support for dissemination/implementation functions, cross-institutional collaboration/networking, and leadership composition. RESULTS/ANTICIPATED RESULTS: In total, 52% of hubs will renew under the new PAR in the next few years, providing an incentive to demonstrate dissemination capacity (although hubs will likely lag in operationalizing these activities until they are funded). A third of hubs (34%) represent more than one academic/research institution, and almost 80% of hubs have more than one clinical affiliate. To accommodate these different levels of institutional complexity, broad diffusion will require multimodal, locally adapted dissemination efforts. Only 25% of hubs have capacity to undertake additional dissemination activities, and only 27% provide formal D&I support, suggesting that additional capacity/support will be needed to operationalize the CTSA dissemination mission. In total, 30% of hubs participate in cross-institutional collaboration/networking, so many may not have existing norms/tools supporting inter-institutional collaboration, but 77% include leadership from outside the School of Medicine, facilitating effective intrainstitutional dissemination. DISCUSSION/SIGNIFICANCE OF IMPACT: Understanding more about CTSA hubs as both adopters and transmitters of innovation can facilitate strategic use of these sites as a built-in dissemination network to amplify the reach and impact of clinical innovation and improve population health. Based on this initial analysis, the CTSA network does not appear to be fully primed for broad, rapid dissemination of innovation across its sites. In-depth interviews are being conducted to investigate CTSA hubs' perceptions of their dissemination capacity and roles as adopters and transmitters of innovation.

2224

Determining if intestinal commensal bacteria enhance the frequency of reassortment of an enteric, segmented virus, reovirus

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OBJECTIVES/SPECIFIC AIMS: The overall goal is to determine if intestinal commensal bacteria play a role in enteric virus evolution. We will use reovirus, an enteric segmented virus, to investigate specific goals. First, we will determine if specific bacterial species enhance the coinfection frequency of 2 separate strains of reovirus. Second, we will determine if the presence/absence of different bacterial species in the microbiota of mice results in different reovirus reassortment frequencies. Finally, we will discover if reassortant reovirus is present in human populations. METHODS/STUDY POPULATION: My first goal is to determine if specific bacterial species enhance the coinfection frequency of 2 strains of reovirus. In our lab, we have a panel of commensal intestinal bacterial strains, as well as a number of lab adapted bacterial strains. We will use this panel of bacteria to determine if reovirus binds to different species of bacteria using a binding assay involving radiolabeled virus. Additionally, we will determine if specific species of bacteria alter the coinfection frequency through a Flow cytometry based assay. This will involve mixing virus with bacteria, infecting cells in culture, and straining for reovirus proteins for flow cytometry. Our second goal is to determine if specific bacteria promote reassortment of reovirus in a mouse model of infection. To do this, we will use gnotobiotic techniques to create mice harboring different intestinal bacteria populations. Mice will be infected with 2 strains of reovirus, and then feces and organs will be collected. Progeny virus will be subjected to a plaque assay on 2 different types of cells. The first type of cells will be normal cells in culture in which all viable viruses will form plaques. The second will be a cell line that stably expresses siRNAs against specific reovirus segments in which only specific reassortants will form plaques. These 2 plaque assays will be used to quantify the total number of viruses present and the total number of reassortant viruses present. Additionally, SDS-PAGE and RT-PCR will be used to confirm reassortants. Our third goal is to determine if reassortant reovirus is present in infected humans. To do this, I will obtain feces from reovirus-infected children and isolate reovirus. One specific reovirus reassortant is known to propogate in dual-infected mice. I will use the plaque assay technique to determine if this reassortant is also present in humans. To determine if other reassortants are present, I will use RT-PCR and SDS-PAGE. RESULTS/ANTICIPATED RESULTS: Based on previous studies with other enteric viruses, we suspect that specific bacterial species bind reovirus strains with different efficiencies. It is likely that a number of bacterial species will promote coinfection. The bacterial strains that binds both reovirus strains at a high efficiency will likely enhance coinfection by the greatest amount. It is likely that mice harboring different bacterial populations will produce different reovirus reassortment frequencies. We predict that bacteria that enhance reovirus coinfection in vitro should also enhance reovirus reassortment in our mouse model. Therefore, mice specifically lacking bacteria that promote coinfection should have significantly lower amounts of reassortant reovirus. It will be important to control for the overall amount of replication within mice with different microbiotas, as this will affect the basal reassortment frequency. We suspect that reovirus reassortants are present in humans. Work done both in vitro and in mouse models indicates that reassortment happens at high frequencies. Additionally, one specific reassortant commonly propogates in mice due to an enhanced cellular attachment phenotype. Therefore, we predict that this reassortant also commonly emerges after coinfection and reassortment in humans. DISCUSSION/SIGNIFICANCE OF IMPACT: Segmented viruses, such as influenza and rotavirus, are important human pathogens. Viral reassortment poses a unique threat to humans, as it enables new viruses to emerge and cause pandemics or epidemics. However, little is known about what factors promote viral reassortment. This study will provide insight into a novel mechanism of segmented virus evolution.

2421

Development and validation of a translational rat model of neonatal abstinence syndrome

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OBJECTIVES/SPECIFIC AIMS: Rodent models can be used to study neonatal abstinence syndrome (NAS), but the applicability of findings from the models to NAS in humans is not well understood. The objective of this study was to develop a rat model of norbuprenorphine-induced NAS and validate its translational value by comparing blood concentrations in the norbuprenorphine-treated pregnant rat to those previously reported in pregnant women undergoing buprenorphine treatment. METHODS/STUDY POPULATION: Pregnant Long-Evans rats were implanted with 14-day osmotic minipumps containing vehicle, morphine (positive control), or norbuprenorphine (0.3–3 mg/kg/d) on gestation day 9. Within 12 hours of delivery, pups were tested for spontaneous or precipitated opioid withdrawal by injecting them with saline (10 mL/kg, i.p.) or naltrexone (1 or 10 mg/kg, i.p), respectively, and observing them for well-validated neonatal withdrawal signs. Blood was sampled via indwelling jugular catheters from a subset of norbuprenorphine-treated dams on gestation day 8, 10, 13, 17, and 20. Norbuprenorphine concentrations in whole blood samples were quantified using LC/MS/MS. RESULTS/ANTICIPATED RESULTS: Blood concentrations of norbuprenorphine in rats exposed to 1–3 mg/kg/d of norbuprenorphine were similar to levels previously reported in pregnant women undergoing buprenorphine treatment. Pups born to dams treated with these doses exhibited robust withdrawal signs. Blood concentrations of norbuprenorphine decreased across gestation, which is similar to previous reports in humans. DISCUSSION/SIGNIFICANCE OF IMPACT: These results suggest that dosing dams with 1–3 mg/kg/day norbuprenorphine produces maternal blood concentrations and withdrawal severity similar to those previously reported in humans. This provides evidence that, at these doses, this model is useful for testing hypotheses about norbuprenorphine that are applicable to NAS in humans.

2525

Development of human cell-based screening assays to detect subject-specific drug-response variability

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OBJECTIVES/SPECIFIC AIMS: The goals of this study are to develop a human-based screening assay for testing individual drug reactions and investigate the mechanism underlying susceptibility to develop diLQT. METHODS/STUDY POPULATION: We derived iPSC-CMs from 10 subjects with a high sensitivity to Sotalol (high-S group) and 10 subjects with no changes in QT interval after administration of the same drug (low-S group). Multielectrode array (MEA) was used to measure field potential duration, a surrogate to the QT interval in the electrocardiogram, in iPSC-CMs under basal conditions and in response to increasing concentrations of Sotalol. Transcriptomic profiling of iPSC-CMs from high-S Versus low-S groups was performed using RNA-sequencing. A parameter sensitivity analysis was performed on the Paci *et al.* iPSC-CM mathematical model to further support the lead hits identified via RNA-sequencing. RESULTS/ANTICIPATED RESULTS: Cardiac differentiation resulted in the generation of iPSC-CMs with appropriate cardiac channel

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expression and response to a hERG blocker E4031. MEA recordings showed a significantly higher response to Sotalol in iPSC-CMs from high-S compared with low-S subjects. Transcriptomic profiling identified upregulation or down-regulation of genes (DLG2, KCNE4, PTRF, HTR2C, CAMKV) involved in downstream regulation of cardiac repolarization and calcium handling machinery as underlying high sensitivity to Sotalol. In silico parameter sensitivity analysis corroborated transcriptomic profiling of select genes; upregulated KCNE4 and downregulated CAMKV were predicted to positively and negatively correlate with iPSC-CM action potential duration when exposed to Sotalol, respectively. DISCUSSION/SIGNIFICANCE OF IMPACT: Our findings suggest subject-specific iPSCs can be used to model functional abnormalities observed in diLQTS and offer novel insights into iPSC-based screening assays for toxic drug reactions. Success of this study may help identify key components underlying diLQT susceptibility to ultimately develop novel therapeutic agents.

2028

Discovery and evaluation of FOXP3 dimerization inhibitors

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OBJECTIVES/SPECIFIC AIMS: Immuno-oncology (IO) strategies are promising new approaches for the treatment of a variety of malignancies, including multiple myeloma (MM). Regulatory T cells (Tregs), which suppress effector T cell function, are a limitation to durable IO responses. The transcription factor FOXP3 is critical for the mature Treg phenotype. FOXP3 homodimerization is required for DNA binding and transcriptional activity, and mutations mapping to the dimerization region are associated with IPEX syndrome, resulting in dysfunctional Tregs in humans. We therefore hypothesize that inhibitors of FOXP3 dimerization will repress Treg suppression and enhance the anti-MM activity of IO. METHODS/STUDY POPULATION: To discover FOXP3 dimerization inhibitors, we are modeling FOXP3 homodimerization in vitro. Currently, we are optimizing an ALPHA screen and an ELISA-based dimerization assay using recombinant full length and truncated versions of FOXP3 to discover peptidomimetics that inhibit homodimerization. Induced Tregs expanded from human PBMCs will be treated with lead biologics and functional assays will be performed. RESULTS/ANTICIPATED RESULTS: Here we demonstrate Treg suppression of T cell proliferation and IFN-γ secretion after 5 days of co-culture under basal conditions. Additionally, we developed a MM/T cell co-culture system to measure anti-MM T cell responses and show decreased anti-MM T cell activity in the presence of Tregs. We expect to exploit the assays outlined here to demonstrate defective Treg suppression when FOXP3 dimerization is inhibited. DISCUSSION/SIGNIFICANCE OF IMPACT: These studies support drug discovery efforts that will ultimately improve IO therapies for patients with MM.

2510

Disparities in navigation to health research among Floridians

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OBJECTIVES/SPECIFIC AIMS: The analyses explore socio-demographic characteristics of community members who are navigated and enrolled in health research through HealthStreet—the CTSA community engagement initiative at University of Florida. METHODS/STUDY POPULATION: HealthStreet utilizes the Community Health Worker model to reach the community, conduct health assessments, provide referrals to medical/social services and link people to health research. We compared never navigated, navigated and not enrolled, navigated and enrolled on demographics, access to care, common health conditions and drug use among this community dwelling population. RESULTS/ANTICIPATED RESULTS: Among the 9581 community members, 51% were navigated to a study; 41% were screened eligible and enrolled (n = 2024) for an overall enrollment yield of 21%. Disparities were found for all variables; never navigated Versus the others were more likely to be African American, never married, reporting less education and less access to care. The navigated and enrolled Versus others were older females who reported more education, food insecurity, more access to care, and higher rates of hypertension, depression, and prescription opioid and marijuana use. DISCUSSION/SIGNIFICANCE OF IMPACT: Our unique and comprehensive data can assist investigators to tailor recruitment efforts that reduce disparities in health research.

2160

Does maternal schistosomiasis affect the humoral and cellular vaccine responses of infants?

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OBJECTIVES/SPECIFIC AIMS: The aims of this study are 2-fold: (1) to determine if maternal schistosomiasis affects maternal immunity to tetanus and/or transplacental transfer of antitetanus toxoid (TT) immunoglobulin G (IgG) from mother to infant and (2) determine the influence of maternal schistosomiasis on infant BCG vaccine immunogenicity. METHODS/STUDY POPULATION: The study will utilize blood samples from a historic cohort of 100 mother-infant pairs from Kisumu, Kenya, a schistosomiasis-endemic area. For the first aim, we will evaluate maternal schistosomal circulating anodic antigen, which has improved sensitivity and specificity to detect active schistosomiasis from serum, and antisoluble egg antigen IgG positivity compared with quantitative maternal anti-TT IgG at delivery and anti-TT IgG cord blood to maternal blood ratio (cord:maternal ratio). For the second aim, we will evaluate association between maternal schistosomiasis as detected by circulating anodic antigen and antisoluble egg antigen IgG at delivery and infant BCG-specific Th1-cytokine positive CD4+ cells at 10 weeks following BCG vaccination at birth. RESULTS/ANTICIPATED RESULTS: We hypothesize that active maternal schistosomiasis will be associated with decreased maternal anti-TT IgG and reduced efficiency of transplacental transfer, as measured by infant cord blood to maternal blood ratio of anti-TT IgG. We also expect that maternal schistosomiasis will be associated with decreased infant immunogenicity to BCG vaccine. DISCUSSION/SIGNIFICANCE OF IMPACT: This is a formative study on infant vaccine immunity using laboratory methodology not previously applied. Understanding infant immunity in the setting of maternal schistosomiasis will inform vaccination strategies and tailor vaccine development in schistosome-endemic areas such as Kenya, where neither TB nor neonatal tetanus have been eradicated. Additionally, our results will inform public health policies to consider integration of antischistosomal agents in antenatal care.

2178

Drug development core facilitates institutional collaboration and translational science innovation

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OBJECTIVES/SPECIFIC AIMS: Drug development is a common research pursuit for basic and clinical scientists that interfaces diagnostic/therapeutic challenges with funding agencies, pharmaceutical industry, regulatory systems, and education. The University at Buffalo Clinical and Translational Science Institute (CTSI) has implemented a Drug Development Core (DDC) with goals that foster team science and collaboration, optimize laboratory use, and networks investigators. Our goals are to foster collaborations within the region and with other CTSAs. METHODS/STUDY POPULATION: The DDC met with 300 potential investigators from 14 departments and several local companies. There were 35 portal requests from 15 departments and 7 companies; 8 were from training programs. For 28 requests, a reviewer provided consultation, while 7 required discussions and review of data. DDC assisted with 15 grant applications (outcomes pending), 10 industry-related new drug development requests and 1 regulatory review. Curriculum reviews noted overlap and gaps. Cross-institute opportunities for M.D.-Ph.D. research mentoring were identified. RESULTS/ANTICIPATED RESULTS: The DDC met with 300 potential investigators from 14 departments and several local companies. There were 35 portal requests from 15 departments and 7 companies; 8 were from training programs. For 28 requests, a reviewer provided consultation, while 7 required discussions and review of data. DDC assisted with 15 grant applications (outcomes pending), 10 industry-related new drug development requests and 1 regulatory review. Curriculum reviews noted overlap and gaps. Cross-institute opportunities

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