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

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