SHORT TALKS

ST001. Genetics & Epigenetics

Maternal overnutrition and increased risk of intergenerational liver disease and cancer – targeting epigenetic mechanisms

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Epidemiological observations indicate that parental overnutrition of diets rich in fat is among the strongest predictors of fatty liver and liver cancer in their progeny. However, the mechanisms underlying this effect are completely unknown. Notably, data from our laboratory show that palmitic acid, one of the most consumed saturated fatty acids in Western diets, has been found to have long-term pro-metastatic effects in tumours through epigenetic mechanisms. This study aims to investigate whether maternal intake of a palmitate-based HFD during pregnancy and lactation predisposes offspring to liver disease and cancer, and if this intergenerational propensity for liver cancer is due to epigenetic changes of the offspring's epigenome in the liver. Preliminary results demonstrate that maternal consumption of a palm oil-enriched high-fat diet (PA-HFD) epigenetically alters lipid metabolism-related genes in the livers of F1 offspring. The livers of these offspring show stable changes in H3K4me3 at promoters, along with transcriptomic changes related to aberrant fatty acid metabolism, oxidation, and inflammation. Metabolome/lipidome studies reveal the accumulation of acyl-carnitines, indicating heightened fatty acid oxidation. Identifying these epigenetic mechanisms as a cause of increased liver disease and cancer risk in offspring due to parental overnutrition has potential clinical implications as a disease biomarker and for developing new therapies.

Keywords: Epigenetics, intergenerational inheritance, palm oil enriched-HFD, fatty liver disease.

ST002. Neuroscience, Psychiatry & Mental Health

Targeting NLRP1 inflammasome activation by GSK3β inhibition for neuroprotection

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Glycogen synthase kinase 3 (GSK3) plays a significant role in physiological and pathological conditions. The excessive activation of this enzyme has a strong correlation with neuroinflammation. Angiotensin II is known to trigger GSK3β activation in the brain. In this study, we investigated whether GSK3β inhibition prevents angiotensin II-induced NLRP1 inflammasome activation in neuronal cells. For this reason, the human cortical neuronal cell line (HCN-2) was treated with Ang II (10 μM) for 6 or 24 h. The changes in GSK3β and NLRP1 gene levels were measured by real-time PCR following Ang II treatments. In addition, the levels of cleaved caspase-1 and NLRP1 were measured by Western blotting after pretreatment with GSK3β inhibitors, namely tideglusib (5 μM) and LiCl (2 mM). Significant increases in GSK3β and NLRP1 gene expressions were observed following Ang II treatment at 24 h ($P < 0.05$). GSK3β inhibition by pharmacological inhibitors decreased the protein expression levels of inflammasome-associated cleaved cas-1. It can be concluded that the design and synthesis of specific inhibitors of GSK3β may assist to prevent NLRP1 inflammasome activation and ultimately protect neuronal cells where angiotensin II contributes to neuroinflammation.

Keywords: NLRP1, GSK3β, neuroinflammation.

ST003. Neuroscience, Psychiatry & Mental Health

The biological effects of 6-hydroxy-L-nicotine in various experimental models of dementia: in silico and in vivo study

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The impact of a nicotinic intermediate, namely 6-hydroxy-L-nicotine (6HLN), was evaluated on memory deficits, anxious behaviour and oxidative stress in two animal models of Alzheimer's disease (AD): a rat (Rattus norvegicus) model induced by brain delivery of beta-amyloid fragment 25–35 (Aβ25-35) and a zebrafish (Danio rerio) model induced by scopolamine (SCOP). 6HLN was delivered chronically to Aβ25-35-treated rats and acutely to SCOP-treated zebrafish and their behavioural performances were evaluated using specific in vivo tasks. The oxidative stress parameters and acetylcholinesterase (AChE) activity were measured from the brain samples of the animals. A set of in silico tools was used to associate the behavioural outcomes with the calculated binding potential of 6HLN into two different allosteric binding sites of α4β2 nAChRs (PDB ID 6CNK). Aβ25-35 and SCOP decreased memory performance and increased the anxiety-like behaviour in the in vivo tests and increased the brain oxidative stress and AChE activity in rats and zebrafish. As compared to nicotine, the pretreatment with 6HLN more effectively ameliorated the memory deficits and anxiety caused by Aβ25-35 or SCOP. Also, 6HLN significantly reduced the oxidative stress and AChE activity in the brain of Aβ25-35- or SCOP-treated animals. Furthermore, we showed that 6HLN indeed binds to α4β2 nAChRs with similar or even higher energy than nicotine and that the binding site at the α4-β2 interface is preferred over the binding site at the α4-α4 interface. 6HLN might improve memory and anxiety-like behaviour by modulating cholinergic activity

and thus might represent a new neuropharmacological agent in AD.

ST004. Clinical Research, Translational Biomedicine & Personalised Medicine

Artificial thymic organoids as a model to study physiopathology of human T cell development

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T-cell differentiation is a key process of the adaptive immune system development that occurs in the thymus. Experimentally, it is difficult to recapitulate this process due to the intricate complexity of the thymus microenvironment, which is the reason why murine models are often used. In order to study T cell differentiation *in vitro*, new systems based on artificial thymic organoids (ATOs) have been developed. In this work, we used ATOs to study T- cell lymphopenias of unknown origin to identify patients' specific T-cell differentiation blockage and help to characterise disease severity and guide diagnosis and treatment. To this end, CD34$^+$ cells were obtained by immunomagnetic selection from peripheral blood of healthy donors and immunodeficient patients. ATOs generated with the stromal cell line MS5 transduced with Notch ligand DLL4 were seeded with CD34$^+$ cells and cultured *in vitro* for 6–12 weeks in the presence of IL-7 and FIt3-L. T-cell differentiation was analysed by flow cytometry. Our results show that ATOs support the differentiation of haematopoietic progenitors along sequential intrathymic maturing stages and their efficient generation of mature T cells. More importantly, studies using CD34$^+$ cells from patients with severe combined immunodeficiency (SCID) revealed specific developmental detects at particular T-cell maturation stages. In conclusion, ATOs represent a solid *in vitro* system to study T-cell maturation of patients with T lymphopenia of unknown origin and to determine if their defect relies on haematopoietic progenitors' intrinsic alterations or extrinsic cues due to thymic microenvironment defects. Therefore, ATOs represent a useful tool for diagnosis and treatment orientation of immunodeficient patients.

ST005. Immunology, Microbiology & Infectious Diseases

Mycobacterium abscessus siderophore biosynthesis as a target to inhibit the iron uptake mechanism

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Mycobacterium abscessus (Mab) is a rapid-growing non-tuberculous mycobacterium, which is emerging as an opportunistic pathogen in patients with lung disorders, such as those with cystic fibrosis. With the aim of searching for new anti-virulence treatments, which do not kill the bacteria but disarm them before attacking the host, we focused on siderophore biosynthesis. Mab produces siderophores to scavenge iron from the host, which is essential for the establishment and maintenance of infection. The salicylate synthase (Mab-SaS), the first enzyme involved in the biosynthesis of siderophores, catalyses the conversion of chorismate into salicylic acid. Its homologue in *M. tuberculosis* (Mtb-MbtI) has already been extensively characterised and identified as a promising therapeutic target, and promising phenylfuran-carboxylate based inhibitors were developed. Taking into consideration the successful work performed on *M. tuberculosis*, the aim of this work is therefore to identify compounds capable of inhibiting the enzymatic activity of the Mab-SaS, starting from the library of compounds developed for Mtb-MbtI. The Mab-SaS was then produced in recombinant form, and its enzymatic activity established by a fluorimetric assay. Upon screening of the compounds belonging to the library of Mtb-MbtI inhibitors, some showed good activity even against Mab-SaS, with IC$_{50}$ values in the low micromolar range, and not behaving as PAINs. These results support the hypothesis that phenylfuran-carboxylate is a promising scaffold for the inhibition of Mab-SaS as well, paving the way for the optimization and rational design of more potent derivatives.

ST006. Computational Biology, Bioinformatics & Artificial Intelligence

A machine learning model for the early prediction of ovarian cancer using real world data

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Ovarian cancer is the leading cause of death in women among all gynaecological cancers. This is mainly due to its generally late stage diagnosis, as the disease presents vague or no symptoms in early stages. Indeed, the cure rate when diagnosed early is very high, but there is currently no established strategy for screening and early detection of this cancer among the female population. Furthermore, as the prevalence of ovarian cancer is low, a universal screening strategy might not be suitable for this disease due to the high cost to healthcare systems and its comparatively low yield. Here, we present a machine learning early prediction model for ovarian cancer exploiting real world clinical data from the Andalusian Public Health System database. The purpose of this model is to carry out a continuous evaluation of patients' data, inferring their monthly risk trajectories in order to anticipate the occurrence of ovarian cancer. Our model was trained with patient electronic clinical history, including routine blood analyses, chronic comorbidities, relevant symptoms and diagnoses, and patterns in patients' access to the public healthcare system. Our model correctly identifies 60% of the ovarian cancer patients, with a false positive rate of 10%. Nearly a fifth of correctly identified ovarian cancers were identified over a year in advance, confirming the usefulness of our model as an early ovarian cancer predictor. This performance could serve to establish a high-risk population to whom to apply a more detailed selective screening strategy.

Keywords: Machine-learning, real world data, ovarian cancer, disease prediction, pre-screening.

ST007. Omics (Proteomics, Transcriptomics, Metabolomics, Metagenomics)

Transcriptomic study of nicotine catabolism in *Paenarthrobacter nicotinovorans* ATCC 49919 using long-read direct RNA sequencing

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The tobacco industry is among the costliest and most damaging regarding land and water use and their consequent contamination with toxic nicotine. Nicotine-degrading microorganisms are the choice method for nicotine decontamination, allowing valuable green chemicals to be extracted from the resulting biomass. *Paenarthrobacter nicotinovorans* ATCC 49919 is an extensively studied soil nicotine-degrading bacterium - the nicotine catabolic genes are sequenced, but we have little knowledge of the interplay between the degradation pathway and the general cellular metabolism. It is essential to understand the mechanisms regulating nicotine catabolism for biotechnological use. Hence, we are working on a metabolic model of the pathway based on a multi-omic study. Here, long-read direct RNA sequencing was applied to study the nicotine-related transcriptome of *P. nicotinovorans* ATCC 49919. The bacterium was grown on citrate medium with and without nicotine. Cells were harvested at three timepoints correlated with nicotine catabolism. Native RNA was polyadenylated for sequencing adapter ligation. Direct RNA sequencing was performed with the ONT MinION coupled to a Flongle adapter. Basecalled data were assessed for differential gene expression between control and nicotine-treatment using the nf- core/nanoseq v3.1.0 pipeline. The 24 sequencing runs produced 1 million reads totalling over 1 Gb. Of the identified 40 genes with nicotine-related expression (p_{adj} <0.1; abs($\log_2$ foldchange) > 1), less than half were previously known to be involved in nicotine catabolism, most being reported here first. This first transcriptomic analysis of nicotine catabolism in *P. nicotinovorans* ATCC 49919 should facilitate its environmental applications and use as a cell factory.

Keywords: Transcriptome, nicotine, direct RNA-sequencing.

ST008. Computational Biology, Bioinformatics & Artificial Intelligence

Natural variation and cellular morphology patterns in epithelial cysts

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A fascinating question in Developmental Biology involves understanding how tissues and organs acquire the shape that is critical to their function, in a process called morphogenesis. The faithful

execution of the morphogenetic program requires an accurate spatiotemporal control of several mechanisms, including changes in cell shape. However, this control allows for certain variations that do not compromise the viability of the organ or organism, giving rise to natural variation. Here, we explore the stochasticity of MDCK (Madin-Darby canine kidney) cysts to understand the causes and consequences of natural variation during epithelial morphogenesis. To achieve this aim, we have developed Carto-Cell, an automatic segmentation method for three-dimensional (3D) epithelial images, enabling high-throughput analysis of hundreds of MDCK cysts. Our method realistically detects the 3D morphology of the whole tissue, and the individual cells composing the cyst, facilitating the quantification of geometric and packing features at tissue and cellular resolution. We found that cysts can adopt different shapes. Furthermore, the analysis of geometric and packing features (depending on shape or time) unveiled several constraints on the natural variation of cystogenesis, demonstrating the robustness of certain features in ensuring process stability. Finally, we concluded this study with the implementation of the "single-cell cartography" approach, which provides insights into the distribution of cellular feature values, revealing cell morphology patterns on MDCK cysts. Taken together, we believe that our strategy can serve as a reference for studying how geometrical constraints drive the self-organisation of epithelial tissues.

Keywords: Segmentation, single-cell cartography, cyst, pattern, variation.

ST009. Cancer Biology & Oncology

Updating conventional therapy: new treatments for cell quiescence in acute myeloid leukaemia

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One of the main obstacles in the approach to acute myeloid leukaemia is the relapse of patients after treatment with conventional chemotherapy, whose main target is proliferative cells. One explanation may be the existence of leukaemic stem cells in a reversible state of quiescence (outside the cell cycle) that confers chemoresistance. The activation of the Hedgehog, Notch and Wnt/β-catenin pathways seem to favour the maintenance of quiescence, so their inhibition could induce the entry of these cells into the cell cycle and improve the efficacy of conventional chemotherapy such as cytarabine, azacytidine and idarubicin. Here, we worked with three human AML cell lines, namely HL-60, OCI-AML3 and KASUMI-1. The cells were treated for 48 h and 72 h with the IC_{50} of cytarabine, idarubicin or azacytidine, previously determined by the group, and different combinations of the drugs Glasdegib, Nirogacestat and PRI-724, inhibitors of the Hedgehog, Notch and Wnt/β-catenin pathways, respectively. To determine the cytotoxicity of the treatments, the WST8 agent was used to obtain a measure of absorbance proportional to the number of viable cells. Combinations of chemotherapy with signalling pathway inhibitors showed a greater reduction in cell viability compared to the monotherapy control at 72 h compared to

48 h of treatment. Likewise, HL-60 showed a pattern more sensitive to cytarabine and idarubicin, while OCI-AML3 and KASUMI-1 were found to be more sensitive to azacytidine. The results obtained show an increased efficacy of conventional chemotherapy in combination with the inhibition of Hedgehog, Notch and Wnt/β-catenin pathways in AML cell lines.

Keywords: Leukaemic stem cell, quiescence, acute myeloid leukaemia, cell cycle, chemotherapy.

ST010. Omics (Proteomics, Transcriptomics, Metabolomics, Metagenomics)

Unravelling the impact of endocrine disruptors on cortical development through the lens of brain organoids

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Endocrine disrupting chemicals (EDCs) are a class of environmental contaminants that interfere with the normal functioning of hormones, leading to various adverse health effects. Neurodevelopment is one of the critical biological processes impacted by EDCs, yet the molecular mechanism of action of such chemicals remains to be fully characterised. Reprogramming of induced pluripotent stem cells (iPSCs) and differentiation of Cortical Brain Organoids (CBOs) allows recapitulation of *in vitro* human developmental processes that closely mimic the structure and function of the developing human brain, thus representing uniquely valuable tools for studying the molecular and cellular effects of genetic and environmental factors on human neurodevelopment. Building on our previous work, that integrated epidemiological evidence with experimental dissection of an EDC mixture associated with neurodevelopmental adverse outcomes, we are now establishing an atlas of hormonal impact on neurodevelopment by combining chronic exposure of CBOs to key hormonal receptor agonists and inhibitors to deeply characterise the impact of hormonal modulation on the developing brain. Additionally, we are investigating in the same model the effects of 7 EDCs and the weighted mixture of them in a dose–response setting, starting from the epidemiologically relevant concentration linked with developmental neurotoxicity. The multi-omics integration of the datasets generated upon these experiments contributes to the ENDpoiNTs and RE-MEND consortia, EU-funded projects aimed at providing regulatory agencies with new tools for risk assessment of endocrine disruptors. In this context our research offers a unique resource, shedding light on the hormonal mechanisms underlying the effects of environmental pollutants on neurodevelopment.

Keywords: Developmental neurotoxicity, environmental pollutants, endocrine disruptors, brain organoids, epidemiology.

ST011. Computational biology, Bioinformatics & Artificial Intelligence

Differences in cellular signalling pathway activation by gender across various cancer types

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This study investigates the influence of gender on cancer development and treatment responses, capitalising on genomic sequencing technology's transformative capabilities. Genomic sequencing has empowered us to explore mRNA's profound impact on cellular function, particularly through the identification of signalling circuits. Simultaneously, gender's role in shaping disease outcomes, notably cancer, has gained prominence. To unravel this complex interplay, we employ Hipathia alongside transcriptomic data from the TCGA project. Hipathia is designed to analyse signal transduction within cellular pathways, utilising KEGG's repository of cellular signalling pathways. These pathways outline relationships between proteins constituting signalling circuits, reflecting cellular function. mRNA levels signify protein presence and activity, with the final protein value indicating circuit activation. Our findings illuminate the most active cellular signalling pathways in different cancer types and their relation to patient gender. This comprehensive analysis deepens our understanding of gender's impact on disease manifestation and potential treatment efficacy. In summary, this research harnesses mechanistic models to decipher gender's role in cancer development and treatment outcomes. These insights pave the way for personalised cancer treatments, offering improved prospects for patients confronting this formidable challenge.

Keywords: Mechanistic models, cancer, transcriptomics, systems biology, gender.

ST012. Cellular & Molecular Biology

Metabolic rewiring of epithelial cells and myofibroblasts during kidney fibrosis

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Chronic kidney disease (CKD) affects 10% of the population, and fibrosis driven by excessive accumulation of extracellular matrix (ECM) is the hallmark of CKD. Myofibroblasts are the key ECM-producing cells and are activated by crosstalk with injured proximal tubule and immune cells. Although metabolic derangement is identified in CKD pathophysiology, the metabolic requirements of kidney cells during this response remain elusive. We characterised the metabolic phenotype of proximal tubular epithelial cells ($CD10^+$) and myofibroblasts ($PDGFR\beta^+$) by using immortalised human cells, kidney organoids and the aristolochic acid nephropathy (AAN) mouse model by combining Seahorse, SCENITH and gene expression technologies. Basally, $CD10^+$ cells relied on fatty acid oxidation (FAO), while $PDGFR\beta^+$ cells mainly depended on glycolysis. Under AA-induced profibrotic stimuli, both FAO and glutaminolysis were impaired in $CD10^+$ cells, whereas both glycolysis and glutaminolysis were increased in $PDGFR\beta^+$ cells. In kidney organoids, AA treatment reduced mitochondrial respiration and enhanced glycolysis. In AAN renal tissue, FAO dependence was reduced in $KIM1^+$ damaged epithelial cells, whereas $PDGFR\beta^+$ cells exhibited enhanced dependence on mitochondrial function, glycolysis and glutaminolysis. This metabolic reprogramming likely contributes to development of kidney fibrosis since FAO gain-of-function in $CD10^+$ cells reduced the expression of markers associated with epithelial cell dedifferentiation. In turn, FAO gain-of-function and both glutaminolysis and glycolysis inhibition reduced the expression of ECM genes in $PDGFR\beta^+$ cells. In kidney organoids, glycolysis inhibition counteracted AA-induced ECM production. Strategies based on the modulation of these metabolic shifts may prove useful in therapies against renal fibrosis and CKD.

Keywords: Metabolism, kidney, fibrosis.

ST013. Computational Biology, Bioinformatics & Artificial Intelligence

Inferring haplotype-specific chromatin contact maps in cancer with Genome Architecture Mapping

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Chromatin structure is key to the proper orchestration of gene regulation. Chromatin misfolding is involved in many diseases including cancer. Recently, Genome Architecture Mapping (GAM) was introduced as a ligation-free method for determining chromatin contacts by sequencing ultrathin cryo-sectioned nuclear slices. Together with the Pombo Lab, we have shown that GAM is well suited for deriving chromatin contacts from minimal input material such as from biopsies, and that it is also an effective tool for haplotype reconstruction and variant phasing. While this observation in principle opens the possibility for inferring haplotype-specific chromatin contacts in any tissue including cancer, phasing currently is limited by the comparatively low variant density of the human genome, and further complicated by frequent somatic copy-number alterations and structural variants present in cancer genomes. To overcome the problem of low read phasing efficiency, we have developed 'Co-Phasing', a novel algorithm which leverages local haplotype information in GAM to phase sequencing reads which do not overlap any variants to their haplotype of origin. Co-Phasing provides the statistical power to determine haplotype-specific chromatin contacts in variant-sparse genomes, including human. This increased resolution will allow the development of new algorithms for the identification of haplotype-specific somatic copy number alterations and structural variants directly from human GAM data. We will benchmark Co-Phasing and these new algorithms on cell lines with and without known structural variants and ultimately on clinical cancer samples. Together, our algorithms will enable novel insights into the interplay of chromosomal instability and chromatin misfolding in cancer.

Keywords: Computational cancer biology, chromatin structure, genome architecture mapping, phasing, chromosomal instability.

FLASH TALKS

P001. Computational Biology, Bioinformatics & Artificial Intelligence

Experimental and computational validation of South African indigenous essential oils against the therapeutic targets of spoilage organisms of tomato fruits

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The need to find an alternative to synthetic fungicides currently used in the control of microbial spoilage in tomatoes has become imperative as farmers continue to experience high postharvest loss. This study investigated the mechanism of antimicrobial properties of commonly used essential oils from South African botanicals using *in vitro* and *in silico* methods. The *in vitro* results showed varying degrees of antimicrobial action against the eight bacteria and six fungi isolates from spoiled cultivars of commonly consumed South African tomatoes with buchu oil eliciting the best effect. A further *in silico* analysis of the constituents of buchu oil obtained through GCMS against the key therapeutic targets [topoisomerases 2As (GyrA, GyrB, TopC, TopE) and ergosterol biosynthetic enzymes (ERG1, ERG11, ERG24)] of the isolated bacteria and fungi, respectively revealed that the oil constituents do not compromise the structural integrity of the investigated targets of the isolates and stabilised and interacted well with the active site amino acid residues critical for the inhibition of the respective targets. Overall, this study lent scientific credence to the structural mechanism of inhibitory action of the oil constituents against the therapeutic targets critical to the survival of spoilage bacteria and fungi in tomatoes. The development of a potent, natural and biodegradable edible coating from the buchu oil and its constituents for use in tomato preservation is underway.

Keywords: Therapeutic target, mechanism of action, essential oil, tomato preservation and biodegradable coatings.

P002. Cellular & Molecular Biology

Structural insights into α-synuclein and tau hetero-aggregates: cross-seeding as a potential mechanism underlying α-synuclein amyloid spreading

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The deposition of misfolded proteins in the form of amyloid aggregates is the hallmark of a range of neurodegenerative disorders. Traditionally, the aggregation of a particular protein has been

associated with the development of a distinct type of neurodegenerative disorder; for example, the deposition of α-synuclein (α-Syn) is the hallmark of Parkinson's disease (PD), but the deposition of tau has been typically associated with Alzheimer's disease (AD). However, recent experimental evidence has shown cross-talk between α-Syn and tau aggregation; moreover, aggregates containing both proteins have been found in PD patients' brains and it has been shown that patients with AD were more likely to develop PD, highlighting the relevance of cross-seeding mechanisms in these diseases. It has been recently shown that α-Syn or tau can aggregate through different pathways, resulting in a myriad of amyloid polymorphs with different toxicities and degrees of infectivity. However, very little is known about the structure and toxicity of hetero-amyloids composed of these two proteins, as well as the details of the acquisition of the amyloid structure when the templating process is compromised. In this project, we are using cryoelectron microscopy to unravel the structural assembly of α-Syn onto disease-relevant tau amyloid aggregates and assessing for the possibility of α-Syn cross-seeding as a potential relevant process involved in the spreading of α-Syn pathology using different cellular approaches. This study will provide valuable insights to guide the development of effective therapeutic strategies that aim at early treatment during the initial phase of disease development.

Keywords: α-Synuclein, Tau, amyloid aggregation, cross-seeding, Cryo-Electron Microscopy.

P003. Cellular & Molecular Biology

ERC2 as a novel disease-associated gene for a myasthenia-like phenotype

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Neuromuscular disorders are a highly heterogeneous group of diseases with the common feature that voluntary movements are affected due to problems in the peripheral nervous system and/or the muscles. Recently, we identified biallelic variants in ERC2 (ELKS/RAB6-Interacting/CAST Family Member 2) in two unrelated patients with comparable NMD phenotypes. ERC2 was not previously associated with a mendelian phenotype. Both patients suffer from distal and proximal muscle weakness with increased fatigue and had their symptom onset in early childhood with a non-progressive course. Trio exome sequencing revealed homozygous variants (NM_015576.3: c.2008G > A, p.A670T in patient 1 and c.2712 + 1G > C, p.Gln856Profs*5 in patient 2) in ERC2 as the most likely disease-causing variants. ERC2 is highly conserved in all vertebrates and encodes a scaffolding protein functioning at the presynaptic active zone with essential roles in neurotransmission. We recently confirmed the expression of ERC2 in the disease-relevant tissues, such as mouse spinal cord and embryonic motor neuron lysates, as well as in hiPSC-derived motor neurons. Therefore, we generated an Erc2 exon 17 KO mouse line by CRISPR/Cas9, resembling the predicted exon skipping outcome of the variant in patient 1. The mouse line is viable and fertile. Similarly, we generated an ERC2 exon 15 KO hiPSC line, that will allow us to perform *in vitro* analyses utilising differentiated motor-neurons. Loss of ERC2 was confirmed for both models by Western blot. A deep phenotypic analysis with mice, as well as biochemical and molecular studies utilising both models will help us to elucidate the pathomechanisms caused by ERC2 mutations.

Keywords: ERC2, neuromuscular disorders, rare diseases, motor neuron, CRISPR/Cas9.

P004. Cellular & Molecular Biology

Investigating novel regulators of DNA damage-induced apoptosis: a forward genetics approach

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DNA damage triggers various cellular responses, including DNA repair, cellular senescence, and apoptosis. Although the core apoptotic machinery activated by DNA damage is well described, recent studies suggest the existence of unknown cell autonomous and systemic signals that can regulate apoptosis. In this study, we utilised *Caenorhabditis elegans* as a model organism to identify novel regulators of DNA damage-induced apoptosis. We performed EMS-induced random mutagenesis on the highly apoptotic mutant *alg-2(ok304)* and screened for suppressor mutations that reverse the highly apoptotic phenotype. To confirm that the identified mutation is causative for the suppression of apoptosis, we employed CRISPR/Cas9 to introduce the candidate mutation into both *alg-2* and wild-type genetic backgrounds. We have verified the candidate gene as an apoptosis suppressor in both genetic backgrounds and are currently pursuing its functional characterisation. This novel regulator is involved in cytoplasmic polyadenylation, a step of translational regulation that is so far understudied due to technical difficulties. However, recent advances in sequencing technologies allow for better understanding of such processes. Our findings shed light on the complex regulation of apoptosis and may have implications for understanding how organisms respond to genotoxic stress.

Keywords: DNA damage, *C. elegans*, apoptosis, polyadenylation.

P005. Computational Biology, Bioinformatics & Artificial Intelligence

CGeNArate: a sequence-dependent coarse-grained model of DNA for accurate atomistic MD simulations of kb-long duplexes

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We present CGeNArate, a new model for molecular dynamics simulations of very long segments of B-DNA in the context of biotechnological or chromatin studies. The developed method uses a coarse-grained Hamiltonian with trajectories that are back-mapped to the atomistic resolution level with extreme accuracy by means of machine learning approaches. The method is sequence-dependent and reproduces very well not only local, but also global physical properties of DNA. The efficiency of the method allows us to recover with a reduced computational effort high quality atomic-resolution ensembles of segments containing many kilobases of DNA, entering into the gene range or even the entire DNA of certain cellular organelles.

Keywords: Coarse-grained, molecular dynamics, chromatin, machine learning.

P006. Cellular & Molecular Biology

Macrophage polarisation changes and disturbed lipid metabolism induced by polystyrene nanoplastics

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In terms of human health risks, nanoplastics (NPs) are currently a main concern due to their potential to accumulate in different environmental compartments and mobility through the food chain. Nevertheless, we still have limited knowledge about their impact and interaction with cellular machinery. To fill this knowledge gap, we evaluated the interaction between NPs and fish cells, both intestinal cells and macrophages, in order to understand which cell organelles are targeted by polystyrene (PS)-NPs and how this could impact cell function. PS-NPs can enter cells by endocytosis, phagocytosis, or passive transport. In this context we analysed different endpoints as indicators of effects triggered by PS-NPs, including, co-localization, ROS increase, transcriptome alterations, and increase in the expression of M1/M2 phenotype-related genes. Once internalised, we found that PS-NPs co-localise with lysosomes but not with mitochondria. We demonstrated that NPs did not trigger the production of reactive oxygen species (ROS), which was corroborated by the fact that neither the oxygen consumption rate (OCR) nor the extracellular acidification rate (ECAR) in mitochondrial respiration were altered. Moreover, RNA-Seq data revealed clear interference of PS-NPs with the lipid metabolism, peroxisomes and PPAR signalling. To explore the role of PS-NPs in M1/M2 balance, the expression of different genes was further assessed to characterise the macrophage phenotype. Overall, our data provided new insights into the potential health risks of PS-NP exposure in living organisms. We demonstrated that PS-NPs in macrophages and gut cells co-localised within lysosomes without triggering ROS production, and in macrophages PS-NPs apparently modulate polarisation towards a M2-like phenotype.

Keywords: Nanoplastics, metabolism, immunology, environment, cells.

P007. Computational Biology, Bioinformatics & Artificial Intelligence

SPACE: STRING proteins as complementary embeddings

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Representation learning has revolutionised sequence-based protein function prediction. Protein interaction networks are another crucial source of information on protein function; however, applying representation learning to networks in a manner that works across species is much harder. The STRING database provides protein networks as well as orthology relations for over 1500 eukaryotes. The aim of the SPACE project is to network embeddings for all proteins in these species, which are directly comparable between species and are complementary to existing sequence embeddings. We propose a method in which we first use node2vec to generate embeddings for each species, and subsequently use the FedCoder model to align them across species based on orthologous proteins. To test SPACE, we generated embeddings for three very distantly related eukaryotes, namely human, yeast, and Arabidopsis. We assessed how well they are aligned, how well they capture network topology by using a simple logistic model to perform link prediction from embeddings, and how well they were in function-related benchmarks, involving KEGG pathways, InterPro families/superfamilies, and subcellular localization. The results showed that the three species-specific networks were successfully aligned in the same space with minimal loss of topological information before alignment. The aligned embeddings outperformed node2vec in all benchmarks. When simply combined with ESM-2 sequence embeddings and trained on a multi-layer perceptron, they also surpassed ESM-2 in the subcellular localization task.

Keywords: Network biology, protein–protein interactions, network embedding, representation learning, deep learning.

P009. Cellular & Molecular Biology

Neural stem cells regulate vascular properties in the adult subventricular zone neurogenic niche

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The neurovascular unit (NVU) and the blood–brain barrier (BBB) are unique features of the CNS vasculature. NVU properties in different brain regions seem to be different. However, the mechanistic insight leading to such differences is less understood. In this study, we characterise vessel heterogeneity and NVU properties in neurogenic and non-neurogenic regions, both at the morphological level as well as at the transcriptomic level. Vessels in the SVZ present a more planar and less branched structure, which gives rise to a reduction in the blood vessel density compared to the vasculature from the cortex. Additionally, the proportion of vessels completely covered by astrocytic endfeet is lower in the SVZ compared to the cortex, while the pericyte coverage is increased. Using the mTmG pericyte reporter mouse model, we have demonstrated that the increase in the coverage is due to a change in pericyte morphology from the SVZ compared to the cortex. In order to investigate whether NSCs can control the properties of vessels located within their own neurogenic niche, we characterise the SVZ vasculature upon NSC depletion in vivo. While no differences in blood vessel density or permeability of a small tracer molecule (NaF) are detected, an increase in pericyte coverage is specifically observed in the SVZ vasculature (and not in other brain regions) upon NSC depletion. To gain insight into the molecular mechanisms underlying the potential crosstalk between NSCs and vascular cells, we analyse ligand-receptor interactions between NSCs, ECs and perivascular cells using single cell RNA sequencing of cells in the SVZ. With a focus on signals deriving from the NSC compartment, we identified molecules like pleiotrophin (Ptn) and midkine (Mdk) highly expressed in NSCs and their respective receptors in ECs and mural cells, suggesting that there might be instructive signalling from NSCs that may induce and maintain vascular cell properties (and in turn NVU characteristics) within their niche, to assure the optimal niche environment for maintaining neurogenesis.

Keywords: Blood brain barrier, pericytes, neural stem cells, astrocytes, neurovascular unit.

P010. Cancer Biology & Oncology

The Drosophila lymph gland as a model for investigating haematopoietic stem cell (HSC) maintenance- Headcase as an example

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The haematopoietic organ of the Drosophila larva, the lymph gland, serves as a simplified representation of mammalian haematopoietic compartments, with the presence of hemocyte progenitors in the medullary zone (MZ), differentiated hemocytes in the cortical zone (CZ), and a haematopoietic niche called the posterior signalling centre (PSC) that signals to the progenitors to control their differentiation. Utilising this model, we have revealed a novel function for Headcase (Hdc), the orthologue of the HECA human tumour suppressor, in maintaining hemocyte progenitors. With genetic interaction studies and rescue experiments, we found that Hdc negatively regulates the insulin/mTOR pathway in the niche. The loss of hdc function leads to cellular stress as indicated by the in vivo reactive oxygen species (ROS) reporter gstD-GFP. According to our model, in hdc mutant larvae, the ROS produced in the niche functions as a signal that triggers the premature differentiation of progenitors. In line with this, we showed that expression of Foxo, a transcription factor that regulates the expression of ROS scavenging enzymes, has a compensatory effect on the phenotype. Furthermore, we found that Hdc is required cell-autonomously in the MZ progenitors to suppress their early differentiation, by regulating distinct signalling pathways, such as EGFR and JNK in the progenitors. Since the molecular pathways controlling progenitor maintenance are highly conserved in Drosophila, we hope that our results will give us more insight into the role of the Hdc orthologue, HECA in mammals and help us to better understand the regulation in HSC niches in vertebrates.

Keywords: HSC, niche, haematopoiesis, tumour suppressor, Drosophila.

P011. Chemistry & Biochemistry

Neurotoxic impact of organophosphate pesticides via inhibition of cholinesterase activity

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Public interest in pesticides and pesticide-free farming has increased in recent years, reinforced by frequent media reports about contamination of food or aquatic ecosystems with pesticide residues. Pesticides are often available on the global market for an extended period of time before delayed adverse health effects in humans are recognised. Some of the most widely employed insecticides and herbicides are organophosphate (OP) compounds, known for their potential neurotoxicity in humans either as a result of chronic exposure to lower doses or acute poisoning. OPs increase the concentration of the neurotransmitter acetylcholine within the synapse by inhibiting the hydrolyzing enzymes acetylcholinesterase (AChE) and butyrylcholinesterase (BChE), resulting in cholinergic crisis, respiratory failure and long-term neurological damage. Our aim was to investigate the neurotoxic potency of several OP herbicides and insecticides by determining the inhibition of human AChE and BChE activity in their presence. Overall, OP insecticides progressively inhibited cholinesterases over time and were more potent inhibitors than the tested herbicides. The docking study identified important interactions within the active site, and cytotoxicity tested in a concentration- and time-dependent manner on neural and liver cells corroborated the neurotoxic impact of tested pesticides. Since medical therapy for restoring enzyme activity includes oxime reactivators that dephosphorylate the cholinesterase active center, we also evaluated the potential of several oximes to reactivate pesticide-inhibited AChE. Our findings could assist in the further development of chemicals safer for use and a better response in case of poisonings.

P012. Obesity, Diabetes & Other Diseases

Impact of increased dietary glucose intake on β-cell functional heterogeneity

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Dietary glucose intake creates a stressful environment leading to an increase in insulin demand that healthy β-cells overcome by going through different functional states. These are described by various levels of expression for both proinsulin and insulin, that result in heterogeneous β-cell populations within the islets. We aimed to characterise how increased glucose intake influences the distribution of these cell populations in a murine model of diabetes. Our experiments were conducted by placing 5 week-old non-obese diabetic female mice (NOD) on sustained high-glucose (HGW), or normal water (NW), for four weeks. Weekly measurements of body weight and glycemia showed no major differences between the two groups. We further employed a complex analysis of immunofluorescence images from cryosections of islets stained against proinsulin and insulin. This allowed us to assess differential levels of expression for both proteins that defined several populations of β-cells. Our results highlighted the occurrence of medium and highly insulin-expressing cells in the HGW group, compared to the control, where these populations were absent. These results suggest that, despite the stressed state of the β-cells due to the immune attack that starts to be present in NOD mice starting with four weeks of age, the additional sustained glucose intake did not affect insulin homeostasis until 9 weeks of age. Thus, this model represents a useful tool in assessing the capacity of β-cell populations to functionally adapt under stressful conditions through a mechanism that remains to be elucidated.

P013. Cancer Biology & Oncology

Assessment of novel therapeutic treatments in *KRAS* mutant colorectal cancer using patient-derived organoids

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Colorectal cancer (CRC) arises from mutations in APC, KRAS and TP53/SMAD2/4. Mutations in the KRAS oncogene activate the KRAS/RAF/MEK/ERK pathway constitutively in 35–45% of CRC, favouring tumour progression and metastasis. In this study, we exploited 3D *in vitro* culture patient-derived organoids (PDOs) to better investigate the role of KRAS in tumorigenesis, since the majority of the knowledge concerning KRAS-targeting in CRC is still missing. We performed drug screening using a panel of eight different compounds targeting the KRAS pathway firstly in the 2D normal colon mucosa NCM460D cells and in CRC cell lines, including DiFi (KRAS WT), HCT116 (KRAS^{G13D}) and LS-174 T (KRAS^{G12D}). We tested 0.1–100 nM and 5 nM-10 μM ranges of drug concentration and evaluated the cell viability after 72 h to

calculate the IC_{50} of each compound. We further repeated the drug screening in $KRAS^{G12A}$, $KRAS^{G12D}$, $BRAF^{V600E}$ and KRAS WT CRC PDOs, and although CRC PDOs responded to the drug treatment with a similar trend to one of the 2D cell lines, we observed that the IC_{50} value of each compound was shifted towards a lower effective concentration in CRC PDOs. This suggests that PDOs represent a more reliable platform to explore new therapeutic strategies in CRC, since they maintain the patient's inter/intra-tumour heterogeneity. The novel $KRAS^{G12D}$ inhibitor MRTX1133 showed an effective IC_{50} 20 times lower (nM) in $KRAS^{G12D}$ PDO than in LS-174 T cells. As a following step, we plan to integrate these data by using scRNA-seq, proteomic analysis and 4i to deepen the $KRAS^{G12D}$ in CRC.

Keywords: Colorectal cancer, oncology, precision medicine, patient-derived organoids.

P014. Obesity, Diabetes & Other Diseases

Changes induced in murine β-cells by pharmacological UPR activation

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Perturbation of endoplasmic reticulum (ER) homeostasis disturbs the optimal glucose-responsive insulin production and secretion, and many studies suggest a relationship with diabetes pathogenesis. The unfolded protein response (UPR) is a major ER regulator mechanism which coordinates adaptive stress-responsive signalling through three sensors, namely IRE1α, PERK and ATF6. Of these three sensors, ATF6 is the least understood UPR branch, with pro-survival and pro-death outcomes. Studies showed compound C147 as a specific activator of ATF6 *in vivo*, with beneficial effects in various organs, however, the impact of C147 exposure on β-cells has not been explored yet. We aimed to assess the physiological and molecular effects of C147 treatment. We used isolated murine islets and three strains of mice (C57Bl6, NOD, NSG RIP-DTR with 50% β-cell ablation). We found that C147 treatment interferes with insulin production and inhibits insulin secretion, *in vitro* and *in vivo*. Additionally, our ipGTT data showed that exposure to two doses of C147 resulted in delayed response to glucose stimulation in NSG RIP-DTR (50%), but had no effect in C57Bl6 or NOD mice. Moreover, by immunofluorescence, we found that C57Bl6 mice treated with C147 have more activated ATF6 and less insulin and proinsulin in the islets, compared to the vehicle-treated mice. These results were completed by the decreased insulin detected by ELISA in the serum of all the C147-treated mice, as compared to the control. Our future studies will determine the mechanism by which C147 administration impairs insulin homeostasis. These will allow for better therapeutic approaches for diabetes that imply UPR modulation.

Keywords: UPR, ATF6, insulin impairment, murine islets, C147.

P015. Obesity, Diabetes & Other Diseases

Dynamics of the physiological parameters during the prediabetic states of a murine model of diabetes

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The Non-Obese Diabetic (NOD) mouse is a model used in experiments regarding type 1 diabetes (T1D) because of the spontaneous development of this disease. Modern diets are rich in sugar, thus developing a model that mimics additional burden on the already stressed β-cells present in T1D patients is of great importance in further research. We hypothesised that feeding NOD mice with a high glucose diet will induce diabetic onset earlier than 12 weeks (12w). For our experiments, we used 4w-old NOD mice that were continuously exposed to high glucose water (HGW) and their corresponding controls with normal water (NW), for 8w, thus covering the prediabetic state of this model. Glycemia and weight of the mice were monitored weekly. Our results showed that sustained glucose feeding did not change weight and blood glucose, although mice from the HGW group showed a trend of smaller weight and higher glycemia than the NW group, with glycemia peaking at 7w. At 8, 10 and 12w of age, we performed an intraperitoneal glucose tolerance test (ipGTT) to observe the physiological response of the β-cells. By 12w of age, the ipGTT analysis displayed a small delay in glucose control. Together, these results suggest that stressed β-cells, which can be found in T1D, have the capacity to adapt to increased insulin demand due to continuous glucose exposure. In conclusion, our model can be used for understanding the mechanisms responsible for the adaptation of β-cells to sustained stress that can be exploited in developing new therapies.

Keywords: NOD, diabetes, hyperglycemia, β-cells, ipGTT.

P016. Genetics & Epigenetics

The yeast Hog1 MAPK controls telomere homeostasis during stress adaptive responses

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Maintaining telomere length is essential for cell survival. Disruption of this length equilibrium is a hallmark of most cancers and it is directly associated with ageing. Recent studies have linked environmental signals with telomere shortening and elongation. However, while the complexes regulating telomere length and its interplay with the replication cell cycle machinery are well described, the molecular

mechanisms that integrate environmental cues to telomeres remain elusive. Here we aim to characterise the molecular mechanisms governing telomere biology during osmostress-adaptive responses, using *Saccharomyces cerevisiae* as a model organism. We focus on deciphering the role of the yeast homologue of p38, the Hog1 SAPK (Stress-Activated Protein Kinase) in regulating telomere length upon stress and basal conditions. An increase in extracellular osmolarity leads to the activation of Hog1 that modulates gene expression and cell cycle progression, both of which are required to ensure cell adaptation and to maximise cell survival. By applying genome-wide chromatin association studies (ChIP-seq), we found that Hog1 binds to virtually all telomeric regions upon osmostress and there is a subsequent recruitment of RNA Pol II. Hog1 activation and chromatin association is linked to transcriptional changes and chromatin remodelling, thus we assessed the role of MAPK on the transcription of noncoding telomeric repeat-containing RNA (TERRA) as well as the physiological relevance of telomere regulation upon osmostress adaptation. Understanding novel regulatory mechanisms during adaptation can help to uncover hidden layers of telomere biology.

Keywords: Telomeres, Hog1, osmostress, *Saccharomyces cerevisiae*.

P017. Computational Biology, Bioinformatics & Artificial Intelligence

CRISPRnet: deep learning and data-driven CRISPR design for network-based multiplexed targeting

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CRISPR/Cas systems have advanced genome editing, but designing specific and efficient guide RNAs (gRNAs) remains challenging. Our proposed approach, CRISPRnet, enhances two current challenges in CRISPR screens: target accuracy and genetic redundancy. CRISPRnet incorporates a deep learning model that predicts on-target effects while also considering genome-wide off-targets. To improve model accuracy, we perform efficiency experiments using data from methods like Surro-seq to complement the predictions. The model is trained on gRNA primary sequences and their corresponding binding energy at different sites, both on-target and off-targets, and uses a classifier to discriminate between them, which operates on RNA embeddings. The generation of these embeddings for gRNA has the potential to be extended to RNA types beyond gRNAs, such as siRNA and miRNA. To address genetic redundancy, we are developing a tool based on graph neural networks. We do this by training a graph neural network model to predict genetic interactions based on other types of networks. These include sequence similarity, physical protein interactions, and functional associations from the STRING database. CRISPRnet has the potential to significantly improve CRISPR-based gene editing and functional genomics research by enhancing guide RNA design and identifying functionally related genes.

Keywords: CRISPR, deep learning, graph neural networks, protein networks.

P018. Computational Biology, Bioinformatics & Artificial Intelligence

Theoretical prediction of nucleosome arrays in yeast

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Nucleosomes are the fundamental organising unit of chromatin in all eukaryotic genomes. By understanding how proteins gain access to DNA-binding sites located within or next to nucleosomes, we gain the knowledge of how crucial biological processes such as transcription, replication or repair occur. It is thus essential to study its positioning and behaviour as it will play a role in determining an organisms' health. In our project titled "a theoretical prediction of nucleosome arrays in yeast" we have developed a model to predict the positioning of nucleosomes in *Saccharomyces cerevisiae*, which combines signal transmission theory and machine learning (ML) tools while incorporating information on physical properties of DNA and known sequence preferences of transcription factors. We demonstrate that nucleosomes in the gene body can be accurately located from signal decay theory, assuming the existence of two emitters located at the beginning and at the end of genes which generate wave signals that can be in phase (leading to well defined nucleosome arrays) or in antiphase (leading to fuzzy nucleosome architectures). We found that first ($+1$) and last ($-$last) nucleosomes are contiguous to regions signalled by transcription factor binding sites (TFBS) and by unusual physical properties of the DNA. Based on this analysis, we have been able to locate the basal positions of nucleosomes with accuracy similar to experimental MNase-seq-based methods. The causal interrelation between nucleosome architecture and genome activity is discussed.

Keywords: Nucleosome positioning, arrays, phase, machine-learning.

P019. Cellular & Molecular Biology

Mog1 protein might participate in cell division and Brugada syndrome

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Mog1 is a conserved protein among eukaryotic organisms which participates in nuclear protein import through Ran-GTP binding, in the establishment of two epigenetic marks (H2Bub1 and H3K4me3), mRNA transcription and export. It is also associated with Brugada syndrome, a ventricular arrhythmia responsible for sudden death in young patients. In 20% of cases, there are mutations in the SCN5A gene, which encodes the α-subunit of the sodium channel type 5, Nav1.5. Mog1 interacts with Nav1.5 and contributes to its transport to the plasma membrane in human cardiomyocytes. In *Saccharomyces cerevisiae*, the voltage-gated

calcium channel Cch1 has structural homology to Nav1.5, and this is why we hypothesise that yeast Mog1 protein might interact with Cch1, and *S. cerevisiae* could be used to study the disease at the molecular level. As a first approach, we looked for genetic interactions between MOG1 and CCH1 under different stress conditions. We found that MOG1 and CCH1 interact genetically when exposed to NaCl, sorbitol and heat stress. On the other hand, in previous studies we found that yeast cells lacking MOG1 gene are bigger than wild type cells which might indicate defects in the cell cycle. There is also evidence for Mog1 contribution to mitotic spindle formation in HeLa cells through Ran GTP interaction. Therefore, we are interested in understanding the putative role of Mog1 in yeast cell cycle. We synchronised cells lacking MOG1 gene at two different stages of the cell cycle, finding that mog1Δ cells show a delay in the formation of anaphase spindles.

Keywords: Mog1, Cch1, cell cycle, Brugada syndrome.

P020. Neuroscience, Psychiatry & Mental Health

Antibiotic-induced gut microbiome dysbiosis alters hippocampal serotonin bioavailability and anxiety-like behaviour

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Gut-Microbiome-Brain (GMB) axis is a dynamic trans-kingdom communication system linking gut microbiome and host central nervous system (CNS). The composition of gut microbiome correlates with host behaviour, and its disruption is implicated in several neurological disorders. Germ-free (GF) mouse model is widely used to investigate the GMB axis; however, dysregulated serotonergic transmission in the GF model limits its scope in studying host-microbiome interplay in anxiety modulation. Here, we used specific pathogen-free (SPF) mice to develop an antibiotics-induced gut dysbiosis model and combined behavioural, neurochemical, gene expression, and multi-omics analysis to dissect the possible role of gut microbial communities in tryptophan metabolism and anxiety regulation. Further, we are analysing the recovery of the gut microbiome at multiple post-antibiotic treatment time points (up to 2 months) to study its correlation with reversal of host behavioural and physiological states. Our results showed a decrease in hippocampal tryptophan (Trp), serotonin (5-HT), and 5-HIAA levels with anxiolytic behaviour in dysbiosis mice. Expression of 5-HT transporter was downregulated in the dysbiosis group, while glucocorticoid, 5-HT, GABA receptors, and TPH2 remained unaffected. Metagenomics revealed increased functional dominance of *Klebsiella* and *Escherichia* species in the dysbiosis group that catalyse Trp into indole in the gut. Our data suggest that perturbations in the gut microbiome composition alter hippocampal 5-HT bioavailability and modulate anxiety-like behaviour *via* the Trp metabolism pathway. 5-HT is a key regulator of anxiety, and low Trp levels in the brain attributes to its reduced bioavailability. We are currently quantifying the host and microbial-derived Trp metabolites from Kynurenine and Indole pathways that will likely explain the low Trp/5-HT levels in dysbiosis mice.

Keywords: Antibiotics, gut microbiome dysbiosis, serotonin, multi-omics.

P024. Clinical Research, Translational Biomedicine & Personalised Medicine

Effect of toxic light on circadian rhythm and oxidative stress

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Night shift work is a subset of exposure to artificial light. Potential pathogenic and carcinogenic effects of suppression of melatonin have been demonstrated. The International Agency for Research on Cancer classified shift work, which disrupts the circadian rhythm, as carcinogenic in 2019. This study aims to understand the relationship between shift work and oxidative stress. The first-morning urine samples were taken from daytime workers ($n = 32$) and night workers ($n = 32$) after working at night and two free days later. Total Oxidant Status (TOS) and Total Antioxidant Status (TAS) were measured with the help of a spectrophotometric method, standardised with creatinine values. The Oxidative Stress Index (OSI) was calculated using the formula [TOS/TAS] × 100. Sleep quality was assessed with the Pittsburgh Sleep Quality Index (PSQI). Statistical analyses were calculated with the SPSSv.21 program. Although there was a significant difference ($P = 0.011$) between PSQI in the day workers and night workers (4.5 ± 1.9 vs 6.2 ± 2.9), this difference was not reflected in the OSI ($P = 0.067$). The OSI were significantly higher in the samples after the shift in the night working group compared to the samples two days later (0.92 ± 0.46 vs 0.68 ± 0.23, $P = 0.026$). Similarly, there was a significant difference in the TOS values between the two samples of night workers (30.75 [9.78–108.84] vs 15.51 [4.98–71.05], $P = 0.017$). Our results indicate that shift work has pro-oxidant effects. Further long-term studies with melatonin, which is known for its antioxidant effect, are suggested to understand the underlying mechanisms and establish the impact of shift work.

Keywords: Night shift work, circadian rhythm, total oxidant status, total antioxidant status, Oxidative Stress Index.

P025. Genetics & Epigenetics

Transcriptional regulation in mosquito immunity: insights from Precision Run-On Sequencing (PRO-seq)

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Arthropod-borne (arbo)viruses are imposing an increasing threat to global health. The medically important Yellow fever, Zika, Dengue and Chikungunya viruses are all transmitted by the *Aedes aegypti* mosquito. Despite the relevance of this mosquito to human health, fundamental knowledge of its transcriptional regulation and response to virus infections is limited. Currently, such studies are restricted by our lack of knowledge regarding regulatory elements. To investigate regulatory elements as well as dynamic responses to immune challenge, we employed Precision Run-On and sequencing (PRO-seq) in *Aedes aegypti* Aag2 cells

stimulated with bacteria. Through mapping of transcription start sites and RNA polymerase at nucleotide resolution, we improve and expand the annotation of regulatory transcriptional elements such as promoters and enhancers. Corrected positioning of the transcription start site results in an improved positioning of TATA box and Initiator elements. Functional genome annotation was followed by differential gene expression analysis. Since PRO-seq assesses real-time transcription by RNA polymerases, independent of RNA stability bias, we detect rapid and dynamic gene expression changes upon immune challenge. Moreover, quantification of RNA polymerase positioning unveils dynamics of polymerase stalling and progression. This allows determination of complex mechanisms that underlie the gene expression changes, such as increased RNA polymerase initiation or promoter-proximal pause release. In conclusion, PRO-seq offers a powerful tool to uncover regulatory elements and transcriptional responses in the immune response of *Aedes aegypti* mosquitoes. The obtained insights on the mosquito's defence will eventually be important to identify novel molecular targets for arbovirus transmission control and disease prevention.

Keywords: Arbovirus, *Aedes aegypti*, immune response, transcriptional regulation, regulatory elements.

P026. Neuroscience, Psychiatry & Mental Health

The RNA binding protein CLUH maintains mitochondrial proteome in axons by ABCE1-mediated translational surveillance

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Local protein synthesis is critical to maintain the integrity of axons. In this context, the transport and the translation of nuclear-encoded mitochondrial proteins assures that mitochondria can supply energy distally. However, the regulatory factors for mitochondrial proteostasis in axons are largely unknown. Clustered mitochondria protein homologue (CLUH) is an RNA binding protein, which binds mRNAs of nuclear-encoded mitochondrial proteins involved in different metabolic pathways. In a neural knock-out (NKO) mouse model of CLUH, axons of developing spinal motoneurons delayed their growth and ultimately degenerated, leading to impaired locomotion. This phenotype was concomitant with reduced levels of ATP primarily in distal NKO mitochondria. In these axons, CLUH target mRNAs and proteins were reduced, while no changes in trafficking of those mRNAs was measured. Interestingly, CLUH interacted with translation initiation and ribosome recycling components, which were also impaired in NKO axons. Cluh absence was accompanied with a general impairment of axonal translation, suggesting a role of CLUH in translational quality control by acting together with other parts of the translation machinery.

Indeed, overexpression of the ribosome recycling factor ABCE1 rescued the translation and growth defects of NKO axons, demonstrating a conserved role of CLUH in translational quality control in axons.

Keywords: Axon degeneration, proteostasis, translation, mitochondria, RNA binding protein.

P027. Immunology, Microbiology & Infectious Diseases

Trafficking of fluorescently labelled glycoproteins during HSV-1 infection

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Herpesviruses are large, complex, double stranded DNA viruses that infect animals and humans in a species-specific manner. Viral envelope proteins play an important role during herpes simplex virus 1 (HSV 1) infection. Besides mediating the interaction of viral particles with host cell membranes to allow virus entry, additional functions in the viral replication cycle have been proposed. HSV-1 drastically changes cellular organisation of host cells to allow efficient replication. The involvement of glycoproteins in key steps of the replication cycle such as secondary envelopment is debated. Previous studies have mostly focused on analysing expression of one glycoprotein at a time. By generating complete, replication competent mutant viruses with fluorescent protein-labelled viral glycoproteins, we were able to track the spatial–temporal expression of HSV-1 glycoproteins gC, gD and gH individually and in combination with each other and with respect to cellular organelles (cis-Golgi, TGN, endosomes and lysosomes) across different stages of viral replication by high-resolution spinning disc microscopy. We observed distinct expression patterns and different kinetics for the different glycoproteins and identified dissimilarities in the individual trafficking pathways by quantifying colocalization of the glycoproteins with host cell compartments and investigating glycosylation patterns. Association of viral envelope proteins with endosomes and the Golgi network in late stages of replication indicated the involvement of these organelles in secondary envelopment. Further investigation is warranted to better determine how sites of secondary envelopment are formed and to dissect the potential additional roles glycoproteins might have during the viral replication cycle.

Keywords: HSV-1, glycoproteins, fluorescence microscopy, secondary envelopment, organelles.

POSTERS

P028. Pharmacology, Toxicology & Nutrition

Luteolin attenuates cisplatin-induced toxicity in the liver of male albino rats

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This present study evaluated the protective effect of luteolin on cisplatin-induced hepatotoxicity in male albino rats. Rats were randomly divided into five groups of seven rats each. Group 1 (control) received normal saline. Group 2 was administered cisplatin only intraperitoneally at a dose of 7 mg/kg on the last day of the experiment. Groups 3 and 4 were pre-treated with luteolin at doses of 50 mg/kg and 100 mg/kg respectively for 7 days before administering cisplatin on the 7th day. Group 5 was treated with luteolin only at 100 mg/kg for seven days. The animals were sacrificed on the 8th day and biochemical evaluation and histological assessment of the liver were carried out. The effect of luteolin on alanine transaminase (ALT), alkaline phosphatase (ALP), total protein and high density lipoprotein (HDL) levels was measured. The activities of the antioxidant enzymes (catalase, superoxide dismutase and glutathione-S-transferase) were also determined. The results showed that treatment with cisplatin elevated ALP and AST levels when compared with the control. HDL and total protein (TP) levels were also reduced while significant induction of lipid peroxidation occurred when compared with the saline-treated group. Cisplatin caused a reduction in the activities of the antioxidant enzymes studied. Pre-treatment with luteolin lowered ALP level significantly and improved the levels of HDL and TP. Activities of antioxidant enzymes were restored. Histopathological examination of the liver confirms the above biochemical findings. The antioxidant properties of luteolin may play a contributory role in its protection offered against cisplatin in the liver.

Keywords: Luteolin, cisplatin, hepatotoxicity, antioxidants, histopathology.

P029. Chemistry & Biochemistry

D-carbamoylases: environmentally friendly development of D-amino acids and their derivatives

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The process whereby hydantoinase and carbamoylase convert chemically synthesised precursors into optically pure amino acids and their derivatives is called the "hydantoinase process". These two enzymes have been found in different types of bacteria. D-carbamoylase hydrolyzes D-carbamoyl amino acid into D-amino acid. D-amino acids have a number of potential applications, namely, in development of semisynthetic antibiotics, peptide hormones, and pesticides. In contrast, to chemical technologies, enzyme-based technologies have been shown to have a number of advantages as they are not harmful to human health, environmentally friendly, sustainable and reusable. An in silico approach allowed us to identify a carbamoylase in Pseudomonas sp. having appropriate properties. Through homology modelling, the 3D structure and properties of carbamoylases were predicted. Applied molecular docking analysis showed that the enzyme has potential to exhibit activity against carbamoyl-D-tryptophan, carbamoyl-para-hydroxy-D-phenylglycine, carbamoyl-D-valine, carbamoyl-D-methionine, carbamoyl-D-phenylglycine, then against carbamoyl-D-phenylalanine, carbamoyl-D-leucine, carbamoyl-D-alanine and possibly less against carbamoyl-beta-alanine and carbamoyl-D-glycine. To prove the concept, molecular dynamics simulation was carried out to simulate the enzyme-ligand complexes. Furthermore, we have cloned the gene coding for D-carbamoylase in Escherichia coli cells. The expressed enzyme has formed "inclusion bodies", which were dissolved with N-lauroylsarcosine. Further research has to be carried out to optimise the enzyme assay parameters.

This study is supported by the SCS MESCS RA [project No. 21 T-2I289].

Keywords: D-carbamoylases, D-amino acids, hydantoinase process.

P032. Cellular & Molecular Biology

Characterisation of a novel SUMO-dependent catenane resolution pathway in interphase

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SUMOylation regulates numerous cellular processes, but what represents the essential functions of this protein modification has remained unclear. To address this, we recently performed genome-scale CRISPR/Cas9-based screens for synthetic lethality relationships with the SUMOylation inhibitor ML-792. These screens revealed that SUMOylation exerts its essential role in cell proliferation by enabling the resolution of toxic DNA catenanes generated during the cell cycle via dual, non-epistatic catenane-processing mechanisms. These mechanisms involve the well-established mitotic BLM-TOP3A-RMI1-RMI2 (BTRR)-PICH pathway and a novel interphase pathway mediated by the poorly characterised protein NIP45/NFATC2IP. Specifically, NIP45 and SUMOylation orchestrate an interphase pathway for converting DNA catenanes into double-strand breaks (DSBs) when such intertwined DNA structures cannot be resolved by Topoisomerase II (TOP2). Subsequently the G2 DNA damage checkpoint is activated and prevents cytokinesis failure and binucleation when BTRR-PICH-dependent catenane resolution is defective. Here, we sought to further characterise the mechanistic underpinnings of the emerging NIP45-dependent catenane resolution pathway. We discovered that the SUMO-targeted ubiquitin ligase RNF4 is an integral component of this pathway, acting in a concerted fashion with NIP45 to orchestrate the conversion of catenanes into DSBs and ensuing G2 cell cycle arrest upon TOP2 inhibition. We are currently exploring the precise mechanisms by which the NIP45-RNF4 partnership drives catenane resolution in interphase via SUMOylation of specific factors and will present our latest insights at the meeting.

Keywords: Catenanes, DNA repair, SUMOylation.

P033. Computational Biology, Bioinformatics & Artificial Intelligence

Integrating AlphaFold and GEMPro for unravelling the environmental impact on *Corynebacterium glutamicum*'s metabolism and human health

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Understanding the impact of environmental factors on human health is of global concern. Our transformative project investigates the intricate relationship between environmental stressors and human health using advanced bioinformatics and metabolic modelling techniques. Our study focuses on *Corynebacterium glutamicum*, a key model organism in industrial applications. The core of our approach lies in integrating AlphaFold2, a state-of-the-art deep-learning protein structure prediction tool, with the GEMPro1 toolbox adapted to Python 3. This innovative integration enables highly accurate 3D protein predictions, allowing us to gain unprecedented insights into crucial enzyme fluxes and regulatory interactions in response to varying environmental conditions. Through comprehensive analyses, we aim to unravel how environmental factors influence *C. glutamicum*'s cellular responses and metabolic behaviour. Understanding the organism's adaptive strategies will shed light on its potential impact on human health in industrial applications and the environment. Beyond fundamental research, our toolbox holds promise for targeted biotechnological interventions. By revealing the interplay between environmental impacts and *C. glutamicum*'s molecular responses, we open new opportunities for sustainable bioremediation and optimised pharmaceutical production. In conclusion, our toolbox integrates AlphaFold-enabled 3D protein structures with genome-scale metabolic models, placing us at the forefront of deciphering the intricate connections between environmental changes, microbial physiology, and human health. This project significantly contributes to understanding environmental impacts on organisms' metabolic processes, utilising *C. glutamicum* as a model system.

Keywords: Systems Biology, GemPro, AlphaFold, Genome Scale Metabolic Models, *Corynebacterium glutamicum*.

P034. Omics (Proteomics, Transcriptomics, Metabolomics, Metagenomics)

Amino acid harvesting and regulation in yeast

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Adaptive stress protection is a critical mechanism that helps organisms to respond to and survive stressors, including environmental, physical, and psychological stress. For a few years, it has been known that amino acids are involved in adaptive stress protection in yeast. In a recent study, the mechanism "Lysine Harvesting" as a preventative antioxidant strategy was found. In this project, the amino acid histidine was found to be harvested as well in yeast and may play a similar role in adaptive stress protection. The amino acid uptake amount may differ between the yeast isolates. To understand the exact mechanisms underlying histidine harvesting, we are working on an approach, which combines QTL mapping with metabolomics. This approach allows researchers to identify the genetic loci responsible for the variation in amino acid harvesting, providing insight into the genetic basis of metabolite production.

Keywords: Amino acid harvesting, metabolomics, high-throughput, yeast, amino acid metabolism.

P035. Immunology, Microbiology & Infectious Diseases

Microbial quality of *Moringa oleifera* (moringa) and *Glycine max* (soya beans) seed protein concentrate-supplemented breads

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Wheat flour contains macronutrients that aid microbial growth under inappropriate storage conditions. Rope-forming bacterial species, yeast and mould are often associated with bread spoilage. The information on microbes present in a product have a considerable effect on its sensory properties and shelf-life of the product. This study was carried out to assess the microbial stability of breads supplemented with moringa and soya seed protein concentrates (MOPC-B & SPC-B) stored at 5°C and 26–30°C ± 0.2°C. Bread samples were baked through a straight dough method with 2%, 4%, 6%, 8%, 10%, 12% MOPC & SPC composite flours and 100% wheat flour (control). Microbiological analysis began after 24 h of baking using aerobic colony count (ACC) and organisms were identified with biochemical tests, microscopy and morphology. The counts were compared to a standard microbial limit. Results obtained revealed that all breads stored at ambient temperature moulded on day 4 of storage, while the average shelf-life of MOPC-B was 6 days. The heterotrophic bacteria count (HBC) ranged from 3.0×10^7–2.40×10^8 cfu/g in MOPC-B, 3.0×10^7–1.96×10^8 cfu/g in SPC-B and 1.2×10^8 cfu/g in the control at 5°C. While the fungi count (FC) for MOPC-B, SPC-B and control ranged from 1×10^3–1.57×10^5 cfu/g, 1×10^3–8.5×10^4 cfu/g and 4×103–1.0×104 cfu/g at 5°C. In all cases and to some extent, microorganisms isolated were *Bacillus cereus, Bacillus spp, Streptococcus faecalis, Micrococcus luteus, Lactobacillus bulgaris., Mucor pusillus, Aspergillus niger, Aspergillus flavus, Rhizopus stolonifer* and *Saccharomyces cerevisae*. These findings show that moringa-supplemented breads had higher microbial stability than soya breads and 100% white bread.

Keywords: Moringa bread, storage, shelf-life, refrigeration, microbial quality.

P036. Cancer Biology & Oncology

Figuring out meningioma progression

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One third of primary brain tumours are meningioma. Since they are considered mostly benign with only about 3% of samples progressing to malignant form, the focus of most scientific research is directed towards more aggressive types of brain tumours such as glioblastoma. However, the malignant form of meningioma is clinically challenging to treat and has a poor prognosis for patients. Detecting leading molecular actors of aberrant signalling in meningioma progression could help in setting effective diagnosis and treatment. Our research is focused on determining the role of biologically conserved pathways – Wnt and Notch – in meningioma progression. Both pathways have been shown to be activated in meningioma with similar roles in transcription of oncogenic genes. Our studies have shown that active β-catenin, a central molecule of Wnt signalling, is translocated in a smaller portion to the nucleus and that translocation is more prominent in atypical meningioma ($P = 0.002$). We detected nuclear expression of *DVL1* which was also related to higher expression of the active β-catenin ($P = 0.029$) and a higher meningioma grade ($P = 0.030$). On the other hand, the *APC* gene, responsible for destruction of β-catenin, was found methylated only in the malignant form of meningioma ($P = 0.000$). Regarding Notch signalling, NOTCH1 and NOTCH2 were translocated to the nucleus in more than 90% of samples, indicating activation in early stages of meningioma progression. Furthermore, methylation of the NOTCH2 promoter site was distinctive to atypical meningioma ($P = 0.000$). Our results show activation of Wnt and Notch signalling at different stages of meningioma progression, suggesting the above-mentioned molecular actors as potential prognostic biomarkers.

Keywords: Meningioma, Wnt signalling pathway, Notch signalling pathway.

P037. Genetics & Epigenetics

Using differentially expressed miRNA for sepsis and DIC diagnosis

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As defined in Sepsis-3, sepsis is a "life-threatening organ dysfunction caused by a dysregulated host response to infection", where a subset, septic shock, presents abnormalities associated with a greater risk of mortality. Furthermore, associated pathologies such as disseminated intravascular coagulation (DIC), worsen the prognosis of patients. However, little is known on the heterogeneity of the pathology and if intrapersonal differences affect the progression. Thus, adequate, robust, and rapid biomarkers are needed for the correct diagnosis and prognosis of patients in a timely manner. The field of epigenetics provides a viable study area which may allow the correct stratification of patients and, consequently, provide the adequate treatment. Recently, microRNAs (miRNAs), a type of non-coding RNA, have been studied for their potential as biomarkers in several pathologies. In this study, we explore different established circulating miRNAs in plasma samples to determine the expression profile that can allow the correct classification of patients into sepsis, septic shock, and the adverse side-effect of DIC. Additionally, we determine the correlation between the levels of these circulating miRNAs and the different clinical and biological parameters that are monitored throughout the development of the septic episode. In all, the described miRNAs could potentially be used in a clinical setting as biomarkers that could provide diagnosis and prognosis of septic patients.

Keywords: Sepsis, septic shock, DIC, biomarker, miRNA.

P038. Immunology, Microbiology & Infectious Diseases

Molecular structures of infection-derived and recombinant secreted NS1 from Dengue and Zika viruses in complex with antibodies

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Higher temperatures due to climate change are causing mosquito-borne diseases, like Dengue and Zika, to spread in cooler regions like southern Brazil and Europe with a ~ 20% increase in burden over the next 30 years. Severe Dengue and Zika infections are characterised by endothelial dysfunction shown to be associated with the secreted nonstructural protein 1 (sNS1), making it an attractive vaccine antigen and biotherapeutic target. However, the biologically relevant structure of sNS1 remains an enigma. sNS1 is believed to be secreted as hexamers that could dissociate and bind to epithelial cell membrane based on recombinant sNS1 (rsNS1)

samples. We found that infection-derived sNS1 (isNS1) appeared as a ~ 250 kDa complex of NS1 and ApoA1 and further determined the cryoEM structures of isNS1 and its complex with a monoclonal antibody. The major species of isNS1 is a complex of the NS1 dimer partially embedded in a High-Density Lipoprotein (HDL) particle. Cross-linking mass spectrometry (XL-MS) studies confirmed that the isNS1 interacts with the major HDL component ApoA1 through interactions with the NS1 wing and hydrophobic domains. We further present high resolution cryoEM structures of ZIKV rsNS1, which appears as stable tetramers in its apo form and when bound to human anti-NS1 antibodies used in our study. Furthermore, our studies demonstrated that the sNS1 in sera from DENV-infected mice, ZIKV-infected mice, and a human dengue patient form a similar isNS1-HDL complex. Our findings expand the structural landscape of NS1 and help to inform the molecular pathogenesis of NS1.

Keywords: Flaviviruses, Dengue, Zika, NS1, cryoEM.

P039. Chemistry & Biochemistry

Evaluation of the protective effect of cardamom (*Elettaria Cardomomum*) according to GPER levels in an experimental bladder ischemia reperfusion model: a biochemical and histopathological study

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Ischemia reperfusion injury is held responsible for the etiopathogenesis of atherosclerosis, myocardial infarction, neurodegenerative diseases, and chronic liver diseases. Cardamom is a plant with antioxidant properties. This study aimed to investigate the effect of cardamom on GPER-1 levels of ischemic bladder tissue in rats. In our study, 24 Wistar Albino rats (weighing 250–300 g) were used. Rats were divided into three groups: ischemia–reperfusion (I/R), sham (physiological saline) and treatment (cardamom extract at a dose of 50 mg/kg) groups. For the treatment and sham groups, cardamom extract and physiological saline were first administered 24 h before ischemia–reperfusion injury occurred. For each group, after anaesthesia and surgical procedures, 30 min of ischemia and 30 min of reperfusion were applied to the bladder with the help of a clamp. Then, the rats in three groups were sacrificed and their bladder tissues were removed. GPER-1 levels for biochemical analysis in tissue samples were determined using enzyme-linked immunosorbent assay. Also, tissue samples for histopathological analysis were evaluated under light microscopy. As a result of biochemical examinations, an increase in GPER-1 levels was observed in the I/R group compared to the sham and treatment groups ($P < 0.05$). There was no significant difference between sham and treatment groups ($P > 0.05$). While histopathologically serious damage occurred in the I/R group, it was noted that Cardamom treatment reduced the damage. It was concluded that increased GPER-1 levels in the I/R group were associated with bladder damage and that GPER-1 levels approached normal with cardamom treatment.

Keywords: Bladder, I/R, Cardamom, GPER-1.

P040. Cellular & Molecular Biology

Mechanistic insights into lipid-based protein sorting from the ER

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Protein sorting in the secretory pathway is crucial to maintain cellular compartmentalization and homeostasis. In addition to coat-mediated sorting, the role of membrane lipids in driving protein sorting during secretory transport is a longstanding fundamental question that remains unanswered. To address this question, we have investigated in the yeast *Saccharomyces cerevisiae* how a special type of lipid-linked cell surface proteins, the GPI-anchored proteins, are differentially exported from the endoplasmic reticulum (ER). We have shown that ceramide drives the clustering and sorting of GPI-anchored proteins into specialised ER exit sites. Here we provide a better comprehension of the potential mechanism for this ceramide-based sorting process.

Keywords: Ceramide, protein sorting, GPI-APs, membrane lipids and secretory pathway.

P041. Pharmacology, Toxicology & Nutrition

Assessment of the physical and chemical properties of seawater samples collected from Turkish coastal stations inhabiting Mediterranean mussels

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Toxic waste and global warming are the main threats to marine ecosystems. Seawater pollution and its chemical parameters are very important for the environment, marine organisms, and public health. Within the scope of this study, water samples were collected from 15 stations in the coastal areas of Turkey, especially from the Marmara, Black Sea, and Aegean regions. Stations were selected according to their potential for facing various anthropogenic pressures and inhabiting Mediterranean mussels. Seawater samples were examined in terms of various chemical parameters that can detect pollution, such as salinity, pH, turbidity, and concentration of dissolved oxygen. In addition, seawater temperatures were determined and recorded on-site. According to these results, dissolved oxygen concentrations varied between 6.62 ± 0.32 and 9.81 ± 0.22 mg/L. Turbidity scores varied between 0.10 ± 0.01 and 4.17 ± 0.78 NTU. Salinity scores varied between 13.55 ± 0.38 and 34.49 ± 1.40 psu. Acidity scores varied between 7.23 ± 0.01 and 7.97 ± 0.05 pH. Seawater temperatures varied between 21.10 ± 0.10 and 27.80 ± 0.15 °C. Coastal marine pollution due to various factors such as industrial activities, human activities, and high population density has not only affected biodiversity in marine environments but also public health. The marine ecosystems near the bay areas and the ports are mostly under the pressure of anthropogenic pollution and are more risky areas for human health. In conclusion, it is possible

to state that according to scores of recorded parameters, Izmir Bay area station is the station under the highest threat in terms of pollution potential.

Keywords: Seawater, Mediterranean mussel, pollution, chemical parameters, sea temperature.

P042. Obesity, Diabetes & Other Diseases

From plate to pancreas: high fat diets and their impact on stressed β-cells

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Diabetes is a complex disease that currently affects half a billion people worldwide and one of the main causes is β-cell dysfunction. A diet based on foods rich in fats may play a role in its increasing incidence. We hypothesised that adapting β-cells to metabolically challenging conditions may lead to their increased resistance and performance in the onset of diabetes. Our aim was to characterise the function of β-cells under both mass ablation and metabolic stress. We used NSG RIP-DTR mice that express the human diphtheria toxin receptor (DTR) driven by the rat insulin 2 promoter (RIP) in an immunosuppressed background. Upon injection with DT, heterozygous NSG RIP-DTR females lose half of their β-cell mass (NSG RIP-DTR50%). The remaining β-cells were additionally stressed by exposure to a 10-week high-fat diet (HFD). Mice were divided into four experimental groups: DT- or vehicle-treated, exposed to HFD or normal diet (ND), respectively. By the end of the 10-weeks diet, serum insulin levels revealed no changes in the ability of the remaining β-cells to secrete the hormone. Glycemia monitoring and the ipGTT revealed that all experimental groups exhibited normal blood glucose fluctuation, except for the NSG RIP-DTR50% on HFD group, which showed a significant delay of glucose control, indicating an abnormal response of the remaining β-cells. Our results showed that a sustained HFD on already stressed β-cells leads to their impaired function. This model will allow thorough characterisation of the mechanisms that precede diabetes and design of better therapeutic strategies.

Keywords: Diabetes, β-cells, high-fat diet, insulin secretion, metabolic stress.

P043. Pharmacology, Toxicology & Nutrition

Effects of an exposure to a mixture of fungicides in human colon cancer cells

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In the context of global warming, fungicides are massively used to limit the proliferation of pathogenic fungi in cereals, fruits and vegetables. Succinate dehydrogenase inhibitor (SDHi) fungicides target succinate dehydrogenase (SDH), the well-conserved complex II of the mitochondrial respiratory chain (MRC). SDH is involved in both cellular respiration and the Krebs cycle, and its genetic inactivation leads to severe outcomes, including cancers. Strobilurin (STR) fungicides also target mitochondria by inhibiting complex III of the MRC. In marketed formulations, SDHi and STR are often combined, so we hypothesise that such mixtures may strongly alter mitochondrial function with potential consequences on tumour phenotype. We explored the toxicity of a fungicide mixture containing SDHi (fluxapyroxad/FLU) and strobilurin (pyraclostrobin/PYR) in HCT116 human colon cancer cells. We showed that the mixture FLU/PYR alters the mitochondrial functions with an increase in mitochondrial ROS production and a decrease in oxygen consumption rate. We also observed that the mixture increases lactate production, suggesting a metabolic switch from oxidative phosphorylation towards glycolysis. The mixture also induces a slow-down in proliferation and changes in cell morphology with cell spreading and lamellipodia. In conclusion, these preliminary results suggest that exposure to the mixture FLU/PYR may lead to a strengthening of the Warburg effect, a well-known metabolic feature of cancer cells. Further studies are needed to decipher the toxic effects of the mixture on other hallmarks of cancer cells.

Keywords: Mitochondria, pesticides, metabolic reprogramming, cancer.

P044. Computational Biology, Bioinformatics & Artificial Intelligence

In silico computational modelling of some bioactive compounds as an insight to possible inhibitors of HER2 breast cancer

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Overexpression of HER2, a type I tyrosine kinase receptor involved in cell proliferation and differentiation, has been related to a variety of malignancies, including breast cancer. Identifying beneficial plant chemicals that can reduce its overexpression could lead to therapeutic benefits for breast cancer patients. Because of its capacity to block carcinogenesis and reduce the proliferation of breast cancer cells, medicinal plants have been proven to be useful in the development of innovative anticancer drugs. In order to find effective therapeutic options for breast cancer, the phytochemical library of plants was screened for inhibitory potentials against HER2 using molecular docking, pharmacophore modelling and ADMET studies. The docking scores of the top 10 compounds in the molecular docking

analysis range from −9.327 kcal/mol to −8.147 kcal/mol. The 10 compounds are arranged in order of binding affinity, and they were found to interact with the same amino acid residues as the reference compound (03Q). The chemicals had hydrophobic contacts with target amino acid residues of the HER2 ATP binding region in addition to one or more hydrogen bond interactions. Gallocatechin appears to be the safest of all the chemicals, with an LD_{50} of 10 000 mg/kg, toxicity class 6, and no inclination towards any of the toxicity check points. This compound could be subjected to further studies to validate its activity against breast cancer.

Keywords: Computational drug design, breast cancer, medicinal plants.

P047. Cellular & Molecular Biology

Perinatal derivatives and environmental pollution: a dissection of the negative impact of BPA on mesenchymal stromal cells of the amniotic membrane

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Nowadays, microplastic pollution has become an increasingly pressing issue, not only for the environmental fallout, but also for the assumed negative effects on human health. Indeed, microplastics can enter the body through ingestion, inhalation, dermal contact and unfortunately also maternal-foetal transmission. Their physical presence in the human body has been associated with deleterious effects at multi-organ level. Recently, microplastics have been detected within the placenta and breast milk. Among the by-products of microplastic degradation, bisphenol A (BPA) has emerged as a harmful chemical, with a possible toxic impact on the reproductive sphere. It thus becomes clear how the effects of microplastics are not limited to adults, but they can also affect early stages of human development. We therefore went to study the impact that BPA may have on properties and functions of mesenchymal stromal cells of the amniotic membrane (hAMSCs), which represents the last barrier separating the foetus from possible toxic substances and pollutants that the mother can come into contact with. Our studies highlight how high BPA concentrations reduce cellular viability and induce the production of oxygen free radicals at the mitochondrial level. The increased oxidative stress led in turn to p53 stabilisation and the induction of the apoptotic pathway in response to increasing concentration of BPA. We are trying to define if the administration of antioxidant compounds could revert the BPA-mediated negative effect in hAMSC.

Keywords: Microplastics, BPA, perinatal derivatives, hAMSC, oxidative stress, pregnancy.

P048. Pharmacology, Toxicology & Nutrition

Toxicity of microplastics and additives in a complex cellular liver model

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Plastics are currently a source of intense concern because they are present in everyday products. Microplastics (MPs) are defined as particles smaller than 5 mm. Humans are exposed to MPs as well as their additives bisphenols (BPs) and perfluoroalkyl substances (PFAS) mainly by ingestion. These contaminants reach organs such as the liver and cause damage related to Non-Alcoholic Fatty Liver disease (NAFLD). The aim here is to evaluate the toxicological impacts of mixtures of MPs and their additives in order to decipher the mechanisms involved in a complex liver cellular model. A co-culture model is being developed with three cell types implicated in NAFLD steps: hepatocytes, stellate cells and Kupffer cells, modelled respectively by HepaRG, LX-2 and THP-1 cell lines. We established different LX-2 cell sub-lineages that all maintain stellate cell marker expression (COL1A1, MMP2, Fibronectin). Moreover, these markers are upregulated by exposure to stellate cell activator (TGFβ 5 ng/mL - 24 h). The cytotoxicity results of the three cell types, independently grown in 2D, revealed sensitivity differences after exposure to MPs (5–150 μg/mL) and additives BPA, BPS, PFOS, and PFOA (100 pM - 100 μM). Oxidative stress assay performed on HepaRG cells did not show modulation of either production of reactive oxygen species or of antioxidant gene expression. Our initial experiments showed an optimal production of compact HepaRG spheroids in agarose micro-moulds. The main prospect of these results is the development of a complex liver model in which the cytotoxic effects of MPs and additives, alone or in combination, will be investigated.

Keywords: Microplastics, additives, liver, 3D culture, toxicity.

P049. Cancer Biology & Oncology

Overcoming radiation therapy resistance in uveal melanoma

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Uveal melanoma (UM) is the most common intraocular malignancy in adults. Radiation therapy is the widely used globe-preserving therapy for UM and often preferred over enucleation. Failures of tumour control in up to 25% of cases have been reported with radiation. Since failure of local tumour control in UM leads to tumour spread outside the eye and consequent

death within a year in half of all UM cases, overcoming radiation resistance is of the utmost importance. However, knowledge is still lacking about factors that determine radiosensitivity of UM. We hypothesise two possible mechanisms responsible for the varying response to radiation, *CDKN2A* gene silencing and enhanced extracellular vesicle (EV) secretion. *CDKN2A* silencing is seen in a third of all UMs. The *CDKN2A* gene is responsible for producing two proteins, p14 protein and p16 protein, which have important roles in cell death (via p53 signalling) and cell cycle regulation pathways, respectively. We will test drugs that work on p14 and p16 pathways to enhance the radiosensitivity of UMs thereby overcoming the effect of *CDKN2A* disruption. Enhanced EV secretion is a mechanism by which cancer cells get rid of their damaged cellular material following irradiation, thereby evading apoptosis. We will test the effect of using inhibitors of EV secretion along with irradiation to increase cancer cell killing. Enhancing the *CDKN2A* mediated signalling pathway and EV targeting would therefore provide additional therapeutic strategies to overcome radiation resistance in UM, which can be used for successful local tumour control and to prevent UM progressing into metastatic disease.

Keywords: Uveal melanoma, radiation therapy, extracellular vesicles, cell death, therapy resistance.

P050. Omics (Proteomics, Transcriptomics, Metabolomics, Metagenomics)

Genetic background effect of proteome response to genetic perturbations

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Functional proteomics aims to assign a biological function to unknown proteins by the study of the proteome profile in selected conditions and the protein interactions. These studies are performed in a large-scale manner, and tend to focus on model organisms and laboratory strains. The genetic background of different strains influences characteristics such as phenotypes and proteome responses; however, this effect remains to be quantified in this context, which is relevant to avoid a skewed functional assignment. The purpose of this study is to characterise the diversity of the proteome response of 10 *Saccharomyces cerevisiae* strains to 29 chromatin-remodelling gene knockouts (KO) and assess the effect of the genetic background in the determination of biological functions. The 10 yeast strains were selected from the 1011 Yeast Isolates Collection, covering the genetic diversity of *S. cerevisiae*. These KOs were made by using CRISPR/Cas9 and Synthetic Genetic Arrays techniques. The proteome was quantified by data-independent acquisition mass spectrometry, with a proteomic depth of 3500 proteins. Then, the proteome response of the KO across the strains will be compared to determine its variability. Further, the enriched Gene Ontology terms will be identified to estimate the consistency of the associated functions. Last, underlying drivers for the differences will be identified.

Keywords: Epistasis, proteomics, genetic background.

P051. Cellular & Molecular Biology

Investigating the roles of teashirt genes in pancreatic endocrine specification

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The generation of insulin-producing β cells from the *in vitro* differentiation of human pluripotent stem cells (hPSC) both for disease modelling and treatment of diabetes has been pursued aggressively in recent years. Current protocols heavily rely on our understanding of pancreatic development in the mouse and other vertebrates. Fundamental differences in the gene regulatory networks governing mammalian pancreatic development do however exist among different species. Pancreatic and duodenal homeobox 1 (PDX1) encodes a well-characterised transcription factor crucial for human pancreatic organogenesis: homozygous loss of PDX1 results in pancreatic agenesis, while heterozygous mutations are associated with β cell dysfunction. Despite its importance in pancreatic specification and glucose homeostasis, surprisingly little is known about the identity of the transcriptional targets downstream of PDX1. To address this knowledge gap, we developed a comparative bioinformatics pipeline incorporating human *in vitro* and *in vivo* gene expression data sets as well as PDX1 ChIP-seq and epigenome data (H3K27ac at active enhancers) to identify candidate effectors of PDX1. From this pipeline, we identified teashirt zinc finger homeobox 2 and − 3 (TSHZ2/3) as potential downstream targets of PDX1 transcriptional regulation. Significantly, TSHZ2/3 expression decreases in hPSC lacking PDX1, and PDX1 ChIP-seq confirmed that PDX1 binds to regions in both genes whose putative enhancers are marked by H3K27ac. Lastly, TSHZ2/3 expression has been documented in the human pancreatic primordium. Here, we outline experimental strategies and preliminary data that we have undertaken to elucidate the roles of TSHZ2/3 in the development of the human pancreas.

Keywords: Teashirt, pancreas, stem cell differentiation.

P052. Cancer Biology & Oncology

Study of cytotoxicity in acute myeloid leukaemia after administration of the 7 + 3 scheme and inhibition of the Hedgehog, Notch and Wnt pathways

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Acute myeloid leukaemia is a clonal disease for which the main treatment is the 7 + 3 (Cytarabine + Idarubicin) regimen. Relapse is common in this disease and appears to be associated with chemoresistance due to quiescence of the CD34^{+} CD38^{−}

clonal population. The entry of cells into quiescence is regulated by signalling pathways such as the Hedgehog, Notch and Wnt/β-catenin pathways. Therefore, inhibition of these pathways in combination with chemotherapy could increase chemosensitivity. HL-60, OCI-AML3 and KASUMI-1 cell lines were treated with the pathway inhibitor drugs called Glasdegib (Hedgehog inhibition), Nirogacestat (Notch inhibition), and PRI-724 (Wnt inhibition) in combination with the 7 + 3 scheme to study cell viability in an absorbance assay. In all cell lines, viability was reduced with respect to the chemotherapy control by the different treatments proposed; although in all cell lines the best treatment was the combination of Glasdegib + Nirogacestat with the chemotherapy drugs. Therefore, it seems that the joint inhibition of Hedgehog and Notch may open a new therapeutic window when combined with the 7 + 3 scheme.

Keywords: Acute myeloid leukaemia, inhibition, Hedgehog, Notch, Wnt.

P053. Obesity, Diabetes & Other Diseases

Linear ubiquitination in metabolic inflammation

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TNF is a key cytokine in chronic inflammation, it induces cell death and gene activation via NF-κB and MAPK signalling. LUBAC is an E3 ligase that generates linear ubiquitin chains and it is composed of HOIP, HOIL-1 and SHARPIN. LUBAC regulates the balance between cell death and inflammatory gene activation upon TNF stimulation. Therefore, we aim to explore the respective contributions of cell death and NF-kB regulated by LUBAC in inflammation associated with obesity. To understand this, we generated a mouse model in which HOIP is specifically deleted in adipocytes (*HoipA-KO*) leading to loss of LUBAC activity, and a second model in which HOIL-1 is catalytically inactive *(Hoil-1C458A)*, resulting in exacerbated LUBAC activity. These mice were challenged with a high-fat diet (HFD) or control diet (CD) for 8 and 16 weeks. *HoipA-KO* mice display exacerbated cell death and inflammation characterised by an increase in infiltration of immune CD45$^+$ and F4/80$^+$ cells in gonadal white adipose tissue (GWAT) as compared to their littermate wild-type control after 8 and 16 weeks of CD, and this was worsened during HFD. This inflammation in GWAT is due to cell death, since deletion of Caspase-8 in adipocytes rescues the inflammation. Moreover, *Hoil-1C458A* mice displayed less cell death and less immune cell infiltration accompanied by reduced formation of crown-like structure. This study emphasises an important role of LUBAC in the pathogenesis of obesity-induced metabolic inflammation and implies that cell death is the fundamental process responsible for inflammation during obesity.

Keywords: Inflammation, obesity, cell death, LUBAC.

P054. Cellular & Molecular Biology

L-Arginine treatment corrects impaired autophagy in GM2 gangliosidosis AB-variant mouse cells

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The GM2 gangliosidosis AB-variant is an extremely rare neurodegenerative disorder caused by a mutation in the *GM2AP* gene. GM2 and GA2 ganglioside accumulation were previously reported in the lysosomes of neural tissues of the Gm2a-defective mouse model. Autophagic impairment is a typical phenotype observed in many lysosomal storage disorders. However, the regulation of autophagic flux has not been studied fully in the Gm2a$^{-/-}$ mouse model. Recent studies have shown that L-arginine supplementation partially improves mTOR activity and restores autophagic flux in GM2 gangliosidosis patient fibroblasts. Here, we explored the regulation of autophagic flux in Gm2a$^{-/-}$ mouse cell lines using L-arginine in addition to EBSS and bafilomycin A1 targeting the autophagic pathway. Accordingly, fibroblast and neuroglia cells derived from WT and Gm2a$^{-/-}$ mice were treated with EBSS medium, bafilomycin A1 (100 nM), and L-arginine (1 mM) for 1-h, 24-h, and 72-h respectively. Autophagic flux markers were analysed by RT-PCR, Western blotting, and immunocytochemistry. We observed that p62 gene expression and protein levels were significantly elevated in Gm2a$^{-/-}$ mouse fibroblasts compared to the control. In addition, EBSS and L-arginine treatment significantly reduced both p62 and LC3-II protein levels in both Gm2a$^{-/-}$ fibroblast and neuroglia compared to untreated Gm2a$^{-/-}$ cells. Altogether, our results suggest that the autophagic flux in Gm2a$^{-/-}$ mouse fibroblast and neuroglia is significantly impaired and can be reversed by starvation and L-arginine treatment.

Keywords: GM2 gangliosidosis AB-variant, autophagy, L-arginine, bafilomycin A1, neuroglia.

P055. Computational Biology, Bioinformatics & Artificial Intelligence

Predicting time to treatment in youth and adolescence diabetes with transformer based neural network

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Diabetes is a highly heterogeneous and complex disease and has been associated with numerous genetic and environmental factors, making early detection challenging. Early detection of diabetes has been associated with reduced risk of diabetic complications, underlining the importance of timely identification and intervention. Here we instead investigate the predictive value of existing clinical data. This study analyzes 3.2 million individuals under the age of 30 years, including 40,510 newly diagnosed diabetes patients, comprising a total of 505 million health-related

occurrences from the Danish National Health Service Registry, the Danish National Prescription Registry, and the Danish National Patient Registry. This dataset serves as the foundation for training a transformer-based network that utilises the longitudinal nature of registries to forecast the necessity of treatment for diabetes. Preliminary results show that early identification of diabetes improved with the inclusion of primary care data compared to secondary care data, emphasising the need for primary care data to correctly identify patients with symptoms that often have debuted long before the hospital patient histories. These results also show how deep learning algorithms have the potential to better stratify patients using heterogeneous longitudinal information yielding timely intervention.

Keywords: Diabetes, deep learning, Electronic Health Registries.

P056. Cellular & Molecular Biology

Deciphering the role of novel isoforms of Fpn1 protein in fungal pathogenesis

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Fungal diseases have become progressively significant in recent years. Because few and far between fungi are efficient pathogens, their pathogenic mechanisms are predisposed to be increasingly intricate, derived largely from adaptations of preceding attributes of the organisms' nonparasitic lifestyles. In the past few years, genetic methods have discerned many fungal virulence factors, and intense knowledge of host reactions has also divulged much about fungal diseases. The pathogenesis of fungi has been seen to be related to iron homeostasis. It plays a significant role in adjusting the immune response by macrophages against these pathogens. Ferroportin (Fpn1), which is an iron transporter, has been deciphered to play a cardinal role in recycling of iron, thereby contributing to iron homeostasis. In the host, the efflux of iron from the intracellular organelles supervised by FPN1 is an important defence strategy to restrict the availability of iron to the intracellular pathogens. Ferroportin works in association with a peptide hormone called Hepcidin in order to maintain the stable iron equilibrium in the body. In this study, we have predicted and confirmed an alternatively spliced novel isoform of Fpn1 in humans. The new isoform shows a difference in the C-terminal domain wherein the last exon is distinct to that of the already reported transcript of Fpn1. We have also performed *in silico* analysis and MD simulations for structural characterisation of the novel isoform.

Keywords: Fungal pathogenesis, ferroportin, hepcidin, iron homeostasis, alternative splicing.

P057. Cellular & Molecular Biology

Prevalence of gastrointestinal parasites and molecular identification of beta-tubulin mutations associated with benzimidazole resistance in *Haemonchus contortus* in goats from selected districts of Uganda

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Gastrointestinal parasites are among the most economically important pathogens of small ruminants. The emergence of anthelmintic resistant *H. contortus* in small ruminants is a serious problem because it undermines effective helminth control and results in reduced productivity. Little is known about resistance to benzimidazoles (BZ) in Haemonchus in goats and sheep in Uganda. A total of 200 goats from 10 districts of Uganda slaughtered at Kalerwe abattoir in Kampala were sampled for *H. contortus* adult worms. Faecal samples were also collected to detect other intestinal parasites. Faecal microscopy and analysis were performed using flotation and sedimentation techniques and it showed that the most prevalent intestinal parasites were coccidia (98%), strongyles (97.5%), Strongyloides (82%), Paramphistomum (74.5%), Moniezia (46%), Fasciola (1.5%) and Trichuris (1%). Most goats had a high intestinal burden of coccidia ($\geq$ 5000 oocyst per gram) and strongyles ($\geq$ 1000 egg per gram), 65% and 67.5%, respectively. The prevalence of *H. contortus* adult worms was 63% (126/200). Sequencing of the partial β-tubulin isotype 1 gene of 54 *Haemonchus contortus* adult male isolates revealed the presence of mutations associated with anthelmintic resistance. The F200Y mutation was the most common mutation (13% of samples with good beta-tubulin sequences) followed by the E198A and E198K mutations, both found in 9% of sequenced samples. Mutation F167Y was not identified in any of the samples and there were no heterozygous individuals for any of the SNPS associated with BZ resistance that were identified in this study.

Keywords: Benzimidazole resistance, *Haemonchus contortus*, gastrointestinal parasites, Beta tubulin genes.

P058. Neuroscience, Psychiatry & Mental Health

Association of CYP1A1 and GSTM1 null polymorphisms with pro- and anti-inflammatory cytokines in the OCD group

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It is thought that the activation of the kynurenine pathway causes inflammation and plays an important role in obsessive-compulsive disorder (OCD) pathogenesis. Cytochrome P450 (CYP) enzyme activity has been shown to be modified by inflammatory cytokines. The members of multigenic GSTs family's subtype μ show a common polymorphism that is characterised by the complete deletion of the gene. It is known that homozygous deletions (null genotype) result in the absence of catalytic activity of the GST enzyme. The null genotypes of GSTs have been associated with oxidative stress-related diseases such as cardiovascular, epilepsy, and psychiatric diseases. We aimed to examine the relationship between pro-inflammatory cytokine interleukin-1beta (IL-1β), anti-inflammatory interleukin-10 (IL-10) and interleukin-4 (IL-4), serum cytochrome P450 (CYP1A1) and glutathione S-transferase1 (GSTM1) null genotype in OCD. A hundred people with OCD and fifty healthy controls were included in our study. Enzyme-linked Immunosorbent Assay (ELISA) was used to determine serum IL-1β, IL-4 and CYP1A1 levels. GSTM1 present/null genotyping was performed using polymerase chain reaction (PCR) from isolated DNA samples. We found that IL-1β levels were significantly increased in the OCD group, whereas IL-10 was decreased ($P < 0.001$, for both). Serum IL-4 levels and GSTM1 present/null genotype distributions were comparable between groups ($P > 0.05$, for both). IL-10 levels were significantly different in the OCD group carrying the GSTM1 null allele compared to the controls ($P < 0.01$). Inflammation and having the GSTM null allele may contribute to the pathology of OCD.

Keywords: Obsessive Compulsive Disorder, IL-1β, IL-4, IL-10, CYP1A1, GSTM1 null polymorphism.

P059. Cardiovascular Diseases

Identification of anti-TB therapy induced ADR genetic markers using *in silico* approaches

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Adverse drug reactions (ADRs) are associated with clinical morbidity and, in severe cases, even mortality. Globally, billions of dollars are spent on managing these ADRs for common and uncommon diseases. Due to these reasons, drug-resistant strains have emerged and are now a serious challenge to TB eradication. To effectively deliver the available treatment regimen and ensure patient compliance it is important to manage ADRs more efficiently. Recent studies have demonstrated that drug outcomes are patient-specific and can, therefore be predicted. A few of these drugs, including a few administered for TB, have shown excellent correlation with response rates and development of ADRs. ADRs were selected based on frequency of occurrence (≥1%). Anti-TB drugs were reviewed to identify the candidate genes (DMETs, HLA). Genes were analysed with different web tools and databases to extract their SNPs. MAF >0.01 were shortlisted using NCBI Gene and dbSNP databases (built 141). SNPs which lay in a functional domain of the gene were prioritised using SNPinfo web server (www.snpinfo.niehs.nih.gov/). Additionally, the same analysis was done for the Indian population. We identified 10 genes which may be directly linked to ADRs to various anti-TB drugs, and four of these have been documented earlier. Nearly 47 genes were identified for indirect association with ADRs by virtue of them being off-targets of the drugs. Lastly, 5 genes were reported for their allelic association with anti-TB DIH. To our knowledge, this is the first review reporting a list of possible genetic markers in context to TB ADRs to such a vast extent. New genes are identified that may be associated potentially with anti-TB drug ADRs. This would translate into not just patient welfare, but would also save billions of dollars spent annually on managing drug-induced ADRs.

Keywords: *In silico*, Anti TB, pharmacogenomics.

P060. Neuroscience, Psychiatry & Mental Health

Evaluation of ischemia modified albumin and TNF-alpha levels in female patients with migraine

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Migraine is a common neurologic disorder, characterised by recurrent episodes of headache related with consecutive construction and dilatation phases of cranial veins. The full pathophysiology of migraine is not completely identified. Current theories suggest that ischemia and neurogenic inflammation may also play important roles in pathogenesis of the disease. In order to evaluate the relations between ischemia and neurogenic inflammation processes with migraine type headache, we measured ischemia modified albumin (IMA) and TNF-alpha levels of 64 female migraine patients aged 20–50 years and 43 healthy age matched female controls. Serum levels of TNF-alpha were detected by commercially available kits based on ELISA method and IMA levels were determined by a colorimetric assay based on decreased binding of Co (II) ions to albumin. TNF-alpha levels were significantly higher in migraine patients than the healthy subjects ($P < 0.05$); however, there was no significant difference for IMA levels between the groups. Our results claimed that neurogenic inflammation is involved in the pathogenesis of migraine, but further investigations are needed in order to evaluate ischemia and oxidative stress processes in migraine type headache, especially carried out in attack and free of attack periods of the disease.

Keywords: Migraine, IMA, TNF-alpha.

P061. Chemistry & Biochemistry

Paraoxonase activities and oxidised-LDL levels in women with migraine type headache

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Migraine which is a common and chronic neurovascular disorder and characterised by severe headache attacks and neurological symptoms is suggested to be associated with increased cardiovascular risk. Paraoxonase (PON1), high density lipoprotein (HDL)-associated enzyme is synthesised in the liver and prevents oxidative modification of low-density lipoprotein (LDL). It is responsible for the antioxidant activity of HDL. We aimed to investigate lipid profile, oxidised LDL levels and PON1 activities as cardiovascular risk factors in women with migraine type headache with and without aura. Forty-five women with migraine type headache and 25 healthy women contributed to this study. Serum lipid profile was measured with routine methods, oxidised LDL concentrations were determined with ELISA technique and paraoxonase activities with a colorimetric assay. HDL-cholesterol levels and paraoxonase activities were decreased while triglyceride and oxidised LDL levels increased in the migraine group compared to the control. There was no significant difference for paraoxonase activities and oxidised LDL levels between migraine with or without aura. Decreased PON1 activities and increased levels of oxidised LDL may cause increased cardiovascular and cerebrovascular risk. However, when we consider the high biological variation and reference change values (RCVs) for these parameters and the limited number of the study group, we can suggest that further investigations with higher numbers of participants are necessary on cardiovascular risk profiles of these patients to delineate the pathogenesis that connects migraine and cardiovascular events.

Key words: Migraine, paraoxonase, oxidised LDL.

P062. Cancer Biology & Oncology

Relationship between cyclin-dependent kinase polymorphisms and prostate cancer risk in Slovak population

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Prostate cancer (PCa) is one of the most common tumours in males. For normal prostate growth, it is necessary to maintain a balance between factors driving cellular growth, proliferation and apoptosis. Alterations in the regulation of the cell cycle are strongly linked to tumorigenesis, so genetic variants in genes critical to control of the cycle are good candidates to have their association with susceptibility to PCa assessed. Among these candidates are cyclin dependent kinases (CDKs). CDKs are serine/threonine kinases that form a complex with cyclin proteins and play a critical role in cell cycle progression. Most CDKs demonstrate substantially higher expression in cancer tissues. We decided to study the association between four selected single nucleotide polymorphisms (SNP) of CDKs (CDK1 rs2448343 and rs1871446; CDK2 rs2069408; CDK4 rs2069502) and prostate cancer risk in the Slovak population. No association was found between all SNP and prostate cancer risk. After analysis of the associations of clinical status and these CDKs polymorphisms, the CDK1 rs2448343 showed a positive association with a higher Gleason score (>7), serum PSA levels ($\geq$10 ng/mL) and pathological T stage ($P > 0.05$). Moreover, we found that the CDK2 rs2069408 polymorphism is associated with higher Gleason score >7 ($P > 0.05$). No significant associations were found for the CDK2 rs2069408 and CDK4 rs2069502 polymorphism with clinicopathological parameters ($P > 0.05$). We can conclude that all selected polymorphisms have no significant impact on prostate cancer risk.

Keywords: Prostate, kinase, cancer, cyclin, polymorphism.

P063. Genetics & Epigenetics

Physiological causes of genome instability in ageing: identification and evaluation of G-loop-binding proteins

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Physiological ageing is accompanied by increased genomic instability. G-quadruplexes (G4s) and DNA:RNA hybrids (R-loops) are structural variations of the genome that form at promoters and transcription start sites and are associated with increased susceptibility to DNA damage. Sites of R-loop and G4 formation overlap strikingly in the genome, suggesting they form simultaneously on complementary strands of DNA, generating so called G-loops. We hypothesise that R-loop formation on the opposite strand of G4s can recruit and stabilise helicase binding which is a crucial step in removing the structures and avoiding transcriptional stress. With age, functionality of helicases is impaired leading to stabilisation of G-loops and increased DNA damage at these sites. We apply the proteomic proximity biotin-labelling approach TurboID with a Protein A-coupled biotin ligase to identify the interactome of G4s. Next, we want to direct the application of Protein A-TurboID towards tissue-derived nuclei, aiming to generate proteomic datasets profiling G4s and R-loops in differently aged mouse tissues. As an orthogonal approach, we are applying genomic mapping technology like G4- and R-loop CUT&Tag to identify sites of G-loops in aged tissue of mice, as well as the co-occupancy of identified interacting proteins. With biochemical approaches like EMSA, we can evaluate direct interaction partners of G-loops. We anticipate that binding of occupation of helicases at G4s is increased in aged tissue and stabilised by R-loops. To expand our understanding of causes of genomic instability during ageing, we will identify where G-loops

are occupied and perturbed by interaction partners by further genomic methods.

Keywords: G-quadruplex, R-loops, epigenetics, genomic instability, ageing.

P064. Immunology, Microbiology & Infectious Diseases

Pathogens co-opt senescent cells to establish chronic infections

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Viruses, bacteria, and parasites such as *Toxoplasma gondii* develop into latent forms leading to long-term chronic infections. However, whether intracellular pathogens exploit host biological processes to establish persistent chronic infections is poorly understood. A potentially attractive pathway for latent forms of pathogens to target is a state of irreversible cell-cycle arrest termed cellular senescence. Senescent cells are known to accumulate with age, potentially due to their reduced clearance via the immune system. Here we show that Toxoplasma infection induces a senescent profile in primary murine neurons *in vitro* and, strikingly, also in murine brains *in vivo*. Specifically, we found that a chronic infection with Toxoplasma leads to increased levels of the senescent markers γH2AX and p21. Furthermore, we showed that the growth of the acute parasite stage is decreased in senescent fibroblasts and that a senescent environment promotes tissue cyst formation – a phenotype we termed Senescence-Induced Stage Differentiation (SISD). Our results suggest that Toxoplasma might be co-opting senescent cells for the formation of tissue cysts, thereby ensuring long-term chronic infection and parasite transmission between hosts.

Keywords: Infection, toxoplasma, senescence, brain, mice.

P065. Cancer Biology & Oncology

Adjuvant effect of statins on brain cancer treatment

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Statins, the most commonly prescribed drugs for cardiovascular diseases, exert their effects by inhibiting the conversion of β-hydroxy-β-methylglutaryl-coenzyme A (HMG-CoA) to mevalonate. This inhibition leads to a decrease in sterol production, which is an important component of cell membranes and it leads to decreased membrane integrity. Statins also exhibit pleiotropic effects, including the suppression of growth, survival, migration of tumour cells, formation of metastasis, angiogenesis, inflammation, as well as support of apoptosis. Recent studies have highlighted the impact of statins in treating various cancer types. The most aggressive of brain tumours is glioblastoma, which is associated with high mortality rates. Our research aims to clarify the molecular mechanisms induced by the presence of statins in brain tumour tissue and explore their potential as an adjuvant treatment for brain cancer. Our project was centered on conducting a comparative analysis of simvastatin's effects on both healthy astrocytes and glioblastoma cells. We monitored the cell's morphology in the presence of simvastatin. We also studied the effect of simvastatin on cell viability and prepared 3D cell spheroids and analysed their responses to simvastatin treatment. At very low concentrations, simvastatin exhibited a supportive effect on healthy cells. As the concentration of simvastatin increased, its inhibitory influence on cell viability became stronger. Another important result is that healthy cells are more sensitive to increased concentrations of simvastatin compared to cancer cells. These revelations showed the potential differential effects of simvastatin on distinct cell types, laying the groundwork for further exploration and application in future treatments.

Keywords: Statins, adjuvant therapy, glioblastoma, astrocytes, inhibition.

P066. Clinical Research, Translational Biomedicine & Personalised Medicine

Identifying cancer-associated genes in myotonic dystrophy type 1 patients

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Myotonic dystrophy type 1 (DM1) is a debilitating autosomal-dominant genetic disorder caused by a trinucleotide expansion of unstable repetitions of CTG in the 3′ untranslated region of the myotonic dystrophy protein kinase (DMPK) gene and is characterised by myotonia, progressive muscle weakness and atrophy. Other features observed in DM1 patients are cardiac complications, sleep disorder, dyslipidemia, and insulin resistance. Studies have shown patients with DM1 are at a high risk of developing certain types of cancers. Recently, we explored the novel metabolism-related targets for DM1 and identified 71 candidate genes not previously associated with DM1 using bibliometrics and automatic text-mining analysis. Furthermore, our data also lead to a direction indicating many of these putative genes could be cancer-associated genes. We aim to investigate the relationship between DM1 and various types of cancer by performing survival analysis using Kaplan–Meier (KM) plots with the identified 71 genes to investigate the relevant cancer-associated genes. Thereafter, we sought to identify differential gene expressions (DGEs) and further validate using molecular techniques. Exploration of data is still ongoing to investigate the signalling pathways also involved with the help of various freeware bioinformatic tools. These approaches may allow the recognition of potential DM1-associated cancer genes. We strongly believe that some of these targets could be validated in patients with

DM1. In conclusion, this study will advance new insights into the relationship between DM1 and cancer.

Keywords: Myotonic dystrophy type 1, metabolism, cancer, DGEs, bioinformatics.

P067. Cardiovascular Diseases

Molecular involvement in a severe paediatric syndrome of multiple diffuse pulmonary fistulas

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Pulmonary arteriovenous malformations (PAVMs) are vascular anomalies, in which there is an anomalous connection between pulmonary arteries and veins. In 80% of cases, PAVMs are present from birth, but clinical manifestations are rarely seen before adulthood. These congenital malformations are typically associated with Hereditary Haemorrhagic Telangiectasia (HHT). HHT is one of the rare diseases, affecting 1 in 5000/8000 individuals. Most of those affected with HHT are due to mutations in genes involved in the TFG-β pathway. However, around 15% of patients do not have a genetic diagnosis and this is a real problem when making a clinical diagnosis in the paediatric age group. Molecular and functional analysis has been performed in a severe case of multiple diffuse fistulas in children in which the mutation causing this phenotype could not be found. The results obtained in the present study indicate that the joint action of two mutated genes, *MMP-3* and *PI4K*, may be involved in the appearance of a rare syndrome of multiple diffuse pulmonary fistulas, whose presence would be related to a variant of HHT of greater aggressiveness and with onset in early childhood.

Keywords: AVMs, HHT, lung, endothelium, angiogenesis.

P068. Cancer Biology & Oncology

A hMYC transgenic zebrafish model discloses the involvement of proteasomal degradation in neutrophils resistance to oncogenic transformation

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Acute Myeloid Leukaemia (AML) is the most common acute leukaemia in adults. Despite being considered a heterogeneous malignancy, AML possesses many genetic aberrations classified as prognostic factors, including overexpression of MYC and downregulation of PP2A: both proteins are essential regulators of cell proliferation, apoptosis, and differentiation, and directly and indirectly, regulate each other's activity. With a new model of zebrafish AML, we can follow the development of AML and verify the effects of different drugs in tumour development. Leveraging the zebrafish larvae for *in vivo* imaging, we studied the impact of hMYC overexpression in neutrophils on early oncogenic transformation. After the generation of a transgenic zebrafish line expressing human MYC under the control of the neutrophil-specific promoter lysozyme (lyz: hMYC), we checked the expansion of neutrophils in zebrafish larvae, revealing an early drastic expansion of neutrophils. Surprisingly, the neutrophil number gradually returned to normal levels from 10 dpf onwards, coinciding with the degradation of hMYC. We investigated effects induced by inhibition of the proteasome on the zebrafish larvae, which would offer line of sight on the potential effects on neutrophil proliferation. As MYC's degradation is regulated by the phosphorylation of two sites mediated by PP2A, the expression of these two phosphorylation has been checked as well as the expression of PP2A. Single-cell RNA analysis is highlighting the mechanisms of proteasomal degradation of oncogenic MYC by neutrophils. These data suggest a mechanism of direct interaction between MYC and the PP2A in acute myeloid leukaemia.

Keywords: AML, neutrophils, zebrafish, CMYC, PP2A.

P069. Cancer Biology & Oncology

Regulation of lysophospholipase PNPLA7 by metabolic signals in an hepatocellular carcinoma cell line

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Hepatocellular carcinoma is one the most frequent causes of cancer-related death worldwide and one of its hallmarks is dysregulation of hepatic lipid metabolism. *Patatin-like phospholipase domain containing protein 7* or PNPLA7 is a membrane-bound lysophospholipase involved in the metabolism of intracellular lysophosphatidylcholine, and is highly expressed in testes, heart and insulin-targeted tissues – liver, skeletal muscles and adipose tissue. It is known to be regulated by metabolic signals such as insulin and fast/feeding cycles, suggesting it plays a role in energy metabolism. Most research regarding this enzyme was performed in rodents and it was shown that deficiency of *PNPLA7* in mouse liver results in reduced secretion of very-low-density lipoproteins, hypoglycaemia, hypolipidemia, as well as low consumption of energy, highlighting a role for PNPLA7 in whole-body energy metabolism. However, the physiological role and regulation of PNPLA7 in the liver is still unknown, especially in hepatocellular carcinoma. In our research, we investigated the effect of metabolic signals on regulation of PNPLA7 in HepG2 cell line in a time-dependent manner. First, our results show that PNPLA7 is upregulated in low and high glucose conditions after 24 h, but downregulated after 72 h. Secondly, insulin increased PNPLA7 levels after 16 h of treatment, contrary to literature data and our previous research on human primary skeletal muscle cells. However, 24-h treatment with insulin decreased PNPLA7 levels. These results suggest that PNPLA7 might be dysregulated in the HepG2 cell line which makes it a potential biomarker and drug development target in hepatocellular carcinoma.

Keywords: Hepatocellular carcinoma, PNPLA7, insulin, glucose.

P070. Chemistry & Biochemistry

Isolation and identification of microorganisms associated with indigenous fermented milk "Nono", kefir and yoghurt

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The present study has been designed with the aim of investigating the species of lactic acid bacteria such as Streptococcus, Lactococcus, Lactobacillus and Enterococcus microorganisms associated with fermented indigenous milk products. A total of 60 samples, 20 from each state, were collected from Jigawa, Bauchi and Plateau States in Northern Nigeria at guided random. The proximate composition, biochemical and physiological properties were determined using standard methods. Lactic acid producing bacteria were isolated using the lactic bacteria culture medium (MRS media). These isolates were duly identified under the microscope using morphological, biochemical characteristics, carbon requirements and molecular parameters. The results of the molecular characterisation revealed that the organism as E1Bau3 having 93.61% pairwise to *Lysinibacillus fusiformis*, while E10Js3 with 79.20% pairwise was *Lysinibacillus sphaericus*, E4Jg1 95.03% pairwise to *Lactobacillus plantarum*. The isolate E7Bau with 98.03% pairwise was identified as *Lactobacillus lactis* and E9Js2 with 99.53% pairwise was found to be *Fractobacillus fructosus*. *Lactobacillus plantarum* (E4Jg1), *Lactobacillus lactis* (E7Bau) and JG4, BAU2 and *Lysinibacillus fusiformis* (E1Bau3) had the highest cellulolytic activity of 28.48 ± 0.21, 25.78 ± 0.21 and 27.54 ± 0.21 μmole/min respectively. *Lactobacillus plantarum* (E4Jg1) had the highest protease activity 640.89 ± 2.23 and JG1 had the highest lipase activity of 352.76 ± 9.86 μmole/min, respectively.

Keywords: Identification, microorganisms, fermented milk "Nono", Kefir.

P071. Immunology, Microbiology & Infectious Diseases

Autoantibodies against complement proteins in membranoproliferative glomerulonephritis

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Membranoproliferative glomerulonephritis (MPGN) is a chronic, inflammatory kidney disease affecting the glomeruli. Dysregulation of the complement alternative pathway (AP), complement gene variations and autoantibodies against complement components (e.g., anti-factor H (FH), C3 nephritic factor (C3NeF)) might cause or associate with MPGN, and they can also be important in diagnosis or treatment. Therefore, in this work, we analysed the presence and role of complement-specific autoantibodies in a previously published MPGN cohort. Serum samples of 100 MPGN patients were examined in ELISA. Autoantibodies were characterised regarding binding site and titre. IgG fraction was isolated from the serum using Protein G column. Immune complexes formed *in vivo* were detected by Western blot. Hemolysis assays with rabbit red blood cells were performed to determine the effect of the autoantibodies on AP-mediated complement activation. On-chip complement activation was investigated using antigen microarrays. We identified four autoanti-FH, six autoanti-Factor B (FB), five anti-C3, and twenty-seven C3NeF positive patients. Autoantibody titers varied from 1:25 to 1:12800. The autoanti-FH binding sites were localised on both the C- and the N-terminus of FH. IgG-FB and IgG-FH complexes could be detected in the IgG fraction of several patients. IgG fraction of some patients influenced the complement AP-mediated hemolysis in normal human serum. Complement and Ig-deposition on some printed complement proteins were significantly different between the MPGN and control groups. Altogether, the analysed complement-specific autoantibodies had distinct effects on complement activation. However, to determine their exact role in MPGN, further investigation is needed.

Keywords: Complement, autoantibody, membranoproliferative glomerulonephritis, alternative pathway, C3NeF.

P072. Cancer Biology & Oncology

Role of autophagy in therapy-induced senescence in thyroid cancer

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Senescence is a stable cell cycle arrest, induced by several anti-cancer treatments. It has long been considered a positive treatment outcome; however, mounting evidence suggests that senescent cells have many detrimental effects, so their targeting has been proposed to improve the anti-tumour response. Interestingly, autophagy is often induced together with senescence, but their interplay is mostly unexplored. Anaplastic thyroid cancer (ATC) is one of the deadliest solid tumours, and the existing therapies are ineffective. What role senescent cells play in the treatment of ATC, and what interplay exists between senescence and autophagy, is unknown. Here, we investigated the characteristics and the crosstalk of these two processes *in vitro*, following different treatments. Three human ATC cell lines were treated with ionising radiation (IR), or senescence-inducer palbociclib. Senescence was assessed by analysing β-galactosidase activity, cell cycle inhibitors levels, and presence of γH2AX foci. Autophagy levels were assessed by analysing LC3B and p62. The functionality of the autophagic flux was assessed by analysing p62 levels in the presence/absence of Chloroquine. IR and palbociclib efficiently induce senescence and autophagy in different ATC cell lines, as indicated by the increase in the markers analysed. The functionality of the autophagic flux seems to be impaired in two out of the three cell lines, and this impairment seems to be cell-line dependent, rather than treatment-related. These differences may uncover a differential sensitivity to the perturbation of autophagy in senescent ATC cells.

Keywords: Thyroid cancer, senescence, autophagy, senolytics, lysosomes.

P073. Immunology, Microbiology & Infectious Diseases

Microbial co-infections in upper respiratory tract: a simultaneous exploration utilising molecular and conventional diagnostic approach at ATBUTH Bauchi, Nigeria

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Microbial coinfections are a significant health concern, particularly with the global rise in tuberculosis cases, an infectious disease. In 2021, the World Health Organisation (WHO) reported that approximately 9.9–11 million people contracted tuberculosis, translating to 134 in 100,000 population. This surge in tuberculosis cases is straining diagnostic facilities. This research aimed to detect commonly found fungal and bacterial pathogens apart from *Mycobacterium tuberculosis* in sputum. The GeneXpert test was used to confirm positive and negative sputum results at the ATBUTH Tuberculosis Laboratory. These samples were concurrently cultured on chocolate, MacConkey, and Sabouraud agar, incubated at 37°C for 18–24 h for bacteria and at 25°C for 3–7 days for fungi at the ATBUTH microbiology laboratory. We used biochemical, gram staining, and phenol mount-tease reactions to identify the isolated bacterial and fungal pathogens. Their genomic DNA extraction was conducted following the Zymo Research Quick-DNA fungal/bacterial miniprep kit's instructions and quantified with NanoDrop One at the ATBU/ATBUTH MOGID research laboratory. Conventional PCR amplification targeted universal primers for 16S rRNA and ITS genes and the amplicons were confirmed after agarose gel electrophoresis. GeneXpert confirmed tuberculosis positive cases accounted for 5.9%. The conventional analysis indicated that 42.7% had bacterial coinfections, with 57.3% showing negative bacterial growth, 8.7% showed fungal coinfections, while 91.3% had negative fungal growth. The most prevalent isolated bacterium and fungus were *Klebsiella pneumoniae* (35%) and *Candida albicans* (31%), respectively. They were followed by *Aspergillus fumigatus* (27%), *Klebsiella oxytoca* (25%), *Staphylococcus aureus* (14%), *Rhizopus* spp (14%), *Aspergillus niger* (13%) and *Streptococcus* spp (7%). *Cryptococcus* spp. (4%) and *Pseudomonas aeruginosa* (2%) had the lowest occurrence among the coinfections. All purified genomic DNA of the most prevalent isolates were checked to be quantitative, and the amplified selected regions detected with visible bands on all the isolates. This study assessed the prevalence of suspected co-infections alongside tuberculosis and adapted the use of both molecular and conventional diagnostics. This approach can enhance the simultaneous approach for diagnosing these microbial infections in individuals, and provide valuable data for physicians to ensure accurate clinical care for human health.

Keywords: Co-infections, PCR, diagnostic, prevalence, health.

P074. Genetics & Epigenetics

Methylation profiling of peripheral blood mononuclear cells in neonatal sepsis

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Neonatal sepsis is a severe clinical complex syndrome that occurs within the first 28 days of life of the newborn and is manifested by an exacerbated systemic inflammatory response of the host against the presence of pathogens of bacterial, viral or fungal origin. Unfortunately, the immune response can damage the host's own tissues causing fatal multi-organ dysfunction. Currently, neonatal sepsis is the most common cause of morbidity and mortality in newborns, and although survival has improved, its aetiology is still not fully understood. Currently, a distinction is made between microbiological sepsis (positive blood culture) and clinical sepsis (with altered clinical manifestations). Therefore, there is a special interest in finding new biomarkers for early diagnosis and appropriate treatment. In recent years, it has been shown that epigenetic changes leading to reprogramming of gene expression in immune cells can occur during infection, including DNA methylation. DNA methylation can influence the regulation of gene expression associated with biological processes such as inflammatory responses by changing DNA methylation patterns. In this work, we aim to identify DNA methylation profiles, particularly in promoters of key genes involved in inflammation, cell differentiation and immune cell function to provide potential tools for understanding the pathophysiology of sepsis and to provide new biomarkers for neonatal sepsis diagnosis and prognosis.

Keywords: Neonatal sepsis, DNA methylation, inflammation, biomarkers.

P075. Computational Biology, Bioinformatics & Artificial Intelligence

Multiple sclerosis drug target discovery and assessment using PPI networks

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Mechanisms behind complex diseases, such as multiple sclerosis (MS), cannot be attributed to individual genes/proteins. Omics

data provide insights at gene/protein level, but the phenotypic effect is elucidated at the system level ("genes do not work alone"). There are multiple ways to affect biological systems behind a disease and single/few variants can rarely explain a phenotype. Furthermore, a disease signal spread over multiple genes/proteins can be difficult to identify without large cohorts. Here, we used a PPI interactome (protein–protein interactions) based on a strong experimental foundation and extracted a high-confidence subset of interactions to find biological systems enriched in MS disease signal. First, gene-level P-values for association to MS (derived from UK biobank) were mapped to the interactome and our own System Significance algorithm was applied to identify sub-networks enriched in the disease signal. Performance was evaluated based on rediscovering effective MS drug targets. In total, we identified 10 networks (219 unique proteins) enriched in disease signals and observed six times more MS drug targets compared to random expectancy and gene-level data alone. The retrieved biological functions aligned with known MS biology (e.g., neuronal degeneration and muscular dystrophy), suggesting this method as a valid approach for the discovery and assessment of novel drug target candidates.

Keywords: Systems biology, network biology, target discovery, protein–protein interactions, multiple sclerosis.

P076. Clinical Research, Translational Biomedicine & Personalised Medicine

Allotopic expression of hydrophobicity-reduced proteins as an approach to overcome mitochondrial dysfunction-related diseases

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Mitochondrial diseases are prevalent genetic disorders characterised by defects in oxidative phosphorylation (OXPHOS). These disorders can result from mutations in OXPHOS protein-encoding genes found in both nuclear and mitochondrial genomes. Mitochondrial DNA (mtDNA) mutations are responsible for approximately 80% of cases in adults and 25% in children. These diseases primarily affect energy-demanding tissues like nerves and muscles, exhibiting diverse clinical symptoms. While direct manipulation of human mtDNA is still in development, alternative approaches for mitochondrial disease therapies, such as allotopic expression, have been proposed. Allotopic expression involves introducing a healthy wild-type copy of the affected gene into the nucleus and targeting the corresponding cytosol-synthesised protein to mitochondria replacing the faulty mitochondrial counterpart. However, several considerations must be addressed, with a crucial focus on the translocation of the precursor protein (immature protein) across two membranes during the import process into mitochondria. The high hydrophobicity profiles of some inner-membrane proteins pose an obstacle to the functional relocalization of mitochondrial genes to the nucleus. Therefore, lowering their average hydrophobicity is essential to

prevent misrouting to the endoplasmic reticulum (ER) and enable proper passage through the inner mitochondrial membrane primary alpha-helix translocon (TIM23). To quantify how the hydrophobicity of each alpha-helix governs the insertion of membrane proteins by TIM23, an apparent free energy of membrane insertion (ΔGXapp) was estimated for each of the 20 amino acids. In this work, we underscore the concept that increasing the $\mu\Delta$Gapp (which decreases hydrophobicity) of certain transmembrane stretches (TMS) may facilitate the import of proteins into mitochondria.

Keywords: Genetic disorder, mitochondrial dysfunction, therapeutics, gene editing, organelle import.

P077. Immunology, Microbiology & Infectious Diseases

Analysing HERV envelope proteins *in silico*: insights into immunosuppression mechanisms

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Human Endogenous Retroviruses (HERVs) are remnants from paleo viral infections that became part of the human genome millions of years ago. During evolution, these retroelements suffered several genetic edits that made them unable to code for proteins. However, HERVs that still have intact ORFs and can code for proteins are subjects of a strict epigenetic repression mechanism in regular tissues. In pathological contexts, nevertheless, they overcome their epigenetic control, resulting in pathological-specific overexpression. Unfortunately, their biological impact on diseases like cancer remains mostly unknown. HERV envelope proteins (Env) are one of the most studied products of HERVs due to their potential interaction with the immune system as a membrane protein; sadly, only Syncytin crystal structures have been elucidated, representing a pivotal advancement in our comprehension of HERV Envs. Here, we used computational models to scrutinise the structural features of several HERV Envs, based on their known sequences, revealing that the usage of rare codons, the absence of signal peptides, and variations in the furin cleavage site, etc., can exert substantial influence on HERV Env biosynthesis, subcellular localization, and overall functionality. Furthermore, it is unclear how the immunosuppressive domain (ISD) present in the Env causes retroviral-induced immunosuppression. We found that HERV-ISD peptides can bind to MHC class I and II molecules and be significantly less immunogenic than other studied epitopes ($P < 0.01$). This suggests that tumours may use the presentation of these immunosuppressive HERV ISD peptides in the MHC complex to evade the immune system and promote tumour growth.

Keywords: HERVs, envelope protein, immunosuppressive domain, MHC complex.

P078. Immunology, Microbiology & Infectious Diseases

The impact of non-antifungal drugs on antifungal susceptibility in *Candida albicans*

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Candida albicans is a commensal of the human body which can turn pathogenic, causing mild to live-threatening fungal infections. Treatment options are limited and often complicated by resistance formation against available standard antifungal drugs. Patients with a high risk of developing a severe fungal infection suffer from underlying co-morbidities, which require the intake of broad drug cocktails. We aim to investigate the impact these non-antifungal drugs have on antifungal susceptibility in *Candida albicans*. By conducting a systematic keyword search on 813 treatment guidelines from the Association of the Scientific Medical Societies, we established a drug library encompassing 129 FDA-approved drugs which are often taken by patients with high risk for fungal infections. The drugs were screened on *Candida albicans* growth; alone and in combination with three different concentrations of the standard antifungals fluconazole and anidulafungin. While eight drugs (~5.7%) reduced fungal growth by more than 50%, 24 drugs (~18.6%) even increased fungal growth by at least 50% when combined with fluconazole and/or anidulafungin. Remarkably, interactions with fluconazole were considerably more potent compared to those with anidulafungin. Checkerboard assays demonstrated that nine drugs – carvedilol, desogestrel, dienogest, doxorubicin, estradiol, levothyroxine, loperamide, mycophenolate and salmeterol – were antagonistic to fluconazole. Future experiments will use *Candida albicans*-infected *Galleria mellonella* larvae to evaluate the effects of the nine identified fungal growth enhancers on larvae survival and fluconazole susceptibility *in vivo*. In the long term, linking specific drugs to decreased antifungal susceptibility might reduce clinical treatment failure in *Candida albicans* infections.

Keywords: Antifungal susceptibility, fungal infection, drug screen, *Candida albicans*, fluconazole.

P079. Chemistry & Biochemistry

Secretome analysis and molecular identification of novel plastic-degrading microorganisms isolated from plastic dumpsites in Abuja, Nigeria

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Plastics are important polymers in our everyday lives which take decades for natural degradation. Continuous and indiscriminate disposal of the various forms of these plastics is a leading cause of environmental pollution which affects both marine and human health. In this study, the ability of locally-isolated microorganisms to degrade plastics was determined. Microbes were isolated from the plastic dumpsite and applied in degrading polyethene (PE), polyvinyl-chloride (PVC), polyethylene-terephthalate (PET) and polyurethane (PUR) plastics using the submerged fermentation method. Aliquots were obtained every 24 h for enzyme screening. Weight loss of the plastics and FTIR analysis of the aliquots were determined. The isolates with plastic-degrading potentials were molecularly identified as *Aspergillus niger, Fusarium solani, Aspergillus fumigatus, Aspergillus oryzae, Pseudomonas spp* and *Bacillus spp. A. niger* and *Pseudomonas spp* showed higher cutinase activity of 2.345 U/mL and 2.196 U/mL, laccase activity of 2.215 U/mL and 3.234 U/mL respectively. *A. oryzae* has higher lipase activity of 2.152 U/mL. *Fusarium solani* showed varying activities for the test enzymes. The best degradation was observed after 10 days of incubation with a 0.45% and 0.3% weight loss by *Pseudomonas spp* and *F. solani* respectively. The Fourier-transform-infrared-spectroscopy (FTIR) analysis of the best fractions revealed the presence of ethers, alcohols and carboxylic acids. The result obtained in this study revealed new novel microbes which can effectively carry out microbial and enzymatic degradation of PE, PVC, PET and PUR plastics. Strain improvement and overexpression of these degrading enzymes for biotechnology applications can provide an eco-friendly and less toxic plastic waste management method.

Keywords: Biodegradation, plastics, microorganisms, enzymes, human-health.

P080. Cancer Biology & Oncology

Targeting undifferentiated cells in neuroblastoma

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Neuroblastoma is the most common extracranial solid tumour occurring in childhood and is characterised by poor outcome in advanced stages, with high frequency of metastasis, relapse and resistance to therapy. It is thought that undifferentiated neuroblastoma cells, frequently named as "neuroblastoma cancer stem cells (NBCSC)", are the main cell population responsible for these processes. Our hypothesis states that there are signalling pathways particularly relevant to NBCSC and their activation is associated with a higher number of metastases, increased aggressiveness, and ultimately, a worse prognosis for neuroblastoma patients. We are interested in identifying pathways that exhibit these characteristics and specifically target them to understand the mechanism behind their activation. One such pathway is the Rho/ROCK signalling pathway, in particular the Rho Associated Coiled-Coil Containing Protein Kinase (ROCK). ROCK is a serine/threonine kinase that acts as downstream effector of some Rho GTPases, regulating contractility, cell adhesion and motility. Although some data from our laboratory and others place ROCK as a possible target in neuroblastoma, its function in the malignant NBCSC has not been explored. In the preliminary work presented, we are using different available specific inhibitors of ROCK in undifferentiated neuroblastoma cells to analyse their function in differentiation

and migration. Our goal is to understand the biology of the NBCSC and identify suitable molecular targets to impact in this cell population.

Keywords: Neuroblastoma, undifferentiated cells, ROCK, inhibitors.

P081. Pharmacology, Toxicology & Nutrition

Microbial contamination in grilled meat (Suya): an emerging environmental and public health challenge

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Ready-to-eat meat products, like Suya, offer numerous nutritional benefits but improper handling and processing can pose environmental and public health threats. Suya, a cherished sub-Saharan African delicacy, stands at the intersection of these challenges due to its susceptibility to microbial contamination and emerging antimicrobial resistance. This study explores the intricate relationship between microbial contamination, food safety, and environmental health. Bacterial pathogens, including Staphylococcus spp., *Escherichia coli*, Bacillus spp., Salmonella spp., and Klebsiella spp., were found to be prevalent in some of the tested samples. Fungal contaminants, primarily Aspergillus spp. (flavus, niger, and fumigatus), along with Penicillium spp., Rhizopus spp., Mucor spp., and *Candida albicans* were also observed. Parasitic infestations, including beef tapeworm, human roundworm, hookworm, *Entamoeba histolytica*, and *Giardia lamblia*, were also discovered, further amplifying health concerns. These microbial contaminants were also identified in spices meant to supplement and improve Suya's organoleptic and nutritional value. A paramount concern is the surge in antimicrobial resistance observed within microbial isolates from the tested samples, a phenomenon with far-reaching implications for both environmental and public health. Introduction of the microbial contaminants have been linked to unhygienic practices during its storage, processing, and packaging, such as bare-hand contact, exposure to vehicular emissions, or other environmental contaminants, and packaging in inked papers with contaminants, which makes it unfit for human consumption. As the world grapples with the complex issue of environmental impacts on human health, this research underscores the urgency of comprehensive food safety measures and hygiene practices across the ready-to-eat-meat production and consumption chain.

Keywords: Antimicrobial resistance, microbial contamination, food safety, public health, hygiene.

P082. Immunology, Microbiology & Infectious Diseases

Investigating the molecular basis of the pro-viral role of ADAR1 in productive HSV-1 infection

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ADARs (Adenosine deaminase acting on RNA) play an important part in immune regulation by modifying dsRNA, effectively disabling self-recognition by immune sensors. Pro- as well as anti-viral effects of ADARs have been described in RNA viruses, but its functions remain unexplored in DNA viruses. Here, we are investigating the role of ADAR1 in the productive infection of herpes simplex virus 1 (HSV-1), an important human pathogen well known as the causative agent of cold sores. Our study shows that HSV-1 replication is significantly impaired in ADAR1 deficient cells, which could be restored by complementing the inadequacy, especially by interferon inducible p150 isoform. Detailed screening into immune pathways revealed that PKR (protein kinase R) autophosphorylation is the principal cause of restrained replication. Knocking down PKR in ADAR1 deficient cells could significantly reinstate viral replication, supplementing earlier observations. Furthermore, activation of PKR and downstream signalling (eIF2a) in the absence of ADAR1 suggests that a translational shutdown is initiated thus preventing viruses from replicating efficiently, concluding a pro-viral role of ADAR1. Currently, we are investigating further the molecular mechanisms, such as, presence of mediator for ADAR1-PKR that leads to activation of the pathway and subsequent translational arrest.

Keywords: HSV1, ADAR1, pro-viral, activation of PKR.

P083. Chemistry & Biochemistry

Repurposing the cholesterol-lowering drug bempedoic acid (ETC- 1002) for targeted cancer treatment

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Bempedoic acid (BA), is a novel drug that has recently been used as a statin replacement in patients with atherosclerosis cardiovascular disease. BA is used to reduce LDL-C. This is accomplished through the metabolic activation of BA by the enzyme ACSVL1. ACSVL1 activates BA and links it to CoA through a thioester linkage to form Bempedoyl-CoA. It is this form of BA that is then responsible for the inhibition of ACLY, the enzyme responsible for generating the main cytosolic pool of acetyl-coenzyme A (AcCoA). By limiting the action of ACLY, the production of AcCoA as the main fatty acid synthesis precursor is limited, therefore reducing fatty acid production. BA's mode of action and its mechanism of activation is linked to ACSVL1 that is found in the liver. Consequently, exploring other routes for the metabolic activation of BA with no tissue association could allow for its repurposing and the selective targeting of cancer cells. Cancer cells have a dependency on fatty acids, and thus increased

fatty acid synthesis is observed. With the increase in fatty acid synthesis thus leading to the dependence on ACLY, utilising BA or BA analogues could be a potential inhibitor for ACLY. With the current metabolic activation for the BA being limited to the liver we would like to explore the CoA biosynthesis pathway as a potential metabolic activation route for BA therefore bypassing the tissue specificity while decreasing fatty acid production. Our proposal is that this decline in fatty acids would affect the rapid cell proliferation.

Keywords: Metabolic activation, cancer, fatty acids, coenzyme A, ATP citrate lyase.

P085. Genetics & Epigenetics

Loss of SIRT7 promotes G-quadruplex DNA mediated genome instability in Hutchinson Gilford progeria syndrome

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Genome instability is a hallmark of ageing and increased DNA damage accumulation leads to numerous premature ageing diseases. In patients suffering from Hutchinson-Gilford-Progeria-Syndrome (HGPS), rapid ageing and associated accumulation of (epi)genetic alterations and instability is caused by the expression of progerin, a protein which disrupts the nuclear lamina, promoting genomic alterations and rapid ageing phenotype. The relationship between double strand breaks (DSBs) and ageing has been established. However, there is an unmet need to identify where age-associated DSBs occur in the genome. We hypothesise that G-quadruplexes (G4s) may elevate ageing-related DSB levels. To generate a suitable cellular model to study DSBs in the context of ageing, we derived induced pluripotent stem cells (iPSCs) from HGPS patient fibroblasts and we differentiated iPSCs into induced mesenchymal stromal cells (iMSCs) and characterised them according to the criteria of the International Society for Cellular Therapy. We further demonstrated that iMSCs express progerin and exhibit rapid ageing phenotype. To remove potential genetic donor biases, we employ the CRISPR-Cas9 technology and perturbation methods to reduce progerin expression in patient-derived iMSCs. Together with the López-Otín lab, we started to establish bone marrow-derived MSC cultures from their previously established HGPS mouse model. In this study, we aim to map age-specific DSBs, genome-wide, on HGPS patient and murine model samples. We will systematically investigate DSBs and G4s formation in the human and murine HGPS rapid ageing models. Ultimately, our study will provide novel insights into the consequences of endogenous DSBs and G4 formation for mammalian ageing.

Keywords: G-quadruplex, DNA double strand breaks, HGPS, DDX21, ageing.

P087. Computational Biology, Bioinformatics & Artificial Intelligence

Unlocking the potential of the miniprotein design platform: addressing research challenges and public demands

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Miniproteins are naturally occurring or engineered protein molecules that are smaller than typical proteins. They have unique properties due to their size and structure, which makes them useful in various healthcare applications. They have many functional groups, enabling strong and specific target interactions. Additionally, they may bypass some issues associated with antibodies, such as bioavailability, complicated production, and potential immune reactions. Their versatility is exemplified in roles such as blocking protein interactions, acting as binders for small molecules, serving as receptor substitutes in diagnostics, and detecting specific protein markers, among other applications. We aim to establish a semi-automated platform that integrates computational protein design and screening to rapidly identify and produce miniproteins. The workflow begins by using knowledge-based and AI methods to design proteins tailored to the target. Subsequently, we employ recombinant or solid-state synthesis to produce these proteins. Finally, we assess the new proteins' binding affinity, stability, and overall secondary structure, primarily utilising Surface Plasmon Resonance (SPR) and circular dichroism (CD). In addition, functional cellular assays will be used to validate the proteins' effectiveness in a cellular context. Our ultimate goal is creating an efficient protocol for protein design targeting diverse applications. The platform's effectiveness will be assessed based on its performance on particular protein targets, leveraged by different groups from our institute. This platform is designed to strengthen research and public health systems by providing timely support in urgent situations.

Keywords: Miniproteins, AI, surface plasmon resonance, drug discovery platform.

P088. Obesity, Diabetes & Other Diseases

MAE-optimised *Enhydra fluctuans* L. phytocompounds for functional food and medicine: antihyperglycemic and cytotoxic evaluation

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This study aims to prove that *Enhydra fluctuans L.*'s bioactive phytocompounds could be a powerful functional food and pharmaceutical compound for diabetes management. This study used *in silico* molecular docking and pharmacokinetic analysis on Enhydra phytochemicals. The phytochemicals showed promise in inhibiting α-amylase and α-glucosidase enzymes, which contribute to high blood glucose levels after meals. Phytocompound binding energies ranged from -8.4 to -4.8 kcal/mol. The analysis also

showed that phytochemicals have low to moderate absorption, distribution, metabolism, and excretion (ADME) and toxicity. The experimental design was created to enable industrial extraction of bioactive phytocompounds from *E. fluctuans* leaf with high yield recovery. Seventeen microwave-assisted extraction (MAE) runs yielded the optimised response variables, including total phenol, flavonoid, tannin, and antioxidant activities (DPPH and FRAP). These results were achieved at 58°C, 803 W microwave power, and 41 min processing time. Thin-layer chromatography (TLC), ultraviolet–visible (UV–Vis) spectroscopy, Fourier-transform infrared (FTIR), and liquid chromatography-mass spectrometry (LC–MS) spectral analysis confirmed 6 of *E. fluctuans*' 13 primary phytocompounds. Enzymatic activity *in vitro* showed significant inhibition of α-amylase (IC$_{50}$ 63.98 ± 3.56 μg/mL) and α- glucosidase (IC$_{50}$ 94.17 ± 7.57 μg/mL). The hemolytic activity was below 2%, meeting ISO standards for biomaterial intervention suitability. The MTT assay showed minimal toxicity at 62.5 μg/mL, while the CAM assay showed no toxicity at any concentration. This research helps food and pharmaceutical professionals, scientists, and industry experts develop antidiabetic foods and medications to help diabetics manage their condition and improve their health.

Keywords: Diabetes mellitus, *Enhydra fluctuans*, phytocompounds, optimization, enzyme inhibitory assay, cytotoxicity.

P089. Cellular & Molecular Biology

Identification and functional characterisation of alternatively spliced novel isoforms of human genes encoding small heat shock protein 8 and deciphering their potential role in defence against environmental and physiological stress

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One of the primary factors for maintaining cell homeostasis is the adjustment of protein synthesis to environmental and physiological threats (proteostasis). A perpetual requirement for proteostasis is essential for adapting to changes in cell environment which can otherwise lead to misfolding and aggregation of proteins which is achieved by an elaborate chaperone network. sHSPs are a unique class of molecular chaperones characterised by a core ACD flanked by variable N-terminal and C- terminal domains manoeuvring an early chaperoning role in case of misfolded proteins, often prior to refolding attempts by ATP-dependent chaperone complexes. Alternative splicing is the phenomenon of removal of specific sequences from a pre-mRNA and the joining together of remaining sequences in order to generate multiple functional RNAs or proteins from a single transcript. There is not much detail available about the alternative RNA splicing of these small heat shock proteins as a co-transcriptional and post transcriptional processes which makes it an intriguing topic to be explored. HSPB8 is one of the comrades of the small heat shock protein family. In the current study we have predicted and confirmed two alternatively spliced novel isoforms of HSPB8 gene. These spliced variants have smaller size owing to a smaller N terminal region and lack several structural motifs that are essential for various functional endeavours of the HSPB8 protein. *In silico* analysis of the conceptually translated

protein was carried out using various bioinformatic tools in order to gain understanding into their properties so as to explore their possible potential in therapeutics.

Keywords: sHSP, alternative splicing, stress, isoform, heat shock.

P090. Cellular & Molecular Biology

FEBS activities for PhD students and young scientists

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The Federation of European Biochemical Societies (FEBS) is a non-profit organisation promoting research and education in molecular life sciences across Europe and neighbouring regions. FEBS has many programmes and initiatives dedicated to early-career researchers. FEBS offers Fellowships to support and promote mobility of young researchers among FEBS countries. Youth Travel Fund grants are available to attend Advanced Courses (lecture courses, workshops, practical courses, and special meetings) organised by experts on different topics. The Young Scientists' Forum (YSF) is a popular event for about 100 selected PhD students and postdocs that takes place in conjunction with the annual FEBS Congress. Participants get the opportunity to share science with peers, attend career skills sessions, meet keynote lecturers, and enjoy a social programme. FEBS provides financial support for participation in the YSF and the ensuing Congress via YSF grants covering registration and accommodation and up to 80% of the travel costs. FEBS supports participation of many young scientists in the FEBS Congress through the FEBS Congress Bursaries scheme. The FEBS-IUBMB-ENABLE Conference, organised by young scientists for young scientists, includes a scientific symposium, a career day, and offers a concrete opportunity to network, explore career options, and gain transferable skills. Discounted registration and travel grants are available to support attendance from around the world. The FEBS Junior Section is an initiative aimed at building a network of young scientists in the molecular life sciences, fostering collaboration and mobility across Europe and beyond. They organise online talks and deliver networking events for young scientists.

P091. Immunology, Microbiology & Infectious Diseases

Unravelling functional consequences of tumour-mediated galectin downregulation in dendritic cells

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Tumour immune-evasion mechanisms remain poorly understood, despite being crucial to improve current immunotherapies. Glycans and their interacting proteins, namely galectins (gals), pose another level of cellular organisation instrumental in modulating immune-cell function and are considered as a novel mechanism

of tumour immune-evasion. Nonetheless, their role in anti-tumour immunity is only recently becoming widely acknowledged. Gals are carbohydrate-binding lectins that modulate immune-cell function by organising and clustering glycosylated cell-surface proteins into functional membrane microdomains, in turn influencing numerous immune-cellular processes. In professional antigen presenting cells, namely dendritic cells (DCs), the role of gals has not yet been characterised. We set out to study galectin function in DCs using knockdown technology on primary DCs. Our results show that gal-deficiency in DCs impairs their capacity to interact and form stable immune synapses with T cells and ultimately promote T cell effector responses. In agreement with our hypothesis that highlights the role of galectins in initiating adaptive immunity, we found galectin expression to be downregulated in DCs upon co-culture with both 2D and 3D tumour microenvironment model systems. Furthermore, cancer patients with low-galectin expression in the DC compartment show a poor prognosis compared to those with high-galectin-DCs. Overall, our data suggest an essential role for galectins during DC-mediated anti-immunity. We hypothesise that disruption of the galectin-mediated interactions could be exploited by malignant cells, posing a novel melanoma immune-evasion mechanism.

Keywords: Dendritic cells, galectins, tumour-immune escape.

P092. Neuroscience, Psychiatry & Mental Health

Amelioration of ageing features in mice through cellular reprogramming

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Although our knowledge about brain physiology has expanded significantly in the last decades, most neurological conditions remain incurable. The mammalian brain has very limited regenerative capacity, as most of its cells are not replaced in normal or pathological situations. Neurons and their connections are established early in life and are designed to age with the individual. Despite the diverse and intricate etiologies of these disorders, advanced age is a major risk factor. Ageing brains undergo cognitive decline associated with loss of homeostasis, and decreased neuronal performance and neuroinflammation. We take advantage of the reprogramming technology to address neural cell rejuvenation. Cell reprogramming has emerged as a method to reverse the age and identity of virtually any cell to an embryonic-like stage by the action of the four Yamanaka Factors (4F). Partial reprogramming (PR), the transient expression of the 4F, has been shown to be sufficient to lead the cells to a youthful state through remodelling the epigenetic landscape. We applied PR to mice at different ages, analysed their memory, learning and motor skills and studied their brains at the histological and gene expression levels. We observe a robust improvement in behavioural tests in animals subjected to PR. Moreover, we measured two epigenetic marks that correlate with ageing in primary astrocytes aged *in vitro*, and both marks were restored to a younger state. We propose that rejuvenation-by-reprogramming of brain cells could have therapeutic potential to modify the course of ageing and thereby reduce disease susceptibility in the central nervous system.

Keywords: Ageing, epigenetic, cell reprogramming, rejuvenation.

P093. Immunology, Microbiology & Infectious Diseases

Bisphenol a negatively impacts cellular vascularization processes related to early pregnancy

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Spiral artery (SA) remodelling is a pregnancy-associated vascular adaptation that supports placental and fetal development. Cellular processes required for successful remodelling include extravillous trophoblasts (EVTs) invasion, vascular smooth muscle cells (VSMCs) switch from contractile to synthetic phenotype, and migration. Previous studies showed that mast cells (MCs) are able to promote these cellular processes. Bisphenol A (BPA), an endocrine-disrupting chemical (EDC) abundantly present in the environment, has been shown to interfere with SA remodelling *in vivo*. Due to their receptors' repertoire, MCs are potential targets of BPA. Our study aims to investigate whether BPA exposure impacts the response of EVTs and VSMCs to MCs *in vitro*. Transwell invasion assays were performed to test the impact of BPA (0.1, 1, 10, 100 μM) on the invasion and migration ability of mice EVTs (SM9-2 cell line) and primary uterine VSMCs when cocultured with MCs (MC/9 cell line). Furthermore, BPA influence on VSMC phenotype switch when cocultured with MCs was assessed through antibody targeting of two phenotype marker proteins, fibronectin and α-smooth actin, after 24 h exposure using immunohistochemistry. When BPA was added to the system, MCs lost their ability to significantly increase EVT invasion, as well as VSMC migration. Furthermore, the significant fibronectin increase observed when VSMCs are cultured with MCs, which is considered an indicator of the switch promotion to the synthetic phenotype, was not observed when cells were exposed to BPA. Our data show that exposure to BPA disrupts mast cell promotion of mice EVTs and VSMCs functionality.

Keywords: Bisphenol A, pregnancy, mast cells, spiral artery remodelling, endocrine disrupting chemicals.

P094. Immunology, Microbiology & Infectious Diseases

ER stress responses in airborne microbial component-induced toxicity

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ER (endoplasmic reticulum) is not only a complex organelle responsible for protein synthesis, folding, and lipid metabolism, but also plays a critical role in sensing cellular stress and maintaining cellular homeostasis. When the ER becomes stressed with toxicants leading to protein misfolding, lipid imbalances, or nutrient deprivation, it triggers the unfolded protein response (UPR) to restore ER homeostasis. If ER stress is prolonged or severe, the UPR can activate pathways that lead to cell death. In this study, we investigated the effects of exposure to airborne microbial components on ER stress at the molecular level via qPCR and western blotting. The protein expression of several antioxidants was regulated by microbial component exposure. Moreover, they have been shown to modulate signals associated with apoptosis. In particular, the expression of CHOP (C/EBP homologous protein) was changed upon treating them. These results suggest that airborne microbial components induce ER stress, associated with apoptosis and inflammation.

Keywords: Air-borne microbial components, toxicity, ER stress, CHOP.

P095. Chemistry & Biochemistry

Effects of α-synuclein proteoforms on the liquid–liquid phase separation and aggregation of α-synuclein

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The aggregation of α-synuclein (αSyn) is linked to a family of neurodegenerative disorders known as synucleinopathies, most prominently Parkinson's disease (PD), which affects more than 6 million people worldwide. Clinically, PD is characterised by motor symptoms, including rigidity and tremor, while cognitive impairment typically manifests at advanced stages. The predominant αSyn isoform is expressed as a 140-amino acid protein (αSyn-140). However, multiple proteoforms of αSyn have been reported, with increasing evidence that these variants are involved in the misfolding and aggregation of αSyn-140. Recently, liquid–liquid phase separation (LLPS) has emerged as a new paradigm in biomolecular self-assembly, leading to the formation of dense liquid-like condensates from initially dilute solutions. Liquid condensates can further undergo liquid-to-solid transition (LST) into aggregate-rich structures. Therefore, this "condensation pathway" (the formation of amyloids through liquid condensates) presents an alternative to the traditionally studied "deposition pathway" (the formation of amyloids directly from monomers) of aggregation. To investigate the involvement of proteoforms in αSyn aggregation, we recombinantly produced a series of αSyn constructs. Using solubility predictors, experimental aggregation assays, kinetic analysis, and fluorescence microscopy, we elucidated the aggregation mechanisms in the deposition pathway and in condensation pathways. We found marked differences in aggregation kinetics, morphologies and phase boundaries between the proteoforms, as well as a modulation in the overall phase behaviour of the predominant αSyn-140. Taken together, these results offer further understanding of the role of αSyn proteoforms in the aggregation of αSyn, offering new insights into the onset and development of synucleinopathies.

Keywords: Neurodegeneration, α-synuclein, liquid–liquid phase separation, amyloid aggregation.

P096. Cellular & Molecular Biology

K29-linked ubiquitylation regulates SUV39H1 stability to promote epigenome maintenance

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K29-linked ubiquitin (Ub) chains represent the most common "atypical" Ub linkage type in unperturbed mammalian cells and have been suggested to facilitate proteasomal degradation of proteins modified by K48-linkages. However, K29-linked Ub polymers (K29-Ub) remain understudied due to a paucity of tools for probing their cellular functions. We generated a Ub replacement system allowing for selective and conditional abrogation of K29-linked Ub chain formation in human cells. Applying this system, we profiled global ubiquitylation and proteome changes resulting from disruption of K29-linked ubiquitylation in order to identify the cellular targets of this modification. Among a range of regulated proteins, we identified and validated the H3K9me3 methyltransferase SUV39H1 as a prominent cellular target of K29-linked ubiquitylation. Furthermore, we demonstrate that K29-linked ubiquitylation and ensuing proteasomal degradation of SUV39H1 is catalysed by the HECT E3 ligase TRIP12, which we show is the main enzyme responsible for K29-Ub formation in the nucleus, and is antagonised by the K29-Ub deubiquitinase TRABID. Stabilisation of SUV39H1 via abrogation of K29-Ub formation leads to an accompanying increase in H3K9me3 levels. Collectively, these findings identify SUV39H1 as an important cellular target of proteasomal degradation via K29-Ub and reveal a key role of K29-linked ubiquitylation in promoting epigenome maintenance.

Keywords: Proteostasis, ubiquitin, degradation.

P097. Cellular & Molecular Biology

The response of photosynthesis in maize and sorghum under salt stress

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Photosynthesis serves as a global stress sensor in plants, algae and cyanobacteria, which has a direct impact on human health. The impact of salinity on photosynthesis in maize (*Zea mays* L. Kerala) and sorghum (*Sorghum bicolor* L. Shamal) was investigated in this study. The plants were grown in a Hoagland solution with different NaCl concentrations (0–200 mM) for 15 days. The effects of salinity on photosynthesis were estimated using chlorophyll fluorescence (PAM and JIP test) and P700 photo-oxidation. The results showed that salt stress leads to: (i) an influence on the effective PSII antenna size (ABS/RC) and PSI photochemistry; (ii) a decrease of the photochemical quenching (qp), the electron transport from QA to the PSI end electron acceptors (REo/RC) and the possibility of their reductions; (iii) an increase of the regulated and non-regulated energy losses. The data also revealed a reduction of the pigment content, an increase in the amount of H_2O_2 and lipid peroxidation, which correspond with decreased membrane stability. The parameters that can be used to evaluate the sensitivity of plants to salt stress were determined.

Keywords: Maize, sorghum, salt stress, chlorophyll fluorescence.

P098. Immunology, Microbiology & Infectious Diseases

How does genetic diversity shape metabolic interactions in *Pseudomonas aeruginosa*?

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Antimicrobial resistance is rapidly increasing in prevalence at least partly because of overuse of antibiotics in human and agricultural clinical settings. *P. aeruginosa* is a Gram-negative bacteria that inhabits a variety of natural environments including soil, water, plants, animals, and humans. As an opportunistic pathogen, it is an important cause of hospital-acquired infection, particularly in immunocompromised and critically ill patients. Due to its versatile genome, it is able to adapt quickly to new environments and can therefore invade a wide range of anatomical sites. *P. aeruginosa* evolves resistance during infections at a very high rate, which is an important challenge for treating infected patients. It has been shown recently that *P. aeruginosa* strains are genetically very diverse and that within-patient diversity leads to larger increases in resistance in response to antibiotic treatment. However, it is also known that not only the genome, but also the metabolic states of bacteria determine antibiotic resistance. It is therefore crucial to understand how the genetic diversity transfers to the metabolic level. By targeting the core component of cell metabolism, the central carbon metabolism, I want to decipher the metabolic programming of *P. aeruginosa* that supports antimicrobial resistance. Based on a bacterial strain collection that contains 27 natural strains and 2 lab strains, I will apply systems-biology based strategies to correlate phenotypes to genotypes by investigating metabolic reactions to the availability of different nutrients.

Keywords: *Pseudomonas aeruginosa*, antibiotic resistance, genetic diversity, central metabolism.

P099. Cellular & Molecular Biology

Study and characterisation of Mip6 export mechanisms

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Eukaryotic gene expression is a process which comprises different interconnected steps, including chromatin modification, transcription, RNA processing, export to cytoplasm, translation and degradation. Mip6 is a protein that participates in some of these steps, having a role in the homeostasis of stress response transcripts. Mip6 is composed of four RRMs and, through the W442 residue in the RRM4, is able to interact directly with the export factor Mex67, which enables its export to the cytoplasm. However, there must be another export pathway, since the nuclear retention that is observed when the Mip6 Mex67 binding is broken is only partial. Using *in silico* approaches, we predicted two putative nuclear export signal sequences that might be Mip6 export mechanisms. One of them is located in the RRM4, next to the W442, and seems to be an unconventional NES of those mediated by the karyopherin Msn5. In contrast, the other one is located in the C-terminal domain of the protein. Thus, in this work, we aim to study both NES as Mip6 export pathways. Our experiments revealed that mutations of amino acids comprising the NESRRM4 provoked a Mip6 nuclear retention; however, these mutations also affect Mip6-Mex67 binding, which could be the reason for this retention. Furthermore, in Pes4, Mip6 paralogous protein, there is also a NES homologous to the one in Mip6; nevertheless, point mutations in this NES provoke its accumulation in cytoplasmic granules under heat shock, but without nuclear retention. Thus, this sequence in Pes4 could not be considered as a functional NES.

Keywords: Nuclear export signal, export pathway, gene expression.

P100. Chemistry & Biochemistry

Nature turning on humanity: earthquake survivors and the importance of laboratory testing

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Environmental and public health are connected. Some occurrences affect us more than others and some can unfortunately be inevitable: natural disasters. An earthquake with a magnitude of 7.8, followed by one similarly strong hit Türkiye on 6 February 2023. People were admitted to hospitals with one thing in common, monitorisation using laboratory testing. We retrospectively analysed earthquake victims that were admitted to Gazi University Hospital between 7 February and 31 March 2023. Sixty-seven adults were investigated regarding their serum total creatine kinase (CK) (Siemens ADVIA®) and serum myoglobin (Roche® cobas) levels and indication for haemodialysis. The relationship was statistically analysed. Total CK and myoglobin turnaround time (TAT) was calculated. Mean serum myoglobin level at admission was 2740.2 ng/mL, mean total CK concentration was 5924 U/L. TAT was approximately 84 min for myoglobin and 148 min for total CK testing. There was a significant ($P < 0.05$) difference between myoglobin and CK levels of patients who underwent haemodialysis ($n = 11$) and those who did not ($n = 56$). Even after extraction, survivors keep facing health risks. CK and myoglobin are essential resources of information for forecasting and managing possible complications. It is inevitable that laboratory testing plays a key role, making it a vital element for appropriate patient care. We cannot prevent earthquakes from occurring, but we can reduce the impact of natural disasters on public health. This is a reminder that risk prevention is very valuable, because life is very valuable. Condolences to everyone affected by the recent earthquake in Morocco on 8 September 2023.

Keywords: Earthquake, creatinine kinase, myoglobin, haemodialysis.

P102. Computational Biology, Bioinformatics & Artificial Intelligence

Computational determination of potential allosteric binding sites for Ecto-5′-nucleotidase

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Ecto-5′-nucleotidase, commonly known as 5′-nucleotidase or CD73, is an enzyme encoded by the NT5E gene in humans. CD73 catalyses the conversion of AMP to adenosine. CD73 is an important regulating molecule of cancer cell proliferation, migration, and invasion *in vitro*, tumour angiogenesis, and tumour immune escape *in vivo*. These important roles of CD73 are demonstrated with preliminary bioinformatics and experimental studies. The aim of this study is to find potential allosteric binding sites of CD73 and perform a virtual screening of FDA-approved small molecules that specifically bind to those potential sites. An elastic network model based on the Essential Site Scanning Analysis (ESSA) method which takes into account amino acid side chains to explore ligand binding effect was used to detect potential ligand binding sites in the open and closed conformations of CD73. The ESSA results were also compared to the results obtained from FTMap and FPocket web servers and alternative binding sites were investigated. Virtual screening (VS) was performed using two different tools: Autodock Vina and e-LEA3D server. Potent molecules that yield high docking scores in both tools were determined. Analysis of docking studies is still ongoing and the stability of the most promising molecules will be examined using short molecular dynamic simulations. Our results would reveal alternative binding sites in CD73 and potent molecules that bind to those sites, which would provide insight into further *in vitro* and *in vivo* studies.

Keywords: Enzymes, molecular docking, virtual screening, allosteric sites, binding sites.

P104. Cellular & Molecular Biology

Sex-specific effects of bisphenol A, its substitutes and benzophenone-3 on T helper 1 cell differentiation

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T cells, known to play a pivotal role in the development of a plethora of diseases, may represent an endocrine-disrupting chemical (EDC) target. Moreover, there is accumulating evidence that endocrine-immune interactions show some sex-specificity. We aimed to study the influence of different EDCs, namely bisphenols and benzophenone-3 (single and mixtures) on T helper 1 (Th1) cell differentiation in a sex-specific approach. Female and male mouse naïve CD4$^+$ T cells were isolated. A specific cytokine cocktail and T cell receptor stimulants were added to induce Th1 cell differentiation. Treatment with different concentrations of bisphenol A (BPA; 0.01–100 µM), its analogs (BPF, BPS; 0.01–100 µM) and benzophenone-3 (BP- 3; 0.001–10 µM) started 24 h after T cell differentiation and lasted for another 72 h. Flow cytometry analyses were applied for detecting changes in specific transcriptional factor expression and cytokine production. Data were analysed with GraphPad Prism after extracting with Flowjo software. High concentrations of BPA (100 µM) and BPS (100 µM) significantly affected the viability of female T cells. A lower concentration of BPA (10 µM) significantly increased Th1 cell differentiation (based on T-bet expression) among female T cells but did not affect male T cells. Notably, mixtures of BPA and BP3 (BPA: BP-3: 0.01:0.1 µM; 1:0.01 µM; 1:0.1 µM) impaired male Th1 cell differentiation (based on T-bet expression) but did not affect female cells. Our results suggest a harmful effect of some bisphenols in supraphysiological concentrations on mouse T cell

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viability. Moreover, the tested bisphenols alone or in mixture with BP-3 affected Th1 differentiation differentially and even displayed sex-specific effects in mice.

Keywords: T helper 1 (Th1) cell differentiation, sex-specific effects, bisphenol A.

P105. Neuroscience, Psychiatry & Mental Health

Does the effect of inflammation on DA system change with age?

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It is now evident that inflammation affects dopaminergic (DA) pathways and may cause damaging effects when it becomes chronic. Chronic inflammation is a common comorbidity of several health conditions, particularly those associated with ageing, and often coincides with a decline in DA function. The decline in function can manifest itself in decreased motivation, impaired reward processing, or reduced motor activity, which significantly impact the quality of life. Whilst both inflammation and ageing negatively impact DA function, a fundamental question remains: how does the association between inflammation and the DA system change with age, or more specifically, with the health status of individuals? To address this question, our study aims to investigate the influence of inflammation on the DA system, assess the potential age-related modulation of this association, and determine whether epigenetic age serves as a more accurate reflection of the ageing process compared to chronological age. Our study will include 40 young adults and 40 seniors, with a balanced representation of inflammatory levels. We will measure blood concentrations of inflammatory biomarkers that correlate with DA-related symptoms. Participants will undergo assessment of their DA system functioning using reward-based learning tasks with generative modelling being exploited to extract behavioural markers. Additionally, we will estimate epigenetic age as a proxy of health status. With this study, we aim to contribute to our understanding of an intricate interplay between ageing, inflammation, and the DA system. This may offer valuable insights for clinical applications, including potential interventions and improved health markers via epigenetic age.

Keywords: Inflammation, dopaminergic system, ageing, reward learning.

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