group's history was a visit from the Program Officer for the UF Clinical and Translational Science Institute in February 2020. Since that time, multiple collaborations have resulted in grants submitted, such as P30 center grants and an innovative R61/R33, as well as numerous publications. DISCUSSION/SIGNIFICANCE: A complex public health emergency like the opioid epidemic requires creativity and collaboration, from laboratory science to interventions in the community, putting it squarely within the sights of translational research. SARB2C will soon enter its fifth year of linking researchers and training the next generation of scientists.

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Creating an In-Person Workshop Series Addressing Core Team Science Principles for Early Career Investigators

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OBJECTIVES/GOALS: A barrier to the proliferation of team science is that academicians are often trained in disciplinary silos where "independent" research contributions are lauded. To tackle some of the most pressing scientific challenges, dismantling silos and increasing team science training efforts that focus on early career investigators is a must. METHODS/STUDY POPULATION: A team science training workshop for early career investigators from varied disciplinary backgrounds was informed by a 20-item needs assessment that addressed essential team science competencies and was completed by early career investigators participating in federally funded professional development programs on our campus. During the workshop, the benefits of cross-disciplinary teaming was discussed. Strategies including team formation, team effectiveness and/or dysfunction, diagnosing team strengths and weaknesses, and teaming in community settings were discussed. Instructional methods included short presentations, video clips, case studies, group discussions, pair and share activities, and panel discussions with expert role models encouraged active learning. RESULTS/ANTICIPATED RESULTS: The impact and value of the workshop series to participant's professional development and knowledge of team science concepts will be evaluated before and after the workshop. Multiple Likert-scale items focused on team science competencies (e.g., confidence in your ability to carry out responsibilities specific to your role on a team, recognize when the team is not functioning well; engage team science practices in on-going research), and open-ended questions (e.g., importance of engaging community partners in academic research teams, vision of what factors contribute to an effective team science collaboration) will be completed by program participants before and after completing the workshop. DISCUSSION/SIGNIFICANCE: Effective collaboration among scientists with expertise in different disciplines is needed to address and solve complex scientific problems. We believe our interactive approach to team competency training sessions would work in a variety of settings and improve team skills.

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Design Lab Methodology Supports Innovation in Clinical Trials

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OBJECTIVES/GOALS: Since 2017, we have used the Design Lab methodology to support investigators taking innovative approaches to clinical effectiveness trial design. To date we have held 12 Design Labs and this year we are creating a handbook that will support dissemination of this approach across the Clinical and Translational Science Award consortium. METHODS/STUDY POPULATION: The Clinical Trial Design Lab brings together a multi-stakeholder group to consider innovative and impactful clinical trial designs. An investigative team is selected from a competitive pool of applicants, after which expert-led consultations support the investigator team to think about evidence generation in the context of the full treatment development pathway. Teams map the stakeholders at each step of this pathway (e.g. clinicians, patients, researchers, funders, industry experts, policy experts, regulatory experts, payers) and consider innovative design solutions. These consultations prepare investigators for an event that involves all stakeholders in a structured and facilitated discussion about trial designs that generate the best evidence and increase potential for health impact. RESULTS/ANTICIPATED RESULTS: The result of our work will be a set of Design Lab principles, a handbook with templates that support stakeholder mapping and structured discussions, and educational resources to accompany the handbook. The work is supported by a literature review that characterizes the multi-component processes included in the Design Lab, situates them within the larger context of team science interventions, and lays groundwork for the development of process metrics and impact evaluation criteria to assess the Design Lab method. In this poster presentation, we will share our multi-component broadly engaged team science approach, provide a brief outline of the principles and educational resources, and include an early version of the evaluation criteria. DISCUSSION/SIGNIFICANCE: Broadly engaged team science supports innovative thinking about study design and is especially important in the development of clinical trials. We have grown the Design Lab program of work over the past seven years and are now able to characterize our team science methodology and support others to use this approach to innovate for health impact.

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Maternal Opioid Use Leads to Aberrant Maternal and Fetal Immunity

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OBJECTIVES/GOALS: Maternal opioid use disorder (OUD) is linked to poor fetal outcomes. While it has been established that

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opioids can cross from maternal to fetal circulation, the mechanisms underlying these adverse outcomes remain poorly defined. This study aims to uncover OUD-associated immunological changes in maternal and fetal circulation. METHODS/STUDY POPULATION: To study the effect of maternal OUD on the maternal immune system at delivery, we collected maternal blood samples at delivery from healthy pregnant women (controls) and pregnant women with a diagnosis of severe OUD. To study the impact of maternal OUD on newborn immunity, we also collected umbilical cord blood (UCB) at delivery. Flow cytometry was used to determine the frequency and phenotype of circulating immune cell subsets and responses to stimulation. Isolated monocytes were stimulated with bacterial/viral agonist cocktails, while T and NK cells were stimulated with PMA/ionomycin. The impact of maternal OUD on circulating immune mediators was determined by Luminex and on monocyte activation markers sCD14 and CRP by ELISA. RESULTS/ANTICIPATED RESULTS: In maternal circulation, OUD was associated with a significant decrease in markers of inflammation, cell proliferation, and activation. Frequencies of immune cell subsets were impacted by OUD, shown by an expansion of CD8+ EMRA T cells, marginal-zone B cells, mDCs, non-classical monocytes, and CD16low NK cells. While no differences were seen in T and NK cell responses to stimulation, monocytes and pDCs had significantly lower responses to bacterial and viral agonist stimulation. Analysis of UCB revealed increased levels of pro-apoptotic/T cell exhaustion mediators and pro-inflammatory cytokines, albeit decreased levels of several chemokines and growth factors. The UCB immune landscape is altered with maternal OUD, as demonstrated by a shift from naive to memory CD8+ T cells and a decrease in pDC frequency. DISCUSSION/SIGNIFICANCE: OUD dampens maternal peripheral immunity, possibly contributing to poor placental function or premature/delayed labor. Monocytes and pDCs lack antimicrobial functionality, suggesting increased infection susceptibility with OUD. Finally, these implications extend to the fetal compartment, shown by heightened immune activation in UCB.

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Dual TGFβR1/MAP4K4 inhibitor reduces kidney injury in a mouse model of renal fibrosis.

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OBJECTIVES/GOALS: Renal fibrosis is a critical pathophysiological event in chronic kidney diseases. Our goal is to determine the ability of dual-inhibitor of transforming growth factor beta receptor 1 (TGFα²R1) and mitogen-activated protein kinase kinase kinase kinase 4 (MAP4K4), TK850, on reducing kidney fibrosis. METHODS/STUDY POPULATION: To test the renal anti-fibrotic action ofdual TK850,8-10-week-old male and female C57BL/6mice with unilateral ureteral obstruction (UUO) induced kidney fibrosis were used. Mice were separated into 3 groups: group 1 contained mice that had UUO surgery (UUO control), group 2 contained mice prophylactically treated with TK850 thatstarted 7 days prior to UUO(UUO-P,20 mpk/d/ip), and group 3 contained mice interventionally treated with TK850 that started3 days after UUO(UUO-I,20 mpk/d/ip). Ten days following UUO the kidneys and blood were collected for analysis. Renal fibrosis was assessed from hydroxyproline content (measure of collagen)and histological collagen analysis using Picrosirius red stain. RESULTS/ANTICIPATED RESULTS: Renal hydroxyproline was increased equally in the UUO kidney of male (5.4 ± 0.41 μg/10mg, n=5) and female mice (5.5 ± 0.50 μg/10mg, n=5) compared to the contralateral control kidney (2.9 ± 0.14 μg/10mg, n=10). TK850 treatment in UUO-P mice (n=10, 3.4 ± 0.24 μg/10mg) and UUO-I mice (4.30 ± 0.20 μg/10mg, n=10) had significantly reduced hydroxyproline levels. Histopathological evaluation revealed that kidney injury increased collagen deposition in the UUO kidney (17.1 ± 0.43% collagen positive area, n=10) compared to the control kidney (2.0 ± 0.23%, n=10). TK850 treatment in UUO-P mice significantly attenuated collagen deposition (10.5 ± 0.38%, n=10), while UUO-I had significantly reduced collagen deposition as well (13.1 ± 0.25%, n=10). DISCUSSION/SIGNIFICANCE: Taken together, these results validate the dual TGFβR1/MAP4K4 inhibitor, TK850 as a potential therapeutic to mitigate renal fibrosis and supports the emergence of a combinational pharmacotherapeutic approach for multi-factorial kidney diseases.

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Investigation of the Epidemiological Differences associated with Post Acute Sequelae of Sars-CoV-2 infection

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OBJECTIVES/GOALS: In this work investigating the epidemiological differences associated with Post Acute Sequelae of SARS-CoV-2(PASC) patho genesis we willassess the sex differences inocular viral persistence and the immunologic profile in tear film obtained from COVID-19 patients. METHODS/STUDY POPULATION: Participants will be enrolled from the NIH funded RECOVER Consortium at the 15 adult hubs in the US and will include those with acute COVID-19 (n=250), followed up at baselineto 48 weeks post infection. RT-PCR will be used to detect viral RNA and electro chemiluminescence assays will be used to detect IgG, IgA1 and IgA2 antibodies.Tear film antibody titers will be measured longitudinally in all participants to assess the kinetics of the immune responses in those who developed PASC and those who did not. Tear film antibody titers will be correlated with antibody titers in the blood and compared between those individuals with or without measurable viral RNA in tear film. RESULTS/ANTICIPATED RESULTS: Logistic regression models will be used assess the association of viral persistence with PASC status controlling for relevant covariates. Linear mixed regression models will be used to assess the association of IgA1/IgA2 with PASC status. We expect to observe delayed clearance of viral RNA and elevation in SARS-CoV-2 specific IgA2/IgA1 in the tear film of patients with PASC compared with those without PASC. Given evidence of increased PASC risk in women we expect to observe higher rates of SARS-CoV-2 ocular viral persistence and higher SARS-CoV-2 specific IgA2/IgA1 ratios in women with COVID-19 when compared to men with COVID-19. DISCUSSION/SIGNIFICANCE: There is concern that PASC will pose a major global health challenge given the scale of the Covid-19 pandemicand the patho genesis remains unclear. This work is highly likely to improve our understanding of the mechanisms of PASC and the reasons why women are more vulnerable to this condition.

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