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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for M.D.-Ph.D. research mentoring were identified. DISCUSSION/SIGNIFICANCE OF IMPACT: The CTSI DDC was well received by investigators. The request process fosters collaboration among researchers with similar interests and identifies core laboratory resources that add innovation to ongoing research, funding applications, education, and interinstitutional planning.

2095

Drug screening and hit identification for night blindness with zebrafish

Logan Ganzen and Yuk Fai Leung

OBJECTIVES/SPECIFIC AIMS: Retinitis pigmentosa (RP), also known as night blindness, is an incurable disease which affects ~1 in 4000 individuals globally. Since there are no effective treatment options for RP, the goal of this project is to identify novel drug treatments that can prevent or slow the disease progression. To this end, we optimized a behavioral assay, visual-motor-response (VMR) assay, to investigate rod function (Ganzen *et al.*, *ARVO*, 2017; Ganzen *et al.*, *IJMS*, 2017). This was done utilizing a transgenic zebrafish RP model expressing human rhodopsin with the Q344X mutation. In this study, we used this model to perform a proof-of-concept screen for drugs which may improve the vision of the larvae. METHODS/STUDY POPULATION: To screen for beneficial drugs, the SCREEN-WELL® REDOX library was chosen for screening. This library was selected to identify a compound that may alleviate any excessive oxidative stress in the diseased retina. The Q344X zebrafish line suffers from significant rod degeneration by 7 days postfertilization (dpf) and displayed deficits in VMR under scotopic conditions (Ganzen *et al.*, *ARVO*, 2017). The Q344X larvae were drug treated beginning at 5 dpf at 10 μM. Compounds that were toxic at this concentration were retested at 1 μM. The 5 dpf stage was chosen as most of the rods are intact, and these concentrations were chosen to optimize the drug effect based on similar studies. Hits were identified by assays that provided a robust and reproducible enhancement in the Q344X VMR. The retinae of any drug hits were dissected from larvae crossed with a rod EGFP reporter line and whole-mounted to analyze rod survival via fluorescence. To determine if drug effects were exerted through the retina, eyeless chokh mutant zebrafish were exposed to the drug and tested with the same assay. RESULTS/ANTICIPATED RESULTS: Of the 84 compounds tested, we identified 1 drug that ameliorated the VMR of the Q344X scotopic VMR. Eyeless chokh mutant zebrafish larvae did not exhibit the same VMR when treated with the same drug. Histological analysis suggested increased rod survival in the drug-treated retina of Q344X mutants. DISCUSSION/SIGNIFICANCE OF IMPACT: These results indicate that the vision of the Q344X zebrafish was improved via this beneficial drug treatment. Since eyeless chokh larvae did not respond to the same treatment, the drug likely mediated its positive effects through the Q344X retina, likely by improving rod survival. Together, our results have identified a beneficial drug that may treat RP.

2038

Effects of bilateral frontal transcranial direct current stimulation (tDCS) on the working memory network: An fMRI-tDCS study in healthy older adults

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OBJECTIVES/SPECIFIC AIMS: The study aimed to determine the effects of bilateral frontal active transcranial direct current stimulation (tDCS) at 2 mA for 12 minute Versus sham stimulation on functional connectivity of the working memory network during an fMRI N-Back task. METHODS/STUDY POPULATION: Stimulation was delivered over bilateral frontal dorsolateral prefrontal cortex via and MRI-compatible tDCS device during an fMRI working memory task in healthy older adults in a within-subject design. RESULTS/ANTICIPATED RESULTS: Active stimulation compared with sham resulted in significant increases in functional connectivity in working memory related brain regions during the N-Back task. DISCUSSION/SIGNIFICANCE OF IMPACT: Older adults typically have reduced functional connectivity compared with young adults. Our findings demonstrate that a single session of tDCS can increase functional connectivity of the working memory network in older adults. Based on this mechanism of effect, tDCS may serve as an adjunctive method for interventions aiming to enhance cognitive processes in older adults.

2060

Exploring gene expression signature shared between obese Zucker rat and human cardiac hypertrophy

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OBJECTIVES/SPECIFIC AIMS: Objectives: To determine genes that are shared between human and obese Zucker rat hypertrophic hearts, in order to identify potential early biomarkers and drug target for heart failure. METHODS/STUDY POPULATION: Four age-paired lean and obese Zucker rats were used. The human data are derived from doi:10.1152/physiolgenomics.00122.2016. RESULTS/ANTICIPATED RESULTS: We expect to find genes that are upregulated and downregulated in Zucker rats and humans that present cardiac hypertrophy. DISCUSSION/SIGNIFICANCE OF IMPACT: The genes and proteins determined from this study will provide future directions in order to determine whether obese Zucker rats are a valid model organism for the development of cardiac hypertrophy.

2116

Exploring Müller cell-cone interactions in human fovea using 3-dimensional volume electron microscopy (EM)

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OBJECTIVES/SPECIFIC AIMS: Müller cells, radial glial cells of the retina, are the principal repository of xanthophyll pigment (lutein, zeaxanthin, meso-zeaxanthin), which are modifiable by diet and visible clinically by autofluorescence imaging. To understand the structural basis of xanthophyll visualization in vivo, we used 3-dimensional electron microscopic reconstruction of Müller cells surrounding one cone in a healthy human fovea. METHODS/STUDY POPULATION: From a 21-year-old male organ donor, dissected retinas were rejuvenated by oxygenated Ames medium then fixed in 4% glutaraldehyde. A tissue block 3.5 mm^2 centered on the fovea was prepared for Automated Tape Ultramicrotomy (Kasthuri *et al.*, *Cell* 162: 648–661, 2015). From 1462 serial 65 nm horizontal sections, an area ~250 × 250 μm was imaged at 6 nm *xy* resolution. Images were stitched and aligned. TrackEM software on a pen display was used to trace, reconstruct, and display cone #5 (of 186) and its contacting Müller cells. RESULTS/ANTICIPATED RESULTS: Cone 5 is ensheathed by 2 types of Müller cells, outer and inner (Dacey, *ARVO*, 2016). The outer cell is first seen at the external limiting membrane (ELM) between cones 5 and 17. Moving inward from the ELM, it tightly wraps around cone 5's fiber in a C-shape profile for 78 μm. This Müller cell also intermittently projects to neighboring cones, 2 of which were close to cone 5 at the ELM. As cone 5's axon approaches the pedicle, it contorts into a corkscrew. The outer cell fluidly molds to this changing shape. At this level, this Müller cell doubles in volume to encompass not only cone 5, but also cone 17 and another Müller cell. In the final 17 μm of the block the Müller cell's volume quickly dissipates as it sends a small projection towards the internal limiting membrane, eventually encasing an OFF midget bipolar cell also associated with cone 5. In contrast to this outer cell, an inner Müller cell adjoining cone 5 spans only 19 μm, interacting directly with cone 5 and the outer cell for 3.9 μm. DISCUSSION/SIGNIFICANCE OF IMPACT: Neural-glial relationships in a human fovea are visible through 3-dimensional volume EM. The volume of Müller cells in the fovea was impressive, consistent with a pivotal role in the health of cone photoreceptors and xanthophyll homeostasis. It is possible that individual glia also ensheath the post-receptoral neurons in a cone-driven circuit, supporting the concept that xanthophylls contribute to neural efficiency in vision.

2036

Extracellular matrix as a novel approach to glioma therapy

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OBJECTIVES/SPECIFIC AIMS: Gliomas are the most lethal and common primary tumor type in the central nervous system across all age groups; affected adults have a life expectancy of just 14 months. As glioma cells invade the surrounding

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