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

Nicole R. Nissim[1,2], Andrew O'Shea[1,2], Lindsey Richards[1,2], Rachel Telles[1,2], Eric Porges[1,2], Ronald Cohen[1,2] and Adam J. Woods[1,2]

[1] Center for Cognitive Aging and Memory, McKnight Brain Institute, Department of Clinical and Health Psychology, University of Florida, Gainesville, FL, USA; [2] Department of Neuroscience, University of Florida, Gainesville, FL, USA

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

Mackenzie Newman, Janelle Stricker and Han-Gang Yu

Department of Physiology, Pharmacology, and Neuroscience, West Virginia University, Morgantown, WV, USA

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)

Ramya Singireddy[1], Kenneth R. Sloan[1], Jeff W. Lichtman[2], Christine A. Curcio[1] and Dennis M. Dacey[3]

[1] University of Alabama, Birmingham, AL, USA; [2] Harvard University, Cambridge, MA, USA; [3] University of Washington, Seattle, WA, USA

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

Mark H. Murdock[1], Jordan T. Chang[1], George S. Hussey[1], Nduka M. Amankulor[2], Johnathan A. Engh[2] and Stephen F. Badylak[1]

[1] McGowan Institute for Regenerative Medicine, University of Pittsburgh; [2] Department of Neurological Surgery, University of Pittsburgh

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

https://doi.org/10.1017/cts.2018.70 Published online by Cambridge University Press