Using short hairpin RNA (shRNA) to reduce ADAR1 expression abrogated the oncogenic potential of human TNBC cell lines, while non-TNBC cells are less susceptible. Different levels of RNA editing of known ADAR1 targets were detected in shRNA-treated human TNBC cell lines, suggesting that ADAR1-mediated RNA editing contributes to TNBC pathogenesis. DISCUSSION/SIGNIFICANCE OF IMPACT: These results indicate critical roles played by the tumor suppressors p53 and ARF in the pathogenesis of TNBC, partially through affecting ADAR1-mediated RNA editing. Further understanding of this pathway could shed light on potential vulnerabilities of TNBC and inform the development of personalized therapies based on patients' genetic signiatures.

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Unraveling the role of Phospholamban (PLN) in humans via the characterization of Induced Pluripotent Stem Cell (iPSC) Cardiomyocytes (CM) derived from carriers of a lethal PLN mutation

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OBJECTIVES/SPECIFIC AIMS: To study the biology of Phosholamban (PLN) in a human relevant model. METHODS/STUDY POPULATION: State of the art stem-cell technologies using iPSC-CMs derived from carriers of a lethal PLN mutation. RESULTS/ANTICIPATED RESULTS: Our preliminary data demonstrate that this particular PLN mutation (L39) results in reduced expression and mis-localization of PLN as well as increased incidence of early after depolarization in isolated iPSC-CMs. DISCUSSION/SIGNIFICANCE OF IMPACT: Phospholamban (PLN) is a critical regulator of Ca++ homeostasis yet many uncertainties still remain regarding its role in humans. Our study will provide unique insights into the pathophysiology of this protein in HF.

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Using infant exertion to tailor treadmill intervention

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OBJECTIVES/SPECIFIC AIMS: This research examined 3 aims to address the need to understand and quantify exertion in infants. Aim 1: Develop a schema to identify and code exertional behaviors in infants during treadmill stepping. Aim 2: Establish feasibility for the schema's use with clinical populations. Aim 3: Pilot the schema in a study designed to induce infant exertion. METHODS/STUDY POPULATION: Aims 1 and 2 were achieved using existing treadmill stepping data. The data used in Aim 1 included eight typically-developing infants (age 7-10 months) who were able to sit independently, but not walk. The data used in Aim 2 came from two separate data sets from infants who took more than 10 steps in a 30-second trial: Data set A included six typically-developing infants (age 2-5 months) who were unable to sit independently (developmentally comparable to atypical populations who might receive treadmill interventions). Data set B included six infants with Spina Bifida (age 3-10 months). Aim 3 was addressed with a prospective study using an exertion model. Pre-walking, typically developing infants (age 8-10 months) underwent five total stepping trials. Trial 1 determined the infant's individualized maximum stepping speed; trials 2-5 were each 60 seconds and alternated between a baseline stepping speed of.20 m/s and the infant's maximum stepping speed determined in trial 1. All video data were coded for step type, step frequency, and exertional behavior. RESULTS/ANTICIPATED RESULTS: Aim 1: Two behaviors were identified and determined to capture infant exertion: foot dragging and leg crossing. Aim 2: The feasibility of capturing exertion with these two behaviors was established for young infants and infants with neuromotor delays, with exertional behaviors increasing with stepping exposure (p< 0.05). Aim 3: Total exertion (foot dragging + leg crossing) was higher in the maximum speed trials compared to baseline trials (p = 0.005). DISCUSSION/SIGNIFICANCE OF IMPACT: Exertion in infants can be quantified. The exertion schema developed with this study will support the development of dosing guidelines for infant treadmill intervention. The next step in this line of research is to examine the correlation between infant exertion and heart rate, in effort to move from behaviorally-informed protocols to more precise, individualized protocols based on the physiological response of the infant.

Biomedical Informatics/Health Informatics

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Biomedical Informatics/Health InformaticsA Preliminary Study of Glaucoma: The Intersection of Genetics and Survey Data from the Health and Retirement Study

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OBJECTIVES/SPECIFIC AIMS: Glaucoma is a leading cause of irreversible blindness worldwide; in the United States alone, over 2.7 million individuals are affected. Various risk factors for glaucoma are known and include age, race/ethnicity, genetics, and ocular measures. Despite numerous studies, molecular and environmental factors that contribute to glaucoma remain elusive. Our objective was to conduct a genome-wide association for glaucoma among black and white HRS respondents, and to determine the feasibility for future analyses examining shared genetic markers between glaucoma and other comorbidities, behaviors, and environmental risk factors. METHODS/STUDY POPULATION: The University of Michigan Health and Retirement Study (HRS) is a longitudinal survey of a representative sample of Americans over the age of 50. Supported by the National Institute on Aging and the Social Security Administration, the HRS is designed to provide reliable data on the decisions, choices, and behaviors of people as they age and respond to changes in public policy, the economy, and health. The study obtains information every two years about income and wealth, health and use of health services, work and retirement, and family connections. Through its unique and in-depth interviews, the HRS provides an invaluable and growing body of multidisciplinary data that researchers can use to address important questions about the challenges and opportunities of aging. Because of its innovation and importance, the HRS has become the model and hub for a growing network of harmonized longitudinal aging studies around the world. Saliva was collected on half of the HRS sample each wave starting in 2006 and respondents were genotyped on the Illumina Human Omni2.5-Quad (Omni2.5) BeadChip at the NIH Center for Inherited Disease Research. We accessed survey results to evaluate prevalence of

glaucoma in this dataset and performed a genome-wide association study (GWAS) adjusting for age, sex, and significant Principal Components and stratifying by self-reported race (White / Black). RESULTS/ANTICIPATED RESULTS: Of 8179 respondents passing quality filters, 6409 (78.40%) were white and 985 (12.05%) were black. Self-reported glaucoma prevalence was 7.85% and 16.34% in white and black respondents, respectively. White respondents had a mean age of 76.97 (SD 7.53) and were 57.25% female. Black respondents had a similar mean age of 74.96 (SD 7.27) and were 62.54% female. More than 87% of both groups were assessed in 2012. Preliminary GWAS analyses did not replicate known glaucoma loci and no variants attained genome-wide significance. A suggestive variant (p<1e-05) in the black population was within 10kb of a known locus, rs1196998. Future analyses will evaluate genetic association with combinations of glaucoma and comorbidities. DISCUSSION/SIGNIFICANCE OF IMPACT: Glaucoma risk is higher in minority groups than in whites, and the majority of reported genetic studies of glaucoma have been performed in individuals of European descent. It is imperative to better understand the role of genetics, environment, and health behavior in glaucoma risk. Further, understanding common mechanisms underlying diseases that co-occur with glaucoma could illuminate novel disease mechanisms that can be targeted for early intervention and/or treatment.

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Characterizing the top 100 articles in benign prostatic hyperplasia literature using bibliometric analysis

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OBJECTIVES/SPECIFIC AIMS: The prevalence of BPH, coupled with associated disability ranging from quality of life impairments to hospitalization, has spurred decades of research into its pathophysiology, diagnosis, treatment, and outcomes. For these reasons, we conducted a study to characterize the current landscape of BPH literature, including the most commonly cited articles impacting the field. METHODS/STUDY POPULATION: We used the Web of ScienceTM databases to conduct a bibliometric analysis of the top 100 leading BPH articles. Bibliometric analyses are quantitative approaches examining the impact of academic literature. We used the following search terms: 'benign prostatic hyperplasia' and 'benign prostatic enlargement.' We identified and characterized the 100 most-cited BPH articles including their citations, journal, author, year, and country through September 2018. RESULTS/ ANTICIPATED RESULTS: The top 100 BPH articles were published between 1978 and 2012. The number of citations ranged from 143 to 2,158 across 26 different journals, including 9 urology-specific journals. The Journal of Urology (5-year impact factor: 4.91) was the most published journal with 26 articles, followed by European Urology (5-year impact factor: 15.66) with 16, and Urology (5-year impact factor: 2.39) with 13. The oldest 10 articles in the top 100 mainly focused on BPH etiology/pathogenesis, while the newest 10 articles mainly focused on medical treatment. The 1990's was the most productive decade accounting for nearly half of the top 100 articles (n=46). Eight authors had two or more first author publications, and 8 institutions had five or more publications in the top 100. Thirteen different countries were represented in the top 100 articles, with the US (n = 64), Italy (n=7), and Germany (n=5) being the most common. The articles were published in the following Web of Science Categories: Urology & Nephrology (n=68), Medicine, General & Internal (n=15), and Endocrinology & Metabolism (n=7). DISCUSSION/SIGNIFICANCE OF IMPACT: This study represents the first bibliometric analysis of the leading 100 BPH articles impacting the academic literature. The literature focus has evolved from BPH pathogenesis/etiology to treatment, and was primarily published in 3 specialty journals. Our findings highlight the most impactful BPH literature, and may be used to guide research and funding priorities for this increasingly common condition.

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Genetic variants in gestational diabetes mellitus

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OBJECTIVES/SPECIFIC AIMS: This study aims to identify genetic biomarkers of GDM and facilitate the understanding of its molecular underpinnings. METHODS/STUDY POPULATION: We identified a cohort of mothers diagnosed with GDM in our longitudinal birth study by mining Electronic Health Records of participants utilizing PheCode map with ICD-9 and ICD-10 codes. We verified each case using ACOG's GDM diagnosis criteria. RESULTS/ANTICIPATED RESULTS: Whole genome sequencing (WGS) data were available for 111 confirmed cases (out of 205) and 706 controls (out of 1,429) from different ancestries (412 EUR, 256 AMR, 56 EAS, 26 SAS and 18 AFR; 49 OTHER). SAS had the highest incidence of GDM at 38.46% and EUR had the lowest at 6.55%. We performed logistic regression using computed ancestry, age and BMI as covariates to determine if any variants are associated with GDM. The top variant (rs139014401) was found in an intron of DFFB gene, which is p53-bound and regulates DNA fragmentation during apoptosis. We will investigate the robustness of 49 identified variants and will separate the cohort by ancestry to detect population-specific differences in the top loci. DISCUSSION/SIGNIFICANCE OF IMPACT: Identification of molecular biomarkers in GDM across different ancestral backgrounds will address a gap in current GDM research. Findings may enhance screening and enable clinicians to identify those at risk for developing GDM earlier in the pregnancy. Early management of mothers at risk may lead to better health outcomes for mother and baby.

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Glycemic Control and Diabetic Peripheral Neuropathy Among Patients on Prescription Opioid Pain Medications in Western New York: Using Data Analytics for Quality Assessment

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OBJECTIVES/SPECIFIC AIMS: I would like to make clinicians aware about prescription opioid use and glycemic control among patients with diabetes. This is a quality of care issue that increases the disease burden for two conditions opioid dependence and diabetic complications. Big data analytics can bring out this quality of care issue and help in changing clinical practice through precision medicine METHODS/STUDY POPULATION: This is a population