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 interdisciplinary planning.

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 10μM. 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 for fluorescence. To determine if drug effects were exerted through the retina, eyeless chokl mutant zebrafish were exposed to the drug and tested with the same assay. RESULTS/APPROACHES: Of the 84 compounds tested, we identified 1 drug that ameliorated the VMR of the Q344X scotopic VMR. Eyeless chokl 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 chokl 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.

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.

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 rats 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 were derived from doi:10.1152/physiogenomics.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.

Exploring Müller cell-cone interactions in human fovea using 3-dimensional volume electron microscopy (EM)
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OBJECTIVES/SPECIFIC AIMS: Muller cells, radial glial cells of the retina, are the primary 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 Muller cells surrounding one cone in a healthy human fovea. METHODS/STUDY POPULATION: From a 21-year-old male organ donor, dissected retinas were rehydrated by oxygenated Ames medium then fixed in 4% glutaraldehyde. A tissue block 3.5 mm² centered on the fovea was prepared for Automated Tape Ultra-microtomy (Kasthuri et al., Cell 162: 648-661, 2015). From 1462 serial 65 nm horizontal sections, an area - 250 x 250 μm was imaged at 6 nm zy resolution. Images were stitched and aligned. TrackEM software on a pen display was used to trace, reconstruct, and display cone i (of 186) and its contacting Muller cells. RESULTS/APPROACHES: Cone 5 is ensheathed by 2 types of Muller 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 Muller cell also interminently projects to neighboring cones, 2 of which were close to cone 5 at the ELM. As cone 5's axon approaches the pedicle, it contours into a croskrew. The outer cell fluidly molds to this changing shape. At this level, this Muller cell doubles in volume to encompass not only cone 5, but also cone 17 and another Muller cell. In the final 17 μm of the block the Muller 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 Muller 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 Muller 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.

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...
OBJECTIVES/SPECIFIC AIMS: To examine how women with OF in Ghana develop strategies for coping in the absence of access to successful surgical repair. To assess the feasibility, acceptability, and appropriateness of an innovation to support coping among women with OF seeking care in a health facility in Ghana. To examine the perceived facilitators and barriers to implementation among all of the stakeholders regarding the innovation.

METHODS/STUDY POPULATION: This study uses a sequential exploratory mixed methods design. The population of study is women in Ghana living with obstetric fistula, as well as additional fistula stakeholders (programmers, policy makers, community leaders). To get an understanding of usual leakage, women carried out at baseline a pad test, where they wore a sanitary pad for 2 hours and leakage freely. We subtracted the dry pad weight from the wet pad weight to estimate urine losses in mL. Then women inserted the cup for 2 hours and again wore a pad and urine leakage was estimated. Acceptability among women with vesicovaginal fistula was measured by questionnaire. Acceptability among additional stakeholders was examined by semistructured interview. Appropriateness was assessed among the user, additional stakeholders, and organizational stake. RESULTS/ANTICIPATED RESULTS: We found a 61% reduction in leakage with the cup which was also perceived by cup users as a reduction in wetness. Notably, one participant who had 4 previous surgical attempts, experienced a 78% reduction in leakage. No adverse events attributable to the use of the cup were observed, unlike some of the strategies currently used to manage leakage. Acceptability was high as most women could easily insert, remove, and wear the cup over the 2-hour period and fistula stakeholders indicated that the innovation was acceptable. In community interviews, women shared various coping and self-care strategies to manage their leaking, other related impairments, and stigma. Women using the cup in the health facility expressed that it was useful. Additional stakeholders found the cup a low-cost, low-tech solution to supplement existing programs. Within the stakeholder interviews we heard that the cultural norms and existing activities of the potential implementation partners align with the innovation approach. Stakeholders revealed various implementation facilitators and barriers. The facilitators to implementation reported in the interviews were related to the intervention and organization characteristics in particular. Stakeholders perceived a relative advantage to self-management. Stakeholders had concerns regarding whether women would find the insertable device acceptable and appropriate—questioning whether potential users would have access to water, soap, and safe space to empty cup. DISCUSSION/SIGNIFICANCE OF IMPACT: The innovation is efficacious, acceptable, adds to current coping strategies, and fits within existing fistula programs. Stakeholders pre-implementation perceptions highlight the importance of partnerships and the need for an evidence base related to effectiveness, acceptability, and cost. Challenges to address include access to resources within these contexts (water, soap, and safe space) and development appropriate counseling message.