vesicle (EV)-based vaccine generated using lab-strain Salmonella against wastewater-derived Salmonella. METHODS/STUDY POPULATION: We isolated Non-Typhoidal Salmonella (NTS) from raw influent wastewater samples collected from two wastewater reclamation facilities (WRF) in Gainesville, FL. Whole genome sequencing was performed on each isolate and compared to sequences of clinically-derived isolates in FL during our study period to identify a clinical and subclinical isolate for assessing EV based vaccine protection. Mouse serum and stool samples were collected from a cohort of EV-vaccinated mice. Surrogates of protection against Salmonella used anti-Salmonella IgA in the feces of these mice, and anti-Salmonella IgG in serum of the mice, by using ELISAs coated with whole cell lysate collected from the two wastewater-derived isolates. RESULTS/ANTICIPATED RESULTS: We have previously shown that an EV vaccine provides protection against Salmonella enterica Serovar Typhimurium, the serovar used in the generation of the EV vaccine. We anticipate that the EV vaccine generates additional protection against the community-acquired strains, which will be characterized by increases in fecal IgA and serum IgG against two community Salmonella isolates that is similar to responses against the serovar used to generate the EV vaccine (Typhimurium). DISCUSSION/SIGNIFICANCE: This study will improve the translation of our vaccine studies by demonstrating the efficacy of our novel EV vaccine against circulating Salmonella isolates.

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A CTS Team Approach to Fetal Hyperinsulinemia in Diabetic Pregnancy and its Effects on Vasculature and Early Life Metabolism

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OBJECTIVES/GOALS: Fetal glucose dynamics mediate many of the adverse outcomes seen in infants of diabetic mothers (IDM). The goals of this study are to identify: (1) rates of blood glucose change in normoglycemic and hypoglycemic IDM; (2) their relation to in-utero insulin exposure; and (3) their transcriptional impacts on placental and umbilical vasculature. METHODS/STUDY POPULATION: Using a longitudinal prospective study design, placental/umbilical cord tissue and maternal hemoglobin A1c (HbA1c) are being collected from mothers diagnosed with Type 1, Type 2, or gestational diabetes mellitus. Blood glucose levels are also collected from their infants at birth, and every 3-4 hours for up to 9 hours to determine the rate of change. Linear regression modeling will be used to determine associations between placental and umbilical endothelial RNA expression, umbilical cord insulin levels, and maternal HbA1c within each diabetic sub-type. Gene expression from endothelial specimens will be compared between diabetic subtypes and between normoglycemic and hypoglycemic infants via paired t-tests using Benjamini-Hochberg procedure for false discovery rate correction. RESULTS/ANTICIPATED RESULTS: We hypothesize the following; (1) glucose levels will have a steeper rate of change in hypoglycemic infants; (2) maternal HbA1c and in-utero insulin levels will correlate with the level of transcriptional change identified in placental and umbilical endothelial samples; (3) a negative association will exist between cord insulin levels and the rate of change in infant glucose levels; and (4) a positive association will exist between cord insulin level and transcriptional change on the placental and umbilical endothelium. DISCUSSION/SIGNIFICANCE: Identifying gene expression changes in diabetic placental/umbilical endothelium, and the role of insulin/glucose in these changes, is key to managing diabetic vasculopathy and its adverse outcomes. Understanding infant insulin response may also guide management of hypoglycemia and decrease the risk for neonatal intensive care unit admission.

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A CTS team approach to identifying thematic constructs related to kratom use during pregnancy and breastfeeding: A qualitative analysis of social media posts

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OBJECTIVES/GOALS: Research on the safety of perinatal kratom use - an herb that acts on opioid receptors - is scarce. Our transdisciplinary clinical and translational science (CTS) team is conducting parallel qualitative analyses of subreddit posts related to kratom use during (1) pregnancy and (2) breastfeeding. METHODS/STUDY POPULATION: Pregnancy- and breastfeeding-related keywords are being used to extract posts and selected metadata from the following subreddit communities: r/kratom, r/quittingkratom, r/pregnant, and/or r/breastfeeding. After the removal of duplicate posts, posts written in a non-English language and those that state in the post text and/or title that they were published by minors (RESULTS/ANTICIPATED RESULTS: Among the eligible posts, the number of unique usernames of the sources publishing the posts; the range of publication dates; and the mean, median, & range of the number of comments per post will be presented. Inter-rater concordance in thematic coding will be computed. A word cloud will be created with the most used nouns from the eligible posts. Verbatim quotes will be shown to illustrate themes depicted in the sample. The quantitative and qualitative analyses will be conducted separately for the posts related to kratom use during pregnancy and breastfeeding. DISCUSSION/SIGNIFICANCE: These findings could assist clinicians in identifying questions that obstetric patients may have regarding the perinatal use of this emerging substance of concern. Further research is needed to validate these findings using other social media data, such as Twitter.

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A novel mouse model of COVID-19

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OBJECTIVES/GOALS: Rodents are the most widely used experimental animals to study disease mechanisms due to their availability and cost-effectiveness. An international drive to investigate the pathophysiology of COVID-19 is inhibited by the resistance of rats and mice to SARS-CoV-2 infection. Our goal was to establish an appropriate small animal model. METHODS/STUDY POPULATION: To recreate the cytokine storm that is associated with COVID-19, we injected angiotensin converting enzyme 2 knockout (ACE2KO) mice (C57BI/6 strain) with lipopolysaccharide (LPS) intraperitoneally and measured the expression of multiple cytokines as a function of time

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and LPS dose. We then chose a minimum dose (500ug/kg) and time (3h) when multiple cytokines were elevated to measure lung injury scores using a point-counting technique on tissue sections stained with hematoxylin and eosin. The data are expressed as mean percentage of grid points lying within the peribronchial and superficial area in up to 20 fields. Percentage of peribronchial and superficial intrapulmonary hemorrhage, congestion, neutrophil infiltration and area of alveolar space were all assessed. RESULTS/ANTICIPATED RESULTS: Compared to the wildtype group (WT-G), the LPS-injected ACE2KO mice (LPS-G) exhibited a higher percentage of peribronchial intrapulmonary hemorrhage [(%): LPS-G, 10.56 ± 2.06 vs. WT-G, 5.59 ± 0.53; p DISCUSSION/SIGNIFICANCE: Establishing this novel mouse model of COVID-19 will facilitate studies investigating tissue-specific mechanisms of pathogenesis in this disease. This model can also be used to discover novel therapeutic targets and the design of clinical trials focusing on diagnostics, treatments and outcomes in COVID-19.

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A Phase 1 and Randomized Phase 2 Clinical Trial of Selinexor and Temozolomide in Recurrent Glioblastoma Among Adults: The Product of a Successful Team Science Approach

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OBJECTIVES/GOALS: Selinexor is a novel XPO1 inhibitor that blocks nuclear export, thus impairing DNA repair and causing apoptosis. Our goal was to conduct preclinical and clinical studies to test our hypothesis that selinexor's efficacy is boosted by priming with temozolomide and is associated with a tissue biomarker. METHODS/STUDY POPULATION: We leveraged a team science approach through the NCI Cancer Therapy Evaluation Program (CTEP) to design preclinical experiments, develop a novel RNAseq analysis pipeline, and use pre-existing clinical experience to open an early phase clinical trial for recurrent glioblastoma. Team members included a CTEP medical officer, cancer biologist, pharmacist, industry scientist, translational scientist, and early career clinician scientist mentored by an expert clinician scientist. Based on preclinical results, participants in the clinical trial experimental arm will receive sequential temozolomide 150mg/m2 on days 1-5 and a starting dose of selinexor 60mg on days 8 and 15 of a 28-day cycle. Participants in the control arm will receive monotherapy temozolomide. RESULTS/ANTICIPATED RESULTS: Sequential treatment of U87 cells and intracranial xenografts had superior DNA damage (É £H2A.X, cleaved PARP) and overall survival compared to combination or single-agent (HR 0.25 [95% CI, 0.07-0.84]; p=0.01, log-rank). We used the top-scoring gene pair method to identify an RNAseq signature associated with response to selinexor. We then designed a trial for first recurrent MGMT methylated glioblastoma. Primary objectives are safety and preliminary efficacy. Secondary objectives are overall response rate, efficacy, and validation of a molecular signature. Phase 1 dose finding (n=12) will be followed by a randomized phase 2 (n=72); using proportional hazards regression, RHR 0.5 with p DISCUSSION/SIGNIFICANCE: The NCI CTEP Project Team employs team science as a framework to successfully develop multidisciplinary collaborations, build investigator trial experience, and lead the way to future research opportunities. Our trial addresses a significant unmet need to offer novel therapies and molecular biomarkers in glioblastoma.

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Addressing complex and urgent problems through innovative team science: The University of Miami Laboratory for Integrative Knowledge (U-LINK)

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OBJECTIVES/GOALS: The goal of U-LINK is to bring together diverse scholars from multiple disciplines to address complex and challenging problems in healthcare, climate change, social equity, and community, through innovative team science, and aligned with the University of Miami's strategic plans. METHODS/STUDY POPULATION: The U-LINK program has supported developmental and implementation projects through a competitive selection process. Developmental funding was intended for teams to develop and refine ideas and to become established as an effective team. Additional funding was provided to teams to advance their projects by conducting data collection and feasibility testing. In addition, U-LINK has supported fellowship for pre-doctoral and affiliated doctoral trainees. Team science training was provided to all teams through didactic lectures and hands-on training. Teams were tracked longitudinally by using surveys and bibliometrics to measure success and impact including scholarly output and follow on funding. Network analysis was performed to analyze research collaboration networks before and after ULINK funding. RESULTS/ANTICIPATED RESULTS: U-LINK has funded pilot programs and initial phases for 57 projects and 13 fellowships in the last three years. Over 400 individuals on teams from 16 schools/academic units collaborated on these projects on topics such as resilience, climate change, social equity and societal challenges, health, and impact of recent legislation on LGBTQ+ community. While data collection and analysis are ongoing, initial results show successful outcomes from U-LINK projects including publications and $29.5m in follow-on external funding. We anticipate network analysis to demonstrate increased and continued multi-disciplinary collaborations among U-LINK teams through co-authorship networks and increase in collaborative grants being submitted and/or funded. DISCUSSION/SIGNIFICANCE: The University of Miami's U-LINK program has demonstrated success in forming interdisciplinary teams that have produced real-world solutions to complex problems by harnessing the inherent diversity and strength across UM's programs.

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An omega-6-derived eicosanoid negatively regulates platelet reactivity of cardiovascular patients at increased risk for thrombosis

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OBJECTIVES/GOALS: This study aimed to investigate the mechanistic effects of the omega-6-derived eicosanoid 12-HETrE on platelets of cardiovascular patients at risk for a recurrent cardiovascular event triggered by thrombosis. 12-HETrE negatively regulates platelet reactivity through binding to the prostacyclin receptor in platelets.

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