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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