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Biological Determinants of Health: Genes, Microbes, and Metabolism Exemplars of Nursing Science

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Abstract

Increasingly, nurse scientists are incorporating ‘omics’ measures (e.g., genomics, transcriptomics, proteomics, and metabolomics) in studies of biologic determinants of health and behavior. The role of ’*omics*’ in nursing science can be conceptualized in several ways: a) as a portfolio of biological measures (biomarkers) to monitor individual risk; b) as a set of combined data elements that can generate new knowledge based on large and complex patient data sets; c) as baseline information that promotes health education and potentially personalized interventions; and d) as a platform to understand how environmental parameters (e.g., diet) interact with the individual’s physiology. In this paper we provide exemplars of nursing scientists who use *omics* to better understand chronic pain vulnerability, risk for a pain-related condition, cardiometabolic complications associated with pregnancy, and as biomarkers of response to a dietary intervention. In addition, we describe challenges and opportunities for nurse scientists who consider using *omics* in their research.

The intent of precision medicine is to move the focus from the “average” patient or “one-size-fits-all” diagnosis and treatments, to individualized healthcare by including an individual’s molecular make up in concert with environment and lifestyle factors. Such an approach capitalizes on recent advances in technologies that allows scientists and clinicians to characterize individuals and families in terms of health risk and treatment response. As such, nursing scientists whose research focuses on the biological determinants of health need to understand and incorporate these approaches into their research.

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Omics is a term used to encompass the collective technologies and approaches used to explore the actions and roles of various molecules that constitute cells. These include *genomics*, which is the study of genes and their function; *transcriptomics*, which is the study of the complete set of RNA transcripts in a cell population; *metagenomics* refers to the study of genetic material taken directly from the community; *proteomics*, which is the study of proteins and their functions; and *metabolomics*, which characterize the chemicals involved in biological function. The number of *omic* methods continues to proliferate, encompassing the study of viral particles in the human body, *viromics*; environmental diversity, *metagenomics*; antibiotic resistant genomes, *resistomics*; changes in gene expressions without a change in underlying DNA, *epigenetics*; and beyond. Our ability to merge *omic* methods with one another will lead to a greater understanding of our physiology, perturbations in health, and the role of the environment.

In this paper, we provide exemplars of the roles of *omics* in understanding biological determinants of health. The first exemplar focuses on genomics, Starkweather uses genomics as potential markers of chronic chronic pain vulnerability in patients with low back pain, while Heitkemper describes the use of genomics to predict responsiveness to a self management program. In the second exemplar, Ferranti explores the link between gut microbiome and the persistence of cardiometabolic dysregulation in the postpartum period in African American women. In the third exemplar, Grossmann provides the rationale for how the examination of the metabolome may provide valuable information on how best to design nutritional interventions for patients with multiple sclerosis. In addition to these exemplars, we describe some of the challenges and opportunities the use of omic measures create.

Nursing Science Exemplar: Genomics

Method Overview

Since the publication of the Human Genome Project, we have known that there are 3.2 billion base pairs of DNA and approximately 30,000 genes. Over the past 25 years, the growth of data regarding genomics has increased exponentially. We know about Mendelian diseases and disease risk within families. A growing list of genes are linked directly or indirectly to disease. In 1993, scientists isolated the Huntington's disease gene on chromosome 4 (Locke et al., 1993). Unlike a monogenic disease, more disorders that are common are likely polygenic disorders determined by many common gene variants. Each of these variants contribute a small piece of the variance in the clinical phenotype. For example, in irritable bowel syndrome (IBS) there are phenotypic variations (e.g., constipation- versus diarrhea-predominant) as well as co-morbid conditions (e.g., chronic pelvic pain, depression) that may result from many interacting genetic alleles that show context-dependent and environmentally-sensitive effects.

The field of nursing science has a growing, albeit still small, number of examples of how genetic information can inform about functional impairment risk, intervention response and symptom expression (Doong et al., 2015; Thompson & Voss, 2009).*Epigenetics* refers to changes in gene expression without a change in the underlying DNA sequence. In other words, there is a change in phenotype without a change in genotype. Genomics, as well as

epigenetic changes, can have far-reaching effects that are involved in some forms of cancer, mental health disorders, and autoimmune diseases. DNA methylation is an example of the most studied epigenetic change that occurs. Bench studies provide impetus for linking methylation of chromatin induced by stressors to expression of behavior (clinical phenotype) (Pacchierotti & Spano, 2015). For example, animal studies indicate that early adverse events (stress, exposure to cigarette smoking) can affect the regulation and expression of genes (Green & Marsit, 2015) particularly those involved in stress reactivity, synaptic plasticity, and ultimately behavioral responses (Li-Tempel et al., 2016). However, the complexity of the epigenome and its impact on genomics is not fully understood. For nursing, omics is an expanding field with multiple opportunities for those trained with the appropriate skill sets(Tully & Grady, 2015; Williams, Tripp-Reimer, Daack-Hirsch, & DeBerg, 2016). The integration of omics in the context of human health has been challenging, however, with growing numbers of nurse scientists in this area of research and increased availability of datasets that include genomic data, there are tremendous opportunities. Nurse scientists are particularly well poised to fill the gap between the bench and clinical research. This is because of their appreciation of person (resilience, motivation, self-efficacy) and environment (family, social context, resources, ethnicity/race, culture) factors that influence outcomes. Below, we provide two patient population exemplars (chronic low back pain and IBS) of nursing scientist work that utilize genomic information.

Chronic Pain Vulnerability: Low Back Pain—Nurse scientists are undaunted by the challenge of studying some of the most complex problems in healthcare, one of those being variation in pain outcomes. Low back pain is one of the most common and costly conditions in the U.S. (Institute of Medicine Committee on Advancing Pain Research & Education, 2011). Although a majority of people experience resolution of low back pain within weeks of onset (usually 4–6 weeks), some individuals continue to have pain long-term, which increases the likelihood of disability. Currently, low back pain is responsible for a third of work-related disability in the U.S. (Mehra, Hill, Nicholl, & Schadrack, 2012). As a highly heterogeneous condition, the source of pain (i.e., pain generator) is unidentifiable through modern imaging in up to 90% of low back pain cases (Chou, Fu, Carrino, & Deyo, 2009). However, sensitization of the peripheral and central nervous system is an important process that may drive the transition from acute to chronic pain. Sensitization occurs through modifications in expression of genes that encode pain-signaling molecules and their receptors, particularly genes associated with neurotrophins, inflammatory mediators and catecholamines.

Altered levels of pain signaling molecules and their receptors may be important for the early steps of nervous system sensitization. Given that levels of gene expression associated with enhanced pain sensitivity are potentially modifiable, further elucidation of the differences in somatosensory function and gene expression over the course of low back pain may provide foundational knowledge to evaluate and guide the development of predictive markers and preventative interventions to reduce the incidence of chronic low back pain.

Starkweather and colleagues simultaneously examined differences in peripheral and central sensitivity and expression levels of pain sensitivity genes at the onset of low back pain and over time in patients with an acute episode that either resolved or became chronic

(Starkweather, Lyon, et al., 2016). Participants enrolled in the study during an acute phase of low back pain and categorized as either “recovered” if their pain resolved in the first six weeks after onset or as “persistent” if their pain continued for six months. Various *omic* measures (genomics, lipidomics) were used during the study to identify the mechanisms underlying the transition from acute to chronic pain. The team’s initial goal was to identify differential expression pain genes at the onset of acute low back pain. They found that participants with acute low back pain had significantly increased expression of prepro-nociceptin (*PNOC*), the precursor of nociceptin, chemokine (C-C motif) ligand 2 (*CCL2*), and cannabinoid type-2 (CB2) receptor (*CNR2*) compared to the healthy no-pain control group (Starkweather, Ramesh, et al., 2016). In addition, dysregulated expression of multiple genes involved in pain processing were identified at the onset of acute low back pain, including *GCH1, CSF1, TRPV1, CALCA, PTGES, GDNF*, and *KCNQ2*.

Compared to the recovered group, patients who developed persistent low back pain had increased expression of *P2X3* and *FAAH*, and lower expression of *SLC6A2, KCNIP3, OPRD1, OPRK1*, and *OPRM1* at baseline. In addition, global methylation was significantly decreased in patients with persistent pain compared to the recovered and healthy no-pain control groups. These data suggest the biological mechanisms leading to chronic pain may be set in motion early, i.e., during the acute phase, and may provide a ‘signature’ to identify patients at risk.

Most recently, Starkweather’s team performed a plasma lipidomic study to compare lipid metabolites between patients with signs of peripheral and central sensitivity and those without sensitization. It is increasingly recognized that lipid molecules play a significant role in pain signaling and are involved in the process of sensitization. Upon tissue injury, membrane-derived phospholipids and oxidative metabolites of polyunsaturated fatty acids released from injured cells excite nociceptive neurons by activating selective G-protein-coupled receptors or ligand-gated ion channels. Activation of pronociceptive receptors by lipid molecules may result in peripheral sensitization seen in acute low back pain. The lipidomic analysis showed that patients with signs of peripheral and central sensitization had significantly higher levels of a triacylglycerol isomer while those without peripheral and central sensitization had higher levels of plasma phosphoglyceride, plasmenyl phosphocholine and phosphatidic acid. Whether these observations are signatures or biomarkers linked to specific pain receptors and sensitization phenotypes will be examined in future studies by her laboratory.

As can be seen, these multi-*omic* measures allow for examination of the products of genes and ultimately the linkage of genetic risk with clinical phenotypes such as chronic low back pain. Starkweather and her interdisciplinary team are planning further studies to evaluate the risk of chronic low back pain at specific gene expression thresholds. The results will help them determine the viability of using an expression panel in guiding personalized treatments. *Omic* measures will also provide a way to evaluate patient responses to specific therapeutics and possibly reveal pathways targeted personalized treatment.

Irritable Bowel Syndrome (IBS)—IBS is a chronic functional condition characterized by intermittent abdominal pain and alterations in bowel habit, e.g., constipation and

diarrhea. Current estimates of the IBS prevalence are 10–17% of the U.S. population. Twin data reveal a genetic predisposition to IBS development. However, given the complexity of the IBS etiology and its variable clinical presentation, other genetic factors such as the presence and combination of rare genetic alleles and epigenetic modification may also be responsible for the different phenotypes.

The bulk of genetic variation between humans is due to rare genetic polymorphisms and these variations are the focus on on-going studies by nurse scientists. Based on its importance to gastrointestinal physiology/pharmacotherapy and depression, a frequent comorbid condition in persons with IBS, researchers have focused attention on the serotonin reuptake transporter (SERT) gene. Heitkemper's team performed whole gene sequencing of the SERT gene from over 400 women and men with and without IBS. They found preliminary evidence that IBS patients with a history of either depression or anxiety were significantly more likely to carry multiple rare, likely functional, variant alleles than IBS patients without psychiatric comorbidity (Kohen et al., 2016). The results of rare genetic variant studies may point to a clear identification of risk for subgroups and/or, more likely, inform us about potential mechanisms leading to symptoms.

In addition to understanding gene variants, there is a need to measure gene expression and examine how products link with clinical phenotypes. Recent advances allow scientists to consider measures of gene expression or transcription factors such as microRNAs (miRNA). miRNAs are small non-coding RNAs, which are single-stranded RNA of 19–24 nucleotides. miRNAs have the ability to modulate the genome post-transcriptionally and as such may signal important roles not only in diseases such as cancer but also in the mechanisms accounting for symptoms such as pain (Andersen, Duroux, & Gazerani, 2014; Flowers, Won, & Fukuoka, 2015). Recently, Fourie, an intramural investigator at National Institute of Nursing Research (NINR), published a preliminary report on two miRNAs found in whole blood of patients with IBS that differed from controls. Both miRNAs are associated with pain and inflammation pathways (Fourie et al., 2014). Advances in blood-based miRNA techniques open up avenues for nurse scientists to study health risk as well as to track responses to therapeutic approaches. Standardization in terms of collection, compartment (serum, plasma, whole blood), preservation methods, and data analytic approach are important elements for consideration.

Recommendations and Resources for Genomics

The NINR integrated genomics as a strategic theme in 2000 and has supported genomic research for the past two decades. In addition to supporting the Summer Genetics Institute (SGI) since 2000, NINR has been providing immersion training in Big Data over the past several years to prepare nurses to engage in the quest for integrating clinical and *omic* data. In the summer of 2016, the NINR hosted a timely one week intensive training class entitled *Precision Health: From 'Omics' to Data Science*. The goal of this training course was to engage and inform a diverse audience of nurse scientists, clinicians, graduate students, and faculty on the latest advances in genomics, pharmacogenomics, nutrigenomics, metabolomics, microbiomics, and data science as well as the associated ethical, legal, and social implications of precision healthcare research. Additional resources include the

genomic databases available, such as the Database of Genomic Structural Variation (dbVar), Database of Genotypes and Phenotypes (dbGaP) and the Database of Single Nucleotide Polymorphisms (dbSNP).

Nursing Science Exemplar: Human Microbiome

Method Overview

With the 2008 launch of the National Institutes of Health Common Fund Human Microbiome Project (HMP), the field of human microbiome research has exploded. Numerous health conditions (e.g., obesity, diabetes) have important associations with the various human microbiome habitats (oral, vaginal, gut, skin). Investigation into the role of the microbiota in maternal-child health outcomes has revealed important associations, particularly with pregnancy outcomes (Vinturache, Gyamfi-Bannerman, Hwang, Mysorekar, & Jacobsson, 2016).

Human Microbiome, Maternal Health and Preterm Birth—Preterm birth affects 1 in 10 pregnancies with African American women most disproportionately burdened (Nelson, Shin, Wu, & Dominguez-Bello, 2016). Infection and inflammation are important contributors to preterm birth, leading researchers to investigate what role the vaginal microbiome may contribute to infection and inflammation, both clinical and subclinical. The vaginal microbiota changes in both composition and stability throughout normal pregnancy (Hyman et al., 2014; Romero et al., 2014). There are also differences in vaginal microbial composition between non-pregnant African American women as compared to women of European ancestry (Collado, Isolauri, Laitinen, & Salminen, 2008). The studies to date examining the role of the vaginal microbiome in preterm birth have produced mixed findings with some studies indicating differences in those who deliver preterm (Bassols et al., 2016; Fugmann et al., 2015; Koren et al., 2012) and other studies finding no differences (Gomez-Arango et al., 2016). In general, limitations of these studies include small sample sizes and lack of racial and ethnic diversity. Addressing these limitations, an ongoing NINR-funded study (NR014800) is examining the biobehavioral determinants of preterm birth in a cohort of nearly 500 African American women. This longitudinal study of pregnant African American women is using a nested case-control design to examine the contribution of the oral, vaginal and gut microbiome to the incidence of preterm birth. This study will contribute to a greater understanding of within-race variability in microbiome changes across pregnancy that may have a role in preterm birth in African American women.

Human Microbiome, Maternal Health and Cardiometabolic Dysregulation—In addition to the role of the vaginal microbiome in pregnancy outcomes, the gut microbiome may also be a significant influence in maternal health. In particular, cardiometabolic complications and hypertensive disorders of pregnancy may be linked to gut microbiota. Similar to the vaginal microbiota, throughout a healthy pregnancy the gut microbiota undergo changes characterized by an increase in bacterial load and an alteration in microbial composition (Amarasekara, Jayasekara, Senanayake, & Dissanayake, 2015; Wu et al., 2016). However, there are few studies that have examined microbiome in concert with pregnancy-associated cardiometabolic complications. Two studies in women with gestational diabetes

mellitus (GDM) found distinct microbiota profiles characterized by a depleted richness in both the gut and the placenta (Guertin et al., 2014). Differences in the gut microbiome appear to persist into the postpartum period among women who had GDM during pregnancy (Park, Sadanala, & Kim, 2015). Similarly, recent studies have found associations between the gut microbiome composition and elevations in blood pressure during pregnancy (Chen et al., 2012) and for a potential role of placental microbiota in the development of preeclampsia (Evans et al., 2014). These findings are promising and indicate a need for further studies to examine the association of the microbiome with cardiometabolic complications longitudinally from pregnancy through postpartum. This approach will also allow for the investigation of potential mechanism(s) by which microbiota influence cardiometabolic risk factors and allow for the expansion of research into populations of ethnic and racial diversity who are most at risk.

Funded by the NIH, Office of Research on Women's Health, Building Interdisciplinary Research Careers in Women's Health (BIRCWH) program (K12 HD085850), Ferranti's team is currently investigating the contribution of the gut microbiome to the persistence of cardiometabolic dysregulation in the postpartum period in the cohort of African American women from the above-mentioned study (NR014800). With these two studies the investigators will be able to longitudinally examine gut microbiome changes in pregnancy and postpartum and how they may contribute to cardiometabolic dysregulation in women who are most at risk for future cardiometabolic disease.

Recommendations and Resources for Genomics

The NIH HMP Data Analysis and Coordinating Center (DACC) maintains a link to the research protocols used for the HMP in addition to new technologies and advances as they become available. As with any clinical or biologic specimen, consideration for the study design, sample collection methods, transport and storage must be well thought out and based on established protocols to assure data integrity, comparisons across studies and accumulation of findings to build the evidence base (Jordan et al., 2017). Nurse scientists are well positioned to investigate the role of the microbiome in human health. The microbiome field necessitates interdisciplinary collaboration, particularly with data scientists, bioinformaticists, microbiologists and genomic experts.

Nursing Science Exemplar: Metabolomics

Method Overview

Metabolomics is a biomarker and pathway analysis approach that utilizes mass spectroscopy and nuclear magnetic resonance technology. Metabolomics is the multi-targeted analyses of low molecular mass (<1000D) endogenous and exogenous metabolites and their pathways. This approach allows for the systematic study of the unique biochemical fingerprints (amino acids, glucose) resulting from cellular processes. Metabolites may be the substrates, intermediates, and products of metabolism. Complementing genomics and proteomics, metabolomics offers the advantage to investigators of linking environmental (diet, stress) factors to cellular responses. Metabolites are found in all body fluids and tissues. The

Human Metabolome Database (www.humdb.ca) contains a list of those metabolites resulting from cellular activities.

Metabolomics has been used to both analyze the impact of environmental factors and provide powerful new insights into disease processes (Baker et al., 2015; Edmands et al., 2015). Metabolomic approaches are increasingly used in the study of diabetes, dyslipidemia, cancer, chronic neurological disorders, pharmaceutics, and nutrition to name a few. Research into the metabotype of individuals during the disease processes has led to new biomarkers of disease status as well as new targets for interventions and the impact of nutritional interventions (Alvarez et al., 2017; McGrath & Young, 2015). Nutritional metabolomics is seeking to identify novel biomarkers of dietary intake to provide objective measures of dietary intake (Schmidt et al., 2015). Some nutritional metabolomic studies are comparing the metabotype of individuals with differing BMI and/or the response to dietary interventions (Baker et al., 2015).

Metabolomic Analysis of a Dietary Intervention in Multiple Sclerosis—An area of interest in nutritional metabolomics is how diet impacts the development, persistence, and symptomatology of autoimmune disease. There have been numerous studies evaluating the impact of dietary interventions on autoimmune diseases such as chronic fatigue syndrome, rheumatoid arthritis, inflammatory bowel disease, and multiple sclerosis (Naviaux et al., 2016; Pieragostino et al., 2015). Multiple sclerosis (MS) is an autoimmune disease producing neurological deterioration (Dendrou, Fugger, & Friese, 2015). Often diagnosed between the ages of 20 and 40 years, MS produces significant physical and cognitive disability leading to reduced quality of life and inability to complete daily activities (Patti & Vila, 2014). MS prevalence is approximately 400,000 in the U.S. and 2.5 million worldwide (Jialal, Huet, Kaur, Chien, & Devaraj, 2012). Although the number of disease modifying medications has proliferated in the past 20 years, the cost for these medications averages more than $60,000 per year (Bin Sawad, Seoane-Vazquez, Rodriguez-Monguio, & Turkistani, 2016) and these medications do little to address the most common and debilitating symptom of MS, MS-related fatigue (Asano & Finlayson, 2014; Ledinek, Sajko, & Rot, 2013). Efficacy of medications used specifically for MS-related fatigue is mixed with some studies finding no impact on reported fatigue (Asano & Finlayson, 2014; Ledinek et al., 2013).

There is some evidence supporting the use of dietary interventions to reduce disease progression and alleviate symptoms such as fatigue. Early studies by Swank recommended a very low saturated fat diet. Results from his work found that individuals who maintained a saturated fat intake less than 20g per day vs. individuals whose intake was 25 or 41g per day exhibited reduced disability as measured by the Expanded Disability Status Score (EDSS) over a period of 30 years (Swank & Grimsgaard, 1988). In 2014, a study proposed a modified Paleolithic diet with exercise and stress reduction. When 19 individuals followed this diet for a year, there was an average decrease in Fatigue Severity Score of 2.2 on a nine-point scale (Bisht et al., 2014). Other recently published dietary interventions include the MacDougal diet and an anti-inflammatory diet proposed by Riccio have demonstrated similarly encouraging results (Riccio et al., 2016; Yadav et al., 2016). The caveat to these

studies is the small samples sizes and lack of true placebo groups. Therefore, additional rigorous research is warranted.

Mechanisms by which diet may influence the progression and/or symptomatology of MS and many other chronic diseases are largely unknown. Hypotheses of how diet may improve MS include reduction of inflammation, alteration of the microbiome, increased nutrient provision for cellular healing, epigenetic changes, increased mitochondrial function, among others. Currently, Grossmann and colleagues use a multi-omics approach (metabolome, microbiome and epigenome analyses) to identify potential biomarkers as well as to gain insights into mechanisms related to dietary interventions in MS and cystic fibrosis(Alvarez et al., 2017).

Recommendations and Resources for Metabolomics

Nurse scientists such as Grossmann, bring great expertise in the clinical identification and characterization of symptoms and symptom clusters. As metabolomic methods continue to mature, metabolomics will offer an additional facet to the already robust symptomatology analyses by adding biofluid (urine, blood, stool) analyses. However, the caveat with metabolomics is its sensitivity. Therefore, design of studies to include metabolomics must carefully consider the methods of collection of biofluids and the metadata collected.

The NIH provides training in metabolomic through the Metabolomics Workbench (www.metabolomicsworkbench.org). The information on the Workbench provides not only detailed information about metabolomic methods, but includes examples of how data may be analyzed and applied. Further, the Workbench provides links to services at the six Metabolomics Resource Cores funded through the NIH. The purpose of these cores is to facilitate the design, data acquisition and analysis for scientists seeking to utilize the power of metabolomics in their research. The NINR has included the use of multi-*omic* methods in its Strategic Plan 2016 and emphasized the importance of metabolomics in symptom science (“NINR. NINR Strategic Plan: Advancing Science, Improving Lives,” 2016).

Opportunities and Challenges

Taken together, we need to view these *omic* measures as part of the ‘toolbox’ for nurse scientists pursuing the biologic health determinants of health that cut across ages and disease states. These tools as well as the integration of data elements (i.e., systems biology) will allow us to uncover the heterogeneity of each individual and open up future possibilities of designing therapies that are personalized or tailored. Nurse scientists through their multilevel focus on the individual, family and community can interweave the biologic with the sociocultural, environmental, and behavioral influences on health. Their incorporation into programs of research mandates team science. Core resources and partnerships with technological and analytic experts and biostatisticians are critical components.

Despite the impressive growth in technologies, there remain challenges in the interpretation, utilization, and translation of *omic* findings. A number of potential pitfalls associated with varying analytic approaches used in sample testing could contribute to false positives, false negatives, and conflicting results (Rehm, Hynes, & Funke, 2016). Sample collection is

critically important in terms of timing, sample storage, and time to analyses. All of which need to follow specified protocols and require careful documentation. For example, normal circadian patterns, nutrition, and medications can influence the levels of numerous metabolites. When using 'omics' measures that are currently available in large datasets, similar data collection issues also need to be considered. Often biologic measures are collected only on a subsample of the participants in the databases (Conley et al., 2015). Thus, nurse scientists need to be prepared to be aware of these potential confounders, in addition to the rapid changes in the *omic* science landscape.

The number of possible biological and environmental measures captured is rapidly increasing. While costs for individual genome, microbiome and metabolome assays are decreasing, the inclusion of data management experts, biostatisticians, and consultants to lead and/or assist with data analyses continues to add to the budget. The availability of collaborators and institutional infrastructure such as Clinical and Translational Science Award (CTSA) are key.

To address the gap between omics and clinical practice necessitates both an integration of omics content into core PhD and health care provider content(Williams & Cashion, 2015). There is a need for the education of a larger cadre of nursing scientists skilled to design experiments, capture data, and analyze data in combination with endophenotypic and phenotypic data. (Greco, Tinley, & Seibert, 2011; Quevedo Garcia, Greco, & Loescher, 2011) In 2013 a Council for the Advancement of Nursing Science (CANS) survey of university websites and their documentation of PhD course content noted that only 4.2% contained 'omics' content.(Wyman & Henly, 2015) As a result of this review, they recommended strategies and opportunities for doctoral programs in nursing to meet the increasing need for nurse scientists prepared to understand and for some to incorporate omics measures into their research.(Wyman & Henly, 2015) The authors also noted that inclusion of changes in practice-based curriculum have outpaced the incorporation of new omics science in nursing doctoral programs.(Conley et al., 2015).

The NINR has been responsive to this need voiced by the nursing scientific community by partnering with other institutes, such as the National Human Genome Research Institute, to provide resources for clinicians and educators (https://www.genome.gov/17517037/health-professional-education/). The NINR's most recent efforts in helping to promote the integration of –omics in nursing science and research will be unveiled soon, through the Omics Nursing Science and Education Network (ONSEN) website. ONSEN will provide a gateway to omics educational resources, information on common data elements, and a database to promote collaboration among nurse scientists. Through these combined efforts, nurse scientists can be prepared to integrate omics in their practice of education, research and clinical patient care. The exemplars described above provide a glimpse of the current opportunities and challenges of *omic* nursing research. As a powerful tool for accelerating a deeper understanding of physiology, perturbations in health, and the role of the environment, the integration of omics holds promise for increasing the impact of nursing research and practice on population health outcomes.

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Highlights

- Multi-omic measures allow for examination of the products of genes and ultimately the linkage of genetic risk with clinical phenotypes such as chronic low back pain.
- *Omic* measures provide a way to evaluate patient responses to specific therapeutics and possibly reveal pathways that can be targeted for personalized treatment.
- Advances in blood-based miRNA techniques open up avenues for nurse scientists to study health risk as well as to track responses to therapeutic approaches.
- There is a need to examine the association of the microbiome with cardiometabolic complications longitudinally from pregnancy through postpartum.
- Nursing scientists are using multi-omics approach (metabolome, microbiome and epigenome analyses) to identify potential biomarkers as well as to gain insights into mechanisms related to dietary interventions in chronic illnesses.
- Nurse scientists through their multilevel focus on the individual, family and community can interweave the biologic with the sociocultural and behavioral influences on ability and disability.