engage in a statewide Facebook (FB) group. METHODS/STUDY POPULATION: Cross-sectional online survey administered via iPads at the MN State Fair in 2018 to adults aged 18+ years residing in MN assessed demographics, social media use, interest in participating in a FB group for biomedical research; and open-ended questions on health topics of interest, and what would keep people engaged in this group. RESULTS/ANTICIPATED RESULTS: Respondents (N=487) were 21% racial minorities and 65% female sex. Most (87%, n=422) had created a personal FB profile. Of these, the proportion who agreed/strongly agreed was: 57% that the FB group sounded interesting, 45% were interested in being part of it, 41% were willing to share it with others, 62% that it would allow the community's thoughts/ideas to be heard and 59% wanted to learn about opportunities to participate in research on health topics they care about. Using content analysis, the top 3 health topics people wanted to learn about were chronic disease and prevention, wellness, and mental health. Top ways to keep people engaged were providing personable, relevant health information; and interactive bi-directional discussions. DISCUSSION/SIGNIFICANCE OF IMPACT: Findings will inform development of a FB group to engage diverse populations in biomedical research.

Mechanistic Basic to Clinical

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A Mouse Model to Study Image-Guided, Radiation-Induced Cardiac Injury and Potential Clinically Targetable Biologic Mediators

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OBJECTIVES/SPECIFIC AIMS: The overall objective of this study is to develop a novel, clinically-relevant, image-guided mouse model for radiation-induced cardiotoxicity, which can be used to gain insight into clinically-targetable, pathophysiologic mechanisms of cardiac injury in thoracic radiotherapy patients. METHODS/STUDY POPULATION: Photon or sham radiation will be administered at differential doses to a defined portion of the heart and/or lungs of C57BL/6 female mice using micro-CT visualization of the heart with Xstrahl's MuriSlice Software applied to the Small Animal Radiation Research Platform (SARRP). Cardiac and lung segments from a subset of mice will be harvested at specific time points for confirmation of radiation targeting, local apoptosis assessment, and evaluation of fibrosis and vascular tissue morphology. Quantitative echocardiography, myocardial 18F-fluorodeoxyglucose positron emission tomography computed tomography (18F-FDG PET/CT), and myocardial perfusion imaging (MPI) with Technicium-99 (Tc-99) sestamibi will be implemented to identify sensitive imaging measures of cardiac injury and asses myocardial mechanics, inflammation, and perfusion deficits, respectively. Concurrently, a multiparametric analysis will be conducted to identify novel, circulating biomarkers of cardiotoxicity. RESULTS/ANTICIPATED RESULTS: We hypothesize that a clinically-relevant mouse model can be generated by the in situ, focal irradiation of a portion of heart and/or lung tissue segments, and can be used to elucidate molecular mechanisms of radiation-induced cardiac damage. We anticipate time-dependent and dose-dependent, focal histopathologic changes in the mouse heart, with cardiac fibrosis development, vascular damage, and cellular apoptosis in irradiated mice. Additionally, we anticipate that our mouse model of focal heart irradiation will reveal radiologic and biochemical changes that can be used to characterize and predict radiation-induced cardiac injury. Specifically, we expect our quantitative echocardiography, FDG-PET, and MPI parameters to identify and characterize cardiac damage that topographically matches histopathological analysis, and expect levels of select biochemical markers to differentially vary with time. DISCUSSION/SIGNIFICANCE OF IMPACT: Our mouse model of radiation-induced cardiotoxicity has the potential to shift current preclinical research paradigms to more closely mimic the radiation plans most commonly administered in clinical practice. The primary technologic innovation to be developed here is the use of the SARRP to deliver image-guided, in situ, focal radiation to a defined portion of the mouse heart. From a conceptual perspective, we propose a novel approach for phenotyping radiation-induced cardiac damage in patients undergoing chest radiation therapy, integrating sensitive radiomic and biochemical markers into a predictive model of cardiotoxicity.

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A TL1 Team Approach to Personalizing Donor Human Milk for the Preterm Infant

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OBJECTIVES/SPECIFIC AIMS: Aim 1: To compare frozen MOM to fresh MOM over time as an agent to inoculate DHM and measure the enrichment of commensal microbes and their beneficial bioactive components similar to MOM. Hypothesis: Frozen or fresh MOM inoculated in DHM will produce similar microbial content to MOM over time allowing for the production of beneficial bacterial compounds that may contribute to host immune response. Aim 2: To determine the effect of MOM storage (fresh vs frozen) on the expansion of bioactive components from live microbiota in DHM. Hypothesis: Both fresh and frozen MOM will produce similar results when inoculated into DHM to restore the microbial content (including their bioactive components) similar to each MOM sample. Aim 3: To compare the microbiome found in a mother's MOM to the microbiome in her infant's stool. Hypothesis: The mother/infant pair will share a common microbiome between the mother's MOM and her infant's stool. METHODS/STUDY POPULATION: Subjects will include 12 pump-dependent mothers of infants born < 34 weeks gestation admitted to the University of Florida Health Shands Hospital, Neonatal Intensive Care Unit (NICU). Inclusion criteria consists of mothers expressing over 100 ml of MOM per day, producing at least 45 ml of MOM at an expression session, at least 18 years of age, and speak English. Mothers are excluded if they have taken antibiotics within 3 days of sample collection, are HIV+, or delivered an infant who has a chromosomal abnormality or is severely ill. An expressed MOM sample will be collected and divided into two fractions: (A) fresh and (B) frozen at -20C for 24 h. The fresh fraction (A) will be processed immediately while the frozen fraction (B) will be processed after 24 h. Each MOM will be inoculated in DHM at dilutions of 10% and 30% and incubated at different time points: 0 h (T0), 2 h

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(T2), 4 h (T4) at 37°C. At each time point, total viable cell counts as well as microbiome analysis through 16S ribosomal shotgun sequencing will be performed and compared for differences. Bacteria isolated from each MOM will be saved, identified through 16S ribosomal sequencing and grown in culture for future studies. Fecal samples from each corresponding infant will be collected within 48 h after collection of the MOM sample. Stools will be homogenized and subjected to DNA extraction to perform 16S ribosomal shotgun sequencing. Microbiome analysis will be conducted, compared between fecal samples as well as with the microbiome of the MOM. RESULTS/ANTICIPATED RESULTS: Study is ongoing. We anticipate similar results with fresh or frozen MOM to that of a previous pilot study, where enriched microbiota similar to MOM was found when fresh MOM was inoculated and incubated in DHM. The microbiome analysis of the infant fecal samples may illustrate the influence that the microbiome of the MOM may have on the development of the infants' gastrointestinal microbiota. DISCUSSION/SIGNIFICANCE OF IMPACT: The purpose of this study is to provide evidence on the ability, timing, and efficacy of inoculating DHM with fresh and frozen MOM. Study results will inform future studies to support the implementation of an inoculation procedural protocol to be used in clinical practice and human milk banking. The description of the MOM microbiome, as well as the gastrointestinal microbiome, will expand scientific knowledge on the role breast milk has on the origins of health and disease.

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Associations between Diabetes Mellitus and Sublingual Microvascular Disease: A Prospective Cross-Sectional Study

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OBJECTIVES/SPECIFIC AIMS: Diabetes mellitus (DM) is a risk factor for the development of microvascular complications. We sought to determine the association between diabetes mellitus status and microvascular circulatory disease, as measured in the sublingual capillary bed. METHODS/STUDY POPULATION: We prospectively recruited adults with cardiovascular (CV) risk factors or established CV disease, with and without DM, who were referred for invasive coronary angiography at an urban tertiary care medical center. All participants underwent non-invasive sublingual sidestream darkfield microscopy. The primary outcome was the perfused boundary region (PBR), a measure reflecting the extent to which red blood cells (RBC) penetrate the sublingual glycocalyx in vessels between 5 and 25 μm in width. RESULTS/ANTICIPATED RESULTS: 57 participants were enrolled. The mean age was 66.1 ± 11.1 years and a majority of participants (66%) were men. DM was present in 18 (31.6%) participants. Sublingual PBR measurements were not different between participants with and without DM overall (1.93μm vs. 1.96μm, p=0.63) or in vessels with high flow (1.48μm vs. 1.59μm, p=0.08). No differences in capillary RBC filling (72.9% vs 73.0%, p=0.95) or perfused microvascular density (3112 vs. 3236 μm/mm2, p=0.32) by DM status were observed. DISCUSSION/SIGNIFICANCE OF IMPACT: In a population of adults with CV risk factors or disease, DM was not associated with impaired sublingual microvascular glycocalyx. Additional investigation into diabetes-induced microvascular impairment is warranted.

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Biomechanical analysis of acute versus chronic aortic dissection flaps

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OBJECTIVES/SPECIFIC AIMS: Thoracic endovascular aortic repair (TEVAR) is more effective in remodeling the dissected aorta in acute versus chronic type B aortic dissection (TBAD). It has been hypothesized that this is due to differences in dissection flap biomechanical and structural properties but has not been confirmed in explanted human aortic tissue. We aimed to characterize and compare differences in tissue biomechanics and microstructure between acute and chronic dissection flaps that may underlie these findings. METHODS/STUDY POPULATION: Dissection flaps were obtained at time of operative repair for patients presenting for open aortic replacement to treat acute type A (ACUTE, n=7) or chronic type B (CHRONIC, n=7) aortic dissection. Given that the current treatment modality for acute complicated TBAD is TEVAR, it was not feasible to acquire acute TBAD flaps for analysis. Tissues were cryopreserved and subjected to biaxial tensile testing in the circumferential and longitudinal directions. Stiffness was quantified by the tangent modulus (TM) in the low and high linear regions of the compiled equibiaxial response curves for each cohort. Extensibility was defined as the intersection of the fitted line from the high linear region with the x-axis, and the degree of anisotropy (DA) was defined as the mean absolute percentage error of the strains in both directions. Flap architecture and collagen fiber organization were also compared between groups using two-photon microscopy. RESULTS/ANTICIPATED RESULTS: Average age of dissection flaps were 3.4±3.4 days in ACUTE and 1,868.7±1,354.0 days in CHRONIC (p=0.011). There were no differences in age, co-morbidities, maximum aortic diameter, and aortic wall thickness. ACUTE exhibited an anisotropic stress-strain response with increased extensibility longitudinally than circumferentially (0.18 vs. 0.09, p=0.022, DA=0.67) while CHRONIC demonstrated an isotropic response with similar extensibility in either direction (0.11 vs. 0.12, p=0.606, DA=0.26). CHRONIC and ACUTE had comparable stiffness in the circumferential direction (TMlow 439.92 vs. 541.08, p=0.729, and TMhigh 1585.19 kPa vs. 1869.35 kPa, p=0.817). In the longitudinal direction, CHRONIC was significantly stiffer than ACUTE (TMhigh 8347.61 kPa vs. 1201.34 kPa, p=0.049) (FIGURE). Microscopy corroborated these findings with greater collagen fiber organization circumferentially than longitudinally in ACUTE and increasing fibrosis, collagen predominance, and straightening of collagen fibers in CHRONIC. DISCUSSION/SIGNIFICANCE OF IMPACT: Compared to ACUTE, CHRONIC exhibited loss of anisotropy with increased tissue stiffness in the longitudinal direction. Increased dissection flap fibrosis and decreased compliance may explain the worse outcomes for aortic remodeling after TEVAR in chronic TBAD. This study offers biomechanical support for early TEVAR in the acute phase of uncomplicated TBAD.

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