# POSTER SESSION ONE

## TL1 AWARDEE PREDOCTORAL ABSTRACTS

### T0: BASIC SCIENTIFIC DISCOVERY

001

#### ABERRANT EXPRESSION OF MITOCHONDRIAL GENES IN RETT SYNDROME CELLS

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**OBJECTIVES/SPECIFIC AIMS** Rett syndrome (RTT) is one of the most prevalent female neurodevelopmental disorders that cause severe mental retardation. Mutations in methyl CpG binding protein 2 (MeCP2) that is present in Xq28 locus are mainly responsible for RTT. Following the normal development until 6–18 months, classic RTT patients show the symptoms, such as loss of language and motor milestone, purposeful hand movement, and normal head growth. Using reprogramming technology, we isolated induced pluripotent stem (iPS) cells from RTT patients' somatic cells. This study aims to investigate the function of MeCP2 in human neurons. **METHODS/STUDY POPULATION** iPSC clones expressing wild-type MeCP2 (RTT-wt-iPSCs), mutated MeCP2 (RTT-mu-iPSCs) or both (RTT-bi-iPSCs) were differentiated into neurons. Transcriptomes were obtained by RNA-seq in iPSCs and neurons. Pairwise comparison was performed to identify differentially expressed genes between wild-type and mutant neurons. These genes were used to determine the cellular signaling pathways affected in MeCP2 mutant neurons. The publicly available transcriptome data from RTT patients brains and immortalized B lymphoid cell lines were obtained and used for comparative analysis with our data sets. **RESULTS/ANTICIPATED RESULTS** We found that mutant neurons differentiated from RTT-iPSCs showed aberrant expression of genes involved in mitochondrial functions, including mitochondrial ribosomal proteins and proteins for electron transports. Gene sets that were known to highly express in Parkinson's diseases and Huntington's diseases were also found to be highly expressed in neurons from MeCP2 mutant RTT-iPSCs. **DISCUSSION/SIGNIFICANCE OF IMPACT** Our results show that MeCP2 regulates important genes for mitochondria, suggesting the importance in investigating the previously less explored function of MeCP2 in energy metabolism.

003

#### AURORA A KINASE IS REQUIRED FOR HEMATOPOIESIS AND COUPLES POLYPLOIDIZATION WITH TERMINAL DIFFERENTIATION IN MEGAKARYOCYTES THROUGH PHOSPHORYLATION OF NF-E2

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**OBJECTIVES/SPECIFIC AIMS** We have recently shown that small molecule inhibitors of Aurora A kinase (AURKA) induce polyploidization and differentiation of normal and malignant megakaryocytes. **METHODS/STUDY POPULATION** To determine the mechanism by which AURKA inhibitors ameliorate the leukemic phenotype, we have examined the functional requirement for Aurka in adult hematopoiesis. **RESULTS/ANTICIPATED RESULTS** Complete loss of AURKA in hematopoietic cells caused a rapid and profound defect in hematopoiesis. To determine whether the observed defects are cell autonomous, we transplanted the cells to lethally irradiated recipients. Upon AURKA deletion, the transplanted mice develop an identical phenotype. Moreover, in competitive transplantation experiments, Aurka-/- cells fail to contribute to hematopoiesis. We next deleted AURKA in megakaryocytes *ex vivo* and observed increased CD41 and CD42 expression as well as increased ploidy. To investigate whether AURKA modulates differentiation of megakaryocytes through interactions with lineage specific transcription factors, we performed co-IP experiments between AURKA and megakaryocyte transcription factors. Results confirmed a robust interaction between AURKA and p45 NF-E2. Additionally, we found that AURKA phosphorylates p45 NF-E2 on the S170 residue. Overexpression of wild-type NF-E2 significantly increased the megakaryocyte population, while overexpression of the S170E mutant was less effective in promoting megakaryocyte differentiation. Finally, we knocked down NF-E2 and treated with Aurora A inhibitors. Strikingly, cells with NF-E2 knocked-down displayed significantly less differentiation. **DISCUSSION/SIGNIFICANCE OF IMPACT** Taken together, our data show that Aurora A kinase is required for adult hematopoiesis and that Aurora A regulates NF-E2 function during megakaryocyte differentiation.

004

#### TRANSCRIPTIONAL CONTROL OF HUMAN CELLULAR METABOLISM BY WASP VENOM: TRANSLATIONAL APPLICATION OF NASONIA VENOM-DERIVED BIOACTIVE PEPTIDES

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**OBJECTIVES/SPECIFIC AIMS** Animal venoms are known sources of biological components with therapeutic value. The goal of this proposal is to explore parasitoid wasp venoms for medical applications. Parasitoid wasps are an immense group (>100,000 species) whose venoms have been underexplored for drug discovery. Wasp venom alters conserved metabolic pathways of the host, presumably to promote survival of the wasp offspring. Because conserved metabolic pathways are targeted while maintaining hosts alive, the venoms of parasitoid wasps are likely to contain drug candidates quite different from venoms previously studied (e.g. snakes, cone snails, spiders) – targeting coagulation, neurophysiology, and immune system. **METHODS/STUDY POPULATION** Illumina Hi-Seq analysis of total RNA extracted from human renal mesangial cells (HRMCs) dosed with a wide range of venom concentrations (128–1/128 reservoirs) and across three timepoints (1 h, 4 h, 24 h). Transcriptomic data was analyzed by CuffDiff analysis as well as Limma (for RNA Seq) to identify dose and time-series trends. **RESULTS/ANTICIPATED RESULTS** Our study organism is the model parasitoid Nasonia vitripennis (NV). We previously found that NV venoms specifically target sugar, lipid, pyruvate, and amino acid metabolism in fly hosts (Sarcophaga bullata). Our analysis of human cells dosed with Nasonia venom recapitulate the most significant of these observed changes to gene expression. Specifically, gene expression changes aggregate in sugar metabolism and steroid hormone biosynthetic pathways. **DISCUSSION/SIGNIFICANCE OF IMPACT** We next aim to determine in which ways parasitoid venoms alter metabolism in human cells, and to identify candidate small molecules and secreted peptides with metabolic effects relevant to human disease.

005

#### 'INCOGNITO' IMMUNE MEMORY CAN DISRUPT TRANSPLANTATION TOLERANCE

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**OBJECTIVES/SPECIFIC AIMS** Vaccination-induced immune memory can cross-react to major histocompatibility complexes (MHC) on donor cells and block graft survival by disrupting tolerance. To avoid this problem, recipients are transplanted with donor grafts for which they have limited preexisting MHC reactivity. Since recipients retain vaccination-associated immunity, we sought to determine whether such immunity that lacks specificity for donor MHC can block tolerance. **METHODS/STUDY POPULATION** We vaccinated C57BL/6 mice with an adjuvant and ovalbumin (OVA). ELISPOT analysis showed strong T cell OVA-specific immunity and limited cross-reactivity to donor-derived BALB MHC. OVA-immune mice were transplanted with BALB grafts and treated with the tolerance-promoting therapy, anti-CD154 and BALB donor-specific transfusion (DST). **RESULTS/ANTICIPATED RESULTS** Relative to control mice, OVA-immune mice did not inhibit BALB tolerance (MST >66d vs >67d, $p$ = ns). However, when vaccinated mice were exposed to DST that expressed vaccine-associated OVA and donor BALB MHC, tolerance was disrupted in 5/6 OVA-immune mice ($p < .03$ vs controls). We found altered fates of graft-reactive T cells *in vivo*: Anti-CD154 normally restrained the primary response to BALB DST, but in response to linked OVA and BALB antigens, preexisting OVA memory disrupted this inhibition and naïve donor-reactive T cells were activated. **DISCUSSION/SIGNIFICANCE OF IMPACT** Seemingly benign ('incognito') vaccine-induced memory that is not directed against donor MHC can disrupt tolerance and drive donor-reactive T cell immunity. Pre-transplant evaluation of anti-donor MHC reactivity, therefore, may not always predict whether preexisting immunity will interfere with tolerance. Vaccinated recipients who have limited donor cross-reactivity may still be at substantial risk for graft rejection if they are exposed to donor cells that express vaccine-associated antigens.

006

#### DIFFERENTIAL PHYSIOLOGIC, AND MOLECULAR CARDIAC RESPONSES TO EXENDIN-4 IN LEAN VS. OBESE OSSABAW SWINE IN THE SETTING OF ISCHEMIA/REPERFUSION INJURY

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**OBJECTIVES/SPECIFIC AIMS** (1) Assess the differential effects of Exendin-4 (EX-4) in lean versus obese/metabolic syndrome (MetS) states on cardiac performance during response to ischemia-reperfusion injury (IRI). (2) Investigate molecular mechanisms responsible for the observed differential effects. **METHODS/STUDY POPULATION** Cardiac contractility was assessed in lean and obese Ossabaw swine at rest, following 30 min occlusion of the left circumflex artery, and 2 hours after the release of the occlusion. Swine received either 24 hours of EX-4 at 30 fmol/kg/min or saline. 10 lean and 10 obese swine were used (5 saline and 5 EX-4 for each group). Affymetrix 3.0 microRNA (miR) microarrays were used to measure differential expression of miRs in normally perfused and IRI territory from 19 of the swine used in this study. **RESULTS/ANTICIPATED RESULTS** (1) Exendin-4, a GLP-1 mimetic, elevated load-independent contractility measures in lean treated swine during ischemia. EX-4 had no effect on this relationship in obese swine. (2) Preliminary microarray analysis demonstrates differential miR expression profiles in lean when vs. obese EX-4 treated swine. This differential

expression is largely lost in the saline control swine. **DISCUSSION/SIGNIFICANCE OF IMPACT** (1) These findings indicate that the cardiac inotropic actions of GLP-1 receptor activation following ischemia/reperfusion injury are abolished in the setting of the obesity/metabolic syndrome. (2) Differential miR expression demonstrates molecular evidence of altered EX-4 treatment effect as a function of lean vs. obese status.

**007**

## BMP SIGNALING REGULATES THE TEMPO OF ADULT HIPPOCAMPAL PROGENITOR MATURATION AT MULTIPLE STAGES OF THE LINEAGE

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**OBJECTIVES/SPECIFIC AIMS** New neurons are generated in the adult brain from stem cells that reside in the hippocampus, a region of the brain important for learning and memory. Novel stimuli increase baseline cell division of neural progenitor cells (NPCs) to rapidly expand the population of new neurons. However, it remains unclear how more new neurons can be generated in a shorter time frame than is usually required for proliferating stem cells to generate new neurons. **METHODS/STUDY POPULATION** Bone morphogenetic proteins (BMPs) are secreted signaling molecules that regulate neural stem cell fate and maturation throughout development. BMP signaling was increased in the hippocampus by lentiviral overexpression of BMP4 and decreased by either overexpression of the BMP inhibitor, noggin, or by conditional knockout of the BMP receptor type 2 (BMPRII). Progenitor maturation status was determined by stage-specific lineage markers. **RESULTS/ANTICIPATED RESULTS** Virally mediated overexpression of BMP4 caused NPC cell cycle exit and slowed the normal maturation of NPCs, resulting in a long-term reduction in neurogenesis. Conversely, overexpression of noggin promoted NPC cell cycle entry and accelerated NPC maturation. Similarly, BMPRII ablation in Ascl1+ intermediate NPCs accelerated their maturation into neurons. **DISCUSSION/SIGNIFICANCE OF IMPACT** We show that BMP signaling in the hippocampus regulates the tempo of NPC maturation at multiple stages along the lineage. Thus inhibition of BMP signaling is a mechanism for rapidly expanding the pool of new neurons in the hippocampus by accelerating the maturation of NPCs into neurons. We propose that BMP signaling modulation presents a potential therapeutic target for stimulating neurogenesis in conditions with a deficit in neurogenesis and cognition.

**008**

## HDAC5 PROMOTES MEF2 REPRESSOR COMPLEX FORMATION IN CARDIAC MYOCYTES

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**OBJECTIVES/SPECIFIC AIMS** Cardiac pressure overload leads to aberrant gene expression resulting in myocardial hypertrophy. Histone deacetylases (HDACs) significantly alter gene expression during hypertrophy. Experiments using HDAC5 KO mice support HDAC5 playing a scaffolding role to recruit Class I HDACs and other corepressors to specific transcription factors. We have demonstrated that HDAC5 recruits the HDAC1-Sin3a complex to the Ncx1 and BNP promoters through its interaction with Nkx2.5 and YY1, respectively. Given these findings, we investigated whether HDAC5 functions similarly to recruit corepressors to other transcription factors. The cardiac transcription factor MEF2 is a very important mediator of cardiac growth and has been shown to regulate genes that are pathologically dysregulated in cardiac hypertrophy. Thus, we hypothesized that Class IIa HDACs recruit corepressor complexes to the promoters of MEF2-regulated genes. **METHODS/STUDY POPULATION** Hearts were harvested from wild-type or HDAC5 knockout mice, homogenized and lysed. Tissue lysates were used for coimmunoprecipitation experiments to determine which corepressors were found in complex with MEF2. **RESULTS/ANTICIPATED RESULTS** In the wild-type ventricle, we identified MEF2 in complex with HDAC1, HDAC3, HDAC4, HDAC5, HDAC9, Sin3a, and CoREST. Interestingly, knocking out HDAC5 eliminated the interaction of HDAC1 and Sin3a with MEF2. We also found that knocking out HDAC5 resulted in an increase in the association of HDAC4 with MEF2 and a decrease in the interaction of HDAC3 and CoREST with MEF2. **DISCUSSION/SIGNIFICANCE OF IMPACT** In the absence of HDAC5, there is a reduction of Class I HDACs and other corepressors in complex with MEF2. This finding supports HDAC5 serving a scaffolding role to form complexes with MEF2, as we have shown with two other transcription factors.

**010**

## MOVING BEYOND INDIVIDUAL LEVEL INDICATORS: INTEGRATING SCHOOL-LEVEL FACTORS INTO UNDERSTANDING YOUTH' BYSTANDER BEHAVIOR

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**OBJECTIVES/SPECIFIC AIMS** Youth bystander programs have been introduced as innovative approaches to prevent teen dating violence (TDV). The bystander literature has focused on the individual factors that can motivate teens to positively intervene. The aim of this project is to identify the mezzo- and community-level factors that can influence adolescents' bystander behaviors. The ultimate goal is to inform the development of efficacious and relevant community-based TDV prevention programs. **METHODS/STUDY POPULATION** Data were collected from 8 community-based and 4 national online focus groups with youth aged 14–18 ($n = 103$). We used a semi-structured interview guide to elicit youths' examples of TDV and initiate a discussion about situational and interpersonal factors that could influence their bystander behavior. Qualitative analysis involved multiple rounds of inductive and deductive coding. Matrices were used to compare codes within and across the focus groups. Coding was done collaboratively within the research team. **RESULTS/ANTICIPATED RESULTS** Youth reported school environments that discourage active bystander behavior. School-level barriers fell into 5 domains: (1) TDV is invisible or minimized; (2) Gender inequitable attitudes about women; (3) Youth feeling of disempowerment; (4) School administration not responsive to TDV; (5) Permissive attitudes about TDV. **DISCUSSION/SIGNIFICANCE OF IMPACT** This study revealed that schools could play a critical role in partnering with youth to modify school climates that are intolerant to TDV and promote active youth involvement. Therefore attention to social context and social norms is paramount for the design and implementation of youth bystander programs.

**011**

## THE ROLE OF TMEM195 IN LEFT-RIGHT CARDIAC DEVELOPMENT

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**OBJECTIVES/SPECIFIC AIMS** Congenital heart disease (CHD) affects 1 in 130 newborns and is a major cause of morbidity in the pediatric population. One cause of CHD is heterotaxy (Htx), a disorder of abnormal left-right (LR) development. Unfortunately, the causes of Htx remain largely undefined, but a recent screen of Htx patients (Fakhro et al 2010) suggests that a mutation in TMEM195 may lead to Htx. TMEM195 is an alkylglycercol monooxygenase that cleaves ether lipids, however, neither its molecular target nor its role in development have been described. The aim of this project is to understand the molecular mechanism by which TMEM195 alters LR cardiac development. **METHODS/STUDY POPULATION** We examined the role of TMEM195 using morpholino (MO) knockdown in Xenopus tropicalis and evaluated the developmental effects by time-lapse imaging, whole mount in-situ hybridization, explant dissections and immunohistochemistry. **RESULTS/ANTICIPATED RESULTS** At a low dose of MO (1ng), we can recapitulate our patient's Htx phenotype in Xenopus. Interestingly, a higher dose MO (2ng) leads to a remarkable gastrulation defect. The gastrulation phenotype is unique and, using time-lapse imaging, shows a developmental sequence in which the blastopore is unable to close following multiple attempts in high dose embryos, but eventually is able to close in low dose embryos. TMEM195 also has an overexpression phenotype, which induces twinning in the embryo. Our results suggest that TMEM195 is critical for wnt signaling indicating a novel mechanism for alkylglycerol monoxygenase in the wnt pathway. **DISCUSSION/SIGNIFICANCE OF IMPACT** Unraveling the role of TMEM195 in wnt signaling will enable us to better understand the relationship between gastrulation errors and defects in the LR axis of development. In addition, the wnt pathway plays a critical role in a myriad of different disease processes including congenital malformations, stem cells, and cancer.

**012**

## PH-ACTIVATABLE NANOPARTICLES FOR TUMOR-SPECIFIC DRUG DELIVERY

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**OBJECTIVES/SPECIFIC AIMS** We aim to develop a pH-activatable nanoparticle (NP) drug delivery system that avoids interaction with healthy cells at pH 7.4 but enters cancer cells by changing surface properties in acidic tumor environment. **METHODS/STUDY POPULATION** Zwitterionic chitosan (ZWC) was synthesized by conjugating succinic anhydride to low MW chitosan. NPs were formed via electrostatic interactions between ZWC and polyamidoamine (PAMAM) at pH 7.4. NP stability was determined using UV-Vis spectroscopy. NP morphology was observed by transmission electron microscopy (TEM). The effect of ZWC-PAMAM complexation was investigated by testing the cytotoxicity, hemolytic activity, and observing cellular uptake of NPs by confocal microscopy at different pHs. **RESULTS/ANTICIPATED RESULTS** NPs were formed when PAMAM dendrimer, a polycationic drug carrier, and ZWC, a chitosan derivative that had negative charges at neutral pH, were mixed in pH 7.4. The formation of ZWC(PAMAM) complex nanoparticles were demonstrated by the increasing turbidity and observed by TEM. ZWC coating protected RBCs and fibroblasts from hemolytic and cytotoxic activities of PAMAM, respectively. That ZWC(PAMAM) particles were taken up at pH 7.4 but not at pH 6.2 indicates that ZWC prevented cell-PAMAM interaction when present on PAMAM but not when the complex dissociated due to the charge reversal of ZWC at low pH. **DISCUSSION/SIGNIFICANCE OF IMPACT** ZWC coating provides a conditional shielding/deshielding which prevents the

pre–mature cellular uptake of PAMAM and allows for preferential uptake of PAMAM by cells in tumors following ZWC deshielding at the acidic environment. ZWC(PAMAM) has the potential to serve as an effective drug carrier to solid tumors.

**014**

## EFFECT OF CARDIAC CIS EQTLS NEAR PROTEIN KINASE C ALPHA ON HUMAN HEART FAILURE

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**OBJECTIVES/SPECIFIC AIMS** Genetic variants in noncoding regions can exert functional effects by altering expression of nearby genes. We have performed genome-wide eQTL studies in human myocardium and identified cis variants that affect expression of Protein Kinase C alpha (PRKCA). PRKCα modulates cardiac function in small and large animal models. The overall aim of this project is to better define the regulatory mechanism at this locus and assess their potential impact on human heart failure (HF). **METHODS/STUDY POPULATION** The region of interest upstream of PRKCα from 10 human samples is cloned into an expression plasmid containing the Luciferace gene. Luciferase expression is then quantified after transfection into HeLa to determine if altered genotype at the candidate eSNP in this region can alter expression of the downstream gene. A second study of SNP association in an existing cohort study of heart failure patients is performed to test whether genotypes at PRKCA regulatory variants associate with time to the combined outcome of ventricular assist device placement, cardiac transplantation or death. **RESULTS/ANTICIPATED RESULTS** I expect that the genotype of the cloned region will alter luciferase expression *in vitro* in the same manner as it associated with PRKCα expression *in vivo*. In addition, I expect to find that the eQTLs that encode for decreased PRKCα expression will be associated with worse HF outcomes. **DISCUSSION/SIGNIFICANCE OF IMPACT** While there is a growing body of literature implicating PRKCA in animal HF the significance of the gene in human disease has yet to be established. The presence of an association between PRKCA eQTLs and HF outcome in humans would suggest a role in human disease. Discovery of the function eSNP encoding for altered PRKCα expression could potentially have pharmacogenomic applications by identifying patients that would most likely respond to therapy targeting PRKCα.

**015**

## NEUROINFLAMMATION IN A CLOSED HEAD INJURY MODEL OF TRAUMATIC BRAIN INJURY

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**OBJECTIVES/SPECIFIC AIMS** Accumulating evidence indicates that a single moderate to severe traumatic brain injury (TBI) increases the risk of developing progressive neurological disorders and dementia. This chronic, neurodegenerative pathology has also been identified in brains that have sustained repeated mild injuries. The goal of this project is to test the hypothesis that the inflammatory response after TBI contributes to cognitive decline. **METHODS/STUDY POPULATION** C57Bl6/J mice (20–30 g) were subjected to lateral closed head injury (CHI) and received either one mild CHI (1 mm), three mild CHI, or severe CHI (3 mm). Edema was measured by MRI at 2, 7 and 30 days postinjury. Astrocyte immunoreactivity and microglial activation were quantified at 7 and 30 days postinjury by histological staining for GFAP and Iba-1, respectively. Long-term potentiation (LTP) was measured in hippocampal slices 3 days postinjury, and learning and memory was assessed with the novel object recognition (NOR) task 7 days postinjury. **RESULTS/ANTICIPATED RESULTS** Seven days after severe CHI, focal T2-pixel hyperintensity was detected in the ipsilateral cortex, indicative of injury-related edema. Astrocyte immunoreactivity and microglial activation were also detected in the injured cortex and hippocampus. LTP was reduced but not entirely diminished after severe CHI. We anticipate that deficits in synaptic plasticity will be accompanied by impairments in learning and memory. We also expect that repeated mild CHI will result in either cumulative or synergistic edema, inflammation, and hippocampal impairments after injury. **DISCUSSION/SIGNIFICANCE OF IMPACT** As impairments in cognition accompany most TBI cases, these findings have important implications for treating human TBI and suggest that targeting this inflammatory response is feasible for therapeutic intervention.

**017**

## HIGH-RESOLUTION IMAGING OF APOE4-INDUCED SYNAPTIC DYSFUNCTION

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**OBJECTIVES/SPECIFIC AIMS** ApoE4 is the most common genetic risk factor associated with late-onset Alzheimer disease. We seek to elucidate the kinetics of ApoER2 and glutamate receptor trafficking with high-resolution imaging and to determine the mechanism by which receptor recycling is retarded intracellularly by ApoE4. Additionally, we will assess the activity of ApoE4 structure correctors on ApoER2 and glutamate receptor trafficking. Structure correctors are compounds that disrupt the domain interaction within ApoE4. **METHODS/STUDY POPULATION** Using standard molecular genetics cloning techniques, fluorescent reporter proteins are cloned into plasmids containing the cDNA sequence for the glutamate receptor subunits GluR1 and GluR2. The ApoE4 structure corrector PH-002 is then applied to neurons and analyzed with optical imaging, electrophysiology and Western blot. Hippocampal field recordings are established by stimulating the schaffer collaterals and recording from the CA1 region. **RESULTS/ANTICIPATED RESULTS** Cell surface biotinylation data demonstrates decreased recycling of receptors in the presence of reelin and ApoE4. The fluorescent reporter proteins will provide visualization of receptor trafficking from the surface to intracellular compartments. We anticipate that the ApoE4 structure corrector PH-002 will release receptors from intracellular compartments and allow trafficking to the cell membrane. **DISCUSSION/SIGNIFICANCE OF IMPACT** We currently lack a clear understanding of the mechanism of ApoE4 suppression of synaptic activity. Building on previous discoveries at this lab, we will establish the mechanism of impairment of ApoER2 and glutamate receptor recycling at a subcellular level using fluorescent imaging. This data will provide a deeper understanding of the interplay between ApoE4 and the pathophysiologic changes seen in Alzheimer disease, thereby providing novel targets for evaluating directed pharmacologic therapy.

**019**

## HUMAN PAPILLOMAVIRUS TYPE 16 ENTRY VIA THE ANNEXIN A2 HETEROTETRAMER SUPPRESSES PRIMARY HUMAN LANGERHANS CELL MATURATION; AN *IN VITRO* EXPERIMENTAL STUDY

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**OBJECTIVES/SPECIFIC AIMS** Human papillomavirus type 16, the most common oncogenic HPV genotype, infects epithelial cells through the annexin A2 heterotetramer (A2t) receptor. During infection, HPV16 also interacts with Langerhans cells (LC), the antigen presenting cells of the epithelium, and induces immune suppression. Here, we examined if internalization of HPV16 into LC is mediated through A2t, and if entry via A2t suppresses LC maturation. **METHODS/STUDY POPULATION** LC were incubated with an A2t-binding HPV16 peptide that is essential for infection of epithelial cells, and subsequently, HPV16 binding was assessed via FACS. Additionally, A2t was down-regulated with siRNA prior to exposure to HPV16, and internalization was measured. To characterize the contribution of A2t in LC maturation, LC were treated with purified A2t, and expression of surface markers and cytokines were analyzed. Lastly, the effect of A2t inhibitors on LC activation was examined. **RESULTS/ANTICIPATED RESULTS** Incubation of LC with an HPV16 A2t-binding peptide blocked binding of HPV by 50% ($p = 0.02$). A down-regulation of A2t decreased HPV16 internalization into LC by 30% ($p = 0.003$). LC exposed to purified A2t showed attenuated secretion of cytokines and decreased surface expression of MHC II by 40% ($p = 0.04$). Conversely, A2t inhibitors prevented HPV16-induced immune suppression of LC as indicated by significantly increased secretion of cytokines and surface expression of MHC II and CD86 (37% and 180% respectively with $p < 0.05$). **DISCUSSION/SIGNIFICANCE OF IMPACT** These results demonstrate that HPV16 suppresses LC maturation through an interaction with A2t, revealing a previously unknown role for this protein in LC and HPV16 immune evasion. Targeting this interaction could prevent HPV16 induced immune suppression and ultimately reduce incidence of HPV-related cancers.

**020**

## AKAP-LBC COORDINATES PKA PHOSPHORYLATION AND INHIBITION OF THE TYROSINE PHOSPHATASE SHP2

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**OBJECTIVES/SPECIFIC AIMS** Pathological cardiac hypertrophy (an increase in cardiac mass resulting from stress-induced cardiac myocyte growth) is a major factor underlying heart failure. Src homology 2-domain containing phosphatase (Shp2) is critical for cardiac function. Mutations resulting in loss of Shp2 catalytic activity are associated with congenital cardiac defects and hypertrophy. We have identified a novel mechanism of Shp2 inhibition that may promote cardiac hypertrophy. **METHODS/STUDY POPULATION** Protein tyrosine phosphatase activity was measured *in vitro* from cell lysates following treatment with forskolin and IBMX to activate PKA, as well as from heart extract from normal and isoproternol-induced hypertrophic mice. **RESULTS/ANTICIPATED RESULTS** We demonstrate that Shp2 is a component of the AKAP-Lbc complex. AKAP-Lbc facilitates PKA phosphorylation of Shp2, which inhibits Shp2 phosphatase activity. We have identified two key amino acids in Shp2 that are phosphorylated by PKA. Utilizing double mutant PKA phospho-deficient (T73A/S189A) and phospho-mimetic (T73D/S189D) constructs, *in vitro* PTP assays indicate that phosphorylation of these residues results in inhibition of Shp2 activity. **DISCUSSION/SIGNIFICANCE OF IMPACT** Overall, our data indicate that AKAP-Lbc integrates PKA and Shp2 signaling in the heart and that AKAP-Lbc-associated Shp2 activity is reduced in hypertrophic hearts in response to chronic β-adrenergic stimulation and PKA activation. Thus, while induction of cardiac hypertrophy is a multifaceted process, inhibition of Shp2 activity through AKAP-Lbc-anchored PKA

is a previously unrecognized mechanism that may promote compensatory cardiac hypertrophy. We are currently investigating the effects of Shp2 phosphorylation by PKA on downstream hypertrophic signaling mechanisms.

021

### BACTERIAL DNA PROMOTES MUCOSAL ANTIBODY PRODUCTION IN NEWBORN INFANTS

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**OBJECTIVES/SPECIFIC AIMS** The absence of the mucosal antibody immunoglobulin A (IgA) in the intestinal tract renders young infants highly susceptible to enteric infections. Moreover, most vaccines administered to newborns and young infants induce limited IgA responses and require multiple boosters to be effective. Therefore, the identification of newborn-specific factors that can enhance the development of protective IgA is essential. **METHODS/STUDY POPULATION** Cord blood mononuclear cells (CBMCs) were isolated by standard ficoll density gradient separation and were stimulated with combinations of bacterial components as well as soluble (IL-21, IL-4) and cognate (anti-CD40) T cell factors. Cells were collected at day 3 for flow cytometry to determine receptor expression. Supernatants were collected on day 7 for ELISAs to determine IgA production. **RESULTS/ANTICIPATED RESULTS** We found the novel combination of the bacterial DNA analogue CpG combined with both soluble and cognate T cell factors (TCF) promoted the production of IgA from B cells of newborns in a direct and CpG dose-dependent manner. Both CpG binding and toll-like receptor 9 (TLR9), a receptor for CpG, were upregulated on B cells after co-stimulation with CpG and TCF. Indeed, IgA production required engagement of and signaling through TLR9 by CpG. Moreover, TLR9 signaling increased surface expression of both IL-21 receptor and CD40, indicating enhanced responsiveness of B cells to T cell help upon exposure to bacterial DNA. **DISCUSSION/SIGNIFICANCE OF IMPACT** Taken together, these data suggest that exposure to bacterial DNA may prime newborn infant's B cell to respond to T cell help and to produce IgA. Thus, bacterial DNA or its analogues (e.g. CpG), could serve as effective adjuvants to enhance local IgA responses to mucosal vaccines and to induce early protection against enteric infections in very young infants.

## T1: TRANSLATION TO HUMANS

022

### NOVEL AMINE OXIDASE INHIBITORS REVEAL NEW THERAPEUTIC STRATEGIES TO REDUCE ISCHEMIA-REPERFUSION DAMAGE IN ISOLATED RAT HEARTS

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**OBJECTIVES/SPECIFIC AIMS** Current therapies to assist outcomes after acute myocardial infarction (AMI) are dependent on fast restoration of flow to the tissue. Upon reperfusion, localized oxidative stress can further damage the myocardium—termed ischemia-reperfusion (IR) injury. To date, inhibitors of epigenetic enzymes show promise in maintaining cardiac contractility and reducing infarct post-IR. Yet, in the vast milieu of epigenetic enzymes responsible for regulation of heart disease, little focus has been allocated to histone demethylases. One of the first identified was the lysine-specific demethylase (LSD1). The intent of this study was to unveil LSD1 as a contributor in IR injury and exploit novel drug discovery as a means to ascertain a mechanism. **METHODS/STUDY POPULATION** A previously classified oligoamine inhibitor of LSD1 (Verlindamycin; IC50 8.5 μM) was i.p. injected (10 mg/kg) in male Sprague-Dawley rats at 18-hrs and 1-hr prior to heart isolation and perfusion by Langendorff model. Ischemia was induced for 30-mins followed by 1-hr of reperfusion. A saline-filled balloon fixed to a pressure transducer in the left ventricle (LV) measured contractile function. After reperfusion, 2-mm cross-sections of LV tissue were collected for measurement of infarct area and protein expression. **RESULTS/ANTICIPATED RESULTS** Verlindamycin preconditioning of hearts maintained LV function after IR injury. Also, increased levels of phosphorylated p38 in verlindamycin-treated rat hearts corroborate a pro-survival preconditioning event. **DISCUSSION/SIGNIFICANCE OF IMPACT** This study reveals the first evidence for histone demethylases as key regulators of IR pathogenesis and provides new targets for therapeutic protection against IR injury. This work will provide new pharmacologic intellect into future preclinical drug design to improve patient outcomes following AMI.

023

### ESTRADIOL MODULATES VISCERAL NOCICEPTION AT THE LEVEL OF PRIMARY SENSORY NEURONS

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**OBJECTIVES/SPECIFIC AIMS** A large body of literature supports the idea that estrogen modulates nociceptive responses in pelvic pain syndromes; however, whether this hormone is pro- or anti-nociceptive remains unresolved. The dorsal root ganglion (DRG) is an important site of visceral afferent convergence and cross-sensitization. Within the context of our hypothesis visceral nociception and nociceptor sensitization appear to be regulated by purinergic P2X3 and vanilloid TRPV1 receptors and 17β-estradiol modulates DRG neurons response to ATP/ α,β-meATP and capsaicin suggesting that visceral afferent nociceptors are modulated by estrogen in the DRG **METHODS/STUDY POPULATION** 17-β estradiol (E2), the most common form of estrogen act on functional properties of P2X3 and TRPV1 receptors in DRG neurons *in vitro*. In this study we used ratiometric technique to study changes intracellular Ca2+ concentration and retrograde labeling to verify viscerally-labeled sensory neurons. **RESULTS/ANTICIPATED RESULTS** DRG neurons from Wt, ERαKO and ERβKO knockout mice responded to P2X3 and TRPV1 activation. Moreover, E2 appears to have different actions on nociceptive signaling depending on the input. E2 attenuated the ATP-induced [Ca2+]i responses and interfered with the μ-opioid receptors (MOP) attenuation of this flux. **DISCUSSION/SIGNIFICANCE OF IMPACT** Based on our data we can propose that E2 can gate primary afferent response to increase or decrease nociception. Our novel data may help to understand the mechanisms of functional disorders such as irritable bowel syndrome, chronic pelvic pain, painful bladder syndrome that can lead to development of new therapeutic interventions.

024

### MEASURING THE INFLUENCE OF THE ENVIRONMENT ON SUPPORT PROVIDED BY CAREGIVERS

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**OBJECTIVES/SPECIFIC AIMS** Caregiving can be physically and emotionally taxing, placing caregivers at risk for negative health consequences. Home modifications such as grab rails near toilets can improve the functional abilities of people with disabilities and may reduce strain for caregivers. The influence home modifications have on reducing caregiver strain is understudied, with no assessments currently available to measure the impact on caregivers. This cross sectional study investigates the feasibility, validity, and interrater reliability of a new assessment to measure the impact of environmental barriers on caregiving. **METHODS/STUDY POPULATION** Two occupational therapists administered the new assessment to family caregivers. During the assessment, caregivers identify problematic caregiving activities and provide self-ratings of performance, satisfaction with performance, and confidence in providing assistance. **RESULTS/ANTICIPATED RESULTS** To date, 10 of 30 planned caregiver dyads have completed the assessment. Caregivers are primarily female (80 %) with an average age of 68 years. They assist spouses ($n = 6$), parents ($n = 2$) and adult children ($n = 2$) with a variety of conditions including dementia, Parkinson's disease, and spinal cord injury. ICCs of the 5 subscales ranged from .96–1.0. The Caregiver Inventory (confidence in caregiving) is positively correlated ($r = .325$) with the self-efficacy scale. Caregivers had positive perception of the assessment with an average rating of 4.2 on a 5-point scale ranging from 1, did not address my concerns, to 5 completely addressed my concerns. **DISCUSSION/SIGNIFICANCE OF IMPACT** The new assessment provides researchers and clinicians with quantifiable measures of the impact of environmental barriers on caregiving.

025

### NEURAL SUBSTRATES OF MOTIVATIONAL EFFECTS ON MOTOR LEARNING: A WITHIN-SUBJECT COMPARISON

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**OBJECTIVES/SPECIFIC AIMS** Learning underlies most skilled behaviors, including recovery of motor control when the neural systems governing learning are disrupted after neurologic disorders. The mechanisms brought to bear for motor recovery are similar to those when nondisabled adults learn new motor skills. Research investigating motivational effects on motor learning in nondisabled adults has identified a variety of manipulations that positively influence perception of capabilities, enhance motivation and improve motor performance and learning. However, the neural processes mediating these skill-learning effects are for the most part unknown. From previous work, a network of regions including the ventral striatum, insula, nucleus accumbens and ventral tegmental area are known to play a role in processing motivation. Our objective is to determine the network of brain areas associated with enhanced motivation for skilled motor performance. **METHODS/STUDY POPULATION** We expect to recruit healthy adults from students attending University of Southern California in 2014–2015. Participants will be asked to balance on a horizontal platform. Prior to the task, they will be given a brief statement to create a positive perception of learning a challenging balance task. Brain activation during observation of videos of adults attempting to balance on a horizontal platform, measured by fMRI, will be compared before and after the statement. **RESULTS/ANTICIPATED RESULTS** We expect that if the provision of the statement engages the motivation network, it will potentiate activation of motor circuits involved during action observation and motor learning. **DISCUSSION/SIGNIFICANCE OF IMPACT** Findings have the potential to improve our understanding of the neural and behavioral mechanisms that mediate successful motor skill learning and may generalize to effective interventions for neurorehabilitation in cases of neurological disorders such as stroke.

026

## ALTERED NEURAL RESPONSES TO AFFECTIVE REPETITION IN PERSONS WITH MILD COGNITIVE IMPAIRMENT

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**OBJECTIVES/SPECIFIC AIMS** Emotional enhancement effects (EEEs) encompass the tendency of arousal or nonneutral hedonic valence to be associated with memory retention, and their status in mild cognitive impairment (MCI) is controversial. We examined the interrelation of neural mechanisms of EEEs and other memory systems in the context of MCI to identify its status both in isolation and in concert with other mechanisms. **METHODS/STUDY POPULATION** 16 participants—8 with MCI, 8 with normal cognitive status—participated in an affective repetition task while event-related potentials (ERPs) were measured. After temporospatial principal components analysis, mixed-model robust 2x2x2 ANOVAs were used with temporospatial principal components analysis. **RESULTS/ANTICIPATED RESULTS** The first temporal component of ERPs was positive-going and left-lateralized, peaking frontally at 930 ms; HAN stimuli were associated with greater positivity in both groups. The second temporal component was positive-going and right-lateralized, peaking frontally at 462 ms; a Group X Affect interaction indicated that HAN stimuli were associated with greater positivity and the difference between HAN and LAP stimuli was greater in persons with MCI. The third temporal component was positive-going and without significant lateralization, peaking frontocentrally at 690 ms; a Group X Repetition interaction was significant such that repetition effects were greater in persons with MCI. Behaviorally, LAP stimuli and repeated stimuli were associated with faster RT and improved accuracy; no group differences were observed. **DISCUSSION/SIGNIFICANCE OF IMPACT** Persons with MCI showed enhanced brain responses to negative emotional stimuli, especially with repetition. Future work will examine these changed neural mechanisms in the context of working memory.

027

## MARKERS OF OXIDATIVE STRESS IN PATIENTS WITH TUMOR NECROSIS FACTOR RECEPTOR ASSOCIATED PERIODIC FEVER SYNDROME

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**OBJECTIVES/SPECIFIC AIMS** Tumor necrosis factors receptor associated periodic fever syndrome (TRAPS) is an autosomal dominant autoinflammatory disease associated with missense mutations in tumor necrosis factor receptor superfamily, member 1A (TNFRSF1A) gene. Our laboratory has recently demonstrated a role for mitochondrial reactive oxygen species (ROS) in triggering the hyper-responsiveness characteristic of cells from TRAPS patients. When the level of ROS generation exceeds the anti-oxidant defense capacity of the cell, oxidative damage to macromolecules including DNA and protein ensues. Our objective is to determine and to compare various oxidative stress markers in TRAPS patients versus control. **METHODS/STUDY POPULATION** Peripheral blood mononuclear cells (PBMC) from TRAPS patients were analyzed for mitochondrial ROS production and quantification of oxidative DNA damage via the DNA adduct 8-oxo-guanine and protein oxidation via protein carbonil content **RESULTS/ANTICIPATED RESULTS** TRAPS patients have increased levels of oxidized DNA and proteins compared controls. Inhibition of mitochondrial ROS by Mito Q can reduce normal cytokine production and reverse hyperinflammatory responses in PBMC from TRAPS patients. **DISCUSSION/SIGNIFICANCE OF IMPACT** Our data suggest that mitochondrial ROS production, 8-oxo-guanine and protein carbonyl content are increased in TRAPS patients compared with non-inflammatory controls. These findings suggest that mitochondrial ROS may be a novel therapeutic target for TRAPS patients.

028

## ROLE OF DTI AND FMRI IN STROKE RECOVERY

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**OBJECTIVES/SPECIFIC AIMS** It has been shown that the fractional anisotropy (FA) of the CST correlates with motor function in stroke patients. Other studies have shown changes in functional connectivity are correlated with motor impairment. Our goal in this project is to predict functional outcomes based on FA and/or resting state connectivity. **METHODS/STUDY POPULATION** Complete data were collected on 31 patients with acute ischemic stroke (lesions: 13 cortical, 4 cortical-subcortical, 11 subcortical, 1 cerebella, 2 undocumented; age range 22–77, 29 right handed, 14 female). Patients were evaluated with motor tests and fMRI for BOLD data at recruitment (within 4 weeks after stroke), 3 months after stroke, and 12 months after stroke. DTI scans were obtained at 3 months and one year post stroke. Motor factor scores were calculated using factor analysis of shoulder flexion, wrist extension, hand dynamometer, nine hole peg, ARA, timed walk/FIM, motoricity and ankle flexion. FA values are measured for each patient within the CST excluding the lesion and the ratio of ipsilesional to contralesional FA values is determined. Pearson correlation coefficients were calculated with homotopic seeds pairs on either hemisphere of the motor network and averaged. SAS was used for multivariable regression to predict 12 month factor score using age, education, acute factor scores, FA ratio, and homotopic BOLD values. **RESULTS/ANTICIPATED RESULTS** Only acute motor factor score and FA ratio were significant predictors of 12 month factor score with $p$ values <0.0001 and 0.0145, respectively. Age, education level, and homotopic BOLD values were not significant after correcting for all other variables. **DISCUSSION/SIGNIFICANCE OF IMPACT** These results suggest FA ratio, although correlated with motor function, provides predictive value to clinical outcomes not explained by acute motor deficits alone.

029

## THE RELATIONSHIP BETWEEN MUSCLE SYMPATHETIC NERVE ACTIVITY AND HEMODYNAMICS IN WOMEN TAKING ORAL CONTRACEPTIVE PILLS

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**OBJECTIVES/SPECIFIC AIMS** The relationship between mean arterial pressure (MAP), muscle sympathetic nerve activity (MSNA), and total peripheral resistance (TPR) is altered in young women versus men and postmenopausal women due to endogenous sex hormone differences. The aim of this study was to determine if exogenous sex hormones in the form of oral contraceptive pills (OCPs) may further affect this relationship. **METHODS/STUDY POPULATION** We performed a retrospective review of 136 premenopausal women in whom MSNA and arterial pressure were measured, including 78 women with natural menstrual cycles in the early follicular phase (26 ± 1 yr) and 58 women in the placebo phase of OCPs (24 ± 1 yr). TPR and cardiac output (CO) were measured in a subset of women in whom continuous intra-arterial blood pressure was recorded. **RESULTS/ANTICIPATED RESULTS** Compared to those with natural menstrual cycles, women on OCPs had greater MAP (89 ± 1 vs. 84 ± 1 mmHg, $p < 0.01$) and tended to have lower MSNA (15 ± 1 vs. 18 ± 1 bursts/100 heart beats, $p = 0.06$). MAP and MSNA were positively correlated ($r = 0.22$, $p < 0.05$), TPR and MSNA were positively associated ($r = 0.41$, $p < 0.05$), and CO and MSNA were inversely associated ($r = -0.44$, $p < 0.05$) in women with natural menstrual cycles ($n = 26$) but not in women on OCPs ($r = 0.15$, $r = 0.11$, $r = -0.01$, respectively; $p > 0.05$; $n = 38$). **DISCUSSION/SIGNIFICANCE OF IMPACT** In summary, there appears to be no relationship between MSNA and hemodynamics in women on OCPs, suggesting that these women may regulate their blood pressure differently than women with natural menstrual cycles.

030

## EFFECTS OF MATERNAL OBESITY ON LIPID METABOLISM, OXIDATIVE STRESS, AND NEONATAL OUTCOMES

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**OBJECTIVES/SPECIFIC AIMS** Over 30% of all pregnant women in the US are obese. Maternal obesity contributes to an altered intrauterine metabolic environment. This may lead to fetal programming of unfavorable neonatal outcomes. Increased maternal lipid oxidation in conjunction with increased oxidative stress levels during obese pregnancy could influence the intrauterine metabolic environment and cause poor outcomes. The purpose of this study is to examine maternal lipid metabolism and oxidative stress (at rest and during low-level exercise) and their relationship to neonatal adiposity and insulin resistance in obese and lean pregnancies. **METHODS/STUDY POPULATION** Twenty ($n = 20$) pregnant women (3rd trimester) will undergo: skinfold anthropometry (body fat percentage (BF%)), submaximal exercise testing (predicted fitness level), indirect calorimetry (lipid oxidation), and blood draws (insulin resistance and oxidative stress) at rest and during exercise. In the neonate, we will use cord blood to measure insulin resistance and skinfold anthropometry and air displacement plethysmography to measure body composition. **RESULTS/ANTICIPATED RESULTS** Data has been collected on 8 lean (BMI = 22.1 ± 1.7 kg/m$^2$, BF% = 18.8 ± 4.0 and 2 obese (BMI: 33.9 ± 0.7 kg/m$^2$, BF%: 36.7 ± 0.8) women. Lipid oxidation rate appears to be higher in the obese group at all times points (rest: lean (L) = 0.11 g/min, Obese (O) = 0.16 g/min; exercise: L = 0.17 g/min, O = 0.27 g/min, recovery: L = 0.12 g/min, O = 0.17 g/min). Plasma triglyceride concentration (L = 140.8 ± 36, O = 230.5 ± 92.0, $p = 0.08$) and C-reactive protein levels (L = 2.8 ± 2.5, O = 11.4 ± 9.0, $p > 0.001$) appear higher in obese pregnancy. **DISCUSSION/SIGNIFICANCE OF IMPACT** Maternal lipid metabolism appears altered in obese pregnancy. Data collection and sample processing

is ongoing. Results will provide enhanced understanding of the intrauterine metabolic environment and its relationship to neonatal outcomes.

031

## PREDICTION OF 3D KINEMATICS DURING CONTRALATERAL AND IPSILATERAL REACHING MOVEMENTS USING ELECTROCORTICOGRAPHY

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**OBJECTIVES/SPECIFIC AIMS** Brain-computer interface (BCI) systems utilizing electrocorticography (ECoG) can potentially restore function after motor impairments. BCIs traditionally use the motor cortex contralateral to an impaired limb, but these areas would be altered after a stroke. While previous studies demonstrate unique neural physiology related to movements of the ipsilateral limb, the encoding of kinematics is uncertain. This study examined the characteristics of ECoG signals during 3D reaching movements of both the ipsilateral and contralateral limbs for BCI applications. **METHODS/STUDY POPULATION** Data was collected from intractable epilepsy patients implanted with subdural ECoG grids. ECoG signals and 3D hand positions were recorded while participants performed 3D center-out reaching movements with either the arm contralateral or ipsilateral to the electrodes. Datasets from both limbs were collected when possible. Common spatial patterns were calculated to maximize the discriminability of kinematic information. These signals were then analyzed to identify the cortical activity and signal characteristics related to movement kinematics of each arm. **RESULTS/ANTICIPATED RESULTS** We found that ECoG signals demonstrated significant spectral power changes during planning and execution of movements of both the contralateral and ipsilateral limb. Furthermore, we demonstrate the utilization of ECoG signals for decoding of 3D movement kinematics of both the ipsilateral and contralateral arms. **DISCUSSION/SIGNIFICANCE OF IMPACT** These results demonstrate the presence of neural representations of kinematics of the contralateral and ipsilateral arms in human ECoG signals. Furthermore, the decoding of kinematic information from ECoG demonstrates the potential for these findings to be extended for development of an ECoG BCI system using the unaffected hemisphere after stroke.

033

## CHOLANGIOCYTE SENESCENCE IN PRIMARY SCLEROSING CHOLANGITIS

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**OBJECTIVES/SPECIFIC AIMS** Primary sclerosing cholangitis (PSC) is an incurable cholangiopathy of unknown etiopathogenesis. Here we tested the hypothesis that cholangiocyte senescence is a pathobiologically important phenotype in PSC. **METHODS/STUDY POPULATION** We assessed markers of cellular senescence and senescence-associated secretory phenotype (SASP) in livers of patients with PSC, primary biliary cirrhosis, hepatitis C, and in normals by in situ hybridization (FISH) and immunofluorescence microscopy (IFM). We tested whether endogenous and exogenous biliary constituents affect senescence and SASP in cultured human cholangiocytes. Finally, we explored signaling mechanisms involved in cholangiocyte senescence and SASP. **RESULTS/ANTICIPATED RESULTS** *In vivo*, PSC cholangiocytes expressed significantly more senescence-associated p16 and γH2A.x compared to the other three conditions; expression of pro-fibroinflammatory SASP components (i.e., IL6, IL8, CCL2, PAI-1) was also highest in PSC cholangiocytes. *In vitro*, several biologically-relevant endogenous (e.g. cholestane 3,5,6 oxysterol) and exogenous (e.g. LPS) molecules normally present in bile induced cholangiocyte senescence and SASP. NRas, a known inducer of senescence, was increased in PSC cholangiocytes and experimentally-induced senescent cultured cholangiocytes; inhibition of Ras abrogated experimentally-induced senescence and SASP. **DISCUSSION/SIGNIFICANCE OF IMPACT** Our data suggest that cholangiocyte senescence induced by biliary constituents via NRas activation is pathobiological important in PSC. Pharmacologic inhibition of NRas with resultant reduction in cholangiocyte senescence and SASP is a new therapeutic approach for PSC.

034

## AUTOPHAGY MODULATION IMPROVES ANDROGEN RECEPTOR BLOCKADE IN CASTRATION RESISTANT PROSTATE CANCER

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**OBJECTIVES/SPECIFIC AIMS** The specific AIMS are as follows: (A) Characterize Castration Resistant Prostate Cancer's cellular response to treatment with Enzalutamide; (B) Identify autophagy as a mechanism of cellular survival in Enzalutamide treated prostate cancer cell lines; and (C) Demonstrate that autophagy modulation improves the treatment effect of Enzalutamide treated prostate cancer cell lines. **METHODS/STUDY POPULATION** LNCaP and PC3 will be stably transfected to express eGFP-LC3. Then, LNCaP and PC3 cells will be treated with several different concentrations of Enzalutamide. Treatment affect on cell growth will be measured using MTT and cell counting. Autophagic flux will be assayed with microscopy and Western blotting. Using microscopy, we will measure autophagic flux by quantifying the number of punctate granules expressing the eGFP-LC3 reporter construct. These results will be confirmed with Western blotting, where key autophagy signalling proteins (i.e. PI3K,Akt,mTOR,p70S6K,LC3-I, and LC3-II) will be quantified. These steps will be repeated with concurrent autophagy inhibition with Metformin and Hydroxychloroquine. To confirm autphagy inhibition, siRNAs will be used to knockdown the expression of the following autophagy proteins: Atg3 and Atg7. **RESULTS/ANTICIPATED RESULTS** Hypothesis: Combination treatment with enzalutamide and metformin/hydroxychloroquine will decrease cell growth in both androgen dependent and independent prostate cancer cell lines. **DISCUSSION/SIGNIFICANCE OF IMPACT** Currently, the most common treatment for metastatic prostate cancer is androgen ablation therapy via chemical castration; however, this is not curative. In established tumors, autophagy has been shown to improve cellular survival in a number of cancers to include prostate cancer. Thus, concurrent autophagy inhibition in prostate cancer could dramatically improve upon currently available treatments.

035

## THE PATHOGENIC ROLE OF ACROLEIN IN MULTIPLE SCLEROSIS

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**OBJECTIVES/SPECIFIC AIMS** Multiple sclerosis (MS) is an autoimmune demyelinating neuropathy affecting nearly 2.5 million people with few treatments currently available. The immune-inflammatory nature of the pathology has prompted investigation of the role of oxidative stress in disease development and progression; however targeting reactive oxygen species for neutralization has had marginal success, prompting the pursuit of an alternate oxidative stress-related target. Acrolein, a highly reactive aldehyde endogenously produced by lipid peroxidation and exogenously from petrol combustion and tobacco smoke, has been implicated as a therapeutic target and biomarker for MS diagnosis and disease monitoring. **METHODS/STUDY POPULATION** n/a **RESULTS/ANTICIPATED RESULTS** In an MS model, EAE, sequestering acrolein using two FDA approved compounds, hydralazine and phenelzine, offered a neuroprotective effect. Each of these structurally distinct drugs can suppress tissue acrolein level, slow disease progression, and decrease symptom severity, suggesting acrolein is likely a key pathologic mediator in MS. The pathogenic role of endogenous acrolein in MS raises the possibility that environmental exposure to acrolein as a pollutant could potentially increase MS risk or exacerbate MS symptoms. Using a respiratory exposure model in combination with urinary detection of an acrolein metabolite 3-HPMA and immunoblotting assessment of tissue acrolein-lysine adducts, we have ascertained that nasal administration of acrolein can cause systemic accumulation of acrolein in mice. Additionally, elevations in urinary 3-HPMA were observed in EAE mice as well as in human MS patients. **DISCUSSION/SIGNIFICANCE OF IMPACT** These findings imply that both environmental and occupational acrolein exposure could potentially contribute to MS risk or exacerbate MS symptoms.

036

## RADIOIMMUNOTHERAPY KILLS ANTIVIRAL-TREATED HIV-INFECTED LYMPHOCYTES *IN VITRO* AND *EX VIVO* FROM HIV PATIENTS

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**OBJECTIVES/SPECIFIC AIMS** Effective antiretroviral therapy (ART) requires strict lifelong adherence to a costly, toxic regimen. ART does not directly kill HIV-infected cells, which persist even in patients with undetectable peripheral viremia. A more permanent solution to eradicate HIV must include a method to eliminate infected cells. Radioimmunotherapy (RIT) kills infected cells in experimental models but the co-interaction of ART and RIT is unknown. **METHODS/STUDY POPULATION** Human lymphocytes were either infected with HIV *in vitro* and cultured in the presence of clinically relevant ART drug combinations, or directly isolated from ART-treated HIV+ patients. Cells were treated with the cytocidal radionuclide Bismuth-213 conjugated to 2556, a human monoclonal antibody to HIV-1 gp41 protein. Gp41 levels were assessed by Scatchard analysis, cell survival by Trypan blue dye exclusion, and viral levels by p24 ELISA and RT-PCR. **RESULTS/ANTICIPATED RESULTS** Although cell surface gp41 expression diminished under ART, sufficient binding sites for 2556 remained. RIT resulted in potent dose-dependent killing of infected cells for all drug conditions, with increased efficacy from co-treatment compared to ART or RIT alone. The observations were confirmed

*in ex vivo* patient cells, with a 20 μCi dose leading to >95% viral reduction in 13 of 15 patient samples. **DISCUSSION/SIGNIFICANCE OF IMPACT** These findings provide the basis for development of an RIT-based eradication strategy in HIV patients on ART.

**038**

## DISABLING NMP4 IMPROVES PTH OSTEOPOROSIS THERAPY

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**OBJECTIVES/SPECIFIC AIMS** The aim of this T1 research is to investigate the potential of Nmp4 as a drug target for improving osteoporosis therapy. **METHODS/STUDY POPULATION** WT and *Nmp4*-KO mice underwent ovariectomy at 12 weeks of age. At 16 weeks mice received PTH (30 μg/kg/day) or vehicle control for 4 weeks. After treatment femurs and L5 vertebrae were collected for μCT analysis. Data were analyzed by 2-way ANOVA. **RESULTS/ANTICIPATED RESULTS** We have previously shown that healthy *Nmp4*-KO mice exhibit an enhanced PTH-induced bone formation but whether this phenomenon persists in mice with osteoporosis is the clinically relevant question. Ovariectomized (ovx) *Nmp4*-KO mice lost bone similarly to ovx WT mice. In the present arm of the study, ovx *Nmp4*-KO showed an enhanced response to therapeutic doses of anabolic PTH compared to their ovx WT littermates. A significant genotype (G) x treatment (T) interaction was observed at the end of the therapy period and the null mice had nearly twice as much bone compared to WT mice (BV/TV 7.2% vs. 3.9%; 2-way ANOVA, G x T $p < 0.05$). Importantly, vehicle treated animals did not differ significantly when analyzed with student's t-test. A significant interaction was also seen for the connectivity density (Conn.D. 69.6 vs. 33.2; G x T $p < 0.05$). Additionally, *Nmp4*-KO mice had more trabeculae (Tb.N G $p < 0.001$) which also had a more plate like structure (SMI G $p < 0.0001$). **DISCUSSION/SIGNIFICANCE OF IMPACT** These data demonstrate that the single gene Nmp4 suppresses the therapeutic efficacy of PTH for treating osteoporosis. We have previously shown that Nmp4 antagonizes the response of bone to multiple anabolic drugs/treatments. Nmp4 or its regulated pathways may provide novel drug targets for treating bone disease.

**039**

## ACOUSTIC AND KINEMATIC QUANTIFICATION OF FOCAL EMBOUCHURE DYSTONIA

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**OBJECTIVES/SPECIFIC AIMS** To develop a method to identify and validate features of focal embouchure dystonia (FED) in brass musicians and quantify its severity. **METHODS/STUDY POPULATION** FED is a task-specific dystonia affecting the control of lower cranial muscles in wind instrumentalists, often leading to professional disability. Little is known about its features or pathophysiology. This is in part due to inadequate knowledge of (1) specific features of FED, (2) physiology of normal embouchure control, and (3) traits that distinguish FED from nondystonic errors. As the deficit in FED is often "heard" better than it is "seen," we sought to quantify the impact of FED on performance using a combination of acoustic and kinematic methods. **RESULTS/ANTICIPATED RESULTS** Two groups of adult brass musicians, those with and without FED, are studied while performing a custom etude composed to explore the range of performance techniques. Reflective markers are placed at 10 points on the face and tracked with a 3D motion analysis system. Sound is recorded with high-fidelity, digitized at 83333 Hz and analyzed using MATLAB. Variables of interest include inter-onset intervals, onset latency time, tone stability, time from tone onset to maximum stability, and pitch accuracy. Measures of quality of life and musical sophistication are obtained from each subject. Comparisons are made between groups and within subjects between least and most impaired playing. An investigator blind to the diagnosis performs all analyses. **DISCUSSION/SIGNIFICANCE OF IMPACT** We have successfully quantified key acoustic variables and found differences between least and most impaired performance within subjects. Inter-group comparisons will be performed when recruitment is complete and the blind is lifted. Acoustic analysis is a useful and powerful approach to quantifying the severity of impairment in brass musicians with FED.

**040**

## HIPPOCAMPAL-CORTICAL RSFMRI NETWORK DYSCONNECTIVITY IN PSYCHOSIS: A SEED-BASED VOXELWISE ANALYSIS

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**OBJECTIVES/SPECIFIC AIMS** Hippocampal (HP) activity increases in schizophrenic psychosis, which may influence functional HP-cortical networks and disrupt normal regional connectivity. We aim to identify changes in HP-cortical networks in resting state fMRI (rsfMRI) networks in people with psychosis (PS) vs. healthy controls (HC). Studying connectivity changes may enable us to define biomarkers of psychosis severity for targeted treatment. **METHODS/STUDY POPULATION** 100 PS (schizophrenia, schizoaffective disorder, and psychotic bipolar I) and 80 HC were included. 5 min long rsfMRI scans were acquired on a 3Tesla Philips scanner. Whole hippocampal seeds and their bilateral cortical networks were defined in the AFNI fMRI analysis package. Results are at a threshold of $p < .01$, $k = 32$ contiguous voxels. High and residual psychosis subgroups (HP and RP) were divided by Positive and Negative Syndrome Scale scores. Connectivity was defined within these subgroups. **RESULTS/ANTICIPATED RESULTS** Compared to HC, PS showed reduced connectivity within the temporal cortex, between HP and anterior cingulate, precuneus, and middle occipital gyrus, as well as cerebellum and caudate, consistent with a limbic dysconnectivity model. Compared to RP, HP showed increased connectivity with right brain, posterior cingulate, precuneus, middle temporal gyrus, and cerebellum. **DISCUSSION/SIGNIFICANCE OF IMPACT** Overall cerebral connectivity is reduced in psychosis; however, HP show increased connectivity with cortical ROIs compared to RP. Strongest changes are locally between HP and limbic structures and basal ganglia. Future analyses include (1) diagnostic specificity of dysconnectivity, (2) correlations between network changes and clinical/cognitive traits, and (3) HP subfield contributions to dysconnectivity, using partial HP seeds. We aim for biologically driven definitions of severe mental illness.

**041**

## "CAPTURING THE ELUSIVE FOE": A NOVEL TELOMERASE PROMOTER-BASED APPROACH TO DETECT MELANOMA CIRCULATING TUMOR CELLS

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**OBJECTIVES/SPECIFIC AIMS** An assay for tracking disease burden in patients with advanced melanoma may help guide treatment decisions. Circulating tumor cell (CTC) analysis requires only peripheral blood so is convenient, safe, and may complement standard assessments. We therefore sought to establish the feasibility of a novel assay in patients with melanoma. **METHODS/STUDY POPULATION** The assay utilizes an adenoviral vector that drives the expression of green fluorescent protein in the presence of elevated telomerase activity, which is present in almost all cancers but not normal cells. Tumor cells are identified based on criteria of fluorescent intensity and size, and are further co-stained for Melan-A to confirm their melanoma origin. The assay was tested on cells in culture, in control blood, and on samples from 10 patients with advanced melanoma. **RESULTS/ANTICIPATED RESULTS** The assay was effective with sensitivity of 92% (95% CI 84.4–99.1%) and specificity of 99% (99.5–99.6%). In a pilot trial, CTCs were identified in 9 of 10 patients with metastatic disease with mean count of 6.0 CTCs/mL (range 0.7–27.1). Linear regression analysis showed CTC counts were significantly increased in patients with greater burden of disease ($p = 0.02$) and decreased in patients after chemotherapy ($p = 0.02$). Detection was not adversely affected by BRAF status, LDH levels, sites of metastases, or history of immune therapy (all $p > 0.05$). **DISCUSSION/SIGNIFICANCE OF IMPACT** This assay was effective in identifying melanoma cells in culture and in patients with metastatic melanoma. Longer follow-up data and serial analysis may further inform this promising assay's role in managing patients with melanoma.

**042**

## THE EFFECT OF ETOPOSIDE IN REGULATING TUMORIGENICITY: TRANSLATING IPSC-BASED MYOCARDIAL THERAPY TO THE CLINIC

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**OBJECTIVES/SPECIFIC AIMS** The advent of induced pluripotent stem cell (iPSC) technology created new opportunities for transplant-based therapeutic strategies. This potential for clinical translation is currently hindered by the risk of dysregulated cell growth. We aimed to demonstrate the effect of etoposide treatment in decreasing teratoma formation by selectively targeting and eliminating the pluripotent cells in the early cardiac progenitor population. **METHODS/STUDY POPULATION** Murine iPSCs were differentiated to early cardiac progenitors, day 7 EBs, and were treated with 0.01 μM etoposide for 24 hours. Immunodeficient mice received iPSC-derived day 7 progenitor cell population (200,000 cells per heart in 15 μl propagation media) into the left ventricle 30 min following coronary ligation. Echocardiography, live cell imaging and histology were performed. **RESULTS/ANTICIPATED RESULTS** Etoposide-treated cell implantation produced none or reduced teratogenicity in the intra-cardiac and extra-cardiac/chest cavity compared to the control untreated group. *In vivo* bioluminescence imaging confirmed the localization and engraftment of transplanted cells in the myocardium four weeks postinjection. Comparatively, the cell population without treatment demonstrated a greater incidence and size of teratoma formation. **DISCUSSION/SIGNIFICANCE OF IMPACT** While experimental evidence increasingly supports the potential of patient-specific stem cell-based therapies, its clinical translation is currently hindered by tumorigenicity. Ensuring patient safety

prior to utilizing the promise of such transplant-based therapeutics remains the highest priority. This study found that pretreatment with genotoxic etoposide could significantly lower the threat of teratogenicity, allowing the ability to harness the clinical-grade application of iPSC-derived therapeutic agents.

044

## CERAMIC UMBILICAL CORD CUTTER

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**OBJECTIVES/SPECIFIC AIMS** Limited-resources preclude the availability of new umbilical cord cutting blades in poor countries, where lack of sterile equipment and aseptic conditions during childbirth lead to umbilical cord infection. Because metal blades have limitations (e.g., rusting, sterilization difficulties, occupational hazard), we designed a novel zirconium oxide ceramic cutting device. The aims of the study were to (1) ascertain the clinical utility of this device to execute a single cut through an umbilical cord, (2) determine life span by measuring its ability to maintain blade sharpness; and (3) evaluate its amenability to sterilization by measuring bacterial adhesion. **METHODS/STUDY POPULATION** Ceramic blades of different geometries were compared to disposable metallic blades by ability to execute a single cut through a human umbilical cord. Blade sharpness (defined by mean square roughness calculated by serial measurements of blades edge peaks and valleys) was used to establish how repeated use and sterilization affected blade loss and cutting performance. Quantitative bacterial cultures measured the effectiveness of sterilization and surface bacterial adhesion. **RESULTS/ANTICIPATED RESULTS** The 6th prototype safely cut umbilical cords with comparable efficiency to disposable blades, and is amenable to repeated sterilization. Unlike disposable metal blades, which rust and fail to sever the cord, the ceramic device remains sharp after >20 uses and is expected to stay effective over numerous cuts. **DISCUSSION/SIGNIFICANCE OF IMPACT** Future work includes design optimization and birth attendant feedback. We propose that the device will reduce neonatal sepsis, improve neonatal outcomes, enhance occupational safety, and mitigate problems related to sharps disposal. Work supported in part by the NIH/NCATS CTSA to UF, TL1 TR000066 and UL1 TR000064.

045

## PROGNOSTIC FACTORS IN OVARIAN CANCER: AN EVALUATION OF 142 PATIENT SAMPLES USING 31 DISTINCT MARKERS

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**OBJECTIVES/SPECIFIC AIMS** Ovarian cancer is the most lethal gynecologic malignancy in the United States. A number of positive prognostic factors exist including the presence of lymphocyte markers. Tumor infiltrating lymphocytes, or TILs, are cells that infiltrate the tumor with the potential to sample, target and destroy tumor cells. Cytotoxic CD8+ TILs have been shown to be most favorable for prognosis in ovarian cancer, although other immune cells including CD3+T cells, CD4+ T cells, and B cells have demonstrated survival benefits as well. Although data for these markers exist, results are not uniform in the literature. Furthermore, a number of other cell protein markers that have been targeted in effective immunotherapies for other cancers such as metastatic melanoma may prove to be favorable in the prognosis of ovarian cancer. For example, in our in-vitro studies, CD137+ TILs are the most cytotoxic subtype among TILs and blockade of PD-1 enhances TIL activity. **METHODS/STUDY POPULATION** We performed Immunohistochemistry experiments using 31 key lymphocyte and tumor markers on 142 ovarian cancer patient samples obtained during tumor debulking. We subsequently analyzed expression of each marker and correlated marker expression with overall survival, histotype, stage, age, debulking grade, and response to chemotherapy. **RESULTS/ANTICIPATED RESULTS** Early results have shown that the presence of CD8+ TILs is positively correlated with overall survival, and many more markers are actively being analyzed. **DISCUSSION/SIGNIFICANCE OF IMPACT** In conclusion, our results further support the vital role of cytotoxic T-cells in the body's natural defense against ovarian cancer.

046

## SIMVASTATIN-CONTAINING MICELLES FOR IMPROVING FRACTURE REPAIR

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**OBJECTIVES/SPECIFIC AIMS** Simvastatin (SIM), a lipid-lowering medication, enhances bone formation via induction of bone morphogenetic protein 2 (BMP2). However, the dose required for this anabolic effect is limited by systemic toxicity. Local application of SIM with carriers such as hydrogels can deliver effective doses, but requires surgical introduction. The aim of this study was to develop and validate a novel SIM-PEG micelle to enhance bone repair without the need for surgical intervention. **METHODS/STUDY POPULATION** IRDye-800CW labeled micelles consisting of an amphiphilic SIM-polyethylene glycol shell and a free SIM core (SIM-PEG) were synthesized. MC3T3 osteoblastic cells were treated with SIM-PEG and BMP expression and signaling were evaluated using qPCR and phosphoSMAD1/5/8 immunofluorescence. Open, stabilized femur fractures were created in 42 7-wk female C57Bl/6 mice. Mice received retro-orbital injection of SIM-PEG on post-op day (POD) 1 ($n$ = 15), POD 7 ($n$ = 12), or saline on POD 1 ($n$ = 15). SIM-PEG localization was assessed by bioluminescence imaging. Fracture repair was assessed by histology and μCT. **RESULTS/ANTICIPATED RESULTS** SIM-PEG induced BMP2 expression and BMP signaling in MC3T3 cells. *In vivo* bioluminescence imaging demonstrated localization of SIM-PEG to fracture sites. Histologic analysis revealed accelerated fracture repair compared to saline control. Although underpowered for this pilot study ($n$ = 3/group), μCT showed a strong trend towards improvements in bone volume fraction and tissue mineral density. **DISCUSSION/SIGNIFICANCE OF IMPACT** SIM-PEG micelles induced BMP2 expression and signaling in osteoblast lineage cells *in vitro* and localized to fracture sites and accelerate repair *in vivo*. SIM-PEG micelles therefore show promise as a single-dose therapy for enhancing fracture healing.

047

## TRANSLATIONAL STUDY OF DIFFUSION TENSOR IMAGING FOR PERIPHERAL NERVE INJURIES

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**OBJECTIVES/SPECIFIC AIMS** Diffusion tensor imaging is a specialized MRI that leverages tissue-specific differences in water diffusion to visualize neural structures. In the central nervous system, DTI has greatly impacted our abilities to map neural pathways in addition to serving as a diagnostic tool for traumatic injury. The use of DTI in the peripheral nervous system is limited, even though current clinical measurements of injured peripheral nerves are vastly insufficient for directing surgical decisions. Outcomes following peripheral nerve repair are currently unknown until late-stage clinical milestones are reached, which can be several months after the initial operation. In this study, we first evaluated DTI in an animal model of peripheral nerve injury and then initiated a human clinical trial for ulnar and median nerve injuries. **METHODS/STUDY POPULATION** Twelve Sprague Dawley rats were anesthetized and underwent partial or complete sciatic nerve transection followed by microsurgical repair. Rats were sacrificed at one hour postrepair and the injured nerves were excised and immersion-fixed with 4% glutaraldehyde/0.5% paraformaldehyde in PBS for 24 hours. Images were acquired using a 2D diffusion-weighted spin echo sequence on a 4.7T MRI scanner. Additionally, two human subjects have been imaged to date, one normal and one injured subject, in a 3T MRI scanner. **RESULTS/ANTICIPATED RESULTS** Rat DTI nerve tract counts in completely transected nerves (1.8 ± 0.92 tracts) were significantly lower than both partially transected (155.8 ± 45.5, $p$ = 0.0136) and control nerves (199.7 ± 94.6, $p$ = 0.0286). Human DTI nerve tracts were severely reduced in the median and ulnar nerves of the injured subject. **DISCUSSION/SIGNIFICANCE OF IMPACT** Animal and human studies support the continued investigation of DTI for peripheral nerve injuries.

048

## ENGINEERING A UNIVERSAL DONOR SKIN GRAFT

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**OBJECTIVES/SPECIFIC AIMS** Every year in the US, 13,000 patients require autografts to treat severe burns. Large severe burns require multiple rounds of autografting and long hospital stays. An allogeneic full thickness universal donor skin graft could cover these wounds in a single surgery, dramatically improving patient outcomes. Therefore, we are pursuing the following aims; (1) Perform an *in vivo* tolerogenic screen to identify the best method for creation of a Universal Donor skin transplant; (2) Validate the *in vivo* screen with an engineered murine skin transplant rejection model; and (3) Create a human full-thickness skin graft with Universal Donor normal immortal diploid human cells. **METHODS/STUDY POPULATION** Murine fibroblasts expressing luciferase and candidate genes have been injected intradermally into the skin of syngeneic or allogeneic mice to assay induction of an immunomodulatory response. These results will inform engineering of murine universal donor skin constructs for transplant rejection experiments. We will then engineer Universal immortal normal diploid human cells and seed them into a decellularized human skin matrix. We will evaluate reconstitution of skin function in a nude mouse model. **RESULTS/ANTICIPATED RESULTS** We have determined that allogenic transplants show a dramatic decrease in luciferase signaling when adaptive immunity is triggered at about 7 days post

transplant by measuring the survival of syngeneic and allogeneic murine fibroblast transplants. We have also shown modulation of the rejection response by some of our candidates. **DISCUSSION/SIGNIFICANCE OF IMPACT** Human primary cells immortalized with hTERT are nononcogenic, genetically stable, and respond normally to differentiation signals. We aim to use these cells to facilitate genetic engineering in a regenerative medicine context, with engineering expression of universal donor genes as an initial indication.

**049**

### IDENTIFICATION AND FUNCTIONAL ANALYSIS OF KEY GENETIC DRIVERS OF CUTANEOUS SQUAMOUS CELL CARCINOMA

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**OBJECTIVES/SPECIFIC AIMS** Currently, effective molecularly driven interventions and risk assessment are not available for preneoplastic lesions because the key genomic drivers of progression from normal tissue to preneoplastic lesion to invasive cancer have not been identified. We have addressed this gap by using cutaneous squamous cell carcinoma (cSCC) as a model, which has a well-characterized progression sequence from a distinct precancerous lesion, the actinic keratosis (AK), to invasive carcinoma. **METHODS/STUDY POPULATION** We have combined RNA-Seq, miR-Seq, and reference exome-Seq on tissue specific, matched human samples at three stages of tumor development. **RESULTS/ANTICIPATED RESULTS** We analyzed 10 matched sets of human skin, AK, and cSCC. Using functional pair analysis, we identified multiple miRNA/mRNA pairs, including miR-181 and its target TGFBR3, as potential drivers of cSCC progression. We show that miR-181 regulates susceptibility to apoptosis, cellular adhesion and motility at least in part through TGFBR3. Primary human keratinocytes and HaCaT cells that overexpress miR-181 or have TGFBR3 knockdown are less susceptible to UV-induced apoptosis, readily form colonies in soft agar, and exhibit hypermotility. **DISCUSSION/SIGNIFICANCE OF IMPACT** Currently, we lack diagnostic predictors of AK progression to cSCC. We propose that miR-181 levels, correlated with TGFBR3 expression, drive disease progression. Better understanding of these mechanisms offers an avenue for therapeutic intervention in both prevention and treatment of cSCC.

## T2: TRANSLATION TO PATIENTS

**050**

### AGE BY CONDITION DIFFERENCES IN A LABORATORY CORRELATE OF ENDOGENOUS PAIN MODULATION: PRELIMINARY ANALYSIS

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**OBJECTIVES/SPECIFIC AIMS** The extent to which age moderates the association between chronic pain and endogenous pain modulation is vague, since few studies have examined such interactions. We present preliminary data comparing a correlate of endogenous pain modulation in older and younger adults, who were either pain-free or experiencing chronic low back pain (CLBP). **METHODS/STUDY POPULATION** 28 adults (mean age = 48.9; *n* of females = 19; CLBP = 17) underwent conditioned pain modulation. This involved (1) 30sec application of constant heat pain with 10sec neutral temperature (33° C) stimulus to the right foot; (2) 45sec cold water immersion (8° C) of the left hand; and (3) repeated 30sec application of heat pain with 10sec neutral temperature stimulus to the right foot. Peak pain intensity (0–100 scale) during heat pain and neutral temperature periods were calculated. Percentage change in peak pain intensity after water immersion was compared using ANOVA modeling. **RESULTS/ANTICIPATED RESULTS** While all groups were similar during the constant heat period, ($F_{3,25} = 1.85$, $p = 0.169$), CLBP young adults demonstrated divergence from the other groups as peak pain intensity increased instead of decreased. Groups were also similar during the neutral temperature period ($F_{3,20} = 2.94$, $p = 0.066$). However, CLBP young adults experienced a 15% increase in peak pain intensity, compared to a 51% decrease for pain-free young adults. **DISCUSSION/SIGNIFICANCE OF IMPACT** While similar in this sample, preliminary indication is of pain modulation decrement in CLBP young adults. Future examination of a larger cohort will enhance our understanding of pain modulation differences, including for older adults which have been previously reported. This work is supported in part by NIH/NCATS Clinical and Translational Science Awards to the University of Florida (TL1 TR000066 and UL1 TR000064).

**052**

### RNASEQ AND ISOFORM-LEVEL PATHWAY ANALYSES REVEAL PATHOLOGICAL PATHS TO DANON DISEASE

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**OBJECTIVES/SPECIFIC AIMS** Lysosomal-associated membrane protein 2 (LAMP2) deficiencies cause Danon disease (Dd). Pathological characteristics include cardiomyopathy and glycogen accumulation in striated muscle. Pathophysiology remains largely unknown. Our goal was to shed light on processes that lead to Dd. We hypothesized that transcriptome profiling and pathway investigations would determine at least one pathway altered in Dd that could lead to glycogen accumulation and perturbations to cardiac muscle homeostasis in Dd. **METHODS/STUDY POPULATION** Case-control study using 3 Dd versus 6 healthy explanted human heart tissues. Ingenuity Pathway Analysis followed RNAseq isoform-level expression profiling. Data were filtrated by fold change = $\pm 5$; $p < 0.05$ for network analyses and $p < 0.05$ for pathway analyses. **RESULTS/ANTICIPATED RESULTS** Our RNA-Seq isoform data coupled with analysis-specific data filtering techniques provide novel molecular and pathway-level insight into pathological mechanisms that might lead to Dd, supporting our hypothesis. Results suggest that transcript modifications occur at the pathway-level in Dd that are associated with glycogen metabolism and signaling at cell junctions. Isoform-level perturbations to these pathways haven't been previously identified. The observed overrepresentation of transcripts associated with cell-sertoli cell junction signaling was unexpected. **DISCUSSION/SIGNIFICANCE OF IMPACT** In-depth exploration of the altered glycogen regulation and cell junction signaling changes may provide conceptual frameworks for understanding pathological systems governing perturbations to cardiac-muscle homeostasis in Dd.

**053**

### PATIENT PERIOPERATIVE MEMORIES

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**OBJECTIVES/SPECIFIC AIMS** Patient perioperative memories have implications for assessing patient satisfaction with the perioperative period, for timing of informed consent, and for provision of medical information. **METHODS/STUDY POPULATION** This was a retrospective study of patients from 2 clinical trials ($n = 7750$) on intraoperative awareness. Patient descriptions of last preoperative and first postoperative memories at 1–3 and 30 days post-op were analyzed and coded into perioperative locations. The proportions of patients who did not remember perioperative locations of interest at 30 days post-op were ascertained. Logistic regression analyses were performed for patients not remembering the OR before surgery and for patients remembering the OR after surgery, both at 30 days post-op. To assess memory stability, coded locations were compared between 1–3 and 30 days post-op. **RESULTS/ANTICIPATED RESULTS** Most patients did not remember the OR before and after surgery ($p < 0.0001$, 54%, 2187/4067; 95% CI, 52.2% to 55.3%). Fifty-six percent of patients did not remember the OR before surgery (3353/5990; 95% CI, 54.7% to 57.2%) and 95% did not remember the OR after surgery (4327/4564; 95% CI, 94.1% to 95.4%). Midazolam dose and age predicted not remembering the OR before surgery. No variable predicted remembering the OR after surgery. Forty-one percent of patients (2077/5122; 95% CI, 39.2% to 41.9%) changed their answer regarding last preoperative location between 1–3 and 30 days post-op, and 40% of patients (1388/3517; 95% CI, 37.9% to 41.1%) changed their answer regarding first postoperative location. **DISCUSSION/SIGNIFICANCE OF IMPACT** Patient perioperative amnesia may argue against assessing patient satisfaction with the perioperative period as well as obtaining consent and providing information close to surgery.

**055**

### TRANEXAMIC ACID USE AND POSTOPERATIVE OUTCOMES IN PATIENTS UNDERGOING TOTAL HIP OR KNEE ARTHROPLASTY: A STUDY OF EFFECTIVENESS AND SAFETY

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**OBJECTIVES/SPECIFIC AIMS** While tranexamic acid (TXA) has been shown to reduce perioperative blood loss, safety concerns remain. We aimed to determine the effectiveness and safety of perioperative TXA use in patients undergoing total

hip or knee arthroplasty (THA, TKA). **METHODS/STUDY POPULATION** We selected THA/TKA patients from the Premier Perspective database (2006–2012; $n$ = 872,416). The primary outcomes were transfusion, thromboembolic events (TE; pulmonary embolism and deep venous thrombosis), acute renal failure (ARF), and combined complications (TE, ARF, cerebrovascular events, myocardial infarction, in-hospital mortality). Multilevel multivariable logistic regression models measured the association between TXA use and outcomes. **RESULTS/ANTICIPATED RESULTS** While not different regarding age and comorbidity index, patients receiving TXA (versus non-TXA patients) showed lower rates of transfusion (6.9% vs. 17.5%), thromboembolic complications (0.6% vs. 0.8%), ARF (1.3% vs. 1.6%), and combined complications (2.0% vs. 2.6%); all P < 0.01. In the multilevel models TXA was associated with significantly decreased odds for blood transfusions (OR 0.34 [95% CI 0.32–0.36]), ARF (OR 0.70 [95% CI 0.61–0.81]), and combined complications (OR 0.74 [95% CI 0.66–0.83]; all $p < 0.0001$), but not TE (OR 0.93 [95% CI 0.75–1.16], $p = 0.51$). **DISCUSSION/SIGNIFICANCE OF IMPACT** This is the first large-scale population based study on safety of perioperative TXA use in orthopedic surgery. We found that TXA was effective in reducing the need for blood transfusions, while not increasing the risk of complications. Thus, our data provide incremental evidence of the potential effectiveness and safety of TXA in orthopedic patients.

**056**

### ELEVATED C-REACTIVE PROTEIN CONTRIBUTES TO PREECLAMPSIA VIA KININ SIGNALING PATHWAYS

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**OBJECTIVES/SPECIFIC AIMS** Preeclampsia (PE) is a serious disease of pregnancy characterized by hypertension and proteinuria. Despite intensive research, the pathogenesis of PE remains a mystery. In our study, we demonstrate a novel interaction between C-reactive protein (CRP) and the Neurokinin B (NKB)/Neurokinin 3 receptor (NK3R) system. **METHODS/STUDY POPULATION** Patient samples were obtained from Memorial Hermann Hospital, Houston, TX. CRP and NKB levels were quantified by ELISA and Western blot in term sera and placenta. Matrigel invasion chambers were used to examine trophoblast cell invasion. To model PE, pregnant C57BL/6 mice were injected with CRP or with NK3R antagonist, SB222200 on E13/14. Blood pressure was monitored via tail cuff. Proteinuria was measured via metabolic cage and ELISA on E17. **RESULTS/ANTICIPATED RESULTS** CRP, an acute phase reactant, is elevated in sera and placentas of PE patients. To determine the role of elevated CRP in PE, we injected CRP into pregnant mice. Injection of CRP induces hypertension and proteinuria, indicating its direct role in PE. CRP is known to bind to phosphocholine on damaged cell membranes. NKB, a placental-enriched peptide and PE-related pathogenic molecule, has been shown to be phosphocholinated, increasing NKB stability and enhancing NK3R activation. Via pulldown, we determined that CRP binds with NKB. Using invasion assays, we revealed that CRP decreases human trophoblast cell invasion, and treatment with SB222200 ameliorates this shallow invasion. Finally, *in vivo* evidence shows siRNA knockdown or SB222200 inhibition of NK3R significantly reduces CRP-induced hypertension and proteinuria in pregnant mice. **DISCUSSION/SIGNIFICANCE OF IMPACT** Our findings demonstrate elevated CRP contributes to PE, and NKB/NK3R is a novel mechanism underlying disease development. These findings indicate both therapeutic targets and diagnostic testing possibilities for PE.

## T3: TRANSLATION TO PRACTICE

**057**

### PHYSICIAN PERCEPTIONS IN THE MANAGEMENT OF MALIGNANT CENTRAL AIRWAY OBSTRUCTION

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**OBJECTIVES/SPECIFIC AIMS** We will assess the perceptions of a cohort of interventional pulmonologists who perform palliative airway stenting for the management of malignant central airway obstruction (CAO). **METHODS/STUDY POPULATION** We have designed a survey targeting provider attitudes related to the efficacy of interventional management of CAO. It will be given to a cohort of approximately 100 board certified Interventional Pulmonologists, with a goal response rate of 70%. The survey will be implemented online via Surveymonkey, and documents related to informed consent will be digitally linked. Responses will be de-identified and recorded in a computerized password protected database. **RESULTS/ANTICIPATED RESULTS** We hypothesize that many providers have intrinsic beliefs that palliative airway stenting improves mortality in CAO, despite of body of evidence suggesting it does not. **DISCUSSION/SIGNIFICANCE OF IMPACT** In its advanced stages, lung cancer can represent a challenge for both patients and providers in terms of the discussion of palliative vs. curative care. Procedures such as airway stenting can alleviate some of the symptoms of malignancies that cause CAO, but there continue to be discrepancies between patients and providers in the perceived efficacy of such interventions. Data has demonstrated that many patients receiving palliative interventions for CAO mistakenly think that their intervention is curative. However, corollary data on the perceptions of the providers is currently limited. This would provide an important link to determining whether providers share the sometimes-unrealistic expectations of many of their patients with advanced malignancies. Additionally, these provider surveys might also help to identify why pragmatic discussions about goals of care are too often delayed until a patient is on the verge of an invasive procedure.

**058**

### IRON SUPPLEMENTATION AFTER MALARIA IS ASSOCIATED WITH NORMALIZATION OF HEME OXYGENASE-1

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**OBJECTIVES/SPECIFIC AIMS** Iron treatment in malaria endemic areas increases the risk of malaria and other infections. Delaying iron treatment in children with malaria and iron deficiency (ID) may mitigate this risk. Oxidative stress may increase symptoms of malaria, or decrease risk by combatting infection. This study examines heme oxygenase-1 (HO-1), an enzyme upregulated under oxidative stress, after iron treatment of children with severe malaria, **METHODS/STUDY POPULATION** HO-1 levels were assessed in Ugandan children with cerebral malaria (CM) ($n$ = 51), severe malaria anemia (SMA) ($n$ = 39) and community children (CC) ($n$ = 52). Upon enrollment, ID children (zinc protoporphyrin (ZPP) >80) received iron immediately ($n$ = 62) or 4 weeks later ($n$ = 54). All children with SMA and CM and 26 CC had a ZPP>80, and were randomized to immediate vs. delayed treatment. 26 CC had a ZPP < 80 and did not receive iron. HO-1 concentrations were assessed at baseline and 1 month, hospitalizations after 1 month were monitored. **RESULTS/ANTICIPATED RESULTS** Children with CM and SMA had similar baseline HO-1 concentrations, and did not differ in the immediate vs. delayed subgroups. HO-1 concentrations were lower in CC than in CM or SMA ($p < 0.0001$). At 1 month, HO-1 in children in the CM and SMA delayed iron groups were increased compared to the immediate iron groups (both $p < 0.05$) and the iron sufficient group (both $p < 0.001$). At 1 month, there was no difference in HO-1 levels between children who received immediate iron and iron sufficient children (all $p > 0.05$). There was no correlation of HO-1 levels at 1 month with readmission ($p > 0.05$). **DISCUSSION/SIGNIFICANCE OF IMPACT** Iron treatment after malaria was associated with normalization of HO-1, which may reflect increased iron for enzymes that reduce oxidative stress. This suggests that ID after malaria leads to greater oxidative stress than iron treatment.

**059**

### IDENTIFYING FACTORS ASSOCIATED WITH MALIGNANT DEGENERATION AFTER LOW-GRADE OLIGODENDROGLIOMA RESECTION

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**OBJECTIVES/SPECIFIC AIMS** Oligodendrogliomas (OG) are rare cancers of the central nervous system which account for approximately 2% of primary brain tumors and 5–20% of gliomas. Low-grade (WHO grade II) OG have median survival estimates of 10–15 years, a more favorable prognosis than other glioma subtypes, which average 4.5–7 years. However, certain low-grade OG will undergo malignant transformation to the anaplastic (WHO grade III) variant (AO), which requires more aggressive treatment and has significantly poorer prognosis. To date, few studies have focused on predictors of transition to AO. Because OG is rare, existing reports often group grade II OG into larger series of low-grade gliomas, which may lead to potential misclassification bias. We aim to determine factors associated with transition to AO among patients with OG. **METHODS/STUDY POPULATION** We will conduct a retrospective chart review of patients who had surgical resection of low-grade OG at UCSF between 2000–2013. We will calculate the prevalence of AO transformation and median malignancy-free survival in the series. We will use univariate and multivariate proportional hazards regression analysis to identify factors associated with malignant degeneration. The potential determinants we plan to evaluate include demographics, presenting symptoms, Karnofsky performance scale, imaging characteristics (e.g., tumor size, location, MRI appearance), biomarkers (e.g., 1p/19q codeletion) and treatment factors (e.g., extent of resection, chemotherapy, radiotherapy). **RESULTS/ANTICIPATED RESULTS** We anticipate that preoperative tumor size and extent of resection will be significantly correlated with the patient's risk of developing AO. **DISCUSSION/SIGNIFICANCE OF IMPACT** The information learned will provide a better understanding of a patient's probability for malignant degeneration, which would influence prognostic implications and improve patients' and clinicians' treatment decision making.

060

## FEASIBILITY PILOT FOR A COMPARATIVE EFFECTIVENESS STUDY OF SCREENING METHODS FOR TYPE 2 DIABETES: DESIGN AND IMPLEMENTATION

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**OBJECTIVES/SPECIFIC AIMS** This pilot will provide critical preliminary data for a comparative effectiveness study, which will compare, using a randomized clinical trial design, three screening tests for diabetes (i.e., fasting plasma glucose, hemoglobin A1c, and point of care testing hemoglobin A1c), as they are used in "real-world" clinical settings. The specific aims of the pilot are: (1) to determine the feasibility of implementation of the study procedures at practice sites; (2) to examine the feasibility of the proposed methods to recruit study subjects; (3) to collect data necessary for sample size calculations for the large study. **METHODS/STUDY POPULATION** We plan to enroll 75 patients from four primary care practices in Rochester, NY, who meet the American Diabetes Association guidelines criteria for diabetes screening. They will receive the study intervention (i.e., recommendation for screening with one of the three tests) during an office visit with their physicians. The results of a glucose tolerance test will serve as the "gold standard" for diabetes diagnosis. **RESULTS/ANTICIPATED RESULTS** The pilot's implementation is currently underway. The expected outcomes at its completion are: (1) Identified barriers and facilitators of implementation of the study procedures at practice sites; (2) Yield from recruitment activities to inform recruitment strategies for the large study; (3) Information needed for planning the sample size of the large study (e.g., point estimates and 95% confidence intervals). **DISCUSSION/SIGNIFICANCE OF IMPACT** In the US, 7 million adults have undiagnosed diabetes and, without changes in current screening practices, the prevalence of undiagnosed diabetes is expected to double by 2050. The results of the pilot will guide the design of a large-scale study, which will provide healthcare decision makers with the evidence-based information needed for improving screening for diabetes.

062

## OROPHARYNGEAL SQUAMOUS CELL CARCINOMA AND HUMAN PAPILLOMAVIRUS IN AFRICAN AMERICAN POPULATIONS

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**OBJECTIVES/SPECIFIC AIMS** (1) To ascertain the proportion of oropharyngeal squamous cell carcinoma (OPSCC) positive for human papillomavirus (HPV) by race (African American vs. Caucasian). (2) To determine overall survival, disease specific survival and recurrence-free survival for OPSCC by HPV status and race (African American vs. Caucasian). **METHODS/STUDY POPULATION** The study will utilize a database of 270 OPSCC patients from Grady Memorial Hospital and Emory University Hospital. The proportion of OPSCC positive for HPV by race will be determined. If HPV status has not been reported as part of the official pathology diagnosis, p16 immunohistochemistry staining will be performed on the paraffin embedded tumor filed within the pathology department. Overexpression of p16 in tumor cells is a surrogate marker for high-risk HPV, and has been shown to be a highly sensitive method for determination of HPV status. The primary outcome will be overall survival, defined as months from time of diagnosis to death. Secondary outcomes will be disease-specific survival and recurrence-free survival. Survival curves will be compared using Kaplan-Meir and log rank tests. **RESULTS/ANTICIPATED RESULTS** (1) The proportion of OPSCC positive for HPV in African American patients will be significantly smaller than the proportion in Caucasian patients, as well as that reported in studies of majority white populations. (2) Similar to other populations, HPV+ African American OPSCC patients will have significantly longer survival than the HPV- patients. **DISCUSSION/SIGNIFICANCE OF IMPACT** There is a large disparity in outcome between African American and Caucasian patients with OPSCC. There is no consensus as to the etiology of this disparity. This study aims to explore a potential biological cause of this disparity.

063

## COST-EFFECTIVENESS OF DABIGATRAN COMPARED TO WARFARIN WITH A MULTIPERSPECTIVE ANALYSIS

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**OBJECTIVES/SPECIFIC AIMS** Recent trials have found that dabigatran and dose-adjusted warfarin are equally effective in stroke prevention in patients with atrial fibrillation. Rates of adverse events and costs of administration and monitoring these two medications vary. We aimed to assess the cost perspectives of each payer (Medicare, health system, patient) in relation to administration, monitoring and adverse outcomes for dabigatran and warfarin. We hypothesized that, due to costs of anticoagulation clinic maintenance, dabigatran is cost-effective from the perspectives of healthcare systems and Medicare, whereas warfarin therapy is more cost-effective from the perspective of patients. **METHODS/STUDY POPULATION** Previous research and original data were collected. Using data from three large, hospital-based anticoagulation services, the costs, reimbursements, staffing ratios, and annual patient load were extracted to assess the financial impact of maintaining anticoagulation clinics. **RESULTS/ANTICIPATED RESULTS** Three large-scale tertiary hospital based anticoagulation clinics were used to acquire an average cost of $63.57 per patient on warfarin annually. Maximum reimbursement was $13.00. In total, the cost of running an anticoagulation clinic over the course of one year was above $1.8 million for the largest anticoagulation clinic. The annual cost of warfarin for the patient was $105.85, and the annual cost of dabigatran for the patient was $661.56. **DISCUSSION/SIGNIFICANCE OF IMPACT** There are substantial costs of anticoagulation clinic services from the view of healthcare systems. This may contrast with the financial incentives for the patient.

064

## DEVELOPMENT OF A LONG-TERM OUTCOME MEASURE IN JIA

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**OBJECTIVES/SPECIFIC AIMS** Juvenile idiopathic arthritis (JIA) is not strictly a childhood disease, but rather a chronic disease that begins in childhood. There is not a single multidimensional outcome measure for adult patients with JIA. To determine which medications or treatment plans will benefit patients the most, more knowledge of the outcomes that patients wish to achieve is necessary. The aim of this project is to develop a multidimensional patient reported outcome instrument generated from all stakeholders to measure the long-term outcomes of JIA in young adults. **METHODS/STUDY POPULATION** We will use qualitative methods to derive a list of JIA outcomes assessed in early adulthood that are important to patients, families, and pediatric rheumatologists. This information will be harmonized into a multidimensional quantitative measure. The content validity will be assessed by cognitive interviews of a national sample of JIA patients. This initial questionnaire will be tested in young adult patients with JIA and refined by factor analysis. The shortened, refined instrument will be given to a population of young adult JIA patients to assess reliability and comparisons to other accepted adult rheumatoid arthritis measures. **RESULTS/ANTICIPATED RESULTS** To date, 13 pediatric rheumatologists from the U.S. have been interviewed regarding physician important long-term outcomes for JIA patients. In-depth interviews of adolescent JIA patients, young adult JIA patients, and parents of children with JIA have been scheduled. **DISCUSSION/SIGNIFICANCE OF IMPACT** This study will begin to develop the foundation for assessing and comparing outcomes in juvenile arthritis patients beyond childhood. With additional studies, the definition of an end outcome will allow for the development of predictive models and the identification of biomarkers, enabling patients to be better informed about their treatment options and expected future outcomes.

066

## LIVER TRANSPLANTATION TRENDS AMONG SOMALIS LIVING IN MINNESOTA

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**OBJECTIVES/SPECIFIC AIMS** Chronic viral hepatitis B and C infections (CHBV/HCV) are the predominant risk factors for liver cancer (HCC) in people from sub-Saharan Africa. The best options for treating HCC are liver transplantation and surgical resection. In order for patients to be eligible for these treatments, HCC must be diagnosed at an early stage. In the United States, minority populations are diagnosed and treated for HCC at a later stage compared to Caucasians. The aim of this study was to determine the proportion of Somali HCC patients who met the eligibility criteria for liver transplant at the time of diagnosis **METHODS/STUDY POPULATION** We identified Somali individuals evaluated for HCC at Mayo Clinic (Rochester, Minnesota) from July 1, 1996 through April 5, 2013. We retrospectively reviewed the electronic medical record to determine each patient's eligibility for liver transplant using the Barcelona Clinic Liver Cancer (BCLC) staging system as well as the Milan criteria for liver transplantation. **RESULTS/ANTICIPATED RESULTS** 44 of 48 Somali HCC patients had the required information to determine whether they met the eligibility criteria for transplant. Of the 44, 12 (27%) were eligible for liver transplant. and only 5 (42%) received liver transplantation. Thus only 5 of 44 (11%) Somali HCC patients received ideal therapy. **DISCUSSION/SIGNIFICANCE OF IMPACT** A substantial proportion of Somali HCC patients are ineligible for liver transplant at the time of HCC diagnosis and the reasons are unclear. Further investigations to understand and eliminate barriers are warranted.

## T4: TRANSLATION TO POPULATION

067

### HEALTHCARE CONTINUITY AND THE OVERUTILIZATION OF MEDICAL PROCEDURES

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**OBJECTIVES/SPECIFIC AIMS** This study investigates whether there is an association between the interpersonal continuity of medical care and the use of overutilized procedures using Medicare claims data. Overutilization of medical procedures is an important driver of healthcare spending in the United States and may be harmful to patients. Procedures are defined as unnecessary when they provide little or no likelihood of benefit to the patient. While evaluating the appropriateness of any given procedure for an individual patient requires extensive clinical evaluation, the prevalence of certain commonly overused procedures can provide information about overutilization in various sectors of the US health system. Care continuity is a core tenet of primary care, and different metrics of interpersonal care continuity quantify the duration, density, dispersion, and sequence of patient-provider interactions. **METHODS/STUDY POPULATION** This study analyzes a 5% sample of 2008 fee-for-service Medicare claims to identify associations between 20 commonly overutilized procedures and two previously validated metrics of care continuity, the Bice-Boxerman Continuity of Care Index (COCI) and the Sequential Continuity Metric (SECON). The claims cover 551,028 men and 900,114 women over the age of 65. **RESULTS/ANTICIPATED RESULTS** The research question is whether COCI or SECON have statistically significant associations in multivariate logistic regression analysis with 20 potentially overutilized medical procedures. **DISCUSSION/SIGNIFICANCE OF IMPACT** This study aims to provide a first step towards validating continuity metrics as a meaningful predictor of overutilization of medical procedures in order to address an unsustainable and harmful increase in unnecessary procedures in the US health system.

068

### COMPARING URBAN AND RURAL CHILD WELFARE INVOLVED CHILDREN'S RISK FACTORS FOR MENTAL HEALTH PROBLEMS

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**OBJECTIVES/SPECIFIC AIMS** In 2012 6.3 million children in the United States were reported to the child welfare system as having been maltreated. These children are at high risk of mental health problems. Most research is based on urban and suburban populations, but 20% of the population lives in rural areas. Using a nationally representative dataset, this study compares the risks for mental health problems in rural and urban child welfare populations. **METHODS/STUDY POPULATION** Data are from the Second Cohort of the National Survey of Child and Adolescent Well-being. The sample was children 6 years and older who remained in their home after a maltreatment report. Mental health status was assessed using the Child Behavior Checklist (CBCL). Child age, race, gender, most severe type of maltreatment, number of children in the home, family poverty, parent age, education and employment were included in analyses. Analyses were conducted separately for rural ($n = 248$) and urban populations ($n = 1145$) to identify unique predictors. Urban and rural was determined using the 2010 Census definition. **RESULTS/ANTICIPATED RESULTS** In the rural population, number of children, caregiver's work status and age, experiencing neglect and child's race were significant predictors of the CBCL score ($F = 4.98$, $p < .001$, $R2 = 18.26$). In the urban population, having been physically abused, child's race, being male and child poverty were significantly related to the CBCL score ($F = 4.35$, $p < .001$, $R2 = 5.75$). **DISCUSSION/SIGNIFICANCE OF IMPACT** Rural children's risk factors for a high CBCL score were related to the family environment and notably poverty was not significant. Urban children's risks were more typical and related to poverty and having been physically abused. Research and practice may need to consider these populations separately to accurately identify mental health risk and need for services.

069

### DRUG IS A MEANS OF PROBLEM SOLVING

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**OBJECTIVES/SPECIFIC AIMS** Commonly it is said that due to curiosity and peer pressure people abuse drug. In a survey of department of narcotic, Bangladesh it was found that 60.98% people abuse drug due to peer pressure and 28.52% due to curiosity. Drug addiction policy of a country depends on the underlying causes for that country. Now the question is what should be policy of Bangladesh? According to the findings how should we make plan to deal with peer pressure and curiosity? If we want to make people capable to deal their curiosity and peer pressure we have to understand why people are being curious with drug and why they are influenced by peer regarding to drug abuse? **METHODS/STUDY POPULATION** To explore the new dimension of motives for drug dependency I have been searching for last seven years on the way of my clinical practice. During this time I have dealt with 200 of male drug dependent person from diverse background. Their age ranged from 16 to 57 years. **RESULTS/ANTICIPATED RESULTS** Among them I have explored the reason behind this curiosity and peer influenced and found that most of them had some specific problems like depressed feeling, social and performance anxiety, low self esteem, communication problems, sleep disturbance, psychosexual dysfunction etc and these problems made them vulnerable for which they are being easily influenced by peer and being curious towards drugs. People had tried to solve or cope with those problems by elicit drugs that made them gradually dependent. During the treatment they could understand their maladaptive ways of problem solving **DISCUSSION/SIGNIFICANCE OF IMPACT** Therefore, people suffering form bio-psychosocial problems are vulnerable to peer pressure and curiosity. So, we have to develop policy to encounter those bio-psychosocial problems faced by people. It should be started from school education so that all people can come to understand their self and can regulate them in a proper way.

070

### PROFILE OF MINORITY HIV VACCINE PARTICIPANTS: LESSONS LEARNED FROM PHASE I HIV VACCINE TRIALS TO INCREASE MINORITY PARTICIPATION

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**OBJECTIVES/SPECIFIC AIMS** To decipher characteristics and experiences of minority volunteers in Phase I HIV vaccine trials in order to improve recruitment and retention strategies of this demographic. **METHODS/STUDY POPULATION** Data was collected over a 5-year span from 280 subjects at the HIV Vaccine Trials Unit at the University of Rochester. To gain in-depth insight, qualitative interviews were conducted with a subset of the sample ($n = 31$), purposefully oversampling for members of minority groups. **RESULTS/ANTICIPATED RESULTS** Demographic data ($n = 280$) revealed that the majority was Caucasian (86%), 8% were black and 6% were Hispanics. Gender composition was 75% male to 25% female. Minorities participants typically had a history of volunteering and were unemployed or students. Motivations were primarily a need to help minorities due to high incidence, knew someone with HIV, financial compensation and altruism. Main concern about participation was uncertainty about unintended side effects and whether scientists provided full disclosure of vaccine mechanism. Knowledgeable and reassuring nurses were cited as key to positive trial experience and alleviating mistrust concerns. The majority of participants were college educated, heterosexual, unmarried and male. Effective recruitment strategies reported by minorities were: One-on-one recruitment, flyers using known faces in the community, and graphically appealing ads in newspapers and on the Internet. Homosexual stereotyping and/or focused content on promotional materials were generally negatively perceived amongst participants. **DISCUSSION/SIGNIFICANCE OF IMPACT** In the U.S., vaccine clinical trial research teams should prioritize minority recruitment and focus recruitment efforts in community settings using culturally relevant materials. Well-informed and culturally responsive vaccine trial staff is integral to minority retention.

072

### BLOOD PRESSURE CONTROL AMONG LOW-INCOME AFRICAN AMERICANS: ARE WE MISSING IMPORTANT OPPORTUNITIES?

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**OBJECTIVES/SPECIFIC AIMS** This study aims to identify the independent contributions of medication regimen, medication adherence, and selected psychosocial factors to blood pressure (BP) control among low-income African American (AA) hypertensive patients. **METHODS/STUDY POPULATION** In this cross-sectional study, 699 low-income AA hypertensive patients underwent a face-to-face interview using validated questionnaires to assess 4 measures: medication adherence, readiness for change, medication adherence self-efficacy, and participatory decision making. The medical record was reviewed for prescribed medications and office BP. The primary outcome, BP control (based on the 2003 national guidelines) was analyzed using multivariate logistic regression. **RESULTS/ANTICIPATED RESULTS** The majority of the study participants were middle-aged ($53.8 \pm 9.9$ years) AA women ($n = 505$, 72.2%) with an annual income less than $12,000 ($n = 231$, 35.5%). BP was controlled in 24% of participants, with the use of $1.9 \pm 1.0$ antihypertensive medications. Participants with uncontrolled and controlled BP were similar in relation to the psychosocial factors and adherence. Medication classification, on the other hand, significantly predicted BP control. Hydrochlorothiazide was prescribed in 64.8% of the controlled participants compared to 57.6% in uncontrolled participants ($p < 0.01$). **DISCUSSION/**

**SIGNIFICANCE OF IMPACT** Our findings highlight the importance of the medical regimen in controlling the BP of low-income AA hypertensive patients.

075

### SOCIAL NETWORKS AND MRI MEASURES OF BRAIN HEALTH IN OLDER ADULTS: THE CARDIOVASCULAR HEALTH STUDY

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**OBJECTIVES/SPECIFIC AIMS** To examine the association between social networks and MRI measures of brain health in community-dwelling older adults. **METHODS/STUDY POPULATION** We examined the cross-sectional association between social networks and measures of brain health assessed via magnetic resonance imaging (MRI) in 1794 older adults from the Cardiovascular Health Study (CHS). Social networks were assessed using the Lubben Social Network Scale, and brain health measures were based on clinicians' semiquanititative visual ratings of brain MRI abnormalities (ventricular enlargement—a marker of gray matter atrophy—and white matters hyperintensities). The association between social networks and brain health measures were examined in logistic regression models. **RESULTS/ANTICIPATED RESULTS** Having a larger social network was associated with less gray matter atrophy and white matter hypertintensities ($p < 0.01$). After adjusting for demographics (age, gender, race, education) and health-related characteristics (hypertension, diabetes, and depression), older adults with larger social networks were less likely to have gray matter atrophy (OR 0.72, 95 CI 0.58–0.90) and less likely to have white matter hyperintensities (OR 0.77, 95 CI 0.62–0.96) than those with smaller networks. **DISCUSSION/SIGNIFICANCE OF IMPACT** These findings are consistent with the hypothesis that having larger social networks could help to preserve brain health in late life.

076

### FACTORS ASSOCIATED WITH HEPATITIS C VACCINE TRIAL PARTICIPATION AMONG RURAL PEOPLE WHO INJECT DRUGS

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**OBJECTIVES/SPECIFIC AIMS** People who inject drugs (PWID) are at high risk for hepatitis C virus (HCV), yet this population is less likely than the general public to be screened and receive medical care for HCV. Behavioral intervention has shown limited ability to decrease HCV incidence among PWID. Candidate HCV vaccines advancing to phase III trials will require at-risk study participants. This study examines willingness to participate (WTP) in a vaccine trial among HCV-negative PWID in Appalachian Kentucky. **METHODS/STUDY POPULATION** 503 illicit drug users were recruited using respondent-driven sampling. Participants were tested for HCV antibodies, and demographic and behavioral data were collected by questionnaire. HCV-negative individuals will be assessed for personal willingness and willingness to encourage drug-using peers to participate in a vaccine trial. Multivariate regression will be used to determine associated factors. **RESULTS/ANTICIPATED RESULTS** Few studies have examined WTP in an HCV vaccine trial. Income and employment are expected to be inversely correlated with WTP, as payment is a key motivator among PWID in past research. Women and nonminorities may report higher WTP, while legal trouble and incarceration may be inhibitory. Given the importance of peer communication in WTP, social network variables will be assessed, particularly with regard to peer encouragement. **DISCUSSION/SIGNIFICANCE OF IMPACT** Given the healthcare barriers and mixed impact of behavioral intervention among PWID, a vaccine is critical to controlling HCV. However, PWID are often stigmatized with unstable lifestyles and low trust in clinicians. Ironically, vaccine trials will rely on recruitment of PWID to establish efficacy. For this reason, characterizing WTP among PWID is critical to actualizing a vaccine against HCV.

077

### LENGTH OF STAY AND THIRTY DAY READMISSION FOR YOUTH/YOUNG ADULTS AGING WITH SICKLE CELL DISEASE

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**OBJECTIVES/SPECIFIC AIMS** As a result of reaching age-dependent cutoff points for insurance eligibility, young adults with sickle cell may experience loss of healthcare access thus higher adverse health events and greater hospital utilization. The objective of this study was to examine variation in length of stay (LOS) and readmission within 30 days of previous discharge between youth (14–17) and young adults (18–20 and 21–26). **METHODS/STUDY POPULATION** We used nonpublic patient level discharge data collected by The Office of Statewide Planning & Development from 2006–2011. Patients with a primary or secondary ICD 9 code of sickle cell anemia or thalassemia were included in the sample. Multilevel logistic and multivariate negative binomial regression was performed to assess the association of age on 30 day readmissions and length of stay (LOS) after controlling for patient demographics and hospital level characteristics. **RESULTS/ANTICIPATED RESULTS** We identified 1,890 patients accounting for 13,335 hospitalizations. Twenty-five percent of hospitalizations resulted in a 30 day readmission. Mean LOS was 6.2 days. Fifty-six percent of hospitalizations were patients ages 21–26. The oldest age group was associated with longer LOS [IRR = 1.2; 95% CI: 1.15–1.26] and increased 30 day readmission [OR = 1.24; 95% CI: 1.02–1.48]. **DISCUSSION/SIGNIFICANCE OF IMPACT** This analysis supports our assertion that readmissions and LOS increases with age among sickle cell patients. Consistent access to wellness care/outpatient services after aging out of children's health services may reduce inpatient utilization.

## KL2 SCHOLAR ABSTRACTS

### T0: BASIC SCIENTIFIC DISCOVERY

078

### MICRO-RNAS AS CANDIDATE PROGNOSTIC BIOMARKERS OF CERVICAL INTRAEPITHELIAL NEOPLASIA

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**OBJECTIVES/SPECIFIC AIMS** Each year thousands of American women are diagnosed with low-grade cervical intraepithelial neoplasia (LG-CIN), an early precursor to cervical cancer. The vast majority of LG-CIN resolves naturally without medical intervention, yet no current clinical test can predict the fate of LG-CIN and thereby inform treatment decisions. We postulate that tiny molecules known as microRNAs (miRNAs) can be used clinically to predict the fate of LG-CIN. Our first objective is to identify candidate prognostic miRNAs by comparing miRNA expression profiles in LG-CIN that resolved naturally to LG-CIN that progressed. Our second objective is to evaluate the feasibility of using Pap smear samples as a surrogate to biopsy for miRNA diagnostic testing. **METHODS/STUDY POPULATION** De-identified, archived clinical specimens were obtained from the Interim LSU Hospital (ILH) Department of Pathology. Clinical specimens consisted of formalin-fixed, paraffin-embedded cervical biopsies and residual Pap smears obtained from women attending the ILH Woman's Referral Clinic for care following an abnormal cytology finding. Total RNA was extracted from the specimens, reverse-transcribed, and tested for small RNAs by Taqman QPCR. **RESULTS/ANTICIPATED RESULTS** To date, we have conducted a pilot study to determine the feasibility of detecting miRNA expression in cervical specimens. Three small RNAs, including two miRNAs (miR-146a and miR-205) are readily detected in both archived cervical biopsy and residual Pap smear specimens. **DISCUSSION/SIGNIFICANCE OF IMPACT** This pilot study demonstrates the feasibility of detecting miRNAs in cervical specimens and is an important first step toward the development of miRNA-based prognostic tests for CIN. Clinical tests that can predict the fate of low-grade CIN represent the next generation of cervical cancer screening programs.

079

### HEMATOPOIETIC STEM CELL EXPANSION BY INACTIVATION OF LATEXIN

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**OBJECTIVES/SPECIFIC AIMS** Hematopoietic stem cells transplantation (HSCT) has been used as standard treatment for various hematological disorders. Even though HSCT has been applied in clinic for decades, regulation of HSC self-renewal and differentiation is still a major challenge to the therapeutic efficiencies of transplantation. This study aims to investigate the novel role of latexin (Lxn) gene in the regulation of HSC self-renewal and expansion and to determine its translational potential in HSCT. **METHODS/STUDY POPULATION** Latexin knockout mice (Lxn-/-) and the litter-mate controls (WT) were generated. The number and function of HSCs and progenitor cells (HPCs) were analyzed by *in vitro* colony forming assay and flow cytometric immunophenotypic analysis and *in vivo* transplantation. Gene expression profile in Lxn-/- HSC was defined by microarray. Lxn protein expression and HSC number in humans were measured and their relationship was determined by correlation analysis. **RESULTS/ANTICIPATED RESULTS** PB cell counts and lineage staining show that the numbers of both myeloid cells and lymphocytes are significantly increased by 50% to 100% in Lxn-/- mice ($p < 0.05$). Lxn-/- BM has 2-fold more HSCs and HPCs

than WT marrow ($p < 0.01$). Upon transplantation, Lxn-/- cells demonstrate nearly two-fold higher reconstitution capacity than WT cells. At the mechanistic level, genes involved in cell-matrix interaction and cell-cell communication are dysregulated in Lxn-/- HSCs. Lxn protein level is negatively correlated with the HSC number in humans ($R = -0.95$). **DISCUSSION/SIGNIFICANCE OF IMPACT** These data indicate LXN is a potential molecular target for enhancing HSC self-renewal and the expansion of stem cells. Future study will focus on the translational potential of antagonism of Lxn activity for HSC expansion and HSCT efficiency in clinic.

**080**

## SYSTEMS APPROACH TO DISEASE RISK PREDICTION AND STRATIFICATION

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**OBJECTIVES/SPECIFIC AIMS** Our main goal is to integrate genetic and other omic data to predict disease risk and drug response, which would improve preventive interventions and treatments. Thousands of genetic variants have been found to be robustly associated with these complex traits but their predictive power is very limited. **METHODS/STUDY POPULATION** Given the growing evidence that many (hundreds or thousands) of variants of small effects are contributing to these traits, we develop methods that take full advantage of this architecture to improve our predictions and our understanding of driving biology. Our prediction method called OmicKriging leverages and integrates similarity in genetic, transcriptomic, even geographic proximity to make optimal predictions. **RESULTS/ANTICIPATED RESULTS** Using seven disease datasets from the Wellcome Trust Case Control Consortium (WTCCC), we show that OmicKriging allows simple integration of sparse and highly polygenic components yielding comparable performance at a fraction of the computing time of a recently published Bayesian sparse linear mixed model method. Using a cellular growth phenotype, we show that integrating mRNA and microRNA expression data substantially increases performance over either dataset alone. Using clinical statin response, we show improved prediction over existing methods. **DISCUSSION/SIGNIFICANCE OF IMPACT** Our results show that an integrative approach that takes full advantage of the emerging polygenic architecture of complex traits can yield predictions that are clinically useful.

**081**

## EOSINIOPHIL-ASSOCIATED PROCESSES UNDERLIE DIFFERENCES IN CLINICAL PRESENTATION OF LOA LOA INFECTION BETWEEN TEMPORARY RESIDENTS AND THOSE INDIGENOUS TO LOA-ENDEMIC AREAS

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**OBJECTIVES/SPECIFIC AIMS** Previous studies have suggested that Loa loa infections among inhabitants of Loa-endemic areas (END) have marked differences in clinical presentation and posttreatment reactions compared to those of temporary residents (TR). Many of these differences are thought to be immune-mediated. Our aim in this study was to identify the immunologic changes that underlie the different clinical presentations in these two groups. **METHODS/STUDY POPULATION** We conducted a retrospective analysis of 186 patients with loiasis (144 TR and 42 END) seen at the National Institutes of Health. **RESULTS/ANTICIPATED RESULTS** The initial clinical presentation differed markedly between the two groups with a statistically significant difference in those having Calabar swelling (50% of END compared to 82% of TR, $p < .001$), eyeworm (71% of END compared to 15% of TR, $p < .001$), and microfilaremia (74% in END compared to 22% in the TR, $p < .001$). The absolute eosinophil counts (AEC) were markedly different between the groups; the geometric mean AEC in TR was two-fold higher than among END ($p = .0003$). Along with the quantitative increase in AEC, individuals in the TR group showed evidence of increased eosinophil activation in that the serum levels of all three eosinophil granule proteins (EDN, EPO, and ECP) at baseline were higher in the TR group compared to END. Baseline serum levels of eosinophil-associated cytokines, including IL-4, Eotaxin, GM-CSF, and IL-5 were all found to be elevated in the TR group compared to the END group ($p < 0.05$ for all cytokines). **DISCUSSION/SIGNIFICANCE OF IMPACT** These data extend earlier observations related to different clinical presentations between END and TR, and explore differences in immunology that may underlie these differences.

**082**

## THAP1 TRANSCRIPTIONAL ACTIVITY IN NEURONAL DEVELOPMENT AND THE NEUROLOGICAL MOVEMENT DISORDER, DYT6 DYSTONIA

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**OBJECTIVES/SPECIFIC AIMS** Dystonia is a neurological movement disorder characterized by prolonged involuntary twisting movements that can cause severe motor disability. DYT6 dystonia is a common inherited form of dystonia recently found to result from dominantly inherited mutations in the gene that encodes THAP1, a zinc finger-containing transcription factor. More than 50 reported THAP1 mutations have been described in clinically diagnosed DYT6 dystonia, including early truncating mutations. However, little is known about the identity of the THAP1-target genes in the nervous system. This has limited our understanding of the effects of DYT6 disease mutations on THAP1 function and designing therapeutic interventions. **METHODS/STUDY POPULATION** For this study, we have utilized mouse model and embryonic stem (ES) cells. We generated THAP1 null and DYT6 disease mutant knock-in mice and ES cells derived from these lines. Using these tools we characterized the CNS lineage genes dysregulated by DYT6-mutations and ultimately identify the key THAP1-mediated biological pathways of the CNS disrupted in DYT6 mutations. **RESULTS/ANTICIPATED RESULTS** This study demonstrates that THAP1 is essential for development and neurogenesis. THAP1 deficient stem cells fail to progress beyond the neural progenitor cell state and form mature neurons, demonstrating the key role of this protein in neural development. Using microarray analysis, we identified THAP1-regulated genes in the neural progenitor cells and the mouse brain tissue. Specifically, among the THAP1-target genes of the nervous system, we identified key pathways dysregulated by the DYT6 disease form of THAP1. **DISCUSSION/SIGNIFICANCE OF IMPACT** Based on our studies, we identify THAP1 as a developmentally essential protein that regulates key aspects of the nervous system development and further define THAP1-mediated pathways crucial for CNS development and DYT6 etiology.

**083**

## AN ESTROGEN RECEPTOR ALPHA FUNCTIONAL MUTANT IS PROTECTIVE IN MURINE LUPUS

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**OBJECTIVES/SPECIFIC AIMS** Lupus is a disease that disproportionately affects females. The etiology of the sex bias is unclear. We previously showed that a functional knockout of estrogen receptor alpha (ERα) resulted in significantly reduced renal disease and increased survival in murine lupus. Dendritic cell development, which requires both estrogen and ERα, is impacted, as is activation status and cytokine production. Due to altered hormonal feedback loops, ERKO mice have hypergonadism and partial endocrine sex reversal which may have immunomodulating effects independent of ERα. Thus, we studied the phenotype of lupus-prone ERKO mice following ovariectomy (OVX) +/- E2 replacement to preserve a physiologic hormonal state. **METHODS/STUDY POPULATION** ERKO and Ex3a strains were backcrossed onto the NZM2410 lupus-prone background. Subsets of mice were OVX'd and E2-pelleted. Mice were sacrificed at 32 weeks. Bone marrow was cultured for 7 days with Flt3L to enrich for dendritic cells which were analyzed by flow cytometry. Kidney and spleen DCs were also examined. **RESULTS/ANTICIPATED RESULTS** NZM2410 ERαKO mice were protected from lupus disease expression (no early deaths; no proteinuria at 32 weeks) if unmanipulated, or if both ovariectomized and E2-repleted. These mice had fewer inflammatory and activated cDCs (CD11c+/CD11b+/MHCII+ cells) from Flt3L-cultured bone marrow, which correlated with increased survival. **DISCUSSION/SIGNIFICANCE OF IMPACT** NZM2410 ERαKO mice were protected from lupus disease expression. Interestingly, protection was lost after ovariectomy if no E2 pellet was administered, suggesting that the protective effect requires E2 (despite the lack of a functional ERα). A protective effect was not observed in lupus-prone Ex3a mice (ERα−/−) regardless of hormonal state suggesting that the functional mutant in ERKO mice, in the presence of estrogen, potentially modulates disease.

**085**

## THE BRAIN DEFAULT MODE NETWORK IN PATIENTS WITH TYPE 1 DIABETES DIFFERS BY HYPOGLYCEMIA AWARENESS STATUS

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**OBJECTIVES/SPECIFIC AIMS** Patients with type 1 diabetes (T1D) often experience hypoglycemia (HG), and can ultimately develop HG unawareness. In the present study we sought to determine the impact of HG and HG unawareness in humans with T1D on the default mode network (DMN), a brain functional network commonly associated with human subjects' introspective, self-referential tasks. **METHODS/STUDY POPULATION** The DMN was measured by resting-state functional MRI during a 2-step hyperinsulinemic clamp [step 1 = 100 mg/dL (NG) and step 2 = 50 mg/dL (HG)] in 11 HG-unaware (5F/6M, age = 44 ± 5 years) and 9 HG-aware T1D subjects (4F/5M, age = 29 ± 5 years) as determined by Cox questionnaire. **RESULTS/ANTICIPATED RESULTS** The comparison of the DMN under the NG and HG conditions did not produce statistically significant differences in either group of subjects. Statistically

significant differences were instead found in the comparison between the aware and unaware groups, showing regional effects that indicated DMN functional connectivity suppression in the posterior cingulate cortex (PCC) of the unaware group ($p < 0.005$). These effects were not related to the glycemic status. The between-group differences in the PCC remained statistically significant also when taking into account the age of subjects. **DISCUSSION/SIGNIFICANCE OF IMPACT** The decreased connectivity of the PCC within the DMN observed in HG-unaware T1D patients is similar to what is observed in Alzheimer's disease, mild cognitive impairment, and type 2 diabetes. The results suggest that HG unawareness, but not single episodes of HG per se, alters the DMN of T1D subjects. Future studies including larger cohorts and nondiabetic controls will be needed to fully evaluate the impact of HG and HG-unawareness on the DMN of patients with T1D.

086

## LOST IN TRANSLATION: DECIPHERING SOCIAL NETWORKING AND INTERCELLULAR COMMUNICATION IN CANCER

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**OBJECTIVES/SPECIFIC AIMS** Intercellular communication is vital to tumor formation and metastasis. Cancer cells harness a little-known entity known as tunneling nanotubes (TnTs) – long narrow actin-based cytoplasmic extensions – to connect distant cells for long-distance communication in cancer. The role of TnTs in cancer, including their ability to transfer genetic materials, is unknown. **METHODS/STUDY POPULATION** We calculated average # of TnTs formed/cell at 24, 48, 72, and 96 hours in colon and pancreatic cancers. We transfected malignant cells with either of two microRNAs (miR-19a & miR-199a) labelled with fluorophore Alexa-488 by *in vitro* transcription and performed fluorescence time-lapse imaging. Invasion chamber assays were also used to separate cells using a membrane filter with pores permissive of TnT formation. Relative miR levels were assessed in recipient cells at 48 hours using qPCR. **RESULTS/ANTICIPATED RESULTS** There was up to a 200-fold difference in formation of TnTs in malignant cells as compared with stromal cells in several forms of cancer, including colon and pancreatic. For colon, a cell line derived from a distant metastatic site formed TnTs at a 7-fold higher rate than the other malignant cell lines by 48 hours; by 96 hours, this difference was 200-fold. TnT-mediated cell-to-cell transport of miR-19a was demonstrated between osteosarcoma and osteoblast cells. Levels of miR-19a were 2.4-fold higher in osteoblast cells after 48 hours of co-culture with osteosarcoma cells. **DISCUSSION/SIGNIFICANCE OF IMPACT** Our 'therapeutic index' demonstrates the rate of TnT formation is remarkably higher in cancer cells. Intercellular transport of miRNAs between cancer and stromal cells via TnTs is a novel mechanism by which miRNAs mediate altered gene regulation in the tumor microenvironment. TnTs represent a potential novel therapeutic target for invasive solid tumor malignancies.

088

## DECREASED DOPAMINE D2 RECEPTORS IN BRAINS OF ALCOHOL PREFERRING MICE

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**OBJECTIVES/SPECIFIC AIMS** A goal of alcohol (ETOH) addiction research is to identify biomarkers that may play a role in its euphoric properties. Our objective was to determine if there are differences in the DA D2 receptor system between mice that prefer or avoid ETOH and to examine changes in DA D2 receptor availability (RA) following chronic ETOH exposure using PET and [18F]fallypride (FP) to measure *in vivo* DA D2 RA. **METHODS/STUDY POPULATION** Male, drug naïve 8-week old high ETOH preferring (HAP) and low ETOH preferring (LAP) mice ($n = 11$ per grp) were administered ETOH (200 proof; 20% v/v) diluted in water using the drinking in the dark procedure for 5 weeks. FP was administered via the tail vein at the start of each 2 h emission scan. Dynamic emission scans were acquired at baseline and after alcohol administration and binding potential (BPND) images of the striatum (ST) were computed using PMOD software. Anatomical regions of interest (ST and cerebellum) were identified using a rodent brain atlas and manually defined on the PET images. DA D2 RA in the mouse ST was calculated as BPND using a reference-region method and t-tests were used for group comparisons. **RESULTS/ANTICIPATED RESULTS** DA D2 RA in the ST of drug naïve HAP mice (4.78 ± 1.0) were significantly lower ($t = 2.27$; $p = 0.03$) when compared to LAP mice (6.38 ± 2.2) (mean ± SD). HAP mice drank significantly more ETOH than LAP mice ($t = -7.02$ $p = 0.0001$). Moreover, HAP mice had a significant decrease in their DA D2 RA following ETOH exposure ($t = 2.74$ $p = 0.04$; –28% change). There were no significant changes in LAP mice. **DISCUSSION/SIGNIFICANCE OF IMPACT** Our findings demonstrate that reduced DA D2 RA exists in drug naïve HAP mice that are further exacerbated by chronic ETOH exposure. This down-regulation of DA D2 RA may influence the drug-seeking behaviors typically seen in HAP mice.

089

## GLUTAMATERGIC REGULATION CAUSES NEUROPLASTIC CHANGES WITH DENDRITIC SPINE CLUSTERING THAT PREVENTS AGE-RELATED SPATIAL MEMORY DECLINE

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**OBJECTIVES/SPECIFIC AIMS** Aging occurs with synaptic alterations in the glutamatergic neural circuitry that leads to cognitive decline. Pharmacological treatments for age-related cognitive decline remain to be developed along with understanding of their neural structural and functional correlates. We tested if we could better regulate the hippocampal aging dysfunctional glutamatergic synapse with the glutamate modulator riluzole. Riluzole has been shown to increase glutamate uptake through glial transporters and is thought to decrease glutamate spillover to the extrasynaptic NMDA receptor while increasing synaptic glutamatergic activity. **METHODS/STUDY POPULATION** Aged rodents received placebo or the glutamate modulator riluzole from 10–14 months of age. We performed behavioral studies along with confocal laser scanning microscopy and neuronstudio spine morphological analysis in the hippocampal formation and prefrontal cortex. **RESULTS/ANTICIPATED RESULTS** Aged treated rats did not present age-related hippocampal cognitive decline in comparison with aged nontreated animals. The underlying neuroplastic change is characterized by dendritic spine clustering in apical thin spines which drive the behavioral performance within a circuitry specificity. **DISCUSSION/SIGNIFICANCE OF IMPACT** Clustering of synaptic inputs along dendritic branches has been shown in electrophysiological studies and computational models to allow nonlinear summation of synaptic strength, greatly expanding neural networks computational powers. In summary, this data further elucidate mechanistic neuroplastic changes in glutamatergic neural circuits with aging and advance therapeutic development to prevent and treat age-related cognitive decline.

090

## DISCOVERY OF BACTERIAL SMALL MOLECULES FROM HUMAN INTESTINAL MICROBIOTA USING FUNCTIONAL METAGENOMICS

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**OBJECTIVES/SPECIFIC AIMS** Changes in human bacterial ecology have been associated with diseases including Inflammatory Bowel Disease (IBD). The mechanisms of how bacteria cause disease are poorly understood due to limitations in growing and manipulating these bacteria *in vitro*. Functional metagenomics circumvents these barriers by placing DNA from uncultured bacteria into a host bacteria that can be easily grown and manipulated *in vitro* (metagenomic clone). Metagenomic clones can be surveyed for the production of new bioactive small molecules using high content imaging. Aim1) Identify novel small molecules from intestinal bacteria using functional metagenomics and high content imaging. Determine the genetic pathways and structure of small molecules. **METHODS/STUDY POPULATION** Metagenomic libraries were created from the stool of patients with IBD and a healthy control. All patients were free of abdominal surgery and recent antibiotics. Metagenomic libraries are placed into E. coli and grown in 384 well plates. Sterile supernatant is transferred to human cells that are observed for changes with high content imaging. **RESULTS/ANTICIPATED RESULTS** In a preliminary screen of ~1000 metagenomic clones, a single clone was discovered that was able to perturb human cellular functions in three cell lines. This clone has been sequenced and the genetic pathways are being determined. We anticipate we will uncover ~20 novel bacterial small molecule in a screen of ~35,000 clones. We will report on the genetic pathways, molecular structure and relationship to human cellular function for all molecules. **DISCUSSION/SIGNIFICANCE OF IMPACT** To date there are only a handful of bacterial small molecules that have been discovered in the human microbiome. Any molecule discovered in this study would have a great impact in our understanding of host-bacterial interactions.

091

## LIGHT EMITTING DIODE-GENERATED RED LIGHT GENERATES REACTIVE OXYGEN SPECIES AND DECREASES FIBROBLAST MIGRATION

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**OBJECTIVES/SPECIFIC AIMS** Skin fibrosis is defined by increased fibroblast proliferation and extracellular matrix deposition. Skin fibrosis–derived fibroblasts have increased migration speed compared to normal skin fibroblasts. Our aim is to determine if light emitting diode-generated red light (LED-RL) 633 nm decreases normal human skin fibroblast migration speed. We hypothesize that LED-RL inhibits fibroblast migration speed through generation of reactive oxygen species (ROS) and is reversed by the anti-oxidant resveratrol. **METHODS/STUDY POPULATION** Using a paired study

design, skin fibroblasts were irradiated with LED-RL and compared to matched bench control plates (BCP) and evaluated using flow cytometry to quantify ROS, quantified by mean fluorescence intensity (MFI). LED-RL effect on migration speed (um/min) alone or with resveratrol 0.001% was measured by time-lapse video microscopy. Differences in treatment groups measured with ANOVA. **RESULTS/ANTICIPATED RESULTS** LED-RL at 160 J/cm$^2$ increased ROS compared to BCP (MFI 5931 versus 5594, $p = 0.03$). LED-RL fluences of 320, 480, 640, and 800 J/cm$^2$ decreased fibroblast migration speed in a dose dependent manner to 86.7%, 83.0%, 74.4%, 58.6% compared to temperature matched controls respectively ($p < 0.05$). Decreases in LED-RL migration speed post-irradiation at 320, 480, 640, and 800 J/cm$^2$ were reversed by 0.001% resveratrol (94.7%, 103.7%, 99.0%, 97.4% relative to matched control, respectively, $p < 0.05$). **DISCUSSION/SIGNIFICANCE OF IMPACT** Mechanistically, decreased migration speeds are likely due to LED-RL generated ROS and are reversed by the anti-oxidant resveratrol. Our findings contribute to the mechanistic understanding of the effect of LED-RL and provide a foundation for future mechanistic and translational studies that contribute to the light-based management of skin fibrosis.

092

### THE NLRP3 INFLAMMASOME IS REQUIRED FOR THE DEVELOPMENT OF HYPOXEMIA IN A LPS/MECHANICAL VENTILATION MODEL OF ACUTE LUNG INJURY

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**OBJECTIVES/SPECIFIC AIMS** Interleukin 1β is a potent pro-inflammatory cytokine that is implicated in the pathogenesis of Acute respiratory distress syndrome (ARDS). We sought to determine the specific role of IL-1β and the molecules that regulate its secretion, Caspase-1 and the NLRP3 inflammasome, in a two-hit model of acute lung injury due to LPS plus MV. **METHODS/STUDY POPULATION** We used a two-hit murine model of acute lung injury in which both inhaled LPS and MV were required for the development of hypoxemia, pulmonary neutrophil infiltration, and alveolar leakage. **RESULTS/ANTICIPATED RESULTS** NLRP3-deficent and Caspase-1-deficient mice had significantly diminished IL-1β levels in bronchoalveolar lavage fluid and were protected from hypoxemia, despite similar neutrophil infiltration and leakage. The IL-1 receptor antagonist Anakinra significantly improved the specific development of hypoxemia without significant effects on neutrophil infiltration or alveolar leakage. MV resulted in increased BAL extracellular ATP and alveolar macrophage apoptosis as triggers of NLRP3 inflammasome activation. **DISCUSSION/SIGNIFICANCE OF IMPACT** NLRP3 inflammasome activation and IL-1β production play a key role in acute lung injury, particularly in the hypoxemia associated with ARDS. Blocking IL-1 signaling in this model specifically ameliorates hypoxemia, without affecting neutrophil infiltration and alveolar leakage, disassociating these readouts of acute lung injury. Mechanical ventilation causes alveolar macrophage apoptosis, a key step in the activation of NLRP3 inflammasome and production of IL-1β.

## T1: TRANSLATION TO HUMANS

094

### EXECUTIVE HOMEOSTATIC NETWORK IN MILD COGNITIVE IMPAIRMENT (MCI)

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**OBJECTIVES/SPECIFIC AIMS** Patients with cognitive deficit encounter stressors requiring overloaded mental effort in their daily lives and this may accelerate their cognitive decline. The executive homeostatic network (EHN) proposes stress regulation as a bidirectional interaction between the central executive network (CEN) and peripheral homeostatic system. In this descriptive correlational study, we examined if the EHN can be used to understand stress regulation in patients with MCI. We tested the associations of two CEN indicators, executive function (EF) and resting-state functional connectivity (rFC) in CEN, with two cardiovascular homeostatic indicators, reactivity and recovery of heart rate variability (HRV). **METHODS/STUDY POPULATION** Data were collected from the preintervention assessment of an ongoing behavioral intervention in MCI. Five patients' data are presented here (mean age 77). More data will be included in the final presentation. EF, including cognitive control, verbal fluency, and working memory, was measured using a computer battery package (EXAMINER) at baseline. rFC was collected by BOLD fMRI at baseline. HRV included heart rate (HR) and high frequency (HF) HRV of electrocardiogram at baseline, in response, and in recovery from a standard task with high executive load. **RESULTS/ANTICIPATED RESULTS** Greater HR reactivity while lower HF HRV reactivity was related to greater cognitive control, but not other EF domains. The rFC in CEN existed taking anterior cingulate cortex as the seed, and were related to HR and HF HRV reactivity and recovery, and cognitive control. **DISCUSSION/SIGNIFICANCE OF IMPACT** These preliminary findings suggest that EHN may be useful in understanding the neurophysiological basis of stress regulation in MCI. These results may provide a basis for developing effective stress regulation interventions for individuals with high risk for dementia.

095

### FEASIBILITY OF VIRTUAL REALITY GAMES WITH CONTRALATERALLY CONTROLLED FUNCTIONAL ELECTRICAL STIMULATION FOR MOTOR TRAINING IN HEMIPLEGIA

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**OBJECTIVES/SPECIFIC AIMS** Investigate the feasibility of a new therapy for restoring stroke-impaired hand function that uses virtual reality (VR) to motivate motor skill practice and contralaterally controlled functional electrical stimulation (CCFES) to assist paretic hand movement. The first objective is to determine if stroke survivors can self-administer VR+CCFES therapy at home. The second objective is to evaluate the efficacy of VR+CCFES to improve function. **METHODS/STUDY POPULATION** A case series trial will enroll 3 stroke survivors with chronic upper limb hemiplegia to be treated with 12 wks. of VR+CCFES – which occurs in lab (therapist administered) and at home (self-administered). Assessments will occur 2x prior to treatment and at weeks 6, 12 (end of treatment), 16 (1 mo. post), and 20 (2 mo. post) by a therapist who will be naïve regarding the treatment that was delivered to the participants. **RESULTS/ANTICIPATED RESULTS** We anticipate that participants will be able to setup and operate the equipment and self-administer daily VR+CCFES at home as shown by electronic logs and diaries. We also anticipate impairment reduction and functional gains as measured by maximum voluntary finger extension, finger movement tracking error, upper extremity Fugl-Meyer, Box and Blocks, and Arm Motor Abilities tests. **DISCUSSION/SIGNIFICANCE OF IMPACT** Stroke is a leading disability causer, with US incidence of 795,000/yr. – 75% suffer reduced hand function. At 6 mos. post-stroke with conventional care, 65% cannot utilize the paretic hand for activities of daily living. Nearly 30% suffer chronic hemiparesis and are caregiver dependent—thus, new therapies are needed. VR and CCFES therapy have independently demonstrated efficacy for poststroke motor relearning, but have not yet been combined even though they are complimentary.

096

### ALTERATIONS IN THE CARDIAC EXTRACELLULAR MATRIX IN END-STAGE HEART FAILURE IN RELATION TO CARDIOMYOPATHY CLASSIFICATION

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**OBJECTIVES/SPECIFIC AIMS** Many cardiovascular diseases (CVDs) promote pathological remodeling of the heart and can lead to development of heart failure. In pathological cardiac remodeling, many extracellular matrix (ECM) proteins are upregulated and show different expression patterns relative to healthy hearts. On the other hand, it is often assumed that the ECM changes are similar regardless of the primary etiology of CVD and classification of cardiomyopathy in end-stage failing hearts. To examine this, we hypothesized that the pattern of myocardial remodeling is dependent upon the type of cardiomyopathy associated with heart failure. The specific aim of this project is to test whether levels and localization of ECM proteins differ between end-stage human heart failure cardiac samples classified as having ischemic cardiomyopathy, dilated cardiomyopathy, or nonischemic cardiomyopathy, relative to control hearts. **METHODS/STUDY POPULATION** End-stage failing human heart samples ($n = 17$; ischemic $n = 7$, dilated $n = 6$, nonischemic $n = 4$) were obtained from cardiac explants from patients receiving a transplant. Control human hearts ($n = 7$) were obtained from donor hearts ineligible for transplant. ECM protein expression was determined by histological analysis, immunofluorescence and immunoblotting. **RESULTS/ANTICIPATED RESULTS** As expected, levels of fibrosis are significantly higher in failing versus control hearts, but preliminary data show that the pattern of fibrosis is different in ischemic cardiomyopathy compared to both dilated and nonischemic cardiomyopathy. **DISCUSSION/SIGNIFICANCE OF IMPACT** These data suggest that investigations into novel treatments to prevent or ameliorate heart failure, in which ECM remodeling is a major complication, may require different strategies for various types of cardiomyopathy.

097

### MODELING OF CANCER STEM CELL STATE TRANSITIONS PREDICTS THERAPEUTIC RESPONSE

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**OBJECTIVES/SPECIFIC AIMS** Targeting the stem cell niche represents a novel approach to eradicate the cells that originate tumors and drive their progression. The complex nature

of interacting niche elements creates a challenge in choosing which elements to target, alone or in combination. Stochastic stimulation techniques allow for the careful study of complex systems in biology and medicine and are ideal for the investigation of strategies aimed at cancer stem cell eradication. **METHODS/STUDY POPULATION** We construct a multiple type branching process model of the breast cancer stem cell niche. We employ a fast and accurate simulation approach to simulate bulk tumor growth dynamics and predict response to therapy. **RESULTS/ANTICIPATED RESULTS** Using data from cell line and mouse xenograft experiments, we estimate frequent rates of interconversion between EMT- and MET-like states in breast cancer stem cells (BCSCs). We find that small alterations in the rate of BCSC symmetric self-renewal give rise to the Gompertzian bulk tumor growth pattern observed in breast tumors. Finally, we simulate the inhibition of microenvironmental cytokines and intracellular signals individually and in combination. We find that slowing self-renewal and disrupting the positive feedback loop between IL-6, Stat3 activation, and NF-κB signaling by simultaneous inhibition of IL-6 and HER2 is the most effective combination to eliminate both EMT- and MET-like BCSC populations. **DISCUSSION/SIGNIFICANCE OF IMPACT** We develop a mathematical model to predict response to therapies targeting the breast cancer stem cell niche. Predictions from our models show excellent agreement with cell line and xenograft experimental data showing the efficacy of combined HER2 and IL-6 blockade, and will be directly tested in planned clinical trials in HER2-positive breast cancer.

**099**

## TRANSLATING ANTI-VIRULENCE STRATEGIES AGAINST STAPHYLOCOCCUS AUREUS INTO HUMAN TISSUES

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**OBJECTIVES/SPECIFIC AIMS** Small molecule inhibitors which ablate *Staphylococcus aureus* virulence signaling *in vitro* and limit tissue injury in wild-type animal models of infection have been identified. These inhibitors have the potential to alter the pathogen's ability to cause disease while minimizing resistance development. The goal of this study was to translate these findings into human disease and evaluate the efficacy of these inhibitors in human tissues. **METHODS/STUDY POPULATION** Using both purified human neutrophils and *ex vivo* abscess fluids obtained from patients presenting to the Emergency Department we characterized the efficacy of inhibiting *S. aureus* virulence. Abscess formation is characteristic of *S. aureus* infection and represents a unique opportunity to examine clinically relevant infection in an *ex vivo* manner. Although *S. aureus* abscesses present commonly to the ED there are significant gaps in knowledge regarding host-pathogen determinants as well as a lack of effective treatment regimens that do not lead to rapid development of antibiotic resistance. **RESULTS/ANTICIPATED RESULTS** We found that lack of virulence inhibition by host factors favors bacterial survival and neutrophil lysis. Conversely, disruption of the S. aureus virulon either genetically or with small molecule inhibitors, results in enhanced host defense and increased bacterial killing. **DISCUSSION/SIGNIFICANCE OF IMPACT** These findings demonstrate the complexity of the host-pathogen interactions in infected tissues. Our findings also demonstrate that anti-infectives can be developed which target bacterial virulence while minimizing resistance.

**100**

## CORRELATION BETWEEN METAGENOMICS AND METABOLOMICS REVEALS ACTIVE BACTERIAL METABOLISM IN THE LOWER AIRWAYS

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**OBJECTIVES/SPECIFIC AIMS** Metagenomics detects the functional potential of the community, while metabolomics identifies the products of active metabolism. Thus, we used shotgun metagenomics and mass spectrometry metabolomics to examine functionally active microbial metabolism in the lower airways. **METHODS/STUDY POPULATION** BAL samples from 20 smokers were obtained by bronchoscopy. Lung microbiome characterized by 16S sequencing as enriched with background predominant taxa (BPT) or with supraglottic predominant taxa (SPT). Metabolite profile in BAL fluid was measured using mass spectrometry. Lower airway metagenome: PICRUSt and shotgun metagenome sequencing (HiSeq) **RESULTS/ANTICIPATED RESULTS** BAL microbiome of 12/20 was enriched with BPT, while 8/20 was enriched with SPT. There were no differences in demographics, clinical characteristics or lung function between the groups. Clustering analysis revealed that the metagenome of pneumotypeSPT was distinct. Using Random Forests for a predictive model, KEGG Ortholog (KO) K01492 was a significant feature associated with pneumotypeSPT (789.8 ± 698.4 counts in pneumotypeSPT, versus 42.1 ± 49.1 in pneumotypeBPT, $p < 0.001$). This KO is part of purine metabolism and inosine biosynthesis, a precursor of adenosine. Evaluation of the metabolome revealed that Adenosine and Threonine tended to be higher in PneumotypeSPT. Since threonine is an essential amino acid synthesized only in microbes we correlated the abundance of the threonine operon (shotgun) with levels of threonine by mass spectrometry ($r^2 = 0.52$, $p = 0.007$). **DISCUSSION/SIGNIFICANCE OF IMPACT** Taken together, correlations between metagenomic and metabolomic data supports viability of the lung microbiome.

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## NUCLEAR RECEPTOR GENES AND CARDIOMETABOLIC HOMEOSTASIS: FROM CELL CULTURE TO THE CLINIC

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**OBJECTIVES/SPECIFIC AIMS** Cardiovascular diseases (CVD) kill 17 million people worldwide annually. Furthermore, the number of patients with multiple CVD risk factors is growing at an alarming rate, and we are facing a global cardiometabolic crisis. Efforts are required to stop this epidemic of worsening cardiovascular health. The nuclear receptor (NR) super family of transcription factors are attractive targets to explore as contributors to the pathogenesis, morbidity and mortality associated with CVD. Genetic variability in some NR genes is associated with cardiometabolic risk factors including high blood pressure, body mass index, lipids and glucose levels. Therefore, we designed cell culture experiments to identify NR genes that contribute to cardiometabolic homeostasis clinically. **METHODS/STUDY POPULATION** Human umbilical vein endothelial cells (HUVECs) were cultured for 24 hours with DMSO (control) or Fenofibrate (FF) 10 μM ($n = 3$) respectively. FF effects on NR gene expression was measured using the Nuclear Receptor & Coregulators Array (SA Biosciences). The NRs that were significantly modulated by FF will be analyzed for associations in the HyperGEN study. **RESULTS/ANTICIPATED RESULTS** Fenofibrate increased the expression of the following 21 genes: *PPARA, ESR1, PGC1B, RXRG, NR0B1, NCOA1, NR6A1, PGC1A, ESR2, NR1D1, ESRRB, PPARG, ESRRG, NR2F1, THRB, NR2E3, RXRA, NCOA2, LXRA, NR0B2*, and *HNF4A*. Genetic variants for these genes will be analyzed for associations with cardiometabolic risk factors in HyperGEN. **DISCUSSION/SIGNIFICANCE OF IMPACT** This ongoing research is timely and significant because of its emphasis on genetic variability in pathways that influence cardiometabolic homeostasis. This effort will capitalize on the availability of unique study cohorts that will collectively contribute to the unknown causes of CVD risk.

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## LOX ROLE IN THE PATHOPHYSIOLOGY OF ENDOMETRIOSIS-ASSOCIATED INFERTILITY

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**OBJECTIVES/SPECIFIC AIMS** Mechanisms related to endometriosis-associated infertility are not well described. We and others have previously shown that lysyl oxidases (LOXs) genes are aberrantly expressed in endometriotic lesions from patients and rats with experimental endometriosis. Also, preliminary analysis of endometrial biopsies obtained from women with endometriosis indicate that there are differences in the levels of LOX protein when compared to fertile controls, however more samples have to be analyzed to validate the results and additional tests need to be conducted to ascertain the mechanisms activated by LOX upregulation. Thus, the aims of our study are: (1) To examine the expression levels of LOX protein and collagen deposition in endometrial biopsies from women with endometriosis-associated infertility and controls. (2) To correlate LOX expression and collagen deposition levels with the results of the *in vitro* fertilization procedures (IVF) (i.e., pregnancy success, live birth). **METHODS/STUDY POPULATION** We will accomplish these aims by immunohistochemistry and collagen-specific staining analysis of endometrial biopsies obtained during the window of implantation and by correlating these data with the results of the IVF technique, obtained by retrospective data analysis of records of subjects recruited at an infertility clinic. **RESULTS/ANTICIPATED RESULTS** We expect that women with endometriosis will have higher LOX protein expression and higher levels of collagen than controls, which may cause alterations in the process of implantation during the IVF technique leading to infertility. **DISCUSSION/SIGNIFICANCE OF IMPACT** Understanding the contribution of LOX to endometriosis-associated infertility may provide the basis for the development of new diagnostic tests and treatments for infertility.

# T2: TRANSLATION TO PATIENTS

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## THE PI3K INHIBITOR GDC-0941 IS SYNERGISTIC WITH LAPATINIB IN UTERINE SEROUS CARCINOMA

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**OBJECTIVES/SPECIFIC AIMS** To determine the effect of PI3K activity in mediating ligand-independent estrogen signaling and endocrine sensitivity in uterine serous

carcinoma (USC). **METHODS/STUDY POPULATION** Drug effect on cell proliferation was calculated via Calcusyn in patient-derived UPSC cell lines ARK 1 and 2. PI3K mutation was analyzed after laser capture microdissection of tumor DNA in 7 consecutive patients with USC. Protein expression, via Western blot, was correlated prospectively with clinical parameters. **RESULTS/ANTICIPATED RESULTS** Fulvestrant, an ER antagonist, rendered the cells significantly more resistant to taxol in ARK1 and 2 ($p$ = 0.035, 0.021 respectively). The concomitant decrease in pERS167 and pAKTS473 with Fulvestrant treatment is independent of baseline ER expression and PI3K mutation. In ARK2, a cell line that is ER-, disrupting AKT signaling via GDC-0941, or with the lapatinib is synergistic with Fulvestrant with Combination Index (CI) 50 of 0.441 and 0.229, respectively. Independent of HER2 amplification or PI3K mutation, lapatinib and GDC-0941 exhibited synergistic cytotoxicity in both ARK1 and 2 (CI50 of 0.577, 0.233). Finally, PI3K mutation and pAKTS473 expression was analyzed in 7 tumor samples. While none harbored PI3K mutation, patients who are chemotherapy resistant had significantly lower expression of baseline pAKTS473 in their tumor samples than those who are chemosensitive, similar to our cell line data. **DISCUSSION/SIGNIFICANCE OF IMPACT** PI3K pathway dysregulation, either via upstream erbB amplification, or downstream constitutive activation of AKT, may be important in mediating endocrine and taxol sensitivity in USC. pAKTS473 may be an important biomarker of drug sensitivity. The combination of PI3K inhibitor and lapatinib is synergistic and warrant further therapeutic investigation.

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## LONGITUDINAL CHANGE IN MYELIN WATER FRACTION IN NEW MULTIPLE SCLEROSIS LESIONS

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**OBJECTIVES/SPECIFIC AIMS** The aim of this project was to quantify change in myelin water fraction (MWF) in new enhancing and nonenhancing multiple sclerosis (MS) lesions. **METHODS/STUDY POPULATION** Five patients with MS had a total of 13 new contrast-enhancing lesions and three nonenhancing lesions (occurring within past six months) on baseline T2prep SPIRAL MRI (Taqc = 10 min) and second SPIRAL MRI at a mean follow-up of 5 ± 1.5 months. The SPIRAL data was analyzed with our postprocessing algorithm, by restricting the relaxing T2 distribution to two Gaussian-shaped peaks corresponding to myelin water and intra/extra-cellular water. A voxel-based paired t-test was performed to compare the mean values of MWF between the lesions at the two time points. **RESULTS/ANTICIPATED RESULTS** 12 of 13 enhancing lesions showed increase in MWF over time (mean 0.0319 ± 0.022 vs. 0.0822 ± 0.046, $p = 0 < 0.0001$). Two of three nonenhancing lesions demonstrated rising MWF values at follow-up (0.0494 ± 0.0327 vs. 0.0528 ± 0.0347, $p = 0.0297$). **DISCUSSION/SIGNIFICANCE OF IMPACT** The ability to study myelin change *in-vivo* could provide insight into the dynamics of remyelination. T2 relaxometry is a MRI technique in which the contribution of water associated with myelin can be represented as MWF. Although MWF is a promising tool to assess myelin change, its use within early, edematous lesions may be influenced by increased water content. This work provides evidence that MWF changes longitudinally within lesions utilizing a clinically feasible acquisition. The higher increase in MWF occurring within contrast-enhancing lesions over nonenhancing lesions suggests that the initial change in MWF may be in part be related to resolving edema, however continued change in older lesions suggests that true remyelination is occurring. This work demonstrates the utility of MWF to study myelin dynamics in new MS lesions.

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## DAILY D2 INTAKE FROM UVB-EXPOSED MUSHROOMS DOES NOT RAISE 25OHD IN DEFICIENT ADULTS WITH FEATURES OF THE METABOLIC SYNDROME

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**OBJECTIVES/SPECIFIC AIMS** The objective of this study was to test the bioavailability of D2 from mushrooms as compared to D3 from supplements (as measured by 25OHD) in a RCT of adults with features of the metabolic syndrome. **METHODS/STUDY POPULATION** We tested the bioavailability of D2 from mushrooms, as measured by 25OHD, in a RCT of adults ($n$ = 43, 49 ± 12y) with confirmed Vit D deficiency at baseline (total 25OHD≤20ng/ml) and features of the metabolic syndrome. Subjects were randomized to 1 of 4 groups, each fed meals containing 100 g mushrooms daily for 4 months: 1)UVB-mushrooms-600 IU D2 + placebo capsules; 2)UVB-mushrooms-4000 IU D2 + placebo capsules; 3)Untreated mushrooms + 600 IU D3 capsules, and 4) Untreated-mushrooms + 4000 IU D3 capsules. Meals contained fresh mushrooms prepared in a variety of self-selected entrees by a chef; these were frozen after cooking and delivered biweekly over 4 months. 25OHD was measured at baseline, 1 and 4 months. **RESULTS/ANTICIPATED RESULTS** Mean baseline 25OHD was 13.1ng/ml with no group differences. Consumption of either low or high dose UVB-exposed mushrooms produced little change in 25OHD (delta = 1.5 and 4.8ng/ml, $p$ = ns), while both doses of D3 increased 25OHD (delta = 7.6 and 20.5ng/ml, p≤0.05). **DISCUSSION/SIGNIFICANCE OF IMPACT** Losses experienced in cooking, freeze-thaw, and storage of UVB-exposed mushrooms, as well as, possible problems with serum transport, tissue uptake and hepatic hydroxylation may explain the poor bioavailability and failure of D2 from UVB-exposed mushrooms to raise serum 25OHD compared to D3 supplements.

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## AAC REVOLUTIONIZES APHASIA THERAPY: CHANGES IN CORTICAL PLASTICITY AND SPOKEN LANGUAGE PRODUCTION

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**OBJECTIVES/SPECIFIC AIMS** To generate pilot behavioral and neuroimaging data, comparing the effect of traditional restorative (TR) and augmentative and alternative (AAC) treatment on the restoration of language recovery in people with aphasia (PWA). **METHODS/STUDY POPULATION** The participants received either 4 weeks of AAC treatment or TR aphasia therapy. Behavioral and fMRI testing occurred pre- and posttreatment. **RESULTS/ANTICIPATED RESULTS** The follow section summarizes preliminary subject-level results for the first 9 participants (4 = AAC and 5 = TR) (target $n$ = 14). BEHAVIORAL FINDINGS (analyses for patients 001–009) Two participants from each group improved by two or more points on the standardized aphasia testing. Two participants who received AAC therapy made numerical increases on dWords, CIUs, and CIUs/minute on the treated story. Carryover to untreated stories with and without AAC was variable; instruction that facilitates generalization may be warranted. NEUROIMAGING FINDINGS (analyses for patients 001–008) The participants exhibited variable lesion sizes (and locations). Five participants exhibited relatively high numbers of lesioned voxels in the region of interest (ROI = left inferior frontal gyrus). Of the 3 remaining participants, 2 exhibited small numbers and 1 did not have any lesioned voxels in the ROI. Pretreatment, LIs were largely right lateralized or bilateral; 6 of the 8 participants demonstrated a leftward shift in activation posttreatment (2/3 in AAC group). **DISCUSSION/SIGNIFICANCE OF IMPACT** This study will provide preliminary behavioral and fMRI data that AAC interventions facilitate language recovery and lay the groundwork for the development for a more efficient and effective approach to aphasia rehabilitation.

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## PROGRESS ON A RANDOMIZED TRIAL OF TRANSCRANIAL DIRECT CURRENT STIMULATION FOR POSTSTROKE APHASIA

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**OBJECTIVES/SPECIFIC AIMS** Aphasia, an impairment of one's ability to understand or use language, impacts one third of stroke victims, and there are no effective medical treatments to improve recovery. Transcranial direct current stimulation (tDCS) is a new technique that safely and noninvasively modulates brain activity and can have a lasting effect on stroke recovery. We hypothesize that tDCS designed to enhance left lateralization of the frontal lobes can improve language function in poststroke aphasia. This approach should induce leftward reorganization of the language network, observable as changes in brain structure, function, and connectivity. **METHODS/STUDY POPULATION** We have begun a randomized double-blind sham-controlled Phase II trial testing whether tDCS can improve language function in people with poststroke aphasia. In addition to clinical measures of language functions, secondary outcome measures include safety and tolerability, cognitive and motor functions, detailed measures of the component processes of language, and multimodal MRI data, including measures of brain function, structure, and connectivity. **RESULTS/ANTICIPATED RESULTS** As of January 2014, 30 subjects have been consented, and 21 have been randomized. Protocol adherence has been good. There have been no adverse events related to treatment. Baseline behavioral and MRI data will be shown. **DISCUSSION/SIGNIFICANCE OF IMPACT** Completion of the study will provide evidence regarding the safety and efficacy of tDCS for aphasia, as well as translational data on the physiological changes induced by treatment.

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## FACTOR VIII MAY PREDICT CATHETER-RELATED THROMBOSIS IN CRITICALLY ILL CHILDREN

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**OBJECTIVES/SPECIFIC AIMS** Identification of critically ill children at increased risk of deep venous thrombosis from central venous catheters can individualize

prevention strategies. We determined whether plasma factor VIII activity and G value are associated with the risk of thrombosis in critically ill children. **METHODS/STUDY POPULATION** We enrolled critically ill children <18 years old within 24 hours after catheter insertion. We excluded children with thrombosis and those anticipated to receive anticoagulation. Once enrolled, we measured factor VIII with one-stage clotting assay and G value with thromboelastography. Children with thrombosis diagnosed with surveillance ultrasonography on enrollment day had prevalent thrombosis while those with thrombosis thereafter had incident thrombosis. We used logistic regression to test the associations. We calculated the sensitivity and specificity of factor VIII >150% and G value >12.4 dynes/cm$^2$. **RESULTS/ANTICIPATED RESULTS** Of 85 children enrolled, 26 had incident and 11 had prevalent thromboses. Factor VIII, but not G value, was associated with incident thrombosis. The odds ratio of incident thrombosis per standard deviation increase in factor VIII was 2.33 ($p$ = 0.01). The sensitivity and specificity of factor VIII was 36.0% and 80.4%, respectively. In contrast, G value, but not factor VIII, was associated with prevalent thrombosis. The odds ratio of prevalent thrombosis per standard deviation increase in G value was 2.61 ($p$ = 0.006). The sensitivity and specificity of G value was 36.4% and 94.6%, respectively. Addition of factor VIII and G value to clinical characteristics seems superior to clinical characteristics alone in identifying incident and prevalent thrombosis, respectively. **DISCUSSION/SIGNIFICANCE OF IMPACT** Factor VIII may predict the development of catheter-related thrombosis in critically ill children.

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## DECREASED MYELIN INTEGRITY IN NORMAL CONTROLS WITH HIPPOCAMPAL ATROPHY

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**OBJECTIVES/SPECIFIC AIMS** There is a critical need for MRI biomarkers of the earliest stages of Alzheimer's disease (AD). While hippocampal atrophy has been identified as one such biomarker, other MRI techniques may identify concomitant changes in other regions and tissue. Thus, this work investigates if diffusional kurtosis imaging (DKI) could reveal alterations in white matter of normal controls (NC) with hippocampal atrophy. **METHODS/STUDY POPULATION** 27 cognitively healthy NC (age = 70.59 ± 8.26; 19F) were studied. Siemens 3T MRI experiments included MPRAGE and DKI. DKI–derived metrics include axonal water fraction (AWF), axial and radial extra-axonal water diffusivity (De,ax and De,rad). Hippocampal atrophy was measured using NeuroQuant (i.e. z-score ≤ –1). Parametric maps were normalized to MNI-152 space. Voxelwise analyses were performed with TBSS running in FSL, with analyses of covariance (for age, sex) performed only in white matter skeleton voxels (FA> = 0.4). Permutation-based statistics were computed using randomise applying TFCE to correct for familywise error ($p$ < 0.05). **RESULTS/ANTICIPATED RESULTS** NC subjects with ($n$ = 12) and without ($n$ = 15) hippocampal atrophy did not differ in demographic characteristics or neuropsychological testing. However, covarying for age and sex, NC with hippocampal atrophy had increased De,ax ($p$ < 0.05) and De,rad ($p$ = 0.05) in several white matter tracts previously implicated in AD, primarily in the left hemisphere. AWF showed no differences between the groups. **DISCUSSION/SIGNIFICANCE OF IMPACT** In our prior publications, we proposed that De,ax and De,rad may be markers of myelin integrity, while AWF reflects axonal density. In extension of that work, these preliminary analyses demonstrate that De,ax and De,rad potentially identify changes in the Preclinical AD phase, suggesting that decreased myelin integrity may be observed very early in the AD process.

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## TRANSLATION OF CONTRAST AGENT FREE CARDIAC FIBROSIS IMAGING

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**OBJECTIVES/SPECIFIC AIMS** Cardiac fibrosis heightens the risk of deadly arrhythmias, particularly in patients with diabetes. Standard of care diagnosis is performed using gadolinium enhanced cardiac magnetic resonance imaging (CMR), however, gadolinium contrast agents are toxic in patients with reduced renal function including diabetics. Recently, we developed and validated a noninvasive and contrast agent free CMR technique for measurement of cardiac fibrosis in mice. In this study, we report on the initial clinical translation and validation against gadolinium CMR. **METHODS/STUDY POPULATION** Fibrotic collagen transfers magnetization (MT) to surrounding bulk water. We visualized this through acquisition of pairs of MT-weighted CMR images in 35 patients referred for standard of care gadolinium enhanced CMR at our institution. MT-weighted data was acquired prior to infusion of gadolinium and validated against gadolinium enhancement. MT contrast was quantified as the normalized change in signal from MT-weighting. **RESULTS/ANTICIPATED RESULTS** Patterns of fibrosis were present in 37% of patients when assessed with gadolinium enhanced CMR. MT-weighted CMR revealed significantly elevated MT contrast in densely fibrotic tissue as defined by gadolinium enhancement compared to healthy tissue (213 ± 22% vs. 142 ± 16%, P < 0.05). In addition, MT contrast demonstrated correlation ($r$ = 0.72) with fibrotic density determined using T1-mapping MRI. Finally, patterns of elevated MT contrast were spatially similar to patterns of enhancement at gadolinium CMR. **DISCUSSION/SIGNIFICANCE OF IMPACT** This work demonstrates the ability to probe for cardiac fibrosis in an entirely noninvasive manner without nephrotoxic contrast agents. Diagnosis in patients currently excluded will help to direct treatment and reduce mortality from adverse cardiac events. Additionally, the translational imaging approach will expedite development, testing, and application of novel anti-fibrotic therapies.

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## POSTURAL SWAY COMPLEXITY: A BIOMARKER FOR POSTCONCUSSION DYSFUNCTION IN YOUTH?

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**OBJECTIVES/SPECIFIC AIMS** The inflammatory process following a concussion takes time to unfold, leaving the brain in a vulnerable state for an unknown period of time. During this vulnerable period, premature return to activity can lead to dangerous outcomes. As the impairments associated with concussions are difficult to detect, there is a critical need to identify biomarkers to help track concussion recovery. This study's purpose was to test complexity characterizations of postural sway as a potential biomarker for postconcussion dysfunction in youth. **METHODS/STUDY POPULATION** Participants included 40 age/gender-matched subjects (20 injured, 20 healthy) with a mean age of 13.23 years. Injured participants were under the care of a physician for a documented concussion. Healthy participants reported a history free of any head injuries. Participants were excluded from both groups if they reported any health condition with potential to affect sway. Participants were instructed to stand as naturally as possible during two-minute trials under eyes-open and eyes-closed conditions on an AMTI force platform. Custom MATLAB code was used to compute the complexity metric Sample Entropy (SampEn) for the time series of the center-of-pressure trajectories in the anterior-posterior and medial-lateral directions for each participant and each condition. A 2 (injury vs healthy) x 2 (eyes open vs. closed) mixed-design analysis of variance (ANOVA) was performed. **RESULTS/ANTICIPATED RESULTS** Injured subjects yielded lower SampEn values than healthy subjects in both directions (p < .05) with Cohen's d values ranging 0.5–0.95. **DISCUSSION/SIGNIFICANCE OF IMPACT** These data provide preliminary support for complexity characterizations of postural sway as a potential biomarker for postconcussion dysfunction in youth.

# T3: TRANSLATION TO PRACTICE

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## PROCESS VARIATION AND DATA QUALITY RISKS IN ELECTRONICALLY COLLECTED PATIENT REPORTED OUTCOMES

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**OBJECTIVES/SPECIFIC AIMS** High quality patient reported outcomes (PRO) data are increasingly needed to support effective and patient-centered care delivery. Our objective in this study was to identify process-related risks to PRO data completeness and accuracy. **METHODS/STUDY POPULATION** We conducted practice site observations and informal interviews with practice staff to ascertain information regarding patient visits across five family medicine practices. Our analysis was framed by a process-oriented approach to data quality assessment and organized patient visit tasks into transaction sources, error sources, and controls. **RESULTS/ANTICIPATED RESULTS** Patient visits at all practices consisted of a common set of tasks, beginning with a patient appointment (transaction source). Subsequent tasks included patient check-in, nurse interview, provider exam and interview, and patient check-out. Each task, as well as wait times between tasks, represents an opportunity to collect PRO data with varying likelihood of data errors (error sources). Eliciting PROs before patients are seen by a clinician increases the time available for the patient to report data, increases the time available to transmit data to an EHR, and frees up clinician time. However, these approaches also prevent a clinical expert from serving as a monitor (control) to maximize data completeness and accuracy. **DISCUSSION/SIGNIFICANCE OF IMPACT** For PRO data to be consistently used in clinical decision making and quality improvement, practices must adopt processes and systems that minimize the risks of data errors. Practices may benefit from validated measures, user-friendly computer-adaptive questionnaires, automated error checking controls, and a practice wide culture that embraces the value of high quality PRO data.

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## ARE HEALTHCARE PROVIDERS A BARRIER TO THE HEALTH OF RURAL SEXUAL MINORITIES?

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**OBJECTIVES/SPECIFIC AIMS** Sexual minorities experience a number of health disparities, and studies suggest that avoidance or delayed contact with healthcare providers (HCPs) may play a role. There is a paucity of research on the provider side of this equation, especially in rural areas where stigma against sexual minorities is still substantial. The aim of this study was to describe factors relating to care of sexual minority patients in the practices of rural HCPs. **METHODS/STUDY POPULATION** survey administered to HCPs and patient care staff practicing in a rural Kentucky county. Participants were recruited via purposive sampling using personal invitations, tabling at physician events, links on social media, and snowball sampling. **RESULTS/ANTICIPATED RESULTS** 64 eligible HCPs completed the survey. 21 counties were represented. 92% reported serving lesbian, gay, or bisexual (LGB) and 56% serving transgender (T) patients; 35% did not know whether they served T patients. 70% reported a nondiscrimination policy including sexual orientation and 47% believed their policy included gender identity. 86% agreed or strongly agreed that they provide quality care for LGB patients and 84% agreed/strongly agreed that LGB patients would feel comfortable in their practice. Only 28% agreed that they would display symbols or materials specifically welcoming of sexual minorities and only 35% would advertise in LGBT media. **DISCUSSION/SIGNIFICANCE OF IMPACT** This study adds to knowledge about the policies, practices, and attitudes of rural providers that relate to their interactions with sexual minority patients and the community. The data indicate a disconnect between provider beliefs about their quality of care for LGBT patients and their willingness to actively change their practice. Interventions including and linking HCPs and the LGBT community are needed to improve care and reduce health disparities.

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## ASSESSING PEDIATRIC CENTRAL LINE VOLUME-OUTCOME EFFECTS ON CENTRAL LINE ASSOCIATED BLOOD STREAM INFECTIONS

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**OBJECTIVES/SPECIFIC AIMS** Assess if hospital volume of central line procedures is associated with central line–associated blood stream infection (CLABSI) outcomes for children in urban community hospitals treating predominantly adult patients. **METHODS/STUDY POPULATION** We used data from the 2011 Nationwide Inpatient Sample. CLABSI was determined using the AHRQ's Patient Safety Indicator and Pediatric Safety Indicator software. Central line procedures were identified from ICD9 codes. We fitted a multilevel logistic regression model with CLABSI as the outcome. Patient-level covariates included age group (child/adult), gender, race/ethnicity, insurance status, and case-mix risk adjustment variables. Hospital-level covariates included teaching status, and quartile variables for: the number of pediatric central lines performed, number of adult central lines performed, and percentage of pediatric discharges. We included patient-, hospital-, and cross-level interactions. **RESULTS/ANTICIPATED RESULTS** Compared to all patients discharged from hospitals with the highest quartile of pediatric central line procedures, those in the lowest quartile were 3.6 times as likely to have a CLABSI ($p < 0.05$). Compared to all adults and just children seen in hospitals with the highest quartile of pediatric central line procedures, children seen in hospitals in the third quartile of volume of pediatric central line procedures were one-third as likely to have a CLABSI ($p < 0.05$). **DISCUSSION/SIGNIFICANCE OF IMPACT** There is a central line volume-outcome effect on CLABSI for all patients associated with the pediatric volume of procedures. Exploring the dynamics associated with this pediatric finding will help identify best pediatric practices translatable to adult patients.

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## CLINICAL AND HISTOLOGIC CORRELATES OF BACKGROUND PARENCHYMAL UPTAKE ON MOLECULAR BREAST IMAGING

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**OBJECTIVES/SPECIFIC AIMS** While evaluating molecular breast imaging (MBI) for adjunct screening in mammographically dense breasts, we observed various levels of background parenchymal uptake (BPU), or uptake of Tc-99m sestamibi in normal fibroglandular tissue (FT). We examined associations of BPU with clinical and histologic breast cancer risk factors. **METHODS/STUDY POPULATION** BPU was assessed on screening MBI exams of 1149 women without implants and no history of breast cancer. BPU was categorized as photopenic (uptake in FT < subcutaneous fat), mild (uptake in FT = fat), or moderate to marked (uptake in FT>fat). ANOVA and chi-square analyses were used to test for association of BPU and clinical factors. In 44 women, prospective core-needle breast biopsy of FT with either photopenic BPU (27 women) or marked BPU (15 women) was performed. **RESULTS/ANTICIPATED RESULTS** BPU was photopenic, mild, and moderate/marked in 22%, 63%, and 14% of subjects, respectively. Moderate/marked BPU was associated with younger age, being premenopausal, and using postmenopausal hormone therapy (all $p < 0.0001$). Prevalence of moderate/marked BPU increased with BI-RADS density; however, prevalence of photopenic BPU also increased with density. Biopsy analysis showed marked samples demonstrated less lobular involution (mostly partial involution) than photopenic samples (mostly complete involution, $p = 0.001$). **DISCUSSION/SIGNIFICANCE OF IMPACT** MBI-depicted BPU is influenced by age and hormonal factors, but FT that appears similar on mammography in women of similar age, menopausal status, and hormone use can demonstrate considerable differences in BPU. BPU may reflect lobular involution status, a factor associated with risk. Mammographic density is also strongly associated with breast cancer risk; these findings suggest that BPU may be an effect modifier of that association.

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## SERUM PHOSPHORUS IN PEDIATRIC KIDNEY TRANSPLANT CANDIDATES IS ASSOCIATED WITH POSTTRANSPLANT ADHERENCE TO IMMUNOSUPPRESSANT MEDICATIONS

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**OBJECTIVES/SPECIFIC AIMS** Nonadherence to low-phosphorus diet and phosphate binders in CKD and dialysis patients is commonly used as a predictor of their posttransplant nonadherence. The objective of this study was to test the hypothesis that pretransplant medication and dietary adherence is associated with posttransplant adherence in pediatric kidney transplant recipients. **METHODS/STUDY POPULATION** Pretransplant adherence to diet and phosphate binders was assessed by serum phosphorus levels during the last 2 years before transplant. Patients were categorized into nonadherent (NA) and adherent (A) using the median serum phosphorus value as a cutoff. Posttransplant adherence was assessed by the number of subtherapeutic and/or undetectable tacrolimus levels (UTL). Posttransplant adherence was analyzed for a 1-year period starting 1 year posttransplant. Statistical methods included chi-square and Mann-Whitney tests. **RESULTS/ANTICIPATED RESULTS** 53 patients (age range 2–20, 12.98 ± 5.57) who received their first kidney transplant in our center between 1990 and 2011 were included in the analysis. Patients were predominantly male (62% vs. 38%) and ethnically identified as Hispanic ($n = 19$), African American ($n = 14$), white ($n = 11$), or other ($n = 9$). In the A group, 40% had at least one UTL during the time of observation, which was statistically significantly lower than in the NA group (69%, $p = 0.037$). The number of UTL episodes was also lower in the A group compared with the NA group (1.1 vs. 2.5 respectively, $p = 0.04$). **DISCUSSION/SIGNIFICANCE OF IMPACT** Pretransplant serum phosphorus levels were significantly associated with posttransplant adherence to tacrolimus in our cohort which may help to justify transplant selection process and help with developing an intervention.

# T4: TRANSLATION TO POPULATION

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## FRONTAL T-AXIS AND QRS-T ANGLE ON ECG IMPROVE RISK PREDICTION OF CARDIOVASCULAR DEATH

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**OBJECTIVES/SPECIFIC AIMS** We evaluated the roles of 2 easily obtained ECG measures, frontal T-axis and QRS-T angle, in risk prediction of CVD death. **METHODS/STUDY POPULATION** We studied 7,865 adults aged 40–90 years without CHD from the NHANES III (1988–1994) study. Frontal T-Axis and QRS-T angle were measured from standard 12-lead ECG using automated software. Frontal T-axis deviation was measured as the absolute difference from 45 degrees, and frontal QRS-T angle was calculated as the absolute difference of the frontal R and T vectors. Mortality and cause of death through 2006 were assessed. **RESULTS/ANTICIPATED RESULTS** The mean age (SD) was 60 (13.5) years, and 1156 CVD deaths occurred in a median follow-up time of 14 years. T-axis deviations and QRS-T angles of greater than 30 degrees occurred in 22% and 40% of the sample, respectively. In multivariate analysis adjusting for traditional risk factors, each 30 degree deviation in frontal T-axis and QRS-T angle associated with an adjusted HR of 1.39 (95% CI 1.31 –1.47) and 1.38 (95% CI, 1.33–1.44), respectively, for CVD mortality. Each measure was more pronounced in adults ≤ 60 years of age (age interaction $p < 0.05$), with an adjusted HR of T-axis and QRS-T angle of 1.49 (95% CI, 1.30–1.71) and 1.43 (95% CI, 1.28–1.59), respectively. With both variables together in an adjusted model, significant sex interactions were found in the younger group only: T-axis was only predictive in men ($n = 1926$, HR 1.34, 95% CI 1.09 –1.66) and QRS-T angle was only predictive in women ($n = 2180$, HR 1.71, 95% CI 1.31–2.22). Together, they improved the C-statistic from 0.78 to 0.81. Also, the continuous net reclassification index improved by 37%. **DISCUSSION/SIGNIFICANCE OF IMPACT** Frontal T-axis and QRS-T angle are simple ECG markers that could be used to improve prediction of CVD death.

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## ENGAGING MALES IN ANTENATAL CARE AND HIV COUPLES COUNSELING: RESULTS FROM A QUALITATIVE STUDY IN RURAL MOZAMBIQUE

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**OBJECTIVES/SPECIFIC AIMS** Antenatal care (ANC) services are offered at 86% of clinics in Mozambique and opt-out HIV testing and antiretroviral (ARV) drugs are provided free-of-charge, yet only 42% of pregnant women received ANC-based HIV counseling/testing. Interventions designed to engage men in ANC have been hypothesized to increase women's service uptake by increasing partner understanding and support for clinical services. We aimed to identify social, logistical, and financial barriers to ANC uptake, including partner accompaniment and participation, in rural Mozambique. **METHODS/STUDY POPULATION** We conducted 15 focus groups with pregnant women, traditional birth attendants, men, and clinicians separately in Inhassunge district in Zambézia province, to identify barriers and facilitators associated with male support for, and engagement in, ANC services. **RESULTS/ANTICIPATED RESULTS** Social norms, including gender inequality that limited women's ability to demand support, alcohol use/abuse by men, and the practice of polygamy were the most commonly cited barriers to women's uptake and male engagement in ANC services. The association of ANC with HIV testing also posed a barrier given high levels of HIV stigma in the community. Women want their partners involved in ANC services, but men are uncomfortable participating until this behavior is less stigmatized; men believed that if a respected man accompanied the male partner to the health facility it would reduce taunting and ridicule by friends. **DISCUSSION/SIGNIFICANCE OF IMPACT** Involving community leaders as community activists who support and accompany expectant couples to ANC should encourage male participation in ANC and HIV testing. Given women's preference for male support, we believe such an intervention would lead to increased uptake of ANC services.

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## THE HOUSING FIRST FIDELITY INDEX: FURTHER ASSESSMENT OF A MEASURE

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**OBJECTIVES/SPECIFIC AIMS** The Housing First Model (HFM) is a form of permanent supportive housing developed to serve chronically homeless individuals with co-occurring mental health and substance use disorders. Because the initial diffusion of HFM occurred without strong programming or fidelity guidelines, a number of programs that have adopted the label "Housing First" are carrying out practices that conflict with the model's basic underlying philosophy. In response to this problem, the Housing First Fidelity Index was designed to measure the degree of implementation of the model. Initial testing of the instrument among a sample of 52 housing organizations provided evidence for its content and discriminant validity. **METHODS/STUDY POPULATION** The current study aims to replicate this research with a larger sample, which will allow researchers to further test reliability of the index. One hundred HFM programs will be randomly selected and recruited from a publicly available list of federally funded housing organizations. Program-level data will be collected from a single case manager at each organization through a structured phone interview. **RESULTS/ANTICIPATED RESULTS** The instrument is expected to have high internal consistency and inter-rater reliability. **DISCUSSION/SIGNIFICANCE OF IMPACT** A valid and reliable fidelity tool will be useful for researchers and practitioners seeking to attribute program outcomes to the HFM.

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## RACIAL DISPARITIES IN SEPSIS ARE ASSOCIATED WITH RESIDENCE IN MEDICALLY UNDERSERVED AREAS

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**OBJECTIVES/SPECIFIC AIMS** To determine the association between residence in a Medically Underserved Area (MUA) and racial disparities in sepsis incidence and outcomes. **METHODS/STUDY POPULATION** Data from all admissions to non-federal South Carolina (SC) hospitals during the year 2010 with the diagnosis of sepsis were collected. A ZIP Code map of the state was overlaid on a map of the state's MUAs in order to identify which ZIP codes were deemed medically underserved. Age and race stratified incidence and mortality rates were compared using chi square. Multivariable logistic regression measured the association between race and sepsis mortality while adjusting for severity of illness and ZIP Code–level covariates. **RESULTS/ANTICIPATED RESULTS** In 2010, there were 16,293 sepsis admissions to non-federal hospitals in SC with 3,395 in-hospital deaths. Two hundred forty six ZIP Codes were identified as MU and represent a population of 1,446,987 over the age of 19 (42.5% of population over the age of 19). Blacks had a higher overall incidence rate of hospital admission for sepsis than whites (6.09 vs. 4.74 admissions/1,000 people, RR = 1.28, $p < 0.0001$) and a higher in-hospital mortality rate from sepsis than whites (13.4 vs. 9.75 deaths/10,000 people, RR 1.34, $p < 0.0001$). The disparities in sepsis incidence and mortality rates were attenuated but persisted in those who live in non-MUA (RR 1.14, $p < 0.0001$ and RR 1.18, $p = 0.004$, respectively). Educational attainment, median income and percent below poverty of the resident ZIP Code did not predict mortality in the regression analysis. **DISCUSSION/SIGNIFICANCE OF IMPACT** Racial disparities in sepsis are associated with but not completely explained by residence in a MUA. Median income, percent below poverty level, and educational attainment at a ZIP Code level did not predict mortality in this dataset.

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## IMPROVING COUPLES' QOL THROUGH A WEB-BASED, COUPLE-ORIENTED PROSTATE CANCER EDUCATION INTERVENTION

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**OBJECTIVES/SPECIFIC AIMS** Prostate cancer (Pca) and its treatment side effects negatively affect QOL, yet patients and partners (couple) often receive suboptimal instructions regarding symptom management to improve QOL. This study aims to improve couples' QOL through an eHealth intervention called Prostate Cancer Education and Resources for Couples (PERC). **METHODS/STUDY POPULATION** A multidisciplinary team of researchers, programmers, couples managing localized Pca, and clinicians from cancer centers developed PERC. PERC incorporates the family involvement module from a theory-based, efficacious, face-to-face intervention to improve QOL after Pca, and the latest evidence from scientific publications and guidelines. Usability testing using observation and qualitative interviews were conducted among three purposefully selected couples managing localized Pca. **RESULTS/ANTICIPATED RESULTS** Couples in usability testing identified strengths and weakness of PERC and provided suggestions to help refine it. PERC includes 6 modules covering topics pertaining to Pca symptoms and partner involvement issues that are integral to QOL. Each module is divided into an information section and an exercise section (e.g., couples share personal experiences with symptoms and develop better management strategies); each module requires 15–20 minutes to complete. Patients and partners are instructed to jointly review the information and complete the exercises. To accommodate the low health literacy of some potential users, PERC content is available in audio and video formats. Feasibility testing of the refined PERC is underway. **DISCUSSION/SIGNIFICANCE OF IMPACT** PERC disseminates a successful intervention to mitigate the impact of men's symptoms on couples' QOL. The innovative Web-based PERC intervention has the potential to improve QOL for more couples at a lower cost. A randomized clinical trial is needed to test its efficacy.

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## RELATIONSHIPS AMONG DYSMENORRHEA, LABORATORY PAIN, AND PSYCHOLOGICAL VARIABLES IN HEALTHY GIRLS AND GIRLS WITH CHRONIC PAIN

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**OBJECTIVES/SPECIFIC AIMS** Research has demonstrated elevated pain responses in women with dysmenorrhea, and studies have also confirmed a relationship between dysmenorrhea and anxiety. We aimed to explore relationships among self-reported menstrual pain ratings, somatization, pain-related anxiety, and acute laboratory pain in a sample of menstruating adolescents with and without a chronic pain condition. **METHODS/STUDY POPULATION** Participants were 85 menstruating girls ages 10–18 (44 healthy, mean age 14.8 years; 41 chronic pain, mean age 15.92 years) who completed questionnaires and laboratory pain tasks involving cold and pressure pain. Menstrual pain (without medication) was rated on a 0 (none) to 10 (extreme) scale. Girls with ratings of "4" and above were classified as having dysmenorrhea. **RESULTS/ANTICIPATED RESULTS** A higher proportion of participants with chronic pain were classified with dysmenorrhea (87.1%), as compared to those without chronic pain (61.8%), $\chi^2>1$, $p < .05$. After controlling for age, healthy girls' rating of menstrual pain was significantly positively correlated with cold and pressure lab pain intensity and somatization ($r$'s = .58, .41, & .36, respectively; $ps < .05$). Menstrual pain ratings in girls with chronic pain were significantly correlated with pain catastrophizing, pain anxiety, anxiety sensitivity, and neuroticism ($r$'s = .59, .61, .44 & .46, respectively; $ps < .05$). **DISCUSSION/SIGNIFICANCE OF IMPACT** Healthy girls' menstrual pain appears related to acute pain intensity and somatic symptoms, whereas menstrual pain in girls with chronic pain is related to psychological aspects of pain. The findings underscore the importance of assessing behavioral and psychosocial variables in girls with dysmenorrhea and addressing anxiety and related constructs in interventions.

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### CIRCULATING ANP GENETIC ASSOCIATION STUDY IDENTIFIES A NOVEL GENE CLUSTER ASSOCIATED WITH STROKE

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**OBJECTIVES/SPECIFIC AIMS** The goal of this study was to identify genetic determinants of plasma atrial natriuretic peptide (ANP) in the general community by performing a large scale genetic association study and to assess its functional significance on clinical outcomes and disease susceptibility. **METHODS/STUDY POPULATION** Genotyping was performed for 200,000 SNPs across 16,000 genes in 893 randomly selected individuals, with replication in 891 subjects from the community. Plasma NT-proANP1-98 concentrations were determined using a radioimmunoassay. **RESULTS/ANTICIPATED RESULTS** Thirty-three genome-wide significant SNPs ($p \leq 3.9$ X 10-7) were identified in the MTHFR-CLCN6-NPPA-NPPB locus and were all replicated. To assess functional significance of this genetic variation, the clinical characteristics and outcomes of carriers of a SNP rs5063 located in NPPA that represented the most significant variation in this genetic locus, was assessed. Carriers of rs5063 had lower ANP levels (1427 vs. 2291 pmol/L, $p < 0.001$), higher diastolic blood pressures (75 vs. 73 mmHg, $p = 0.009$) and were at an increased risk for stroke as compared to wild-type subjects ($p = 0.009$) independent of age, sex, diabetes, hypertension, atrial fibrillation, and cholesterol levels (hazard ratio 1.6, $p = 0.004$). **DISCUSSION/SIGNIFICANCE OF IMPACT** This is the first large scale genetic association study of circulating ANP levels performed with replication that identified genetic variants in the MTHFR-CLCN6-NPPA-NPPB cluster to be significantly associated with ANP levels. The functional significance of this variation relates to lower ANP levels, higher blood pressures and an increased risk for stroke in the general community

## RESEARCH SCHOLAR/TRAINEE ABSTRACTS

### T1: TRANSLATION TO HUMANS

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### REPURPOSING OF DRUGS IN HEPATOCELLULAR CARCINOMA

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**OBJECTIVES/SPECIFIC AIMS** The overall goal was to study *in vitro* efficacy of repurposed drugs in hepatocellular carcinoma (HCC) cell lines. We also evaluated alterations in microRNA upon cell treatment. **METHODS/STUDY POPULATION** We tested four generic drugs (metformin, simvastatin, salsalate, and valproic acid) alone and in different combinations, in treating hepatocellular carcinoma cell lines HEPG2, SNU449 and HuH7. We performed cell proliferation assays and flow cytometric analysis of apoptosis vs necrosis. Toxicity of a particular drug (or drug combination) on HCC cells was measured with the effectiveness measure Ed = (1-exp(-48(λ0–λd))X100, where λd and λ0 are cell growth rates under the specific treatment or no-treatment, respectively. Real-time PCR was used to validate microRNA expression upon treatment with the most effective combination on HCC cell lines. **RESULTS/ANTICIPATED RESULTS** 1.) Valproic acid is not effective alone, but works synergistically when added to metformin. This combination proved the most effective regimen and was used for microRNA analysis. 2.) MicroRNA-10b, –212, 181c and Let-7f were upregulated after 48 hrs of treatment with metformin 20 mm and valproic acid 5 mM, the most effective dosing strategy tested. **DISCUSSION/SIGNIFICANCE OF IMPACT** Currently, sorafenib is the only FDA-approved drug for HCC. As the incidence of hepatocellular carcinoma continues to rise, finding new clinically effective and cost-effective therapeutic options are much desired. This microRNA analysis can help further understand potential carcinogenic pathways in HCC as well as elucidate the targets of this repurposed therapy in HCC. These results can be useful in designed diagnostic tools to personalize the effect of therapy in planned future studies in humans.

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### IMMUNOLOGIC EXPLANATION FOR FAILURE TO CONTROL VIRAL SKIN INFECTIONS IN ATOPIC DERMATITIS

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**OBJECTIVES/SPECIFIC AIMS** To study the frequency of INFγ producing vs. IL13 and IL22 producing cells among CLA- and CLA+ skin homing T cells in activated blood of atopic dermatitis (AD) patients as compared to controls. **METHODS/STUDY POPULATION** Blood from 12 AD patients and 12 healthy controls was activated by PMA/Ionomycin and subsequently stained by a 12-color antibody panel to be analyzed by flow cytometry. INFγ+, IL22+ and IL13+ in CLA- and in CLA+ skin homing T cells percentages were compared between the two patients groups. **RESULTS/ANTICIPATED RESULTS** We measured a positive trend of Th2 (IL13) and Th22 (IL22) populations in CLA+ lymphocytes of AD vs. controls ($p = 0.05$ and 0.1 respectively). However, most striking was that although we noted a lower frequency of INFγ producing cells in AD vs. controls irrespective of CLA status, this difference was highly significant in CLA+ population (12.6% vs. 22.5%; $p < 0.05$). Additionally an imbalance of INFγ/IL13 producing cells was noted in the AD population, which showed a significantly lower ratio (1.4) compared to normal controls (3.9)($p < 0.05$). **DISCUSSION/SIGNIFICANCE OF IMPACT** We demonstrated that although there is no global cytokine production defect, AD patients harbor a selective defect in INFγ+ expression in skin homing CLA+ T cells with a relative predominance of IL-13 and IL-22 CLA+ skin homing cells. These data provide a fundamental immunologic explanation for skin specific viral dissemination in AD despite lack of other visceral involvement.

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### EFFECT OF INTRANASAL ILOPROST ON A MURINE MODEL OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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**OBJECTIVES/SPECIFIC AIMS** Inflammation, in part arising from the pulmonary vasculature, is critical for the development and progression of chronic obstructive pulmonary disease (COPD). We hypothesized that a treatment directed at the pulmonary vasculature, the prostacyclin analog iloprost, would reduce systemic inflammation in a murine model of COPD. **METHODS/STUDY POPULATION** Nineteen mice were given intratracheal elastase (1 U/mouse) on days 1 and 15, and intratracheal LPS (10 μg/mouse) on days 6, 13, 19, 27, and 50. Three days after the final LPS dose, 1 group ($n = 9$) received intranasal iloprost (5 μg/mouse) and another ($n = 10$) received the same volume of intranasal saline given at time 0, 6 hours, and 24 hours. All mice were sacrificed and bronchoalveolar lavage fluid was collected. Cytokines (IL-1β, IL-2, IL-4, IL-5, IL-10, GM-CSF, IFN-γ) were measured in the serum and BALF by Biorad multiplex assay. **RESULTS/ANTICIPATED RESULTS** There were no differences in BALF cytokines between iloprost and placebo (all $p > 0.05$). There were significant reductions in serum IL-5 (2.5 ± 0.7 for iloprost vs. 11.3 ± 0.7 for saline, $p = 0.0001$) and serum IFN-γ (11.1 ± 8.6 vs. 83.4 ± 14.3, $p = 0.0004$). There were statistically nonsignificant reductions in serum GM-CSF (18.9 ± 17.4 vs. 63.5 ± 34.0, $p = 0.07$) and serum IL-2 (11.5 ± 1.8 vs. 14.6 ± 2.2, $p = 0.07$) with iloprost compared to saline. **DISCUSSION/SIGNIFICANCE OF IMPACT** In a murine model of COPD, intranasal iloprost decreased systemic inflammation without a change in measured BALF cytokine levels. These data suggest that iloprost may preferentially attenuate systemic inflammation, rather than having a local effect on airway inflammation. Further study with long-term administration of iloprost is warranted to investigate if reductions in systemic inflammation may alter disease progression in COPD.

### T2: TRANSLATION TO PATIENTS

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### IMPACT OF BODY MASS INDEX ON ICU LENGTH OF STAY IN CRITICALLY ILL ELDERLY PATIENTS.

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**OBJECTIVES/SPECIFIC AIMS** With the aging US demographics, increasing number of older adults are being admitted to ICUs and their clinical outcomes are being investigated enormously. Our study seeks to determine the impact of BMI on ICU length of stay in the elderly. **METHODS/STUDY POPULATION** We conducted a retrospective cohort study of elderly (age 65 and over), admitted to the medical ICUs of two tertiary-care academic hospitals from 2009 to 2013. ICU length of stay (LOS) was estimated, using the product-limit method and compared, using the log-rank test. Significantly associated ($p < 0.05$) factors with LOS were included in a multivariable proportional hazards (Cox) regression. For all analyses, patients who died in the ICU were considered censored, since the outcome of interest was days until discharge alive from the ICU. **RESULTS/ANTICIPATED RESULTS** Electronic medical records of all 1,266 subjects meeting inclusion criteria were reviewed. Patients were classified into three age groups (65-<75, $n = 413$; 75-<85, $n = 467$; ≥85, $n = 386$) and four BMI groups (underweight, <18.5, $n = 91$; normal, 18.5-<25, $n = 461$; overweight, 25-<30,

$n$ = 414 and obese, ≥30, $n$ = 300). There was a significant association between age and BMI ($p$ < 0.0001). BMI was also significantly associated with gender, CAD and COPD. When comparing subjects to the BMI group of 18.5-<25, overweight patients had shorter ICU-LOS (hazard ratio: 1.31; 95 % confidence interval: 1.07–1.59, $p$ < 0.008}, whereas underweight subjects had increased ICU-LOS (HR: 0.61; 95 % CI: 0.39–0.96, $p$ < 0.0339). ICU-LOS in obese patients (BMI>30) did not differ from the 18.5-<25 BMI group. **DISCUSSION/SIGNIFICANCE OF IMPACT** Our study indicates that underweight older patients, with BMI <18.5, have increased ICU length of stay. Furthermore, overweight status signals a positive indicator of shorter ICU stay in the elderly.

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### TOWARD PATHONEUROCHEMICAL PROFILING OF MULTIPLE SCLEROSIS: SINGLE-SESSION MEASUREMENT OF GLUTATHIONE, GABA AND GLUTAMATE WITH MAGNETIC RESONANCE SPECTROSCOPY AT 7 TESLA

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**OBJECTIVES/SPECIFIC AIMS** Our long-term goal is to examine function and interplay of neurochemicals involved in multiple sclerosis (MS) pathology. Imbalanced glutathione (GSH), γ-aminobutyric acid (GABA) and glutamate metabolism have been speculated to play a role in the onset and development of MS. We implemented magnetic resonance spectroscopy (MRS) methods at 7-T for the noninvasive quantification of GSH, GABA and glutamate in a single session. **METHODS/STUDY POPULATION** Five healthy volunteers (3 male, age 23–55 years) and a female MS patient (58 years) were studied with MRS in an 8cc volume placed on midline occipital cortex. GSH and GABA were measured in an interleaved fashion with J-difference editing (JDE, TE 74 ms) and the Stimulated Echo Acquisition Mode (STEAM, TE 10 ms, TM 50 ms) was used to detect glutamate. The total session time did not exceed 1 hour. All MR methods and processing were customized. **RESULTS/ANTICIPATED RESULTS** GSH, GABA and glutamate were detectable in all sessions. Average line widths of 11.3 ± 0.9 Hz and 11.2 ± 1.3 Hz were achieved for the 2-ppm N-acetyl aspartate (NAA) resonance of the noninverted JDE condition and STEAM, respectively. Glutamate could be reliably separated from glutamine and NAA. Neither baseline nor first order phase corrections were necessary. As proof-of-principle, GSH, GABA and glutamate were detected in an MS patient. **DISCUSSION/SIGNIFICANCE OF IMPACT** The single-session quantification of various neurochemicals key to MS pathology with MRS at 7-T is presented. The achieved data quality allows the investigation of further metabolites relevant to MS such as NAA, myo-inositol, creatine and cholines. The established methodology is expected to serve as a clinical MS research tool to investigate disease severity.

## T4: TRANSLATION TO POPULATION

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### LEVERAGING CLINICAL DATA FOR PUBLIC HEALTH SURVEILLANCE: COLORADO HEALTH OBSERVATION REGIONAL DATA SERVICE (CHORDS)

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**OBJECTIVES/SPECIFIC AIMS** CHORDS, a health surveillance system, blends electronic health record (EHR) data across healthcare systems. Monitoring population health data identifies demographic and/or place-based risk factors for health processes/outcomes and targets intervention. **METHODS/STUDY POPULATION** CHORDS, a Colorado Clinical Translational Sciences Institute multiagency partnership, combines: (1) a normalized data model (HMORN virtual data warehouse or VDW) (2) a federated query service (PopMedNet), and (3) a regional data sharing governance model based on multiple national efforts. A phased implementation plan guided implementation. Patient demographic and clinical measures tracked in EHRs (i.e., body-mass index) are extracted from EHR, geocoded, and loaded into a site's VDW for federated query. When possible, aggregated patient data were supplemented with community resource data (e.g. grocery stores). **RESULTS/ANTICIPATED RESULTS** A local instance of PopMedNet was developed and tested with data formatted to VDW specifications. Analysis of geocoding capacity across sites showed accurate mapping results for 95% of patient files. Initial review of data for one county showed combined EHR representation for 30% of adults and 50% of children. **DISCUSSION/SIGNIFICANCE OF IMPACT** Federated query of EHR data is possible for monitoring local, regional and national health trends. Geocoded data allow place-based built environment analysis. The CHORDS network has the potential to facilitate data-driven decision making with accurate, timely, local health data to implement and evaluate clinical- and community-based interventions.

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### 12-MONTH OUTCOMES OF COMMUNITY ENGAGEMENT VS. TECHNICAL ASSISTANCE FOR DEPRESSION QUALITY IMPROVEMENT: A PARTNERED CLUSTER RANDOMIZED, COMPARATIVE EFFECTIVENESS TRIAL

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**OBJECTIVES/SPECIFIC AIMS** To compare two approaches to implement depression quality improvement (QI), community engagement and planning (CEP) and resources for services (RS), effects on clients' mental health-related quality of life (MHRQL) and service-use costs over 12-months. **METHODS/STUDY POPULATION** Matched health and community programs ($n$ = 93) in 2 communities randomized to CEP or RS. Measurements: baseline, 6 and 12-month self-reported, client MHRQL, and cost measures. Enrolled adults ($n$ = 1,013) with depressive symptoms on 8-item Patient Health Questionnaire-≥10: 85% minority. Interventions: CEP and RS to implement depression QI. Primary outcomes: 12-item Mental Composite Score (MCS-12)≤40 or poor MHRQL at 6 and 12-months; Secondary outcomes were behavioral hospital nights; RS&CEP implementation & service-use costs over 12-months. **RESULTS/ANTICIPATED RESULTS** There was no significant difference in clients' with poor MHRQL (MCS-12≤40: RS 50.5%, CEP 44.8%, $p$ = 0.113) at 12-months, but CEP improved MHRQL in ≥1 follow-ups (6 or 12-month, MCS-12>40, RS 70.1%, CEP 77.3%, $p$ = 0.006). Path analysis suggested CEP had an indirect association with 12-month MHRQL through MHRQL at 6-months ($p$ = 0.039). CEP decreased the percentage with any behavioral hospital nights over 12-months (RS 13.4%, CEP 8.4%, $p$ = 0.024). CEP implementation costs were higher with no significant differences in 12-month service-use costs. **DISCUSSION/SIGNIFICANCE OF IMPACT** Compared with RS, CEP had more clients with improved MHRQL at 6 or 12-months and had higher implementation but similar service-use costs.

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### SCIENCE CAFÉS: ENGAGING SCIENTISTS AND COMMUNITY THROUGH HEALTH AND SCIENCE DIALOGUE

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**OBJECTIVES/SPECIFIC AIMS** Engagement of the community through informal dialogue with researchers and physicians around health and science topics is an important avenue to build understanding and affect health and science literacy. Science Cafés are one model for this casual interchange; however the impact of this approach remains under researched. **METHODS/STUDY POPULATION** The Community Engagement Key Function of the Clinical and Translational Science Institute of Southeast Wisconsin hosted a series of Science Cafés in which topics were collaboratively decided upon by input from the community. Topics ranged from Personalized Medicine to Alzheimer's and Dementia to BioMedical Innovation. **RESULTS/ANTICIPATED RESULTS** A systematic evaluation of the impact of Science Cafés on attendees' self-confidence related to five health and scientific literacy concepts showed statistically significant increases across all items (Mean differences between mean retrospective prescores and postscores, one tailed, paired samples t-test, $n$ = 141, $p$ < 0.0001 for all items). The internal consistency of the five health and scientific literacy items was excellent ($n$ = 126, α = 0.87). Thematic analysis of attendees' comments provides more nuance about positive experience and suggestions for possible improvements. **DISCUSSION/SIGNIFICANCE OF IMPACT** The evaluation provides important evidence supporting the effectiveness of brief, casual dialogue as a way to increase the public's self-rated confidence in health and science topics.

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### EDUCATING TRANSLATIONAL RESEARCHERS USING DISTANCE EDUCATION

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**OBJECTIVES/SPECIFIC AIMS** The recent IOM report of the CTSA program emphasized the need for flexible, online training of translational researchers. Launched in May 2010, The George Washington University's School of Medicine and Health Sciences Graduate Program in Clinical and Translational Research (CTR) is unique in that it is offered completely online, facilitating greater participation by students with demanding clinical, teaching, and research responsibilities. **METHODS/STUDY POPULATION** Using innovative teaching methods, the program is designed to build collaborative skills while allowing flexibility to participate asynchronously and on a part-time schedule. The rigorous curriculum is aligned with the CTR Core Competencies. Students create an individualized program of study through electives

and independent study coursework. Use of faculty-led, interactive online discussion boards, group and individual projects, and other collaborative tools simulate today's distributed teams. **RESULTS/ANTICIPATED RESULTS** 51 students from a variety of disciplines have enrolled in the program, and 13 have graduated. Self-efficacy in research skills, as measured by Clinical Research Appraisal Inventory (CRAI), shows an increase across all areas. Feedback from students, graduates and their mentors is positive. **DISCUSSION/SIGNIFICANCE OF IMPACT** The CTR Program illustrates an effective use of distance education in the training of clinical and translational researchers. Due to its asynchronous online format, the program (1) has a global outreach, attracting researchers across geographical boundaries, (2) provides flexibility to accommodate the demanding schedules of clinicians and other researchers, while maintaining a rigorous program of study, and (3) emphasizes the team science and leadership skills referenced as areas of desired interest by the IOM.

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### AN ETHICAL FRAMEWORK FOR DISCLOSING INDIVIDUAL GENETIC FINDINGS TO PATIENT OR RESEARCH PARTICIPANT'S RELATIVES

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**OBJECTIVES/SPECIFIC AIMS** The translational science enterprise has imbued the research community with an urgent drive for discovery and the application of cutting-edge findings towards clinical effectiveness and societal benefit. The need for policies that prudently leverage the vast amount of potentially clinically relevant data is ever increasing as we acquire a better understanding of the genetic determinants of disease. Screening for genetic markers holds the potential to not only better treat and care for our patients, but may also impact the lives of many others at risk for chronic diseases. **METHODS/STUDY POPULATION** Much prior work has focused on disclosing actionable genetic findings to research participants and to some extent, relatives of a deceased participant. A framework for disclosing actionable genetic findings to the relatives of living patient and/or research participant has been less examined. Respecting the values and honoring the dignity of the patient/participant can be harmonized with the disclosure of findings to other stakeholders who have a medical interest in that information. **RESULTS/ANTICIPATED RESULTS** Here we develop guidance for actionable genetic information disclosure to relatives that balance providing important, clinically relevant findings while mitigating overreporting that may confound health care decisions or result in individual harms. Key points for the framework include scientific validity, clinical utility, informed consent, authorization, a centralized notification service and genetic counseling. **DISCUSSION/SIGNIFICANCE OF IMPACT** The information disclosed should be limited and actionable with appropriate safeguards along with administrative oversight to protect individual rights and maximize benefit. We have developed a comprehensive framework that will impact the health of clinical research participants, patients and communities.

## RESEARCH PROFESSIONALS ABSTRACTS

### T0: BASIC SCIENTIFIC DISCOVERY

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### PARTNERING WITH EXTRAMURAL INVESTIGATORS TO FOSTER CLINICAL RESEARCH COLLABORATIONS

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**OBJECTIVES/SPECIFIC AIMS** For 60 years, the Clinical Center (CC) has served as a model institution for transforming scientific advances into innovative clinical therapies for a wide range of patients. Following a 2010 report by the Congressionally established NIH Scientific Management Review Board to make Clinical Center resources more widely available to the extramural community, a new NIH grant was created, "Opportunities for Collaborative Research at the NIH Clinical Center (U01)." In 2013, 12 NIH institutes launched the pilot of this competitive funding program to solicit interest. The new grant required an extramural applicant who served as the PI on the grant to partner with at least one NIH intramural investigator co-PI. Some of the clinical project had to utilize CC resources. Proposals had to align with the research priorities of one of the 12 supporting Institutes. A total of 74 letters of intent were submitted with 51 grant applications received. **METHODS/STUDY POPULATION** NA **RESULTS/ANTICIPATED RESULTS** NA **DISCUSSION/SIGNIFICANCE OF IMPACT** Lessons learned from the pilot included (1) interest in additional NIH institutes participating as sponsors; (2) more details than provided by conventional letters of intent for enough information to make support decisions for individual projects prior to grant submission, and (3) enhanced communications with intramural and extramural investigators. Potential investigators required assistance regarding identifying intramural partners and budget development for Clinical Center and intramural research costs. Program enhancements for the second cycle addressed these needs and included three new institute sponsors for the 2014 cycle, the implementation of a new XO2 preapplication process to facilitate the letters of support from the institutes, and creation of a new CC Website designed to facilitate communication between investigators.

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### ROLE OF ANGIOTENSIN AND NITRIC OXIDE IN INSULIN RESISTANCE OF OBESITY

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**OBJECTIVES/SPECIFIC AIMS** Regulation of insulin secretion by pancreas and its effects on skeletal muscle and fat by nitric oxide (NO) was previously published. Many clinical and mechanistic studies suggest that angiotensin II (AII) inhibition improved insulin sensitivity. We have published recently the complex interactions of AII and NO. In this study we examined the role of AII and NO in insulin resistance of obesity. **METHODS/STUDY POPULATION** Obese ZSF rats, previously characterized in our laboratory were used as a model of insulin resistance. Lean ZSF rats were used as controls. ZSF rats from 8th week were fed high calorie diet to maintain hyperglycemia while lean rats were fed standard diet. All rats were sacrificed at 26th week and blood and urine collected and skeletal muscle harvested for cell cultures and homogenates for protein expression. In addition hamster pancreatic β cells in culture were examined for insulin secretion using ELISA assay with or without angiotensin blockers. **RESULTS/ANTICIPATED RESULTS** Our studies indicated that high glucose-mediated and not basal insulin release was regulated by NO. Angiotensin converting enzyme inhibitors (ACEi) and receptor blockers (ARB) increased insulin secretion rate [18 ± 4 vs. 7 ± 2 ng/ml $p < 0.01$] from islet β cells and also increased glucose uptake in a time dependent fashion and both these effects were blocked by NO inhibitors. Furthermore, our studies showed increased IRS-1 phospho-serine compared to phospho-tyrosine in the rat muscle of ZSF rats vs. lean (79% vs. 5% of total IRS-1), which was decreased by ARB (68%). Angiotensin inhibition also increased the free fatty acid levels and improved insulin signaling by increasing adiponectin and NO levels in obese rats. **DISCUSSION/SIGNIFICANCE OF IMPACT** These data indicate that insulin secretion as well insulin resistance is modulated by NO and AII both in basal state and in obesity induced insulin resistance.

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### A VESICULAR SEQUESTRATION-TO-OXIDATIVE DEAMINATION SHIFT IN PARKINSON DISEASE

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**OBJECTIVES/SPECIFIC AIMS** Profound putamen dopamine (DA) depletion is a neurochemical hallmark of Parkinson disease (PD). A shift from vesicular sequestration to enzymatic oxidative deamination of cytosolic DA contributes to the low putamen DA content. An analogous sequestration-to-deamination shift might occur in myocardial sympathetic nerves in PD. If so, then tissue contents of the deaminated metabolites 3,4-dihydroxyphenylglycol (DHPG) and 3,4-dihydroxyphenylacetic acid (DOPAC) would be elevated relative to those of the parent catecholamines. **METHODS/STUDY POPULATION** We measured levels of NE, DA, DHPG, and DOPAC in apical myocardial tissue from 23 PD patients and 23 controls. Data from mice with very low activity of the type 2 vesicular monoamine transporter validated the neurochemical approach. **RESULTS/ANTICIPATED RESULTS** Myocardial NE, DA, and DHPG were decreased in PD ($p < 0.0001$ each), whereas DOPAC was not. Among 16 patients with severe NE depletion (2.0% of control), DHPG:NE averaged 11.2, DOPAC:DA 27.5, and DOPAC:NE 163 times control ($p < 0.0001$ each). Vesicular storage in residual nerves was estimated to be decreased by 73–91% in this subgroup. **DISCUSSION/SIGNIFICANCE OF IMPACT** Most PD patients have severe myocardial NE depletion, which is associated with markedly decreased vesicular storage in the residual nerves. A vesicular sequestration-to-oxidative deamination shift may be part of the death process in catecholamine neurons in PD.

### T1: TRANSLATION TO HUMANS

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### DIVERGENT GENOME WIDE TRANSCRIPTIONAL PROFILES FROM IMMUNE CELL SUBSETS ISOLATED FROM LUPUS PATIENTS WITH DIFFERENT ANCESTRAL BACKGROUNDS

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**OBJECTIVES/SPECIFIC AIMS** Systemic lupus erythematosus (SLE) is a complex multisystem autoimmune disease of uncertain etiology. Patients from different ancestral backgrounds demonstrate differences in clinical manifestations and autoantibody profiles. In this study we examined genome-wide transcriptional patterns in major immune cell subsets across different ancestral backgrounds. **METHODS/STUDY POPULATION** Peripheral blood was collected from 21 African American (AA) and 21 European American (EA) SLE patients, 5 AA controls, and 5 EA controls. CD4+ T-cells, CD8+ T-cells, monocytes and B cells were purified by flow sorting. Each cell subset from each subject was run on an Illumina gene expression array ($n = 208$ arrays). Differentially expressed genes (DEGs) were determined by comparing cases and controls of the same ancestral background. **RESULTS/ANTICIPATED RESULTS** The overlap in DEG lists between different cell types from the same ancestral background was very modest (<1%). Typically between 5–10% of DEGs were shared when comparing the same cell type between different ancestral backgrounds (for ex., CD20 AA vs. CD20 EA). Quantitative measurement of global IFN-stimulated gene (ISG) expression revealed that AA subjects demonstrated more concordance across all studied cell types than EA patients. One subgroup of patients showed higher ISGs expression in all cell types, and the other subgroup had higher ISG expression only in T and B lymphocytes. **DISCUSSION/SIGNIFICANCE OF IMPACT** We find striking differences in gene expression between different immune cell subsets and between ancestral backgrounds in SLE patients. The IFN signature is diverse, with different transcripts represented in different cell populations, and signature-positive cell subsets differed in EA vs. AA patients.

## T2: TRANSLATION TO PATIENTS

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### SEVEN DEADLY SINS: BIAS IN COMPARATIVE EFFECTIVENESS RESEARCH

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**OBJECTIVES/SPECIFIC AIMS** The prohibitive expense of randomized clinical trials and the relentless explosion of novel biomarkers fuel the popular campaign to exploit big data and electronic health records in comparative effectiveness research. Despite the advances in information and medical technologies and in research design and statistical analysis, generating valid and reproducible findings from data streaming through fire hoses remains a challenge. Research methods must account not only for patient heterogeneity but also for the timing of dynamic treatment regimens and complex sequence of short- and long-term outcomes. **METHODS/STUDY POPULATION** Drawing on recent experience in the design, data collection and analysis of studies comparing varying massive transfusion protocols for trauma resuscitation, the PRospective Observational Multicenter Major Trauma Transfusion Study (PROMMTT) and the Pragmatic Randomized Optimum Plasma and Platelet Ratios Trial (PROPPR), we describe seven common, sometimes overlapping biases through examples and resolution strategies.The list includes (1) indication bias, (2) survival bias, (3) time-varying treatment, (4) time-dependent confounding, (5) time-varying intervention effects, (6) nonrandom missing data mechanisms and (7) collider bias. **RESULTS/ANTICIPATED RESULTS** Causal diagramming and appropriate data selection and analysis plans are illustrated to help investigators avoid pitfalls. False hope for electronic record systems may be an 8th sin. Effective mitigation strategies require diverse clinical, epidemiologic and statistical perspectives and vigilance. **DISCUSSION/SIGNIFICANCE OF IMPACT** Minimizing bias across research settings and specialties can help pave the way for higher impact discoveries and more clinically meaningful translation.

## T3: TRANSLATION TO PRACTICE

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### TRACKING & MONITORING PILOT RESEARCH PROJECTS

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**OBJECTIVES/SPECIFIC AIMS** To address the NIH requirements for collecting key metrics and monitoring effectiveness of internal awards and services in real time, the Indiana Clinical and Translational Sciences Institute (ICTSI) needed to create an efficient reporting system. Building on the strengths of existing software tools, the Indiana CTSI created a simple solution to gathering critical data for reporting. This presentation shares how the ICTSI streamlined reporting processes to obtain real time information, monitor progress of projects, identify and respond to barriers to research, and report the outcomes from PIs awarded pilot funding. **METHODS/STUDY POPULATION** na **RESULTS/ANTICIPATED RESULTS** The creation of an integrated system for data collection from our pilot funding programs was a key concern from the initiation of the CTSA. Over the first 3 –4 years of the ICTSI, a grants management system was built and REDCap became available. Combining these programs with other available software, we created a process that allowed data to be shared across the ICTSI. This Pilot Grant Reporting System includes the grant application, progress reports with key outcomes, and program evaluation surveys. Progress reports can be sent to investigators within minutes and then shared with all managers of the ICTSI programs in real time as they are submitted. So, what once took hours or days to input the data into a usable format for reporting now can be done within minutes. Additionally, because the process is an interweaving of software, each part can be modified as needed by any program or CTSA. **DISCUSSION/SIGNIFICANCE OF IMPACT** Obtaining and extracting data easily allows the ICTSI to monitor progress and success of its funded PIs in order to provide quick intervention if issues develop within any given project. Most importantly, these tools, used as a single system, allow us to provide current information to stakeholders on demand.

## T4: TRANSLATION TO POPULATION

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### DIMENSIONS OF LEADERSHIP IN ONLINE HEALTH COMMUNITIES

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**OBJECTIVES/SPECIFIC AIMS** Examine leadership behaviors in online health communities, and predict when leadership occurs. **METHODS/STUDY POPULATION** In addition to conventional research design methods, social network analysis provides a different way of thinking and measuring processes and outcomes that account for the relationships with others and how those relationships are embedded within the data. Eight diverse health Facebook pages were selected to represent a target population of those people interested in health. A random sample was taken over a six month duration. **RESULTS/ANTICIPATED RESULTS** The study explores leadership in online health and wellness communities. (1) What are the leadership characteristics associated with online leaders in health communities? (2) To what extent do characteristics moderate or enhance online leadership? (3) Can leadership be predicted based on online participation in communities? **DISCUSSION/SIGNIFICANCE OF IMPACT** This contribution of knowledge will enhance the understanding of leadership within healthcare by identifying characteristics that distinguish leaders in an online community by identifying mechanisms that facilitate diffusion in technology-mediated environments. Second, it will demonstrate a mixed method analytical approach to examine user behavior in large-scale complex networks. Third, it creates interdisciplinary bridges for future research by blending research in leadership, social science, psychology, linguistics, communication, consumerism, and healthcare. This will address subsidiary areas, (1) developing a specific linguistic and structural model that can be used to identify leaders in other large-scale networks. (2) improving the design and functionality of online communities to facilitate user engagement such as proactively link potential users with leaders in online communities to assist with motivation and lifestyle change to improve health key indicators.

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### ITHS E-PORTAL LEARNING CENTER: AN ONLINE LEARNING REPOSITORY FOR TRANSLATIONAL HEALTH SCIENCES

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**OBJECTIVES/SPECIFIC AIMS** CTSA programs have widely adopted the use of online repositories of educational content to advance integrated and interdisciplinary education, training, and career development. However, a key challenge is management and integration of online content to ensure its usefulness and impact. The Institute of Translational Health Sciences (ITHS) has an exceptionally rich and extensive library of online offerings for research training and faculty development, thereby providing an excellent opportunity to develop and evaluate a learner-centered educational environment, ITHS E-Portal Learning Center. **METHODS/STUDY POPULATION** Researchers we serve focus on diverse areas—from basic science to clinical trials to outcomes evaluation—and are located across a 5-state region, thereby increasing the challenge of creating comprehensive relevant programming. To address these needs, we developed the ITHS Competency Framework and constructed the ITHS E-Portal. Specifically, we grounded our work in the existing CTSA Core Competencies for Clinical and Translational Research, and developed three ITHS Competency Domains: Research Initiation, Data Analysis and Management, and Professional Regulations and Skills. We used these three domains to classify our existing extensive ITHS online content. In addition, we followed the ADDIE (Analysis, Design, Development, Implementation, Evaluation) instructional design model, to ensure the effectiveness of our online knowledge system. **RESULTS/ANTICIPATED RESULTS** We will describe the process, E-Portal results, and lessons learned. We believe our work exemplifies a best practice of

research training and faculty development within and across organizations, and a model that could be adopted both by CTSAs. **DISCUSSION/SIGNIFICANCE OF IMPACT** na

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### PRISM ONLINE TRAINING: A FREE, CUSTOMIZED, EFFECTIVE PLAIN LANGUAGE TUTORIAL FOR RESEARCHERS

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**OBJECTIVES/SPECIFIC AIMS** Clear communication between researchers and the public is essential for promoting translational science and ensuring that new therapies reach the people who need them. Group Health Research Institute (GHRI) created the Program for Readability In Science & Medicine (PRISM) in 2005 to provide research professionals with effective plain language training and tools to support clear communication with study participants and the public. PRISM's public-domain resources include an online training developed in October 2010 with support from the University of Washington Institute of Translational Health Sciences (see http://tinyurl.com/prismtoolkit). **METHODS/STUDY POPULATION** We collected evaluation data via an optional 10-item survey at the end of the course. Content for the hour-long tutorial covers: (1) background on health literacy; (2) communication challenges in research and links to helpful tools; (3) specific plain language strategies paired with pre-post examples; and (4) interactive editing examples and exercises. **RESULTS/ANTICIPATED RESULTS** After three years, more than 1,000 users from across the U.S. and abroad had registered. Frequent users included: investigators and research staff (36%); health educators (16%); clinicians (10%); IRB administrators or members (8%); and medical writers/editors (7%). Of 396 users who completed the evaluation, the vast majority provided high ratings: 94% said the course was a good use of their time; 94% said they learned strategies they could apply immediately; and 95% said they would recommend the course to others. **DISCUSSION/SIGNIFICANCE OF IMPACT** PRISM Online Training is an effective way to boost the plain language skills of research professionals. Plain language training deserves consideration as a strategy for helping translational researchers communicate more clearly with communities and study participants—helping boost engagement and dissemination efforts.

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### FACTORS THAT FACILITATE OR HINDER TRANSITION TO INDEPENDENCE FOR CLINICAL AND TRANSLATIONAL RESEARCHERS: A QUALITATIVE STUDY

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**OBJECTIVES/SPECIFIC AIMS** To understand the personal, professional, and environmental factors that facilitate or hinder transition from a mentored career development award (NIH K12 or KL2) to independent funding. **METHODS/STUDY POPULATION** Semistructured interviews, based on the Rubio model of physician-scientist career success, with 40 former KL2 or K12 scholars at 9 CTSA institutions. 20 had transitioned to independence; 20 had not, at least 2 years after the end of their last K award. **RESULTS/ANTICIPATED RESULTS** Initial analyses revealed several themes. Institutional and professional factors important for facilitating independent funding included: mentors who were generous with time, advice, networks and resources; protected time for research; and a strong community of researchers in a similar content area or discipline. Personal facilitators included resilience, initiative to steer one's career, autonomy, and building one's research network. Researchers used a growth mindset and self-determination components (competence, relatedness, and autonomy) to overcome hurdles. Lack of any of these factors was a barrier to transitioning. A few participants had challenging personal circumstances that derailed their careers, or found non-research opportunities that better suited their interests and needs. **DISCUSSION/SIGNIFICANCE OF IMPACT** Institutions should focus on training faculty in networking, the growth mindset, and taking initiative, and make sure mentors understand the multifaceted nature of successful mentorship. Chairs should protect junior faculty members' time, and facilitate research autonomy and research communities.

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### IDENTIFYING CORE COMPETENCIES FOR STUDY COORDINATORS WORKING IN CLINICAL & TRANSLATIONAL RESEARCH (CTR) TEAMS

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**OBJECTIVES/SPECIFIC AIMS** Study coordinators (SCs) play a critical role on research teams, however standardized training based on job duties and tasks is lacking. To shape training at the University of Michigan (U-M) using competency-based approaches, the Michigan Institute for Clinical & Health Research (MICHR) sought to define core competencies for SCs engaged in CTR. U-M coordinators have widely diverse CTR roles. The purpose of this activity was to 1) familiarize stakeholders about competencies and competency-based education; 2) build consensus for common competencies rather than adopt existing standards from professional sources. **METHODS/STUDY POPULATION** An advisory group of experienced SCs, research, and compliance specialists from U-M was created to define job responsibilities and tasks of SCs engaged in CTR. Resources were provided (e.g. SoCRA, ADA, NIH Nursing & Patient Care Services, Fundamentals of Clinical Research for the Clinical Research Nurse) to guide creation of U-M specific competencies. Six domains were identified. Subgroups defined competencies in each domain. Drafts were compiled and refined by MICHR staff into competency statements which were further refined by the advisory group. U-M competencies were then mapped to existing competencies from SoCRA to assess scope, emphasis, overlap, and identify potential gaps. **RESULTS/ANTICIPATED RESULTS** 3 of 6 domains included in both U-M and SoCRA competencies were similar. U-M placed more emphasis on protocol development and data management and included new domains for informed consent, recruitment, and U-M system requirements. **DISCUSSION/SIGNIFICANCE OF IMPACT** U-M developed 18 competency statements in 6 domains, similar to but not identical with SoCRA competency statements. Differences reflect institutional perspectives and will be used as a basis for designing competency-based educational curricula for SCs.

# POSTER SESSION TWO

# TL1 AWARDEE PREDOCTORAL ABSTRACTS

## T0: BASIC SCIENTIFIC DISCOVERY

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### THE RELATIONSHIP OF LOSS OF CONSCIOUSNESS ACCOMPANYING HEAD INJURY WITH BRAIN VOLUME AND EXECUTIVE FUNCTIONING IN OIF/OEF VETERANS

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**OBJECTIVES/SPECIFIC AIMS** Traumatic brain injury (TBI) is associated with neuropathophysiological changes resulting in decreased brain volumes across the range of TBI severity. Cognitive changes after injury can be detected by neuropsychological testing and involve domains of memory, attention/concentration, and executive skills. Loss of consciousness (LOC) accompanying head injury predicts atrophy, and repetitive injury has an additive effect on cognitive dysfunction and neuropathological burden. Objectives: to examine the impact of LOC on brain volume and characterize the relationship of brain volume changes postinjury with cognitive functioning. **METHODS/STUDY POPULATION** Participants were 49 military veterans from Iraq or Afghanistan who suffered mild TBI (mTBI) and underwent neuropsychological testing and structural magnetic resonance imaging (MRI) upon return. Controls were 38 age-matched civilians without mTBI who underwent MRI. Veterans were divided into groups based on number of sustained LOC. Brain volumes, normalized for subject head size, were estimated with SIENAX software. **RESULTS/ANTICIPATED RESULTS** Volumetric comparisons using ANCOVA with age as a covariate showed significant differences between the control group and veterans who had sustained mTBI with 1 LOC on peripheral grey matter ($p < .001$) and white matter volumes ($p < .001$). Brain volume and LOC were not related to executive performance. **DISCUSSION/SIGNIFICANCE OF IMPACT** Findings support the relationship of LOC with brain atrophy but suggest that the relationship may be complex and nonlinear, possibly mediated by other factors such as cognitive reserve and injury parameters.

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### THE SMALL MOLECULE DNA METHYLATION INHIBITOR SGI-110 AS AN OVARIAN CANCER CHEMOSENSITIZER

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**OBJECTIVES/SPECIFIC AIMS** Ovarian cancer (OC) progression is associated with accumulation of epigenetic changes leading to transcriptional silencing of tumor suppressor genes. Therapeutic interventions targeting the OC methylome reverse drug resistance and induce clinical responses. Our previous preclinical evaluation demonstrated that SGI-110 (Astex Pharmaceuticals), an analogue of decitabine, resensitized platinum-resistant OC cell lines to cisplatin (CDDP) and reduced the CDDP IC50 in the A2780 OC cell line. SGI-110 treatment induced significant demethylation and subsequent transcriptional derepression of tumor suppressors and differentiation-associated genes in A2780 ovarian cancer cells. **METHODS/STUDY POPULATION** We assessed SGI-110 in combination with CDDP to retard the growth of platinum sensitive or drug resistant human ovarian cancer xenografts. Mice were injected with SGI-110 (2 mg/kg or 5 mg/kg, SQ.) or CDDP (2 mg/kg or 4 mg/kg, IP.) treatment or in combination in a biweekly or QD5 regimen. **RESULTS/ANTICIPATED RESULTS** Significant antitumor activity was observed in the single SGI-110 and SGI-110 + CDDP treatment in both the biweekly and QD5 regimen mice bearing an A2780 OC xenograft. Pyrosequencing analysis of LINE1 was used to reaffirm global demethylation by SGI-110 treatment. SGI-110 treatment resulted in derepression of tumor suppressor genes in tumors. Mass spectrometry was used to analyze the amount of platinum-DNA damage induced by CDDP treatment using mass spectrometry. **DISCUSSION/SIGNIFICANCE OF IMPACT** The results of our preclinical study support our recently activated clinical trial using SGI-110 in combination with carboplatin in patients with recurrent, platinum-resistant OC.

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## INVESTIGATING THE PHENOTYPIC CONSEQUENCES OF DUF1220 COPY NUMBER VARIATION

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**OBJECTIVES/SPECIFIC AIMS** DUF1220 is a protein domain that shows a dramatic human-specific increase in copy number, and is associated with an evolutionary increase in brain size and with brain size in the human population. A major challenge in studying DUF1220 has been acquiring accurate copy number estimates of domain subtypes (clades). The objectives of this study were to acquire accurate DUF1220 domain copy number measurements, identify the normal spectrum of copy number variation in a healthy population and determine the association of copy number with neurodevelopmental and neuropsychiatric phenotypes. **METHODS/STUDY POPULATION** We used droplet digital PCR, a novel method for assaying copy number, to determine DUF1220 clade copy number in control and diseased populations. Brain size was estimated using fronto-occipital head circumference (FOC) z-score. Autism spectrum diagnosis was determined using ADIR and ADOS criteria. Case samples were obtained from Baylor College of Medicine and Rutgers University while control samples were obtained from Rutgers University and the Coriell Institute. All samples were obtained with IRB approval. **RESULTS/ANTICIPATED RESULTS** Controls exhibited a broad copy number range. Multiple phenotype associations with DUF1220 copy number were identified. These include a novel association with autism severity and confirmation of an association with brain size. **DISCUSSION/SIGNIFICANCE OF IMPACT** These findings further elucidate the role of a complex gene family in neuropsychiatric and neurodevelopmental disease. These data also highlight the relevance of this gene family to autism severity and suggest an integral role in neurodevelopment. Future research will continue to determine the association between DUF1220 copy number and neurocognitive function and dysfunction.

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## RECOMBINANT MELITTIN PROTEIN THERAPY FOR TREATMENT OF HIGH GRADE ASTROCYTOMA

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**OBJECTIVES/SPECIFIC AIMS** Grade IV astrocytoma, or glioblastoma, is among the most feared diagnosis in medicine. Melittin is a cell lytic peptide that has shown promise in glioblastoma treatment. Protein therapeutics are prone to aggregation and degradation: both processes leading to inactivation of the molecule. Hydrogels have shown promise in protecting proteins, but modes of reversible protein attachment to hydrogels are lacking. We sought to (1) build a novel protein anchor using the natural affinity of glutathione s-transferase (GST) to its cofactor, glutathione (GSH); (2) examine the ability of this anchor to immobilize proteins in physiological environments; (3) test whether protein maintains activity while it is immobilized, and after it is released. **RESULTS/ANTICIPATED RESULTS** GSH fused to the green fluorescent protein (GFP), or melittin, could be attached to poly (ethylene-glycol) diacrylate (PEGDA)-GSH. A thrombin cleavage site between the GST and the fused therapeutic protein served as a proteolytic releasing factor, and at physiologic levels of thrombin, GFP or melittin was released in a short time frame (< 1 hour). GST-melittin induced significantly lower cell death in U118 MG than GST-melittin + active thrombin. Thrombin-mediated melittin release from a small number of PEGDA-GSH microspheres induced morphologic changes in U118 MG cancer cells. **DISCUSSION/SIGNIFICANCE OF IMPACT** GSH can be conjugated to many polymers already being used as platforms for drug delivery. Due to this ease of creation, and the already high numbers of therapeutic proteins being purified with GST fusion anchors, we believe the GST/GSH anchor to be a promising component of future protein delivery systems.

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## JAK/STAT INHIBITION TO PREVENT POSTTRAUMATIC EPILEPTOGENESIS

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**OBJECTIVES/SPECIFIC AIMS** Numerous studies have suggested that traumatic brain injury (TBI) significantly increases the chance of developing epilepsy. Inhibitory neurotransmission is altered in patients with epilepsy. This alteration has been correlated with a decrease in the expression of the GABAAR α1 gene (Gabra1). The JaK/STAT pathway has been shown in other models of epilepsy to drive a decrease in transcription of Gabra1. This study investigated whether the JaK/STAT pathway is activated and if there were any alterations in GABAAR levels after a TBI. **METHODS/STUDY POPULATION** TBI was performed on mice with and without the JaK/STAT inhibitor (WP1066). The mice were allowed to recover and their hippocampi were collected at 6, 24, 48, 72 hrs, 1 and 16 weeks after injury. Protein and mRNA levels for the GABAAR and JaK/STAT proteins were analyzed at the above time points. Animals were also EEG monitored from 10–16 weeks to determine if a TBI caused seizures. **RESULTS/ANTICIPATED RESULTS** We found that the JaK/STAT pathway is activated as early as 6 hr after TBI and activation continues 72 hrs postinjury. Also, we were able to inhibit the JaK/STAT pathway activation 6, 24 and 48 hrs after injury by using WP1066. We found that the α1 subunit of the GABAA receptor was decreased 48, 72 hrs, 1 and 16 weeks postinjury and that this decreased was prevented with administration of WP1066. We were also able to generate epileptic mice 10 weeks after TBI. **DISCUSSION/SIGNIFICANCE OF IMPACT** The activation of the JaK/STAT pathway may contribute to the altered levels of the α1 subunit of the GABAA receptors and may contribute to the development of epilepsy after a TBI. Future studies will determine if blocking this pathway with WP1066 alters the development of epilepsy after experimental TBI.

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## LEFT ATRIAL REMODELING IN HEART FAILURE WITH PRESERVED EJECTION FRACTION

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**OBJECTIVES/SPECIFIC AIMS** Left atrial (LA) dilatation is common in patients with heart failure and preserved ejection fraction (HFpEF), however little further is known about LA structural remodeling or phasic function. Our objective was to define alterations in LA structure and function in a large animal model of HFpEF. **METHODS/STUDY POPULATION** We studied 9 elderly male and female mongrel dogs subject to bilateral renal wrapping and aldosterone administration (HFpEF group) and 10 young dogs undergoing sham surgery (controls). LV and LA volumes and function were assessed by echocardiography and cardiac magnetic resonance imaging. LV and LA pressure volume relationships (PVR, admittance catheter) were recorded 8 weeks postsurgery and tissue sections were obtained for histological analyses (fibrosis and cell size). **RESULTS/ANTICIPATED RESULTS** HFpEF dogs displayed elevated blood pressure and concentric LV remodeling. LA maximal, minimal, and reservoir volumes were greater in HFpEF than controls. LA stroke volume and active emptying fraction were higher while the proportional contribution of LA conduit function to LV stroke volume was reduced. Hemodynamic evaluation confirmed an increase in LA contractility and altered LA-LV coupling. The end-diastolic PVR was steeper in HFpEF and diastolic capacitance reduced at high LA pressure, but greater at low LA pressure. LA autopsy mass was increased and cardiomyocyte cross-sectional area greater in HFpEF. LV fibrosis was similar between HFpEF and controls however LA fibrosis was significantly reduced in HFpEF. **DISCUSSION/SIGNIFICANCE OF IMPACT** This model of HFpEF is characterized by LA hypertrophy, dilatation and increased contractility indicating greater reliance on atrial function to maintain cardiac output at rest. Our results also demonstrate decreased LA compliance and suggest less efficient atrial compensation may occur at higher filling pressures.

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## HOST PROTEOME CHANGES FOLLOWING INFECTION WITH THE LANGAT VIRUS: IDENTIFICATION OF NOVEL TARGETS FOR TICK-BORNE FLAVIVIRUS CONTROL

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**OBJECTIVES/SPECIFIC AIMS** Tick-borne flaviviruses (TBFs), including the neglected Powassan/deer tick virus located in North America, are a complex of +ssRNA strand arboviruses transmitted by ticks that cause encephalitis and hemorrhagic fever, leading to mortality and morbidity in human hosts. Limited treatments exist to prevent flavivirus transmission, which occurs worldwide. Our overall goal is to identify host proteins essential for flaviviral infection. **METHODS/STUDY POPULATION** Langat virus (LGTV) is a mildly virulent biosafety level 2 TBF traditionally used for TBF studies. The annotated genome (available at VectorBase.org) of the model tick vector, *Ixodes scapularis*, was released in 2008, allowing for more in depth post-genomic analyses of this tick vector. A tick embryonic cell line, *I. scapularis* ISE6, has been developed to study pathogen-host interactions. **RESULTS/ANTICIPATED RESULTS** We have characterized LGTV growth in ISE6 cells, developed a LGTV-ISE6 proteomic screen to identify candidate host proteins, completed KEGG (genome.jp/kegg) pathway analyses along with Gene Ontology function/InterPro domain analyses, completed cell viability/growth analyses, and completed functional compound assays to determine candidate proteins essential for virus replication. Currently, energy-associated and glutamate metabolic enzymes are being evaluated to show "proof of concept" in functional studies. Specific RNA interference and targeted proteomic studies are also underway. **DISCUSSION/SIGNIFICANCE OF IMPACT** By focusing on certain host protein targets or their pathways, development of small compounds against these targets or possibly anti-tick vaccines is our long term goal to reduce virus transmission.

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## MOLECULAR DETERMINANTS OF BRAF FUSION DRUG RESPONSE

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**OBJECTIVES/SPECIFIC AIMS** In this study, we characterize protein-protein interactions and posttranslational modifications that underlie BRAF fusion oncogenic signaling and susceptibility to pharmacological targeting. **METHODS/STUDY POPULATION** Our group and others have recently described BRAF fusion genes as activating components of the MAPK pathway in up to 80% of pediatric low grade gliomas. We established cell-based model systems expressing frequently occurring KIAA1549-BRAF fusions and FAM131B-BRAF fusion genes in order to examine their associated signaling and potential therapeutic targeting utilizing a combination of mutagenesis and phenotypic assays. **RESULTS/ANTICIPATED RESULTS** Our results demonstrate the role of BRAF-fusion phosphorylation in determining paradoxical activation and sensitivity to targeted small molecule inhibitors. **DISCUSSION/SIGNIFICANCE OF IMPACT** While cells expressing BRAF fusions display resistance and MAPK activation in response to approved small molecule inhibitors, second generation BRAF inhibitors overcome phosphorylation-dependent feedback dysregulation to successfully attenuate BRAF-fusion signaling.

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## IDENTIFICATION OF ER-ALPHA BINDING PROTEINS IN TAMOXIFEN-RESISTANT BREAST CANCER CELL LINES

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**OBJECTIVES/SPECIFIC AIMS** Estrogen receptor-α-positive (ERα+) breast cancer accounts for 70% of breast cancers diagnosed in the US. These tumors rely on estrogen signaling for sustenance of growth and therapeutic agents such as tamoxifen (TAM) have been designed to take advantage of this dependence. However, 40% of patients who receive TAM eventually develop resistance. The biological functions of ERα are mediated through interactions with coregulatory proteins; therefore, we aim to characterize the network of proteins that interact with ERα in the scenario of TAM resistance to identify novel, druggable targets to restore the sensitivity of ERα+ breast tumors to TAM. **METHODS/STUDY POPULATION** The network of ERα binding proteins will be identified using human breast cancer cell lines (MCF-7, MCF-7-T and T-47-D). These cell lines are intrinsically sensitive to TAM and TAM-resistant derivatives of each cell line are being generated. To stringently identify ERα binding proteins, we will perform tandem affinity purification of a triple-tagged ERα protein that is stably expressed in both TAM-sensitive (parental) and TAM-resistant (derivative) breast cancer cell lines. **RESULTS/ANTICIPATED RESULTS** We have developed the purification scheme and generated the model system comprised of TAM-sensitive and TAM-resistant cell lines. The initial characterization of TAM-resistant cells revealed increased proliferation, decreased ERα protein expression and decreased sensitivity to TAM treatment when compared to TAM-sensitive counterparts. **DISCUSSION/SIGNIFICANCE OF IMPACT** The successful completion of this research has the potential to impact treatment of ERα+ breast cancer in two ways: first, these proteins may be measured at the time of breast cancer diagnosis to identify patients who may be resistant to TAM treatment; or second, these proteins may be targeted by other drugs in combination with TAM to restore TAM efficacy.

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## AUTOPHAGY INHIBITION IN GLIOBLASTOMA ENHANCES TYROSINE KINASE INHIBITOR EFFICACY

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**OBJECTIVES/SPECIFIC AIMS** Glioblastoma (GBM) is the most common central nervous system tumor and patients have an average survival time of 12–14 months with standard treatment. GBM therapy is ineffective and new therapies need to be explored. Receptor tyrosine kinases (RTK) are under investigation as potential targets in treatment for GBM, including the TAM (Tyro-3, Axl, MerTK) family that is found to be upregulated in 95% of patients. Unfortunately, singular therapy RTK inhibitors have been shown to be ineffectual. Recent evidence has shown increased autophagy during RTK inhibition and chemotherapy is cytoprotective. Combination therapy of autophagy inhibitors and TAM inhibitors could prove to be an effective GBM therapy. **METHODS/STUDY POPULATION** Glioma cell lines, adult and pediatric, were transduced with GFP-mCherry-LC3 for detection of autophagy via flow cytometry. These lines were transduced with shRNA against MerTK and Axl or treated with tyrosine kinase inhibitor (TKI) and cell number and viability were determined by trypan blue exclusion. **RESULTS/ANTICIPATED RESULTS** MerTK, specifically, is increased under DNA damage conditions, such as radiation, a standard treatment of GBM. TAM inhibition by shRNA or TKI in glioma cells reduced viability and increased autophagy levels. Combined TAM inhibition and standard therapeutics of GBM increased autophagy compared to individual manipulation. Subsequently, when autophagy is inhibited alongside TAM inhibition, cell counts are reduced and viability is decreased compared to individual treatments. **DISCUSSION/SIGNIFICANCE OF IMPACT** These *in vitro* data suggest inhibiting autophagy and TAMs concomitantly could provide an effective treatment for GBM.

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## URINARY IRON EXCRETION: NOVEL MECHANISMS TO REDUCE BODY IRON STORES

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**OBJECTIVES/SPECIFIC AIMS** Chelation is the only current treatment for iron overloading in transfusion dependent diseases, such as sickle cell disease (SCD), β-thalassemia major, or myelodysplastic syndromes. The cost of Medicare-billed hospital admission for SCD patients was $9,828–$50,852 per patient per year with 42% of the cost attributed to chelation. High cost of treatment, decreased quality of life and side effects of chelation cause poor compliance to therapy and increased morbidity. The development of therapies that utilize novel mechanisms to clear iron from the body is critical to treat iron overload. The flaky-skin anemia (fsn) mouse has the unique ability to excrete iron through its urine. The fsn mouse and an allelic mutant, hea, possess a mutation in the Ttc7 gene. We hypothesize these mutations in fsn and hea mice result in decreased transferrin bound iron reabsorption in the kidney, resulting in elevated iron excretion in the urine. **METHODS/STUDY POPULATION** We utilized fsn, hea, and wild-type (WT) kidney cells to compare relative mRNA levels using quantitative real-time PCR (qRT-PCR). Flow cytometry was used to measure transferrin bound iron uptake in fsn, hea, and WT kidney cells. **RESULTS/ANTICIPATED RESULTS** Preliminary qRT-PCR data indicates a 60% decrease in Steap3 mRNA in 5 day old hea kidney compared to WT. Interestingly, fsn mice at 5 days show no significant difference in mRNA compared to WT. However, adult fsn mice (~5 weeks) show lower Steap3 mRNA by northern blot. Ongoing experiments are being performed in 5 day old kidneys of fsn, hea, and WT mice to demonstrate the role of Steap3 and other iron metabolism genes (TfR1, Dmt1, PIP5K, and Fpn1) in regulating iron reabsorption. **DISCUSSION/SIGNIFICANCE OF IMPACT** Identifying the mechanism of Ttc7 in iron reabsorption will provide targets for therapy to decrease body iron levels in iron overloading.

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## ACYLCARNITINES AND INHERITED DISORDERS OF FATTY ACID OXIDATION: FROM CLINICAL DIAGNOSTICS TO ACTIVE PLAYERS IN DRIVING INFLAMMATION AND MYOPATHY

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**OBJECTIVES/SPECIFIC AIMS** Acylcarnitine patterns in the blood or urine have been used for decades as clinical biomarkers of fatty acid oxidation disorders (FAOD).

These inherited metabolic disorders of fat combustion arise due to deficiencies in enzymes associated with utilization of fatty acids by the mitochondria. Under these conditions of impaired beta-oxidation, fatty acids and metabolic derivatives such as acylcarnitines increase in the bloodstream and tissues, overwhelming the body's ability to utilize them. FAOD patients routinely experience outward symptoms in muscles (myopathy and/or rhabdomyolysis), but the origins of this are not known. Often, patients do not display symptoms until the body experiences an additional stress such as infection/illness, intense exercise, or fasting, conditions of high fatty acid mobilization. **METHODS/STUDY POPULATION** In our present study, we utilize cell-based models and patient samples to examine the correlation between acylcarnitines, inflammation, and indices of myocyte stress. **RESULTS/ANTICIPATED RESULTS** Long-chain acylcarnitine moieties activate cell stress signaling processes in muscle and immune cells. **DISCUSSION/SIGNIFICANCE OF IMPACT** These metabolites may contribute to the pathophysiology seen in FAOD patients.

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## ADJUVANT CATIONIC NANOLIPOSOMES INDUCE ANTI-CANCER IMMUNITY IN A MURINE MODEL OF BREAST CANCER

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**OBJECTIVES/SPECIFIC AIMS** Nanoparticles, such as liposomes, provide opportunities to present immune modulators as multivalent ligands for enhanced activity. In this study, nanoliposomes containing monophosphoryl lipid A (MPL) and 1,2-dioleoyl-3-trimethylammonium-propane (DOTAP) were created to stimulate a cytotoxic immune response *in vitro* and *in vivo* using a murine breast cancer model. **METHODS/STUDY POPULATION** DOTAP-MPL liposomes were used to treat cultured 4T1 murine breast cancer cells for 24 hours, and cell death was characterized by flow cytometry. Next, bone marrow derived dendritic cells were cultured and treated the nanoliposomes to determine the change to the co-stimulatory surface markers. Finally, immune competent mice bearing 4T1 tumors were treated with nanoliposomes +/– interleukin-12 (IL12). The response was characterized by tumor volume change, bioluminescence, and immunohistochemistry. **RESULTS/ANTICIPATED RESULTS** The cationic nanoliposomal formulation containing MPL and the cationic DOTAP induced anti-tumor activity following intratumoral administration. Addition of recombinant IL12 further suppressed tumor growth and augmented T helper-1 cell (Th-1) polarization, with enhanced tumor infiltration by cytotoxic T cells, dendritic cells, and M1 macrophages, as well as amplification of interferon gamma secretion. Mice bearing dual tumors displayed arrest of tumor growth in both treated and distant tumors. **DISCUSSION/SIGNIFICANCE OF IMPACT** The goal was to create an immune-based therapy against breast cancer, a disease with significant mortality risk in advanced stages. The data clearly demonstrates that adjuvant MPL-liposomes combined with localized IL-12 therapy block tumor growth, stimulate a Th-1 bias of the tumor microenvironment, and induce cancer-specific immune responses.

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## METABOLITE MARKERS OF BRAIN SWELLING IN PEDIATRIC CEREBRAL MALARIA

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**OBJECTIVES/SPECIFIC AIMS** Metabolomic approaches can assess a unique range of chemical signatures, discover biomarkers, and examine host-parasite interactions in the setting of malaria. We have previously identified novel parasite-generated metabolites in the plasma of patients with mild malaria. Here, we aim to enumerate small molecule profiles and explore their role in mechanisms of severe disease. **METHODS/STUDY POPULATION** We conducted an untargeted lipid-phase metabolite analysis of 16 plasma samples from a pediatric cerebral malaria cohort enrolled in the Blantyre Malaria Project (Blantyre, Malawi) from 2009–2013. Consent was obtained and clinical, laboratory and neuroimaging data was collected in accord with IRB-approved protocols. **RESULTS/ANTICIPATED RESULTS** 681 total lipid features were identified in the mass range of 50.0–2000.0 Da and above the threshold of 100 ion counts after normalization of intensities. The 5 markers with the highest median intensity were shown to have a mass-to-charge ratio and retention time of 197.8062@0.3404, 758.5698@5.2697, 195.8095@0.3404, 874.7872@14.8139, and 802.5585@5.2775, respectively. We have identified some unique metabolites, as well as presence of metabolites in the arachidonic acid pathway, which is consistent with published data. **DISCUSSION/SIGNIFICANCE OF IMPACT** We will analyze 60 additional samples with Metabolon, screening samples from a confirmed library of approximately 4,000 targets. Further analysis will be conducted using paired samples of ill and convalescent children ($n = 15$). We will carry out association studies of metabolite profiles with important clinical outcomes such as degree of brain swelling and mortality. This will help identify disease mechanisms and potentially develop biomarkers of severe disease.

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## ACUTE LYMPHOBLASTIC LEUKEMIA CELLS STIMULATE ADIPOCYTE LIPOLYSIS AND UTILIZE ADIPOCYTE-DERIVED FREE-FATTY ACIDS TO PROLIFERATE IN AN *IN VITRO* MODEL

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**OBJECTIVES/SPECIFIC AIMS** Obesity is associated with the development and progression of many cancers, including acute lymphoblastic leukemia (ALL), the most common childhood malignancy. Prior, we have shown that adipocytes interact with and protect ALL cells. Here, we aim to show that ALL cells (1) stimulate adipocyte lipolysis, (2) internalize, and (3) utilize adipocyte-derived free-fatty acids (FFAs) for proliferation. **METHODS/STUDY POPULATION** (1) To test ALL cell stimulation of adipocyte lipolysis, FFA release and adipocyte lipid content were measured following exposure to ALL-conditioned media. (2) To determine ALL uptake of adipocyte-derived FFAs, murine or human ALL cells were co-cultured with BODIPY-FFA laden adipocytes and analyzed by flow cytometry. (3) To determine the localization and utilization of these FFAs, ALL cells incubated with BODIPY-FFA were evaluated by microscopy and thin layer chromatography. ALL cell proliferation and expression of lipogenic enzymes were analyzed after exposure to adipocytes and/or a lipogenesis inhibitor, TOFA. **RESULTS/ANTICIPATED RESULTS** ALL-conditioned media reduced adipocyte lipid content by 16.8 ± 7.1% ($p = 0.047$). ALL cells, co-cultured with BODIPY-labeled adipocytes, accumulated BODIPY-FFAs within membranes and lipid droplets. Adipocyte co-culture reduced, non-significantly, ALL expression of the lipogenic enzyme, ACC1, by 40.3 ± 10.2% ($p = 0.06$, $n = 3$). ALL cell proliferation, inhibited by TOFA ($6.1 \pm 1.1 \times 10^4$ vs. $41.9 \pm 4.7 \times 10^4$ cells, $p = 0.004$, $n = 3$), was rescued by adipocyte conditioned media (ACM, 29.8 ± 9.2 $\times 10^4$, $p = 0.045$ vs. TOFA, $n = 3$). **DISCUSSION/SIGNIFICANCE OF IMPACT** We have shown how adipocytes and ALL cells interact through the provisioning of adipocyte-derived FFAs. This may lead to improved strategies for treating obese pediatric patients with ALL.

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## LRRK2 DEFICIENCY LEADS TO ABNORMAL ACCUMULATION OF BLOOD PRODUCTS AND MACROPHAGES IN THE KIDNEY

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**OBJECTIVES/SPECIFIC AIMS** Therapeutic inhibitors for the leucine-rich repeat kinase 2 gene, LRRK2, are currently under development for the treatment of Parkinson's disease. In rodents, LRRK2 deficiency leads to an adverse kidney phenotype: a striking accumulation of dark pigment in the cortex and medulla associated with defects in autophagy and oxidative stress. Despite these changes there are no signs of kidney dysfunction. We sought to understand the impact of LRRK2 function on kidney physiology and the potential compensatory and/or protective mechanisms prevalent in this rat model. **METHODS/STUDY POPULATION** To evaluate the potential compensatory/protective mechanisms, we explored the role of LRRK2 in cisplatin induced acute kidney injury (AKI). **RESULTS/ANTICIPATED RESULTS** There was a lack of increased susceptibility in KO animals to renal dysfunction following cisplatin induced AKI. The proximal tubule cells (PTCs) that accumulate pigment due to loss of LRRK2 have little or no LRRK2 expression in WT animals compared to the collecting duct that have the highest LRRK2 expression. PTCs become rich with abnormal blood products encompassed in LAMP1 positive vesicles filled with hemoglobin, increased H-ferritin and lipofuscin, causing the extreme pigmentation in the kidney. Cytoprotective factors like HO-1 become strongly induced, providing potential protection for subsequent kidney injury. CD68+macrophages are recruited to PTCs. LRRK2 expression is also high in CD68+macrophages and these cells are responsible for hemoglobin recycling. We found LRRK2 deficiency leads to decreased hemoglobin turnover in these cells. **DISCUSSION/SIGNIFICANCE OF IMPACT** Our data suggest that LRRK2 deficiency in the kidney results in defects in renal cells other than those that normally express LRRK2, probably resultant from altered kidney and macrophage homeostasis.

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## THE FITNESS COST OF FLUOROQUINOLONE RESISTANCE (FQ-R) ON CLINICAL STRAINS OF PSEUDOMONAS AERUGINOSA DIFFERS BY GENOTYPE, AN EXPERIMENTAL *IN VITRO* STUDY

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**OBJECTIVES/SPECIFIC AIMS** FQ-R is highly prevalent among clinical P. aeruginosa strains. We have shown that the more virulent genotype, exoU+, predominates in the

FQ-R population while exoS+ is more common among FQ-susceptible strains. We aim to investigate this observed co-selection of antibiotic resistance and virulence. We hypothesize that FQ-R conferring mutations impose a lower fitness cost on exoU compared to exoS strains, allowing for better adaptation to FQ exposure in the clinical environment. **METHODS/STUDY POPULATION** Isogenic mutants containing a FQ-R-conferring point mutation were created from 3 exoU and 3 exoS clinical isolates. Head-to-head competition experiments were performed to compare fitness of parents vs resistant mutants. Strains were grown in co-culture and colonies of each strain were enumerated every 24 h. Metabolic fitness of the strains was assessed using Phenotype Microarray plates (Biolog) which allowed for comparison of growth on 96 different carbon and nitrogen substrates. **RESULTS/ANTICIPATED RESULTS** The resistance mutation reduced the mean fitness of exoS strains but had minimal effect on exoU strains (average mutant:parent ratios: 1.5 for exoU strains and 0.3 for exoS strains). Growth on carbon substrates was similar among all strains. When growth on nitrogen substrates was compared between mutants vs. parents, reduction in growth was observed on an average of 77/96 compared to 50/96 substrates for exoS and exoU strains, respectively. **DISCUSSION/SIGNIFICANCE OF IMPACT** These results suggest that the acquisition of a FQ-R-conferring mutation imposes a lower fitness cost for exoU vs. exoS strains, which provides a biological explanation for the observed predominance of the virulent exoU genotype in FQ-R subpopulations and supports the hypothesis of co-selection of resistance and virulence.

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### MICROBIOTA TRANSPLANTATION RESTORES NORMAL FECAL BILE ACID COMPOSITION IN RECURRENT CLOSTRIDIUM DIFFICILE INFECTION

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**OBJECTIVES/SPECIFIC AIMS** Fecal microbiota transplantation (FMT) is a highly effective treatment for recurrent *Clostridium difficile* infection (CDI), but the mechanisms of this treatment, where healthy donor fecal material is delivered to the patient's colon, are poorly understood. However, it is known that the physiology of *C. difficile* is heavily impacted by bile acids produced in the liver and modified by colonic bacteria. Some bile acids such as taurocholic acid promote *C. difficile* spore germination, while others such as lithocholic and deoxycholic acid inhibit germination and/or growth of vegetative organisms. To investigate the effects of FMT on fecal bile acid metabolism, we performed targeted bile acid analysis and metabolomics studies, along with analysis of the composition of fecal microbiota, on fecal samples from 12 R-CDI patients treated with FMT. **METHODS/STUDY POPULATION** Fecal samples were collected before and 7–22 days posttransplant, along with donor samples. The V6 region of the bacterial 16S rRNA gene was amplified from these samples, sequenced using Illumina technology, and analyzed using mothur. Metabolites were extracted in 50% acetonitrile and analyzed by UPLC-MS. **RESULTS/ANTICIPATED RESULTS** Following FMT, fecal bacterial communities shifted away from pre-FMT samples and towards to donor samples. Primary bile acids, including taurocholic acid, significantly decreased, while secondary bile acids, including deoxycholic acid and lithocholic acid, significantly increased following FMT. These changes were associated with increases in groups of bacteria known to transform primary to secondary bile acids. **DISCUSSION/SIGNIFICANCE OF IMPACT** These shifts in bile acid composition may represent a move towards an environment unsuitable for *C. difficile* germination and/or growth, and therefore may be a mechanism of FMT.

## T1: TRANSLATION TO HUMANS

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### BMI AND FAT TASTE SENSITIVITY IN HUMANS: IS THERE A LINK?

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**OBJECTIVES/SPECIFIC AIMS** Fatty foods are often highly flavorful and associated with obesity. This has prompted hypotheses of associations between nonesterified fatty acid (NEFA) taste sensitivity and body mass index (BMI) with mixed findings. We hypothesized: (1) there is no association between BMI and NEFA detection threshold sensitivity; (2) high habitual dietary fat intake correlates with decreased NEFA taste sensitivity; and (3) increased hunger correlates with improved NEFA taste sensitivity. **METHODS/STUDY POPULATION** Detection threshold testing of oleic acid (OA) was conducted over 7 visits using a modified staircase procedure with a 2-down, 1-up rule and 5 reversals. The average of the last 4 reversals determined the threshold. Testing ended when 5 reversals had taken place or when the participant had tasted all concentration levels without 5 reversals. 48 subjects completed testing (17 male and 31 female; 8 Asian, 5 Black, 33 Caucasian, 1 Mixed, 1 Unknown); BMI: 18.9–47.2 kg/m$^2$. **RESULTS/ANTICIPATED RESULTS** Hypothesis 1: There is little to suggest that BMI influences baseline sensitivity to oleic acid as no differences in baseline sensitivity were seen between groups. Improvement over time was noted in the lean and overweight-only groups. This likely reflects improved testing performance rather than increased sensitivity. Hypothesis 2: The strength of association between higher fat intake and lower sensitivity was strongest among lean/overweight individuals. This may reflect underreporting by the obese. Hypothesis 3: No consistent pattern of associations between thresholds and hunger were observed. **DISCUSSION/SIGNIFICANCE OF IMPACT** This work documents that humans can taste NEFA. This study also suggests that lean and overweight participants live in the same sensory world when it comes to NEFA taste. Exploration as to why obese participants did not learn over time should be undertaken.

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### MODELING PRESSURE WAVEFORMS OF ESMOLOL AND NICARDIPINE IN A NORMAL AORTA

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**OBJECTIVES/SPECIFIC AIMS** The relationship of hypertension and wall stress on the progression of aortic disease is well established. Pressure waveforms are a good way of comparing the effects of medications to discover which may exert higher wall stress. No analyses have compared the effect of antihypertensive drugs for pressures exerted on the aorta. In this work, we compare the pressure waveforms of two common anti-hypertensive medications against a normal waveform. We also aim to provide a 3D model of an aorta to use in future simulations. **METHODS/STUDY POPULATION** A literature search for trials on normotensive patients given esmolol or nicardipine was performed to identify relevant hemodynamic data. The changes in systolic and diastolic pressure, heart rate and mean arterial pressure were used to calculate the changes in a normal pressure waveform. Dynamic CT-scans were used to create a 3D computational model of an aorta for comparing the effects of these medications. **RESULTS/ANTICIPATED RESULTS** Esmolol exhibited a decrease in systolic, diastolic, pulse pressure, and mean arterial pressure (−19.4, −4.0, −15.4, and −9.1 mmHg) compared with the normal waveform. Nicardipine demonstrated an increase in systolic and pulse pressure (4.0 and 9.0 mmHg) with decreases in diastolic and mean arterial pressure (−5.0 and −2.0 mmHg). A workable 3D model of a normal aorta was created from dynamic CT-scans. **DISCUSSION/SIGNIFICANCE OF IMPACT** In this study, pressure waveforms provided a noninvasive way to look at the effects of medications on the aorta. The results from nicardipine raise concern for complications of enlarging aneurysms or dissection of the aorta since an increase in maximum pressure likely correlates with higher wall stress. In the future, these data can be used in computer simulations to measure the magnitude and find points of maximal wall stress in the aorta.

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### COMPARISON OF THE ORAL AND LUNG MICROBIOTA IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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**OBJECTIVES/SPECIFIC AIMS** We will determine the similarity of the chronic obstructive pulmonary disease (COPD) lung tissue microbiota to other oropharyngeal microbiota. **METHODS/STUDY POPULATION** Twenty patients with COPD undergoing lung lobectomy will have their lung tissue, bronchus, nose, and mouth swabbed in the operating room using sterile technique. Microbiota at each site will be determined by 16S rRNA V3 sequencing using Illumina MiSeq. Diversity indices will be calculated using Mothur and taxa will be identified using RDP Classifier. Principle coordinate analysis will be used to illustrate similarities between each sample. **RESULTS/ANTICIPATED RESULTS** We expect that the lung tissue and bronchial microbiota are similar to the oral microbiota. This will implicate aspiration as a source of the COPD lung microbiota and validate the oral microbiota as a surrogate for the COPD lung microbiota. **DISCUSSION/SIGNIFICANCE OF IMPACT** COPD is the third leading cause of death, but the mechanisms driving its progression are poorly understood. Inflammation in response to the lung microbiota is one potential mechanism. Using bronchoalveolar lavage, we showed that the COPD lung microbiota consists of oral bacteria, either due to aspiration or contamination from the oropharynx. We will determine if oral bacteria are the result of aspiration by determining the similarity of the COPD lung tissue microbiome to other oropharyngeal microbiota. Determination of the true COPD lung microbiota will lay the foundation for further work and may implicate aspiration as a factor in COPD progression. In future studies, the oral microbiota may be used as a readily accessible surrogate for the lung microbiota.

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### INTRAOPERATIVE ELECTROENCEPHALOGRAM SUPPRESSION AND POSTOPERATIVE DELIRIUM

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**OBJECTIVES/SPECIFIC AIMS** Electroencephalogram (EEG) suppression, a phenomenon sometimes seen during deep anesthesia, may place patients at risk for

adverse postoperative outcomes such as delirium. The primary aim of this study was to determine whether patients with longer duration of EEG suppression experience higher rates of postoperative delirium. **METHODS/STUDY POPULATION** Patients undergoing surgery at Barnes-Jewish Hospital with anticipated intensive care unit (ICU) admission were eligible. Duration of EEG suppression was prospectively tracked using one channel of frontal EEG. Delirium was measured twice daily from postoperative day 1 until day 5 or ICU discharge, whichever came first, using the Confusion Assessment Method for the ICU. Logistic regression was used to quantify the association between duration of suppression and incidence of delirium, adjusting for age, sex, American Society of Anesthesiologists physical status, Charlson comorbidity index, sensory impairment, heavy alcohol use, surgery type, opiate dose, blood transfusion, and mean end tidal anesthetic concentration. **RESULTS/ANTICIPATED RESULTS** Overall 175 of 775 patients (26%, 95%CI 23% to 30%) experienced delirium, with a median (interquartile range) of 2 (1 to 3) positive assessments. The logistic regression included 521 patients. Each minute of EEG suppression increased the odds for experiencing delirium (adjusted odds ratio 1.009, 95%CI 1.001 to 1.017). **DISCUSSION/SIGNIFICANCE OF IMPACT** These results suggest that EEG suppression is predictive of postoperative delirium. It would be useful to test if titrating anesthetic drug administration to reduce EEG suppression leads to reduced incidence of delirium.

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## NEURAL RESPONSE TO REWARDS AND ADOLESCENT CANNABIS AND TOBACCO USE: PRELIMINARY FINDINGS FROM A STUDY OF FRN AND EEG SPECTRA

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**OBJECTIVES/SPECIFIC AIMS** Cannabis and tobacco use commonly co-occur in adolescents and co-occurrence may contribute to addiction severity and poor treatment outcomes. Dysfunction in the neural processing of rewards is associated with substance use disorders (SUDs) and developmentally informed models are needed. We aim to examine the relationships between adolescent cannabis and tobacco use and two electrophysiological (EEG) markers of reward processing: the feedback-related negativity (FRN) and theta (4–8 Hz) oscillatory activity. **METHODS/STUDY POPULATION** A cross sectional study design to compare adolescent tobacco users ($n = 50$) stratified by cannabis use status with age and gender matched controls on EEG measures. Dense-array EEG technology, utilizing 128-channel Hydro-cell Geodesic Sensor nets and a reward-feedback task will be used. **RESULTS/ANTICIPATED RESULTS** Presented are preliminary analyses from 12 adolescent smokers and 15 age and gender matched non-smokers. The FRN amplitude, latency, theta power, and inter-trial phase coherence (ITC) between smokers and nonsmokers were examined using repeated measures ANOVAS with Greenhouse Geisser correction. Significant main effects for feedback condition (win, lose, and draw) were seen in FRN amplitude ($F1,26 = 5.48$; $p = 0.008$), FRN latency ($F1,26 = 8.35$; $p = 0.001$), theta power ($F1,25 = 5.22$; $p = 0.015$), and ITC ($F1,25 = 11.22$; $p < 0.001$). However, no main effects for FRN amplitude ($F1,26 = 0.21$; $p = 0.79$), FRN latency ($F1,26 = 0.22$; $p = 0.79$), theta power ($F1,25 = 2.45$; $p = 0.11$), or ITC ($F1,25 = 2.57$; $p = 0.09$) were observed between the adolescent smokers and controls in this preliminary analysis. **DISCUSSION/SIGNIFICANCE OF IMPACT** Improved understanding of reward processing deficits in adolescents with SUDs may help in the development of targeted prevention and intervention strategies.

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## LONGITUDINAL CHARACTERIZATION OF GUT MICROBIOTA IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE

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**OBJECTIVES/SPECIFIC AIMS** We propose a novel pilot study to explore the longitudinal relationship between the fecal microbiome of patients with inflammatory bowel disease (IBD) and its relationship to intestinal inflammation by obtaining repeated stool samples over the course of one year. **METHODS/STUDY POPULATION** Since the commencement of our IRB-approved prospective study in June of 2013, we have collected 96 samples from 22 children (17 CD, 5 UC) with active IBD. We plan to characterize the fecal microbiota through 16S rRNA profiling and sequencing. We will then analyze the microbial profile of each sample and its relationship to fecal calprotectin (a measure of intestinal inflammation) by using enzyme-linked immunosorbent assay (ELISA). We will control for diet, maintenance therapy, prednisone use, antibiotic use, and disease phenotype. **RESULTS/ANTICIPATED RESULTS** Preliminary results will be presented at the 2014 Translational Science Meeting. **DISCUSSION/SIGNIFICANCE OF IMPACT** Over the past decade significant advances in technology have enabled an improved characterization of the vast array of organisms in the intestinal microbiome, yet an understanding of the effect of the microbiome on health and disease is just beginning. Numerous cross-sectional studies have established that individuals diagnosed with IBD have intestinal microbiomes that are significantly altered from their healthy counterparts, suggesting that the microbiome of diseased individuals is intricately involved with the disease pathogenesis. However, little is known about how the intestinal microbiota changes over the course of the disease. This is the first study to explore the microbial changes in IBD patients over the course of their illness. The potential impact of this analysis is far-reaching, as it will not only provide more awareness into the pathogenesis of IBD, but also support future avenues to explore new therapeutic opportunities.

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## CONE PHOTORECEPTOR STRUCTURE IN SUBJECTS WITH INHERITED RETINAL DEGENERATION AT 12 MONTHS IN A RANDOMIZED TRIAL OF SUSTAINED-RELEASE CILIARY NEUROTROPHIC FACTOR

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**OBJECTIVES/SPECIFIC AIMS** No treatments have been shown to slow visual loss in retinitis pigmentosa (RP), an inherited retinal degeneration. The current study uses adaptive optics scanning laser ophthalmoscopy (AOSLO), a high-resolution imaging system, to assess cone survival in subjects with RP participating in a randomized trial of ciliary neurotrophic factor (CNTF). **METHODS/STUDY POPULATION** Eight subjects (16 eyes) with RP were randomized to receive a CNTF implant in one eye and sham surgery in the fellow eye. Visual acuity (VA), visual fields, and full-field electroretinography (ERG) were tested at each visit. Retinal layers were imaged with spectral-domain optical coherence tomography (SD-OCT) and AOSLO. A masked, interim 12-month analysis was performed. Cone spacing data was available for 4 of 8 subjects. **RESULTS/ANTICIPATED RESULTS** Analyzing the 16 eyes together, VA improved slightly (+2.25–3.25 letters, $p = 0.01$), but the area of peripheral visual field seen was significantly lower by 213.9–322.5 total degrees seen ($p < 0.001$) after 12 months. ERG amplitudes and retinal thickness did not differ significantly from baseline. Cone spacing increased slightly for the 4 subjects at 12 months ($p = <0.01$). **DISCUSSION/SIGNIFICANCE OF IMPACT** In this masked assessment of 4 of 8 subjects, cone spacing measures increased over 12 months, consistent with diffuse photoreceptor loss. A future, unmasked analysis may show a decelerated rate of cone loss in CNTF-treated eyes. The results suggest that cone spacing is a sensitive outcome measure of RP progression over 12 months.

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## OPTICAL PARAMETER INFERENCE FOR LASER ABLATION IN BRAIN

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**OBJECTIVES/SPECIFIC AIMS** Postmarket studies are investigating MR-guided laser-induced thermal therapy (MRgLITT) as a neurosurgical treatment. While MRgLITT has powerful real-time guidance of treatment delivery, brain MRgLITT stands to benefit from effective planning to inform physicians' laser fiber placement. Predictive models have been researched but lack reliable physical data, *e.g.,* optical parameters. This abstract explores improving parameter data via machine learning of optical parameter data obtained from prior MRgLITT procedures. **METHODS/STUDY POPULATION** The method has three components: training data, a physics model, and a parameter search algorithm. The training data was MR thermal imaging from 19 MRgLITT oncological brain ablations in 7 patients. The physics model is a Green's function bioheat model for homogenous tissue. The search algorithm is a gradient-based quasi-Newton method and limited to the optical absorption, $\mu_a$. All remaining thermal parameters are assumed constant to demonstrate feasibility. **RESULTS/ANTICIPATED RESULTS** To three significant figures, the descriptive statistics for $\mu_a$ were 2300 $m^{-1}$ mean, 2320 $m^{-1}$ median, 510 $m^{-1}$ st. dev., 1470 $m^{-1}$ min. and 3130 $m^{-1}$ max. The mean-normalized st. dev. was 22.2%. The inverse problem took 27 min. to optimize all 19 datasets. **DISCUSSION/SIGNIFICANCE OF IMPACT** As expected, the recovered mean is biased by modeling approximations of the relatively simple underlying physics model. However, the standard deviation adjusted for mean's bias is smaller than literature values and indicates an increased accuracy in the characterization of parameters relevant to MRgLITT planning. This investigation was designed to run efficiently, but it demonstrates the potential optimization of more sophisticated bioheat models that incorporate the data's uncertainty into the predictions, *e.g.,* stochastic finite element methods.

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## SUBCLINICAL INJURY IN PEDIATRIC RENAL TRANSPLANT PATIENTS: ACE2 AND ANG-(1–7) AS NOVEL BIOMARKERS

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**OBJECTIVES/SPECIFIC AIMS** Develop noninvasive biomarkers of early and chronic subclinical renal graft injury using Ang-(1–7) and ACE2. **METHODS/STUDY POPULATION** Prospective cohort study of children undergoing renal transplantation. The urinary Ang-(1–7), Ang II, ACE2 and ACE will be compared to outcomes of early injury using urine NGAL/creatinine and chronic injury using Cortical Fractional Interstitial Fibrosis Volume on biopsy specimens. Kaplan-Meier statistics, Cox models and frailty models will assess predicting time to outcomes. ROC curves, sensitivity and specificity will assess the clinical predictive value. Donor type and cold ischemia time will be controlled for as confounders. **RESULTS/ANTICIPATED RESULTS** The urinary ratio of Ang-(1–7) to Ang II and of ACE2 to ACE should predict early and chronic graft injury. The ratios will correlate to existing measures of early injury (urine NGAL/creatinine) and chronic injury (Cortical Fractional Interstitial Fibrosis Volume). **DISCUSSION/SIGNIFICANCE OF IMPACT** These are novel potential biomarkers and have not been previously evaluated in this population. The results may enable more prompt diagnosis and more effective treatment. The results may help to better understand how graft injury over time culminates in graft loss. Future studies could evaluate pharmacologic pathway modifiers to prevent or treat graft injury. The goal is to prolong healthy function and survival of transplanted kidneys and improve quality of life.

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## FUNCTIONAL ACTIVITY OF A NOVEL T-CELL RECEPTOR LIKE BI-SPECIFIC ANTIBODY

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**OBJECTIVES/SPECIFIC AIMS** Acute myeloid leukemia (AML) is the most common leukemia in adults. A novel therapy for these patients utilizes the human leukocyte antigen (HLA)-A2 restricted peptide PR1. We have developed a bi-specific T-cell engaging (BiTE) antibody that engages PR1/HLA-A2 on leukemia cells and CD3 on T-cells (h8F4 BiTE), facilitating targeted T-cell therapy against the leukemia. The objective of these studies is to determine if the h8F4 BiTE has activity against AML *in vitro*. **METHODS/STUDY POPULATION** Here we demonstrate successful construction, expression, and purification of the h8F4 BiTE antibody. Flow cytometry tested the binding specificities of each targeting region of the antibody using PR1-pulsed T2 cells, pp65-pulsed T2 cells, wild-type Jurkat cells and CD3-lacking mutant Jurkat cell line J.RT3-T3.5. Flow cytometry investigated T-cell activation after h8F4 BiTE engagement with PR1-pulsed T2 cells and healthy donor PBMC. **RESULTS/ANTICIPATED RESULTS** The h8F4 BiTE antibody showed increased binding to PR1-pulsed T2 cells compared with T2 pulsed with irrelevant CMV peptide pp65. The antibody demonstrated 6.8 fold higher binding to wild-type Jurkat cells compared to the CD3-lacking mutant Jurkat cell line J.RT3-T3.5. Next we show that upon 24h incubation in the presence of h8F4 BiTE and PR1-pulsed T2 cells, both CD4 and CD8 T-cells increase their surface expression of CD69, CD25, CD71 compared to controls. **DISCUSSION/SIGNIFICANCE OF IMPACT** The h8F4 BiTE is novel in that PR1 is an intracellular antigen rather than a conventional surface marker, and these studies will open up possibilities for targeting additional tumor antigens. This novel BiTE antibody will provide a safer and more potent treatment option for patients with aggressive myeloid leukemias that will improve upon currently available highly toxic standard therapies.

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## FROM LEAD CONTAMINATION TO CLEANUP AND BEYOND: SORTING OUT THE DIFFERENCES IN EXPOSURE POTENTIAL AND REALITY FOR USE IN TARGETED PUBLIC HEALTH INTERVENTIONS

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**OBJECTIVES/SPECIFIC AIMS** The fact remains that despite the reduction of lead (Pb) sources in the environment, low income, minority urban children continue to be at higher risk of having elevated blood lead levels (EBLLs) compared to other children due to the persistence of Pb in soil from legacy Pb sources. **METHODS/STUDY POPULATION** This research focuses on two neighborhoods [Martindale-Brightwood (MB) and NearWest] both with former Superfund sites located in the urban center of Marion County, Indianapolis, Indiana to compare spatial soil-Pb distribution and BLLs for children ages 0–5 living in the two separate areas. **RESULTS/ANTICIPATED RESULTS** High resolution sampling and mapping of soil-Pb and BLLs for both neighborhoods reveal discordant regions with some areas exhibiting high soil-Pb yet low BLLs and vice versa. Scanning electron microscopy (SEM) will be used to ascertain Pb speciation of soil-Pb in MB and NearWest and will help determine bioavailability of the high soil-Pb areas (exposure potential). **DISCUSSION/SIGNIFICANCE OF IMPACT** The final stage of research will combine these results along with address level BLL data to determine reasons for differences in exposure reality and assign block level specific public health interventions to reduce future exposures for children.

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## MULTIPARAMETRIC MAGNETIC RESONANCE IMAGING OF THERMOCHEMICAL ABLATION

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**OBJECTIVES/SPECIFIC AIMS** To assess the ability to monitor thermal and chemical changes in tissue during thermochemical ablation (TCA) procedures using fast chemical shift magnetic resonance imaging (MRI). **METHODS/STUDY POPULATION** A TCA injection was performed in *ex vivo* bovine liver by simultaneously injecting 1mL of 10M acetic acid and 1mL of 10M sodium hydroxide through an angiocatheter. The injection was simultaneously monitored by a 2D multigradient recalled echo MRI sequence. Independent temperature measurements were made using a fluoroptic probe adjacent to the catheter. Changes in proton resonance frequency (PRF), T2* relaxation rate, and T1-weighted signal were assessed by applying an autoregressive moving average model to the multigradient echo data. **RESULTS/ANTICIPATED RESULTS** The fluoroptic probe measured a 7.5°C temperature increase from the exothermic acid/base reaction. A two peak model was used on a 2x2 ROI near the catheter tip to measure changes in MRI parameters. A second chemical species was detected during injection with a chemical shift consistent with sodium acetate. A rapid decrease in PRF corresponding to 13.9°C increase in temperature was observed during injection. The spatial distribution of heating was largely heterogeneous and is the likely cause of the discrepancy between the fluoroptic probe and MR derived temperature estimates. During injection, the T1-weighted signal and T2* relaxation rate of the water protons rapidly decreased before slowly returning to their original values during cooling. **DISCUSSION/SIGNIFICANCE OF IMPACT** In this experiment we showed the feasibility of using multiparametric MRI to monitor changes in tissue during TCA. Further research into monitoring these procedures will be critical in evaluating the clinical potential of TCA for tumor ablation procedures.

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## THE INVOLVEMENT OF WNT SIGNALING IN POLYCYSTIC KIDNEY DISEASE

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**OBJECTIVES/SPECIFIC AIMS** Autosomal dominant polycystic kidney disease (ADPKD) causes progressive cysts of the nephron resulting in end stage renal disease (ESRD) during the 5th–7th decade of life. Therapies to safely reduce cyst formation and slow the onset of ESRD are needed. Targeting the Wnt pathway may be a potential therapeutic target to treat PKD. The Wnt signaling pathway plays a key role in the differentiation and proliferation of epithelial cells during development and is upregulated in explanted cystic kidneys. I hypothesize that aberrations in Wnt signaling play a role in cyst initiation and expansion in polycystic kidney disease. **METHODS/STUDY POPULATION** To test this hypothesis, I will (1) determine changes in Wnt signaling, proliferation and Wnt related cellular phenotypes in mouse models of ADPKD and (2) determine if direct interactions between cilia proteins and Wnt pathway proteins regulate Wnt signaling. **RESULTS/ANTICIPATED RESULTS** Preliminary results with a canonical Wnt reporter assay show that overexpression of the PKD disease causing protein, polycystin-1, in HEK cells also transfected with the downstream canonical Wnt pathway protein, β-catenin, has reduced ability to activate the Wnt pathway compared to cells transfected only with β-catenin as well as cells transfected with β-catenin and a loss of function polycystin-1 mutant (E2771K). **DISCUSSION/SIGNIFICANCE OF IMPACT** These results agree with previously published literature that cilia proteins, such as polycystin-1, suppress Wnt signaling and support the hypothesis that Wnt signaling may be upregulated in PKD cells. This study will develop a clear understanding of the regulation of Wnt signaling by ciliary proteins and the protein interactions that mediate these effects in order to establish if modulation of Wnt signaling can ameliorate cyst burden and survival of patients.

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## GENETICS AND MOLECULAR MECHANISMS OF GRAY PLATELET SYNDROME

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**OBJECTIVES/SPECIFIC AIMS** The aim of this project is to study the molecular mechanisms of Gray Platelet Syndrome (GPS), caused by defects in NBEAL2. GPS is a rare autosomal recessive bleeding disorder characterized by thrombocytopenia and mispackaged platelet alpha granules. Little is known about alpha granule biogenesis, and the role of NBEAL2 in this process is not understood. I aim to determine the expression patterns and associated proteins of NBEAL2 to begin to learn more about

this elusive protein. **METHODS/STUDY POPULATION** Relative tissue expression of NBEAL2 was determined by qPCR of a human cDNA library. Cellular localization was determined by immunofluorescence and cellular fractionation in megakaryocytes with a novel antibody to NBEAL2. Associated proteins will be determined by co-IP and mass spectrometry. **RESULTS/ANTICIPATED RESULTS** qPCR showed highest NBEAL2 expression in CD33+ (myeloid lineage) cells. Despite homology with NBEA, a brain specific protein, NBEAL2 expression was low in the brain. Cellular fractionation showed NBEAL2 in the fraction containing small vesicles and the endosomal marker Rab7. Immunofluorescence of NBEAL2 in megakaryocytes showed punctate staining, suggesting a vesicular localization. **DISCUSSION/SIGNIFICANCE OF IMPACT** Many genes involved in platelet biogenesis have been reported, yet the mechanism of alpha granule biogenesis is not known. Alpha granules are improperly packaged in GPS. Understanding the localization and associated proteins of NBEAL2 will help elucidate the mechanism of granule biogenesis. These results suggest a vesicular localization of NBEAL2 which agrees with data that suggests an endosomal origin of alpha granules.

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## METABOLOMIC ANALYSIS FOR DUCHENNE MUSCULAR DYSTROPHY

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**OBJECTIVES/SPECIFIC AIMS** Duchenne muscular dystrophy (DMD) is an X-linked genetic disorder in which the absence of the dystrophin protein causes sarcolemma fragility resulting in incorrect muscle cell physiology and function. Eventually, failed muscle regeneration leads to the progressive loss of ambulation in early teens, and the boys succumb to the disease in the third decade of life. Despite the rapid rate of disease progression, there are few accepted surrogate endpoints and the FDA approved clinical outcome measure lacks sensitivity. As a result, there is a dire need for a biomarker to track disease progression in DMD. **METHODS/STUDY POPULATION** Our approach for biomarker discovery in DMD has been two-fold: (1) analysis of tissues and serum from a mouse model with a single, conserved mutation leading to the lack of dystrophin; and (2) correlating the phenotypical differences observed with DMD subjects to metabolomic measures of urine and serum. In preclinical studies, we compare differences in the muscle (*in vivo*/*ex vivo*) and serum metabolomes of dystrophic mice (mdx) at two stages of the disease. For the clinical study, we determine the urine and serum metabolome from a cohort of 125 DMD boys where their phenotype and rate of disease progression has been determined. **RESULTS/ANTICIPATED RESULTS** Preliminary analysis has revealed metabolomic differences in the mouse model at two stages of the disease. Metabolomic screens of both urine and serum are being correlated with biochemical markers of inflammation and the rate of disease progression. **DISCUSSION/SIGNIFICANCE OF IMPACT** Metabolic profiles and MR properties of dystrophic muscles can be used to characterize different stages of DMD with the potential of becoming a biomarker. Supported in part by the CTSI TL1 TR000066 and UL1 TR000064.

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## ZEBRAFISH AS A TRANSLATIONAL MODEL FOR THE STUDY OF NICOTINE AND ETHANOL USE

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**OBJECTIVES/SPECIFIC AIMS** Cigarette smoking is the single most preventable cause of death and excess healthcare costs in the United States. Treatment challenges can be partially attributed both to the limited efficacy and availability of pharmacotherapeutics, and also to genetic factors. Addressing this healthcare crisis using traditional paradigms of drug development and human genetic studies is costly and protracted, limiting the emergence of new medications and genetically-informed personalized treatment strategies. As an alternative strategy, we developed a translational zebrafish model to address this clinical need. **METHODS/STUDY POPULATION** We leveraged a larval zebrafish behavioral model of nicotine and ethanol response for drug repositioning and forward genetic screening of a catalogue of mutants. **RESULTS/ANTICIPATED RESULTS** We established predictive clinical validity with current medications, varenicline and bupropion. We identified additional clinically available compounds that block the nicotine response including apomorphine, betaxolol, topiramate, zolpidem, three benzodiazepines, and four herbal supplements. Counter evaluation with ethanol-induced locomotor activation, reveals largely stimulus-specific responses. Combination treatment of varenicline and bupropion show increased efficacy over monotherapy, recapitulating the efficacy seen in recent clinical trials, as do apomorphine and topiramate when tested in combination with varenicline, although to a lesser extent than bupropion. The genetic screen has identified genes modulating the responses to nicotine, varenicline, and/or ethanol, and likewise shows largely stimulus-specific responses. **DISCUSSION/SIGNIFICANCE OF IMPACT** The medications and genes identified here are primed for small cost-effective studies for human clinical evaluation such as pilot clinical trials and pharmacogenetic studies.

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## DIFFERENTIATING PANCREATIC CYSTIC NEOPLASMS BY GLOBAL PROTEASE SPECIFICITY

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**OBJECTIVES/SPECIFIC AIMS** Short of pancreas removal, there is no definitive technology that differentiates benign, premalignant and malignant pancreatic cystic neoplasms. As a result, some patients die from undiagnosed cancers, while others undergo unnecessary pancreatic resections with considerable morbidity. We sought to characterize proteolytic signatures of pancreatic cyst fluid specific to different stages of pancreatic carcinogenesis in order to risk stratify lesions. **METHODS/STUDY POPULATION** We used a novel protease substrate profiling technology, Multiplex Substrate-Profiling by Mass Spectrometry (MSP-MS), that can detect and classify endo- and exopeptidases in a complex sample. This assay consists of a diverse library of 228 tetradecapeptides designed by incorporating all combinations of neighbor and near-neighbor amino acid pairs to provide maximum specificity information. We applied this assay to cyst fluid derived from 4 low risk and 4 high risk lesions as determined by current clinical guidelines. **RESULTS/ANTICIPATED RESULTS** The proteases in the samples generated 773 cleavage sites in the low risk category and only 285 in the high risk category. Interestingly, only 220 of the sites were shared between groups. The signature from the low risk group had a trypsin-like specificity with Arginine and Lysine preferred at the P1 position, whereas the high risk group had minimal trypsin-like specificity and predominantly showed amino- and carboxypeptidase activity. **DISCUSSION/SIGNIFICANCE OF IMPACT** These data suggest that protease profiling of pancreatic cyst fluid may facilitate risk stratification of pancreatic cystic lesions and help guide clinical decision making. MSP-MS offers a unique technology to both identify active proteases in clinical samples of interest and measure total and specific proteolytic activity despite the presence of endogenous inhibitors.

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## VANCOMYCIN TOLERANCE AND CLINICAL OUTCOMES IN *STAPHYLOCOCCUS AUREUS* BACTEREMIA

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**OBJECTIVES/SPECIFIC AIMS** To evaluate the relationship between vancomycin (VAN) tolerance and clinical outcomes in patients treated for *Staphylococcus aureus* bacteremia (SAB). **METHODS/STUDY POPULATION** Forty-one clinical *S. aureus* blood isolates were collected from the University of Kansas Hospital. VAN minimum inhibitory concentrations (MIC) and minimum bactericidal concentrations (MBC) were determined by broth microdilution (BMD) according to Clinical and Laboratory Standards Institute (CLSI) recommendations. The MBC was defined as the lowest concentration of VAN with ≥99.9% killing at 24 h. VAN tolerance was defined as an MBC/MIC ≥32. Treatment failure was defined as a composite of 30-day mortality and persisting symptoms of SAB for ≥5 days of treatment. **RESULTS/ANTICIPATED RESULTS** VAN tolerance was observed in 18 (43.9%) of isolates. The majority (66.7%) of VAN tolerant strains were methicillin susceptible *S. aureus* (MSSA). On bivariate analysis, we found a statistically significant difference in treatment failure in those with VAN tolerant isolates (61.1% vs. 26.1%; $p = 0.024$). No cases of elevated VAN MIC (>1 mg/L by BMD) were observed. **DISCUSSION/SIGNIFICANCE OF IMPACT** To our knowledge, this is the first study demonstrating an association between VAN tolerance and treatment failure, regardless of methicillin susceptibility. A recent study by Holmes et al. demonstrated an association between elevated VAN MIC and increased 30-day mortality in patients with SAB; however, elevated VAN MIC was also predictive of mortality in those who received flucloxacillin (a β-lactam) for MSSA SAB. This suggests that elevated VAN MIC may simply be a marker for some pathogen-specific factor that has not yet been elucidated. Our finding that VAN tolerance was associated with treatment failure is consistent with this hypothesis. Further research is needed to determine optimal treatment of VAN tolerant SAB.

# T2: TRANSLATION TO PATIENTS

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## DEVELOPMENT, TESTING, AND REFINING THE FAILURE TO RESCUE SEVERE SEPSIS SURVEILLANCE SYSTEM – "SEPSIS SNIFFER"

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**OBJECTIVES/SPECIFIC AIMS** To develop and test an automated alert algorithm ("sniffer") for the detection of failure to rescue severe sepsis after diagnosis. **METHODS/STUDY POPULATION** Retrospective cross-sectional study using

independent derivation and validation cohorts. We examined all adult first-admissions to the medical ICU at Mayo Clinic in Rochester, MN, from January through March 2013 ($n$ = 587). Algorithm validation was performed against the "gold standard" of manual chart review by two trained reviewers, with one super-reviewer for cases of disagreement. Algorithm development and testing was performed using iterative recursive data partitioning and critical appraisal of false positive and negative alerts. **RESULTS/ANTICIPATED RESULTS** The ability of the first iteration of the severe sepsis sniffer on the derivation cohort to detect severe sepsis and/or septic shock was suboptimal: 59% sensitivity, 97% specificity, 92% Positive Predictive Value, and 83% Negative Predictive Values. Critical appraisal of false positive and negative alerts, along with iterative introduction of new clinical variables into the algorithm was then performed: 82%, 97%, 93%, and 92%. Preliminary testing on the validation cohort validates this optimization approach: 80%, 96%, 92%, and 91%. Recursive data partitioning and validation of the failure to rescue domain are anticipated to further refine the sniffer for eventual implementation in the clinical setting. **DISCUSSION/SIGNIFICANCE OF IMPACT** Sepsis remains one of the most expensive conditions treated in US hospitals, with an aggregated cost of $20 billion per year. As current sepsis alert systems have tested detection performance, but failed to demonstrate improvement in clinically meaningful endpoints, an improved approach is necessary to develop and validate a clinically useful sepsis alert system.

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## ACUTE REDUCTIONS IN DAILY PHYSICAL ACTIVITY NEGATIVELY IMPACTS GLYCEMIC CONTROL WITHOUT CHANGING INSULIN MEDIATED BLOOD FLOW

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**OBJECTIVES/SPECIFIC AIMS** Increases in blood flow (BF) in response to insulin plays a critical role in insulin mediated glucose disposal. 7 days of aerobic exercise in individuals with type 2 diabetes has been shown to increase insulin mediated BF and improve glycemic control (GC). Further, our lab demonstrates that reduced physical activity impairs GC in healthy individuals. The purpose of this study was to determine if an acute transition to reduced physical activity (from >10,000 to <5,000 steps/day) for 5 days (RA5) reduced insulin mediated BF and GC in parallel, and if 1 day return to activity (>10,000 steps/day) (RTA1) restored these outcomes. **METHODS/STUDY POPULATION** We recruited 12 healthy, recreationally active men (Age: 25 ± 1.4yrs, Fat: 19.2 ± 1.0%) to undergo RA5 followed by RTA1. Oral glucose tolerance tests (OGTT) were performed to increase insulin at baseline (BL), RA5, and RTA1. Measures of insulin sensitivity (matsuda index) and insulin mediated femoral artery BF were made during the OGTT. Free living measures of GC were made via continuous glucose monitoring systems for 48 hours prior to BL, RA5, and RTA1. Meals were provided for the duration of the study. **RESULTS/ANTICIPATED RESULTS** BF increased to the OGTT but was not impacted by changes in activity ($p > 0.05$). The matsuda index trended to be decreased by RA5 ($p = 0.1$). GC measures of peak postprandial blood glucose response were significantly elevated to RA5 (BL: 113 ± 3; RA5: 123 ± 5; RTA1: 125 ± 5 mg/dL; $p > 0.05$) and remained elevated during RTA1. CONGA, a measure of blood glucose variability, trended to be elevated by RA5 and remained elevated during RTA1 ($p = 0.09$). **DISCUSSION/SIGNIFICANCE OF IMPACT** Thus, acute reductions in physical activity impaired GC; however insulin mediated BF was not affected. Further, it appears that RTA1 is not sufficient to normalize GC following RA5.

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## EFFECTS OF AEROBIC EXERCISE ON FITNESS AND ASSOCIATED SECONDARY OUTCOMES IN INDIVIDUALS WITH SCI

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**OBJECTIVES/SPECIFIC AIMS** Physical deconditioning and ambulatory impairments are prevalent after incomplete spinal cord injury (iSCI) and are associated with depressive symptomatology, pain, and fatigue. However, there is limited evidence for changes in these outcomes following rehabilitation. Aerobic exercise training (AET) has been widely used as a treatment approach in other clinical populations and may play an important role in reducing depressive symptomatology, pain, and fatigue. The specific aim of this study is to quantify the effects of AET on cardiorespiratory fitness and examine associated secondary outcomes, including depressive symptomatology, pain, fatigue, and quality of life in ambulatory individuals with iSCI. **METHODS/STUDY POPULATION** Ten ambulatory individuals with iSCI will complete six weeks of AET (18 sessions, 30 minutes per session). Outcome measures will include: cardiorespiratory fitness ($VO_2$ peak), depressive symptomatology (PHQ-9; Hamilton Rating Scale for Depression), pain intensity and interference (Brief Pain Inventory), fatigue severity (Modified Fatigue Impact Scale), quality of life (SF-36), and ambulatory status (walking speed; WISCI-II; walking endurance). In addition, the Patient Reported Outcomes Measurement Information System (PROMIS) short-form instruments for emotional distress-depression, pain interference, and fatigue will be used. **RESULTS/ANTICIPATED RESULTS** Six weeks of AET will increase $VO_2$ peak, decrease depressive symptomatology, pain intensity and interference, and fatigue severity, as well as improve quality of life and ambulation. **DISCUSSION/SIGNIFICANCE OF IMPACT** This study will lay the foundation for further investigation aimed at developing exercise based therapeutic strategies to effectively target functional impairments and associated secondary outcomes in individuals with iSCI.

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## CORRELATION OF SNPS WITH FINE NEEDLE ASPIRATION CYTOLOGY AND HRT IN POSTMENOPAUSAL WOMEN AT HIGH RISK FOR BREAST CANCER

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**OBJECTIVES/SPECIFIC AIMS** Our primary goal was to identify single nucleotide polymorphisms (SNPs) associated with abnormal benign breast tissue cytology in a postmenopausal cohort at high risk for breast cancer development. Our secondary goal was to identify specific SNPs associated with cytological abnormalities as a consequence of HRT use. **METHODS/STUDY POPULATION** Breast tissue was sampled by random periareolar fine needle aspiration (RPFNA) and epithelial cells were characterized as to whether they exhibited cytologic evidence of hyperplasia with atypia. DNA was isolated from buccal cells for assessment of 117 SNPs likely to be associated with breast cancer risk because of their involvement in steroid metabolism, receptor function, cell cycle control, DNA repair and/or carcinogen metabolism. Logistic regression analysis identified specific SNPs associated with (1) atypia under any hormone condition; (2) atypia while on HRT; (3) atypia while not on HRT; and (4) worse cytology while on HRT compared to off HRT. **RESULTS/ANTICIPATED RESULTS** Our initial cohort included 258 women; 102 were aspirated only while on HRT, 96 only while off HRT and 60 both on and off HRT. Results have shown promising associations between specific polymorphisms and worse cytologic abnormalities while on HRT. An independent validation cohort of 48 women with RPFNA both on and off HRT will be genotyped for the 117 initial SNPs and 60 new SNPs identified through a review of current literature. **DISCUSSION/SIGNIFICANCE OF IMPACT** HRT is an important treatment option for women experiencing symptoms of menopause. However, certain types of HRT can modestly increase breast cancer risk depending on the type, dose, duration of use and differences in genetic factors. Specific SNPs may identify women for whom HRT is most likely to promote precancerous changes.

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## ROLE OF DIHYDROXYQUINOLINE (DHQ) IN *PSEUDOMONAS AERUGINOSA* PATHOGENICITY

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**OBJECTIVES/SPECIFIC AIMS** *Pseudomonas aeruginosa* (Pa) is responsible for high mortality in cystic fibrosis (CF) patients. The Pseudomonas quinolone system (Pqs) produces 2,4-Alkylquinolones that activate virulence factor production. Dihydroxyquinoline (DHQ) is produced in the highest concentration among quinolones, but has no known function. The purpose for our study was to determine the relationship of DHQ with virulence factor production and quantify the levels of DHQ in CF patients chronically infected with Pa. **METHODS/STUDY POPULATION** Virulence related to DHQ production was assessed using the Caenorhabditis elegans infection model. The ability of DHQ to activate transcription through PqsR was measured by RT-PCR and pqsA'-LacZ reporter construct within *E. coli*. The amount of DHQ in stable and exacerbated CF patient sputum samples was quantified by LC-MS. **RESULTS/ANTICIPATED RESULTS** C. elegans challenged against Pa wild-type strain PAO1 had a median survival time of 216 h ($n$ = 113), while nematodes with the DHQ-only mutant had a median survival time of 240 h ($n$ = 113, PAO1- ΔpqsB no sig. difference) and the quinolone-null mutant was unable to kill all of the nematodes within 240 h ($n$ = 113, ΔpqsAB- ΔpqsB/PAO1 $p < 0.001$). Transcriptional analysis determined that DHQ activates PqsR to initiate transcription of the operon. Preliminary data generated from sputum samples from outpatients maintaining their lung functions contained a median DHQ concentration of 227 μg/ml (± 393, $n$ = 11), while the median DHQ concentration from hospitalized patients contained 465 μg/ml (± 234, $n$ = 2) DHQ. **DISCUSSION/SIGNIFICANCE OF IMPACT** This study demonstrated DHQ is an important component of the Pqs system for virulence factor production and may also be used as a biomarker for exacerbated disease stage, since DHQ is linked to both virulence factor production and toxicity towards the host.

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## ASSESSING THE BURDEN OF GENETIC DISEASES CAUSED BY GROSS DELETIONS IN ACUTELY ILL NEWBORNS BY WHOLE GENOME SEQUENCING (WGS)

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**OBJECTIVES/SPECIFIC AIMS** The 4,023 known Mendelian diseases are major causes of mortality in newborns. Recently we proved the concept of universal genetic disease diagnosis in 50 hours by WGS. For this project our specific aims are to: (1) Develop a bioinformatics pipeline to detect deletions in WGS with high sensitivity, (2) Determine the sensitivity and specificity of deletion predictions, and (3). Use this pipeline in a set of acutely ill newborns with well characterized phenotypes to determine the burden of genetic diseases caused by deletions. **METHODS/STUDY POPULATION** 8 software tools for detection of deletions in WGS were deployed. Their sensitivity, specificity and precision were assessed in simulated and test WGS. The best tools are being developed into a bioinformatic pipeline whose performance is being compared with that of SNP arrays and to identify deleterious deletions in disease genes that match phenotypes in 26 trios with ill newborns. **RESULTS/ANTICIPATED RESULTS** Deletions predicted by both Breakdancer (BD) and GenomeStrip (GS) in simulated WGS had 94% specificity and 83% sensitivity. 95% of deletions predicted by both BD and GS in WGS of the HapMap individual NA12878 were true positives by SNP arrays and the Integrated Genome Viewer. **DISCUSSION/SIGNIFICANCE OF IMPACT** Rapid WGS has shown initial utility for timely diagnosis of genetic diseases caused by nucleotide variants in newborns. Array hybridization and SNP arrays have relatively low sensitivity for deletions. A WGS pipeline that integrates high sensitivity deletion predictions with a comprehensive set of candidate disease genes will allow for the measurement of the burden of genetic diseases caused by deletions in ill newborns. Prospectively, this pipeline may increase the diagnostic yield of WGS in ill newborns with possible genetic diseases

## T3: TRANSLATION TO PRACTICE

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### UVEITIC MACULAR EDEMA OUTCOMES: RESULTS OF A RANDOMIZED CONTROLLED TRIAL

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**OBJECTIVES/SPECIFIC AIMS** To compare outcomes of uveitic macular edema from a randomized controlled trial (RCT) and assess differences by subtype. **METHODS/STUDY POPULATION** We conducted a secondary analysis of macular edema outcomes from a RCT comparing methotrexate and mycophenolate mofetil for non-infectious intermediate, posterior or pan- uveitis. Patients underwent monthly optical coherence tomography (OCT) scans. We defined macular edema as a macular thickness >2 standard deviations above normal retinal thickness. We determined subtype by OCT fluid patterns and categorized these as cystoid, diffuse or serous. Six-month outcomes included resolution, defined as normal macular thickness and absence of OCT fluid, and % change in retinal thickness. **RESULTS/ANTICIPATED RESULTS** 33 out of 80 enrolled patients had macular edema at baseline, and 25 completed follow-up. Of the 35 eyes with macular edema at baseline, 24 (69%) eyes resolved with antimetabolite therapy. Edema resolution was achieved in 3/9 (33%) eyes with cystoid edema, 1/4 (25%) eyes with diffuse edema, and 20/22 (91%) eyes with serous retinal detachments (SRD) ($p = 0.0002$). SRDs, due to Vogt-Koyanagi Harada (VKH) in 86% of cases, were more likely to resolve compared to cystoid ($p < 0.001$) and diffuse ($p = 0.02$) edema. There was no detectable difference in resolution of macular edema or % change in retinal thickness based on treatment arm. **DISCUSSION/SIGNIFICANCE OF IMPACT** First-line corticosteroid-sparing antimetabolite therapy resolved uveitic macular edema in 69% of cases. SRDs, especially those secondary to VKH, respond particularly well to antimetabolite therapy, whereas cystoid and diffuse macular edema do not reliably resolve.

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### ACHIEVING ECOLOGICAL VALIDITY IN ACTIVE AGING PREVENTIVE INTERVENTIONS

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**OBJECTIVES/SPECIFIC AIMS** The aims of this study were to: (1) identify important elements required to culturally center a health promotion interventions to augment both the ecological validity and the overall external validity of a treatment study and (2) develop a culturally sensitive activity-based health promotion intervention for Hispanic older adults who live alone. **METHODS/STUDY POPULATION** A sequential transformative mixed method design guided by the Ecological Validity Model was used for the content validation of the intervention. In Phase I, six Hispanic experts in aging completed a content validity exercise to determine the preliminary content of the health promotion program. In Phase II, two focus groups with six key community members in each group were conducted in two activity centers for the elderly in Puerto Rico to determine the content and the structure of the new intervention. Data analysis included content validity ratio (CVR) and rigorous directed thematic content analysis. **RESULTS/ANTICIPATED RESULTS** The CVR exercise resulted in a total of 7 themes that reached the minimum CVR of .49 for a panel of 18 persons. The analysis of the qualitative data revealed culturally sensitive elements in the dimensions of language, person, metaphors, content, concepts, goals, methods, and context that were used to develop the working version of the intervention protocol. **DISCUSSION/SIGNIFICANCE OF IMPACT** The use of a mix method design to capture the community as well as the aging expert voices resulted in the successful development of a culturally sensitive intervention protocol that will be used to assess its feasibility and acceptability in a future study. The Ecological Validity Model can be used as a guide for developing culturally sensitive interventions to others ethnic minority groups.

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### COST ANALYSIS OF A NUCLEIC ACID AMPLIFICATION TEST FOR PULMONARY TUBERCULOSIS

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**OBJECTIVES/SPECIFIC AIMS** The CDC recommends using a nucleic acid amplification test (NAAT) to diagnose pulmonary tuberculosis (TB) but there is a lack of data on NAAT cost-effectiveness. This study evaluated the cost of testing all acid-fast bacillus (AFB) smear positive respiratory specimens with a NAAT to rule out TB at a large urban hospital with a high prevalence of TB/HIV. The objective was to determine cost-effectiveness of a NAAT. **METHODS/STUDY POPULATION** This study included patients at Grady Memorial Hospital (GMH) in Atlanta, GA with an AFB+ respiratory specimen from 1/2002–6/2008. Test characteristics of the NAAT (AMPLIFIED MTD, Hologic Gen-Probe, San Diego, CA) were determined using culture as gold standard. A cost analysis of routine use of NAAT versus no use of NAAT was conducted using decision analysis models. Relevant costs were laboratory tests (e.g. NAAT, $174/test), hospital rooms (standard and isolation), TB medication, and contact investigations. Cost inputs were determined from GMH and total costs by calculating resources consumed per patient tested with NAAT and not tested with NAAT. **RESULTS/ANTICIPATED RESULTS** 949 patients were included. 445 (47%) were HIV+. Positive predictive value (PPV) of AFB was 27%, and significantly higher for HIV- (56%) than HIV+ (19%) (RR = 2.9, 95%CI 2.4–3.7, $p < .0001$). The NAAT had high sensitivity (99.6%) and specificity (99%). Average cost per patient tested with the NAAT was $9922 versus $11848 without NAAT; average cost savings were $1925 per AFB+ specimen tested with NAAT. **DISCUSSION/SIGNIFICANCE OF IMPACT** Routine use of NAAT for AFB+ respiratory specimens was cost saving to the healthcare system. Due to the low PPV of an AFB+ specimen for TB, use of a NAAT allowed for avoidance of unnecessary TB treatment, airborne infection isolation while hospitalized, and contact investigations by the local health department.

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### SIZER MAP TO INVESTIGATE SIGNIFICANT FEATURES OF THE RATE OF CHANGE OF BODY-WEIGHT PROFILE FOR HIV INFECTED PATIENTS IN IEDEA STUDY

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**OBJECTIVES/SPECIFIC AIMS** This work involves standardized data collected on HIV-positive patients initiating antiretroviral therapy (ART) in five regions of the International Epidemiologic Databases to Evaluate AIDS (IeDEA) collaboration. Our objective is to understand the pattern of body-weight change in HIV patients initiating stavudine (d4T) containing first line regimens versus non-d4T regimens. **METHODS/STUDY POPULATION** Significant Zero Crossings of Derivatives (SiZer) is a powerful graphical tool for exploring structures in curves by mapping areas where the first derivative is significantly increasing, decreasing or no change. These maps provide information about the time at which the changes in the rate of increase or decrease in patient weight occurred. By doing so, we explored the durability of weight gain in these two types of ART regimens. Patients with at least one baseline and one postbaseline body weight measure within first 4 years of follow up were analyzed. **RESULTS/ANTICIPATED RESULTS** A total of 185,010 patients from South Africa (65.6% of the cohort), East-Africa (21.9%), West Africa (8.3%), Central-Africa (3.2%), and Asia-Pacific (0.9%) were included. We compared patients with d4T (53.06%) vs. non-d4T (46.94%) for each region. The SiZer map for South Africa showed that weight in d4T-treated patients did not significantly increase after 54.8 weeks compare to 105.4 weeks for non-d4T treated patients. Similarly, the other four regions showed that weight increases lasted at most 53–76 weeks in d4T-treated patients vs. 59–80 weeks in patients receiving non-d4T-based regimens. **DISCUSSION/SIGNIFICANCE OF IMPACT** The results from the SiZer maps showed that the patients treated with d4Tcontaining ART regimens experienced weight gains for shorter periods and even decreasing or static weight change when compared to non-d4T treated patients.

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## PHASE II STUDY MONITORING QOL AND BIOMARKERS OF MUCOSITIS IN H&N CANCER PATIENTS UNDERGOING RT UTILIZING A PERSONALIZED HUMIDIFICATION DEVICE

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**OBJECTIVES/SPECIFIC AIMS** (1) To determine whether the use of a personalized, handheld humidification system during a course of radiation therapy (6 weeks) will result in improvement in head and neck-specific quality of life (QOL) compared with historical experience. (2) To correlate the MDASI-HN subscale or overall score with the clinician graded mucositis score at 6 weeks and 12 weeks. (3) To assess the rate of feeding tube placement and rate of hospitalization by 12 weeks. (4) Conduct a feasibility analysis assessing patient compliance. (5) Analyze salivary inflammatory biomarkers at baseline, 6 and 12 weeks. **METHODS/STUDY POPULATION** A single arm study of 20 adult patients >18 years old of the use of a personalized sterile humidification device for head and neck cancer patients undergoing radiation therapy. Patients used the humidification system twice daily for 30 minutes, for 12 weeks. They completed the MDASI HN questionnaire and their saliva was collected at baseline, 6, and 12 weeks after the start of radiation therapy. **RESULTS/ANTICIPATED RESULTS** Our preliminary data show that patients have larger changes in their MDASI-HN subscale score than initially hypothesized. Patients with higher compliance had a smaller increase in MDASI-HN subscale score. Salivary marker and other correlative data are pending. **DISCUSSION/SIGNIFICANCE OF IMPACT** Our preliminary data do not yet establish that increased usage of the humidification device quantitatively improves quality of life. However, in patients for whom usage is feasible, this practical, drug-free therapy produces a number of indicators of benefit. If personalized humidification succeeds in improving oral hygiene and reducing inflammatory biomarkers, it should be explored for other forms of cancer treatment related mucositis.

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## PATIENT ACTIVATION AND FUNCTIONAL RECOVERY IN PATIENTS UNDERGOING PRIMARY TOTAL KNEE OR HIP ARTHROPLASTY

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**OBJECTIVES/SPECIFIC AIMS** To assess patient activation on recovery following primary total knee or hip arthroplasty. **METHODS/STUDY POPULATION** In this prospective study, we will enroll patients undergoing primary hip or knee arthroplasty. Activation will be assessed pre-op using the Patient Activation Measure (PAM), a questionnaire addressing personal competencies. Results will be analyzed to determine a correlation with PAM scores and post-op outcomes. Individuals will be stratified into one of four PAM stages: Stage I (persons not taking an active role in their health), Stage II (persons lacking confidence for self-management), Stage III (persons beginning to take action), and Stage IV (persons adopting behaviors of health support). PAM will be measured at baseline. Post-op outcomes of pain, disability, physical and mental health, and patient satisfaction will be evaluated with the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), Short Form-36 (SF-36) and Hip and Knee Satisfaction Score, respectively, at baseline, 6 weeks, and 12 months. **RESULTS/ANTICIPATED RESULTS** We expect pain and disability to decrease after surgery. We expect Stage-IV subjects to experience greater decrease in pain than Stage-I subjects. We expect physical and mental health to improve post-op with greater improvements in patients in Stage IV compared to Stage I. **DISCUSSION/SIGNIFICANCE OF IMPACT** Given increased demand of arthroplasty, we seek to address modifiable factors placing individuals at poor outcome risk. A recent study showed high activation subjects with chronic disease were more likely to use self-management services than low activation individuals. In another study, high patient activation was associated with better recovery after lumbar spine surgery. We will explore the relationship of patient activation to reduction in pain and disability and improvement in physical and mental health in this population.

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## ANALYSIS OF LENGTH OF STAY (LOS) AMONG PATIENTS WITH INTELLECTUAL AND DEVELOPMENTAL DISABILITIES (IDD) AT STRONG MEMORIAL HOSPITAL

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**OBJECTIVES/SPECIFIC AIMS** The purpose of this study is to determine LOS and inpatient experience discrepancies between patients with and without IDD admitted to Strong Memorial Hospital (SMH) in Rochester, NY in 2012. Electronic Medical records (EMR) will be used to (1) Estimate the difference in LOS between patients with and without IDD and assess the impact of pre- and posthospitalization factors on LOS and (2) Estimate the impact of inpatient interventions on LOS for patients with IDD **METHODS/STUDY POPULATION** All patients with a history of IDD and an inpatient stay during the 2012 calendar year at SMH will be matched to twice as many non-IDD patients by gender, age, and diagnosis related group (DRG). Fifteen inpatient interventions of IDD patients including invasive medical interventions (i.e., catheter, line days), adverse events (i.e., secondary infections, falls), and use of support services (i.e., physical/occupational therapy, advocacy presence) will be examined in 150 patients who belong to the 3 DRG groups with the longest LOS in the IDD group. **RESULTS/ANTICIPATED RESULTS** The primary outcome will be a confidence interval of LOS between the IDD ($n = 935$) and non-IDD ($n = 1870$) groups will be compared. Regression analysis accounting for the effects of age, sex, DRG, code status, and discharge location will be calculated. The secondary outcome will be a linear multivariate regression to measure the strength between the inpatient interventions and LOS. **DISCUSSION/SIGNIFICANCE OF IMPACT** Average intensive outpatient residential settings for adults with IDD cost $370/day and the average cost for hospitalization for patients at SMH in 2012 was $2,787/day. It is prudent to examine the factors that will limit the length of hospitalization. Use of advocates and improved staff knowledge in the care of patients with IDD may both decrease LOS and complications of hospital admission.

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## SICKLE CELL DISEASE AND SEXUAL HEALTH EDUCATION FOR YOUTH: A SOCIAL SKILLS MODEL

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**OBJECTIVES/SPECIFIC AIMS** Youth with sickle cell disease (SCD) do not receive adequate SCD genetic inheritance and sexual health education. As more individuals with SCD live into childbearing years, education is needed. To assess interest in a SCD inheritance and sexual health education program, we conducted a single center pilot study among youth with SCD. Secondarily, we studied the feasibility of program implementation. **METHODS/STUDY POPULATION** We used a mixed methods approach. Patients aged 11–19 years were approached in an urban hospital. Semi-structured interviews were conducted, recorded and transcribed. Qualitative data were analyzed and coded to identify themes. These results served as drivers for content of a social skills-based education program. Sisters Informing Sisters about Topics on AIDS (SISTA) also provided a framework for the curriculum. The program was assessed using member-check. Feasibility was measured and defined as at least 50% of individuals consenting to participate. **RESULTS/ANTICIPATED RESULTS** Twenty of 35 youth (57%) consented. All participants from the qualitative analysis demonstrated knowledge deficits and/or interest in SCD genetic education. Nineteen (95%) demonstrated deficits in sexual health knowledge and/or requested education. Seventeen (85%) demonstrated knowledge gain in SCD genetics and/or sexual health. Twelve (60%) reported engaging in sexual activity, seven (35%) in risky behaviors, and three (15%) reported past STI diagnosis. An education program and pre/posttest measures were created and assessed. **DISCUSSION/SIGNIFICANCE OF IMPACT** Youth with SCD lack understanding of both SCD genetic inheritance and sexual health. With feasibility supported, the next phase of research will address the efficacy of implementing a genetic and sexual health education program.

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## TREATMENT OF SUPRAVENTRICULAR TACHYCARDIA IN INFANTS: ANALYSIS OF A LARGE, MULTICENTER DATABASE

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**OBJECTIVES/SPECIFIC AIMS** Describe treatment of SVT in infants with and without congenital heart disease (CHD). **METHODS/STUDY POPULATION** We identified infants treated for SVT (1998–2012) in 348 neonatal intensive care units managed by the Pediatrix Medical Group. We defined acute therapy as any typical acute therapy used on day 1 of treatment, and prophylactic therapy as any typical prophylactic therapy used after day 1 of treatment or on day of hospital discharge. CHD was defined as any heart defect excluding patent ductus arteriosus. A chi-square test was used to compare therapies over time and across diagnosis groups. **RESULTS/ANTICIPATED RESULTS** We identified 2848 infants including 367 (13%) with CHD. Underlying arrhythmia diagnoses included atrial flutter ($n = 448$, 16%), Wolf Parkinson White Syndrome ($n = 200$, 7%), and SVT of unspecified origin ($n = 2200$, 77%). Median (25%, 75%) gestational age and birth weight were 37 weeks (34, 38) and 2955 g (2210, 3522). Median postnatal age at diagnosis was 2 days (0, 8). Overall, 1348 (47%) received acute therapy, 2523 (89%) received prophylactic therapy and 1040 (37%) received both. Digoxin was the most frequently prescribed prophylactic agent but use has declined (100% in 1998 to 62% in 2012, $p = 0.02$) and beta blockers are now more frequently prescribed (0% in 1998 to 64% in 2012, $p < 0.001$). Amiodarone was used more often in infants with CHD for acute ($p = 0.004$) and prophylactic therapy ($p = 0.001$). Multidrug prophylactic therapy was used in 35% of infants and use did not differ in infants with or without CHD ($p = 0.61$). **DISCUSSION/SIGNIFICANCE OF IMPACT** SVT therapy in infants varies greatly. Trends include increasing

preference for beta blockers over digoxin and increased amiodarone use in infants with complex CHD.

## T4: TRANSLATION TO POPULATION

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### MORBIDITY OF PEDIATRIC MINOR INJURIES SUSTAINED AT HOME

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**OBJECTIVES/SPECIFIC AIMS** (1) Describe the length of morbidity following ED treatment in children with a minor injury compared to uninjured sick controls. (2) Assess the impact of HUD-defined housing quality on length of morbidity. **METHODS/STUDY POPULATION** The Children's Housing Assessment for Safe Environment (CHASE) study used a case-control design to compare housing quality in a group of children injured at home ($n = 104$) to a group of uninjured sick controls ($n = 72$). The mean age of the children was 2.7 years. All children were treated in the ED and discharged home. We conducted a secondary analysis to assess short-term, parent-reported clinical and functional outcomes in the groups. We modeled the impact of housing quality on clinical and functional outcomes using Poisson regression. Quality was determined using the US Department of Housing and Urban Development Housing Quality Standards and defined by the number of domains passed. **RESULTS/ANTICIPATED RESULTS** Following ED treatment, injured vs. sick children experienced an average duration of morbidity of 4.5 days vs. 7.6 days ($p = 0.031$). On average, the children's homes passed 3.4 of 5 HUD domains, which did not vary between the groups ($p = 0.448$). Preliminary Poisson regression models showed that an increase of one HUD domain passed was associated with a 10% decrease in duration of morbidity when controlling for gender, age, housing type, and household income ($p < 0.001$). **DISCUSSION/SIGNIFICANCE OF IMPACT** The morbidity outcomes of children sustaining a minor injury at home were similar to those of children treated for an acute illness in the ED. Overall, injured and sick children came from houses that did not significantly differ in quality, as measured by HUD domains. Decreased housing quality was associated with a longer duration of morbidity.

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### DETECTION OF RARE GENETIC VARIANTS THAT PREDISPOSE TO PANCREATIC CANCER: PROOF OF PRINCIPLE USING EXOME SEQUENCING DATA

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**OBJECTIVES/SPECIFIC AIMS** We hypothesize that rare variants can explain the missing heritability of pancreatic cancer (PC). To determine whether this hypothesis can be feasibly tested, we conducted a proof-of-principle analysis using exome sequencing data of 23 Mayo Clinic PC patients. **METHODS/STUDY POPULATION** 23 PC patients were recruited to the registry of the Mayo Clinic SPORE in Pancreatic Cancer. Pre-treatment blood samples and tumor samples were obtained. Exome sequencing was performed and variants were called and annotated. Sequencing and data preparation were performed at OICR. We conducted stringent filtering for candidate variants: (1) Variant Effect Predictor was used to determine the minor allele frequency (MAF) for all variants based on the 1000 Genomes resource. (2) All variants with MAF>0.02 in the European population were filtered out. (3) SIFT and POLYPHEN was used to filter out all nonsynonymous variants that were not predicted to be functional. (4) All rare and functional (indels, stoploss/stopgain, or deleterious nonsynonymous variants) variations were retained for further consideration. **RESULTS/ANTICIPATED RESULTS** The total number of potential interesting rare functional variants in each of these patients ranges from 125 to 541. Among them, the number of indels, stoploss/stopgain, and deleterious nonsynonymous variants are from 18 to 195, 4 to 29, and 93 to 365, respectively. The number obtained is computationally tractable and can be feasibly explored to identify susceptibility variants/genes. **DISCUSSION/SIGNIFICANCE OF IMPACT** In this preliminary proof-of-principle analysis, we found a computationally manageable number of candidate rare functional germline genetic variants in PC patients. We have shown we can feasibly determine new predisposition genes/variants of this cancer using exome sequencing-based study design.

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### HEALTHY COMMUNITIES INSCIED OUT: INDIA IN FOCUS

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**OBJECTIVES/SPECIFIC AIMS** Integrated Science Education Outreach (InSciEd Out) is a K-12 program focused upon achieving science education excellence through student-directed scientific research. The objective of this project is to execute a pilot run of InSciEd Out New Delhi, aiming to cultivate flagship partners for assessment of a curriculum intervention improving student science and facilitating positive gains toward building early healthy behaviors. **METHODS/STUDY POPULATION** As per the study design, teaching teams from Sachdeva Public School and Modern School in New Delhi are recruited for a 3-week internship. Students in participating teacher interns' classrooms will be our study population. The outcome will be evaluated via pre and post assessments based on novel InSciEd Out metrics that include: Evolution of Experimental Design, Next Generation Paper, and Talking Drawings. **RESULTS/ANTICIPATED RESULTS** We anticipate full curriculum implementation in grades 4–8 classrooms by the teacher interns with advances in student science proficiency through increased science interest, aptitude, and confidence. Healthy behavioral trends are also expected via gains in knowledge, attitudes, and intents. Preliminary data on teacher assessment suggests positive reception of our internship with some gains in pedagogical and scientific understanding. **DISCUSSION/SIGNIFICANCE OF IMPACT** As global development hinges upon fostering science, technology, and innovation, improving K-12 education is the key to nurture scientists and science-literate citizens. InSciEd Out's metric-driven, multidisciplinary framework has potential to extend student science beyond rote knowledge to application in critical and topical community-based problems. This research thus carries great import for both advancing scientific research and improving community and global health.

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### NICOTINAMIDE AND ITS EFFECT ON ADIPOGENESIS IN HUMAN UMBILICAL CORD–DERIVED MESENCHYMAL STEM CELLS: THE HEALTHY START STUDY

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**OBJECTIVES/SPECIFIC AIMS** The role of fetal programming in the early development of obesity is an important area of focus for chronic disease prevention. Maternal diet during pregnancy represents a specific *in utero* exposure with the potential to impact fetal development. Little is known in human populations as to what specific nutrient exposures impact fetal programming, in particular fat accretion. The micronutrient niacin, specifically its amide form, nicotinamide, has been linked to increased adipogenesis through inhibition of the de-acetylase Sirtuin 1 (SIRT 1). This protein controls expression of the key adipogenic gene, peroxisome proliferator-activated receptor gamma (PPAR-γ), which can be measured in cultures of adult human mesenchymal stem cells (hMSCs). This project explores the novel hypothesis that adipogenesis mechanisms are accelerated and adiposity increased in infants born to mothers with increased dietary nicotinamide consumption during pregnancy. **METHODS/STUDY POPULATION** Using umbilical cord-derived hMSCs collected from 100 neonates enrolled in the Healthy Start Study, a large population-based pre-birth cohort, we will expose these cells to nicotinamide in culture and analyze them for levels of key adipogenic proteins, CCAAT/enhancer binding protein (c/EBP) alpha and fatty acid binding protein 4 (FABP4), as well as PPAR-γ and SIRT 1. **RESULTS/ANTICIPATED RESULTS** The findings will be compared to adiposity of these infants at 24 hours after birth measured by air displacement plethysmography (Pea Pod). **DISCUSSION/SIGNIFICANCE OF IMPACT** This project will allow us to better understand the potential cellular, nutrient-driven mechanisms responsible for in-utero fat accretion and fetal programming of obesity.

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### AN ASSESSMENT OF DOG BITES BY BREED

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**OBJECTIVES/SPECIFIC AIMS** The purpose of this retrospective chart review was to evaluate the cases of dog bite in the UC Davis Health System over the calendar years 2012 and 2013. Our hypothesis entering this investigation was that that certain breeds of dog, specifically pit bulls, were more likely to cause greater injury than other animals. This investigation had four specific aims: (1) To assess what percentage of the dog bites that present to are due to pit bulls, (2) the impact of breed on length of treatment and follow-up, (3) the impact of breed on consultation, and (4) the impact of breed on pharmacotherapy used for treatment. **METHODS/STUDY POPULATION** This investigation collected the charts of all bog bites, coded as either dog or animal bite, who presented to the UC Davis Emergency Department (ED). These 547 patient charts were reviewed dog breed, body part injured, if the animal was provoked, consulting service, pharmacologic treatment, repair technique used, as well as all available information on the animal including vaccination status, familiarity with the victim. **RESULTS/ANTICIPATED RESULTS** We anticipate that pit bull bites will account for a minority of the dog bites that present to the ED, but that these injuries will require a greater degree of care, consultation, intervention, and follow-up than other dog breeds.

**DISCUSSION/SIGNIFICANCE OF IMPACT** This investigation looking dog bites by breed is not an attempt to vilify pit bulls or any breed of dog. The purpose of this investigation is to gain knowledge for developing decision support algorithms to be used when a new patient enters the health system. If pit bull bites do require a higher level of care than other dog bites, this information will allow a health system to provide the appropriate resources quicker and more effectively to pit bull bitten patient.

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## WELLNESS GOAL SETTING AND ATTAINMENT AMONG INDIVIDUALS WITH CO-OCCURRING PHYSICAL AND MENTAL ILLNESS

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**OBJECTIVES/SPECIFIC AIMS** Patient-centered care models increase the patient's role in selecting and prioritizing health goals, particularly for those with multiple chronic conditions. This study seeks to understand the association between participant characteristics and (1) health goal setting and (2) goal achievement. **METHODS/STUDY POPULATION** The Wellness Incentives and Navigation study is an RCT that assigned Medicaid enrollees with co-occurring physical and mental health conditions to receive regular health coach support and a flexible wellness account. An intake questionnaire assessed wellness risks as well as demographics, health and functional status. With a health coach applying motivational interviewing techniques, the participant chose identified wellness risks to address, set specific goals, and discussed strategies for achievement. Progress toward goal achievement was assessed during monthly calls and quarterly in-person meetings. Descriptive statistics, chi-square tests and logistic regression were used to explore factors associated with goal setting and achievement. This work is supported in part by the NIH/NCATS Clinical and Translational Science Awards to the University of Florida TL1 TR000066 and UL1 TR000064. **RESULTS/ANTICIPATED RESULTS** 515 intervention participants enrolled and set wellness goals. Although almost all participants triggered health limiting, emotional and pain-related risks, participants prioritized weight (80%), nutrition (61%), smoking (53%) and sedentary behaviors (46%). Additional analyses examine the relationship between participant characteristics and goal setting and achievement. **DISCUSSION/SIGNIFICANCE OF IMPACT** Understanding the factors that influence patient health goal setting and achievement is important to support patient decision making and out-of-clinic efforts towards wellness.

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## ALLOCATING CLINICAL PHARMACY SERVICES: RETROSPECTIVE COHORT STUDY TO EVALUATE PATIENTS WITH DIABETES

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**OBJECTIVES/SPECIFIC AIMS** To determine pharmacist's intervention in patients with controlled and uncontrolled diabetes, with a goal to improve clinical pharmacy resource allocation **METHODS/STUDY POPULATION** 572 eligible patients with diabetes were selected from the UMHS Patient-Center Medical Home (PCMH) clinics. These patients were either well-controlled (HbA1c ≤ 7%) or poor-controlled (HbA1c > 7%). We assessed clinical pharmacists' interventions (therapeutic-related, medication reconciliation, and other) in these two groups of patients using data from the PharmD Intervention Checklist. Well-controlled patients were subdivided into those with one versus multiple visits. **RESULTS/ANTICIPATED RESULTS** Among the eligible patients, 321 had a known HbA1c value at baseline. Of the 321 patients, 34.0% had controlled HbA1c and 66.0% had uncontrolled HbA1c. Patients with uncontrolled diabetes were associated with receiving more therapeutic and patient education interventions ($p < 0.001$). In patients with controlled diabetes, 67.0% had multiple visits and 33.0% had one visit. Among these patients, 20.6% and 2.8% received any hypertension medication intervention (multiple vs. one visit, $p = 0.019$), 11.0% and 0% received any hyperlipidemia medication intervention (multiple vs. one visit, $p = 0.051$). The multiple-visit group had a higher number of total non-therapeutic interventions compared to patients with one-time visit (7.90 vs. 1.08, $p < 0.001$); this finding was driven by patient education services. **DISCUSSION/SIGNIFICANCE OF IMPACT** Overall, patients with uncontrolled diabetes received more therapeutic and patient education interventions than controlled diabetes. About one-quarter of controlled patients received medication interventions for hypertension or hyperlipidemia, and nontherapeutic interventions appeared to be the basis of multiple visits. A cost model will be developed.

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## "BUT DOC, WHAT'S THAT CHEMO GONNA COST ME?" NOVEL ANALYSIS OF PATIENT–PROVIDER COST CONVERSATIONS AT THE POINT OF CARE

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**OBJECTIVES/SPECIFIC AIMS** In the setting of breast cancer clinic visits: (1) Determine the frequency of healthcare cost discussions. (2) Elucidate the factors associated with greater odds of healthcare cost discussion. **METHODS/STUDY POPULATION** Sample includes 1000 transcripts of patient-provider interactions from clinic visits for breast cancer management from around the United States. Transcript source was a large, nationwide corpus of audio-recorded point of care conversations owned by Verilogue, Inc. All eligible transcripts were screened by two reviewers for the presence of a cost conversation (any mention of financial costs related to healthcare or health problems). **RESULTS/ANTICIPATED RESULTS** 1.) 23% of breast cancer clinic visits contained a cost conversation (226/1000; 95% CI, 20–26%) 2.) The odds of cost being discussed in an NP/PA clinic visit were 2.2 times higher than the odds of a cost discussion occurring in an MD visit. ($p < 0.001$, 95% CI: 1.4, 3.3). Notably, patient age, race, insurance type, employment status, or the presence of metastatic disease did not affect the odds of cost discussion. **DISCUSSION/SIGNIFICANCE OF IMPACT** It is critical that physicians and patients discuss healthcare costs so that they choose a treament course that is medically and financially optimal. Failing to discuss costs can lead to financial burden or nonadherence. Although past studies suggest that few patients ever discuss treatment costs with their physicians, this study suggests that cost discussion occurs more commonly (about one of four breast cancer visits). Only NP/PA clinic visits were associated with increased odds of cost discussion (OR = 2.2) thereby reinforcing the idea that the occurrence of cost conversation is a complex phenomena.

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## ANALYSIS OF INSECTICIDE-TREATED NET OWNERSHIP AND USE IN MALAWI AND RELATION TO ACCESS TO CARE

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**OBJECTIVES/SPECIFIC AIMS** A chief malaria prevention tool is the Insecticide Treated Net (ITN), today mostly the Long-Lasting Insecticidal Net (LLIN). Malawi is a small southeast African nation of 16 million people that began distributing ITN/LLINs in 2007 for free at government health facilities (HFs) to pregnant women and under-5 children. This program increased net ownership, but fell short of universal coverage. The objective of this study was to better understand social and spatial correlates of net ownership that might inform future anti-malaria interventions. **METHODS/STUDY POPULATION** We examined ITN/ILLN ownership and use during a 2011 cross-sectional study in the Machinga District of rural Malawi. We hypothesized that differences in net condition and use were associated with household malaria prevalence; that most of those surveyed had obtained their ITN/LLIN from a local health facility; and that distance from residence to health facility was associated with a decreased probability of owning an ITN/LLIN. Standard multivariable regression methods were used to evaluate characteristics of nets and related variables at the household and coarser spatial scales. We evaluated Euclidean and walking distances between household geolocations and the Machinga District Hospital and their association with net ownership. **RESULTS/ANTICIPATED RESULTS** Preliminary results showed that net possession ranged from 26 – 76% of households in each village. Machinga District Hospital was the source for 80% of nets. Spatial analyses suggested that distances from village centroids (Kuhn Kuenne method) to the Machinga District Hospital are related to village-level net ownership. **DISCUSSION/SIGNIFICANCE OF IMPACT** Further understanding of these relationships may help inform multilevel anti-malaria interventions in Malawi.

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## CHOICES: REPRODUCTIVE AND SEXUAL HEALTH DECISION MAKING AMONG WOMEN IN WESTERN KENYA

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**OBJECTIVES/SPECIFIC AIMS** (1) Utilize a multidisciplinary translational research approach to better understand the reproductive and sexual health decision making among HIV-infected women in Kenya. (2) Identify appropriate reproductive health counseling and strategies, potentially reducing unintended pregnancy, STI acquisition, and HIV transmission. **METHODS/STUDY POPULATION** Existing scientific literature and focus group data from other studies conducted among the target population, HIV-infected women in sub-Saharan Africa, were reviewed to identify the factors that may influence women's reproductive and sexual health decision making. **RESULTS/ANTICIPATED RESULTS** Key topics that emerged from the focus groups and literature review include: age, education, employment status, HIV status, number of living children, ethnic group, contraceptive knowledge, cultural norms, and costs and availability. These topics will now be used to develop a survey instrument which will be implemented in the next phase of the project. This survey instrument will also include: (1) demographics; (2) knowledge of family planning (FP) methods and sexually transmitted infections (STI); (3) fertility desires; and (4) an assessment of perceived pleasure related to the use of FP methods. Additionally, a matrix will be developed for discrete choice analysis to ascertain the relative importance of these factors in determining if FP methods are used and how they are chosen. We will

implement the survey in two AMPATH clinics. **DISCUSSION/SIGNIFICANCE OF IMPACT** Findings from this research will assist the HIV care and treatment program in providing appropriate reproductive health counseling and services, thereby reducing sequelae including unintended pregnancy and STI acquisition.

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### TARGETING SCHOOL-AGE CHILDREN WITH INFLUENZA VACCINATION REDUCES THE COMMUNITY RISK OF MEDICALLY ATTENDED INFLUENZA-LIKE ILLNESS

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**OBJECTIVES/SPECIFIC AIMS** Influenza is a significant vaccine-preventable public health burden. School-located influenza vaccination (SLIV) programs could substantially enhance the suboptimal coverage levels achieved under existing delivery strategies. This work explores the effectiveness of a routine SLIV program in Alachua County, Florida, in reducing the community risk of medically attended influenza-like illness (ILI). **METHODS/STUDY POPULATION** For the 2011/12 and 2012/13 influenza seasons, age-group specific attack rates (AR) for ILI-associated outpatient visits are estimated from routine surveillance and census data. SLIV program effectiveness is estimated as 1 minus the attack rate ratio for Alachua County versus a comparison region: the surrounding 12 counties or all of Florida, excluding Alachua. **RESULTS/ANTICIPATED RESULTS** For all age groups and both epidemic seasons, Alachua had a substantially lower AR for ILI-associated visits than Region-3 or Florida. During the 2011/12 season, the AR among 5–17 year-olds was 103 per 100,000 (CI: 73, 145) in Alachua versus 597 (CI: 571, 625) in Region-3 and 523 (CI: 514, 531) in Florida. The overall effectiveness of the program was 80% (CI: 72%, 86%) among 5–17 year-olds in Alachua compared to Florida. The indirect effectiveness among 18–44 was 59% (CI: 51%, 60%), 45–64 was 48% (CI: 26%, 64%). The trend is similar for 2012/13, with significant effectiveness under-65, but lower than the previous year. **DISCUSSION/SIGNIFICANCE OF IMPACT** Our results show that high immunization coverage among school-age children through the program reduced the risk of medically attenuated ILI infection in the target age group and, more interestingly, among older members of the same community. SLIV programs can significantly reduce the influenza-associated public health burden in communities

## KL2 SCHOLAR ABSTRACTS

### T0: BASIC SCIENTIFIC DISCOVERY

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### INHIBITION OF PURINERGIC RECEPTOR SIGNALING BLOCKS EARLY HIV-1 INFECTION

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**OBJECTIVES/SPECIFIC AIMS** Human immunodeficiency virus (HIV-1) causes a chronic infection that can be controlled with antiretroviral medications. However, individuals living with HIV are at increased risk of cardiovascular disease, cancer, and neuropathy due to chronic inflammation of unknown etiology. Recent studies indicate that adenosine triphosphate (ATP) release and purinergic signaling is required for HIV-1 infection. Purinergic receptors detect extracellular ATP as a danger signal released from dying cells. We propose that ATP is a key signaling molecule that links HIV-1 infection and HIV-associated inflammation. **METHODS/STUDY POPULATION** We have developed fluorescent-tagged viral constructs that allow us to visualize discrete stages of infection. Using flow cytometry and confocal microscopy, we are able to determine the step at which purinergic antagonists block cell-cell infection. Using primary isolated CD4+ T cells, we can observe inhibition of HIV infection in the presence of purinergic inhibition. **RESULTS/ANTICIPATED RESULTS** Purinergic antagonists can potently block HIV-1 infection at an early stage of infection. We find that inhibitors are potent at blocking infection by cell-associated HIV and cell-free virus. This occurs before initiation of viral membrane fusion but does not appear to interfere with coreceptor localization. **DISCUSSION/SIGNIFICANCE OF IMPACT** Purinergic inhibitors can potently block HIV productive infection at the level of viral membrane fusion. Our studies explore a novel mechanism of therapeutic targeting in HIV-1 that may also act on inflammatory and cell death pathways associated with chronic infection. We propose that targeting this pathway would represent a potent new form of antiretroviral therapy that may reduce both viral burden and associated inflammation.

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### EFFECTS OF RHINOVIRUS (RV) 39 INFECTION ON AIRWAY HYPER-REACTIVITY (AHR) TO HISTAMINE AND CARBACHOL IN HUMAN AIRWAYS

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**OBJECTIVES/SPECIFIC AIMS** RV infection is associated with asthma exacerbations. We hypothesized that airway infection with RV39 would induce AHR, a diagnostic feature of asthma, in lung tissue derived from deceased organ donors with and without a history of asthma. **METHODS/STUDY POPULATION** Precision cut lung slices (PCLS) were prepared from cadaver lungs and cultured *ex vivo*. Airway viability was confirmed microscopically by ciliary motility, by bronchoconstriction with carbachol, and subsequent bronchodilation with isoproterenol. Cumulative dose response curves for carbachol- and histamine-induced contractility (as a biomarker for AHR) were measured using slices derived from asthmatic ($n = 4$) and nonasthmatic donors ($n = 1$) before and after infection with RV39. **RESULTS/ANTICIPATED RESULTS** Overall, RV39 infection of PCLS from donors with a history of asthma failed to stimulate enhanced AHR within 48h. In one donor, RV39 induced histamine-specific AHR (EC50 was reduced from 109 nM to 30nM after 48h; $p < 0.01$) with little change in responsiveness to carbachol (EC50 81nM to 109nM; $p$ = NS). By contrast, RV39-infected PCLS derived from a donor without a history of asthma were less responsive to histamine (EC50 40nM to 200nM) with no change in response to carbachol (EC50 200nM to 180nM). **DISCUSSION/SIGNIFICANCE OF IMPACT** RV39 induced AHR in human PCLS airways derived from 1 of 4 donors previously diagnosed with asthma. AHR to histamine, but not to carbachol in a subset of 'asthmatic' airway provides insights into a potential mechanism by which viral infections and atopy could synergize to induce asthma exacerbations. Human PCLS provide an outstanding platform with which to dissect these interactions.

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### REVERSE PHARMACOGENETIC MODULATION OF THE NUCLEUS ACCUMBENS SUPPRESSES ADDICTION-RELATED BEHAVIORS

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**OBJECTIVES/SPECIFIC AIMS** Drug development for psychiatric conditions has produced no substantial improvement in efficacy over the past 40 years, largely because most psychiatric illness involves focal dysfunction in specific brain circuits, but the vast majority of drug targets are expressed widely across numerous functionally distinct brain regions, precluding specific pharmacological targeting. We propose a solution to this problem called "reverse pharmacogenetics." Unlike classical pharmacogenetics, which modifies a drug regimen to match a patient's individual genetic profile, reverse pharmacogenetics uses techniques from gene therapy to modify a patient's gene expression to respond optimally to a specific drug. In this study, we used a preclinical mouse model to evaluate the feasibility of this approach for the treatment of addiction. **METHODS/STUDY POPULATION** We first assessed the predictive validity of a limited access ethanol consumption paradigm by confirming that electrolytic lesions of the nucleus accumbens core decreased ethanol consumption, recapitulating the effects of similar lesions in humans. We then used this paradigm to test the effect of modulating activity in the nucleus accumbens using the Designed Receptors Exclusively Activated by Designer Drugs (DREADDs) hM3Dq and hM4Di. **RESULTS/ANTICIPATED RESULTS** We found that increasing activity with hM3Dq had no effect, but suppressing activity with hM4Di reduced alcohol consumption to a similar extent as lesioning without affecting consumption of water or sucrose. **DISCUSSION/SIGNIFICANCE OF IMPACT** These results may represent early steps toward a novel neurosurgical treatment modality for alcohol dependence that is reversible and externally titratable, yet highly targetable and less invasive than current approaches such as lesioning or deep brain stimulation.

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### VASCULOGENIC POTENTIAL OF ADIPOSE STROMAL CELLS IN HYPERGLYCEMIC ENVIRONMENT

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**OBJECTIVES/SPECIFIC AIMS** Adipose Stromal Cells (ASC) have been shown to play a regenerative therapeutic role in early stage diabetic retinopathy (DR), a leading cause of blindness in working-age adults. We have shown that ASC in co-cultures with human retinal endothelial cells (HREC) enhance endothelial survival and collaborate to form vascular networks. In this study we evaluated the effects of hyperglycemia on bioactivity of ASC and its ability to maintain sustained vascular networks. **METHODS/STUDY POPULATION** Human ASC expressing both pericyte and mesenchymal cell surface markers were exposed to varying doses of glucose (5.5 mM to 100 mM) for 7 days. For vascular network formation (VNF) assay, ASC were co-cultured with HREC at a 6:1 ratio. Total tube length (TTL) of the networks was assessed by MetaMorph software. Accumulation of bioactive molecules secreted into the media by ASC exposed to physiological and hyperglycemic conditions was evaluated by ELISA and confirmed by Western blotting. **RESULTS/ANTICIPATED RESULTS** ASC cultured under chronic hyperglycemic state secreted both VEGF and HGF at the same rates as those cells incubated with physiological glucose level. Similarly, vascular networks at high glucose levels were the same as observed in normal glucose cultures. Short term (6 days)

pre-treatment of ASC monolayers with 25 mM glucose did not affect their vasculogenic potency and was able to promote HREC survival to the same degree as media conditioned by ASC in control environment. **DISCUSSION/SIGNIFICANCE OF IMPACT** Our findings demonstrate that ASC have a high tolerance to hyperglycemia, suggesting that ASC could be a potential candidate for cell therapy in DR. In our future studies we will explore the significance of specific biomolecules in this vascular stabilization.

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### TARGETED DEGRADATION OF A MUTANT G-PROTEIN: TOWARD A NOVEL UVEAL MELANOMA THERAPY

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**OBJECTIVES/SPECIFIC AIMS** Uveal melanoma is the most common intraocular tumor in adults. Oncogenic mutations in the genes *GNAQ* or *GNA11*, encoding heterotrimeric G-protein α subunits $G\alpha_q$ and $G\alpha_{11}$, respectively, drive more than 80% of uveal melanomas. These mutations "lock" the proteins in the active conformation and cause constitutive mitogenic signaling. Selective removal of these oncoproteins from the cell could specifically inhibit proliferation of uveal melanoma cells. We aim to develop ligands specific for the common Q209L mutant of human $G\alpha_q$ as a first step toward targeted degradation of this oncoprotein. **METHODS/STUDY POPULATION** Peptide bacteriophage display was used to find peptide ligands selective for recombinant $G\alpha_q$ Q209L, and fluorescence polarization analysis was used to assay synthetic peptide binding to recombinant $G\alpha_q$. **RESULTS/ANTICIPATED RESULTS** Multiple phage clones were isolated that showed preferential binding to $G\alpha_q$ Q209L over wild-type protein. These sequences are being optimized and binding is being validated with synthetic peptides. The most selective binders will be incorporated into Proteolysis TArgeting Chimeras (PROTACs) to selectively degrade $G\alpha_q$ Q209L in uveal melanoma cells. **DISCUSSION/SIGNIFICANCE OF IMPACT** We have identified peptide-expressing phage that selectively bind $G\alpha_q$ Q209L. Validated PROTACs based on these sequences will remove mutant $G\alpha_q$ from cells by proteasomal degradation. This selective targeting of oncogenic $G\alpha_q$ Q209L will open an important new avenue for development of targeted therapies for uveal melanoma, a highly metastatic cancer that lacks effective drug therapies.

## T1: TRANSLATION TO HUMANS

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### FEASIBILITY OF GENOME-WIDE GENE EXPRESSION ANALYSIS (GEA) OF INFLAMMATORY BOWEL DISEASE (IBD) FORMALIN-FIXED, PARAFFIN-EMBEDDED (FFPE) MUCOSAL BIOPSY SPECIMENS

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**OBJECTIVES/SPECIFIC AIMS** Archival FFPE specimens are used as a source of genomic material for whole-genome GEA in numerous studies with variable results. We evaluate the feasibility of conducting GEA using archival FFPE mucosal biopsy specimens from patients with IBD. **METHODS/STUDY POPULATION** Fresh mucosal biopsies are obtained from 9 IBD cases undergoing surveillance endoscopy at MSSM. Each case is matched to ten (15um) sections from (1) an FFPE biopsy (collected during the same procedure), and (2) an archival biopsy taken >12 months prior. Total RNA is purified using standard protocols for fresh or FFPE tissues, respectively. Genomic content/purity is estimated by optical density, and RNA fragmentation is assessed via capillary electrophoresis. Genome-wide GEA is performed on a subset of cases using the Illumina DASL HT-12 v4 whole-genome array. Validation of individual gene expression levels is performed by qRTPCR. **RESULTS/ANTICIPATED RESULTS** Average RNA concentration obtained from each biopsy differed among fresh (212, sd 84 ng/ul), new FFPE (36, sd 13 ng/ul), and aged FFPE (27, sd 19 ng/ul). RNA integrity was uniformly high (RIN ≥7) in the fresh biopsies, and very low (RIN ≤2.0) among all the FFPE specimens. We will examine number and overlap of probes detected across matched new and aged FFPE, compared to that of fresh biopsy specimens. We will calculate the inter- and intra-individual variability in fold-change, across sample types and among technical replicates. **DISCUSSION/SIGNIFICANCE OF IMPACT** Our results will evaluate the utility of the WG-DASL assay for genome-wide expression profiling in FFPE mucosal biopsies. If feasible, these methods have the potential to allow identification of novel gene signatures associated with clinical outcomes using a large archive of IBD cases with extensive clinical and follow-up data.

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### A PILOT STUDY OF WHOLE GENOME SEQUENCING IN BACTERIAL SPECIATION AND ANTIBIOGRAM PREDICTION

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**OBJECTIVES/SPECIFIC AIMS** (1) Study the accuracy of whole genome sequencing (WGS) in bacterial speciation, in comparison with the current laboratory standards, in real time from the same clinical samples. (2) Validate the known genetic determinants for various antibiotic resistances. **METHODS/STUDY POPULATION** Under an IRB-approved protocol, we are currently collecting fresh bacterial culture samples from Scripps Central Laboratory. Sequence data is generated after DNA processing and sequencing, which is then assembled and employed to determine the pathogen species using a bioinformatics pipeline established from our previous study. We will then assess the accuracy of WGS in bacterial speciation by comparing the genomic approach to the current standards. The sensitivity and specificity of WGS in antibiogram prediction will be assessed by comparing the known genetic determinants for various antibiotic resistances to the antimicrobial resistance profiles, generated in the Phoenix Automated System. **RESULTS/ANTICIPATED RESULTS** Our previous study in whole genome sequencing of 418 clinical MRSA isolates found that only 373 (89%) samples were determined as MRSA by WGS. While it appears that WGS can provide better accuracy in speciation, errors and contamination during handling and storage can't be ruled out, considering the samples were collected retrospectively. We anticipate this prospective study will provide a better understanding of the accuracy of WGS in bacterial pathogen speciation. **DISCUSSION/SIGNIFICANCE OF IMPACT** Several recent studies have demonstrated the potency of whole genome sequencing in bacterial characterization and antibiogram prediction. However, there is still a lack of real-time studies to assess its clinical validity and our pilot study is set to accomplish this goal.

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### THE NEUROCIRCUITRY OF INFLAMMATION IN DEPRESSION

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**OBJECTIVES/SPECIFIC AIMS** Evidence suggests a cause and effect relationship between inflammatory cytokines and behavioral symptoms relevant to a number of psychiatric illnesses. Previous neuroimaging studies have demonstrated that administration of inflammatory stimuli or cytokines changes activity of basal ganglia nuclei to mediate depressive symptoms. Whether the effects of inflammation extend beyond the basal ganglia to other brain regions to contribute to specific behavioral symptoms is unknown. This study examined whether increased inflammation in depression affects functional connectivity between the basal ganglia (striatum) and other brain regions to mediate depressive and neurocognitive symptoms. **METHODS/STUDY POPULATION** Wakeful resting-state fMRI pilot data were obtained from 17 currently depressed patients with low versus high inflammation (C-reactive protein <3 versus ≥3mg/L). Seed-to-whole brain correlations were computed and compared between groups using four predefined striatal seeds. **RESULTS/ANTICIPATED RESULTS** Depressed patients with high inflammation exhibited attenuated functional connectivity between three striatal seeds and thirteen cortical or subcortical brain regions. Of these thirteen significant relationships, inflammation-related attenuation of connectivity between ventral striatum and both anterior cingulate cortex and amygdala correlated with symptoms of anhedonia and anxiety, whereas compromise of three frontostriatal circuits related to affective and cognitive processing were associated with decreased psychomotor performance. **DISCUSSION/SIGNIFICANCE OF IMPACT** Understanding inflammation-associated alterations in neurocircuitry that mediate specific depressive behaviors is important for identifying strategies to diagnose and treat behavioral symptoms in patients with increased inflammation.(IRB00039107)

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### PILOT STUDY TO ASSESS APOLIPOPROTEIN C-III REDUCTION VIA COLCHICINE

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**OBJECTIVES/SPECIFIC AIMS** (1) Prospective cohort study of low-dose colchicine in patients with gout, pericarditis, or history of hypertriglyceridemia to assess reduction of apolipoprotein C-III (apoC-III), very low density lipoprotein (VLDL), and triglycerides (TG); to establish more accurate effect size (*d*) (2) Assess secondary endpoints for changes in apolipoprotein A-I (apoA-I), apolipoprotein B (apoB), high density lipoprotein (HDL), low density lipoprotein (LDL), and total cholesterol (TC). **METHODS/STUDY POPULATION** Our IRB-approved protocol involves an enrollment strategy with two approaches: (1) patients with gout or pericarditis (both acute or recurrent) (2) if after 3 weeks of enrollment our $n \leq 10$ subjects, we will enroll patients from a Lipid Registry with history of hypertriglyceridemia (TG ≥ 150 mg/dL) and administer colchicine in off-label fashion. Baseline vertical auto profile panel (VAP) along with serum for apoC-III testing will be performed before colchicine administration. After 6 weeks of colchicine (0.6 - 1.2 mg/day), we will reanalyze same labs. We will assess % reduction of TG, VLDL, and apoC-III levels, along with analysis of secondary endpoints. **RESULTS/ANTICIPATED RESULTS** In our laboratory, we have observed a 60% reduction of

apoC-III *in vitro* using colchicine ($IC_{50}$ = 6–7 nM) against a hepatocellular carcinoma cell line. We anticipate that *d* of colchicine in humans may be less than 60% and may only be clinically significant above 30%. **DISCUSSION/SIGNIFICANCE OF IMPACT** The association between hypertriglyceridemia and cardiovascular disease is known but how TG levels ultimately lead to cardiovascular outcomes is a subject of continued debate. We look to illustrate a new lipid lowering strategy with colchicine and translational studies look to identify new therapeutic targets of lipid metabolism.

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### CHARACTERIZATION OF P450 ENZYMES INVOLVED IN TRIMETHOPRIM PRIMARY METABOLITE FORMATION

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**OBJECTIVES/SPECIFIC AIMS** Trimethoprim-sulfamethoxazole (TMP-SMX) is an antibiotic associated with idiosyncratic adverse drug reactions (IADRs). These IADRs are believed to result from an immune response to reactive metabolites (RMs). Recently, TMP metabolite-NAC adducts have been identified in urine of children taking TMP-SMX. TMP RMs are believed to form through direct oxidation to an imino-quinone methide and via conversion of a primary metabolite, 4-desmethyl-TMP, followed by oxidation to a quinone methide. *In vitro* data suggest that TMP bioactivation is catalyzed by cytochrome P450 enzymes (CYPs), although specific enzymes have not been identified. Thus, we set out to identify the CYPs involved in TMP 4-demethylation as well as those CYPs involved in the formation of additional stable, primary metabolites. **METHODS/STUDY POPULATION** Human liver microsomes (HLMs, $n$ = 16) characterized for CYP activity were incubated with TMP (5 μM). Rates of TMP formation were plotted against marker CYP rates and evaluated by linear regression. Rates of TMP primary metabolite formation were also determined in recombinant CYPs to assess the ability of individual CYPs to catalyze formation of TMP metabolites. **RESULTS/ANTICIPATED RESULTS** Rates of 4-desmethyl-TMP formation in HLMs correlated with CYPs 2C8 ($r^2$ = 0.87) and 2C9 ($r^2$ = 0.50), however virtually all recombinant CYPs catalyzed formation of 4-desmethyl-TMP to some extent. Rates of formation for the stable metabolites, Cα-OH-TMP and TMP 1-N-oxide, correlated strongly with CYP3A4/5 enzyme activity ($r^2$ = 0.94) in HLMs and with the recombinant enzymes. **DISCUSSION/SIGNIFICANCE OF IMPACT** Our *in vitro* data identify CYPs 2C8 and 2C9 as significant contributors to the formation of 4-desmethyl-TMP. Further studies characterizing the roles of CYPs in other steps leading to TMP RM formation are required to estimate the impact of CYP variability on TMP bioactivation *in vivo*.

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### METABOLOMICS COMPARISON OF IRRADIATED AND NONIRRADIATED STORED DONOR RED BLOOD CELLS

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**OBJECTIVES/SPECIFIC AIMS** To investigate the changes in the patterns of metabolites that occur during donor red blood cell (RBC) storage with and without preceding gamma irradiation. **METHODS/STUDY POPULATION** CPDA-1 RBC units from 6 volunteer human donors were split into 2 bags on the day of collection. One of each pair of bags was irradiated with 25Gy. RBC units were serially sampled over 35 days (d) of storage, and metabolites were identified and quantified using a Fourier Transform Mass Spectrometer. Discriminatory metabolites within and between samples were identified using multilevel sparse partial least squares discriminant analysis (msPLSDA) approach in R. Patterns of the top 600 most discriminatory metabolites were compared using score plots and hierarchical clustering. Candidate metabolites were further evaluated by pathway enrichment analysis using a false discovery rate of 5%. **RESULTS/ANTICIPATED RESULTS** In principal component analysis, a distinct separation was noted in samples stored ≤7 d and samples stored >7 d. Among donor RBCs stored from 2 to 7 d, irradiated and nonirradiated samples clustered together. By contrast, donor RBCs stored ≥10 d demonstrated a distinct separation of metabolites between irradiated and nonirradiated samples as well as by the duration of storage. In hierarchical clustering analysis, similar patterns between stored and irradiated samples were seen. Significant differences among samples were noted in four candidate pathways, including those involved in arachidonic acid ($p$ = 3.3 E-33) and linoleic acid ($p$ = 1.61 E-11) metabolism. **DISCUSSION/SIGNIFICANCE OF IMPACT** Metabolomic characteristics differ between fresh and stored blood and gamma irradiation accentuates these differences as the age of blood increases. Metabolites involved in the cellular membrane may be important biomarkers of the RBC storage lesion.

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### COMPARISON OF TIME-RESTRICTED FEEDING VERSUS GRAZING TO IMPROVE GLUCOSE TOLERANCE, VASCULAR FUNCTION, AND INFLAMMATION

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**OBJECTIVES/SPECIFIC AIMS** Time-restricted feeding (TRF), which involves eating early in the day followed by a daily 15–20 hour fast, has recently emerged as a promising intervention to combat diabetes and obesity. In rodents, TRF improves glucose tolerance, reduces inflammation and weight gain, and preserves β–cell mass better than calorie-matched grazing. We will conduct the first pilot study of TRF in humans in order to test the hypothesis that TRF improves glucose homeostasis, vascular function, and inflammation better than grazing. **METHODS/STUDY POPULATION** In this crossover pilot study, 8 obese men (BMI 30–50 kg/m$^2$) aged 30–65 years old with prediabetes will be randomized to either 5 weeks of TRF or grazing, followed by a 7-week washout period, and then 5 weeks of the other eating schedule. Calories and meal frequency will be matched in each arm, but the TRF arm will involve eating all meals within about 6 hours starting in the morning (18-hour daily fast) versus 12 hours (12-hour fast) for the grazing arm. Before and after each arm, glucose homeostasis will be measured by an OGTT and vascular function will be assessed via applanation tonometry and orthogonal polarization spectroscopy. Markers of inflammation will also be measured. **RESULTS/ANTICIPATED RESULTS** We anticipate that TRF will improve glucose homeostasis and reduce inflammation better than grazing, but that vascular condition may or may not change within the short timeframe for this pilot study. **DISCUSSION/SIGNIFICANCE OF IMPACT** If successful, this study may provide novel insight into the role of meal timing in health and may lead to a new lifestyle intervention to reduce diabetes risk. Moreover, this study may help overturn the common wisdom that grazing is good for health.

## T2: TRANSLATION TO PATIENTS

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### PATIENT-CENTERED OUTCOMES IN OLDER ADULTS WITH EPILEPSY

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**OBJECTIVES/SPECIFIC AIMS** Persons 60 and older have the highest incidence of epilepsy. There is a lack of self-management interventions for this population. While interventions exist for younger adults, the uniqueness of older adults may make existing interventions less effective for older adults. There is a need for development of patient-centered self-management interventions for older adults with epilepsy. In order to build such interventions, outcomes important to older adults with epilepsy must be described. The purpose of this study was to describe, from the perspective of older adults with epilepsy, self-management outcomes. **METHODS/STUDY POPULATION** Qualitative description was used. Older adults with epilepsy were recruited via purposive sampling. Each engaged in a semistructured interview. Interviews were analyzed via content analysis. **RESULTS/ANTICIPATED RESULTS** 20 older adults participated. Six themes emerged. Themes included Maintaining Normalcy, We Want to be Involved, Well-Equipped, Seizure Freedom, Fitting Epilepsy in with Other Conditions, and Incongruence with Provider Goals. **DISCUSSION/SIGNIFICANCE OF IMPACT** Members of this sample are chiefly concerned with maintaining normalcy. These results go beyond existing literature by describing precise ways in which older adults with epilepsy hope to attain outcomes. Few participants noted the desire to achieve seizure freedom. Results also indicate that older adults desire to become involved in treatment decisions. Also, participants desire to more easily manage multiple diseases. Finally, this sample noted that their epilepsy care providers are not aware of their self-management goals, and that providers' goals are incongruent with theirs. Interventions for this population need to be individualized to meet older adults' goals. Given the rift between participants' and providers' goals, interventions may also need to include a component assisting older adults with patient–provider communication.

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### IMPACT OF JAUNDICE ON ADULTS WITH SICKLE CELL ANEMIA

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**OBJECTIVES/SPECIFIC AIMS** Jaundice, yellow discoloration of the skin and mucous membranes, may be the most visible manifestation of disease in sickle cell anemia (SCA). The impact of jaundice on the daily lives of patients with SCA has not been reported. This study aims to assess the effect of jaundice on the health-related quality of life (HRQOL) of adults living with SCA. **METHODS/STUDY POPULATION** This study was an IRB-approved cross-sectional 15 question survey of adult patients with SCA from a convenience sample. The survey was divided into three subscales (personal, relational, and behavioral) where items were presented in a 5-point Likert scale. Additional data collected included serum total bilirubin (TB), hemoglobin, reticulocyte count (%) and self-report of current treatment for SCA (hydroxyurea [HU], chronic blood transfusions, or other). We tested for associations between survey subscales and TB, reticulocyte count, or hemoglobin. **RESULTS/ANTICIPATED RESULTS** We surveyed 100 subjects (58% female) with SCA. The median age was 25 years (range: 18–63), and the median TB was 2.5 mg/dL (range: 0.4–13.8). TB positively correlated with the 3 subscales. We compared these correlations between 'treatment' and 'no treatment' groups and observed strong correlations in the 'no treatment' group (personal, $r$ = 0.55, $p$ < 0.0001; relational, $r$ = 0.63,

$p < 0.0001$; behavioral, $r = 0.52$, $p = 0.0002$). **DISCUSSION/SIGNIFICANCE OF IMPACT** Jaundice negatively impacts the lives of many adults with SCA and appears to be mitigated by disease-modifying therapies. Our study results suggest jaundice should be represented in HRQOL assessment tools in adults with SCA. Prospective studies are needed to clarify potential benefits of disease-modifying therapies, particularly HU, on the burden of jaundice in SCA. This work was conducted with support from Center for Translational Medicine, NIH/NCATS Grant Number KL2TR001103. Content is the sole responsibility of the authors.

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### *IN VITRO* VIRUS DETECTION USING VOLATILE GAS ANALYSIS

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**OBJECTIVES/SPECIFIC AIMS** Viral respiratory tract infections cause morbidity in asthma and COPD. Early diagnosis may improve outcomes. Volatile organic compound (VOC) analysis has potential for rapid, early, and noninvasive diagnosis. Our goal was to determine if VOCs emitted from cultured primary tracheobronchial epithelial (TBE) cells distinguish between cells infected with human rhinovirus (HRV) and control cells. **METHODS/STUDY POPULATION** Primary TBE cells were collected from a single explanted trachea and grown in multiple cultures. Half the cells were infected with HRV 1B, MOI 1. Headspace VOCs were sampled with solid-phase microextraction (SPME) fibers at 12-, 24-, and 48-hours and analyzed on gas chromatography / mass spectrometry (GC/MS). Cell viability was measured. Student's t-test was used to identify pooled VOC differences between the healthy and HRV-infected cells. Relevant VOCs were identified using a NIST database. **RESULTS/ANTICIPATED RESULTS** Many similar VOCs were seen in all cell groups; however, unique VOCs were seen in the HRV group compared to controls at each time point ($n = 5$ VOCs at 12-h; $n = 2$ at 24-h; and $n = 9$ at 48-h). These were products of oxidative stress: long-chain hydrocarbons, aldehydes, ketones, and esters. All cells remained alive as confirmed by light microscopy and Alamar blue stains. **DISCUSSION/SIGNIFICANCE OF IMPACT** This is one of the first studies to show that VOC emanations differ between control and HRV-infected TBE cells. Unique and low-concentration VOCs (parts-per-billion) can be used to determine if a TBE cell is infected with HRV. Future studies will evaluate this method to identify early viral infections, including other important respiratory viruses (e.g. influenza), *in vivo*.

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### IMPAIRED NEURAL FUNCTIONING FOLLOWING INTERNALLY FOCUSED COGNITION IN OBSESSIVE-COMPULSIVE DISORDER

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**OBJECTIVES/SPECIFIC AIMS** Obsessive-compulsive disorder is associated with excessive absorption in distressing thought or images, which may be due to an inability to disengage from an internally focused (IF) cognitive state. IF cognition is linked to the "default mode network" (DMN), a large-scale brain system that is hyperactive in OCD. Externally focused (EF) cognition, by contrast, is subserved by a fronto-parietal network (FPN) involved in acting on information in the environment. We previously reported reductions of FPN during target detection (TD) when it follows an IF task compared to an EF task. This suggests that excessive IF in OCD may impact patients' subsequent FPN functioning. To test this hypothesis, we examined associations between brain activity during TD and prior cognitive state in patients with OCD and controls. **METHODS/STUDY POPULATION** fMRI data were obtained from 12 healthy individuals and 13 OCD patients. Subjects imagined personal event scenarios that were positive or negative (IF condition) or performed a Stroop task (EF condition) for 12–18s before switching to a target detection (TD) task requiring attention to external information (15s). **RESULTS/ANTICIPATED RESULTS** OCD patients made more errors during TD blocks after imagining negative personal scenarios (negative IF) than controls. On these same blocks, OCD patients showed less activity in FPN and increased activation in DMN. These group differences were not found for other TD block types. **DISCUSSION/SIGNIFICANCE OF IMPACT** OCD may involve a deficit in the ability to recruit FPN regions that are required for redirection of attention away from negative internal states.

## T3: TRANSLATION TO PATIENTS

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### CAN CAROTID PLAQUE THICKNESS MEASUREMENTS PREDICT SYMPTOMATIC DISEASE IN HIGH GRADE CAROTID ARTERY STENOSIS?

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**OBJECTIVES/SPECIFIC AIMS** There has been renewed interest in evaluating imaging techniques for risk stratification beyond luminal stenosis severity in carotid atherosclerotic disease. We correlated recently proposed CT markers, soft and hard plaque thickness measurements on axial CTA source images, with symptomatic disease status in high-grade carotid disease. **METHODS/STUDY POPULATION** Soft plaque and hard plaque thickness were measured using a recently validated technique using CTA source images in subjects with ≥70% extracranial carotid artery stenosis. We used multiple logistic regression analysis to measure the strength of association between each 1 mm increase of soft plaque thickness and symptomatic disease status while controlling for the percent degree of NASCET stenosis and any additional covariate risk factors found to be statistically significant. **RESULTS/ANTICIPATED RESULTS** A total of 42 of 76 subjects meeting inclusion criteria had symptomatic carotid disease. Compared to asymptomatic subjects, those with symptomatic carotid disease had significantly larger soft plaque and total plaque thickness measurements and smaller hard plaque thickness measurements. For every 1 mm increase in maximum soft plaque thickness, there was approximately a 2.7 times greater likelihood (OR = 2.7) of prior ipsilateral stroke or TIA ($p < 0.0001$). Conversely, for each 1 mm increase in hard plaque thickness, there was 45% (OR = 0.55) decreased likelihood of prior ipsilateral stroke or TIA ($p = 0.007$). **DISCUSSION/SIGNIFICANCE OF IMPACT** Increasing maximum soft plaque thickness measurements are strongly associated with symptomatic disease status in carotid artery stenosis, a finding which may translate into a widely accessible stroke risk stratification tool in high-grade carotid artery atherosclerotic disease.

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### NEURAL CORRELATES OF RUMINATION AMONG ADOLESCENTS WITH A HISTORY OF DEPRESSION

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**OBJECTIVES/SPECIFIC AIMS** Studies of depressed adult populations suggest rumination is associated with increased activation in medial regions of the brain including the anterior and posterior cingulate cortexes (ACC and PCC respectively). To date, no studies have examined the neural correlates of rumination among remitted adolescents. **METHODS/STUDY POPULATION** Eleven adolescents (7 female) with major depressive disorder in full or partial remission ages 15–18 (M = 16.64, SD = 1.21) participated in an fMRI scan. Approximately one week before the scan date participants were asked to generate four personal sad memories. During the fMRI scan, participants were reminded of each memory and subsequently presented with rumination or distraction prompts in four event-related jittered blocks followed by visual analogue scale (VAS) measures of rumination and sadness. **RESULTS/ANTICIPATED RESULTS** VAS measures of sadness and rumination verified that adolescents thought about their feelings more during rumination blocks compared to distraction blocks ($t = 4.68$, $p < .01$) and reported greater sadness following rumination ($t = 7.2$, $p < .01$). Rumination resulted in greater activation in medial regions including the PCC, cingulate, and thalamus, as well as the ACC and superior medial gyrus when compared with distraction. Rumination induction also led to greater activation in the inferior frontal gyrus and the medial temporal gyrus. **DISCUSSION/SIGNIFICANCE OF IMPACT** These findings demonstrate that inducing rumination within the scanner is feasible among adolescent populations and that, similar to adults, youth activate medial regions when ruminating. Future research will examine whether rumination-focused interventions can modulate brain networks supporting rumination, decreasing risk for depressive relapse.

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### THE YOUNG CHILD BRIEF BEHAVIORAL SCREEN: PRELIMINARY RESULTS

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**OBJECTIVES/SPECIFIC AIMS** Early identification of disruptive behavior problems is required to reduce the serious long-term consequences of this public health problem. Accurate brief screening methods could improve low rates of physician recognition of young children with behavioral issues. Preliminary results are reported of an ongoing validation study of a new screening tool, the 7-item parent-report Young Child Brief Behavioral Screen (YCBBS). **METHODS/STUDY POPULATION** Parents ($n = 98$) of children ages 3–5 seen at a university pediatric primary care clinic completed the YCBBS at baseline and at 2-week follow up and rated its acceptability. Physicians ($n = 27$) in the same clinic also rated acceptability of the YCBBS in practice. Preliminary descriptive and psychometric analyses are reported. **RESULTS/ANTICIPATED RESULTS** Internal consistency of the YCBBS was .78. Test-retest reliability was high ($\rho = .78$, $p < 0.001$). Baseline YCBBS scores were significantly higher among parents who believed their child has emotional or behavioral problems (M = 4.80, SD = 3.05) compared to those who did not (M = 2.74, SD = 2.33), $t(35.168) = 3.05$, $p < 0.01$. Most parents agreed/strongly agreed that the YCBBS was short enough for use during their child's appointment (86%), that it would be a good idea for their child's doctor to ask these questions (77%), and

that primary care would be a good place to ask these questions (88%). Most physicians agreed/strongly agreed that the YCBBS was short enough for use in primary care (100%), that primary care is an appropriate venue for this tool (96%), and that they would use this tool in their own practice (74%). **DISCUSSION/SIGNIFICANCE OF IMPACT** Parents and physicians are still being enrolled in this study. Early results of the psychometric properties of the YCBBS are promising. Future analyses will examine construct and criterion-related validity to determine its potential utility in early identification of young children with behavior problems.

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## QUANTITATIVE MELANOMA SCREENING BY OPTICAL IMAGING

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**OBJECTIVES/SPECIFIC AIMS** This pilot study aims to determine the dependence of diagnostic precision on wavelength. It remains to be elucidated whether the morphological aspects of disease as manifest in the ultraviolet, visible or near-infrared spectrum has any bearing on diagnosis. **METHODS/STUDY POPULATION** We developed 30 computer-vision metrics on Red/Green/Blue dermoscopic images of melanomas and nevi. 12 classification algorithms (i.e., neural networks, linear discriminant analysis) were trained on 88 lesions and tested on 32 lesions in a test set of 60 melanomas and 60 nevi. The choice of the training and test sets was random and repeated ten times. We calculated the diagnostic sensitivity and specificity for each classification algorithm for each wavelength (i.e. red, green or blue). **RESULTS/ANTICIPATED RESULTS** 17 of the metrics (such as the variance of pigmented network branch lengths and brightness) were significant discriminators, having higher values ($p < 0.05$) for melanomas versus dysplastic nevi with mild to moderate dysplasia. Surprisingly, the metric measuring boarder asymmetry (i.e, degree of symmetry of the silhouette of the lesion), proved to be ineffective at differentiating melanoma from nevi ($p = 0.84$). Overall, the blue channel yielded the best diagnostic accuracy and the red channel yielded the poorest diagnostic accuracy. **DISCUSSION/SIGNIFICANCE OF IMPACT** The 2 main findings of this study were (1) border asymmetry of a lesion provided little diagnostic value, (2) while imaging in the near-infrared spectral range provides little diagnostic value, imaging in the blue light spectral range provides significant discriminating power. Ongoing work aims to further investigate these preliminary findings.

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## POSTTRAUMATIC STRESS DISORDER IN INTENSIVE CARE UNIT SURVIVORS: A META-ANALYSIS

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**OBJECTIVES/SPECIFIC AIMS** To conduct a systematic review and meta-analysis of prevalence, risk factors, and prevention/treatment strategies for posttraumatic stress disorder (PTSD) symptoms in intensive care unit (ICU) survivors. **METHODS/STUDY POPULATION** We searched PubMed, Embase, CINAHL, Psyc INFO, and Cochrane Library through July 15, 2012 for studies including: (1) adult general ICU survivors, (2) validated PTSD instruments ≥1 month post-ICU, and (3) ≥10 patients with substantial PTSD symptoms. **RESULTS/ANTICIPATED RESULTS** The search identified 3,243 titles/abstracts, with 28 eligible articles (25 unique cohorts; $n = 3,428$). Between 1–6 months post-ICU (5 studies; $n = 429$), the pooled mean [95% CI] Impact of Events Scale (IES) score was 19 [16–22], and the pooled prevalences of clinically important PTSD symptoms [95% CI] were 23% [17–29] and 42% [33–51] using thresholds ≥35 and ≥20. Between 7–12 months post-ICU (5 studies; $n = 698$), the pooled mean IES score was 17 [9–24], and pooled prevalences of PTSD symptoms were 17% [10–26] and 34% [22–50]. ICU risk factors for PTSD symptoms included benzodiazepines and memories of frightening ICU experiences. PTSD symptoms were associated with worse quality of life. In European studies: (1) an ICU diary was associated with a significant reduction in PTSD symptoms; (2) a rehabilitation manual was associated with significant symptom reduction at 2 months but not 6 months; and (3) a nurse-led ICU follow-up clinic did not reduce PTSD symptoms. **DISCUSSION/SIGNIFICANCE OF IMPACT** Clinically important PTSD symptoms occurred in 1/4 of ICU survivors 1-year post-ICU, with higher prevalence in those who were young, had comorbid psychopathology, received benzodiazepines, and recalled frightening ICU experiences. In European studies, ICU diaries reduced PTSD symptoms.

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## COOLING OF LIMBS: A COOL THERAPY FOR TREATMENT OF ESSENTIAL TREMOR

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**OBJECTIVES/SPECIFIC AIMS** Standard treatment for essential tremor (ET) is oral medications but many patients show lack of efficacy or develop side effects. Nonpharmacological therapy such as cooling of limbs is promising but only three small scale studies have been conducted. This study aimed to determine the therapeutic effects of limb cooling in a large cohort of essential tremor patients. **METHODS/STUDY POPULATION** ET patients with partial response to medications were enrolled. Demographics and scores on Fahn-Tolosa-Marin Tremor Rating Scale (TRS) were obtained. Dominant arm was cooled to a desired temperature of 59°F achieved with application of icepack to the ventral and dorsal surface of forearm for a period of 10 minutes. Handwriting tests before and immediately after cooling were scored by a blinded rater. Tests included determination of pen control, writing legibility and performance on line drawing test (LDT). Pen control was assessed by ability to draw as many dots as possible over 5 seconds within a predefined circle. For LDT, subjects were asked to draw as many horizontal lines as possible between two predefined vertical lines on a sheet of paper over 20 seconds. **RESULTS/ANTICIPATED RESULTS** 42 patients with mean age 69.1 years and mean disease duration 10.5 years were enrolled. Mean total score on TRS was 40.6. Mean score for dominant arm (average of rest, posture and intention arm motor item) was 2.6. Objective assessment found improvement in pen control and handwriting legibility. LDT scores before cooling (mean 0.93) on a paired t-test showed significant improvements ($p = 0.04$) from those after cooling (mean 0.61). **DISCUSSION/SIGNIFICANCE OF IMPACT** In this large cohort of ET, preliminary evidence shows limb cooling is beneficial. We plan to conduct a randomized controlled blinded study in conjunction with physiological evaluation for further elucidation.

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## EXPERT HEURISTIC EVALUATION OF ONLINE COPDFLIX PATIENT EDUCATION CENTER

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**OBJECTIVES/SPECIFIC AIMS** Because of limited access to hospital-based pulmonary rehabilitation, patients with chronic obstructive pulmonary disease (COPD) are rarely provided with adequate patient education materials. To improve the quality of COPD patient education, we are developing and testing the usability of a novel social media resource center for respiratory therapy videos called "COPDFlix". **METHODS/STUDY POPULATION** A heuristic evaluation was conducted as part of a larger study to determine whether our COPDFlix prototype adhered to recognized Website usability guidelines for older adults. A purposive sample of 3 health IT experts evaluated COPDFlix against 18 heuristics in 4 usability categories (interaction and navigation; information architecture; presentation design, & information design). Experts rated 76 subcriteria across these categories using 4-point scales (1 = "no problem" or satisfies the heuristic; 2 = "minor hindrance" or possible issue that will probably not hinder the user; 3 = "serious problem" that may hinder the user; or 4 = "task failure" preventing the user from going forward). Experts also provided explanatory qualitative comments for each subcriteria rating. **RESULTS/ANTICIPATED RESULTS** Evaluators rated the majority of heuristic subcriteria as either a "minor hindrance" (14%) or "no problem" (57.9%); however, 61 usability violations were identified across the 18 heuristics. Only 2 of the 18 heuristic categories were rated as "major" violations with mean severity scores ≥3. **DISCUSSION/SIGNIFICANCE OF IMPACT** Quantitative severity ratings with qualitative technical feedback from experts helped to prioritize usability problems and design solutions within the COPDFlix prototype. Of the 61 violations identified, 52 (85.2%) were addressed during the Web modification process, leading to 26 total design modifications.

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## CLASSIFYING PATIENT STATEMENTS ABOUT UNCONTROLLED PAIN IN PRIMARY CARE

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**OBJECTIVES/SPECIFIC AIMS** To characterize how primary care patients discuss uncontrolled pain and opioids during primary care visits. **METHODS/STUDY POPULATION** We reviewed transcripts of routine primary care visits recorded as part of a clinical trial comparing interventions to facilitate discussion of depression symptoms in a general primary care population. First, we reviewed transcripts to identify patients on chronic opioids (taking at least 1 opioid/day for >90 days). Second, we iteratively reviewed transcripts to develop and apply a coding system to identify strategies patients used to express poorly controlled pain. Our final coding system was adapted from Street's system for coding patient participation and comprised 4 types of patient statements: *concerns* (statements expressing negative emotions about pain), *questions*, *requests for action* (e.g. referral) and *assertive statements*. **RESULTS/ANTICIPATED RESULTS** We identified 26 eligible transcripts (mean age 53.6; 38% female). Patient concerns were the most common statement type ($n = 84$, 55%) followed by questions ($n = 32$, 21%), requests for action ($n = 22$, 14%), and assertive statements ($n = 16$,

10%). Statement topics were classified as follows: general pain and suffering ($n$ = 43, 28%); pain-related functional impairment ($n$ = 31, 20%); nonopioid pain treatments ($n$ = 44, 29%); opioids ($n$ = 29, 44%); and diagnostic uncertainty ($n$ = 7, 5%). All but one patient request for opioid prescriptions involved refills of existing opioid prescriptions. No direct requests for higher opioid doses were observed. **DISCUSSION/SIGNIFICANCE OF IMPACT** Patients were more likely to mention uncontrolled pain indirectly rather than make direct requests. Statements about opioids comprised a minority of all patient statements. Contrary to conventional wisdom, direct patient requests for higher opioid doses appear uncommon in routine primary care visits involving patients on opioids for chronic pain.

## T4: TRANSLATION TO POPULATION

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### A PROPOSED RISK-BASED DEFINITION OF SMALL FOR GESTATIONAL AGE

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**OBJECTIVES/SPECIFIC AIMS** Customized fetal growth curves have been proposed which characterize "term-optimal weight" based on maternal demographic factors, and the relationship between small-for-gestational-age (as defined by low percentiles on these curves) and adverse neonatal outcomes has been shown to be stronger than population-based models. These standards exclude pathological factors such as smoking, hypertension and diabetes, though subsequent analyses have incorporated these factors and estimated their associations with outcome. We propose an alternative approach which simultaneously predicts expected week of delivery, birth weight, and risk of neonatal outcomes based on potentially incomplete data on maternal characteristics. This one-step modeling approach is used to define functions mapping birth weight to the risk of each outcome, specific to each week of delivery. **METHODS/STUDY POPULATION** A Bayesian network (BN) which expressed the assumed causal relationships among predictors and outcomes (i.e., nodes and directed edges) was prespecified based on prior literature. The probability distribution for each node in a BN is defined conditional on only its parent nodes. Conditional distributions were fit using 1 million randomly selected records from the 2005 NCHS Linked Birth Data Files. **RESULTS/ANTICIPATED RESULTS** Variance in birth weight was reduced most by knowledge of week of delivery (26.1%), plurality (8.4%), and adequacy of prenatal care (2.1%). For singleton births, estimated probability of NICU admission was minimized for birth weights between 3000–4000 g; increased risk was observed for deliveries of ≤37 weeks gestation but still <10% when birth weight was between 3000–4500 g. **DISCUSSION/SIGNIFICANCE OF IMPACT** Our model can be used to define risk-based thresholds for small-for-gestational-age given week of delivery. Further development with richer databases is planned.

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### UNDERSTANDING THE RELATIONSHIP BETWEEN PREGNANCY INTENTION AND PRETERM BIRTH

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**OBJECTIVES/SPECIFIC AIMS** (1) To assess the relationship between unintended pregnancy, maternal depression, maternal anxiety disorders and preterm birth. (2) To examine the relationship between unintended pregnancy, preterm birth, other maternal psychiatric symptoms, such as perceived stress, and social support. **METHODS/STUDY POPULATION** I am performing a secondary analysis of a prospective cohort of 2654 pregnant women (37% unintended pregnancy) in Connecticut and Massachusetts interviewed before 17 weeks and at 28 weeks gestation, and 8 weeks postpartum. Using descriptive statistics, bivariate analysis, and multivariable logistic regression techniques, I am assessing the effect of pregnancy intention on preterm birth and exploring whether any effect is mediated by depression and/or anxiety, or moderated by socioeconomic and biological factors such as stress and social support. **RESULTS/ANTICIPATED RESULTS** Preliminary bivariate analyses suggest that unintended pregnancies are more likely to result in preterm births ($p$ = 0.019), are associated with major depressive disorder before ($p$ = 0.00) or during pregnancy ($p$ = 0.00), general anxiety disorder before ($p$ = 0.00) or during pregnancy ($p$ = 0.00), panic disorder before ($p$ = 0.01) or during pregnancy ($p$ = 0.00), and posttraumatic stress disorder before pregnancy ($p$ = 0.01). Women with unintended pregnancies are also more likely to smoke cigarettes during the pregnancy ($p$ = 0.00), use illicit substances ($p$ = 0.00), and to report prior sexual abuse ($p$ = 0.00), including abuse before age 18 ($p$ = 0.00). Data analysis is ongoing. **DISCUSSION/SIGNIFICANCE OF IMPACT** Despite the public health significance, solid prospective data on the relationship between unintended pregnancy, depression and the risk of preterm birth is lacking. Understanding this relationship is crucial because interventions targeting the modifiable risk factors of unintended pregnancy and/or depression may be developed and implemented to decrease preterm birth.

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### COMPARISON OF PSYCHOMETRIC CHARACTERISTICS OF SPANISH WORD RECOGNITION TESTS

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**OBJECTIVES/SPECIFIC AIMS** About 40% of older adults have hearing loss. Word recognition measures are used in the routine audiological test battery to evaluate communication difficulties, conduct differential diagnosis of auditory pathologies, and determine candidacy for amplification, implantation, and assistive technology. In English, the type of words used for speech recognition testing is well established. In Spanish, however, the most appropriate type of words is yet to be established. In order to effectively manage Hispanic patients with hearing loss, it is imperative to determine the appropriateness of the types of Spanish words (mono-, bi-, or tri-syllable) that should be used for word recognition testing. Research on Spanish speech recognition tests was mostly done over 30 years ago, where methodological issues related to inadequacy of speech recordings were consistently highlighted. The aims of the current project, guided by the previous research, are to develop digital recordings of six Spanish word lists and to use the recordings to obtain and compare psychometric data from listeners with normal hearing. **METHODS/STUDY POPULATION** Six word lists that include the three syllabic types of Spanish words will be digitally recorded using a single speaker. Psychometric functions for each word will be obtained for 24 listeners with normal hearing. **RESULTS/ANTICIPATED RESULTS** Significant performance differences among the three syllabic types of Spanish words are anticipated. **DISCUSSION/SIGNIFICANCE OF IMPACT** The results will be used to establish homogeneous word lists for use in the evaluation of Hispanic patients with hearing impairment. The inclusion of standardized clinical word recognition protocols into best practice models will ultimately improve quality of care, diagnosis, prognosis, and rehabilitation efforts.

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### CONSTRUCT VALIDITY OF THE ADHD RATING SCALE-IV IN HIV-EXPOSED UGANDAN CHILDREN

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**OBJECTIVES/SPECIFIC AIMS** Few studies have examined ADHD—the paradigmatic clinical neurocognitive disorder of childhood—in sub-Saharan Africa (SSA) where risk factors for neurocognitive delay are prevalent. This study aimed to evaluate the construct validity of the ADHD Rating Scale-IV (ADHD-RS-IV) in a group of Ugandan children. **METHODS/STUDY POPULATION** Neuropsychological and demographic data were collected in a nonclinical sample of children born to HIV-infected mothers. Internal consistency of the ADHD-RS-IV was assessed with Cronbach's alpha. Construct validity was assessed via exploratory factor analysis (EFA); tests of convergent validity (correlation with executive function (BRIEF) and TOVA ADHD score); and divergent validity (correlation with KABC-II Mental Processing Index (MPI)). **RESULTS/ANTICIPATED RESULTS** 179 children (54% female; mean age 7.8 yrs (SD 2.0)) were assessed for ADHD in 2013. The mean score on the ADHD-RS-IV was 12.7 (SD 8.6). Using DSM-IV symptom criteria cutoffs, the point prevalence of ADHD was 6.7%. The ADHD-RS-IV showed good internal consistency (alpha = 0.80.) EFA suggested a one-factor solution (Eigenvalues: F-1 = 4.44, F-2 = 0.63) explaining 81% of the variance. ADHD symptom scores were strongly correlated with the BRIEF ($p$ < 0.001) and poorly correlated with the KABC-II MPI ($p$ = 0.11) and TOVA ADHD Score ($p$ = 0.43). **DISCUSSION/SIGNIFICANCE OF IMPACT** The ADHD-RS-IV demonstrated good internal consistency, a unitary factor structure, and good convergent validity with measures of executive function, but not with visual performance tasks among Ugandan HIV-exposed children. The one-factor solution differs from international reference samples and raises questions about the validity and transferability of the ADHD construct in SSA.

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### RETROSPECTIVE COHORT OF CHILDREN WITH POSITIVE CYSTIC FIBROSIS NEWBORN SCREEN

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**OBJECTIVES/SPECIFIC AIMS** This study evaluates phenotype prediction based on CFTR genotypes identified by the 3-step California (CA) model: Immunoreactive trypsinogen, CFTR mutation panel, and CFTR DNA sequencing (unique to CA). **Hypothesis**: Among children with a positive NBS for CF, those carrying one CF-causing mutation plus a variant identified by sequencing are at decreased risk for classic CF phenotype compared to those carrying two CF-causing mutations during the first five years of life. **METHODS/STUDY POPULATION** Data from the CA Department of

Public Health for all children with a positive NBS for CF from 2007–2011 was used and grouped into 2 cohorts: Group 1 (G1) children carrying two known CF-causing mutations (panel or sequenced), and Group 2 (G2) children with one CF-causing and any other CFTR mutation (sequenced); all followed for 2–6 years. **RESULTS/ANTICIPATED RESULTS** 668 children were included (G1 = 220,G2 = 448). G2 children were at decreased risk of early classic CF compared to those from G1 based on sweat test results (≥60mEq/L in G2 9% vs. G1 90%, $p < 0.0001$), pancreatic insufficiency proportion (G2 6% vs. G1 72%, $p < 0.0001$), growth (weight for length Z score, $p < 0001$), and *Pseudomonas aeruginosa* infection free probability (G2 92% vs. G1 81%; Log-rank test $p < 0.0001$). **DISCUSSION/SIGNIFICANCE OF IMPACT** While CF-causing mutations identified by the California 40-panel and sequencing were significantly associated with early classic CF phenotype, the prognosis for those with one CF-causing and atypical variant detected by sequencing is unclear. Applying multivariate and hierarchical modeling may better predict which CFTR mutations are linked to a high risk for early classic CF disease.

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### SELF-REPORTED MEMORY PROBLEMS, INSOMNIA AND SHORT SLEEP IN ADULT-ONSET CANCER SURVIVORS IN THE UNITED STATES: A CROSS-SECTIONAL STUDY

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**OBJECTIVES/SPECIFIC AIMS** Memory problem is a debilitating adverse effect of cancer and its treatments. We examined the relationships between self-reported memory problems (SRMP) and sleep disorders in adult-onset cancer survivors. **METHODS/STUDY POPULATION** We used data from 151 adults, 41–64 years old, cancer survivors who completed the 2007–2008 National Health and Nutrition Examination Survey. Population-weighted binary logistic regression analyses examined SRMP as outcome and included age, sex, education, race-ethnicity, income, and overall health as covariates. Sleep duration was categorized as very short (≤ 4 hrs), short (5–6 hrs), normal (7–8 hrs) or long (≥ 9 hrs). Initial insomnia was assessed as difficulty falling asleep. Middle insomnia was assessed as difficulty maintaining sleep. Late insomnia was assessed as waking too early. These insomnia subgroup were categorized as none, mild (<15 days/month) and severe (≥ 15 days/month). A combined insomnia variable categorized individuals as insomnia if they had severe insomnia of any type (early, middle, late). **RESULTS/ANTICIPATED RESULTS** Overall, presence of insomnia was associated with SRMP ($p < 0.0001$). Severe initial insomnia was associated SRMP ($p = 0.006$). Mild and severe middle insomnia were associated with SRMP ($p = 0.007$ and $p < 0.0001$, respectively). Late severe insomnia was associated with SRMP ($p = 0.037$). Additionally, long sleep was negatively associated with SRMP ($p = 0.019$). Among participants without a history of cancer ($n = 2{,}001$), none of the sleep variables were associated with increased likelihood of memory problems ($p > 0.05$). **DISCUSSION/SIGNIFICANCE OF IMPACT** Insomnia predicted SRMP but only in participants with a history of cancer, indicating that sleep may be a mechanistic pathway through which cancer impact memory.

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### MERCURY EXPOSURE, EPIGENETICS, AND CARDIOMETABOLIC RISK

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**OBJECTIVES/SPECIFIC AIMS** This study hypothesizes that methylmercury (MeHg) and inorganic mercury exposure (I-Hg) will (1) associate with differentially methylated loci, (2) will influence cardiometabolic risk factors, and that (3) DNA methylation changes will mediate Hg-cardiometabolic outcome relationships. **METHODS/STUDY POPULATION** Dental professionals with occupational (I-Hg via amalgams) and environmental (MeHg via fish consumption) Hg exposures were recruited at an American Dental Association (ADA) meeting. Questionnaire data (e.g., exposure sources, health history) was collected. Cardiometabolic risk factors (e.g., blood pressure, cholesterol profile, glycated hemoglobin) were measured. In a subset of male dentists with a range of Hg exposures ($n = 48$), DNA methylation was quantified in blood leukocytes across the genome via the Infinium BeadChip. Top regions differentially methylated by Hg biomarker levels based on statistical and biological significance will be validated via pyrosequencing using blood leukocyte DNA from all participants ($n = 426$) and a subset of matched saliva DNA ($n = 230$). **RESULTS/ANTICIPATED RESULTS** Total Hg was quantified in biomarkers of MeHg (geometric mean (95% CI): hair 0.60 (0.55–0.67) μg/g; blood 3.68 (3.39–3.99) μg/L) and I-Hg (urine 1.31 (1.20–1.42) μg/L). Hair and blood Hg levels are positively associated with glycated hemoglobin ($p = 0.03$). Statistical analyses will evaluate relationships between Hg and cardiometabolic risk factors and mediation of these relationships by differentially methylated regions. **DISCUSSION/SIGNIFICANCE OF IMPACT** By evaluating relationships between MeHg/I-Hg, cardiometabolic outcomes, and genome-wide DNA methylation, results are expected to improve Hg risk assessment and prevent Hg toxicity.

## RESEARCH SCHOLAR AND TRAINEE ABSTRACTS

### T0: BASIC SCIENTIFIC DISCOVERY

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### CORTICAL GRAY MATTER VOLUME DIFFERENCES IN FEMALE ADOLESCENTS WITH SUBSTANCE AND CONDUCT PROBLEMS VERSUS CONTROLS

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**OBJECTIVES/SPECIFIC AIMS** Conduct disorder (CD) and substance use disorder (SUD) are strongly comorbid, highly prevalent in adolescents, and separate behavioral manifestations of the highly heritable underlying liability called behavioral disinhibition (BD). Only one recent study has shown structural differences in adolescent girls with CD. We extend that literature by examining gray matter (GM) volume in adolescent girls with CD/SUD. **METHODS/STUDY POPULATION** We acquired high-resolution structural images of 25 female patients (ages 14–18) and 21 controls of similar ages, using a 3T MR system. Statistical Parametric Mapping version 8 (SPM8), voxel-based morphometric (VBM8) toolbox and the DARTEL algorithm were used to spatially normalize, segment, and register the images. The tissue probability maps were custom generated using the TOM toolbox. A custom brain template was also generated, by and for use in DARTEL. We tested group differences in regional GM volume with analyses of covariance, adjusting for age and IQ. **RESULTS/ANTICIPATED RESULTS** Female adolescents with CD/SUD, when compared to controls, showed reduced gray matter volume in: medial orbitofrontal cortex, left ventrolateral prefrontal cortex, right dorsolateral prefrontal cortex, medial prefrontal cortex, cingulate gyrus, bilateral somatosensory and motor cortices, and bilateral angular gyri. There were no regions where patients showed increase GM volume. **DISCUSSION/SIGNIFICANCE OF IMPACT** Compared to controls, female adolescents with CD/SUD show structural abnormalities in brain regions involved in executive decision-making, inhibition, and reward processing, regions that are relevant in rule-breaking behavior and BD.

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### HEME OXYGENASE-1 EXPRESSION PREVENTS DOXORUBICIN-INDUCED CARDIAC TOXICITY

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**OBJECTIVES/SPECIFIC AIMS** Heme oxygenase-1 (HO-1) is an inducible enzyme that degrades pro-oxidant heme into carbon monoxide, biliverdin, and iron. We have shown that HO-1 expression prevents heart failure secondary to acute cardiac injury. Here, our objective was to determine the role of HO-1 expression in delayed onset heart failure (DOHF) caused by doxorubicin (DOX). **METHODS/STUDY POPULATION** Mice were treated with DOX (18 mg DOX per kg of body weight, administered IV as three 6 mg/kg doses given over one week) to study DOHF by echocardiography. **RESULTS/ANTICIPATED RESULTS**. HO-1 overexpression in humanized transgenic (HBAC) mice prevents body weight loss (4% vs 15% in WT, $p < 0.05$, $n = 10$) and systolic dysfunction (ejection fraction 67% vs 51% in WT mice, $p < 0.05$, $n = 5$) at day 14 after DOX treatment. DOX-induced DOHF, characterized by dilation of the left ventricle (3.22 mm vs 3.55 mm in WT mice, $p < 0.05$, $n = 5$) and wall thinning (0.89 mm vs 0.61 mm in WT mice, $p < 0.05$, $n = 5$), is also prevented by HO-1 overexpression. Histological evaluation demonstrated that HO-1 overexpression prevents cardiomyocyte necrosis and secondary inflammation in necrotic foci. DOX increases the proportion of CD45+ cells in the heart of WT mice relative to vehicle treated controls (1.42% vs 0.62%, $p < 0.01$, $n = 5$), while HO-1 expression inhibits the infiltration of CD11b+ mononuclear phagocytes ($p < 0.05$, $n = 5$). HO-1 overexpression also decreases myocardial fibrosis detected by picrosirus staining 60 days after DOX treatment, which is exacerbated in HO-1 deficient mice. Transmission electron microscopy also revealed that HO-1 expression prevents cardiomyocyte ultrastructural changes, which included vacuolization of the cytoplasm and significant dilatation of the sarcoplasmic reticulum. **DISCUSSION/SIGNIFICANCE OF IMPACT** HO-1 expression represents a potent therapeutic target to prevent DOX-induced DOHF.

## T1: TRANSLATION TO HUMANS

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### MICRORNA EXPRESSION IN FFPE HEPATOCELLULAR CARCINOMA TISSUE AND NONTUMOROUS ADJACENT TISSUE

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**OBJECTIVES/SPECIFIC AIMS** Prognosis following curative hepatocellular carcinoma (HCC) resection depends on the complete removal of tumorous tissue, but characterization of tumor versus nontumor tissue by histological methods alone may not be accurate. Molecular analysis, particularly of microRNA (miR) expression may aid in this characterization. We aimed to compare the miR expression profiles in formalin-fixed, paraffin embedded (FFPE) human HCC tissue with the miR expressions in adjacent, nontumor tissue isolated from the same patients. **METHODS/STUDY POPULATION** miR expression profiles of ten FFPE liver sections from primary HCC tumor ($n = 5$) and adjacent nontumor ($n = 5$) tissue were evaluated using the nCounter Analysis System (NanoString Technologies). Samples were Caucasian male ages 46–74 years; mean tumor size = 5.14 cm. Analysis was performed between groups with a priori statistical significance of $p \leq 0.05$. **RESULTS/ANTICIPATED RESULTS** Of the 805 miRs quantified, 11 had significantly differential counts. miR-424-5p, miR-30e-5p, miR-130a-3p, miR-200b-3p, miR-101-3p, miR4455, miR324-5 and miR429 were down-regulated in tumor compared to nontumor tissue, while miR-21-5p, let-7d-5p and miR-4454 were up-regulated. **DISCUSSION/SIGNIFICANCE OF IMPACT** Our results confirm the reported dysregulation of miR-21-5p, miR-30e-5p, miR-200b, and miR-429 in HCC, while identifying for the first time the up-regulation of miR-4454 and let-7d-5p. These differential miR profiles will potentially aid in the characterization of tumor and nontumor tissue and help clinicians in determining the postresection prognosis of HCC patients. Additionally, the identified miR species offer valuable insights into the microenvironment of liver tumors.

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### PHENOTYPIC CHARACTERIZATION OF SUBJECTIVE, MOTOR AND RISK-TAKING RESPONSES TO ACUTE INTRAVENOUS (IV) ALCOHOL IN SOCIAL DRINKERS

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**OBJECTIVES/SPECIFIC AIMS** The aim of this study was to characterize the subjective, motor, and risk-taking responses following acute IV alcohol administration in social drinkers. **METHODS/STUDY POPULATION** 24 male and female healthy social drinkers underwent 2 infusion sessions on separate days in counter-balanced order: alcohol clamp and biphasic (mimicking a standard oral exposure) paradigms at target BrAC of 0.06 +/- 0.005%. Subjective measures (Drug Effects Questionnaire and Biphasic Alcohol Effects Scale), motor performance (completion time for Grooved Pegboard Task (CT-GPT)), and risk-taking (Balloon Analog Risk Task) were assessed at baseline (B1), 20 min (B2), and 110 min (B3) during the infusion. Initial response (IRA = B2-B1) and adaptive response (ADA = B3-B2) were examined for differences between paradigms, and the effect of sex, family history of alcoholism (FHA) and recent drinking history (RDH). **RESULTS/ANTICIPATED RESULTS** Both paradigms resulted in precise exposure profiles across subjects, although the biphasic profile showed greater inter-individual variability. Subjective measures of feeling alcohol effects, liking alcohol effects, high, stimulation and sedation showed significant IRA that were associated with RDH but not with FHA. ADA for these subjective measures were also associated with RDH, while ADA for wanting more alcohol was associated with FHA. CT-GPT showed high inter-individual variability, with a significant IRA that was sustained with minimal adaptation, and no FHA or RDH differences. Risk taking behavior showed minimal IRA and a significant ADA with increased risk taking in the FHN group. **DISCUSSION/SIGNIFICANCE OF IMPACT** These results show that IV alcohol results in significant subjective and motor responses in social drinkers. Subjective responses were found to be associated with RDH, while FHA did not appear to have much influence in this sample.

## T2: TRANSLATION TO PATIENTS

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### IDENTIFYING THE ROLE OF MOLECULAR MIMICRY IN SLE IMMUNE COMPLEX DISEASE

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**OBJECTIVES/SPECIFIC AIMS** Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease associated with circulating immune complexes and characterized by poorly understood relapses and remissions. Albeit human dsDNA epitopes are the presumed antigenic components of these immune complexes, no literature was identified confirming these epitopes to be exclusively of human origin. SLE patients following vegan diets often achieve remission by unknown mechanisms. Literature review supports the ability of intact segments of ingested animal DNA to enter circulation. The commercial reagents used to test SLE patients for auto-antibodies utilize as target tissue not normal human cells but calf, rodent, fowl, sheep, or HELA cells. Additionally, Epstein-Barr viral (EBV) protein (EBNA-1) has been documented to bind SLE autoantibodies. These data suggest that SLE symptoms might follow a model of molecular mimicry seen in rheumatic heart disease. Thus, the immune complex antigenic epitopes in SLE patients may include beef, EBV, etc. **METHODS/STUDY POPULATION** In order to identify a subpopulation of SLE patient who react to ingested and foreign DNA, we will be isolating DNA from SLE patients' DNA-antibody complexes and sequence the DNA to determine its origin (i.e., self DNA, self-other nucleic acid, EBV, bovine, rabbit, other). Next we will search the DNA database to identify other biological sources containing the epitope. Furthermore, we will determine the DNA nucleotides that constitute epitopes of the isolated DNA antigens. **RESULTS/ANTICIPATED RESULTS** n/a **DISCUSSION/SIGNIFICANCE OF IMPACT** Subpopulations of SLE patients may achieve enhanced control through identification of exogenous antigenic sources which contribute to disease through molecular mimicry.

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### EXERCISE-INDUCED PULMONARY HYPERTENSION BY STRESS ECHOCARDIOGRAPHY: IS FURTHER WORKUP WARRANTED?

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**OBJECTIVES/SPECIFIC AIMS** To study the prevalence of exercise-induced pulmonary hypertension (EIPH) in subjects referred for stress echocardiography (SE). To evaluate subsequent intra-cardiac hemodynamics in a subgroup of subjects with EIPH by SE who were referred for right heart catheterization (RHC). **METHODS/STUDY POPULATION** In a retrospective analysis of 5001 consecutive stress echocardiograms, we identified 100 subjects with EIPH who had a subsequent RHC. We defined EIPH on SE as pulmonary artery systolic pressure (PASP) >50 mmHg or TR velocity > 3.2m/s. Clinical, echocardiographic and hemodynamics findings were analyzed to identify predictors of abnormal hemodynamic findings on RHC (rest mean pulmonary artery pressure (PAP) >25 mm Hg, exercise mean PAP > 30 mm Hg or PVR > 3 or PCW > 15 mm Hg at rest or with exercise). **RESULTS/ANTICIPATED RESULTS** Prevalence of EIPH during routine SE is 11.4%. Abnormal hemodynamics on RHC were present in the majority of subjects with EIPH by SE. Abnormal hemodynamics were associated with older age, smoking, HCV infection, dilated left atrium (LA), lower exercise capacity and higher E/e′ ratio. Dilated LA (odds ratio (OR) 4.4 [95% confidence interval (CI): 1.3, 14.4, $p = 0.02$]) and age >55 years (OR 5. [95% CI: 1.8, 14.1; $p < 0.01$]) were independently associated with increased odds of abnormal RHC. **DISCUSSION/SIGNIFICANCE OF IMPACT** Subjects with EIPH by SE, have a high prevalence of abnormal hemodynamics on RHC. The majority of the subjects (85%) with abnormal RHC required exercise to demonstrate abnormal hemodynamics. Dilated LA and older age were independent predictors of subsequent abnormal findings on RHC. Identification of these factors will help guide referral of EIPH subjects for invasive testing.

## T3: TRANSLATION TO PRACTICE

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### ANATOMICAL CORRELATION OF POSTSTROKE LIMB SPASTICITY

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**OBJECTIVES/SPECIFIC AIMS** Poststroke spasticity is a common disabling complication after stroke. This study aims to investigate the anatomic correlation of poststroke limb spasticity, we hypothesize that the disruption of corticospinal tract (CST) is associated with poststroke spasticity. **METHODS/STUDY POPULATION** We retrospectively analyzed a cohort of 29 stroke patients with upper extremity spasticity with modified Asthworth Spasticity Scale (MASS) ≥ 2 on any of 3 muscle groups (biceps, wrist flexors and finger flexors). Clinico-demographic information was retrieved from medical records. CT or MRI scan of brain were reviewed by two vascular neurologists to determine whether the stroke lesion(s) affect the key segments of corticospinal tract: primary motor cortex (PMC), premotor and supplemental motor cortex (PM), centrum semiovale (CS), corona radiata (CR), posterior limb of internal capsule (PLIC), cerebral peduncle(CP) and brain stem (BS). **RESULTS/ANTICIPATED RESULTS** Patients average 55.7 years old with the majority of them having suffered ischemic stroke (93%). Patient had moderate to severe disability (modified Rank Scale = 3.5 and NIHSS total score = 6.5). They presented with severe spasticity (MASS = 3.7) and motor deficit (NIHSS arm subscore = 2.6). The percentage of patients having lesions along the CST are: PMC: 45%, PC: 48%; SO: 48%; CR: 76%; PLIC: 48%; CP: 11% and BS: 7%. 83% of patients have lesions affecting CST at multiple locations. There is no correlation between of number of lesions and severity of spasticity. **DISCUSSION/SIGNIFICANCE OF**

**IMPACT** Our data suggests that injury to corticospinal tract by stroke is associated with poststroke limb spasticity.

## T4: TRANSLATION TO POPULATION

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### SCREENING FOR CORONARY ARTERY CALCIFICATION USING DESR

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**OBJECTIVES/SPECIFIC AIMS** Dual-energy subtraction radiography (DESR) improves the ability to detect and diagnose thoracic abnormalities. We discovered that the "bone enhanced" image, not available with standard radiography, dramatically improves the identification of coronary artery calcium (CAC) deposits. CAC has been identified as a significant risk factor in the prediction of a future coronary event. The presence of CAC is frequently determined by CT which can be expensive and increase the risk of malignancy. DESR is a low cost, low radiation dose test that could be used for routine pulmonary and CAC screening. **METHODS/STUDY POPULATION** A total of 3327 dual energy subtraction chest radiographs in electric power workers were evaluated for the presence of CAC. Workers were 19–70 years old and were predominantly white males. The average interval between DESR exams was 3–39 months with an average interval of 11.7 ± 8 months. **RESULTS/ANTICIPATED RESULTS** 89 cases of CAC were identified in single DESR examinations and 77 cases were identified in subjects with sequential examinations. 14 cases were identified as false positives (FP). The minimum FP rate was 18.2 %. The CAC prevalence rate = 4.6%. Recent research has suggested that a calcium score similar to the Agatston score can be calculated from DESR CAC images with good linear correlation between CT and DESR scores. **DISCUSSION/SIGNIFICANCE OF IMPACT** CAC was identified using DESR in a working population of with a prevalence rate of 4.6% similar to other CT screening studies. Millions of workers are offered free annual screening by their employers. Because of the high prevalence and morbidity related to the identification of CAC, the concurrent identification of CAC while screening for occupational pulmonary disease may save many more lives that identification of pulmonary disease alone.

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### REIMAGING RESEARCH ETHICS: IMPERATIVES FOR TRANSLATIONAL SCIENCE

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**OBJECTIVES/SPECIFIC AIMS** Translational science emphasizes the dynamic interplay between scientists, clinicians, research participants, and the public, all of whom are invested in improving the health of individuals and their communities. While holding great promise, the success of this enterprise depends upon the creation of an environment grounded in mutual trust, respectful dialogue, and sustainable relationships among a variety of stakeholders. It also requires research scientists and their teams to be cognizant of the unique concerns, expectations, rights, and interests of research participants and to engage these concerns in ethically responsible ways. **METHODS/STUDY POPULATION** We stipulate that traditional forms of compliance oriented training in the protection human subjects are insufficient for ethically conscientious translational science. We offer a new approach, one that is grounded in the subject-practitioner relationship but broadened to account for the ethical challenges inherent in team-based science. **RESULTS/ANTICIPATED RESULTS** We describe emerging refinements in the researcher's role with respect to the moral task of protecting human subjects' rights and welfare and reestablishing these duties within a translational, team-based context. **DISCUSSION/SIGNIFICANCE OF IMPACT** By understanding and integrating the subject's values and concerns along with those of the multidisciplinary team, this relationship–based approach emphasizes: (1) respecting participants' social reality, local culture, community context, and preference history; (2) designing democratic processes which promote fairness in decision making procedures; (3) promoting transparency with regard to scientific motivations for recruitment and funding mechanisms; and (4) developing measures to increase trustworthiness, thus building and sustaining confidence in the translational research enterprise.

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### IDENTIFYING MECHANISMS FOR HEALTH DISPARITIES: YOUTH VOICE EXPECTATIONS FOR SURVIVAL

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**OBJECTIVES/SPECIFIC AIMS** In national studies, a sizable minority of otherwise healthy youth report they think they will die young. Belief in risk for premature death is more prevalent among youth of color, and may become a self-fulfilling prophecy as youth give up on self-care and investment in the future. This qualitative study addresses: (1) when and where survival expectations originate and (2) how perceptions about survival impact health behaviors and decision making. **METHODS/STUDY POPULATION** Data are from ongoing focus groups with youth living in the Twin Cities metro area of Minnesota ($n$ = 4 out of 12 planned). Groups include 5–7 youth, organized according to gender and developmental stage of adolescence: early (12–14 yrs); middle (15–17 yrs); and late (18–21 yrs). Individual interviews are planned with youth who have completed a focus group ($n$ = 15). Thematic analysis reveals perceptions by youth of messages received about survival and related health decision making. **RESULTS/ANTICIPATED RESULTS** Findings to date make clear that youth are actively thinking about their longevity. Youth perceive messages from multiple contexts related to their future prospects and likelihood of survival; however messages in the home and among friend contacts are given more weight. Youth perceptions about their survival are related to choices made about timing of parenthood, experimentation with risk, and personal care. **DISCUSSION/SIGNIFICANCE OF IMPACT** Translation: (1) Clarify the relevance of social context for youth survival perceptions; (2) Inform the development of community-based interventions to improve youth survival beliefs. Discussion: Examination of youth survival expectations represents a unique mechanism to address health disparities by: (1) establishing a link between survival perceptions and health behaviors; and (2) identifying developmental contexts to facilitate future orientation and decisional capacity.

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### FEASIBILITY OF HOME-BASED HIV RAPID TESTING (HRT) AMONG AFRICAN AMERICANS

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**OBJECTIVES/SPECIFIC AIMS** More than half of people living with HIV in the US are African American, yet nearly 40% of blacks have never completed an HIV test. As a result, the majority are diagnosed either with AIDS or low CD4 approaching AIDS, suggesting that testing is not occurring early in the process. OraQuick, the first FDA approved in-home HIV rapid test (HRT) has potential to increase HIV testing rates; however, there are several concerns for using this approach in vulnerable communities, including lack of counseling for persons who test positive and lack of processes to link such persons to HIV care. A pilot study was conducted to determine whether community health workers (CHWs) paired with HRT could be a potentially efficacious mechanism to increase HIV screening and improve access to HIV care among African Americans in Miami, Florida. **METHODS/STUDY POPULATION** Eligible participants were between 18–60 years old, self-identified as African American, and were either HIV negative or had an unknown HIV status. Participants were randomized to either HRT paired with a CHW (experimental condition) or HRT alone (control condition). Both groups received pre and posttest counseling and linkage to care in the event of a positive result. Successful completion was defined as completing HRT and if positive, being linked to care by a CHW. **RESULTS/ANTICIPATED RESULTS** Experimental participants were significantly ($p$ = 0.05) more likely than control participants to successfully complete the test and, if positive, get linked to HIV care (100% vs. 83%). **DISCUSSION/SIGNIFICANCE OF IMPACT** CHW-assisted HRT may be a promising strategy to increase HIV testing and access to HIV care among African Americans in Miami, Florida. Larger studies among diverse populations are needed to determine if results can be generalized to other populations.

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### THE ROLE OF COMMUNITY ENGAGEMENT IN INCREASING TRANSLATIONAL HEALTH RESEARCH PARTICPATION BY HSIPANICS IN THE WWAMI REGION

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**OBJECTIVES/SPECIFIC AIMS** The goal of the Institute for Translational Health Science's (ITHS) Hispanic Community Outreach Program (HCOP) is to increase participation by Hispanics in translational research in the WWAMI region (Washington, Wyoming, Alaska, Montana, Idaho). **METHODS/STUDY POPULATION** As of 2012, HCOP has conducted outreach to investigators, community-based organizations (CBOs) and clinics that serve Hispanics in the WWAMI region. The HCOP's outreach activities have included phone calls, site visits, and participation in community events and conferences, resulting in a growing network of potential research partners. This network has evolved over time through personal contacts and referrals, reflecting the importance of interpersonal relationships and trust when engaging communities. To track its work, the HCOP maintains a database that includes level of engagement (LOE). The LOE is scored on a graded scale of 1–5 where 1 indicates a minimal LOE and 5 indicates a high LOE. **RESULTS/ANTICIPATED RESULTS**: To date, the HCOP has made contact with 42% academic, 52% CBO and 6% policy. The majority of HCOP's initial contacts had LOE scores in the 1–2 level. HCOP has partnered in Diabetes Self Management grant, has been awarded a NIH small conference grant for a regional conference on Latino health. In addition, the HCOP has awarded pilot funding for community engaged research. **DISCUSSION/SIGNIFICANCE OF IMPACT** Community engagement appears to be an effective strategy for increasing

the participation of Hispanics in translational health research. More research is needed to develop tools and methods for assessing the effectiveness of community engagement and its impacts on the health of communities.

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### SLEEP FEAR—A POTENTIALLY MODIFIABLE FACTOR CONTRIBUTING TO NOCTURNAL ANS AROUSAL IN URBAN MINORITIES

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**OBJECTIVES/SPECIFIC AIMS** Minorities living in stressful urban environments have disproportionate illness burdens. Stress can lead to compromised sleep and altered autonomic nervous system (ANS) activity both of which have been linked to adverse health outcomes. People living in stressful neighborhoods may feel that their safety is compromised when they sleep. We examined the role of fear of sleep in the association between neighborhood stress and nocturnal ANS activity. **METHODS/STUDY POPULATION** 64 healthy urban-residing African Americans (age 18–35) completed the City Stress Inventory (CSI) with subscales that assess neighbor disorder and exposure to violence, the Fear of Sleep Index (FOSI) which assesses sleep fear–related thoughts and behaviors, and two 24-hour ambulatory EKG recordings as part of a larger study. Low frequency (LF) and high frequency (HF) components of heart rate variability were derived from the EKG data, and LF-to-HF ratios (LF/HF), an index of sympathetic tone, and normalized HF (nHF), an index of parasympathetic tone, during time in bed were computed. **RESULTS/ANTICIPATED RESULTS** Time-in-bed nHF was significantly correlated with neighborhood disorder and FOSI total score ($r = -.281$, $p = 0.027$; $r = -.338$, $p = 0.008$, respectively). Hierarchical regression analysis indicated that the relationship with neighborhood disorder was accounted for by FOSI ($\beta = -.103$, $p = 0.499$ for neighborhood disorder; $\beta = -.277$, $p = 0.072$, $\Delta r^2 = .052$ with FOSI). **DISCUSSION/SIGNIFICANCE OF IMPACT** Sleep fears may be a modifiable risk factor that impacts long term health among residents of stressful urban environments.

# RESEARCH PROFESSIONAL ABSTRACTS

## T3: TRANSLATION TO PRACTICE

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### MENTORING INTERVENTIONS: IMPACT ON CAREER DEVELOPMENT

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**OBJECTIVES/SPECIFIC AIMS** Mentoring is critical for academic success, yet few mentors are formally trained and many fear the complexities that diversity introduces. We used Self-Determination Theory (SDT) as the basis for mentoring interventions to promote career satisfaction and academic productivity of underrepresented minorities in research. Our specific aims were to assess the impact of these mentoring interventions on: (1) the protégés overall career satisfaction (2) satisfaction with the career development experience of both mentors and protégés. **METHODS/STUDY POPULATION** Our randomized trial of 152 mentor/protégé dyads compared: (1) education for mentors; (2) peer mentoring; (3) combination of education for mentors and peer mentoring; (4) control/ usual practice. Participants were mentors and their protégés at 3 medical schools and 8 universities, who were randomized in dyads. Protégé participants were grad students, fellows and junior faculty who were underrepresented by race, ethnicity, gender, disability or socioeconomic status. We used an evaluation instrument from the Rochester CTSA, which was administered at the beginning of the study and at the end of 1 year. The instrument asks mentors and protégés to rate their satisfaction with the overall mentor relationship and interactions within 8 career development domains. **RESULTS/ANTICIPATED RESULTS** Both mentoring education and peer mentoring had a significant effect ($p < .05$) on the perceived amount of time together and overall usefulness of the mentoring experience. Compared to controls, protégés in groups that received any intervention discussed a wider range of topics. The impact of these interventions on discussions of work-life balance was especially striking. **DISCUSSION/SIGNIFICANCE OF IMPACT** Mentoring interventions based on SDT may improve overall satisfaction with the mentoring experience for underrepresented groups. Long-term follow up is needed to determine effects on academic productivity and retention.

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### THE MENTORED-TO-INDEPENDENT TRANSITION: SURVEY OF CTSA EDUCATION AND CAREER DEVELOPMENT (EDCD) LEADERS

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**OBJECTIVES/SPECIFIC AIMS** The transition from mentored to independent (MtoI) research is a critical juncture for a clinical investigator. Members of the CTSA EdCD Key Function Committee were surveyed about resources to support this transition and predictors of success. **METHODS/STUDY POPULATION** An EdCD faculty leader at each institution was invited to complete an online survey (RedCAP). U of Utah and Mt. Sinai IRBs determined the project to be nonhuman subjects research. Summary statistics are reported. **RESULTS/ANTICIPATED RESULTS** 54 of 62 institutions responded (87%). 28 institutions reported creating mentor training or development programs and 24 reported establishing forums to conduct mock study sections during the CTSA award period. Bridge funding was endorsed most often as an important institutional resource. Respondents reported that nontraditional career success metrics such as participation in team science were less valued by institutions than leadership positions. Data were reported for 914 scholars supported by the CTSA KL2 mechanism. 68% were medical doctors, 19% were nonclinician PhDs, and 12% were from other clinical fields. 53% of KL2 scholars were female and 12% were underrepresented minorities. Among scholars who completed KL2 support 2 or more years ago, 40% had received independent research funding; 56% of these were NIH RO1 awards, 44% from other sources. Funding success did not differ by gender or minority status among the KL2 scholars. **DISCUSSION/SIGNIFICANCE OF IMPACT** Institutions have expanded support for the MtoI transition during their CTSA award periods. Non-NIH sources represent a large proportion of first independent awards. The authors acknowledge the EdCD KFC members for their contributions to this project.

## T4: TRANSLATION TO POPULATION

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### BUILDING INFRASTRUCTURE: COMMUNITY-ACADEMIC GRANT WRITING SERIES LESSONS LEARNED

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**OBJECTIVES/SPECIFIC AIMS** To strengthen community and academic infrastructure for sustainable partnered research, UCLA CTSI Community Engagement and Research Program (CERP) developed a Community-Academic Grant Writing Series, a no-cost, 12-week workshop conducted between April and June 2013 with three goals: (1) to identify organizations and investigators who were ready to write a partnered proposal, (2) introduce diverse sources of funding and standard grantsmanship language, and (3) how to demonstrate evidence of partnership. **METHODS/STUDY POPULATION** Eligible teams included at least 2 representatives from the partnering community organization and an academic investigator. Of the 18 teams that submitted LOIs, 10 with varying levels of grant writing experience were invited to participate. Weekly feedback helped CERP staff iteratively review goals and modify the program. Teams were tracked to determine outcomes. **RESULTS/ANTICIPATED RESULTS** On average, 22 people attended each week, and all teams were represented, each week. At the end of the workshop, the majority of attendees (93.3%) indicated they understood the benefits of partnering, could identify appropriate grant funding opportunities (86.6%), and understood foundation and NIH grant writing language (84.2% and 68.8%, respectively). At 6 months after completion of the workshop, four teams had submitted proposals, and two were successfully funded ($1.4 million awarded). **DISCUSSION/SIGNIFICANCE OF IMPACT** We have early evidence that participating in a grant writing workshop enhanced infrastructure (both self-efficacy and funding) for partnered research. We plan to modify the series based on these early experiences and the recommendations of the participants (e.g., offer distinct short NIH or foundation grant writing tracks) to address the needs of both novice and experienced writers.

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### COMMUNITY-BASED PARTICIPATORY RESEARCH BY YOUTH: A BOOMERANG MODEL OF LEARNING FOR STEM TEACHERS

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**METHODS/STUDY POPULATION** A core principle in Community-Based Participatory Research (CBPR) is a bidirectional flow of information between investigators and community. We have extended this paradigm to include a team of Clinical Research Knowledge Brokers (trained in CBPR and Health Sciences), to high-school STEM teachers/club mentors to youth in health science clubs. Each club member conducts CBPR projects on relevant health issues in their neighborhoods. In principle, diffusion of knowledge occurs at each step between science and cultural perception. The student benefits from the series of experiential processes to consider design, conduct, organization, analysis, interpretation and presentation. We now report on the teacher benefit consequence of this model. STEM teachers, lay educators without formal training in Health Sciences, have little experience of project teaching. Changes

mandated in STEM education now emphasize experiential education. The experiential process of CBPR provides an opportunity not only for the student but their mentors. We illustrate this process where a club teacher, initially hesitant to go beyond their prior level of comfort, has been encouraged to learn and mentor new concepts. Sharing of the student project with the program team provides an environment for the teacher to also be mentored in new fields. In this bi-directional flow of learning, the teacher leads the student through the process of CBPR. In return, the student leads the teacher to new fields of health science. This boomerang of learning, an interesting inversion of classical education, is enhancing teacher education skills.

# POSTER SESSION THREE

# KL2 SCHOLAR ABSTRACTS

## T0: BASIC SCIENTIFIC DISCOVERY

**306**

### PHARMACOLOGICAL TREATMENT OF REPETITIVE BEHAVIOR IN AN ADOLESCENT MOUSE MODEL

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**OBJECTIVES/SPECIFIC AIMS** Restricted, repetitive behaviors are extremely common in children with neurodevelopmental disorders. These repetitive behaviors can range from highly cognitive restricted interests and insistence on rituals or sameness, to repetitive motor patterns and self-injurious behavior. Unfortunately, our understanding of the neural pathophysiology that mediates these maladaptive behaviors is lacking. Accordingly, treatment is challenging. Animal models of repetitive behaviors allow researchers to identify the neurobiological basis of these particular maladaptive behaviors without the influence or complication of other biological problems associated with the disorders. Animal models also allow for the determination of clinical efficacy of potential pharmacological therapies before clinical experimentation is attempted in the very vulnerable human populations. **METHODS/STUDY POPULATION** Our laboratory uses the deer mouse model, which exhibits spontaneous repetitive behavior when raised in a standard laboratory environment. **RESULTS/ANTICIPATED RESULTS** We have characterized the individual differences and trajectory of repetitive behavior development in deer mice. Furthermore, we identified specific deficiencies in basal ganglia circuit function in mice with high rates of repetitive behavior - specifically, reduced function of the indirect pathway of the basal ganglia. As such, we developed a triple drug cocktail targeting dopamine D2, adenosine A2a, and glutamate mGluR5 receptors to increase indirect pathway function. This drug cocktail significantly reduces repetitive behavior in adolescent mice. **DISCUSSION/SIGNIFICANCE OF IMPACT** These data suggest that our drug cocktail is safe and effective at reducing repetitive behavior in adolescent mice. We are currently investigating whether early drug exposure (i.e., chronic administration immediately postweaning) can alter the trajectory of repetitive behavior development.

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### WHOLE GENOME SEQUENCING OF RESPIRATORY VIRUSES FROM CLINICAL NASOPHARYNGEAL SWABS

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**OBJECTIVES/SPECIFIC AIMS** Respiratory infections cause the greatest morbidity and mortality of all pediatric ailments accounting for ~20% of mortality for children younger than 5, one quarter of all hospitalizations, and between 33% and 59% of general practitioner consultations. Despite the enormous medical burden caused by respiratory viruses the specific genetic variation that influence transmission, virulence, and pathogenesis are poorly understand for most viruses. The objective of this study is identify genetic variation in clinical respiratory viruses that influence these critical processes. **METHODS/STUDY POPULATION** We are developing a novel method to enrich viral genomes from clinical nasopharyngeal swabs, which will enable us to conduct deep whole genome sequencing on an Illumina MiSeq. We will conduct whole genome viral sequencing of respiratory syncytial virus, influenza A, human metapneuomivirus, and rhinovirus from residual nasopharyngeal swabs obtained during the peak 2013–2014 respiratory infection season in the state of New Mexico. **RESULTS/ANTICIPATED RESULTS** We will use reference guided and *de novo* assembly approaches to characterize the complete viral genomes and identify genetic variation of individual clinical viral isolates. We anticipate that through bioinformatics analysis of the clinical viruses we will identify novel genetic variation that may effect transmission, virulence and pathogenesis of the virus. **DISCUSSION/SIGNIFICANCE OF IMPACT** Our results will provide crucial insight into the genomic diversity of clinical viral strains, pathophysiology of infection, and may provide understanding of genetic causes of resistance to antiviral therapies.

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### PKA/AMPK SIGNALING IS A MEDIATOR OF THE ANTI-PROLIFERATIVE EFFECT OF ADIPONECTIN ON MULTIPLE MYELOMA CELLS

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**OBJECTIVES/SPECIFIC AIMS** Obesity increases the risk of developing multiple myeloma (MM). Adiponectin is a cytokine produced primarily by adipocytes, but paradoxically decreased in obesity. Animal studies have implicated adiponectin in the progression of MM; its effects on human MM cells is unclear. **METHODS/STUDY POPULATION** Herein, we evaluated the effects of prolonged exposure to adiponectin on the survival of human MM cells as well as putative signaling mechanisms. **RESULTS/ANTICIPATED RESULTS** We found that adiponectin activates PKA, which leads to decreased AKT activity and increased AMPK activation. AMPK, in turn, induces cell cycle arrest and apoptosis. Adiponectin-induced apoptosis may be mediated, at least in part, by the PKA/AMPK-dependent decline in the expression of the enzyme acetyl-CoA-carboxylase (ACC), which is critical to lipogenesis and thus cell survival. Importantly, supplementation with palmitic acid, the preliminary end product of fatty acid synthesis, rescues MM cells from adiponectin-induced apoptosis. Furthermore, 5-(tetradecyloxy)-2-furan carboxylic acid (TOFA), an ACC inhibitor, exhibited potent anti-proliferative effects on MM cells that could also be inhibited by fatty acid supplementation. **DISCUSSION/SIGNIFICANCE OF IMPACT** The effect of adiponectin to reduce survival of MM cells appear to be mediated via its ability to suppress lipogenesis. Our findings suggest that activators of the PKA/AMPK pathway, or inhibitors of ACC, may be useful adjuvants in the treatment of MM. Moreover, the anti-myeloma effect of adiponectin supports the concept that decreased circulating levels of the adipokine, as occurs in obesity, promotes MM tumor progression.

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### SIRT1 AS A POTENTIAL THERAPEUTIC TARGET IN ANDROGEN INDEPENDENT PROSTATE CANCER

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**OBJECTIVES/SPECIFIC AIMS** SIRT1 is highly expressed in prostate cancer cell lines. Its expression was higher in the androgen independent prostate cancer cell lines PC3 and DU145. It was reported that transgenic SIRT1 expression induces prostate carcinogenesis. We hypothesize that SIRT1 acts as an oncogene in androgen independent prostate cancer. **METHODS/STUDY POPULATION** We treated androgen independent and dependent prostate cancer cells with SIRT1 Inhibitor IV, (S)-35. The effectiveness measure reported is the proportion of cells killed by the corresponding dose of SIRT1 inhibitor after 48 hours of exposure. Data were analyzed by a new mathematical measure of effectiveness (PMID: 22934946). Looking for potential biomarkers for treatment/response, the alterations of microRNA was determined. **RESULTS/ANTICIPATED RESULTS** We found a dose response effect of SIRT1 inhibitor in androgen independent prostate cancer cell proliferation. Specifically, in DU145 cells, the effectiveness after 48 hours of exposure to the inhibitor increased from 8.5% at 38 nM to 80.4% at 1000 nM [95% CIs, (−7.9, 24.9) and (76.9, 83.9), respectively. Similarly, for PC3 cells, the effectiveness increased from 2.9% at 38 nM to 69.0% at 1000 nM dose. Doses of 38 nM were not significantly toxic to any of the investigated cell lines, and the SIRT1 inhibitor was significantly toxic to the Lncap androgen dependent cell line only at 1000 nM. The overall effectiveness of SIRT1 inhibitor in preventing DU145, PC3 and Lncap proliferation was 44112.1 ($p < 0.001$), 40064.4 ($p < 0.001$) and 16828.4 ($p = 0.08$), respectively. Currently, we are investigating the usefulness of microRNAs expression for monitoring the effect of SIRT1 inhibitor. **DISCUSSION/SIGNIFICANCE OF IMPACT** SIRT1 inhibition may be effective in treating androgen independent prostate cancer.

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### A PEDIATRIC MOUSE MODEL OF ANTHRACYCLINE-INDUCED CARDIOTOXICITY

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**OBJECTIVES/SPECIFIC AIMS** Exposure to anthracycline chemotherapies results in cardiac fibrosis. We have developed a novel pediatric mouse model of acute anthracycline-induced cardiotoxicity to study the myocardial cellular changes that

occur during early postnatal exposure. **METHODS/STUDY POPULATION** Starting at two weeks of age, the anthracycline doxorubicin (5 mg/kg, $n = 8$) or saline control ($n = 4$) was injected into the peritoneal cavity of C57BL6/J mice weekly for five weeks. Animals were evaluated at the following ages: acute exposure- 3 wks and 5 wks; treatment recovery- 7 wks and 11 wks. Analyses included: (1) echocardiography, (2) quantitation of left ventricle (LV) neutrophils, fibroblasts, and collagen, and (3) myocyte cross-sectional area. **RESULTS/ANTICIPATED RESULTS** A marked decreased in ejection fraction was observed at all time points evaluated, with an average decrease of 20% (all $p < 0.05$). In addition, no difference in LV mass was noted in treated animals, indicating that LV growth and development was preserved. Histologic analysis of LV revealed no difference in myocyte cross-sectional areas ($p = 0.89$) but increased collagen during treatment recovery. In contrast, increased neutrophils were noted with the following percentages: 3 wks (22%), 5 wks (56%), 7 wks (38%) and 11 wks (45%). A large decrease in fibroblast numbers was noted at 3 wks (45.3%; $p < 0.05$), and this was not different at later ages. Experiments using cultured cardiac fibroblasts indicated doxorubicin directly induces the DNA damage response pathway and collagen I expression. **DISCUSSION/SIGNIFICANCE OF IMPACT** Collectively, our data utilizes a novel mouse model to show early doxorubicin treatment induces cardiac dysfunction that is accompanied by distinct histologic and cellular changes in the LV.

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## OPTIMIZED DATA ACQUISITION FOR INTERVENTIONAL CONE-BEAM COMPUTED TOMOGRAPHY USING PATIENT-SPECIFIC ANATOMICAL KNOWLEDGE AND DEFINITIONS OF IMAGING TASK

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**OBJECTIVES/SPECIFIC AIMS** CT systems tend to use only very general information to guide data acquisition (e.g., via technique charts based on rough patient size and anatomical targets). Because interventional imaging studies are typically conducted after diagnostic imaging and with very specific imaging goals, a great deal of patient- and task-specific information is available that can be used to guide acquisitions. Moreover, with increasingly flexible imaging devices like robotic C-arms that are capable of breaking free from traditional acquisition orbits, there is untapped potential to customize imaging acquisition to the patient and task for improved image quality and/or dose reduction. **METHODS/STUDY POPULATION** Previously acquired imaging studies and specific definitions of imaging task are used to predict image quality for arbitrary acquisition geometries using a mathematical framework that includes a model of human observer performance. This predictor is used to optimize and prospectively define an x-ray source trajectory that maximizes imaging task performance. **RESULTS/ANTICIPATED RESULTS** The acquisition design methodology is applied to the scenario of postoperative bleed detection using 3D-capable robotic C-arms in endovascular embolization of intracranial aneurysms. Superior visualization of bleeds around embolization coils is demonstrated using the designed trajectory as compared with traditional acquisition methods. **DISCUSSION/SIGNIFICANCE OF IMPACT** Mathematical observer models have been used to characterize and optimize the design of imaging devices; however, this work breaks new ground in translating the same methodologies to prospectively tailor data acquisitions of imaging systems to the specific patient anatomy and to specific detection tasks, as opposed to traditional protocols based on heuristics and general measures of image quality.

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## THE ANTI-ASTHMA HERBAL MEDICINE ASHMI ACUTELY INHIBITS AIRWAY SMOOTH MUSCLE CONTRACTION VIA PROSTAGLANDIN E2 ACTIVATION OF EP2/EP4 RECEPTORS

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**OBJECTIVES/SPECIFIC AIMS** We sought to determine whether acute *in vivo* ASHMI administration inhibits airway hyperreactivity in a murine model of allergic asthma and acetylcholine induced tracheal ring constriction *ex vivo* and to elucidate the cellular mechanisms underlying these effects. **METHODS/STUDY POPULATION** Ovalbumin-sensitized mice received a single oral ASHMI dose 2 hours prior to intravenous acetylcholine challenge. Airway hyperreactivity was determined by invasive airway measurements. Myography was used to determine the effects of ASHMI on acetylcholine-induced constriction of tracheal rings from asthmatic mice with or without epithelial denudation. The effect of cyclooxygenase inhibition and EP2/EP4 receptor blockade on ASHMI attenuation of acetylcholine contractions were evaluated. Tracheal cAMP and PGE2 levels were measured by ELISA. **RESULTS/ANTICIPATED RESULTS** A single acute oral dose of ASHMI dramatically reduced AHR in response to acetylcholine provocation in ovalbumin-sensitized mice ($p < 0.001$). In *ex vivo* experiments ASHMI significantly and dose-dependently reduced tracheal ring constriction to acetylcholine ($p < 0.05$–$0.001$) which was epithelium-independent and associated with elevated cAMP levels. This effect was abrogated by cyclooxygenase inhibition or EP2/EP4 receptor blockade. ASHMI also inhibited contraction to high K+ ($p < 0.001$). ASHMI increased tracheal ring PGE2 release in response to acetylcholine or high K+ ($p < 0.05$ for both). **DISCUSSION/SIGNIFICANCE OF IMPACT** ASHMI produced direct and acute inhibition of AHR *in vivo*, blocked acetylcholine-induced tracheal ring constriction via the EP2/EP4 receptor pathway. These data suggest that ASHMI may be a valuable alternative to beta-adrenergic agonists.

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## GRAPH THEORETICAL ANALYSIS OF GENOMOME-SCALE DATA IDENTIFIES NOVEL RACE SPECIFIC MOLECULAR ACTIVATION DURING COMMUNITY-ACQUIRED PNEUMONIA

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**OBJECTIVES/SPECIFIC AIMS** In the US, the incidence and mortality rate of community-acquired pneumonia (CAP) are higher in black compare to white Americans. The objective of our study was to identify novel racial differences in molecular network activation during CAP. **METHODS/STUDY POPULATION** A nested case-control analysis was performed on a multicenter inception cohort study. Self-identified black ($n = 22$) and white ($n = 22$) adults with radiological diagnoses of CAP at emergency department (ED) admission were matched 1:1. Written consent was obtained from the patient or proxy. Whole blood transcriptomic data were employed to construct co-expression graphs for each racial group. Pearson correlation coefficients and spectral thresholding were applied. Innovative graph theoretical methods were invoked to detect densely connected subgraphs and provide differential structural analysis. **RESULTS/ANTICIPATED RESULTS** Novel race differences in molecular network activation were observed between the two groups. Three subgraphs demonstrated a perfect connection in the white group only and were comprised of genes involved in the circadian loop, cell adhesion, mobility, proliferation, tumor suppression, NFκB, and chemokine signaling. Similarly, one subgraph in the black group was identified and was comprised of genes involved in DNA/mRNA processes, and apoptosis. **DISCUSSION/SIGNIFICANCE OF IMPACT** Racial disparity in CAP may thus, in part, be a functional consequence of molecular mechanisms by which diverse racial groups respond differently to infection.

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## SPATIAL LEARNING AND MEMORY DEFICITS CORRELATE WITH HYPOCRETIN-1 LEVELS IN HIV-POSITIVE WOMEN

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**OBJECTIVES/SPECIFIC AIMS** Antiretroviral treatment increases the survival of HIV-positive individuals. As a result, HIV-positive individuals live longer but nearly 50% have decreased quality of life due to HIV-associated neurocognitive disorders (HAND). HIV entrance to the brain during early infection results in hippocampal neuronal loss, which alters the establishment of long-term memory and spatial navigation. Hypocretin (hcrt-1), also known as orexin, is a neurotransmitter associated with alertness. It also regulates sleep, appetite, energy consumption. Recently it has been associated with cognitive impairment in neurodegenerative disorders, although its role is controversial and not well understood. Preliminary data from our laboratory shows that hcrt-1 CSF levels are increased in HIV-positive women from the Hispanic/Latino Longitudinal Cohort when compared to HIV-negative controls and are correlated with HAND severity. Our goal in the present study is to correlate CSF and serum hcrt-1 levels with impaired spatial navigation in HIV seropositive women. **METHODS/STUDY POPULATION** To test this we will measure CSF hcrt-1 levels by means of an ELISA in HIV-positive women. We will correlate hcrt-1 CSF and serum levels with spatial navigation impairment in HIV-positive women. A computer-based program, known as Memory Island, will be used to determine spatial navigation impairment. **RESULTS/ANTICIPATED RESULTS** We expect that hcrt-1 levels will be proportional with navigational impairment in HIV-seropositive women. **DISCUSSION/SIGNIFICANCE OF IMPACT** This correlation will establish the prospect of the hypocretin system as a possible therapeutic target for HAND.

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## USING EXERCISE AND MRI TECHNIQUES SENSITIVE TO BLOOD OXYGENATION AND BLOOD VOLUME TO ASSESS SKELETAL MUSCLE PERIPHERAL VASCULAR FUNCTION

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**OBJECTIVES/SPECIFIC AIMS** MRI is the gold standard for evaluating soft-tissue pathology. More recently, MRI techniques have been used to assess tissue and organ function in real-time. Of particular interest are MRI techniques sensitive to vascular structure (blood vessel size and density) and function (blood oxygenation and blood volume) called the blood oxygenation level-dependent (BOLD) effect. BOLD based imaging, in combination with brief muscle contractions, has been used to assess the peripheral vascular function of skeletal muscle in healthy, obese, and diabetic populations. The purpose of this project is to extend our preliminary findings with BOLD based imaging at 7T using improved imaging techniques and an MR compatible exercise device. **METHODS/STUDY POPULATION** Four subjects (2 M), aged 31.3 ± 9.6 yrs, 172.1 ± 6.4 cm tall, body mass of 63.4 ± 12.3 kg, participated in the study. Scanning was performed on a Philips 7T scanner. The subject's foot was secured in an exercise device capable of measuring plantarflexion force. Regions-of-interest 2–3 $cm^2$ in size were drawn in the soleus muscle with care to exclude resolved vessels and connective tissue. Peak signal intensity was calculated as the highest percentage increase from baseline. Muscle force was calculated as the highest force achieved during each contraction. **RESULTS/ANTICIPATED RESULTS** Postcontractile BOLD transients on the order of 3–5% peak change were observed in the soleus muscles following a 2-s plantarflexion contraction. **DISCUSSION/SIGNIFICANCE OF IMPACT** BOLD based imaging of peripheral vascular function is feasible at 7T using improved imaging techniques and standardized exercise protocols.

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### DETECTION OF PANNEXIN AND ECTO-ATPASE ACTIVITY IN HUMAN DENTAL PULP

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**OBJECTIVES/SPECIFIC AIMS** ATP signaling may participate in the neurosensory process associated with dental orofacial pain. In this study, we investigated whether pannexins, which are similar to connexins by forming ATP-permeable hemichannels, are present in human dental pulp. We also assessed the presence of ATP degradation machinery by evaluating the existence, distribution, and functional activity of ecto-ATPase enzymes in dental pulp. **METHODS/STUDY POPULATION** Extracted human third molars were collected from dental clinic patients. Immunofluorescence and enzyme histochemistry staining were used to assess the existence of pannexin and functional ecto-ATPase activity, respectively, in dental pulp. **RESULTS/ANTICIPATED RESULTS** Immunofluorescence experiments demonstrated that pannexin3 is expressed in odontoblasts with processes extending into dentin tubules. Pannexin3 was also detected in dental pulp nerve trunks. In addition, the presence of functional ecto-ATPase activity was observed by histochemistry in the odontoblast layer, subodontoblast layer, and nerve trunks in dental pulp. **DISCUSSION/SIGNIFICANCE OF IMPACT** Our results provide evidence that the functional machinery required for ATP release and degradation is present in dental pulp. This finding supports a role for ATP signaling in dentin sensitivity and dental pain.

## T1: TRANSLATION TO HUMANS

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### TOWARD MOLECULAR DIAGNOSIS OF EARLY ONSET SEPSIS USING UMBILICAL CORD BLOOD

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**OBJECTIVES/SPECIFIC AIMS** To perform an exploratory validation study to evaluate performance and operational characteristics of our novel polymerase chain reaction-high resolution melt analysis (PCR-HRMA) assay for diagnosis of early onset neonatal sepsis (EONS) using umbilical cord blood (UCB). **METHODS/STUDY POPULATION** We are performing a clinical validation study based on a case-control study design. Utilizing a novel technique for aseptic collection of high volume UCB, our team has established a prospective repository of newborn blood. Case definitions include newborns (72 hours of age) with culture-proven or clinical sepsis. Controls include newborns without concern for infection. PCR-HRMA results using higher volume of discarded UCB procured sterilely from newborns with case defining EONS versus healthy controls will be compared. The diagnostic accuracy of our eubacterial PCR will be summarized using Receiver Operating Characteristic (ROC) curve analysis, and the AUC, sensitivity, specificity, positive and negative likelihood ratio of the eubacterial PCR assay will be determined as performance outcome measures. **RESULTS/ANTICIPATED RESULTS** We anticipate that our proposed approach will achieve and AUC ≥ 0.9 in diagnosis of EONS. **DISCUSSION/SIGNIFICANCE OF IMPACT** EONS is a devastating illness of the newborn caused by bacterial infection of the blood that results in severe systemic illness. Currently available blood tests for detection of EONS have major limitations. We expect that the combined use of our PCR-HRMA with higher volume UCB will enable timely and accurate diagnosis of EONS. Potential impact include early effective intervention, reduced emergence of antimicrobial resistance with more selective usage of antibiotics, and ultimately, improved survival from one of the most devastating newborn illnesses.

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### CREATING A PHARMACEUTICAL STYLE REGULATORY AFFAIRS GROUP IN AN ACADEMIC SETTING

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**OBJECTIVES/SPECIFIC AIMS** The Duke Translational Medicine Institute (DTMI) Regulatory Affairs (RA) team serves as a no-cost resource to the investigator community at Duke University. Primary support comes from the CTSA grant. The goal of the group is to provide regulatory and quality assurance support to research teams from preclinical to late phase clinical studies. **METHODS/STUDY POPULATION** The DTMI RA team provides support in four main areas in facilitating translational science: (1) regulatory strategy, (2) GMP manufacturing and testing of investigational drugs and biologics, (3) guidance and assistance with IND/IDE preparation and submission, including electronic submissions, and (4) assistance with setting up meetings with FDA at key points in the drug/biologic development timeline. A major focus of the DTMI RA group is to assist Duke investigators in the preparation of IND/IDE applications. In addition to working with internal sponsor-investigators, the DTMI RA group supports industry-funded proof of concept and Phase I projects in the Duke Clinical Research Unit by providing full regulatory support including maintaining electronic INDs. **RESULTS/ANTICIPATED RESULTS** The DTMI RA team has established a sophisticated regulatory service, assisting Duke investigators to meet FDA requirements for their research. In the past 5 years, DTMI RA has filed over 300 submissions to the FDA, including 58 initial IND applications and 6 original IDE applications and facilitated 20 pre-IND/pre-IDE meetings. The DTMI RA team also filed a Biological License Application for the Carolinas Cord Blood Bank product (DuCord) that received marketing approval in October 2012. **DISCUSSION/SIGNIFICANCE OF IMPACT** Thus, through the establishment of a regulatory service with significant expertise in drug and device development, DTMI RA has contributed to advance basic findings through the translational spectrum.

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### GENETIC DETERMINANTS OF THE ENDO-CANNABINOID SYSTEM AND THREAT PROCESSING IN HUMANS

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**OBJECTIVES/SPECIFIC AIMS** Patients with posttraumatic stress disorder (PTSD) are unable to suppress fear responses and negative appraisals from threat memories. Family and twin studies support that a genetic susceptibility regarding the processing of threatening events could increase the risk for PTSD. Research in rodents demonstrates that pharmacological enhancement of the endo-cannabinoid (eCB) system results in a faster extinction of threat memories. In humans, differences in eCB activity can result from genetic variations of the receptor gene (CNR1) and the enzyme that breaks down the eCB ligands (FAAH). Our objective is to correlate cognitive appraisals and physiological responses to threat with genetic determinants of the human eCB system. **METHODS/STUDY POPULATION** In adult, human subjects with PTSD and healthy controls, we will measure physiological (skin conductance) responses during a classical fear conditioning and extinction protocol. We will evaluate cognitive appraisal by measuring their reaction time to a threat versus neutral words appearing on a computer monitor during the cognitive conflict task. We will also gather a psychological profile with clinical anxiety questionnaires. For analysis, subjects will be grouped and compared according to their CNR1 & FAAH genotypes. **RESULTS/ANTICIPATED RESULTS** We hypothesize that the eCB system is associated with threat processing in humans, and that healthy participants, depending on their genotype, have significantly different threat processing measures. We also hypothesize that PTSD patients compared to healthy humans, carry differences in allelic frequencies of the genotypes studied from the eCB system. **DISCUSSION/SIGNIFICANCE OF IMPACT** Our long term goal is to determine pharmacogenetic markers of human responses to threats, to identify at risk individuals, and therapeutic targets that enhance treatments in favor of PTSD patients.

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### IMPACT OF GESTATIONAL DIABETES MELLITUS ON PLACENTAL FATTY ACID TRANSFER TO THE INFANT

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**OBJECTIVES/SPECIFIC AIMS** The Impact-LA study aims to (1) Evaluate the mechanisms by which human placental tissue fatty acid (FA) binding and transport

is regulated (2) Determine the effects of perturbations in the placental tissue FA transport and binding system secondary to biochemical and metabolic dysregulation on infant growth and neurodevelopmental outcomes. **METHODS/STUDY POPULATION** Placental tissue will be collected at delivery and blood samples from normal and overweight women with ($n$ = 20) and without GDM ($n$ = 20) at 24–28, 32, 36 weeks and delivery. Gene and proteomic profiles in placenta and FAs in blood will be analyzed. **RESULTS/ANTICIPATED RESULTS** This translational study builds on previous preclinical findings by identifying how placental transmembrane transport and intracellular binding and trafficking of LCPUFAs alters clinical infant outcomes in GDM (Apgar scores, adiposity, maturity). **DISCUSSION/SIGNIFICANCE OF IMPACT** Up to 18% of all pregnancies in the U.S. are complicated by GDM. Normal fetal development and growth depends on placental transfer of nutrients including the long chain polyunsaturated FAs (LCPUFAs). Women with GDM have impaired placental transport of the LCPUFAs, docosahexaenoic acid (DHA, 22:6n-3) needed for neural and retinal development, and arachidonic acid (AA,20:4n-6) required for growth. This decrease in transfer is evident in the face of adequate DHA and AA maternal plasma and erythrocyte levels. The mechanisms underlying this phenomenon are not fully understood. Thus, the translational value of this work is to decrease negative infant outcomes associated with low LCPUFA transfer and determine the mechanisms so that nutritional strategies can be designed.

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## MUSCLE-DERIVED STEM CELLS (MDSC) STIMULATE THE EARLY REPAIR OF ISCHEMIC MUSCLE

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**OBJECTIVES/SPECIFIC AIMS** Muscle ischemia and necrosis are common factors in two devastating conditions, critical limb ischemia (CLI) in the limb muscles of some patients with type 2 diabetes (T2DM), and Duchenne's muscular dystrophy (DMD) in the muscles of children with inactive dystrophin. Adult stem cells are studied for DMD therapy although not as yet in CLI, but the repair of the damaged myofibers is still inefficient. Since MDSC implanted in the muscle stimulate angiogenesis and myogenesis, their early repair efficacy on the damaged gastrocnemius has been compared in: 1) a CLI/T2DM model induced by femoral artery ligation in db/db mice, and b) a DMD model with severe muscle damage, the old mdx mouse with notexin injury in the gastrocnemius. **METHODS/STUDY POPULATION** Mice were left untreated (UT), or received MDSC at injury (SC), and nondiabetic intact (ND-UT) or wild-type (WT-UT) untreated mice were controls. **RESULTS/ANTICIPATED RESULTS** At 3 weeks, in CLI versus UT, SC did not reduce mortality or leg loss. In CLI and mdx, SC helped muscle repair by increasing SC activation and myofiber central nuclei, and reducing apoptosis, but did not affect the compensatory overexpression of VEGF in UT versus WT-UT. SC stimulated myofiber formation in mdx but not in CLI, and reduced myofibroblasts in CLI but increased it in mdx. SC reduced in CLI lipodegeneration and apoptosis, and increased smooth muscle and BDNF but also collagen (mdx not evaluated). Myostatin/follistatin ratio was increased by SC in both CLI and mdx. **DISCUSSION/SIGNIFICANCE OF IMPACT** MDSC stimulated early muscle repair but not angiogenesis in two ischemic conditions, with partial counteraction by myostatin overexpression. GRANT SUPPORT: National Institute on Minority Health and Health Disparities of the National Institutes of Health under award number R25 MD007610.

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## NEUROMEDIN U RECEPTOR 2 AS A NOVEL THERAPEUTIC TARGET TO TREAT OBESITY

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**OBJECTIVES/SPECIFIC AIMS** Safe and effective approaches for the treatment of obesity are needed. Although studied as distinct pathways for decades, feeding and reward processes are now thought to be driven by overlapping neural circuits. Studying this "overlap" may provide insight into the basis of obesity and lead to novel therapeutic targets for this disorder. An innovative target in this regard is neuromedin U (NMU), a peptide shown to suppress food intake and cause weight loss. These effects of NMU may be related to actions at the NMU receptor 2 (NMUR2) in the hypothalamus, particularly in the paraventricular nucleus (PVN) which is enriched for NMUR2. **METHODS/STUDY POPULATION** To investigate the role of NMUR2 signaling in the PVN, we utilized RNA interference to selectively knockdown NMUR2 gene expression (NMUR2-KD). We then evaluated food intake, body weight, and feeding behavior. In addition, we tested small molecule agonists of NMUR2 for the first time in animal models of food intake. **RESULTS/ANTICIPATED RESULTS** When the rats were fed a nonobesogenic diet, the NMUR2-KD produced no significant effect on food intake or body weight. However, when the rats were fed an obesogenic diet, NMUR2-KD rats ate significantly more food and gained significantly more weight than controls. Furthermore, we identified two small molecule NMUR2 agonists that were functional *in vivo*. We found that acute subcutaneous administration of the compounds significantly decreased rats' 24-hour intake of obesogenic food compared to controls. **DISCUSSION/SIGNIFICANCE OF IMPACT** Taken together, these data indicate that NMUR2 is a valid therapeutic target to treat obesity. These studies have identified a novel small molecule NMUR2 agonist that is functional in animal models and has provided new insights into the mechanisms of complex reward-related behaviors like feeding and.

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## PRECLINICAL RECOVERY RATES OF CIRCULATING TUMOR CELLS IN BREAST CANCER: AN *IN VITRO* EXPERIMENTAL STUDY

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**OBJECTIVES/SPECIFIC AIMS** Most circulating tumor cell (CTC) assays rely on the detection of epithelial cell surface markers such as the epithelial cell adhesion marker (EpCAM). We aimed to evaluate the ability of a CTC assay using immunomagnetic enrichment followed by flow cytometry (IE/FACS) to detect CTCs across known molecular subtypes of breast cancer. **METHODS/STUDY POPULATION** Ten breast cancer cell lines were acquired from the ATCC, authenticated and stratified according to subtype: HER2 positive, luminal A, luminal B and basal-like. Cell lines were spiked into peripheral blood (PB) from healthy female donors. IE/FACS was performed using EpCAM ferrofluid via a magnetic separator followed by incubation with Thioflavin T, CD45, and EpCAM antibody-fluorochromes. Absolute cell counts and recovery rates were determined using the TruCOUNT method (BD Biosciences) with acquisition of 35,000 beads. **RESULTS/ANTICIPATED RESULTS** Analysis by molecular subtype did not show differences between groups ($p$ = 0.23). Table 1 Recovery Rates from PB Cell Line (%) SKBR3- 51.0 MDA-MB-453- 70.6 T47D- 11.4 MCF7- 24.4 BT474- 47.6 MDA-MB-751- 50.8 SUM 149- 72.9 SUM 190- 58.3 MDA-MB-231- 7.04 Hs578T- 0.84. **DISCUSSION/SIGNIFICANCE OF IMPACT** Significant variation occurred in recovery rates of cells depending on cell line type. IE/FACS detected a portion of CTCs from each of the 10 cell lines, including some aggressive basal cell lines that would be anticipated to undergo epithelial to mesenchymal transition (EMT).

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## DEVELOPMENT OF AMYGDALA-PREFRONTAL CIRCUITRY FROM CHILDHOOD TO YOUNG ADULTHOOD

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**OBJECTIVES/SPECIFIC AIMS** To characterize the normal development of functional connectivity between the amygdala and prefrontal cortex (PFC) from childhood to young adulthood in the context of social and emotional information. **METHODS/STUDY POPULATION** Participants were 57 healthy children and young adults with a mean age of 16.08 ± 5.28 years (age range: 7 to 25 years), of which 33 participants were female. All participants were free of lifetime diagnosis of Axis I or Axis II disorder. Functional magnetic resonance imaging (fMRI) data were acquired while participants performed a modified Emotional Face Assessment Task (EFAT). Participants viewed a trio of faces and were instructed to match the expression (angry, fearful, happy) as the target face. Face matching blocks were interspersed with shape-matching blocks (circles, rectangles, or triangles). Psycho-Physiological Interaction (PPI) analyses were performed to examine functional "coupling" between the amygdala and PFC during fearful faces versus circles. **RESULTS/ANTICIPATED RESULTS** Age was negatively correlated with functional connectivity between the amygdala and several PFC regions including rostral anterior cingulate cortex (ACC), ventral lateral PFC, and dorsolateral PFC (uncorrected $p < 0.005$, cluster size = 20). Specifically, a developmental transition from positive to negative connectivity is observed between amygdala and rostral ACC during adolescence. **DISCUSSION/SIGNIFICANCE OF IMPACT** Results suggest that adolescence is the critical transitional phase for the development of amygdala-PFC circuitry. Positive or immature amygdala-rostral ACC connectivity in children may reflect intrinsic bottom-up amygdala signaling to PFC regions, and negative functional connectivity in adulthood may reflect mature top-down inhibitory regulation.

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## GENERATING BIOENGINEERED HUMAN INTESTINAL TISSUE USING INTESTINAL ORGANOIDS AND ACELLULAR MATRICES

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**OBJECTIVES/SPECIFIC AIMS** Our goal is to develop new treatment strategies for patients with short bowel syndrome (SBS) by using decellularized extracellular matrices (ECMs) and *in vitro* generated intestinal tissue called "induced human intestinal organoids" (iHIOs). We hypothesize that decellularized ECM can provide the appropriate architectural support and instructive signals to guide iHIOs to take on the topology, architecture and function of normal intestine. **METHODS/STUDY POPULATION** Porcine and human small intestine were decellularized through a series of detergent, DNase and solvent washes. iHIOs were generated according to established methods. iHIOs were physically placed onto ECM and then cultured together in iHIO growth media for various times before recellularization was assessed. **RESULTS/ANTICIPATED RESULTS** Our results demonstrate that iHIOs can successfully reseed both porcine and human acellular intestinal scaffolds. Given iHIOs contain both epithelial and mesenchymal cell populations, we observe appropriate epithelial and mesenchymal cell distribution on the scaffolds. We also detect epithelial expression of villin and mucin, markers of enterocytes and goblet cells, respectively. **DISCUSSION/SIGNIFICANCE OF IMPACT** SBS results in poor nutrient adsorption due an insufficiency of healthy intestine. Improved therapeutic options are desperately needed. This is the first demonstration of the ability to successfully reseed acellular ECMs with iHIOs and is an important first step in being able to develop bioengineered intestine for transplantation.

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### URINARY CELL MRNA PROFILES PREDICT HUMAN KIDNEY ALLOGRAFT STATUS

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**OBJECTIVES/SPECIFIC AIMS** Acute rejection (AR), a serious complication in kidney transplantation, is diagnosed using the biopsy procedure which is invasive and can have complications of bleeding, graft loss, and even death. Noninvasive diagnosis of AR is therefore a major objective in transplantation. **METHODS/STUDY POPULATION** Because acute rejection is characterized by inflammatory cells gaining access to the renal tubular space, we reasoned that profiling of urinary cells would offer a noninvasive means of diagnosing AR. To test our hypothesis, we developed urinary cell mRNA profiling methodology and investigated whether levels of mRNAs encoding immunoregulatory proteins are diagnostic and/or prognostic of AR. **RESULTS/ANTICIPATED RESULTS** In our single center studies, urinary cell levels of mRNA for perforin and granzyme B, PI-9, CD103, IP-10 and CXCR3 or Foxp3 differentiated kidney graft recipients with AR from those without AR. Our single center studies led to a multicenter Clinical Trials in Organ Transplantation-04 in which 4300 urine specimens from 485 kidney graft recipients were collected and profiled. This study, in addition to confirming the results from our single center studies, discovered and validated a 3-gene signature of 18S rRNA-normalized measures of CD3ε mRNA, IP-10 mRNA, and 18S rRNA diagnostic and prognostic of AR in the kidney allograft. Our signature reflected also the potency of immunosuppressive therapy. **DISCUSSION/SIGNIFICANCE OF IMPACT** Our development of noninvasively ascertained biomarkers of kidney allograft status, in addition to minimizing the number of invasive biopsies, opens opportunities for personalizing immunosuppressive therapy.

## T2: TRANSLATION TO PATIENTS

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### PROTEIN CHARACTERISTICS OF RECURRENT PANCREATIC CANCER

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**OBJECTIVES/SPECIFIC AIMS** Pancreatic ductal adenocarcinoma (PDAC) is deadly, with 5-year survival of 6%. The only cure for PDAC is surgical removal of the tumor, yet 5-year survival for those with surgically treated disease is only 20% due to postoperative recurrence. We aim to identify and characterize functionally important protein pathways and subnetworks associated with recurrence of disease after surgery. **METHODS/STUDY POPULATION** We will screen 80 matched primary frozen PDACs: 40 with recurrent disease after surgery, and 40 without recurrent disease with the Protein Pathway Array (PPA) using antibodies for protein and phosphoproteins associated with cell proliferation, stem cell, epithelial-mesenchymal transition (EMT) and invasiveness/metastasis. The PPA is comprised of three integrated elements: a one or two dimensional gel electrophoresis immunoblot or bead array, image acquisition and analysis of data, and integration of these results by computational network analysis. PPA can identify and characterize the functionally important protein pathways and subnetworks that associate with the development and metastatic potential of cancers. **RESULTS/ANTICIPATED RESULTS** Statistical analysis and classification packages such as SAM and PAM, as well as clustering and visualization tools such as BRB will be used to select those differentially expressed proteins and phosphoproteins between those with and without recurrent disease. **DISCUSSION/SIGNIFICANCE OF IMPACT** Identification of functionally important signaling pathways and subnetworks associated with PDAC recurrence would allow for identification of patients at high-risk of disease recurrence and provide opportunities for targeted therapy in patients at high-risk of recurrence.

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### PILOT CLINICAL TRIAL OF VITAMIN D SUPPLEMENTATION IN SECONDARY PROGRESSIVE MULTIPLE SCLEROSIS

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**OBJECTIVES/SPECIFIC AIMS** To design a pilot clinical trial to test the potential neuroprotective effects of vitamin D supplementation in secondary progressive multiple sclerosis. **METHODS/STUDY POPULATION** A 2 year randomized double blind placebo controlled study is proposed. Co-primary endpoints will include diffusion tensor imaging of the corticospinal tract and cortical thickness. Secondary endpoints will include a variety of clinical, self-report, cognitive, and optical coherence tomography measures. Neurofilament light chain, a biomarker of neurodegeneration, will be measured in cerebrospinal fluid at baseline and every 12 months. Vitamin D deficient patients will be randomized to vitamin D supplementation regimens targeting low (40 ng/ml) or high (80 ng/ml) levels. Vitamin D doses will be adjusted every 3 months based on serum vitamin levels. Study visits will occur every 3 months and MRI studies will be conducted at baseline and every 6 months. Sample size estimates were created using a mixed effect model of a longitudinal DTI study. Blood and cerebrospinal fluid will be banked. **RESULTS/ANTICIPATED RESULTS** Sample size estimates using diffusion tensor imaging showed that a sample size of 20 subjects in each arm will have a power >90% to detect a 30% change in mean and longitudinal diffusivity. A National Multiple Sclerosis Society Grant was submitted for a target funding date of October 2014. An application for an IND exemption will be made to the local institutional review board. **DISCUSSION/SIGNIFICANCE OF IMPACT** The proposed clinical trial will be a preliminary assessment of the potential neuroprotective effects of a widely available, low cost and safe compound. The results will assist in the design and feasibility of a larger multicenter phase II trial of vitamin D in secondary progressive multiple sclerosis and will provide a rich clinical and imaging dataset plus banked blood and cerebrospinal fluid samples.

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### MULTIPARAMETRIC 3T WHOLE-BODY MRI IN FACIOSCAPULOHUMERAL MUSCULAR DYSTROPHY

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**OBJECTIVES/SPECIFIC AIMS** To address the need for validated outcome measures in muscle disease, we examined the feasibility of multiparametric hybrid continuous table movement (CTM) and multistation whole body MRI (WBMRI) in subjects with facioscapulohumeral muscular dystrophy (FSHD). **METHODS/STUDY POPULATION** Subjects with FSHD were scanned using a 3T Siemens Tim Trio scanner. CTM was used to obtain axial T2-weighted, T1-weighted, and Dixon imaging. A multistation Set-n-Go diffusion weighted imaging sequence with a monopolar encoding scheme was used to measure muscle diffusion characteristics. Regions of interest were drawn in leg muscle groups to calculate mean ADC values. Total acquisition times were recorded. Muscles were scored for fat infiltration on T1 and edema-like change on T2 images. Muscle strength testing and timed function testing were performed at the time of the scan. **RESULTS/ANTICIPATED RESULTS** Eleven subjects (ages 20–65) were imaged; 92–118 muscles were scored per scan. Frequency and severity of muscle disease on T1 and T2-weighted images were analyzed by subject and by muscle. Mean fat infiltration scores for leg muscles were significantly associated with strength and walk times. Affected muscles in the legs were associated with lower ADC map values than unaffected muscles. Mean scan time was 53 ± 8.8 (range 37–66) minutes. **DISCUSSION/SIGNIFICANCE OF IMPACT** Multiparametric WBMRI with hybrid CTM and multistation imaging at 3T is feasible with high diagnostic quality and clinically acceptable scan time, making it a promising tool for tissue characterization and monitoring treatment response in FSHD.

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### AN ACTIVITY MONITOR AND MOBILE DEVICE INTERVENTION IS FEASIBLE AMONG OLDER ADULTS

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**OBJECTIVES/SPECIFIC AIMS** Sedentary behavior and physical inactivity are prevalent, increase with age, and are associated with negative health outcomes. Electronic activity monitors that sync with mobile devices are potentially effective tools for

increasing autonomous (volitional) motivation and physical activity. The purpose of this study was to investigate the feasibility and acceptability of activity monitors and tablets among older adults. A secondary goal was to investigate intervention effects on predictors of autonomous motivation. **METHODS/STUDY POPULATION** Ten sedentary, overweight or obese older adults aged 55–79 (60 ± 4.38 years old, 29.87 ± 3.39 kg/m$^2$ BMI, 7 female) were recruited into a 6-week preexperimental pilot study. Participants received a Jawbone Up activity monitor and a mini tablet with the Up application ("app") installed. They attended weekly brief counseling meetings and were instructed to wear and sync the monitor daily. Usage data were abstracted from the app, and acceptability and psychological data were self-reported at baseline and 6 weeks. **RESULTS/ANTICIPATED RESULTS** Participants wore the monitors 402 out of a possible 420 days (6 weeks × 10 participants). Participants agreed or strongly agreed that they would continue to wear the monitor (9/10), they found the tablet easy to use (10/10), and that the application provided useful ideas (8/10). Participants reported never (6/10) or almost never (4/10) having technological problems. Perceptions of autonomy ($p = 0.004$), competence ($p = 0.001$), and relatedness ($p = 0.022$) significantly increased from baseline to 6 weeks. **DISCUSSION/SIGNIFICANCE OF IMPACT** Mobile health interventions that use mini tablets and activity monitors are feasible and acceptable among older adults. Activity monitor interventions hold promise for increasing autonomous motivation and physical activity in this age group.

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## FEASBILITY STUDY: COUPLE THERAPY FOR COUPLE VIOLENCE

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**OBJECTIVES/SPECIFIC AIMS** This study aims to understand whether the couple therapy is effective in preventing situational couple violence. The interplay between changes in violence and the emotion regulation of partners in relation to each other will be investigated in a couple context. Aim 1: Examine the associations between violence and each partner's psychophysiological regulation in terms of Hypothalamic Pituitary Adrenal (HPA) activity and Parasympathetic Nervous System (PNS) activity. Aim 2: Examine the longitudinal effects of couple therapy on IPV and each partner's psychophysiological regulation in terms of HPA and PNS activity. **METHODS/STUDY POPULATION** This study has a longitudinal design over 8 weeks of couple therapy. Data will be collected in three different time points: pretest, posttest, and follow-up. Eight couples will be divided into control and intervention groups. Data will be collected in the form of self-report and partner-report measures, as well as physiological markers. **RESULTS/ANTICIPATED RESULTS** We anticipate to diminish situational couple violence and its consequences, as well as demonstrate the feasibility of couple therapy via biomarkers. **DISCUSSION/SIGNIFICANCE OF IMPACT** Many programs designed to prevent intimate partner violence solely target male offenders. Domestic violence shelters and other facilities traditionally support only female victims by offering therapy and educational programs. However, recent findings on separate batterer intervention programs indicate that these programs do not work as well as expected. Furthermore, in contrast to widespread expectations, couples who experience situational couple violence may still want to remain together. Therefore, for some couples it is important to be able to improve the relationships and end the violence within the couple.

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## THE SYMPTOMATIC IMPACT OF CONGENITAL AND CHILDHOOD ONSET MYOTONIC DYSTROPHY TYPE-1

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**OBJECTIVES/SPECIFIC AIMS** Characterize the impact and prevalence of symptoms in congenital and childhood myotonic dystrophy (CDM/ChDM). Clinician scientists need to obtain a global characterization of the course of disease manifestations and symptoms in CDM/ChDM to prepare for new treatments, such as antisense oligonucleotides. **METHODS/STUDY POPULATION** We distributed a survey representing 348 symptoms and 19 themes to participants in the US National Registry of DM1 Patients and Family Members, the Canadian Neuromuscular Registry, and the Swedish Health System. All CDM/ChDM participants developed symptoms before 16 years of age and were younger than 40 years of age. A parent of each participant completed a parent-proxy survey and those over age 5 received an age-appropriate survey. **RESULTS/ANTICIPATED RESULTS** Prevalent themes reported by CDM/ChDM participants involved problems with hands or fingers (80.2%) and communication issues (82.93%). The symptoms with the greatest impact on quality-of-life involved communication issues (impact score: 1.35) and gastrointestinal (GI) issues (impact score: 1.11). In many cases, there was agreement between parent and participant responses with an overall weighted Kappa of 0.33, though this was dependent on individual symptoms. The prevalence and relative impact of specific ChDM/CDM manifestations depended upon the age of symptom onset, disease duration, and CTG repeat length. **DISCUSSION/SIGNIFICANCE OF IMPACT** Patients and parents identify a wide range of symptoms that affect quality-of-life in the ChDM/CDM population, many of which may be underrecognized. This research will allow the creation of a disease-specific patient reported outcome for this population.

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## PRESERVED COGNITION IN DISORDERS OF CONSCIOUSNESS CORRELATES WITH INTEGRITY OF EEG MARKERS OF CORTICO-THALAMIC DYNAMICS

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**OBJECTIVES/SPECIFIC AIMS** Standard bedside behavioral tests used to diagnose disorders of consciousness (DOC) require direct observation of motor functions to assess level of consciousness. Recent case reports challenge the bedside diagnoses by using fMRI or fEEG which can detect covert responses even in the setting of severe motor impairment. However these novel methods have limited availability and high potential of false negative and false positive findings. Conventional EEG analysis also bypasses motor functions, however it is readily available and is a well-established correlate of brain integrity. We hypothesized that conventional EEG features correlate with preserved high-level cognitive abilities and may be used to characterize patients with DOC. **METHODS/STUDY POPULATION** 62 research admissions (2–5 days each) in a cohort of 44 subjects with DOC (11 patients with multiple admissions). Evaluations included conventional visual analysis of awake and sleep EEG, functional MRI (fMRI) or functional EEG (fEEG) during motor imagery tasks, structural brain imaging (CT or MRI), FDG-PET, and standard behavioral testing. **RESULTS/ANTICIPATED RESULTS** Five subjects were found to have evidence of command following via fMRI and/or fEEG. Taken against the results across all subjects, these five subjects demonstrated relatively intact awake EEG integrity and preservation of sleep spindles. **DISCUSSION/SIGNIFICANCE OF IMPACT** Our results suggest that preserved cortico-thalamic dynamics as marked by the presence of relatively intact awake EEG and sleep spindles may be required of preserved cognition. These findings support a simple strategy to use conventional EEG to stratify DOC patients for possible unrecognized consciousness.

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## MULTIPLE-STRATEGY INTERVENTION PROGRAM TO PROMOTE ADHERENCE TO TREATMENT OF BIPOLAR DISORDER AT RISK OF CARDIOVASCULAR DISEASE PATIENTS

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**OBJECTIVES/SPECIFIC AIMS** A rationale and design is provided for a novel psychosocial intervention targeting treatment adherence in Hispanic patients with bipolar disorder (BD) who are at risk for cardiovascular disease (CVD). CVD is the leading cause of morbidity and mortality among patients with BD. Nonadherence to prescription medication for BD and CVD is a serious concern as untreated or undertreated BD with CVD can have a significant impact on patient's health, and also on society in general with its financial implications. There are no studies that target nonadherence to treatment in BD patient at risk of CVD factors in Puerto Rico. A key aspect of tailoring intervention for this population is the influence of family members in the process of adherence to medication and healthy behaviors. We propose to develop and test a psychosocial intervention that will form part of a manual tailored to promote concordance to medication treatment that address risk factors for CVD in BD patients. This study will test feasibility and acceptability, and short-term improvements in adherence behavior, manic and depressive symptomatology, and lab based measures of CVD risk. **METHODS/STUDY POPULATION** Stage 1a we will carry out focus groups and collaboratively develop the manual. Stage 1b will be a pilot study employing an open single group design where each subject is his own control. A pre- and posttests will be given in two-time point repeated measures. Assessment will include the administration of scales to determine adherence to treatment, mood symptom assessments, and laboratory measures of CVD risk components. Pharmacy records will be used as an objective measure of medication adherence. The sample is of 40 patients from two sites: ASSMCA and a Community Mental Health Clinic.

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## IDENTIFICATION OF OPTIMAL STIMULATION SITE FOR CERVICAL DYSTONIA SYMPTOMS

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**OBJECTIVES/SPECIFIC AIMS** Dystonia is characterized by abnormal posturing due to sustained muscle contraction, which not only leads to pain but also causes significant

disability. In cervical dystonia (CD), botulinum toxin is the gold standard treatment, but has limitations—painful, frequent injections as well as expected adverse events. New therapeutic targets are needed in this disorder. We aim to identify the optimal stimulation site for transcranial magnetic stimulation (TMS) therapy of CD. **METHODS/STUDY POPULATION** In a randomized, sham-controlled, blinded-rater prospective study, seven CD subjects are given a 15-minute session of low-frequency (0.2 Hz) rTMS over the primary motor cortex (MC), dorsal premotor cortex (dPM), supplementary motor area (SMA), anterior cingulate cortex (AC) and a sham condition. The primary outcome measure is change in the Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) score pre- and postintervention. Secondary outcome measures will include physiologic markers and patient symptom rating. **RESULTS/ANTICIPATED RESULTS** Two men and one woman (mean age = 53 years) have completed all 5 sessions. Preliminary analysis of the main outcome measure reveals the median change in TWSTRS score pre- and postintervention by site was 0 (MC), 0 (SMA), 0 (Sham), 2 (dPM), and 0 (ACC). TWSTRS mean beginning score at the beginning of the trial was (12.3, SD 6.7) and at the end (3.6, SD 1.2). **DISCUSSION/SIGNIFICANCE OF IMPACT** These preliminary results suggest a role of rTMS in modulating CD symptoms. Based on three subjects, dPM is a premotor area to be targeted in further rTMS studies. The effect over time with improved preintervention TWSTRS scores deserves further evaluation. While there is a larger effect seen with dPM targeting, the timing of rTMS delivery may play a role in the symptom improvement seen in these subjects.

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## RANDOMIZED CONTROLLED TRIAL OF MINDFULNESS-BASED STRESS REDUCTION (MBSR) FOR PERSISTENTLY FATIGUED CANCER SURVIVORS

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**OBJECTIVES/SPECIFIC AIMS** Cancer-related fatigue (CRF) is the most prevalent, persistent, and disabling symptom reported by cancer survivors. Effective CRF treatments that are acceptable to patients are critically needed. The purpose of this trial was to assess the efficacy of MBSR compared to an active control for CRF. **METHODS/STUDY POPULATION** Fatigued breast ($n$ = 60) and colorectal ($n$ = 17) cancer survivors were randomized to 8-week MBSR (meditation/yoga) or fatigue education/support groups. Primary outcome was Fatigue Symptom Inventory interference subscale (FSI-I). Secondary outcomes included attentional function, sleep disturbance, depression, and anxiety. Symptoms were assessed at baseline (T1), postintervention (T2), and 6-month follow-up (T3). **RESULTS/ANTICIPATED RESULTS** Both groups showed reductions in FSI-I scores, with a trend favoring MBSR at T2 ($d$ = −0.36, $p$ = 0.14). Improvements for both groups were sustained through T3. The MBSR group reported significant improvements in attentional function compared to the education/support group at T2 ($d$ = 0.81, $p$ = 0.0008) and T3 ($d$ = 0.59, $p$ = 0.018). Other symptoms assessed showed nonsignificant trends favoring MBSR at T2. **DISCUSSION/SIGNIFICANCE OF IMPACT** Both interventions were helpful in producing sustained reductions in fatigue interference; however, MBSR holds a clear advantage in improving attentional function.

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## ENHANCING MOTIVATION FOR PHYSICAL ACTIVITY TO REDUCE FALL RISK

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**OBJECTIVES/SPECIFIC AIMS** The overall objective of this research is to develop an intervention, Ready~Steady, designed to enhance motivation for engaging in physical activities known to reduce falls. It has 3 components: interpersonal motivation, intrapersonal motivation, and physical activity. Content within the motivational components is based on theoretical and empirical evidence that explains why certain psychosocial factors influence older adults' motivation for engaging in physical activity. Content within the physical activity component is based on an established falls prevention protocol for light intensity physical activities. The objective in this study is to determine if both motivational components are essential to the intervention. Specific Aims include: (1) Compare at baseline, 1 week and 6 month follow-up, physical activity behavior, fall risk and occurrence, and psychosocial processes between participants randomized to 1 of 4 treatment conditions: (a) Ready~Steady, (b) Ready~Steady minus the interpersonal motivation component, (c) Ready~Steady minus the intrapersonal motivation component, and (d) Usual Care (physical activity); (2) Ascertain the utility of Ready~Steady and how outcomes were achieved. **METHODS/STUDY POPULATION** A randomized controlled trial and qualitative focus group interviews will be used for Aims 1 and 2 respectively. Adults will be targeted for the study who speak English and have risk(s) for falling as indicated by being >69 years old and having low levels of physical activity. **RESULTS/ANTICIPATED RESULTS** This research will determine if both motivation components are essential to the Ready~Steady intervention. **DISCUSSION/SIGNIFICANCE OF IMPACT** Results will inform how the next iteration of Ready~Steady should be shaped. This research will improve the intervention and underlying theory; optimize future intervention research design; and build a practical science behind the intervention for translation.

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## METHYLATION BIOMARKERS FOR CANCER SURVEILLANCE IN LYNCH SYNDROME

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**OBJECTIVES/SPECIFIC AIMS** Colorectal cancer (CRC) accounts for more than 1,000,000 deaths annually worldwide. While most CRC occurs sporadically, up to 30% of cases have a hereditary component. Lynch syndrome results from germline inactivation of DNA mismatch repair genes, accounting for up to 5% of all CRC. Lifetime risk of CRC in individuals with Lynch syndrome approaches 70%. Although colonoscopy has been found to be effective in reducing CRC related mortality in families with Lynch syndrome, interval tumors developing between colonoscopic exams have been reported. Stool DNA testing has been shown to be an effective early detection method for CRC and high risk polyps. The utility of methylation profiles in stool DNA testing has yet to be studied. Our goal in the present study is to explore the feasibility of methylated genes highly discriminant in sporadic colorectal neoplasia for use in the stool detection of Lynch related neoplasia. **METHODS/STUDY POPULATION** We will study the top 20 most discriminant methylated gene markers for sporadic colorectal neoplasia identified in a recent whole methylome project. The 5 most discriminant markers for Lynch syndrome neoplasia will be first selected using tissue. These genes will then be tested on archived stool from Lynch patients with colorectal neoplasms and Lynch controls without neoplasms to estimate their sensitivity and specificity. **RESULTS/ANTICIPATED RESULTS** We hypothesize that there is substantial overlap in the DNA methylation profiles of colorectal neoplasms in Lynch syndrome and those that occur sporadically. **DISCUSSION/SIGNIFICANCE OF IMPACT** Lynch syndrome DNA-methylation profiles may be used for the development of biomarkers that could potentially be useful in assessing clinical outcomes and establishing screening and surveillance algorithms.

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## TISSUE ENGINEERING MICROVESSELS TO PERFUSE ISOLATED GLOMERULI *IN VIVO*

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**OBJECTIVES/SPECIFIC AIMS** More than 400,000 patients receive treatment for end stage renal disease in the United States. Kidney transplantation is the most effective therapy, but there are not enough donor organs to meet the rising demand. Tissue engineering of a kidney is a potential solution to this organ shortage. **METHODS/STUDY POPULATION** Our laboratory has previously reported that human umbilical vein endothelial cells transduced with the anti-apoptotic protein Bcl-2 (designated Bcl-2-EC) can spontaneously organize into perfused microvessels within type I collagen/fibronectin gels when implanted in immunodeficient mice. As a first step in tissue engineering of renal microvasculature, we combined Bcl-2-ECs with microdissected intact whole rat glomeruli in type I collagen gels and implanted them within immunodeficient mice. **RESULTS/ANTICIPATED RESULTS** We observed that rat glomeruli remained viable for up to two weeks, and maintained podocyte specific podocin staining. Using GFP-expressing rat glomeruli and intravital rhodamine dextran injection, we saw that all glomeruli were perfused by microvessels derived from Bcl-2-ECs at 15 days. However, in the absence of Bowman's capsule and tubular outflow, several glomeruli lost their glomerular capillary tuft morphology and became perfused capillary plexi. Transmission electron microscopy revealed endothelial swelling, loss of endothelial fenestrae, and podocyte foot process effacement after 10 days *in vivo*. **DISCUSSION/SIGNIFICANCE OF IMPACT** Anastomosis of capillaries derived from Bcl-2-ECs with isolated glomeruli provides proof of concept that self-assembled microvessels can perfuse specialized organ structures. We hypothesize that addition of tubular outflow would ameliorate some of the morphological changes observed, and that tissue engineered constructs described here could be further modified to engineer functional kidney tissue in the future.

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## CLOPIDOGREL PHARMACOGENETICS IN OUR BIOBANK COHORT

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**OBJECTIVES/SPECIFIC AIMS** The CYP2C19 (C19) variant genes are independent predictors of reduced clopidogrel efficacy in patients with acute coronary syndrome. Using our Biobank cohort (high cardiovascular disease prevalence and rich racial diversity), we investigate generalizability of the impact of C19 polymorphism in a heterogeneous population [i.e. various clopidogrel indications and 3 racial/ethnic groups]. Aims: (1) Describe the C19 allele distribution of our cohort within each racial group. (2) Investigate the additive effect of clopidogrel treatment and C19 variant genotype on major adverse cardiovascular events (MACE) while adjusting for potential confounders. (3) Assess if race and/or clopidogrel indication modifies the effects C19 polymorphism on clopidogrel effectiveness. **METHODS/STUDY POPULATION** A retrospective cohort study of our Biobank patients. (1) Preliminary query using electronic selection algorithm yielded potential eligible patients (2) Manual review to confirm eligibility and to abstract covariates/outcomes data. (3) Merger of phenotypic and genotypic data. (4) Cox proportional hazards model will be performed for main analysis. **RESULTS/ANTICIPATED RESULTS** 1091 patients were eligible for final analysis: Mean age 68, Male 58%, Hispanic 44%, White 26%, Black 18%. 512 patients (47%) with no MACE during study period; 333 patients (31%) and 155 (14%) had 1 and >2 outcomes of interest respectively. Median time on clopidogrel was 26 months (range 3–48 months); median times to 1st and 2nd event were 11 and 19 months respectively. Pending regression analysis results. **DISCUSSION/SIGNIFICANCE OF IMPACT** The valuable data generated from this exploratory study will serve as an essential next step in a line of inquiry that may lead to a larger prospective pharmacogenetic trial. Our goal is to aid physicians make more informed decisions regarding the choice of antiplatelet agents.

## T3: TRANSLATION TO PRACTICE

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### EVALUATION OF HEALTHCARE PROFESSIONALS' INFORMATION MANAGEMENT DURING OLDER ADULTS' TRANSITIONS FROM HOSPITAL TO HOME CARE

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**OBJECTIVES/SPECIFIC AIMS** Older adults who require skilled home healthcare (SHHC) services after hospital discharge are at high risk of hospital readmission. Care transitions are often executed by SHHC professionals, yet little is known about the SHHC information management process. The aim of the study was to identify (1) critical tasks in SHHC workflow, and (2) challenges faced by SHHC professionals in information management for older adults requiring SHHC services after hospital discharge. **METHODS/STUDY POPULATION** Qualitative research methods using ethnographic techniques (direct observations and interviews). We observed and interviewed 15 SHHC staff, 5 older adults, and their 5 family caregivers from hospital discharge to the end of the first SHHC home visit. Participants came from 9 medical/surgical units in 2 hospitals, a skilled nursing facility, and an affiliated SHHC agency. Data collection took place during multidisciplinary rounds, patient bedside and home visits, and office work involving transmittal of referrals to the SHHC agency. We used conceptual frameworks informed by human factors engineering to guide data collection. **RESULTS/ANTICIPATED RESULTS** SHHC workflows were complex, with a high reliance on other individuals and on access to information for success. We identified four primary challenges for SHHC providers in completing tasks: (1) difficulty locating relevant patient information; (2) obstacles accessing physicians for orders; (3) inadequate support to track concurrent referrals; and (4) uncertainty of care plans due to changes in patient's clinical status. **DISCUSSION/SIGNIFICANCE OF IMPACT** The challenges identified are potential risks to older adults' safety and quality of care during hospital/SHHC transitions. Future studies could identify the extent to which these challenges could be targets for intervention to enhance older adults' safety.

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### EFFECT OF A NOVEL FLUORIDE DELIVERY SYSTEM ON THE PROGRESSION OF DENTAL CARIES IN 12–15 YEAR OLDS

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**OBJECTIVES/SPECIFIC AIMS** Interproximal caries (IC) is a problem that has traditionally lacked appropriate preventive treatment options. The high incidence of IC can be attributed to the failure of preventive agents from reaching these surfaces (between teeth) adequately. Approximately, 18% of interproximal surfaces develop caries and 40% of healthy coronal tooth structure may require removal for access to a minimal inaccessible amount of decay. Fluoride is the most commonly used primary preventive agent; has anticaries effect, prevent demineralization, and promote remineralization of early caries. A novel fluoride-releasing therapy was recently developed in a unique disk form of insertion between teeth. The aim of this study is: to evaluate the efficacy of a fluoride-releasing disk in the progression of incipient interproximal dental caries. **METHODS/STUDY POPULATION** A study design will be employed using a single-center, randomized, double-blind clinical trial. Calibrated examiners will evaluate children following the International Caries Detection and Assessment System (ICDAS), and it will be used as gold standard; scores will be calculated to evaluate incipient IC. The Canary System® will be used to detect and monitor incipient interproximal decay, and correlate results within assessment methods. Fluoride therapy disks will be professionally applied to 12-to-15 year olds. **RESULTS/ANTICIPATED RESULTS** Fluoride disks will provide a clinically significant reduction of incipient IC (≥10%) compared to conventional fluoride gel preloaded tray. **DISCUSSION/SIGNIFICANCE OF IMPACT** Provide evidence-based data showing that a novel therapeutic fluoride releasing vehicle is a clinically effective treatment option to prevent the progression in IC; encourage CBPP to implement this fluoride therapy alternative.

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### MEASURING COLLABORATION AND COMMUNICATION BETWEEN SPECIALISTS AND GENERALISTS OVER A VIDEO TELEMEDICINE INTERFACE

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**OBJECTIVES/SPECIFIC AIMS** Health information technology (HIT) is emerging as a facilitator of interspecialty (i.e., generalist-specialist) communication. Previously unexamined is the quality of provider communication. This study will video-record and analyze specialist-generalist communication over the video telemedicine interface. **METHODS/STUDY POPULATION** We digitally recorded 20 video telemedicine sessions, one specialist and several generalists per session, at multiple medical centers over six months. Transcribed sessions and video-recordings were uploaded into Transana and analyzed using sociolinguistic methodology and discourse analysis. Sessions were divided into 5 components: collaborative talk (> 2 participants talking within 10-seconds), case discussion (consult question, case presentation, plan), formal didactic, social talk and other (technical problems). **RESULTS/ANTICIPATED RESULTS** Generalists repeated the consult question several times before it was addressed by the specialist. The specialist spoke longer than all generalists combined and interrupted more. The videotelemedicine sessions facilitated collaboration that was most evident in case presentation (57.5% of total session length) and social talk (8.9% of total session length). During social talk, participants offered personal life experiences that demonstrated a collaborative interpersonal relationship. **DISCUSSION/SIGNIFICANCE OF IMPACT** While video telemedicine may enable interspecialty collaboration, there may be misalignment of communication patterns. Qualitative analysis is ongoing to elucidate the dynamics underpinning communication difficulties. Results from our study will inform broader efforts to improve the generalist-specialist interface.

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### IMPLEMENTATION OF FEEDING GUIDELINES FOR INFANTS WITH INTESTINAL ABNORMALITIES REQUIRING SURGICAL INTERVENTION

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**OBJECTIVES/SPECIFIC AIMS** Infants with intestinal abnormalities, such as necrotizing enterocolitis or gastroschisis, are prone to intestinal resection, feeding difficulty, and prolonged exposure to parenteral nutrition (PN), putting them at risk for parenteral nutrition-associated liver disease (PNALD), defined as a persistent direct bilirubin >2mg/dl in the absence of other liver disease. Our objective is to develop and implement new feeding guidelines for infants requiring intestinal procedures/resection to reduce the time to reach feeding goals and the incidence of PNALD. **METHODS/STUDY POPULATION** A multispecialty team developed postprocedure feeding guidelines based on evidence and consensus. Retrospective clinical data at our center was collected for infants <6 months old from 2007–2012 who required PN following intestinal resection, abdominal wall closure, ostomy, or peritoneal drain. Guidelines were implemented October 2013. A pre- and postanalysis of time to reach feeding goals and incidence of PNALD will be performed. **RESULTS/ANTICIPATED RESULTS** 82 historical control infants were identified (preguidelines) from 2007–2012. The median time to initiate feeding was 17 days, median time to reach 50% enteral feeding was 34 days, and 66% of infants developed PNALD. We anticipate earlier time to reach feeding goals and decreased incidence/severity of PNALD after implementing the guidelines. **DISCUSSION/SIGNIFICANCE OF IMPACT** A standardized approach to initiating and advancing enteral feeding has potential to improve growth, promote gut adaptation following injury and/or resection, and reduce exposure to PN, thereby reducing the incidence of PNALD.

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### THE DEVELOPMENTAL CLINICAL INSTRUMENT: STRUCTURED DATA COLLECTION FOR THE AUTISM CLINICAL EXAM

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**OBJECTIVES/SPECIFIC AIMS** Despite high fidelity use of the Autism Diagnostic Observation Schedule (ADOS) and Autism Diagnostic Interview (ADI-R), case-ascertained ASD samples continue to possess heterogeneity due to a myriad of physical, medical and psychological conditions inherent to the disorder. The physician's clinical exam provides an opportunity to recognize such phenotypic variability. But clinical exam data typically resides in unstructured free text forms. We developed the Developmental Clinical Instrument (DCI), which standardizes the documentation of an autism-focused clinical exam. Objectives: To implement the DCI at an autism research center as a means of standardizing the collection of embedded data elements and to facilitate the rapid generation of cross sectional data for specific data elements in our study population. **METHODS/STUDY POPULATION** The DCI was used to structure documentation of study physicians' clinical examination at the Seaver Autism Center for Research and Treatment. The clinical examination is one part of the IRB approved assessment protocol that also includes the ADOS, ADI-R, and other cognitive and adaptive measures. Reports were rapidly generated to reflect cross sectional data. **RESULTS/ANTICIPATED RESULTS** Clinician buy-in and compliance with the DCI was high. In this population of research subjects, cross sectional data reflecting the distribution of each data element contained in the medical history of the DCI was generated. A chart reflecting this data is displayed in figure 1. **DISCUSSION/SIGNIFICANCE OF IMPACT** The DCI facilitates structured data collection for the autism-focused clinical examination. When used with a customized data capture system, the DCI can facilitate the generation of reports that display distributions of specific data elements within a population.

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## BLOOD PRESSURE TREATMENT IN PEDIATRIC KIDNEY TRANSPLANT RECIPIENTS

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**OBJECTIVES/SPECIFIC AIMS** Over 50% of pediatric kidney transplant recipients (PKTRs) have uncontrolled blood pressure (BP) which is associated with poor outcomes. Our aim was to understand provider treatment of uncontrolled BP in our PKTR population. **METHODS/STUDY POPULATION** All visits between 6/2011 and 2/2013 for 86 PKTRs >3 mos from transplant in 6 clinics and cared for by 11 MDs were analyzed. The mean of 2 manual BP readings was recorded in our electronic health record (EHR). BP measurement technique, mean BP, and BP percentile were extracted from the EHR. Charts were reviewed to determine prescribed therapy for visits where BP was not controlled according to national guidelines. Treatment was grouped into three categories: medication, behavior modification and observation. Visits were coded according to the most aggressive therapy (medication > behavior > observation). **RESULTS/ANTICIPATED RESULTS** Of 697 visits, patients had isolated uncontrolled systolic BP (S-HTN) in 115 (16%), isolated uncontrolled diastolic BP (D-HTN) in 99 (14%), and combined uncontrolled systolic and diastolic BP (C-HTN) in 100 (14%). Patients had controlled BP in 383 (55%) of visits. Medication was more likely to be modified in visits with C-HTN (49%) and iSBP (37%) than those with iDBP (22%) (C-HTN vs. iDBP, $p < 0.001$; iSBP vs. iDBP, $p = 0.018$). MDs increased medication more often in patients with more severe uncontrolled HTN than for those with less severe HTN (51% vs. 28%, $p < 0.02$). **DISCUSSION/SIGNIFICANCE OF IMPACT** Providers adjusted medication therapy in only about half of visits where both systolic and diastolic BP were not controlled. They treated isolated uncontrolled systolic BP even less often but more often than they treated isolated uncontrolled diastolic BP. A more aggressive approach by providers to adjust medication therapy may be required to improve overall BP control in PKTRs.

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## ASSOCIATON OF PULMONARY FUNCTION WITH ADIPOSITY AND METABOLIC ABNORMALITIES IN MINORITY ADOLESCENTS

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**OBJECTIVES/SPECIFIC AIMS** While Inflammation and adiposity are two mechanisms for obesity-mediated alteration of pulmonary function (PFTs), the role of metabolic abnormalities is not known. We hypothesized that metabolic abnormalities influence PFTs, independent of truncal (waist circumference (WC) > 90th percentile) and general adiposity (BMI > 95th percentile) in minority adolescents. **METHODS/STUDY POPULATION** PFTs were compared between adolescents with general or truncal adiposity and normal weight, and between those with metabolic abnormalities (homeostatic model assessment of insulin resistance (HOMA-IR) in the top quartile or High Density Lipoprotein (HDL)<40mg/dl) and normal metabolic profile. **RESULTS/ANTICIPATED RESULTS** Obese adolescents had lower residual volume (RV), RV/total lung capacity (TLC) ratio, expiratory reserve volume (ERV) and functional residual capacity (FRC) and higher inspiratory capacity (IC) than normal-weight adolescents but did not differ in $FEV_1$/FVC ratio. Those with high HOMA-IR had lower $FEV_1$/FVC ratio, RV, RV/TLC ratio, ERV, FRC and higher IC; those with low HDL had lower $FEV_1$/FVC ratio and RV/TLC ratio. After adjusting for adiposity, HOMA-IR was a predictor of ERV ($\beta = -1.4$, $p = 0.02$) and $FEV_1$/FVC ratio ($\beta = -0.5$, $p = 0.03$), and HDL a predictor of $FEV_1$/FVC ratio ($\beta = 0.1$, $p = 0.01$). General adiposity was a predictor of FRC ($\beta = -0.5$, $p < 0.001$), IC ($\beta = 0.3$, $p < 0.001$), RV ($\beta = -0.8$, $p < 0.0001$), and RV/TLC ratio ($\beta = -0.2$, $p < 0.0001$), and truncal adiposity was a predictor of RV ($\beta = -20.3$, $p = 0.03$) and FRC ($\beta = -13.8$, $p = 0.004$). **DISCUSSION/SIGNIFICANCE OF IMPACT** Metabolic abnormalities were independent predictors of ERV and FEV1/FVC ratio. Truncal adiposity predicted RV and FRC, conferring additional risk above general adiposity, which predicted RV and RV/TLC ratio. Hence, metabolic assessment of obese adolescents may identify those at risk of developing obesity-associated pulmonary morbidity.

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## PEOPLE JUST DON'T UNDERSTAND: A CROSS-SECTIONAL SURVEY OF LOW-INCOME URBAN PATIENTS AND MEDICAID ELIGIBILITY UNDER THE ACA

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**OBJECTIVES/SPECIFIC AIMS** Medicaid expansion has potential to improve the health of uninsured safety-net populations and reduce emergency department (ED) visits. We evaluate if demographics predict ED patients' correct perception of Medicaid eligibility under the Affordable Care Act (ACA). **METHODS/STUDY POPULATION** We enrolled consecutive patients age 18–65 in a cross-sectional study at an urban, safety-net hospital from June to July 2013. Demographics, income and immigration status, self-reported knowledge of the ACA, and belief if they would qualify for Medicaid expansion were assessed. Age, income and immigration status were used to predict which patients would actually qualify. **RESULTS/ANTICIPATED RESULTS** Among 1150 patients, 68% (786) had heard of the ACA. Of these, 41% (319) were unsure if they would qualify for Medicaid expansion, 49% (387) believed they would qualify, and 10% (80) believed they would not qualify. Of those who believed they would be eligible, 170 (44%) were not eligible and 217 (56%) were eligible based on demographics. Those who incorrectly believed they would be eligible were more likely to be Spanish-speaking (66% vs. 41%, $p < 0.01$) and Latino (80% vs. 63%, $p < 0.01$); they were also more likely to be legal permanent residents for less than 5 years (9% vs 0%, $p < 0.01$), or undocumented immigrants (51% vs 1%, $p < 0.01$). **DISCUSSION/SIGNIFICANCE OF IMPACT** The focus for education and enrollment campaigns for Medicaid expansion should be tailored for Spanish language and Latino populations. This improve enrollment efforts and expand the health benefits of insurance to the widest population possible. The educational programs should clarify immigration and other eligibility requirements of the Medicaid expansion and manage patient expectations and beliefs about their potential medical coverage.

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## MEDICAL DECISION MAKING CAPACITY OF INDIVIDUALS WITH NEWLY DIAGNOSED BRAIN METASTASES: A PILOT STUDY

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**OBJECTIVES/SPECIFIC AIMS** To investigate medical decision making capacity (MDC) in patients with newly diagnosed brain metastasis. **METHODS/STUDY POPULATION** Participants were 32 adults with newly diagnosed brain metastases and 32 demographically matched healthy controls. We evaluated MDC using the Capacity to Consent to Treatment Instrument (CCTI) and its four clinically relevant consent standards (expressing choice, appreciation, reasoning, and understanding). Capacity impairment ratings (no impairment, mild/moderate impairment, and severe impairment) on the consent standards were also assigned to each participant with brain metastasis using cut scores referenced to control performance. **RESULTS/ANTICIPATED RESULTS** The brain metastases patient group performed significantly below controls on consent standards of understanding and reasoning. Relative to controls, approximately 50% of the participants with brain metastases demonstrated capacity compromise (mild/moderate or severely impaired categorical ratings) in MDC. **DISCUSSION/SIGNIFICANCE OF IMPACT** Approximately half of patients with brain metastases have reduced capacity to make medical decisions. This impairment is demonstrated shortly after initial diagnosis of brain metastases. Future investigations might pursue the use of interventions to support or improve MDC in this patient population.

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## CHALLENGES FACED BY LUNG CANCER SURVIVORS IN CONTRAST TO OTHER CANCER SURVIVORS IN THE US

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**OBJECTIVES/SPECIFIC AIMS** Lung cancer is the second leading cancer in the US yet there is a paucity of research regarding the needs of lung cancer survivors. Most

data are extrapolated from research in other cancer types. We sought to compare health status and quality of life of lung cancer survivors relative to other cancer survivors in a national sample. **METHODS/STUDY POPULATION** Data was obtained from the 2010 Cancer Control Supplement of the National Health Interview Survey for breast, prostate, colon, and lung cancer respondents. Responses regarding health status, health utility and survivorship care were examined using univariate and multivariate analyses. **RESULTS/ANTICIPATED RESULTS** There were 838 respondents with a history of breast ($n$ = 398), prostate ($n$ = 255), colon ($n$ = 151), or lung ($n$ = 60) cancer. Lung cancer patients reported fair or poor overall quality of life for 39% of respondents compared to 18% colon, 11% breast, and 9% prostate. After adjustment for age and marital status, the odds for better quality of life were higher for all cancer types compared to lung cancer survivors (colon OR 2.03 [95% CI 0.88–4.66] breast OR 3.59 [95% CI 1.55–8.33] and prostate OR 2.97 [95% CI 1.28–6.91]). Lung cancer patients also reported significantly higher degree of financial problems compared to all other cancer types (colon OR 0.46 [95% CI 0.24–0.87] breast OR 0.45 [95% CI 0.25–0.81] and prostate OR 0.30 [95% CI 0.16–0.56]). After full adjustment lung cancer survivor quality of life was only significantly lower than breast cancer survivors (OR 3.24 [95% CI 1.19–8.78]). **DISCUSSION/SIGNIFICANCE OF IMPACT** Lung cancer survivors report survivorship needs differently compared to other cancer types. These differences underscore the limitations of applying survivorship care models based solely on other cancer types to this unique population.

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## A MULTIOBSERVER STUDY OF THE EFFECTS OF INCLUDING POINT-OF-CARE PATIENT PHOTOGRAPHS WITH PORTABLE RADIOGRAPHY

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**OBJECTIVES/SPECIFIC AIMS** To evaluate whether the presence of facial photographs obtained at the point-of-care of portable radiography leads to increased detection of wrong-patient errors. **METHODS/STUDY POPULATION** In this prospective study, 166 photographs were obtained from 30 patients when they underwent portable chest radiography. Consecutive radiographs from the same patients resulted in 83 unique pairs (new and prior radiograph) for interpretation. Radiographs were combined with corresponding photographs to generate composite radiograph-photograph pairs. To simulate wrong-patient errors, mismatched pairs were generated by pairing radiographs from different patients. Ninety radiologists with 21 ± 10 (mean ± SD) years of experience each interpreted a unique randomly chosen set of 10 radiographic pairs, containing up to 10% mismatches. Radiologists were randomly assigned to interpret radiographs with or without photographs. The number of mismatches identified and interpretation times were recorded. **RESULTS/ANTICIPATED RESULTS** With the introduction of photographs error detection increased from 31% (9/29) to 77% (23/30) ($p$ = 0.006). The odds ratio for error detection with photographs to detection without photographs was 7.3 (95% CI: 2.29, 23.18). Observer qualifications, training, or practice in cardiothoracic radiology did not influence error detection. A small increase in interpretation time was calculated: without and with photographs were 59 ± 22 and 61 ± 25 sec., respectively ($p$ = 0.77). **DISCUSSION/SIGNIFICANCE OF IMPACT** Facial photographs obtained simultaneously with portable chest radiographs increased the detection of wrong-patient errors. This technique offers a means to increase patient safety through correct patient identification.

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## LITTLE CHILDREN, BIG CHALLENGES: INCARCERATION—STATEWIDE DISSEMINATION OF RESOURCES FOR CHILDREN WITH INCARCERATED PARENTS

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**OBJECTIVES/SPECIFIC AIMS** The number of children with an incarcerated parent has increased nearly 80% in the past 20 years. Almost 2.7 million children have a parent in state or federal prison and millions more have a parent in local jails. Despite the growing need, few resources exist to support young children and families impacted by incarceration. In June 2013, Sesame Street released a new initiative, Little Children, Big Challenges: Incarceration, to address this need. The initiative includes multimedia resource kits containing a DVD, guide for parents and caregivers, and children's storybook. All resources, with supplemental materials, are bilingual and also available electronically. **METHODS/STUDY POPULATION** Minnesota was chosen as one of ten states to pilot the dissemination of this initiative. We used a "snowball contact" strategy. Ordering was completed via an online Google form or by mail or email request. **RESULTS/ANTICIPATED RESULTS** During the first 18 weeks of dissemination, we dispersed 20,200 multimedia kits to 167 providers in 81 cities across the state of Minnesota. Resources were made available to a diverse group of community partners, including prisons and jails, reentry service providers, child protection agencies, educators, public health nurses, hospitals and clinics, and local nonprofit organizations. **DISCUSSION/SIGNIFICANCE OF IMPACT** Kits continue to be disseminated in Minnesota and other pilot states. Monthly evaluation surveys will be completed by providers to investigate how the resources are being used. This current project was limited in that we were only able to track the location and perspectives of providers, not parents and caregivers who directly used the resources. Future research should investigate the dissemination and utilization patterns of these groups more thoroughly.

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## ACUTE RESPIRATORY DISTRESS SYNDROME INCREASES THE RISK OF DELIRIUM IN ICU PATIENTS

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**OBJECTIVES/SPECIFIC AIMS** ICU delirium and Acute Respiratory Distress Syndrome (ARDS) are both associated with poor clinical outcomes in survivors. We hypothesized that ARDS is an independent risk factor for delirium in mechanically ventilated patients, and that delirium is an important contributor to poor outcomes in ARDS patients. **METHODS/STUDY POPULATION** Prospective cohort study of 564 consecutive patients in 5 medical and surgical ICU's at two academic hospitals between May and September 2011. Delirium and level of consciousness was assessed daily for up to 14 days in the ICU using the Confusion Assessment Method-ICU (CAM-ICU) and Richmond Agitation and Sedation Scale (RASS), respectively. ARDS was defined as acute respiratory failure not fully explained by cardiac failure with bilateral infiltrates and PaO2/FiO2 ratio < 300. **RESULTS/ANTICIPATED RESULTS** 58% of the cohort was intubated and 30% of intubated patients had ARDS; the overall incidence of delirium was 43%. The prevalence of delirious patients increased with worsening respiratory failure (35% in nonintubated patients, 68% in intubated patients, 88% in ARDS patients; $p < 0.001$). Patients with ARDS had a higher risk for delirium compared to intubated patients without ARDS after adjusting for confounders such as age, comorbidities, APACHE IV, sepsis and sedative use (OR 6.3 vs OR 2.5). Delirium was more strongly associated with in-hospital mortality than ARDS in adjusted analyses (OR 2.2, 95% CI 1.1–4.2) vs (OR 1.8, 95%CI 0.6–5.3). **DISCUSSION/SIGNIFICANCE OF IMPACT** Delirium is a common and important driver of clinical outcomes in ARDS, and may mediate poor functional and cognitive outcomes. Future studies investigating cognitive and functional outcomes in ARDS patients need to account for delirium. Efforts to prevent and decrease delirium in ARDS patients may improve outcomes of ARDS survivors

# T4: TRANSLATION TO POPULATION

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## COLORECTAL CANCER SCREENING AMONG CANCER SURVIVORS IN THE US

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**OBJECTIVES/SPECIFIC AIMS** Background: Survivors of cancer from an organ are often at a higher risk for malignancies arising in other organs. It is uncertain if lower screening rates for those other cancers contribute to this finding. Aim: To determine adherence to colorectal cancer (CRC) screening guidelines among US adults with a personal history of cancer other than CRC **METHODS/STUDY POPULATION** Methods: We used the 2007 Health Information National Trends Survey (HINTS) and identified 4,297 respondents (weighted population size = 81,812,374) who were at least 50 years old and did not have a personal history of CRC. There were 3,507 (weighted population size = 70,347,024) respondents without any history of cancer and 790 respondents (weighted population size = 11,465,351) with a personal history of cancer other than CRC. We defined being current with CRC screening as the use of fecal occult blood testing (FOBT) within 1 year, sigmoidoscopy within 5 years, or colonoscopy within 10 years. We compared cancer survivors to those without any history of cancer in CRC screening adherence and used logistic regression models to calculate odds ratios (OR) and 95% confidence intervals (CI). Survey weights were used in all analyses and variance estimations were performed using Taylor series linearization to account for the complex survey design. **RESULTS/ANTICIPATED RESULTS** When compared with respondents without a history of cancer, cancer survivors were more likely to be current with CRC screening (73.9% vs 60.5%, OR = 1.54; 95%CI:1.21–1.96). **DISCUSSION/SIGNIFICANCE OF IMPACT** Although survivors of cancers other than CRC were more likely to be up-to-date, approximately one out of every four of these cancer survivors is not compliant with CRC screening guidelines. There is a need to actively promote CRC screening.

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## PEDIATRIC TYPE 2 DIABETES: AN EPIDEMIOLOGICAL STUDY OF ELECTRONIC MEDICAL RECORDS IN LOUISIANA

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**OBJECTIVES/SPECIFIC AIMS** Prediabetes and diabetes increased in prevalence from 9% to 23% over the past decade among U.S. adolescents. This unprecedented rise in type 2 diabetes (T2D) portends an earlier onset of diabetic retinopathy, neuropathy, kidney failure, myocardial infarction, and stroke. The objective of this study is to examine the contributors to the onset of T2D in adolescence via an analysis of electronic medical records (EMRs). **METHODS/STUDY POPULATION** All pediatric patient encounters ($n$ = 356,693) at 7 Louisiana State University public hospitals and 80 primary care clinics from the years 2006 to 2012 were examined via the LA-EMR database. T2D cases were identified using the appropriate ICD-9 codes (250*). **RESULTS/ANTICIPATED RESULTS** A total of 2,904 unique patients (67% female) were diagnosed with T2D before age 19 years. The majority of cases (92.9%) were classified as T2D without complication and not stated as uncontrolled. Four percent were classified as uncontrolled T2D, and less than 1 percent each was classified as T2D with complication including ketoacidosis or a renal, ophthalmic, or neurological manifestation. At diagnosis, patients were on average 16.1 ± 3.7 years. The majority (57.9%) were African American, with 38.5% white and 3.6% other race/ethnicity. The predominant insurance coverage was Medicaid (58.4%), followed by uninsured (18.2%), commercial (9.3%), and self-pay (7.0%). Mean body mass index (BMI) was 30.8 kg/m$^2$ and mean BMI percentile was 81.2. Fifty-two percent were considered hypertensive based on elevated blood pressure percentile. **DISCUSSION/SIGNIFICANCE OF IMPACT** The high number of diagnosed pediatric T2D cases in the LA-EMR database is a tremendous advantage over prior clinical trials and epidemiological studies, providing sufficient power to examine the contributors to and consequences of the early onset of T2D.

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## RISK FACTORS ASSOCIATED WITH BRONCHIOLITIS IN THE PUERTO RICAN POPULATION

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**OBJECTIVES/SPECIFIC AIMS** Bronchiolitis is the leading cause of respiratory compromise and hospitalization in infants younger than 2 years of age. Studies suggest that bronchiolitis is a major factor for subsequent wheezing episodes and asthma. Whether viral bronchiolitis is causal or an early manifestation of future asthma remains uncertain. Given that bronchiolitis has a different epidemiological behavior and outcome in the Puerto Rican population, it becomes important to identify other risk factor(s) that can contribute to its high, yearlong prevalence, frequency and severity. The objective is to determine the risk factor(s) associated with bronchiolitis in Puerto Rican children and evaluate the association of atopic risk factors with bronchiolitis severity. **METHODS/STUDY POPULATION** This study will recruit 307 Puerto Rican patients, less than 24 months of age with a clinical diagnosis of bronchiolitis at 4 emergency departments of the Metropolitan area during a 6-month period. Risk factors will be assessed by a physician-administered survey inquiring about demographic data, medical history and environmental exposure concerning the patient. Bronchiolitis severity will be assessed with a bronchiolitis severity score. **RESULTS/ANTICIPATED RESULTS** Risk factors in the Puerto Rican population are strongly associated with atopy and directly correlated with disease severity, frequency and management. **DISCUSSION/SIGNIFICANCE OF IMPACT** Identify Puerto Rican children who may present a severe clinical course of disease, who do not present traditional risk factors. It will improve prevention (through improved immunization strategies) for the population at risk of severe disease, improve treatment of bronchiolitis infection (by establishing a clinical pathway for bronchiolitis in PR), and reduce recurrent wheezing prevalence.

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## LIFESPAN PREDICTORS OF CARDIOVASCULAR MORBIDITY IN INDIVIDUALS REACHING MIDDLE AGE: THE BOGALUSA HEART STUDY

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**OBJECTIVES/SPECIFIC AIMS** To determine the individual contribution of cardiovascular (CV) risk factors measured longitudinally from childhood to adulthood, as well as their cumulative burden, on CVD morbidity **METHODS/STUDY POPULATION** The study cohort comprised 118 noninstitutionalized individuals aged 25–46 years; 44.1% black and 63.6% female. These participants had at least 3 traditional CV risk factors measurements since childhood and self-reported information on adult CVD morbidity. Mean follow up period was 14.3 years. CVD was defined as positive personal history of one or more of the following: angina, percutaneous coronary intervention, coronary artery bypass grafting, myocardial infarction and/or stroke. The area under the curve (AUC) was used to assess the cumulative burden of risk factors. **RESULTS/ANTICIPATED RESULTS** After accounting for the effect of age, race, sex, and cigarette smoking, significant predictors of CVD were: childhood body mass index (BMI) (odds ratio [OR], 1.36; 95% confidence interval [95% CI] 1.12–1.62) and non–high density lipoprotein cholesterol (non-HDL-C) (OR, 1.22; 95% CI, 1.15–1.73); adulthood BMI (OR, 1.13; 95%CI, 1.02–1.24), systolic blood pressure (SBP) (OR, 1.32; 95%CI, 1.07–1.65) and non-HDL-C (OR, 1.39; 95%CI, 1.11–1.56); and long-term cumulative burden of BMI (OR, 1.29; 95%CI, 1.21–1.37) and non-HDL-C (OR, 1.47; 95%CI, 1.38–1.71) **DISCUSSION/SIGNIFICANCE OF IMPACT** The observed associations of childhood / adulthood cardiovascular risk factors and their long-term cumulative burden on adult CVD morbidity, are indicative of the individual impact of these risk factors in the development of heart disease. Hence, risk factor-oriented interventions (through primordial prevention early in life) must continue to be implemented to avoid further deleterious effects caused by risk factors and subsequent disease complications.

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## PREVALENCE AND CHARACTERISTICS OF METABOLICALLY HEALTHY OBESE AMONG INDIVIDUALS WHO UNDERWENT BARIATRIC SURGERY

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**OBJECTIVES/SPECIFIC AIMS** Recent studies describe a unique subset of obese individuals with normal metabolic profiles despite having excess weight called "metabolically healthy but obese (MHO)." Our aim was to determine factors associated with the MHO phenotype among bariatric surgery patients. **METHODS/STUDY POPULATION** We conducted a retrospective study of 710 adults who underwent bariatric surgery at The Johns Hopkins Center for Bariatric Surgery between 2008 and 2010. We defined MHO by the absence of both diabetes and hypertension. We used multivariable logistic regression to examine the association between MHO and potential risk factors including age, sex, race, smoking status, BMI and presence of liver disease on liver biopsy. **RESULTS/ANTICIPATED RESULTS** The sample was 78% female, 77% White and 48% less than 45 years old. The prevalence of MHO was 28.7%. MHO patients were significantly more likely to be non-Hispanic white OR = 1.89 (95% CI: 1.14–3.14), younger OR = 4.07 (95% CI = 2.63–6.27), and female OR = 2.05, (95% CI = 1.15–3.63) and less likely to have liver steatosis OR = 0.40 (95% CI = 0.18–0.89) or NASH OR = 0.31 (95% CI = 0.16–0.62). **DISCUSSION/SIGNIFICANCE OF IMPACT** Among bariatric surgery patients, MHO was relatively common especially in patients who were White, younger, females and with less liver injury. Further studies are needed to understand the role of MHO as a predictor of bariatric surgery outcomes.

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## IMPACT OF DIZZINESS ON QUALITY OF LIFE AMONG THE ELDERLY IN PUERTO RICO

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**OBJECTIVES/SPECIFIC AIMS** The purpose of this study is to gather empirical data by exploring the self-perceived quality of life (QOL) of the elderly suffering from dizziness in PR. The specific aims are to establish the association between dizziness and QOL among a group of elderly in PR, and to evaluate the risk of falls within this population. **METHODS/STUDY POPULATION** We will use the Dizziness Handicap Inventory to explore the QOL among a group of 80 elders suffering from dizziness; and use the Tinetti Balance Assessment Tool to evaluate the risk of falling among this group. We will perform a descriptive statistical analysis including measures of central tendency and variability, use a chi-square/Fisher's exact test to assess the association between the variables, and use multivariate analysis to assess the risk of falling. **RESULTS/ANTICIPATED RESULTS** The QOL of the elderly in PR is adversely affected by dizziness and its associated risk of falling. **DISCUSSION/SIGNIFICANCE OF IMPACT** Currently, 13% of the population in Puerto Rico (PR) are people 65 years of age and older. About 30% of the elderly experience dizziness. Dizziness-related falls can result in loss of mobility, hindering independence, and ranks as the leading cause of fortuitous death among the elderly. Nearly 30% of seniors are at risk of falling each year. The commonly accepted medical approach for the treatment of dizziness in PR is prescribing medication to suppress the symptoms, which frequently overlooks proper diagnosis of the underlying etiology. Furthermore, there is little attention given to the impact of dizziness, and the associated risk of falling, on the quality of life of the elderly in PR. Our findings will provide healthcare professionals with new, first-hand, culturally-appropriate, empirical data to better manage dizziness in the elderly PR population.

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## VALIDATION OF A SCREENING TOOL TO IDENTIFY SURVIVORS OF GENDER-BASED VIOLENCE AMONG DISPLACED WOMEN IN COLOMBIA AND ETHIOPIA

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**OBJECTIVES/SPECIFIC AIMS** Worldwide, the number of women displaced by conflict who have experienced gender-based violence (GBV) is likely underreported. Routine screening for GBV can lead to earlier and improved services for survivors with the goal of ameliorating the sequelae of GBV. We have developed and validated the ASIST-GBV, a tool to identify survivors of GBV among displaced women. **METHODS/STUDY POPULATION** The ASIST-GBV was formulated after a formative research phase. In the validation phase, we administered the questionnaire to displaced women 15 and older in Ethiopia and Colombia. Both known survivors of GBV and displaced women who were not identified as survivors were recruited. All women were also asked if they had experienced GBV. Participants were regarded as screening positive for GBV if they reported experiencing one of six types of violence. Item response theory (IRT) was used to assess the range and precision of the ASIST-GBV to detect experiences of GBV. **RESULTS/ANTICIPATED RESULTS** In Ethiopia, 64.8% of the 428 women recruited screened positive for GBV using the ASIST-GBV tool. In Colombia, 44.9% of the 69 women enrolled screened positive for GBV with the ASIST-GBV tool. IRT confirmed that the scale is unidimensional and provides estimates across a range of severity. **DISCUSSION/SIGNIFICANCE OF IMPACT** The ASIST-GBV tool is able to screen for GBV across a range of experiences. Moreover, it is acceptable to displaced women who are at high risk of GBV. A challenge with the development of this questionnaire is the absence of a gold standard, making validation of the tool difficult. However, this demonstrates the novelty of and the need for the ASIST-GBV.

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## A BEHAVIORAL ECONOMIC APPROACH TO IMPROVE HUMAN PAPILLOMAVIRUS (HPV) VACCINATION

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**OBJECTIVES/SPECIFIC AIMS** Our objective is to measure the impact of a behavioral economic intervention based on principles of loss aversion and escalation of commitment on HPV vaccination rates. **METHODS/STUDY POPULATION** In October 2013 we began a demonstration project to compare the impact of a delayed cash reward (Intervention) compared to usual care (Control) on HPV vaccine series completion. We recruit unvaccinated adolescents (11–17 yr) and a parent from two General Pediatric clinics. A personal deposit account is created and each participant is given a document resembling a bank deposit form showing a $25 credit at the time they receive the first dose and a $25 deposit after receiving the second dose of the vaccine. After receipt of the third dose, the participant is given the $50 in cash. If a participant does not show up for an appointment a letter is sent to remind families how much money ($50) they are at risk of losing. **RESULTS/ANTICIPATED RESULTS** A total of 366 dyads have been approached to date, 212 were ineligible, 113 declined to participate and 41 are enrolled. Of those who declined participation the parent declined (85%) more often than adolescent and primary reasons were questions about the vaccine or no interest in participating in (any) research. After enrollment, four participants were found to have previously received 1 dose of the vaccine and three were found to have previously received 2+ doses of the vaccine; none remembered receiving the vaccine at the time of enrollment. **DISCUSSION/SIGNIFICANCE OF IMPACT** To date, the enrollment rate does not differ from other pediatric trials at our institution. Parents appear to find the intervention acceptable but this will be studied in-depth via phone interviews after enrollment is complete. Seven parents (17%) who enrolled in the study were unaware of their child's HPV vaccination status.

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## AN EDUCATIONAL INTERVENTION TO PROMOTE ANTIBIOTIC STEWARDSHIP IN THE LONG-TERM CARE ENVIRONMENT (ABLE)

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**OBJECTIVES/SPECIFIC AIMS** To use an educational intervention targeted towards long-term care facility (LTCF) staff to improve the assessment and clinical interventions for LTCF residents with potential infections, to reduce inappropriate antimicrobial use and to advance antimicrobial stewardship practices in LTCFs. **METHODS/STUDY POPULATION** We developed an educational program that addresses the care of older adults with infections while advancing antimicrobial stewardship principles. Provider education consists of 5 case-based discussions offered via videoconference. Nursing staff education consists of 6 self-paced modules offered via a Website. We use a survey to test the influence of this education on the knowledge, confidence and beliefs of LTCF staff toward the care of older adults with infections. We will also test the impact on antimicrobial prescriptions at each LTCF. **RESULTS/ANTICIPATED RESULTS** Preliminary results indicate improved knowledge among all providers following the intervention. Compared to those with higher knowledge scores, providers with lower knowledge scores prior to the intervention also reported lower confidence in their ability to determine length of antibiotic therapy and to appropriately narrow or stop existing antibiotic therapy. We anticipate that while total antibiotic use at each facility may show little to no change, there may be a shift from broad- toward narrow-spectrum agents. **DISCUSSION/SIGNIFICANCE OF IMPACT** LTCFs often lack resources to implement antimicrobial stewardship. The ABLE program is a simple, adaptable and scalable means to deliver targeted education directly to people who care for LTCF residents. In future work we will examine whether our intervention impacts the overall antibiotic utilization and spectrum of antibiotic regimens prescribed in study facilities.

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## PATIENT FACTORS ASSOCIATED WITH ONLINE SYMPTOM ASSESSMENTS IN ONCOLOGY CARE

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**OBJECTIVES/SPECIFIC AIMS** At-home online symptom assessments can provide important information for clinicians. However, patient use of this technology is often under 40%. Our objective is to identify explanatory or contributory patient-level factors associated with the completion of online symptom assessments. **METHODS/STUDY POPULATION** Nonmetastatic breast cancer patients ages 18–55 ($n = 82$) were recruited at the Lombardi Comprehensive Cancer Center within 5 years of treatment. Patients completed one in-clinic assessment and an online at-home assessment within the next month. Symptoms were measured by the PROMIS® Profile-57. We used chi-square and t-tests to identify differences in online participation ($p < 0.05$), and a multivariate logistic model to estimate effects of each factor on completing an online assessment. **RESULTS/ANTICIPATED RESULTS** Overall, 61% completed an online assessment. Multivariate logistic models indicated that patients in follow-up care, controlling for symptom severity, co-morbidities, and education level were 4 times more likely to log-on than patients in active treatment ($p < 0.05$). Among patients in treatment, ($n = 39$) a higher depression score was associated with lower participation after adjustment (OR: 0.88, $p < 0.05$). All other symptoms and beliefs were not significant. **DISCUSSION/SIGNIFICANCE OF IMPACT** Breast cancer patients in post–acute care were more likely to track their symptoms online than those currently receiving treatment. Elevated depression scores further decreased online participation rates for this group. These findings suggest that online symptom assessment may be difficult to use during treatment. Furthermore, depressed patients in treatment may miss important screening opportunities. Additional research is needed to determine to effective use and integration of online symptom assessment over the full course of oncologic care.

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## IMPROVING ASTHMA SCREENING IN SICKLE CELL DISEASE

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**OBJECTIVES/SPECIFIC AIMS** Asthma is common in children with sickle cell disease (SCD) (prevalence approximately 30%). Experts recommend children with asthma and SCD receive spirometry and care by asthma specialists, but pulmonary clinic visits were uncommon in our patients with SCD (5/300 (2%) in 2011). We hypothesized that a screening program would improve asthma screening and increase appropriate referrals to pulmonary clinic. **METHODS/STUDY POPULATION** We conducted a single center, prospective quality improvement project in a pediatric hematology clinic and infusion center using a previously validated asthma screening questionnaire (ASQ) (in those ≥2 years old) and spirometry(≥5 years old). Children with a positive asthma screening questionnaire or abnormal spirometry were referred to pulmonary clinic. **RESULTS/ANTICIPATED RESULTS** We screened 157 of approximately 300 clinic patients. Fifty-eight (37%) had a positive ASQ and 32 (20%) had abnormal spirometry. A positive ASQ was 76% sensitive (95% CI 63–86) and 86% specific (77–92) for a physician diagnosis of asthma. Abnormal spirometry had a poor correlation with a physician diagnosis of asthma (kappa 0.18, $p = 0.006$). Sixty children (38%) screened positive, of which 100% were referred to pulmonary clinic. Twenty-five (42%) of these made a pulmonary appointment, and 13 (22%) kept the appointment. Of the 107 with interpretable spirometry, 14 (13%) had abnormal spirometry despite a negative ASQ. **DISCUSSION/SIGNIFICANCE OF IMPACT** Asthma questionnaires improved screening and referrals in our pediatric SCD population. Though abnormal spirometry did not correlate well with a physician diagnosis of asthma, a substantial minority of children had abnormal spirometry without a diagnosis of asthma and could likely benefit from pulmonologist evaluation and treatment as well.

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## ALTERED INTESTINAL BARRIER FUNCTION IN NEONATES AFTER CARDIAC SURGERY

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**OBJECTIVES/SPECIFIC AIMS** Intestinal barrier dysfunction may contribute to feeding intolerance in neonates after cardiac surgery. We sought to determine perioperative intestinal barrier function using urine lactulose/mannitol (L/M) ratio measurements and its correlation to early breastmilk feeds in neonates requiring cardiac surgery. **METHODS/STUDY POPULATION** This was a single-center, prospective, randomized pilot study of neonates requiring cardiac surgery. Subjects were randomized to one of two preoperative feeding groups: (1) NPO vs. (2) trophic breastmilk feeds. At three time points (pre-op, post-op day 7 and post-op day 14), subjects were administered an oral lactulose/mannitol solution and subsequent urine L/M ratios were measured, with higher ratios indicative of increased intestinal permeability. Trends over time in the mean urine L/M ratios for each group were estimated using a general linear mixed model. **RESULTS/ANTICIPATED RESULTS** Twenty-seven neonates were enrolled. In the NPO group, the mean urine L/M ratios at pre-op, post-op day 7, and post-op day 14 were 0.06, 0.12, and 0.17 respectively. In the trophic breastmilk feeds group, the mean urine L/M ratios at pre-op, post-op day 7, and post-op day 14 were 0.09, 0.19, and 0.15 respectively. Both groups had significantly higher L/M ratios at post-op day 7 and 14 compared to pre-op ($p < 0.05$). In the trophic breastmilk feeds group, there was a trend for the L/M ratios to increase from pre-op to post-op day 7 followed by a slight decline. Group differences over time were not statistically significant but power was limited to detect this. **DISCUSSION/SIGNIFICANCE OF IMPACT** Neonates have increased intestinal permeability and disrupted intestinal barrier function after cardiac surgery extending to at least post-op day 14. Further studies to identify mechanisms of intestinal injury and therapeutic interventions are warranted.

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### MIXED-METHODS DESIGNS FOR EFFECTIVE HEALTH SERVICES RESEARCH

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**OBJECTIVES/SPECIFIC AIMS** Colorectal cancer (CRC) is the 2nd highest cause of US cancer death, but screening rates are low, especially among safety-net populations. CRC screening involves complex processes, multiple levels, and many steps. Improving CRC screening completion requires new ways of assessing these complex multilevel processes. Our Parkland-UT Southwestern PROSPR Center team (part of NCI's Population-based Research Optimizing Screening through Personalized Regimens [PROSPR] network) is studying factors affecting cancer screening completion. **METHODS/STUDY POPULATION** Our mixed-methods study: (1) comprehensively characterizes the CRC screening process; and (2) tests hypotheses about the CRC process. Since organizational variables vary between clinics or longitudinally at clinic- or system-level, hierarchical random intercept logistic regression modeling helps us identify characteristics predicting screening completion. Our outcomes are: (1) completion of CRC screening among primary care patients at average risk for CRC, and (2) completion of CRC diagnostic evaluation among patients with abnormal screening results. Cross-tabulations will explore steps associated with screening completion failure. **RESULTS/ANTICIPATED RESULTS** Baseline CRC screening rates were 31.9%, with modest variation. We have articulated the CRC care continuum and assessed clinic-level variation: screening rates in our 11-clinic system range from 11.1% to 24.5%, with substantial heterogeneity in modality (ie. FIT = 0.7–19.7%; colonoscopy = 4.2–15%). Several likely nodes of screen failure and modality variation have emerged. **DISCUSSION/SIGNIFICANCE OF IMPACT** Mixed methods capture otherwise opaque, dynamic, and complex systems. Such designs allow us to identify small but significant system functions influencing screening delivery. These designs will bolster future research on complex systems, helping maximize efficiency, reduce costs, and improve patient-centered outcomes.

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### ELECTRONIC HEALTH RECORD (EHR) DATA EXTRACTION COUPLED WITH MANUAL VALIDATION TO EVALUATE PREDIABETES SCREENING AND COUNSELING PRACTICES WITHIN THE PRIMARY CARE SETTING

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**OBJECTIVES/SPECIFIC AIMS** To evaluate gaps in identification and counseling of individuals with prediabetes **METHODS/STUDY POPULATION** We previously extracted EHR data from 46,779 adult primary care patients to evaluate prediabetes screening practices. The current manual validation substudy was undertaken to confirm validity of EHR-based data queries and to evaluate counseling practices for patients with evidence of prediabetes. Data obtained through manual verification were entered into a REDCap database, as seen by a front end user of the EHR. Descriptive evaluation of counseling practices for evidence of prediabetes was performed. **RESULTS/ANTICIPATED RESULTS** Coded EHR data indicated <40% of individuals with risk factors were screened for diabetes. 42% of individuals with labs indicating prediabetes had a coded diagnosis of prediabetes. Manual validation of 10% of charts with labs indicative of prediabetes demonstrated 100% accuracy of EHR data extraction. Chart evaluation indicated 63% of individuals were contacted within 1 year of lab in prediabetes range. The most common counseling terms were "diet" (36.8%) and "exercise" (24.5%), while terms "prediabetes" and "risk of diabetes" were used less often (15.8%, 7.1%, respectively). **DISCUSSION/SIGNIFICANCE OF IMPACT** Manually validated EHR data queries confirm a significant gap in screening for, diagnosis and counseling of individuals with prediabetes in the primary care setting. EHR-based data abstraction will permit study of effects of targeted interventions to help close these identified gaps.

## RESEARCH SCHOLAR AND TRAINEE ABSTRACTS

### T0: BASIC SCIENTIFIC DISCOVERY

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### THE IMPORTANCE OF HDL IN HEART TRANSPLANTATION

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**OBJECTIVES/SPECIFIC AIMS** To study the metabolic HDL changes post–heart transplant. **METHODS/STUDY POPULATION** 101 Patients (Pt.) with heart transplant were studied. 65 Pt. were males and 36 were female, with a mean age of 51 years. **RESULTS/ANTICIPATED RESULTS** Pre- and postmetabolic changes were: (1) BMI ($25 \pm 4 - 28 \pm Kg/m^2$, $p < 0.05$). (2) Systolic blood pressure ($107 \pm 13 - 131 \pm 20$, $p < 0.05$). (3) Diastolic blood pressure ($70 \pm 13 - 81 \pm 10$ mmHg). (4) Fasting blood sugar ($107 \pm 37 - 117 \pm 55$ mg%) N.S. (5) Total cholesterol ($170 \pm 55 - 189 \pm 32$mg/dl), $p < 0.05$. (6) Total HDL ($38 \pm 16 - 52 \pm 17$mg/dl), $p < 0.05$. (7) Total LDL ($99 \pm 20 - 83 \pm 15$mg/dl) N.S. (8) Triglycerides ($163 \pm 10 - 188 \pm 12$mg/dl) N.S. **DISCUSSION/SIGNIFICANCE OF IMPACT** Our data shows that all the Pt. developed Mets. The HDL of the whole groups increased from 38 mg/dl to 52 mg/dl. These changes are not explained only by the immunosuppressive treatment, HDL has a role as an anti-inflammatory agent which is inherent in the lipoprotein characteristics. 16 Pt. died of rejection. The HDL of the rejected Pt. increased from $47 \pm 22$ to $71 \pm 40$ mg/dl, $p < 0.007$. This increase persisted through the course of the rejection period. The mean age of the transplanted heart was 22 years. The rejection occurred in less than 5 years. (3.5 years). Seven autopsies were done. Five of them showed severe atherosclerotic changes in the coronaries and aorta. This is probably explained on basis of dysfunctional HDL. Probably the high levels and persistent elevation of HDL in the rejected group can be used as a biomarker to predict rejection.

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### WEIGHT LOSS IS NOT THE ONLY FACTOR AFFECTING THE METABOLIC CHANGES AFTER BARIATRIC SURGERY

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**OBJECTIVES/SPECIFIC AIMS** The purpose is to describe other factors than weight loss producing the metabolic changes observed. **METHODS/STUDY POPULATION** A retrospective analysis of 102 patients records. **RESULTS/ANTICIPATED RESULTS** 97% had Roux-N-Y surgery with a mean age of 39 years. 79.4 were females and 20.6 were males. 44% were diabetics. Metabolic Changes: (1) BMI ($kg/m^2$) - $47 \pm 9 - 33 \pm 7$), $p < 0.0001$; (2) weight (lbs.)- $285 \pm 62 - 198 \pm 54$), $p < 0.0001$; (3) cholesterol (mg/dl) - $169 \pm 30 - 151 \pm 30$, $p < 0.0001$; (4) LDL (mg/dl)- $101 \pm 27 - 86 \pm 25$, $p < 0.0001$; (5) triglycerides (mg/dl)- $112 \pm 47 - 84 \pm 22$, $p < 0.0001$; (6) FBS (mg/dl) - $98 \pm 25 - 87 \pm 20$, $p < 0.0001$. *HDL mg/dl) - $44 \pm 10$ to $49 \pm 13$, $p < 0.0006$. *Not significant The correlation factor was poor between weight loss and measured factors (.1-.5). **DISCUSSION/SIGNIFICANCE OF IMPACT** These results shows that the metabolic changes are a result of other factors than weight loss: (1) Up-regulation of Glu)-1 protein producing and increase in reabsorption of glucose. (2) Inflammation of the Jejunal mucosa producing adaptation (atrophy- proliferation) reducing cholesterol absortion. (3) More degradation of LDL. (4) No degradation of HDL. In summary the changes in blood sugar and lipids are complex and should be studied further as well as changes in gut microbiota.

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## OSTEODYSTROPHY IN METABOLIC SYNDROME: A BONE MORPHOMETRIC STUDY

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**OBJECTIVES/SPECIFIC AIMS** Metabolic syndrome (MS) represents a constellation of hypertension, obesity, hyperglycemia, hyperlipidemia with high renal and cardiovascular risk. However the nature of bone disease in MS remains poorly understood. The aim of this study is to examine the bone changes in MS. **METHODS/STUDY POPULATION** We used obese ZSF rats, first characterized in our laboratory as a model of MS and Sprague Dawley (SD) rats as controls. They were studied from 8th week in two groups one group sacrificed at 16th week and the other at 32nd week. Femur bones harvested at sacrifice were stored at 4C in until used for morphometric analysis. Dual-energy x-ray absorptiometry (DXA) studies were performed on whole femur while the distal femur and the mid-shaft were used to study the trabecular and cortical bone respectively. Bone mineral density (BMD) expressed as gm/cm$^2$ and bone mineral content (BMC) in grams were measured and data (mean, SE and p value) was analyzed using Students paired t-test. **RESULTS/ANTICIPATED RESULTS** Both ZSF and SD rats gained weight by 32 weeks (744 ± 23 vs. 522 ± 10 g, $p < 0.00001$) but ZSF rats gained twice as much as SD rats (175 vs. 83 g). In the femur, the BMD in ZSF rats (0.1935 ± 0.0016) was lower than the SD rats (0.2221 ± 0.005, $p < 0.001$) at 16 weeks as well as 32 weeks (0.2178 ± 0.0058 vs. 0.2328 ± 0.0039, $p < 0.001$). Similar results were seen in cortical and trabecular bone. This was despite a modest increase in BMD from 16th to 32nd week in ZSF rats but not in SD rats. The BMC was lower in ZSF than SD rats at 16 weeks but not at 32 weeks in the femur, cortical and trabecular bone. With aging, ZSF rats higher BMC than SD except in cortical bone. **DISCUSSION/SIGNIFICANCE OF IMPACT** These results underscore the presence of severe bone disease characterized by low BMD with MS despite some increase in BMC. Future studies are needed to understand the mechanisms to better treat the osteodystrophy of MS

## T1: TRANSLATION TO HUMANS

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## PRENATAL VITAMIN D DEFICIENCY IMPAIRS MAJOR AIRWAY AND PULMONARY DEVELOPMENT IN MURINE MODEL

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**OBJECTIVES/SPECIFIC AIMS** Epidemiologic studies have linked gestational vitamin D deficiency to pediatric respiratory diseases, although mechanisms have not been defined. As the major airways share similar cartilaginous structure to joints, we hypothesize that vitamin D deficiency during airway development may have deleterious effects on the airway and pulmonary supportive tissues **METHODS/STUDY POPULATION** We utilized vitamin D–deficient diet and UV blockade to develop a vitamin D–deficient mouse model. We developed a tracheal ultrasound technique to measure diameter *in vivo* with postmortem airway casting validation. FlexiVent was used to measure lung physiology. Mid-tracheal cross-sections estimated tracheal cartilage area and thickness. Morphometric lung development utilized standard mean linear intercept (MLI) and radial alveolar count (RAC). **RESULTS/ANTICIPATED RESULTS** Tracheal diameter measured with ultrasound was smaller in offsprings of vitamin D–deficient mice compared to littermate controls (0.72 mm vs. 0.90 mm; $p < 0.01$). Lung function indicated increased resistance (R), elastance (E) and reduced compliance (C) in vitamin D–deficient mice (R = 2.01 vs. 1.52, $p < 0.05$; E = 87.35 vs. 57.07, $p < 0.001$; C = 0.012 vs. 0.019, $p < 0.001$). Histology demonstrated decreased cartilage width of tracheal rings in vitamin D–deficient pups (0.44 mm vs. 0.68 mm, $p = 0.027$). Vitamin D–deficient mice had alveolar simplification with increased MLI (30.8 vs. 25.5 microns, $p < 0.0001$) and decreased RAC (10.1 vs. 13.8 septae, $p < 0.0001$) **DISCUSSION/SIGNIFICANCE OF IMPACT** Prenatal vitamin D deficiency impairs airway development, alveolar maturation and lung function. Smaller tracheal diameter, thinner tracheal cartilage and alveolar simplification lead to increased airway resistance and diminished lung compliance. Development of murine model helps investigating preventive and therapeutic strategies involve vitamin D.

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## CHARACTERIZATION OF MOOD STATES DURING INTRAVENOUS (IV) ALCOHOL SELF-ADMINISTRATION IN SOCIAL DRINKERS

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**OBJECTIVES/SPECIFIC AIMS** Computer-Assisted Self-Infusion of Ethanol (CASE) is a method of IV alcohol self-administration (IV-ASA) that provides individuals with access to ad lib self-infusions of alcohol in a laboratory setting. The study aimed to examine changes in mood states during IV-ASA and how these changes may be related to perception of alcohol effects, personality and recent drinking history. **METHODS/STUDY POPULATION** Social drinkers ($n = 73$) underwent an IV-ASA session that included a 25 minute priming phase, where subjects were prompted to push a button to receive 4 standardized alcohol infusions, followed by a two hour phase with ad lib access to the same infusions. Recent drinking history, alcohol expectancy effects and the UPPS-P impulsivity scale were assessed at baseline. During the session, subjective responses were measured using the Profile of Mood States (POMS), Drug Effects Questionnaire (DEQ) and Alcohol Urge Questionnaire (AUQ). **RESULTS/ANTICIPATED RESULTS** Results indicated significant changes in the POMS measures of Tension/Anxiety (TA), Confusion/Bewilderment (CB), and Vigor/Activity (VA), following the priming phase. Individuals with high scores for VA had heavier drinking histories, greater IV-ASA, and greater urge for alcohol. Individuals with high scores for CB had lighter drinking histories, lower IV-ASA, and greater feelings of alcohol effects on the DEQ. POMS measures of CB and TA were positively associated with the UPPS-P measure of negative urgency as well as expectancy effects of power and aggression. **DISCUSSION/SIGNIFICANCE OF IMPACT** These findings indicate that changes in mood states, particularly vigor and activity, following a priming dose of alcohol, are associated with recent drinking history, and predict greater rates of IV-ASA and subjective response to alcohol during self-administration in social drinkers.

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## A CASE-CONTROL COMPARISON OF GENE EXPRESSION AND METHYLATION PROFILES ASSOCIATED WITH POSTTRAUMATIC STRESS DISORDER

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**OBJECTIVES/SPECIFIC AIMS** The heterogeneous outcomes of trauma exposure warrant interest in biological predictors of PTSD and its common psychiatric and medical comorbidities. Recent research has suggested that significant life experiences alter gene expression and induce changes in DNA methylation. To date, most PTSD research has been limited to specific pathways, but emerging methods are examining genome-wide expression and methylation patterns to explore mechanisms of stress on biology. **METHODS/STUDY POPULATION** We preliminarily explored genome-wide gene expression and methylation differences of trauma-exposed individuals with PTSD (cases) vs. resilient controls. DNA and RNA were extracted from blood samples of 24 young-adult African American men and women (i.e., 12 cases, 12 controls) who had been evaluated in a larger study and were analyzed by the Affymetrix GeneChip Exon 1.0 ST expression array and the Illumina Infinium HumanMethylation450 BeadChip methylation array. **RESULTS/ANTICIPATED RESULTS** Whereas 3992 genes were differentially expressed (FDR-adjusted $p < 0.05$, fold change >2) in cases vs. controls, no differential methylation patterns were found. The 100 most upregulated genes and the 3 significantly down-regulated genes were selected for network analyses using Ingenuity Pathway Analysis. Twenty-seven genes were associated with 3 gene networks, 2 of which were involved in immune response and 1 in cell cycle control. **DISCUSSION/SIGNIFICANCE OF IMPACT** Our results suggest that many genes and gene networks have increased peripheral expression with PTSD, which may be associated with cellular and immunological function, but this does not appear to be the consequence of methylation changes. Future research should elucidate mechanisms of up-regulated gene expression in the development of PTSD.

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## PROMOTING TRANSLATIONAL RESEARCH THROUGH DATA QUALITY ASSESSMENT WITH ELECTRONIC HEALTH RECORD DATA

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**OBJECTIVES/SPECIFIC AIMS** Electronic health record (EHR) data have an increasingly critical role in translational research. Understanding data quality is crucial to data mining and analytic approaches for conducting research. Yet, little is understood about data quality in clinical settings. A systematic framework for monitoring data quality is key to future translational research with EHR data. This work aims to identify data quality issues within an existing EHR data sharing infrastructure. **METHODS/STUDY POPULATION** We analyzed EHR data quality from Data QUEST, a federated network of semantically aligned clinical data repositories (CDRs) among primary care clinical practices. The analyses incorporate five attributes of data quality (fitness-for-use, semantic variability, accuracy, completeness, and reliability) explored via three testing protocols. **RESULTS/ANTICIPATED RESULTS** The first testing protocol found content domains such as demographics were often imprecisely recorded or missing. The second testing protocol found 1–3.8% of diagnosis codes (ICD-9) and 1.8–3.5% of medication (NDC) codes did not comply with standard coding schemes. The third testing protocol revealed EHR data fluctuate substantially between clinics, across years, and by disease. **DISCUSSION/SIGNIFICANCE OF IMPACT** Results indicate several key EHR data quality issues critical to data mining and analytics for translational research, emphasizing the need for methodology to address the complexity of these issues. Collaborations between biomedical informaticians and clinical scientists

was crucial to design and interpretation of our evaluation. Data quality assessment needs to be integrated with EHR data sharing infrastructures and future work should focus on refining concrete data quality methodology to ensure best use of EHR data for translational research.

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## MYELOID-DERIVED CELLS RESIDE IN SUBCUTANEOUS ADIPOSE TISSUE BUT ARE NOT FOUND IN CIRCULATION: A DC-EXPRESSING BDCA-1 CD206 AND HEMATOPOETIC PROGENITOR CELLS

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**OBJECTIVES/SPECIFIC AIMS** This is an observational study which requires 2 visits for screening and collection of samples, blood and subcutaneous adipose tissue (SAT). We have phenotyped leukocytes by flow cytometry in SAT and blood in lean (BMI ≤ 24.9 kg/m$^2$) and obese (BMI ≤ 30 kg/m$^2$) subjects to identify inflammatory cells, which may help us to understand the causes and consequences of obesity in order to determine how these cells might be implicated in the initiation and/or progression of metabolic syndrome and inflammatory diseases. **METHODS/STUDY POPULATION** (1) Isolation of AT cells from SAT. (2) Isolation of leukocytes from blood. (3) Stimulation of blood cell populations with PMA,ionomycin, for cytokine responses. (4) Phenotyping of AT and blood cells and ICS by multiparametric flow cytometry. **RESULTS/ANTICIPATED RESULTS** We have found that there is a higher percentage of monocyte/DC populations in obese SAT than in lean SAT and also higher than in blood. In the monocyte/DC population, obese samples have a higher percentage of cells expressing BDCA-1 which do not express CD163, a monocyte/macrophage marker.These BDCA-cells have low levels of CD14 and have been characterized as inflammatory DCs in rheumatioid arthritis and some type of cancers. CD4 T lymphocytes from blood of obese subjects have higher expression of pro-inflammatory cytokines (IFNg and IL-17A) than lean subjects. **DISCUSSION/SIGNIFICANCE OF IMPACT** These data may contribute to understanding the pathophysiology of inflammatory disease associated with obesity.

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## GENITAL TRACT (GT) HIV SHEDDING AND MUCOSAL IMMUNITY IN RWANDAN WOMEN ON PROGESTERONE CONTRACEPTION

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**OBJECTIVES/SPECIFIC AIMS** Studies suggest an increased risk of HIV transmission in women using depot medroxyprogesterone acetate (DMPA). Mechanisms include alterations in GT viral shedding and mucosal immunity reflected by changes in immune mediators, endogenous antimicrobial activity and the microbiome. We hypothesized that DMPA use would be associated with detectable GT HIV-1 RNA, less E. coli activity and higher levels of immune mediators in cervicovaginal lavage (CVL). **METHODS/STUDY POPULATION** Cross-sectional comparison of Rwandan women using CVL from 4 groups of premenopausal women: (1) HIV+ cycling ($n$ = 18) (2) HIV+ on hormonal contraception (HC), DMPA or levonorgestrel ($n$ = 18) (3) HIV- cycling ($n$ = 19) (4) HIV- on HC ($n$ = 18). Outcomes were HIV-1 RNA and mediator levels in CVL and plasma and CVL *E. coli* activity. Associations of HC/cycling with CVL and plasma viral loads (VL) were assessed using chi-square/Fisher's exact tests. ANOVA/Kruskal-Wallis tests compared differences in *E. coli* activity and mediators among the groups. **RESULTS/ANTICIPATED RESULTS** 28% of HC users vs. 11% of cycling women had detectable CVL HIV-1 RNA, $p$ = 0.40. HIV+ HC users had significantly lower CVL myeloperoxidase (MPO), a neutrophil marker important in innate mucosal defense, compared to HIV+ cyclers, $p$ = 0.02. Vaginal pH was higher in HC compared to cycling women in both HIV+ and HIV-s, suggesting an association between HC and decreased protective lactobacilli; there was no significant reduction in E. coli activity. **DISCUSSION/SIGNIFICANCE OF IMPACT** HIV+ Rwandan women on HC were more likely to have detectable CVL HIV-1 RNA, lower levels of CVL MPO and higher vaginal pH. Progesterone dominant HC may modify the mucosal environment to promote HIV shedding via alteration of innate defense & a decrease in lactobacillus dominant flora. Larger studies assessing microbiota are needed to confirm the findings and evaluate alternative forms of contraception.

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## A NOVEL PRECLINICAL MODEL TO EVALUATE TSLP IN NORMAL AND MALIGNANT B CELL PRODUCTION

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**OBJECTIVES/SPECIFIC AIMS** Overexpression of CRLF2 is linked to pediatric B cell acute lymphoblastic leukemia (B-ALL) with poor outcome. CRLF2 is a component of the receptor activated by the cytokine, TSLP. The objective of the proposed studies was to use a novel xenograft model to evaluate the role of TSLP-induced CRLF2 signals *in vivo* in normal and malignant human B cell production. **METHODS/STUDY POPULATION** Mouse TSLP does not act on human cells and thus classic human-mouse xenograft models do not provide TSLP that can activate human CRLF2. We have developed a novel xenograft model system composed of mice that express human TSLP (hTSLP+ mice) and mice that lack human TSLP (hTSLP– mice). We transplanted hTSLP+/– mice with human hematopoietic stem cells and with human CRLF2 B-ALL cells to study the role of TSLP in normal and malignant B cell production. **RESULTS/ANTICIPATED RESULTS** TSLP targeted pro-B cells to induce a 3–5 fold increase in normal B cell production. In mice transplanted with a CRLF2 B-ALL cell line, TSLP increased survival and proliferation of leukemia cells. Microarray analysis comparing gene expression in primary CRLF2 B-ALL cells isolated from hTSLP+ and hTSLP– xenograft mice identified 565 genes that are differentially regulated (>2 fold up or downregulated; $p$ < .05). Ingenuity Pathway and Gene Set Enrichment analyses will be used to determine the signaling pathways regulated by hTSLP *in vivo* in the hTSLP+/– xenograft model. **DISCUSSION/SIGNIFICANCE OF IMPACT** The identification of genes downstream of TSLP-CRLF2 signaling has the potential of providing drug targets for combination therapy to effectively treat CRLF2 B-ALL. The hTSLP+/– xenograft model will provide an important tool for evaluating the *in vivo* efficacy of these and other drugs to treat B cell leukemia.

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## THE OLFACTORY IDENTIFICATION IN SCHIZOPHRENIA

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**OBJECTIVES/SPECIFIC AIMS** This survey evaluated responses of identification towards olfactory stimulation on schizophrenic patients in relationship to their chronicity of the illness. **METHODS/STUDY POPULATION** There were a total of 600 adult subjects, men and women which were participants in this study. Patients with low chronicity of schizophrenia $n$ = 200, patients with high chronicity of schizophrenia, $n$ = 200 and participants with normal control $n$ = 200 were part of the three groups of participants. Schizophrenia of low chronicity implies from 0 to 6 months since the first episode and high chronicity shows from 3 to 10 years of chronicity since the first episode. The University of Pennsylvania Smell Identification Test,UPSIT,was applied. **RESULTS/ANTICIPATED RESULTS** A two way ANOVA, (this is a treatment times(x) the total number of correct answers of identification) was calculated. The results confirmed the interrelation of the variables as a significant effect of the variable treatment or diagnosis. We could observe an important difference in statistics between the two groups (of low and high chronicity) and between these the group that was under normal control. When we put an olfactory stimulus, the patients in both experimental groups (low and high groups of schizophrenic chronicity) they performed a certain number of correct identifications statistically less than the number of correct answers of the normal subjects. The difference in the number of correct identifications in low and high conditions of severity were in statistics significant. The group of high chronicity had a high number of identifications which were not correct to the stimulus, in relationship with the patients of the low group with severity. **DISCUSSION/SIGNIFICANCE OF IMPACT** There is a curve that goes down in the capacity to identify olfactory stimulus this was observed as a direct function of the progression of schizophrenia or of the level of chronicity of the sickness.

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## METABOLOMIC ANALYSIS REVEALS NOVEL SMALL MOLECULE PLASMA MARKERS OF HYPERACUTE ISCHEMIC STROKE

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**OBJECTIVES/SPECIFIC AIMS** Based on prior proteomics studies, we find many accompanying small metabolites and peptides to be better markers for hyperacute ischemic injury, because small molecules can cross BBB easier than larger proteins. Here we use metabolomics approach to identify small molecule biomarkers in acute ischemic stroke patients. **METHODS/STUDY POPULATION** 537 plasma metabolites from acute ischemic stroke patients (< 6hr stroke onset) and control samples were identified and quantified by LC-MS followed by statistical analysis. **RESULTS/ANTICIPATED RESULTS** Principal components analysis (PCA) revealed that stoke patients and controls can be well distinguished by their composite metabolic profile. T-test identified several differentially expressed metabolites between stroke patients and controls. Stroke patients had significantly reduced level of citrate (control: 7.39 ± 0.08; stroke: 7.17 ± 0.12; $p$ = 0.0057), and elevated glutamate (Glu) (control: 4.28 ± 0.27;

stroke: 5.12 ± 0.33; $p$ = 0.006), and plasma lactate (PLA) (control: 5.40 ± 0.19; stroke: 5.69 ± 0.10, $p$ = 0.0029). Other novel mediators were identified. **DISCUSSION/SIGNIFICANCE OF IMPACT** Using metabolomics analysis, we found increased Glu and PLA and decreased citrate in acute ischemic stroke patients within 6 hours of stroke onset. Glu, an excitatory neurotransmitter, and PLA, a known apoptotic marker, were both found in CSF and peri-infarct zone of ischemic stroke. Citrate is not only important in energy metabolism, but also binds blood calcium to prevent clot formation. This is a proof-of-concept study and an initial attempt to understand early metabolic landscape of hyperacute ischemic stroke directly in patients; these results highlight potential central nervous system's contribution to peripheral metabolic contents.

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## METABOLOMIC ANALYSIS REVEALS LONG-TERM DECREASE OF HOMOCYSTEINE POST-PFO CLOSURE

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**OBJECTIVES/SPECIFIC AIMS** PFO can increase the risk of stroke by enabling direct mixing of venous and arterial circulation, serving as a conduit for venous clots to the brain. We previously found that PFO disturbs pulmonary filtration of factors such as serotonin (5HT), and creates a prothrombotic state. In the context of endovascular PFO closure, a bedside model to understand PFO circulatory signaling, we performed a full metabolomic profile of other mediators that may respond to PFO closure. **METHODS/STUDY POPULATION** Patients were recruited in accordance with IRB approval. Plasma was sampled from left (LA) and right (RA) atria pre- and post-PFO closure and also from venous blood 3 months postclosure ($n$ = 70). A discovery metabolite screening was performed. **RESULTS/ANTICIPATED RESULTS** With prespecified analysis adjusting for multiple comparison, we identified homocysteine (HCY) with the most prominent change after PFO closure. While HCY levels in the left atrium (LA) and right atrium (RA) were comparable preclosure (pre-LA: 5.61 ± 0.09; pre-RA: 5.30 ± 0.48), HCY immediately decreased in LA postclosure (post-LA: 4.56 ± 0.04) and remained low in peripheral venous blood at 3-month follow-up (4.57 ± 0.06; $p$ = 0.0036). **DISCUSSION/SIGNIFICANCE OF IMPACT** We found PFO closure immediately reduces HYC in left atrial (arterial) blood, and this effect persists in peripheral venous circulation at 3 months postclosure. Our results suggest that HCY, a major factor in promoting atherosclerosis and procoagulable state, may have an important role in PFO related stroke, and that PFO endovascular closure may improve circulatory profile in PFO stroke patients over time. Studies in a larger patient cohort and validation of other important metabolites are ongoing.

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## PERSONALIZED METABOLOMICS OF IDENTICAL TWINS VS. GENERAL STROKE POPULATION

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**OBJECTIVES/SPECIFIC AIMS** It is often challenging to disentangle genetic from environmental factors that influence proteomic and metabolic profiles. While there is strong genetic contribution to the metabolic profile of a newborn at birth, in adulthood the balance of these changes in the context of stroke or therapeutic response are not well understood. To probe this intricate balance, we study a pair of rare identical twins who both had PFO-related strokes at age 45, and compare their metabolomic profiles to other age/risk factor matched PFO stroke patients. **METHODS/STUDY POPULATION** We investigate changes in the venous and arterial metabolomic profiles between PFO stroke twins and general PFO stroke patients pre- and post-PFO closure. In accordance with IRB, plasma was sampled from left (LA) and right (RA) atria pre and postclosure. **RESULTS/ANTICIPATED RESULTS** PCA analysis shows that at baseline preclosure, the profiles of the twins were indistinguishable from age/risk factor matched unrelated PFO strokes patients. However, when analysis was adjusted for PFO closure, the ratio of changes pre vs postclosure clustered twin patients very closely in PCA analysis (red dots). Thus at a cutoff of >1.2-fold change, we found that most of the closure-related changes are consistent between twin patients in both venous (22 out of 29, 75.86%) and arterial (23 out of 37, 62.16%) plasma. **DISCUSSION/SIGNIFICANCE OF IMPACT** We found that while at baseline the metabolomic profiles of the adult PFO stroke twins have little in common, they respond very similarly to endovascular PFO treatment, compared to nonrelated stroke patients. Our data suggest that genetic influence may be more prominent in response to a specific treatment such as PFO closure. Larger studies are needed to understand these important changes in PFO related stroke to individualize treatment better.

# T2: TRANSLATION TO PATIENTS

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## INTRAVENOUS GHRELIN ADMINISTRATION INCREASES ALCOHOL CRAVING IN ALCOHOL-DEPENDENT HEAVY DRINKERS

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**OBJECTIVES/SPECIFIC AIMS** Animal and human studies suggest a role of ghrelin in the neurobiology of alcohol dependence and craving. We tested the hypothesis that intravenous (IV) administration of exogenous ghrelin acutely increases alcohol craving in alcohol-dependent (AD) individuals. **METHODS/STUDY POPULATION** This was a double-blind placebo-controlled human laboratory study. Non–treatment seeking AD heavy drinking individuals were randomized to receive IV ghrelin 1mcg/kg, 3 mcg/kg or 0 mcg/kg (placebo), followed by an alcohol cue-reactivity procedure, during which participants were exposed to neutral (juice) and alcohol cues. 45 individuals received the study drug. The primary outcome was the increase in alcohol craving ("urge"), assessed by the Alcohol Visual Analogue Scale. **RESULTS/ANTICIPATED RESULTS** Repeated measures of ANCOVA revealed a group effect across ghrelin doses in increasing alcohol craving ($p$ < .05). A dose-specific examination revealed a significant effect of ghrelin 3 mcg/kg vs. placebo in increasing alcohol craving ($p$ < .05) with a large effect size (d = .94). By contrast, no significant ghrelin effect was found in increasing either urge to drink juice or food craving. No significant differences in side effects were found across the three groups. **DISCUSSION/SIGNIFICANCE OF IMPACT** This is the first human demonstration that IV ghrelin increases alcohol craving in AD heavy drinking individuals. Although the small sample requires future confirmatory studies, the present findings suggest that ghrelin-related effects were specific for alcohol craving. As such, this study provides preliminary evidence that ghrelin may play a role in the neurobiology of alcohol craving, thus representing a novel potential pharmacological target for treatment.

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## A DOUBLE-BLIND, PLACEBO-CONTROLLED RANDOMIZED PILOT STUDY OF THE EFFECTS OF BACLOFEN ON ALCOHOL-TOBACCO CO-USE AND ALCOHOL CUE-REACTIVITY IN ALCOHOLIC SMOKERS.

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**OBJECTIVES/SPECIFIC AIMS** There is presently no approved single treatment for dual alcohol and nicotine dependencies. This pilot study investigated the effects of baclofen in alcoholic smokers. **METHODS/STUDY POPULATION** This was a double-blind, placebo-controlled study with 30 alcoholic smokers randomized to baclofen 80 mg/day or placebo. A subgroup ($n$ = 18) participated in an alcohol cue-reactivity experiment. **RESULTS/ANTICIPATED RESULTS** There was a significant baclofen effect, compared to placebo, on the percent(%) days of abstinence from alcohol-tobacco co-use ($p$ = 0.03). Alcohol dependence severity moderated baclofen effects, with the higher severity group having the greater baclofen response ($p$ = 0.002). There was also a strong treatment effect on the reduction in the %days of alcohol-tobacco co-use in both groups, and the difference in this outcome reached significance in favor of placebo ($p$ = 0.04). In the cue-reactivity substudy, there was a trend toward significance for a baclofen effect on alcohol urge ($p$ = 0.058) and a significant baclofen effect on salivation ($p$ = 0.001), but no significant medication-by-cue type interaction. **DISCUSSION/SIGNIFICANCE OF IMPACT** Baclofen may represent a unique pharmacotherapy for alcoholic smokers.

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## INFLUENCE OF FLUORESCEIN ANGIOGRAPHY ON THE DIAGNOSIS OF ZONE IN RETINOPATHY OF PREMATURITY

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**OBJECTIVES/SPECIFIC AIMS** To determine how fluorescein angiography (FA) influences the selection of the fovea as it relates to the zone diagnosis in retinopathy of prematurity (ROP). **METHODS/STUDY POPULATION** A prospective Web-based survey displayed a set of 8 cases (16 eyes) with fundus images asking 9 ophthalmologists for a zone diagnosis (I, II, III) that was compared to the diagnosis made by indirect ophthalmoscopy. Experts also identified the fovea, and the linear distance from the optic nerve to the marked fovea was calculated. This process was then repeated with the same clinical cases but included the corresponding FAs. **RESULTS/ANTICIPATED RESULTS** In 4 eyes, there was a increased mean linear distance of 0.97 ± 0.48 mm to the fovea on the color fundus image compared to the paired FA, $t(9) \geq 4.807$, $p < 0.001$. In cases with a Zone I no plus disease clinical diagnosis, experts chose Zone I in 20 of 40 responses (50%) with the color fundus images and in 21 responses (53%) when shown the color fundus and FA. In cases with a Zone I with plus disease clinical diagnosis, experts chose Zone I in 18 of 40 responses (45%) with the color fundus images and in 28 responses (70%) when shown the color fundus and FAs. In cases with a Zone II diagnosis, experts chose Zone II in 76 of 80 responses (95%) with the color fundus images, and in 74 responses (93%) when shown the color fundus and FAs. **DISCUSSION/SIGNIFICANCE OF IMPACT** The influence of FA on the diagnosis of ROP remains unknown. In cases of Zone I with plus disease diagnosis, the use of FA in conjunction with color fundus images improves the sensitivity of a Zone I diagnosis by ROP experts without significant changes to the specificity.

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### CAN HYPER-REACTIVITY TO UNLOADING REACTION CAUSE ANKLE-GIVING WAY IN PATIENTS WITH FUNCTIONAL ANKLE INSTABILITY?

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**OBJECTIVES/SPECIFIC AIMS** Ankle giving-way or feelings of ankle joint stability after severe ankle sprain is a key component in the diagnosis of functional ankle instability (FAI). However, the etiology of ankle giving-way phenomenon remains unclear. This study examined whether the hyper-reactivity to "unloading reaction" in FAI ankles and duplicate dramatic unloading reaction, similar to ankle giving-way, can be reproduced in a laboratory setting. **METHODS/STUDY POPULATION** We studied the unloading reaction in 24 subjects with unilateral FAI (65% females; mean age: 34.2 ± 7.7 years). A trapdoor device with a tilt platform causing sudden 30° ankle supination was used in testing both ankles in random order on two different days three days apart. The first five trials of sudden trapdoor drop occurred without nociceptive electrical stimulation ("no stim") and were followed by five trials of the combined trapdoor drop with nociceptive stimulation ("with stim"). The nociceptive stimulation was applied about 0.015 s after the trapdoor release. Unloading reaction was quantified by a key variable: maximal reduction in total body weight (RBW) recorded by two force platforms at least 0.5 seconds after the trapdoor release. **RESULTS/ANTICIPATED RESULTS** The averaged RBW in the injured ankles was 120.6 ± 188N under "with stim" condition, which was significantly greater ($p < 0.05$) than 61.9 ± 69.5N (uninjured ankles, "with stim"), 57.6 ± 52.3N (injured ankles, "no stim"), and 54.5 ± 55.1N (uninjured ankles, "no stim"), respectively. **DISCUSSION/SIGNIFICANCE OF IMPACT** This study demonstrates significant increase in unloading reaction on the injured ankles when tested under sudden ankle stretch and nociceptive stimulation. This finding may help to better understand the etiology of ankle giving way and should be considered for intervention effectiveness in patients with FAI.

## T3: TRANSLATION TO PRACTICE

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### BIOMEDICAL RESEARCH TO TRANSLATIONAL MEDICINE

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**OBJECTIVES/SPECIFIC AIMS** Drug discovery in academic institutions and industries predominantly occurs separatey. With increasing drug prices, new drug disapprovals and regulatory constraints, with the persistence of inevitable "patent cliff" and funding impediments creating the "Valley of Death," a collaboration between academia and industry with a translational medicine (TM) vision offers a favorable remedy. This will ensure that bounty of biomedical research is "translated" into clinical benefits catering to the unmet needs of oncology, inflammation or metabolomics. This review article underscores the relevance of TM for progress in R&D, identifies logjams in its execution, discusses propitious mitigation strategies and highlights global efforts taken in this direction. **METHODS/STUDY POPULATION** We facilitated vital affiliations, innovative thinking and offered tools for speedy and effective translation of biomedical research into clinical applications thereby bridging the translational gap while providing an appropriate platform for professionals to learn, network and make crucial strategic decisions. **RESULTS/ANTICIPATED RESULTS** Even though promising initiatives are being taken, no translational educational metrics have been developed to assess the success of such translational programs in Australia and Asia. A robust management and government support can further aid in funding and coordination between translational research organizations. Observations on advances in leading countries will also be discussed. **DISCUSSION/SIGNIFICANCE OF IMPACT** TM helps in improving the quality of human healthcare by providing innovative solutions for hard-to-cure diseases and streamlines resources necessary to support meaningful research endeavors hence encouraging economic growth. Heeding emerging biomarkers from regulatory and human prognosis perspective, cordial nexus amidst academia and industry and tenacious approaches to promote TM globally can render optimism regarding winning the translational race.

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### USING A HACKATHON AS A PRACTICAL AND EFFECTIVE WAY TO TEACH OUT-OF-THE-BOX THINKING AND INNOVATION

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**OBJECTIVES/SPECIFIC AIMS** We demonstrate how a hackathon can be used as a practical way to stimulate out-of-the-box thinking and teach innovation. **METHODS/STUDY POPULATION** Thirty students enrolled in a summer internship program participated in a hackathon. Learning effects were derived from qualitative analyses of students' self-evaluations and comparison of concept maps drawn before and after the experience. **RESULTS/ANTICIPATED RESULTS** The students generated 270 unique ideas addressing a challenging problem, childhood obesity. This group of students, diverse in terms of age, school level, and background, learned how to ideate and as a result of the hackathon has now a much better understanding of what it takes to innovate in the healthcare environment. **DISCUSSION/SIGNIFICANCE OF IMPACT** The hackathon inspired two student teams to continue on the innovation pathway beyond their summer traineeship.

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### RISK FACTORS FOR COMPLICATION AFTER SECOND TRIMESTER UTERINE EVACUATION

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**OBJECTIVES/SPECIFIC AIMS** To determine the association between obesity and complications after second trimester surgical abortion. **METHODS/STUDY POPULATION** We conducted a retrospective cohort study of 4,534 women who underwent second-trimester abortions from 2009 to 2013 at San Francisco General Hospital (SFGH). All procedures identified as having a complication were reviewed by the authors. We compared the risk of any complication in women with BMI <30 to those with BMI ≥30. Secondary outcomes were individual complications, including cervical laceration, hemorrhage, uterine atony, anesthetic complications, uterine perforation, and retained products of conception. **RESULTS/ANTICIPATED RESULTS** Of the 4,534 second trimester abortions, 9.8% met criteria for complication. In the unadjusted analysis, BMI ≥ 30 was not associated with abortion complication (OR = 1.02 [95% CI: 0.82–1.28]), nor was it associated with any individual complications. Parity and gestational age were associated with any complication, with 13% increased odds for each additional birth (95% CI: 1.06–1.20), and 3% increased odds for each additional day of gestation (95% CI: 1.03–1.05). There was a trend toward increased complication risk among women with a history of two or more cesarean sections (OR = 1.4 [95% CI: 0.98–1.87]). **DISCUSSION/SIGNIFICANCE OF IMPACT** The overall 9.8% complication rate in this study is higher than previously reported. Two possible explanations are: (1) SFGH is a high-risk referral center, and (2) we may have used a more inclusive definition of complication. We found no increased risk of abortion complication among obese women in unadjusted analyses. Adjusted analyses must be conducted before we can conclude that obesity is not a risk factor. These data will help to develop evidence-based referral guidelines for women seeking abortion.

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### THE EFFECT OF VITAMIN D REPLETION IN THE CONTEXT OF VITAMIN D BINDING PROTEIN LEVELS

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**OBJECTIVES/SPECIFIC AIMS** (1) To determine the effect of vitamin D repletion on vitamin D binding protein (DBP) levels (2) To determine the effect of DBP levels on the change in PTH and calcium in response to vitamin D repletion. **METHODS/STUDY POPULATION** Vitamin D–deficient (25(OH)D <20ng/ml) adults ($n = 150$) were randomized to receive either 50,000 IU of vitamin D3 or placebo weekly for 8 weeks. 25(OH)D, parathyroid hormone (PTH), calcium and DBP levels were measured. Linear regression analysis was used to determine if DBP levels were correlated with baseline PTH levels and changes in PTH and calcium levels in response to vitamin D3. **RESULTS/ANTICIPATED RESULTS** Blacks had lower total 25(OH)D (12 vs. 15 ng/ml, $p <$ 0.001) and DBP levels (119 vs. 234 mg/ml, $p < 0.001$) than nonblacks. DBP levels were

similar before and after vitamin D3 or placebo treatment ($r = 0.98$, $p < 0.001$). Baseline total 25(OH)D levels were a significant determinant of baseline PTH levels ($p < 0.001$). The change in total 25(OH)D was associated with the change in PTH ($p < 0.001$) and calcium levels ($p < .05$). In contrast, DBP levels were not a determinant of baseline PTH ($p = 0.57$) nor significantly related to changes in either PTH ($p = 0.53$) or calcium levels ($p = 0.88$). **DISCUSSION/SIGNIFICANCE OF IMPACT** DBP levels are stable in blacks and nonblacks, and do not change with correction of vitamin D deficiency. Even for individuals with total 25(OH)D levels < 20 ng/ml, blacks have significantly lower DBP levels than nonblacks. However, within this range of total 25(OH)D, DBP levels do not influence the effect of vitamin D repletion on PTH or calcium levels.

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### CENR-CER BRIDGE BUILDING: A WORKSHOP AND FRAMEWORK FOR BEGINNING A NECESSARY DIALOGUE BETWEEN RESEARCHERS

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**OBJECTIVES/SPECIFIC AIMS** Our objectives were as follows: (1) Describe the differences between CER and CEnR; (2) Discuss how attending this workshop brought practitioners of these two disciplines together; and (3) Identify ways to make collaboration effective and beneficial. **METHODS/STUDY POPULATION** We implemented a full-day, interactive workshop to foster dialogue on problems and needs related to CEnR and CER. We executed facilitated workgroups that explored, through a case example approach with four local research projects (2 CEnR-related and 2 CER-related), questions relevant to specific and broad issues deemed as challenging to the research discipline. To assure a standard variety exploring each case, workgroups were carefully predetermined based on participant areas of interest, type of research and institutional representation. **RESULTS/ANTICIPATED RESULTS** The workshop convened participants from four academic institutions, two health service organizations, and over twelve other organizations (seven were community-based and active in community-academic partnerships). The products of the facilitated workgroups produced themes outlining similar and dissimilar challenges for CEnR and CER. We synthesized these themes and developed preliminary framework for establishing dialogue aimed at developing strategies that will close the gap on barriers to collaborative research. **DISCUSSION/SIGNIFICANCE OF IMPACT** This information can inform other CTSAs with a few practical actions for building a bridge between CEnR and CER including; (1) a method for gathering a constituency of experts from local institutions to begin a dialogue (2) an initial set of questions for key stakeholders to explore; and (3) a basic framework of challenges and priority impact areas for common ground in removing barriers to collaboration.

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### PREDISCHARGE ASSESSMENT OF PATIENTS HOSPITALIZED FOR HEART FAILURE (HF)—A PROSPECTIVE STUDY

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**OBJECTIVES/SPECIFIC AIMS** Evaluation of heart failure patients at the time of discharge **METHODS/STUDY POPULATION** We prospectively enrolled 99 consecutive patients admitted with HF over 4 months at a tertiary care center. History and physical examination, inferior vena cava (IVC) ultrasonographic measurements, valsalva response using Finipress and laboratory tests were obtained at the time of discharge. These patients were followed at 30 days by telephone to record 30-day readmission rates. **RESULTS/ANTICIPATED RESULTS** A total of 99 patients (mean age 60.8 ± 15.9 years, women 46%) were included. There were 22% patients with systolic dysfunction (EF < 40%) and 77% with HF with preserved ejection fraction. Mean JVP was 4.2 ± 1.9 cm and it mildly correlated with lower extremity edema ($r^2 = 0.22$, $p = 0.049$) and pulmonary crackles ($r^2 = 0.35$, $p = 0.0001$). Mean weight loss was 3.4 ± 4.5 kg over 5.5 ± 4.3 days. Valsalva response was abnormal in 30% of the patients (absent over shoot or square wave response). Calculated right atrial pressure based on IVC diameter was 7.5 ± 4.3 mmHg. BNP at discharge was significantly lower than admission BNP (582 ± 805.6, $p < 0.001$). The readmission rate was 25% in these patients and there were additional 13 emergency room visits. **DISCUSSION/SIGNIFICANCE OF IMPACT** In this cohort of patients admitted with HF, significant number had signs of clinical or subclinical congestion that could explain the high readmission rate

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### ASSOCIATIONS OF POSTOPERATIVE WOUND DEHISCENCE: A COHORT STUDY OF MEDSTAR ELECTRONIC HEALTH RECORD DATA USING EXPLORYS

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**OBJECTIVES/SPECIFIC AIMS** Agency for Healthcare Research and Quality (AHRQ) patient safety indicators (PSI's) were developed to metric hospital complications and adverse events. PSI-14 measures postoperative wound dehiscence, which occurs in 0.5–3.4% of abdominopelvic surgeries, and carries a mortality of up to 40%. PSI-14 has been shown to impact morbidity, length of stay, healthcare costs and readmission rates. The purpose of the current study is to investigate associations between PSI-14, and medical and surgical co-morbidities. **METHODS/STUDY POPULATION** Cases of abdominopelvic surgery and postoperative wound dehiscence were identified from the MedStar Health System cohort between January 1, 2008 and December 31, 2012 using the Explorys platform. Patient-related comorbidities including age, sex, presence of COPD, ascites, anemia (Hct <30), malignancy, body mass index (BMI >30 kg/m$^2$), nutritional status (albumin <3.5 g/dL), chronic steroid use, immunosuppression, associated autoimmune disease, and diabetes were exported via Explorys. Logistic regression model was used to examine the association between wound dehiscence and comorbidities. C-statistic and Hosmer-Lemeshow were used to assess the models discrimination and calibration. **RESULTS/ANTICIPATED RESULTS** Of 26422 eligible patients, 786 (2.97%) had postoperative wound dehiscence. Chronic obstructive pulmonary disease (COPD), ascites, albumin <3.5, infection, and opioid use after surgery were significantly associated with wound dehiscence adjusted for age, gender and BMI ($p < 0.05$,C = 0.82, hosmer-lemeshow = 4.0). **DISCUSSION/SIGNIFICANCE OF IMPACT** Opioid use after surgery remained a significant risk factor for wound dehiscence even after adjusting for other risk factors.

## T4: TRANSLATION TO POPULATION

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### QUALITY OF LIFE IN CANCER PATIENTS: LATENT CLASS AND LATENT TRANSITION ANALYSIS

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**OBJECTIVES/SPECIFIC AIMS** Translational quality of life (QOL) research relies on methods to obtain and interpret patient data at multiple time points. While cancer patients are likely to report poor QOL, they do not always experience similar QOL impairment. Classifications based on QOL impairment and the change in these over time is unclear. We describe classes of lung cancer patients based on QOL, examine class transitions over time, and identify the variables predicting class membership. **METHODS/STUDY POPULATION** Lung cancer patients in the population-based Cancer Care Outcomes Research and Surveillance Consortium completed EQ-5D questionnaires near diagnosis and >1 year postdiagnosis) ($n$ = 1396). Using latent class (LCA) and latent transition analysis (LTA) we determined QOL latent classes and the transitions between classes across time. Predictors of class membership and transitions included age (<65, ≥65 years), gender, race, cancer stage, treatment, depression, comorbidities, and pain interference (PI). **RESULTS/ANTICIPATED RESULTS** The sample was 52% male, 40% <65 years, 81% white, and 36% ≥Stage III cancer. LCA identified four classes at diagnosis and follow-up: (1) poor QOL, (2) pain with depression, (3) mobility problems, and (4) good QOL. The probability of remaining in class was 0.76, 0.75, 0.68, and 0.53, for classes 3, 4, 2, and 1 respectively. Classes 1 and 2 had only 0.25 and 0.14 probability of improving to class 4 and 0.30 and 0.10 probability of transitioning to class 3, respectively. Minorities, PI and comorbidities were more likely to be associated with class 1, 2, and 3 at diagnosis compared to class 4. Baseline class membership was the primary predictor of class membership at follow-up. **DISCUSSION/SIGNIFICANCE OF IMPACT** Findings show four classes of patients based on QOL. The stability of classes suggests that patients with any impairment at diagnosis were unlikely to show improvement at follow-up.

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### SUBSTANCE ABUSE STIGMA AND ENGAGEMENT IN HIV CARE: A MIXED METHODS INVESTIGATION

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**OBJECTIVES/SPECIFIC AIMS** (1) Examine levels of substance-abuse stigma (SA stigma) among PLHIV with co-occurring substance use. (2) Assess the effects of HIV stigma on retention in HIV care and medication adherence among PLHIV with co-occurring substance use. (3) Assess the effects of SA stigma on retention in HIV care and medication adherence among PLHIV with co-occurring substance use. (4) Describe how dual stigmas (HIV + SA stigma) affect retention in care and medication adherence among PLHIV with co-occurring substance use. (5) Explore the relationship between stigmas, medication adherence, and retention in care through the perspective of PLHIV with co-occurring substance use, using focus group methods. **METHODS/STUDY POPULATION** Participants are recruited from the 1917 Outpatient HIV Clinic located at the University of Alabama at Birmingham ($n$ = 200). An explanatory-sequential mixed methods design is being used. Phase 1 includes data collected through a self-administered, iPad survey as well as medical record data. Phase 2 focus groups will provide a contextual understanding the results of phase 1. **RESULTS/ANTICIPATED RESULTS** It is anticipated that participants will report higher levels

of SA stigma than HIV stigma. Further, it is hypothesized that individuals who report higher levels of stigma (SA, HIV, and/or dual stigmas) will have lower levels of HIV medication adherence and retention in HIV care. **DISCUSSION/SIGNIFICANCE OF IMPACT** Because HIV-infected substance users are the population least likely to be adequately engaged in HIV care and to adhere to HIV medications, it is critical that researchers continue to identify ways to improve health behaviors and outcomes in this population. This study will help us to understand how health-related stigmas affect HIV care among these patients. Results from this study will help us to develop targeted interventions that will improve engagement in HIV care, health outcomes, and quality of life among this population.

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### MENTORED EXPERIENCE TO EXPAND OPPORTUNITIES IN RESEARCH (METEOR) PROGRAM

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**OBJECTIVES/SPECIFIC AIMS** A strategic goal of the CTSA Consortium is to support training and career development of clinical and translational scientists, with emphasis on those from underrepresented backgrounds (URM). Unlike other short-term summer programs, the METEOR Program, launched in June 2012, provides a long-term mentored educational experience to incoming URM medical students at George Washington University (GW) to increase their participation and success. Promoted as a competitive fellowship opportunity, each student is paired with a clinical or translational research mentor with whom to work through the duration of medical school. **METHODS/STUDY POPULATION** To date, there are 7 students. Using a comparison group of non-METEOR medical students who participated in a similar summer research program, a mixed methods study is underway. Research skills self-assessments and qualitative interviews are being conducted. A workshop in mentoring the diverse trainee will be held in March. **RESULTS/ANTICIPATED RESULTS** The METEOR Program is successful in increasing research skills and interest, and establishing mentoring relationships. **DISCUSSION/SIGNIFICANCE OF IMPACT** The program addresses the critical challenge of mentoring URM students since, like most medical schools nationally, GW has few URM faculty, and some non-URM faculty may feel less equipped and comfortable serving as mentors to URM mentees. Our goal is that participation in the METEOR Program will enhance URM medical students' overall experience in medical school and research skills, and encourage them to consider careers as clinical and translational researchers. Through training, mentors improve their mentoring skills for URM and non-URM medical students and other trainees. The METEOR Program may serve as a model for other mentorship programs.

## RESEARCH PROFESSIONALS ABSTRACTS

### T0: BASIC SCIENTIFIC DISCOVERY

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### PROMOTING DIVERSITY IN THE CLINICAL AND TRANSLATIONAL RESEARCH WORKFORCE

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**OBJECTIVES/SPECIFIC AIMS** To address the problem of health disparities through a concerted effort to recruit and train doctoral-prepared minority candidates for successful careers in clinical and translational research. **METHODS/STUDY POPULATION** A 10-year postinception review of the CRECD programs at Morehouse School of Medicine and the University of Puerto Rico highlights significant contributions to addressing the workforce disparities challenges in CTR. **RESULTS/ANTICIPATED RESULTS** Over the ten-year period, the MSM program successfully graduated 34 doctoral and pre-doctoral trainees with a 75% retention rate for faculty vs. 60% AAMC comparator. Individual doctoral-level trainees at MSM successfully applied for and received grant funding totaling $11 million and participated in program funding amounting up to $56 million. Graduates at MSM have achieved academic advancement to associate professor and professor and other leadership positions, exceeding MSM peers. Trainees have published approximately 135 publications and made over 197 presentations. The UPR program has enrolled 68 doctoral trainees and graduated 44. These scholars come from diverse professional backgrounds (32 physicians, 13 from dental medicine and various disciplines, including 14 PhDs). The majority are Hispanic women (38). Evaluation results show that after five years of graduation 50% of graduates are actively conducting clinical research, 75% have published at least once in peer-reviewed scientific journals, and 68.8% have submitted at least one grant proposal. **DISCUSSION/SIGNIFICANCE OF IMPACT** The CRECD programs have been instrumental in significantly promoting diversity and addressing disparities in the CTR workforce and efforts must be made at the national level to expand this program.

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### FROM EPILEPSIES TO AUTISM: A NOVEL COMPUTATIONAL BIOSTATISTICS APPROACH FINDS THE "MISSING HERITABILITY" IN GWAS

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**OBJECTIVES/SPECIFIC AIMS** Almost a decade after the completion of the Human Genome Project, the medical advances hoped for from genome-wide association studies (GWAS) have not yet been realized. **METHODS/STUDY POPULATION** Here, we present a computational biostatistics approach, combining an adaptation of u-statistics for multivariate structured data to linkage disequilibrium, recombination hotspots, and chromosomal topology with "study-specific genome-wide significance" accounting for MAF-significance correlation, nonrandomization bias, and multiplicity among overlapping wide-loci. **RESULTS/ANTICIPATED RESULTS** The prevalence of autism spectrum disorders (ASD) has increased 20-fold over the past 50 years to >1% of children. Although twin studies attest to a high degree of heritability, the genetic risk factors are still poorly understood. From results in childhood absence epilepsy, we had hypothesized that axonal guidance and calcium signaling are involved in autism as well.Results from two independent populations of <1000 subjects confirmed this hypothesis. Epistasis between impaired growth factor dephosphorylation and variations in chloride and potassium channels suggests the time of accelerated neuronal growth at 9–24 months of age as the period where treatment with ion channel modulators could prevent progression to more severe forms of autism. **DISCUSSION/SIGNIFICANCE OF IMPACT** By extension, the same computational biostatistics approach could yield profound insights into the etiology of many common diseases from subpopulations among the genetic data already collected and into risk factors for treatment failures or side effects from phase III studies.

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### CAMPR-BASIC: A CTSA PILOT GRANT MECHANISM FOR ACCELERATING TRANSLATIONAL SCIENCE AT COLUMBIA UNIVERSITY

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**OBJECTIVES/SPECIFIC AIMS** In 2006, the Irving Institute for Clinical & Translational Research was charged with helping bridge basic and clinical/translational research to bring effective, efficient strategies into healthcare. We developed a novel pilot award, the CaMPR initiative (Collaborative and Multidisciplinary Pilot Research)—to support the formation of newly configured investigative teams from different disciplines to tackle a significant health problem at the cellular, individual, or community level. To date, CaMPR investigators have been largely based in clinical departments. **METHODS/STUDY POPULATION** CaMPR-BASIC takes the next step by offering support for collaborations between researchers from basic science departments from across the university and clinical investigators on the medical campus. Applicants must form a new collaborative team of two principal investigators at the level of assistant professor: one from a basic science department and one from a clinical department. The new team may not have produced any publications together nor shared research funding in the past. Projects must be focused at the preclinical level, with relevance to a clinical problem. The goal is to bring clinical focus and experience to preclinical research, i.e., to ensure that the cell or animal model is appropriate, that the target molecule is specific, and that the preclinical approach has potential for significant translation to humans. **RESULTS/ANTICIPATED RESULTS** In yr 01 (2012), just four applications (led by 2 PhDs and 2 MDs) from the same basic science department were received for the two, $40,000 awards. In 2013, with enhanced outreach to basic scientists, 13 applications from 6 basic science departments were received; 12 led by investigators with a PhD or MD/PhD. **DISCUSSION/SIGNIFICANCE OF IMPACT** Winners to be selected in March 2014.

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### NONALCOHOLIC STEATOHEPATITIS: ROLE OF INFLAMMATION AND OXIDATIVE STRESS

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**OBJECTIVES/SPECIFIC AIMS** Nonalcoholic steato-hepatitis (NASH) and its precursor NA fatty liver disease (NAFLD) occurs in 5–20% of the population, It is a frequent complication of metabolic syndrome (MS) and omay lead to hepatic cirrhosis and carcinoma. While several mechanistic pathways have been incriminated, the pathogenesis remains largely unclear. We hypothesized that severe mitochondrial oxidative stress presumed to cause hepatic injury is the result of cytokine mediated inflammatory damage. **METHODS/STUDY POPULATION** To test our hypothesis we used obese ZSF rats which develop florid MS and Sprague Dawley rats as controls. The control rats were fed normal chow while test group is fed high calorie high fat diet

to maintain hyperglycemia. The rats were sacrificed at 36th week after blood and urine were collected and then liver harvested. Liver slices from both groups were incubated in William's media E with and without sc-358755, a TNFα -anatagonist for 8 hours. The tissue extracts and the media were then examined for the amount of 8 hydroxy deoxyguanosine (8-OHdG), a marker of mitochondrial DNA oxidation by HPLC. **RESULTS/ANTICIPATED RESULTS** Our results showed that ZSF rats at 36 weeks exhibited MS with hypertension, diabetes, obesity, hypertriglyceridemia and renal failure. That ZSF rats also develop NASH was shown previously by us and others. The 8-OHdG levels were in the hepatic tissue of ZSF rats while control rats. Treatment with TNF antagonist decreased 8-OHdG levels in liver in obese ZSF rats from to 2158 ± 92.6 SE to 136 ± 11.3SE pM/ml ($p < 0.0001$). There was no demonstrable effect in controls. **DISCUSSION/SIGNIFICANCE OF IMPACT** Our studies demonstrated that inhibition of inflammation in the liver ameliorated oxidative stress, These findings suggest that inflammatory cytokine cascade could potentially initiate mitochondrial damage and oxidative stress that ultimately leads to NASH.

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## PRECLINICAL STUDIES OF MART-10, A LESS CALCEMIC VITAMIN D ANALOG, FOR CANCER PREVENTION AND TREATMENT

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**OBJECTIVES/SPECIFIC AIMS** Calcitriol, the active form of vitamin D3, has potent anti-tumor activity. However, it can cause hypercalcemia and is not suitable for clinical applications. Analogs of calcitriol that are less calcemic but exhibit potent anti-tumor activity would be good candidates as therapeutic agents. Here, we summarize the results from preclinical studies of a new generation of vitamin D analog, 2α-(3-hydroxypropyl)-1α,25-dihydroxy-19-norvitamin D3 (MART-10). **METHODS/STUDY POPULATION** The *in vitro* studies were conducted using various cancer cell lines. Western blot and, in some cases, real-time RT-PCR were used for measuring the expression of CYP24A1 and biomarkers for cell cycle, apoptosis, cell invasion and epithelial-mesenchymal transition. Cell cycle and apoptotic analyses were also accomplished by flow cytometry. In addition, the anti-tumor activity of vitamin D compounds *in vivo* was studied by a xenograft model. **RESULTS/ANTICIPATED RESULTS** MART-10 is much more resistant to the degradation caused by CYP24A1. The analog is 100–1,000 folds more potent than calcitriol in inhibiting cancer cell growth through a greater upregulation of p21 and p27, leading to a more profound cell cycle arrest. MART-10 is also more active than calcitriol in stimulating the apoptosis and inhibiting the metastatic potential of MCF-7 breast cancer cells. In a xenograft model using BxPC-3 pancreatic cancer cells, MART-10 suppressed tumor growth to a greater extent compared to calcitriol, without inducing hypercalcemia and weight loss. **DISCUSSION/SIGNIFICANCE OF IMPACT** In conclusion, MART-10 is a promising candidate as a drug for the prevention and treatment of various cancers.

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## DOES BLENDED DELIVERY ENHANCE LEARNING ABOUT GRANT APPLICATION DEVELOPMENT?

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**OBJECTIVES/SPECIFIC AIMS** Since 2008, scholars at the University of Michigan have been mentored over 3 face-to-face (F2F) workshops to develop NIH career development award applications. Sessions start with a lecture followed by small group activity for feedback and critique of applications in development. The passive lecture portion was not the best use of F2F time. We explored online delivery of the lecture portion to better utilize F2F time for active learning. **METHODS/STUDY POPULATION** Online lectures were made available 2 weeks prior to the F2F session for self-paced learning. These were re-recorded in 2013 in a studio to replace lower grade videos from the 2012 blended learning pilot. Each video was bookended with the same questions to check pre- and postknowledge gaps. Scholars then worked on their application drafts for peer and mentor feedback at the next F2F session. Impact of online lectures was assessed by measuring knowledge errors (e), defined as percentage of incorrect responses to questions embedded in the modules. **RESULTS/ANTICIPATED RESULTS** We hypothesized a change in knowledge errors (e) across all modules. We found a reduction from 29.67% (pre video lecture) to 3.38% (post video lecture). Using a paired, two-tailed t-test, this reduction was found significant ($p = 0.01$). The largest changes were found in questions that pertained to training and mentoring plan section contents, and goals of the NIH K funding mechanism. Amongst modules, the greatest change occurred in the career development plan module. **DISCUSSION/SIGNIFICANCE OF IMPACT** Although blended delivery requires a high investment in design and development, it promises engaged and active learning. In our program, online modules permitted greater F2F collaboration. Reduction in knowledge errors helped scholars in drafting specific sections of the award application just in time for their next F2F workshop in the series.

## T2: TRANSLATION TO PATIENTS

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## GENDER DIFFERENCES IN TREATMENT WITH OPIOID ANALGESICS AND OTHER DRUGS IN PERSONS WITH DIABETES: A POPULATION-BASED ANALYSIS

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**OBJECTIVES/SPECIFIC AIMS** To examine gender differences in Schedule II/III opioid analgesic (OA) prescriptions (Rx) in a cohort with diabetes mellitus (DM). **METHODS/STUDY POPULATION** From Blue Cross Blue Shield of Texas data for 1/2008–12/2011, 278,348 persons had DM diagnosed, of whom 51,656 were 18–64 and 12+ months in a plan covering Rxes. Among persons with OA Rxes, days covered by OA pills (>98% short acting) after the 1st Rx were analyzed as <1 month/<120 pills vs longer/> = 120 pills. We also examined Rxes for other drugs for chronic noncancer pain (CNCP): benzodiazepines (benzos), zolpidem, and antidepressants. We created variables for 5 types of CNCP, mental health conditions, and alcohol abuse. Bivariate analyses were conducted by gender. **RESULTS/ANTICIPATED RESULTS** Among 51,656 persons with DM, 21,936 (42.5%) were women and 21,515 (41.7%) prescribed OAs. More women used OAs than men (46.3 vs 38.2%, $p < 0.001$). Among OA users, proportions on benzos, zolpidem, and antidepressants were twice those of OA nonusers and proportions with comorbid CNCP, mental health and alcohol abuse were also twice those of nonusers. Among OA users, longer term OA therapy was the same for women and men (15%) but more women were prescribed other drugs (benzos 22.4 vs. 13.3%; zolpidem 11.5 vs. 8.8%, and antidepressants 33.2 vs. 16.5%, respectively), $p < 0.001$ for all comparisons. Among OA users, women were also more likely to be diagnosed with CNCP and mental health conditions than men. **DISCUSSION/SIGNIFICANCE OF IMPACT** In a statewide privately insured DM cohort, treatment with potent OAs is very common, especially for women. Among OA users, more women were prescribed other drugs such as benzos and zolpidem than men. These data point to research opportunities to address use of potentially risky drugs especially by women with DM.

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## THE BENEFITS OF COMPREHENSIVE REGULATORY SUPPORT FOR ACADEMIC SPONSOR-INVESTIGATORS

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**OBJECTIVES/SPECIFIC AIMS** Clinical research conducted at academic medical centers can require FDA oversight through the Investigational New Drug (IND) or Investigational Device Exemption (IDE) designation. Investigator-initiated research requires the investigator to serve as a sponsor-investigator and the "holder" of an IND/IDE. This role involves complex submissions to and interactions with the FDA, but investigators may be poorly prepared or resourced to meet these additional obligations. An increasing number of academic medical centers offer regulatory support for sponsor-investigators. Presently, we describe one high-volume and comprehensive regulatory support program at a large medical center. **METHODS/STUDY POPULATION** Services include regulatory gap analysis, regulatory strategy, technology transfer assistance, protocol refinement, regulatory submissions, (pre-IND and pre-Sub (IDE) meeting support, IND/IDE application submission, IND/IDE life-cycle maintenance support), FDA meeting preparation and engagement, and industry interaction. Select case studies will reveal both specific challenges and successful approaches. **RESULTS/ANTICIPATED RESULTS** As compared to industry, FDA regulatory compliance is challenging for underresourced sponsor-investigators. The assistance of regulatory professionals can impact translational initiatives, research execution, and marketing pathways. **DISCUSSION/SIGNIFICANCE OF IMPACT** Given the complexity of FDA regulatory requirements, comprehensive regulatory support for sponsor-investigators can accelerate study execution and completion and is a growth asset to the academic research enterprise.

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## INTREPID: INTENSIVE RESEARCH TRAINING FOR EARLY ACADEMIC CLINICIANS

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**OBJECTIVES/SPECIFIC AIMS** Early academic clinicians often lack clinical research skills, but duties limit time for extended training. We hypothesized that an intensive short-term program could promote rapid acquisition of translational research skills and improve probability of successful research. **METHODS/STUDY POPULATION** We developed INTREPID (INtensive Training in Research statistics, Ethics, and Protocol Informatics and Design), a 24-day program (134 classroom hours) in clinical research methodologies. 4 integrated courses were developed via faculty collaboration: research

methods, ethics, biostatistics, and bioinformatics/programming. Participants committed 100% protected time. Seminars and didactics were complemented by laboratory (PASS and "R" programming) and discussion groups. Assignments included readings, problem sets, protocol development, study critiques, quizzes, programming, database query and presentations. Graduates received an NYU/NY State Certificate of Completion + 9 credit hours. **RESULTS/ANTICIPATED RESULTS** The inaugural class comprised 6 trainees from a range of departments. All held MD or PhD degrees; 1 had an MPH. Rank ranged from fellow to assistant professor. Upon completion, trainees demonstrated competency in "R" and basic statistics, protocol development and critical reading. On survey graduates reported they would recommend the program to colleagues. 6 months postcompletion all graduates continued to recommend the program; 4 rated INTREPID "very effective," and 2 "effective" in addressing knowledge gaps. **DISCUSSION/SIGNIFICANCE OF IMPACT** An intensive program to build investigational skills for medical researchers across disciplines is feasible and requires significant commitment of time and resources from faculty and participants. We plan to offer INTREPID annually.

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### A MODEL FOR MULTISITE COLLABORATION: THE RARE DISEASES CLINICAL RESEARCH NETWORK (RDCRN)

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**OBJECTIVES/SPECIFIC AIMS** The goal of RDCRN is to advance clinical research in rare diseases involving multiple institutions. **METHODS/STUDY POPULATION** To facilitate multisite clinical REESRACH for rare diseases, the Office of Rare Diseases Research (ORDR), now located in NCATS, in collaboration with six NIH Institutes/Centers (ICs) established the RDCRN. The RDCRN is unique in its approach to addressing rare diseases as a group. The RDCRN is a network of 17 distinct clinical research consortia, a central Data Management and Coordinating Center and 95 Patient Advocacy Groups (PAGs). Each consortium stuies a group of at least three related rare diseases. The direct involvement of PAGs in RDCRN is a major feature of this network. **RESULTS/ANTICIPATED RESULTS** Each consortium conducts at least two multisite clinical studies, develops a training program and involves PAGs as research partners. Collectively, the RDCRN is studying 200 rare diseases in natural history and clinical trials at more than 400 clinical sites located in the US and in 14 countries with 86 active protocols. There have been 134 trainees in the current cycle of RDCRN. More than 15,000 patients have enrolled in protocols. **DISCUSSION/SIGNIFICANCE OF IMPACT** This program has helped facilitate identification of biomarkers for disease risk and disease severity/activity, and measures of clinical outcome applicable to clinical trials. It also has encouraged development of new approaches for diagnosis, prevention, and treatment of rare diseases.

## T3: TRANSLATION TO PRACTICE

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### CREATION OF A MULTIINSTITUTIONAL CTSA-SPONSORED OBSTETRICS REGISTRY FOR ADVERSE RARE EVENTS (RARE)

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**OBJECTIVES/SPECIFIC AIMS** Childbirth is the most common reason for hospitalization in the US, yet limited evidence informs treatment for many serious, but uncommon, pregnancy complications. We sought to assess the feasibility of developing a multiinstitutional database among CTSA centers to evaluate treatments and outcomes for four rare obstetrical events: placenta accreta, monochorionic twins, maternal congenital heart disease, and mechanical ventilation during pregnancy. **METHODS/STUDY POPULATION** Members of the National Perinatal Research Consortium (NPRC) were awarded pilot funds by our respective CTSAs for a multisite project. We piloted use of CTSA IRBshare for a federated IRB and developed and implemented a multiinstitutional REDCap database for abstraction of cases identified by querying administrative and clinical data at our institutions. **RESULTS/ANTICIPATED RESULTS** We encountered opportunities and challenges for multiinstitutional collaboration. We easily implemented our database using REDCap's secure, Web-based application. However, we could not use IRBshare as planned, because exempt IRB applications are excluded. We also encountered challenges creating multisite data use agreements for our shared database. Institutional variation in ICD9 and CPT codes also affected the sensitivity and specificity of case-finding queries. **DISCUSSION/SIGNIFICANCE OF IMPACT** This project demonstrates that CTSA-supported multiinstitutional collaboration is feasible, but roadblocks exist. Addressing these barriers may advance opportunities for collaborative clinical and translational research, as recommended by the IOM report.

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### BUILDING MENTOR NETWORKS: A PILOT PROGRAM

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**OBJECTIVES/SPECIFIC AIMS** Beginning fall 2012, Dr. Zwanziger, Head, CCTS educational program (REACH), Dr. Valenta, Director, REACH Mentoring Programs, and the Head of Emergency Medicine collaborated on a mentoring process for junior faculty interested in research careers in Clinical/Translational Sciences. Zwanziger and Valenta developed a template including an academic development plan and a personal network development map—the focus of their initial meeting with each junior faculty member: For the Academic Development Plan (1) Verbally exploring individual's short- and long-term goals; (2) Verbally introducing formal educational opportunities in REACH; (3) Assigning Linda Pololi's 2006 article "Career Development for Academic Medicine—A Nine Step Strategy;" (4) Assigning "research goals/gaps homework" for which faculty member documents research goals and identifies personal gaps in skills/tasks; (5) Reviewing NCATS Core Competencies for Clinical and Translational Research; and For the Personal Network Development Map; (6) Assigning "network definition homework" for which faculty reads and completes Kathy E. Kram's 2009 exercise "Defining Your Developmental Network" and has instructions for the online UICollaboratory Research Profiles. At the follow up meeting, about two weeks after the initial meeting, the written plans were reviewed. Each faculty member was provided feedback on written goals and suggestions on ways to address knowledge and skills gaps. A report describing findings and recommendations in terms of individual development needs was prepared for the department head. This process contributed to strategic thinking and helped the faculty develop a research program plan. With this activity template, the department implemented a mentorship model for the entire department that utilizes both assigned innovation mentors and peer-group mentors.

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### CA-MRSA TREATMENT AND RECURRENCE IN COMMUNITY HEALTH CENTERS (CHCS)

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**OBJECTIVES/SPECIFIC AIMS** Methicillin-resistant *Staphylococcus aureus* skin/soft tissue infection (SSTI) in persons without previous healthcare exposure (CA-MRSA) is an emerging infectious disease. This project built a research/learning collaborative among CHCs, CDN, a practice-based research network, & RU-CCTS. **METHODS/STUDY POPULATION** With 6 NYC-area CHCs, we followed 129 SSTI patients, developed specimen collection/transport, conducted culture/sensitivity and molecular analyses, integrated the spectrum of translational research from a genetic determinant of antimicrobial resistance to treatment and patient-centered/clinical outcomes, conducted focus groups and transdisciplinary analyses of treatment by outcomes, approached ways to control recurrence. **RESULTS/ANTICIPATED RESULTS** Of wound (40% MRSA+, 18% Methicillin-sensitive *S. aureus*) and nasal (16% MRSA+) specimens, 12% of cases had MRSA in wound and nasal samples. Common MRSA strains were USA300 (85%), USA1100 (6%), NY/CloneV (4%), NY/Japan (4%). Patients received antibiotics and incision/drainage (I&D) (59%), antibiotics (25%), I&D (6%), or observation (3%); 3-month recurrence was 31%; by treatment, 7%, 39%, 0%, 67%, respectively. Clinicians and patients expressed concerns about recurrence. **DISCUSSION/SIGNIFICANCE OF IMPACT** This mixed methods study shows that CA-MRSA recurrence is a significant clinical challenge and patient concern. The association of treatment with recurrence confirms CDC recommendations, with similar I&D outcomes with/without antibiotics. Future studies will focus on whether molecular analyses can predict recurrence and strategies to prevent recurrence.

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### SEEING THE INVISIBLE: AN EXAMPLE OF HOW "SUPPORT MECHANISMS" AFFECT IMPLEMENTATION

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**OBJECTIVES/SPECIFIC AIMS** Disseminating interventions is hindered by a lack of concrete information on how "implementation support mechanisms" work in diverse settings. We give an example of how such mechanisms affected a quality improvement intervention. **METHODS/STUDY POPULATION** Definition: Implementation support

mechanisms are the approaches, methods, structures, and resources through which an intervention is introduced to future implementers. They include communication strategies; role of persons introducing the intervention; training mode; and other assistance. Such mechanisms are rarely acknowledged in the D&I literature; thus we lack practical information on how they influence success. **RESULTS/ANTICIPATED RESULTS** The "ALL Initiative" intervention increases rates of diabetic patients taking cardioprotective medications. It worked well at Kaiser Permanente (KP); we are "translating" it into 11 community health centers (CHCs). Support mechanisms include: Organizational structure, communication, and incentives (KP used top-down implementation; the CHCs used staff engagement and direct support); On-site staff (KP's clinician 'champions' encouraged uptake; in the CHCs, the study team met with clinic staff, and hired and trained site coordinators); Clinic engagement (KP staff were not explicitly asked to provide feedback; CHC staff were asked to help adapt the intervention). **DISCUSSION/SIGNIFICANCE OF IMPACT** Implementation support mechanisms are usually 'invisible' in D&I reporting / evaluation. To address this: (1) Extend D&I models to include support mechanisms as a cohesive group needing consideration. (2) Increase awareness about the need to attend to these mechanisms. (3) Conduct research on these mechanisms. (4) Develop methods for identifying/measuring these mechanisms in diverse situations.

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## THE COMMUNITY BASED RESEARCH PARTICIPANT EXPERIENCE IN COMMUNITY HEALTH CENTERS

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**OBJECTIVES/SPECIFIC AIMS** Participant-centered measures of the clinical research experience offer insight into the quality of the research experience and provide measures of trust and human subject protections (e.g., informed consent). We recently reported such outcomes and benchmarks from 15 academic research centers using a validated instrument. Here we extend this approach to 5 community health centers (CHCs) that are part of a research/learning collaborative with CDN, a practice-based research network and RU-CCTS. Our goal is to collaboratively develop participant-centered measures for community based research at CHCs. **METHODS/STUDY POPULATION** We conducted 7 participant-focus groups ($n = 30$) and 4 clinician groups ($n = 42$) to assess themes of importance to research participants. Moderators' guides were informed by prior participant-centered outcomes research. Discussions were recorded, transcribed and analyzed by the PI and a qualitative analyst. A gap analysis compared themes from community-based versus academic-based research. **RESULTS/ANTICIPATED RESULTS** Common participant themes included informed consent, trust, and a near-universal desire for disease-centered education and support groups. Clinician themes included: participant trust, clinician trust, risk/benefit, and time management. Compensation was viewed by clinicians and participants as both a benefit and a source of mistrust. **DISCUSSION/SIGNIFICANCE OF IMPACT** Community-based research participants describe multiple themes surrounding their research experiences, some distinct from those reported by academic research participants. Additional research is needed to broaden representation from community participants in order to develop/validate a set of community-specific outcome measures. (NIH-NCATS UL1TR000043).

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## IMPROVING EVIDENCE-BASED MEDICATION ADHERENCE AMONG ADULTS WITH TYPE 2 DIABETES THROUGH ADAPTATION, EDUCATION AND MOTIVATION

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**OBJECTIVES/SPECIFIC AIMS** The objective of the study was to incorporate evidence-based medication use into patient self-care, the diabetes self-management, and the decision support functions of the electronic medical record system of a local federally qualified community health center (FQHC). **METHODS/STUDY POPULATION** We used a community health worker (CHW) approach with the innovation of motivational interviewing (MI) to adapt and customize Comparative Effectiveness Research Summary Guides (CERSGs) for Consumers and deliver the content of CERSGs to adults with type 2 diabetes. Adults with type 2 diabetes ($n = 460$) were randomly assigned to the MI-CHW group to receive MI by trained CHWs or to the control group to receive general diabetes education by CHWs (GE-CHW) who are not trained in MI. All study participants were followed during monthly one-on-one in-person and phone-administered counseling sessions over a 12-month intervention period. The delivery of the CHW intervention was based on the psycho-social needs, stage of readiness of the study participants, and enhanced patient-provider communications. **RESULTS/ANTICIPATED RESULTS** Study participants in MI-CHW intervention group and GE-CHW control group experienced a significant increase in medication adherence ($p < 0.001$) and diabetes-self management ($p < 0.001$) over the 12-month intervention period. Furthermore, the clinic was successful in incorporating evidence-based oral and insulin medications into its drug panel. **DISCUSSION/SIGNIFICANCE OF IMPACT** This CHW intervention was effective in improving evidence-based medication adherence among adults with type 2 diabetes, most likely through enhanced patient-provider communications and the patient's willingness to work with the care team.

## T4: TRANSLATION TO POPULATION

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## MENTORING FOR LEADERSHIP SUCCESS IN TRANSLATIONAL RESEARCH; THE VALUE OF AN IDP

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**OBJECTIVES/SPECIFIC AIMS** Mentoring is a crucial step in achieving career success. It is critical to the success of the scholars to create a culture that encourages, supports, and invests in their career development. The individual development plan (IDP) serves as a communication tool between mentor and scholar as both navigate this experience. This is an interactive process that requires full involvement of both to be effective. However, a lack of understanding of the usefulness of the IDP, and lack of effective mentor training, particularly in a non–research intensive institution, are a substantive barrier to an effective IDP. **METHODS/STUDY POPULATION** Here we describe a mechanism to facilitate the success of the IDP in career planning. The program had three core components: (1) workshops orienting the mentor and scholar to the usefulness and importance of an IDP, (2) writing an individual development plan for a scholar, and (3) a follow-up plan for ensuring that the IDP is put into action. In the workshops they receive training to face challenges of the mentoring process during the IDP development. The workshop addressed to mentors is focused on the mentor-scholar relationships where the pros and cons of the IDP are discussed with mentors to help strategize the meeting with the scholar. Mentors engage in brainstorming and interactive discussions to review an IDP and examine measures of success. **RESULTS/ANTICIPATED RESULTS** We have had some early experience implementing the program. Following the workshops, self-ratings of knowledge and confidence of participants in issues of career development and leadership were significantly better. **DISCUSSION/SIGNIFICANCE OF IMPACT** The development process described here is tailored to local needs, but may be transferable to other groups.

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## THE ASSOCIATION OF VITAMIN D WITH URINARY INCONTINENCE IN OLDER ADULTS

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**OBJECTIVES/SPECIFIC AIMS** Our objective was to evaluate the association of urinary incontinence (UI) with vitamin D deficiency in a community-based longitudinal study. **METHODS/STUDY POPULATION** The University of Alabama at Birmingham Study of Aging subjects participated with in-home assessments and provided a blood sample for 25-hydroxyvitamin D. Data from 24 hour dietary recall was used. UI was assessed every 6 months for up to 42 months. The association between incident UI and vitamin D status was evaluated using multivariable logistic regression and Cox proportional hazard models adjusted for gender and ethnicity. **RESULTS/ANTICIPATED RESULTS** Of 350 participants (175 male, 147 black, mean age 73.6 ± 5.8), 54% were vitamin D deficient (<20 ng/mL) and 78.9% were vitamin D insufficient (<30 ng/mL). Participants with vitamin D deficiency/insufficiency had lower dietary intake of calcium, phosphorus, and vitamin D ($p < 0.001$). Among the 187 subjects with no UI at baseline, 57.2% were vitamin D deficient and 81% were vitamin D insufficient. For these 187 subjects, the mean baseline 25(OH)D level was 20.5 ng/mL ± 9.7. 175 of the 187 subjects had follow-up evaluation for incident UI over 42 months and incident UI occurred in 37%. Cumulative incident UI was associated with vitamin D insufficiency at baseline (aOR = 2.21 [0.93–5.21], $p = 0.04$), but there was no association between baseline vitamin D deficiency and incident UI (aOR = 1.18 [0.60–2.31], $p = 0.6$). After adjustment, the association between vitamin D insufficiency and time until incident UI suggested a trend ($p = 0.06$), but no association between vitamin D deficiency and time to incident UI ($p = 0.6$). **DISCUSSION/SIGNIFICANCE OF IMPACT** These results provide preliminary evidence of an association between vitamin D and incident UI in older adults.

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## COLLABORATIVE MODEL TO ENGAGE PRACTICE CHAMPIONS

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**OBJECTIVES/SPECIFIC AIMS** Practice-based research networks (PBRNs) support clinical and translational science by conducting research where most patients receive

their healthcare, and by allowing community-based patients to participate in research. Engaging practice champions in development of research projects may improve the degree to which research reflects the needs and priorities of real world practices and communities. **METHODS/STUDY POPULATION** The WWAMI region Practice and Research Network (WPRN) Coordinating Center (CC), based in the Institute of Translational Health Sciences, developed a collaborative model to engage practice champions in development and implementation of a network-wide study of patient preferences for obesity treatment. The research team, comprising an academic investigator, a research scientist and five WPRN practice champions, identified a research topic of importance, and developed study questions, methods and protocol. The CC reviewed the collaborative process and will report results of a focus group interview with the five participating practice champions to assess facilitators and barriers to successful engagement of practice champions. **RESULTS/ANTICIPATED RESULTS** The CC identified facilitators of practice champion engagement in the research development process, which included offering champions options for different levels of involvement, empowering champions to make study decisions, and adequate support from academic investigators and WPRN staff. Barriers included competing demands for practice champions and lack of external funding. **DISCUSSION/SIGNIFICANCE OF IMPACT** Our collaborative research model engaged practice champions in development and implementation of a network wide study. This model has the potential to transform practice-based research to practice-engaged research. Approaches to scale up this model across diverse research projects are needed.

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## THE PROSPERA CLUB: A COMMUNITY-BASED PROJECT WITH EXPECTING AND PARENTING TEENS IN NEW MEXICO

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**OBJECTIVES/SPECIFIC AIMS** New Mexico has one of the highest teen birth rates in the nation. Given that teen birth and graduation rates are associated with health and economic outcomes, the Prospera Club aimed to promote health and well-being and investigate the factors that influence expecting and parenting teens' participation in community-based projects through collaboration with the GRADS (Graduation, Reality and Dual-Role Skills) program. **METHODS/STUDY POPULATION** Life-skills and health workshops were presented to teen mothers and young parents ($n = 27$) at four different high schools in New Mexico with GRADS programs. Semistructured interviews ($n = 14$) were then conducted in-person or over the telephone with participants exposed to the workshops. The interviews focused on experiences participating in the project, attitudes towards participating in a community-based project, and perceptions about the motivators and barriers to participating in community-based projects. Content analysis of the interview data was conducted. **RESULTS/ANTICIPATED RESULTS** All participants had a positive experience participating in the project. They highlighted that they gained knowledge that was beneficial for them and their children, the educational material and presenters were engaging, and the types of presentation materials used were effective. The majority of participants revealed that the key factors that keep them from participating in community-based projects are their inconsistent school and work schedules, not having transportation, and not having child care. **DISCUSSION/SIGNIFICANCE OF IMPACT** The workshop topics and content were shown to be valuable to participants. Furthermore, future T4 community-based research with young parents needs to consider the barriers to participating in such projects, even when the community is enthusiastic about the plan.

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## CA-MRSA OUTREACH AND EDUCATION WITH ESTHETICIANS

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**OBJECTIVES/SPECIFIC AIMS** Methicillin-resistant *Staphyloccocus aureus* skin/soft tissue infections (SSTI) in persons without healthcare facility exposure (CA-MRSA) is an emerging infectious disease. The CA-MRSA Project (CAMP), a research collaborative among CDN, RU-CCTS and local CHCs, found that 10% of MRSA+ lesions were seen on the head and neck region. Extending public health education efforts beyond the healthcare setting is crucial to preventing infection transmission and minimizing recurrence. **METHODS/STUDY POPULATION** CAMP expanded to recruit 9 barbershops/hair salons in neighborhoods near 3 participating CAMP CHCs and trained the estheticians ($n = 43$) in identifying SSTIs and infection control. Research staff conducted on-site 2-hour workshops on CA-MRSA, occupational health standards, and infection prevention. Each trained worker was provided with referral cards to offer to clients they suspected of having a SSTI. Pre-post knowledge tests were administered to determine knowledge gain, attitudes, and practices regarding CA-MRSA infection. **RESULTS/ANTICIPATED RESULTS** We observed statistically significant increases in knowledge about infection prevention (8.6%, $p = 0.0135$) and CA-MRSA risks (26.4%, $p < 0.0001$). Although there were few referrals to CHCs for care, the estheticians found the information useful for their professional practice. **DISCUSSION/SIGNIFICANCE OF IMPACT** Reaching beyond the clinical setting to partner with community institutions, such as barbershops, is key in translating research into improved population health. CAMP recruited a cadre of non–health professionals and provided them with training on CA-MRSA to deepen our engagement with the community. Future community-engaged research projects will leverage these connections to improve community health. (Funding: NIH-NCATS#UL1-TR-000043)

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## VISUALIZING COMMUNITY ENGAGEMENT METRICS TO REDUCE PARTNERSHIP BARRIERS AND ILLUSTRATE SUCCESSES

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**OBJECTIVES/SPECIFIC AIMS** Community engagement (CE) metrics can theoretically shed light on how successful an institution is in translating research discoveries into improved population health. However, at present there are no consensus metrics to evaluate such programs. **METHODS/STUDY POPULATION** To address the need to identify metrics for community-engaged research, we at RUCCTS developed a monitoring/evaluation platform that can be used by academic and community partners to highlight successes and identify areas for improvement. Metrics were identified for each of the core's goals and then the metrics were translated into key performance indicators (KPIs). Data collection tools were developed in REDCap for most of the KPIs, and summary data is graphically displayed in a dashboard that is viewed by core directors, staff, the CTSA PI, and community partners to monitor progress towards the goals. **RESULTS/ANTICIPATED RESULTS** In the first year of this monitoring/evaluation system, 6 of 9 KPI targets were achieved mid-cycle, including the number of requests from Clinical Scholars to the CE Core for assistance developing community-engaged research protocols, building collaborations with communities, and sharing research authorship with community partners. Early identification of unattained targets allowed for timely program adjustment. **DISCUSSION/SIGNIFICANCE OF IMPACT** We conclude that CE metrics can help monitor program progress and the dashboard format facilitates visualization of actionable data to illustrate success in engaging partners, reaching out to underserved communities, and increasing research capacity. It facilitates identification of progress and opportunities for early course correction to attain program goals. (Funding: NIH-NCATS#UL1-TR-000043).

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## A NEW METHODOLOGY TO ENGAGE STAKEHOLDERS IN DEVELOPING RESEARCH PROJECTS

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**OBJECTIVES/SPECIFIC AIMS** Following Jeffery's Roadmap for Meaningful Stakeholder Engagement used by industry, we are investigating a new method to engage minority community members in developing a research project. **METHODS/STUDY POPULATION** The study is being conducted in two rural South Texas counties. Asset mapping was conducted to identify each community's key constituencies. A key contact in each community was recruited from the local Agri-Extension program to assist with recruiting a professional advisory board and engaging stakeholders. Different stakeholder sampling strategies—respondent-driven and purposive—will be used in each county to identify 65 Hispanic stakeholders. Structured group meetings will generate and prioritize ideas following Concept Mapping methods. Each county's ideas will be rated and compared on a survey of a population-based sample of Texans. **RESULTS/ANTICIPATED RESULTS** The Roadmap emphasizes understanding the target population, internal preparation, and alignment to establish trust. Lessons to date are: (1) Internet resources for asset mapping are often outdated, too general, or irrelevant and must be supplemented by personal contacts; (2) Advisors must be recruited with care to avoid polarizing certain groups; (3) Stakeholders need to be oriented to a research topic with culturally appropriate materials, so we have developed bilingual videos of local Hispanic persons with the condition of interest (chronic pain) and with primary care providers to frame the discussions. **DISCUSSION/SIGNIFICANCE OF IMPACT** This project will adapt the Roadmap for Stakeholder Engagement to ensure that researchers can partner with stakeholders from underrepresented communities to address their ideas, needs, and values.

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## COMMUNITY ENGAGED SCHOLARS: TRAINING ACADEMIC AND COMMUNITY PARTNERS FOR RESEARCH

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**OBJECTIVES/SPECIFIC AIMS** At the South Carolina Clinical and Translational Research Center for Community Health Partnerships (SCTR/CCHP), we offer the

Community Engaged Scholars (CES) Program with the specific aim of providing training and pilot funds for community and academic partners who have collaboratively identified a priority question for study. **METHODS/STUDY POPULATION** At least one academic and one community partner work with the identified community to develop a draft proposal for a research study using community engaged research methods. The proposals are reviewed by a panel of persons from SCTR/CCHP Academic and Community Advisory Board Members, and selected teams participate in interactive group learning to enhance community based participatory research plan development, implementation, and dissemination. Following the training, each team received up to $10,000 for implementation of their proposed research project. **RESULTS/ANTICIPATED RESULTS** Each year for the past four years, 3–6 teams have been selected as Community Engaged Scholars. The teams have participated in CES Program training and implemented pilot research. The pilot projects have focused on child and adolescent health ($n = 5$); prenatal health ($n = 1$); and chronic health conditions ($n = 8$) including HIV/AIDS, cancer, diabetes, hypertension, lupus, Alpha-1, and kidney disease across diverse communities. Following the pilot, CES teams have submitted and received research funding from foundations, Centers for Disease Control, National Institutes of Health, and Patient Centered Outcomes Research Institute. **DISCUSSION/SIGNIFICANCE OF IMPACT** CES Program research training with community and academic partners can be an effective method for addressing community priorities and improving health of diverse populations, and for training research teams.

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## WILLINGNESS TO SHARE SPECIMENS AND DATA IN A SAMPLE OF PARTICIPANTS USING PARTNERED APPROACHES

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**OBJECTIVES/SPECIFIC AIMS** Studies suggest that ethnic minorities participate at lower rates in research, specifically genetic research, than Whites. Lack of representation prevents translation of genetic research to reduce racial/ethnic disparities in health outcomes. Using partnered methods, we assessed willingness to share specimens and data for research in a community-based sample of African American (AA) and Latino residents in a low income community of South Los Angeles. **METHODS/STUDY POPULATION** Eligible adult residents participated in a 2-hour in-home interview, clinical evaluation, laboratory and functional tests. During informed consent, participants were asked for their approval to allow investigators to: (1) store their de-identified data for future use, (2) obtain additional DNA for research purposes, and (3) share their samples with other researchers. Bivariate and multivariable analyses were used to examine associations with demographic and clinical characteristics. **RESULTS/ANTICIPATED RESULTS** Of 258 screened, 29 were ineligible and 23 refused. Among enrolled participants ($n = 206$), 75% were AA, 25% Latino, 71% female, with mean age of 44.8 years (SD = 16.1). All participants completed the interview. Of the 199 who completed lab testing, 75% consented to storing de-identified data, 69% consented to additional DNA collection, and 75% consented to have their samples shared with other researchers. These findings did not differ by demographic or clinical characteristics in unadjusted or adjusted analyses. **DISCUSSION/SIGNIFICANCE OF IMPACT** In this community partnered research project, we found high rates of willingness to store and share specimens and data and slightly lower rates of willingness to share DNA for research. These rates were comparable for AAs and Latinos.

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## SUCCESSFUL STRATEGIES FOR RECRUITMENT OF AFRICAN AMERICANS INTO CLINICAL STUDIES

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**OBJECTIVES/SPECIFIC AIMS** Barriers to participation in clinical trials in African Americans (AA) include lack of awareness about trials, economic factors, mistrust and communication issues. Objectives are: (1) examine recruitment challenges and experiences; (2) determine best practices for researchers to engage AA communities in clinical studies. **METHODS/STUDY POPULATION** We reviewed 50 studies conducted at a historically black institution to determine the type, duration and enrollments. A survey was sent to study coordinators to obtain data on recruitment and retention strategies, challenges and dropout rates. We also interviewed 25 study coordinators on challenges and recruitment strategies. The coordinators had diverse cultural backgrounds. **RESULTS/ANTICIPATED RESULTS** Studies range from cross-sectional to prospective. The prospective studies have follow-up periods from 3 to over 24 months. The 22 completed studies achieved recruitment rates of over 50%; 12 had over100% recruitment rates. For 8 studies with dropouts, the average rate was 23.3%. Barriers are lack of trust, life circumstances, low education, lack of interest; in the elderly, the inability to have study partner. Recruitment strategies include field-based, special advertisements and snowballing. Strategies to barriers are informational sessions, rapport, phone calls and caring attitudes. **DISCUSSION/SIGNIFICANCE OF IMPACT** AA seems to be more trusting to participate in a study if their PCP is involved and through community outreach strategies. This is especially true in studies involving medication usage. Minimum risk studies were very successful in recruiting AA < 30 years old. Ongoing rapport, showing caring attitude improves retention rates. Successful recruitment strategies of AA is paramount to better understand the ways researchers can improve current strategies in order to increase minority participation in clinical trials.

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## PILOTING RANDOM SAMPLING FOR A COMMUNITY REGISTRY & BIOREPOSITORY

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**OBJECTIVES/SPECIFIC AIMS** To present results of pilot efforts undertaken prior to implementing a full-scale population random sampling of households. **METHODS/STUDY POPULATION** Adult volunteers are recruited to participate in the MURDOCK Study Community Registry and Biorepository. Pilot efforts to recruit participants from a random sampling of households were conducted on 2 occasions to provide insight prior to enrolling a full representative sample ($n = 15{,}000$ individuals). 100 households were targeted in each pilot effort, testing outreach approaches, staffing models, marketing techniques and home visits. Individuals in all households were given the opportunity to learn more about the study, or enroll in their homes or off-site. Neighborhood ambassadors, who are also study participants, were added to the second pilot effort. **RESULTS/ANTICIPATED RESULTS** The first pilot effort consisting of mailings, phone calls and home visits recruited no new participants. The second pilot with revised mailing materials (personalized letter, study flyer and magnet), community advertising, and inclusion of neighborhood ambassadors for home visits resulted in enrollment of at least one individual from 9% of the 100 households. Use of neighborhood ambassadors was perceived as positive and participant-centered. Based on ambassador feedback, a third pilot with revised recruitment methods, including study-sponsored community events, increased visibility of yard signs and marketing materials, is underway (completion March 2014). **DISCUSSION/SIGNIFICANCE OF IMPACT** It is critical that the recruited cohort be representative of the local population's composition with selection of an unbiased sample. Piloting random sample recruitment strategies has shown that traditional techniques require refinement and more participant-centered approaches to optimize recruitment efficiency.

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## THE ART OF GRANTSMANSHIP: AN EXPERIENTIAL APPROACH

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**OBJECTIVES/SPECIFIC AIMS** Beginning in May 2011, the Multi-disciplinary Training and Career Development (MTCD) Core of the Puerto Rico Clinical and Translational Research Consortium (PRCTRC) initiated the Art of Grantsmanship workshop series. The goal is to provide early and mid-career investigators with experiential training and mentoring in grant writing with the goal of increasing their success in securing extramural research funding. **METHODS/STUDY POPULATION** Early stage investigators from the three PRCTRC consortium members were invited to apply for participation in workshop series in grantwriting skills. Using Webinar and face-to-face formats, researchers participated in14 sessions, delivered over 4.5 months. Content included identifying funding sources, building effective collaborations, the grant writing/submission process, effective writing and proposal development, budget development, and working with the institution for a successful electronic submission. **RESULTS/ANTICIPATED RESULTS** From May 2011 through June 2012, a total of 21 individuals participated in the program, representing researchers across the clinical and translational continuum. From these, 9 participants submitted applications to NIH and CDC, with 4 funded. **DISCUSSION/SIGNIFICANCE OF IMPACT** Moving forward, we are evaluating variables serving as support or hinder proposal submission. We have begun Phase II of the program, focusing on those who submitted a proposal but were not funded. This phase will provide individualized mentoring and career development in this skill. This project was supported through grants from the National Center for Research Resources (U54 RR 026139-01A1) and the National Institute on Minority Health and Health Disparities (8U54 MD 007587-04) from the National Institutes of Health.

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## INTERACTION BETWEEN GSTT1 AND GSTP1 AS A MODULATOR OF RISK FOR AUTISM SPECTRUM DISORDERS

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**OBJECTIVES/SPECIFIC AIMS** The etiology of autism spectrum disorders (ASD) is believed to be multifactorial with interplay between genes and potential interaction with environmental factors contributing to disease risk. Some studies have reported that ASD are linked with oxidative stress, and that sequence variation in the family of glutathione S-transferase (GST) genes involved in detoxification of xenobiotics may be implicated in their pathogenesis. **METHODS/STUDY POPULATION** The Jamaican Autism Study enrolled 111 pairs of age- and sex-matched ASD cases and typically developing (TD) controls between 2–8 years of age. The association between polymorphisms in GSTT1, GSTP1, and GSTM1 and ASD susceptibility was investigated. **RESULTS/ANTICIPATED RESULTS** Using univariable conditional logistic regression (CLR) models to evaluate main effects, no significant associations between ASD and the three GST genes were found (all $p > 0.16$). However, a significant interaction between GSTP1 and GSTT1 was identified when multivariable CLR was applied. In children heterozygous for the GSTP1 Ile105Val polymorphism, there was a significantly increased odds of also having the GSTT1 null genotype in ASD cases when compared to TD controls (matched odds ratio (MOR) = 2.97, $p = 0.03$) assuming a genotypic genetic model. Similarly, the odds of GSTT1 deficiency was also higher in the ASD group for GSTP1 heterozygotes [MOR = 2.91, $p = 0.04$] under an overdominant model. **DISCUSSION/SIGNIFICANCE OF IMPACT** Our findings suggest that interaction between GSTT1 and GSTP1 may influence individual susceptibility to ASD. Replication in other populations is warranted.

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### ASSESSING APPLICABILITY OF STATISTICAL COMPETENCIES FOR CLINICAL AND TRANSLATIONAL RESEARCHERS

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**OBJECTIVES/SPECIFIC AIMS** Statistics is an essential component of training for a career in clinical and translational science (CTS). However, statistics can be especially challenging or frustrating for CTS learners. Our research question was: what depth of statistical knowledge do different CTS learners require? **METHODS/STUDY POPULATION** For three types of CTS learners (PI, co-investigator, informed reader of the literature), each with three different backgrounds in research (no previous research experience, reader of the literature, previous research experience) 18 experts in biostatistics, epidemiology, and research design proposed a competency level for 21 different areas of statistical knowledge. **RESULTS/ANTICIPATED RESULTS** Statistical competencies were divided into basic, intermediate, and high levels. For all competencies, learners who intended to become principal investigators (PI) had a different proposed competency level than those who intended to read the research literature. Learners who intended to become co-investigators also differed from those intending to become PIs for several competencies. For most competencies, less training was proposed for those with more research background, but the opposite trend was observed for a few challenging competencies. **DISCUSSION/SIGNIFICANCE OF IMPACT** Our results show there are three levels of statistical competencies, and that attainment of these levels varies by the learner's research background and career goal. Learners with different career goals need different statistical coursework. Scholars would benefit from baseline knowledge assessment to identify statistical competencies upon which to focus their coursework. In conclusion, our results suggest statistical coursework can be individually tailored to increase learning potential while minimizing time in the classroom.

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### ANALYSIS OF OPIOID USE AMONG VETERANS

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**OBJECTIVES/SPECIFIC AIMS** To examine opioid use among veterans at the population-level to inform new policies and practices to optimize opioid prescribing. **METHODS/STUDY POPULATION** All Veterans with at least two outpatient visits at any Veterans Administration (VA) facility in FY09, FY10 or FY11 and had at least one Those who were in a VA nursing home, domiciliary, enrolled in hospice care, or diagnosed with cancer were excluded. The prevalence of chronic opioid use, chronic pain conditions, mental health (MH) and substance abuse disorders (SUD) and the average daily morphine equivalent dose (MED) for chronic and nonchronic users was calculated. **RESULTS/ANTICIPATED RESULTS** In FY09, FY'10 and FY'11 1,006,479, 1,060,731 and 1,096,422 respectively Across all years mean age was 58; 92% were male; 71% were Caucasian, 21% were non-Caucasian and unknown in 8%. The prevalence of chronic opioid use (91 or more days in a fiscal year) was 49.4% in FY09, 50.0% in FY10 and 51% in FY11. The MED among chronic users and nonchronic users was 44.8 and 22.4 respectively in FY09; 44 and 21.9 in FY10; 42 and 21.4 in FY11. The prevalence of MH and SUD was similar for chronic and nonchronic users. Chronic pain conditions were more common among chronic opioid users. Use of long-acting opioids was fairly uncommon across all years but was more prevalent in chronic opioid users. **DISCUSSION/SIGNIFICANCE OF IMPACT** Chronic opioid use is slowly increasing in FHA although the mean MED may be decreasing. MH and SUD were similar between the chronic and nonchronic users. Policies to address opioid use in Veterans should include strategies that decrease length of time opioids are prescribed.

# ADDITIONAL ABSTRACTS

# TL1 AWARDEE PREDOCTORAL ABSTRACTS

## T0: BASIC SCIENTIFIC DISCOVERY

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### DIFFERENTIAL RAPID SYNAPTIC POTENTIATION IN NUCLEUS ACCUMBENS CORE VERSUS SHELL DURING COCAINE CUE-INDUCED RELAPSE AND EXTINCTION

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**OBJECTIVES/SPECIFIC AIMS** The purpose of this study was to determine whether transient synaptic potentiation occurs in accumbens core and shell subcompartments during cued reinstatement of cocaine seeking and day 14 of extinction training after cocaine self-administration. **METHODS/STUDY POPULATION** Using a rat model of cue-induced reinstatement of cocaine seeking, we quantified changes in dendritic spine diameter in the accumbens core and shell of animals given 15 min of either cue-induced reinstatement or extinction compared to baseline after cocaine withdrawal and yoked saline. **RESULTS/ANTICIPATED RESULTS** Transient synaptic potentiation was seen in accumbens shell during extinction ($F(2, 137) = 64.73$, $p < 0.001$) and accumbens core during reinstatement ($F(2, 153) = 87.72$, $p < 0.001$); spine heads were larger at baseline in animals withdrawn from cocaine and further expanded fifteen minutes into extinction training or reinstatement. **DISCUSSION/SIGNIFICANCE OF IMPACT** Rapid synaptic potentiation occurred in rats during extinction and reinstatement in brain regions previously shown to be necessary for these behaviors. A future step in this research might involve activating matrix metalloproteinases during extinction training, which are necessary for spine head expansion. Besides providing further evidence for the role of spine head expansion in extinction, MMP activation might offer a pharmacotherapy synergistic with d-cycloserine and cognitive behavioral therapy for treating human drug addicts. This publication was supported by the South Carolina Clinical & Translational Research (SCTR) Institute, with an academic home at the Medical University of South Carolina, NIH/NCATS Grant number TL1 TR000061.

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### BLUE LIGHT EMITTING DIODES MODULATE KEY FIBROBLAST CELL FUNCTIONS ASSOCIATED WITH SKIN FIBROSIS

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**OBJECTIVES/SPECIFIC AIMS** Skin fibrosis is a characteristic finding in multiple skin diseases of varied pathogenesis. Skin fibrosis is characterized by increased fibroblast proliferation, migration speed, and extracellular matrix deposition. We previously found that light emitting diode (LED) red light can alter human skin fibroblast proliferation and migration rate. Here we hypothesized that 415 nm LED blue light (LED-BL) can modulate fibroblast proliferation, migration speed, and may be mediated by reactive oxygen species (ROS) modulation. **METHODS/STUDY POPULATION** To test these hypotheses, human skin fibroblast cells were irradiated using commercially available LED-BL. Each plate was matched with a temperature regulated "bench control plate" (BCP), to ensure that the measured effect was a result of LED-BL treatment and not due to other environmental factors. We assessed cellular proliferation by cell counting. Cellular migration speed was measured by time-lapse video microscopy imaging. We assessed LED-BL–induced modulation of reactive oxygen species generation measured by flow cytometry. **RESULTS/ANTICIPATED RESULTS** LED-BL at fluences of 30 J/cm$^2$ and 80 J/cm$^2$ significantly decreased cell proliferation at 48 hours postirradiation (55.1% and 51.7% decrease compared to BCP, respectively, $p < 0.01$). LED-BL fluences of 30 J/cm$^2$ and 80 J/cm$^2$ decreased fibroblast migration speed by 18.7% and 67.7% of that of BCP ($p < 0.01$), respectively. A fluence of 80 J/cm$^2$ significantly increased ROS levels by 7.6% ($p < 0.05$) compared to BCPs. **DISCUSSION/SIGNIFICANCE OF IMPACT** We conclude that LED generated blue light modulates human skin fibroblast functions that are associated with fibrosis. We envision that our findings will serve as the foundation for future translational studies on light-based management of fibrotic skin disease.

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## THYROID HORMONE DISRUPTION BY PERSISTENT ORGANIC POLLUTANTS THROUGH ALTERED CALCIUM DYNAMICS IN PITUITARY THYROTROPH CELLS

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**OBJECTIVES/SPECIFIC AIMS** Polychlorinated biphenyls (PCBs) and polybrominated diphenyl ethers (PBDEs) are ubiquitous environmental contaminants detected at high levels in human tissues due to their widespread use as flame retardants in consumer products. Both PBDEs and PCBs can disrupt circulating levels of thyroid hormones (THs); however, the mechanism of disruption has not been determined. Select PBDE and PCB congeners alter intracellular calcium dynamics by enhancing activity of the ryanodine receptor (RyR). Thus, we aimed to investigate whether PCBs and PBDEs disrupt the hypothatlamic-pituitary-thyroid axis by altering the calcium-induced hormone release from pituitary thyrotroph cells. **METHODS/STUDY POPULATION** We analyzed the effects of PBDE and PCB congeners at multiples doses on intracellular calcium dynamics of the pituitary thyrotroph cell line TaT1 using rapid acquisition single cell imaging. We then evaluated disruption of the cellular secretion of thyroid stimulating hormone (TSH) during exposure to environmentally relevant doses of PBDE and PCB congeners using a TSH ELISA assay. **RESULTS/ANTICIPATED RESULTS** We anticipate that congeners capable of activating RyR will disrupt calcium dynamics and alter TSH release from thyrotroph cells in a dose dependent manner. **DISCUSSION/SIGNIFICANCE OF IMPACT** Thyroid hormones regulate a number of cellular processes that are sensitive to disruption such as fetal growth and neurodevelopment, regulation of metabolism, cardiac function, and reproduction. Disruption of TH homeostasis by PCBs and PBDEs may contribute to thyroid disorders and complex neurodevelopmental disorders such as attention deficit hyperactivity disorder and autism spectrum disorders. Therefore, it is critical to determine the molecular mode of toxic action of these environmental contaminants in order to understand the risk of exposure.

## T1: TRANSLATION TO HUMANS

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## DNA METHYLATION AND PREDICTION OF SURVIVAL AND TIME-TO-RECURRENCE IN CHILDHOOD GERM CELL TUMORS USING SEMISTRUCTURED RECURSIVELY PARTITIONED MIXTURE MODELS

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**OBJECTIVES/SPECIFIC AIMS** Germ cell tumors (GCTs) represent a heterogeneous group of neoplasms classified together because they arise from a common precursor cell, the primordial germ cell. The etiology of GCTs is not well elucidated, although genetic and epigenetic pathways are implicated. Additionly, the long term clinical implications epigenetic alterations may have for patients is still uncertain, particularly regarding their utility in determining disease prognosis. We sought to identify epigenetic markers associated with poor prognosis and tumor characteristics by performing an epigenome wide analysis of methylation in a large sample of childhood GCT. **METHODS/STUDY POPULATION** Using the Infinium HumanMethylation450 BeadChip array (Illumina, San Diego, CA), we assessed methylation with respect to survival, time to recurrence, and tumor histology using a semisupervised recursively partitioned mixture modeling (SS-RPMM) algorithm in a sample of childhood GCT ($n$ = 111). **RESULTS/ANTICIPATED RESULTS** GCTs segregated into two methylation classes. Class membership was significantly associated with tumor histology ($p < 0.001$), but not survival ($p = 0.71$) or disease recurrence ($p = 0.38$). **DISCUSSION/SIGNIFICANCE OF IMPACT** While power was limited to detect differences in methylation class with respect to survival and recurrence, tumor histology—a strong predictor of tumor aggression and treatment resistance—was found to significantly differ with respect to methylation. These findings provide a strong rationale for future studies of methylation in GCT.

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## ATHEROSCLEROTIC PLAQUE QUANTIFICATION, BIOCHEMICAL CARDIAC CALCIFICATION ASSESMENT, AND F-NAF CARDIAC UPTAKE IMAGING IN OSSABAW SWINE

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**OBJECTIVES/SPECIFIC AIMS** Vascular calcification increases risk of fatal cardiac events in coronary artery disease (CAD) patients making early diagnosis and clinical intervention extremely important. $^{18}$F-NaF uptake has been investigated as an *in vivo* biomarker of calcification and high-risk atherosclerotic plaque. Here we compared measures of cardiac health: CAD by intravascular ultrasound (IVUS), total myocardial calcium by biochemical assessment, and global cardiac uptake of $^{18}$F-NaF by positron emission tomography (PET). **METHODS/STUDY POPULATION** Metabolic syndrome (MetS) Ossabaw swine ($n$ = 14) with CAD underwent ECG-gated PET/computed tomography (CT) scans and IVUS prior to euthanasia. Standard uptake values (SUV) were measured to determine$^{18}$F-NaF uptake in regions of interest (ROI) around the entire heart. IVUS percent plaque burden was measured using Image J software. Flash frozen left ventricular samples were used to measure deposited calcium by HCl extraction of the tissue. **RESULTS/ANTICIPATED RESULTS** Coronary plaque burden ranged between 19–28%. HCl extraction of left ventricular calcium ranged between 0.834–1.704 µmol/g. Total global cardiac $^{18}$F-NaF SUV ranged from 132–544. Spatial resolution did not permit accurate quantification of $^{18}$F-NaF in epicardial coronary arteries. There was no significant correlation between measures. **DISCUSSION/SIGNIFICANCE OF IMPACT** These data suggest global cardiac $^{18}$F-NaF PET uptake does not correlate with coronary plaque burden measured by IVUS or total cardiac calcium measured by HCl extraction. Therefore, this discrepancy must be further explored to validate $^{18}$F-NaF PET imaging as a*n in vivo* biomarker for calcification.

## T2: TRANSLATION TO PATIENTS

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## REAL-WORLD ASSESSMENT OF BILATERAL UPPER EXTREMITY ACTIVITY

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**OBJECTIVES/SPECIFIC AIMS** A key goal of rehabilitation is to improve upper extremity (UE) function in everyday life following impairment. While useful for measuring UE function inside the clinic, standardized assessments do not objectively measure UE activity that occurs in the real-world. Accelerometry can be used to quantify real-world UE activity, but referent values for UE activity measured by accelerometry are not available. The purpose of this study is to provide referent values of real-world UE activity, which can be used by clinicians and researchers to aid in goal selection for patients and to interpret outcomes when examining intervention effectiveness. **METHODS/STUDY POPULATION** Accelerometers were placed on each extremity of 74 nondisabled participants and worn for 25 hours while participants went about their normal, daily routines. Accelerometry data was processed using custom-written software to derive several measures of real-world UE activity. **RESULTS/ANTICIPATED RESULTS** The mean duration of nondominant and dominant UE activity was 8.6 (SD 2.0) and 9.1 (SD 1.9) hours, respectively. The mean ratio of activity duration between the nondominant and dominant UEs was 0.95 (SD 0.06), indicating that the duration of activity between UEs was equivalent. Either UE was active for 11.61 (SD 1.98) hours, but simultaneously active for 8.65 (SD 1.89) hours. The mean acceleration across both UEs was 1.93 (SD 0.48) m/sec$^2$, which corresponds to low-to-moderate activity intensity. The mean ratio of acceleration between the UEs was 0.91 (SD 0.15), indicating that activity intensity was similar between UEs. **DISCUSSION/SIGNIFICANCE OF IMPACT** These referent values provide objective information on real-world, bilateral UE activity. Clinicians and researchers can use these values in conjunction with clinical assessments to set outcome goals and evaluate treatment interventions for a variety of patient populations with UE impairment.

## T3: TRANSLATION TO PRACTICE

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## STIGMA AND DISORDERS OF SEX DEVELOPMENT (DSD)

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**OBJECTIVES/SPECIFIC AIMS** Assess perceptions/experiences of stigma in parents of DSD-affected children and compare that to reports by parents of children affected by epilepsy, another chronic condition associated with stigma. **METHODS/STUDY POPULATION** 155 parents of 108 DSD-affected children (newborn–16y; mea$n$ = 4.9y ± 3.7) participated in one of two studies. Parent participants completed one of two questionnaires tapping their perceptions/experiences of stigmatizing situations related to their child's diagnosis (1 = little to no perceived/experienced stigma to 5 = high amount of perceived/experienced stigma). The questionnaires comprised two subscales: child- and parent-focused stigma. Items were further categorized as asking about (1) perceptions, (2) experiences, (3) future worry, or (4) feelings. **RESULTS/ANTICIPATED RESULTS** Overall, parents reported low levels of stigmatizing perceptions/experiences (mea$n$ = 1.80 ± .57). However, a notable minority reported moderate to high levels of concern on several items. Parents expressed significantly more concerns about stigma on child- than on parent-focused items and on questions asking about perceptions or future worry. Mothers reported higher levels of stigma than fathers. 46,XY DSD was associated with greater reported stigma than 46,XX DSD or sex chromosome DSD. Reported stigma was not associated with child age. Parents of DSD-affected children, overall,

reported lower levels of stigma than did parents of children with epilepsy. **DISCUSSION/SIGNIFICANCE OF IMPACT** High levels of experienced stigma related to DSD, while limited in the aggregate, are present for a notable minority of parents. These experiences may mediate the association between the presence of DSD and overall psychosocial adaptation and quality of life. The findings also suggest that DSD-related stigma may be more salient in certain situations/subgroups of patients, which can inform management.

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## GERIATRIC ASSESSMENT AS PREDICTORS OF HOSPITALIZATION IN SENIOR ADULTS WITH CANCER

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**OBJECTIVES/SPECIFIC AIMS** Hospital readmission (HRA) is a common, costly problem. Little is known on risk factors for HRA in older adults with cancer. This study aims to identify factors associated with 30-day HRA in a cohort of older medical oncology patients. **METHODS/STUDY POPULATION** In a retrospective cohort study of adults over age 60 hospitalized to an Oncology Acute Care for Elders Unit of Barnes-Jewish Hospital from 2000–2008, standard geriatric screening tests were administered in routine clinical care. Clinical data were obtained through medical record review. 30-day readmission was ascertained through electronic medical record review. **RESULTS/ANTICIPATED RESULTS** 798 patients were identified. 77% were white and 52% male. Thoracic (33%), hematologic (19%), and gastrointestinal (17%) malignancies were most common. The 30-day HRA rate was 31.5%. In multivariate analysis, factors associated with readmission were: age [odds ratio (OR), 0.95/year; 95% confidence interval (CI), 0.92–0.98], black race (1.77; 1.14–2.74), complete dependence (2.2, 0.9–5.36) and some dependence (0.51, 0.22–1.19) in feeding, complete dependence (2.25, 1.4–3.62) and some dependence (1.51, 0.97–2.33) in shopping, and the presence of a second cancer (2.18, 1.03–4.62). Discharge to hospice (0.24, 0.10–0.59) was associated with lower odds of HRA, while discharge with home health (1.48, 0.96–2.29) or supportive care (1.56, 0.89–2.74) were associated with greater odds. **DISCUSSION/SIGNIFICANCE OF IMPACT** HRA was common and higher than previously reported rates in general medical populations. We identified several previously unrecognized factors associated with increased risk for HRA. This knowledge can be used in future research to develop interventions to reduce preventable HRA.

## T4: TRANSLATION TO POPULATION

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## SINUSITIS FROM AN INSTITUTIONAL PERSPECTIVE: DEFINING THE BURDEN OF DISEASE AT THE UNIVERSITY OF MICHIGAN

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**OBJECTIVES/SPECIFIC AIMS** We plan to create a novel database from which to measure the burden of disease of sinusitis at the institutional level. We will first define the proportion of sinusitis-related visits from all outpatient visits at an institutional level. We will then compare institutional disease burden with national indicators, specifically the NAMCS/NHAMCS database. **METHODS/STUDY POPULATION** We identified patients with visits to primary care and the emergency department at the University of Michigan between 1/1/2005 and 12/31/2011. We then recorded primary visit purpose using the first three ICD-9 diagnosis codes associated with each visit. Patients with visits related to acute and chronic sinusitis were identified by ICD-9 codes 461.x and 473.x respectively. Number of visits to ENT or Allergy clinics for patients with sinusitis-related visits were recorded as an estimation of additional resource burden for sinusitis. **RESULTS/ANTICIPATED RESULTS** We identified 393,370 patients with primary care or emergency department visits over the defined time period. Of these, we will identify the proportion of patients whose visits were associated with sinusitis and compare this to the 1–2% of patients who suffer from this disease on a national level as indicated by studies of the NAMCS/NHANES database. **DISCUSSION/SIGNIFICANCE OF IMPACT** Sinusitis is one of the most commonly diagnosed diseases in the United States, yet little work has been done to identify institutional-level disease burden and patient populations. By defining an institutional level database of sinusitis patients, we can then conduct further subgroup analysis to better study this prevalent disease at a patient-level as our additional work as expanded on.