exemplify the therapeutic potential of modulating endothelial CD39 activity, as well as the potential for using SNPs within the gene coding for CD39 as a cardiovascular disease marker.

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Development of osteoclast derived exosomes for vascular calcification therapy

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OBJECTIVES/GOALS: The global incidence of calcific aortic valve disease (CAVD) increased 3.5-fold since 1990. No preventative or therapeutic pharmaceutical therapies exist for CAVD. We will establish the therapeutic potential of osteoclast-derived exosomes though characterization of contents and mechanisms of action to protect against mineralization. METHODS/STUDY POPULATION: Exosomes were purified from conditioned media collected from murine myeloid precursor cells, RAW264.7 (control), and osteoclasts induced to differentiate from RAW264.7 cells (OD). Protein content of exosomes was determined using proteomic analyses. Nucleic acid contents will be identified by sequencing mRNA, miRNA, and DNA. The calcification prevention and reabsorption abilities of control and OD exosomes will be tested using human valvular interstitial cells (VIC) and smooth muscle cell calcification assays and acellular osteologic disc assays, respectively. Comparison between cellular and acellular systems will help identify mechanisms of action, and demonstrate potential therapeutic viability of OD exosomes in preventative vs resorptive treatments. RESULTS/ANTICIPATED RESULTS: OD exosomes, but not control exosomes, prevented calcification in VIC in vitro. OD exosomes contained osteoclast-specific proteins including TRAP, MMP6, cathepsin K, and bone reabsorption factors including V type proton pumps, ATPases, and integrins. These genes are also involved in resorptive activities, and were highly upregulated in OD compared to control exosomes. We anticipate miRNA signatures associated with mineral resorption will also be present. Increased knowledge of exosome cargo will illuminate their mechanism of action and allow future work to engineer increased efficacy. We also anticipate a therapeutic response when OD exosomes are applied after calcification has begun, showing exosomes promote calcium reabsorption. DISCUSSION/SIGNIFICANCE: Establishing therapeutic potential and examining mechanisms of action will pave the way for OD exosomes as a CAVD treatment. Analysis of exosome contents will determine active molecules to be enhanced in future studies. This work will lay a foundation for moving into aortic valve organoid models, which are accepted by the FDA for preclinical trials.

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Understanding drivers of post-Ebola syndrome (PES) in pediatric survivors of Ebolavirus disease: characterization and the way forward.

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OBJECTIVES/GOALS: Ebolavirus disease survivors report persistent, debilitating health concerns dubbed Post-Ebola Syndrome (PES). Attention to PES in young survivors is lacking, we describe PES in pediatric EVD survivors in Eastern Sierra Leone. Additionally, we introduce our proposal investigating differential presentations of PES in pediatric survivors. METHODS/STUDY POPULATION: EVD survivors were enrolled a median of 2.5 years after resolution of disease. Survivors were eligible if listed in a national register maintained by the Sierra Leone Association of Ebola Survivors. Household contacts (HCs) were identified by survivors. Participants were assigned into three comparison groups: pediatric (7-11), adolescent (12-17) and young adult (18-25). A self-reported symptom questionnaire, and a physical exam were conducted. Variables were clustered within organ system and compared across groups. RESULTS/ANTICIPATED RESULTS: Pediatric survivors had lower levels of long-term sequelae compared to adolescents and young adults. Symptoms and abnormal physical exam signs increase with age. Musculoskeletal, psychiatric, ophthalmologic, and GI signs and symptoms were significantly different between groups. Pediatric survivors had significantly more persistent sequelae than age-matched HCs with no history of EVD; particularly within the cardiac/GI (p=.006) and psychiatric/neurological (p=.025) clusters. PES is heterogeneous with respect to age, calling for a deeper understanding of age-based differences. Even the youngest group of survivors experienced significantly more sequelae than HCs, highlighting the elevated symptom burden in these children over their peers. DISCUSSION/SIGNIFICANCE: Understanding mechanistic drivers will ultimately improve targeted treatments for PES. We will characterize symptom groups defining PES in children, determine the relationship between accelerated aging and PES in this population, and test how immune profiles associated with accelerated aging relate to the development of PES in children.

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Fostering academic-community research teams to conduct community-engaged research in environmental justice communities: The RISE Communities R25 program

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OBJECTIVES/GOALS: Residents of environmental justice (EJ) communities experience significantly higher rates of negative health outcomes associated with poor air quality. Low-cost air sensors may supplement regulatory monitoring to better measure air pollution at local scales, but widespread application of this technology remains limited due to many challenges. METHODS/STUDY POPULATION: To address these obstacles, we designed a training program to equip community and academic research partners with the skills and knowledge to successfully apply low-cost sensors in community-engaged environmental health research. The R esearch Innovations using Sensor Technology in Environmental Justice Communities (RISE Communities) program was established through an NIEHS R25 award in 2022 and has three specific aims: 1) Foster community-academic partnerships through research education, training, and team development activities, 2) Provide technical training in the application of low-cost sensors for indoor, outdoor, and personal air monitoring in EJ communities, and 3) Establish a community of practice to address air quality in communities nationwide. RESULTS/ANTICIPATED RESULTS: We hosted our first cohort in August 2023, training five community-academic research teams in team collaboration, community-engaged research, and technical skills for collecting and analyzing data from PurpleAir sensors. Each team received 12 sensors to take to their home EJ

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communities to begin their projects. Community of practice development continues through interactive webinars and development of a web-based repository of training videos and discussion board posts. Evaluation data show high participant learning and satisfaction, with mean confidence scores improving on 6/8 metrics. Evaluation data also suggest several areas for improvement such as more time spent in teams for planning and additional opportunities for interaction within the cohort and with program instructors for problem-solving. DISCUSSION/SIGNIFICANCE: Effective training for team-based community-engaged research requires careful planning for team development and study implementation. Longitudinal training and support for the technical aspects of utilizing air sensors is also critical to team success. The RISE Communities program is actively recruiting for future training cohorts.

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Multimodal assessment of sleep in individuals with chronic post-concussive symptoms: A Pilot Study

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OBJECTIVES/GOALS: Weaimed to compare subjective and objective sleep in individuals with chronic post-concussive symptoms. We hypothesized an association between self-reported sleep quality and objective sleep parameters, which is different for concussed and control cohorts. METHODS/STUDY POPULATION: 28 individuals with chronic post-concussive symptoms and 13 age-matched controls (no concussion history) completed the ISI, PSQI, PROMIS Depression, Anxiety, Stress and Cognitive questionnaires at enrollment. Objective sleep parameters were obtained for a minimum of 7 days and up to 30 days with a validated sleep monitoring device placed under the subject's bed (Emfit). For each night, raw activity data per minute were analyzed to determinein-bed, sleep, wake, andout-of-bedtimes. These measures were used to calculate total sleep time (TST), sleep onset latency (SOL), and wake after sleep onset (WASO) for each night. RESULTS/ANTICIPATED RESULTS: Concussed individuals reported worse sleep with PSQI and ISI scores significantly higher than controls. They also showedsignificant associations between PSQI and Dep ression, ISI and Depression, and ISI and Anxiety scores. There was no difference between objective sleep parameters in the concussed and control cohorts (in-bed/sleep/wake/out-of-bed times, TST, SOL, and WASO). Instead, higher PSQI, ISI, Depression, Anxiety, and Stress scores (greater symptom burden) were all associated with later sleep times, where as higher Cognitive scores (greater cognitive function) were associated with earlier sleep times, regardless of g roup status. DISCUSSION/SIGNIFICANCE: Concussed individuals report worse subjective sleep but no differences to controls when objectively assessing sleep. Depression/anxiety, and not concussion status, determine objective sleep parameters. Psychiatric comorbidities should inform the treatment of post-concussive sleep disturbances.

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Aerodynamic Size Distribution of SARS-CoV-2 Aerosol Shedding

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OBJECTIVES/GOALS: We designed the Biocascade Exhaled Breath Sampler (BEBS) to characterize viral aerosol shedding among individuals with influenza and other respiratory virus infections. We first aimed to test the BEBS on volunteer COVID-19 cases and report the aerodynamic size distribution of exhaled breath aerosol particles carrying SARS-CoV-2 RNA. METHODS/STUDY POPULATION: From June 15 through December 15, 2022, we recruited 27 PCR-confirmed COVID-19 cases from a college campus and the surrounding community to provide 30-minute breath samples into a well-validated Gesundheit-II (G-II) exhaled breath aerosol sampler. Among these individuals, 17 provided an additional exhaled breath sample into the newly designed BEBS. We quantified samples for viral RNA using reverse transcription digital polymerase chain reaction (RT-dPCR) and determined the viral RNA copies collected within two aerosol size fractions (≤5 μm and >5 μm in diameter) from the G-II, and four aerosol size fractions (<1.15 μm, 1.15–3.2 μm, 3.3–8.2 μm, and >8.2 μm) from the BEBS. RESULTS/ANTICIPATED RESULTS: Individuals with a SARS-CoV-2 Omicron BA.4 or BA.5 infection shed virus in aerosols at an average rate of 7.5x103 RNA copies per 30-minute G-II sample, with 78% of the total RNA in aerosols ≤5 μm in diameter. Among the BEBS samples, 10% of the total viral RNA was detected in aerosols <1.15 μm, 43% in 1.15–3.2 μm, 37% in 3.3–8.2 μm, and 10% in the >8.2 μm size fraction. Based on viral RNA loads, our results indicate that exhaled aerosols ≤3.2 μm contribute the majority of SARS-CoV-2 inhalation exposure. DISCUSSION/SIGNIFICANCE: Our data provide additional evidence that respirable aerosols contribute to the spread of SARS-CoV-2. Thus, our data suggest that mitigation measures designed to reduce infectious aerosol inhalation, such as ventilation and the use of air cleaners and respirators, are needed to control the spread.

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Alexithymia impacts vulnerability for cognitive decline in healthy elders via frontal lobe connectivity during response inhibition, especially in women

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OBJECTIVES/GOALS: This project aimed to examine the impacts of biological sex and alexithymia on frontal lobe connectivity in executive functioning (EF)-related neural networks during successful inhibition as a means to index vulnerability for future cognitive decline. METHODS/STUDY POPULATION: Healthy, cognitively intact older adults (n=43, 33 female, Mage=79) completed the 20-item Toronto Alexithymia Scale (TAS-20) and the stop-signal task in this study. We used electroencephalography (EEG) source estimation to investigate EF-related frontal connectivity during successful inhibition in stop-signal task trials. Connectivity was measured in bilateral frontal ROIs relevant to inhibition using time series correlations over the N200 (186-350ms) and P300 (340-616ms) time windows, associated with the inhibitory

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