in motor learning, which could be attributable to differences in task protocols and/or genetic background. These results highlight the importance of $Ca_V1.3$ in a variety of behaviors, which may help explain why variation in $Ca_V1.3$ expression and function has pleiotropic effects in humans.

4097

Transcriptome and molecular analysis of erythropoietin-induced hypertension

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OBJECTIVES/GOALS: High blood-pressure (BP) is a common adverse effect of erythropoietin (EPO) therapy among patients with chronic kidney disease on hemodialysis, and even among otherwise healthy individuals who receive EPO. In human genetics, EPO is associated with not only red blood cell traits, but hypertension (HTN) as well. Currently, there is no vascular gene expression data available in the setting of EPO-induced HTN that may explain precise role of key cellular players in its hypertensive etiology. Our aim is to characterize vascular transcriptome to identify key cellular players in EPO-induced HTN. METHODS/STUDY POPULATION: 10-12 week C57BL/6 male and female mice were randomly divided into two groups 1. Vehicle (0.9% saline-VEH), 2. EPO, (N = 4). VEH and EPO were intraperitoneal administered (EPO 75U/30g, 3 times/week) for 20 days. Blood-pressure was measured non-invasively via tail-cuff plethysmography. We characterized in-vivo transcriptome response of mouse descending aorta to EPO-HTN and vehicle control group by high-throughput RNA-sequencing. RESULTS/ANTICIPATED RESULTS: Systolic blood pressure (SBP) was significantly higher in EPO treatment, compared to vehicle (males and females combined SBP VEH 116.29±6.21, EPO 129.57±4.59, mean±s.d., adjusted P = 0.0012). Comparison of in-vivo transcriptional differences between vehicle and EPO-treated reveal statistically significant changes in cellular pathways consistent with hypertension such as upregulation of RAS signaling pathway and oxidative stress. In-vitro mouse aortic smooth muscle cells, EPO markedly increased phosphorylated-ERK activity, suggesting increased RAS activity. DISCUSSION/SIGNIFICANCE OF IMPACT: This study highlights the importance of previously unknown vascular key players and advances our understanding of the transcriptional events associated with EPO-induced hypertension.

4547

Understanding the molecular mechanism of natural killer cell deficiency to improve natural killer cell *in vitro* differentiation for therapeutics

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OBJECTIVES/GOALS: Natural killer (NK) cells are a potential cancer therapeutic but expanding NK cells efficiently *in vitro* is difficult. Natural killer cell deficiency (NKD), a primary immune deficiency affecting only NK cells, is caused by defects in several DNA replication proteins. By studying NKD we will achieve better NK cell *in vitro* differentiation. METHODS/STUDY POPULATION: One patient with NKD has a compound heterozygous mutation in the essential DNA replication protein MCM10. We hypothesize that in individuals with NKD, dramatic telomere erosion from abnormal DNA replication leads to premature senescence and the loss of NK cells. To test our hypothesis, we will knockout one allele of MCM10 or over express *MCM10* in NK cells isolated from blood. We will then monitor telomere length, expansion and cytotoxic activity of these NK cells. To understand the role of MCM10 in early stages of NK cell development we will deplete MCM10 in induced pluripotent stem cells and differentiate these cells into NK cells. During this differentiation we will monitor progression through NK cell developmental stages as well as telomere length and senescence markers. RESULTS/ANTICIPATED RESULTS: Telomeres insulate chromosomes and induce permanent growth arrest (senescence) when they are critically short. We have demonstrated that depletion of a DNA replication protein causes telomere erosion and increases senescence markers. NK cells have shorter telomeres and lower telomerase expression than other immune cells. We predict, this relatively poor telomere maintenance sensitizes NK cells to telomere loss upon depletion of replication proteins. During *in vitro* differentiation, we expect NK cell precursors to undergo premature senescence secondary to telomere shortening. Furthermore, we expect supplementation of DNA replication proteins will enhance NK cell expansion and maturation. DISCUSSION/SIGNIFICANCE OF IMPACT: NKD patients have provided the scientific community with clues as to what proteins NK cells rely on for their development. This project aims not only to understand why these proteins are critical, but to harness that information for cellular anti-cancer therapeutics.

4117

UNIQUE VAGINAL MICROBIOME POPULATIONS AND MICROBIAL GENE CONTENT AMONG WOMEN WHO NATURALLY CONTROL HIV PROGRESSION

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OBJECTIVES/GOALS: The role of the vaginal microbiome (VM) in HIV disease progression is poorly understood. We examined VMs of HIV+ Elite Controllers (ECs) and HIV+ Long-Term Non-Progressors (LTNPs) compared to controls: HIV-positive antiretroviral (ARV) treated (HIV+ATs) and HIV-negative women in the Women's Interagency HIV Study (DC/Chicago/Atlanta sites). METHODS/STUDY POPULATION: VMs were surveyed via both V3/V4 region of 16S rRNA gene amplicon sequencing and metagenomics sequencing in 67 women across 4 study groups: 1) LTNPs (CD4 >500 cells/mL for 5+ years without ARVs) (n = 7) and 2) ECs (HIV RNA <80 copies/mL for 2+ years without ARVs) (n = 8), matched with 3) HIV+ ATs (on ARVs for ≥1 year with CD4 increase ≥100 cells/mm^3) (n = 34), and 4) HIV- women (n = 18). Metagenomes were characterized from specimens collected at two time points: 1) vaginal swabs collected 2016-2017 (n = 62) and 2) cervicovaginal lavage collected 2002-2016 (n = 35; DC/Chicago only). We used VIRGO (human vaginal non-redundant gene catalog), a newly developed referencing framework to comprehensively catalog VM gene content, taxonomy and functions. RESULTS/ANTICIPATED RESULTS: Women were 89% African American with a mean age of 46 years (SD 8.8). The most prevalent species were *Gardnerella vaginalis* (predominant in 34%),

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Lactobacillus iners (predominant in 21%), and *L. crispatus* (predominant in 14%). 90% of LTNP and 45% of EC samples were *Lactobacillus*-dominant vs. 28% of HIV- and 30% of HIV+ATs. *L. crispatus* and *L. iners* in ECs/LTNPs had significantly different gene content and greater gene richness vs. controls. *G. vaginalis*-predominant communities were found in 66% of HIV- and 68% of HIV+ATs, compared to 46% of EC and 0% of LTNP. The *G. vaginalis* strains present in EC/LTNP also showed significantly lower gene richness and different gene content vs. controls. DISCUSSION/SIGNIFICANCE OF IMPACT: These results suggest unique VM communities among EC/LTNP, and led us to hypothesize that differential regulation of vaginal immunity drives the observed differences. The similarity between VMs of HIV- and HIV+ATs warrants further study. Larger longitudinal VM studies are needed to assess associated functional pathways and understand the etiology of VM association with HIV progression. CONFLICT OF INTEREST DESCRIPTION: The authors have no conflicts of interest to disclose.

4412

Unraveling the role of the interaction between enteric virus and commensal bacteria in a physiological relevant model of human intestinal epithelium

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OBJECTIVES/GOALS: In the crowded environment of the intestine, selected commensal bacteria and enteric viruses interact. The biological significance of this interaction, in either normal or pathological condition is not known. To study this interaction, we are developing a physiologically relevant model of an human intestinal epithelium. METHODS/STUDY POPULATION: Intestinal biopsies (ileum region) and fecal samples of 6 healthy and 6 active Crohn's patients are being collected to derive human intestinal enteroid (HIE) lines. 2D-polarized HIE will be first characterized with studies of epithelial permeability, tight junctions and cell type composition, and co-cultured with matching fecal samples. The (co-)cultures will be then infected with human norovirus (HNoV), our model enteric virus, and infection will be quantified by RT-qPCR. In addition, the interaction of HNoV with bacteria derived from healthy or Crohn's will be determined quantitatively by flow cytometry (viral tagging) and qualitatively by 16S sequencing of the total *versus* HNoV-bound bacterial species. RESULTS/ANTICIPATED RESULTS: Crohn's patients are characterized by a microbiome dysbiosis and, in particular, by a high abundance of *Enterobacteriacae*. HNoV interacts with *Enterobacter cloacae*, and interestingly, HNoV infection is associated with exacerbation and reactivation of Crohn's disease. By re-creating the intestinal milieu of healthy and Crohn's patients, we expect that the kinetics of infection by HNoV will be higher in Crohn's as compared to healthy volunteers. In addition, by studying the composition of the HNoV-bound bacterial component of Crohn's versus heathy volunteers, we will be able to identify the contribution of selected bacteria to the expected increase of infection. DISCUSSION/SIGNIFICANCE OF IMPACT: With this study, we will fill the gap of knowledge on the importance of commensal bacteria and enteric virus interactions in healthy and diseased condition. This new knowledge will be paramount for the identification of novel strategies to combat highly prevalent virus infections.

Clinical Epidemiology/Clinical Trial

4216

A TL1 team approach to investigate attention and learning at the intracranial network level and assess the effect different cognitive rehabilitation strategies have on measures of attention and learning

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OBJECTIVES/GOALS: 1) Investigate the network level interactions of attention and learning during an attention network task (ANT) and an implicit learning contextual cueing (CC) task. 2) Assess the effect attention rehabilitation strategies have on *behavioral and neural responses pre/post-attentional intervention.* METHODS/STUDY POPULATION: This study involves refractory epilepsy patients with implanted intracranial electrodes and moderate-to-severe traumatic brain injury (m/sTBI) survivors. In epileptic patients, we will identify connectivity of cortical regions via the ANT, which probes components of attention (alerting, orienting, and executive control) and a CC task that probes implicit learning. We hypothesize that modulation of attention and learning can be seen at the network level. In TBI we will assess improvement following two attention rehabilitation paradigms behaviorally; and use our results from epileptic patients to guide measurement of treatment-related neuroplastic change via scalp electroencephalography. RESULTS/ANTICIPATED RESULTS: When the proposed objectives are complete, we expect to determine how the implicit learning rate in m/sTBI changes as a result of both direct attention and metacognitive-strategy training, and discern the neuroanatomical networks associated with attention and implicit learning based on connectivity results. We expect to identify intracranial regions and networks that exhibit modulatory effects associated with attention and implicit learning. Additionally, we anticipate that deficits in attention will be mitigated following training and hypothesize that implicit learning rate will improve in TBI patients as a result of both attentional rehabilitation paradigms. DISCUSSION/SIGNIFICANCE OF IMPACT: Characterizing intracranial activity in epilepsy patients will give electrophysiology data unattainable in TBI patients. This intracranial perspective will enable us to propose mechanisms of action that may result from our interventions and enable critique of current rehabilitation treatments.

4109

Acceptability of a Tenofovir Disoproxil Fumarate Intravaginal Ring for Human Immunodeficiency Virus Pre-Exposure Prophylaxis Among Sexually Active Women

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OBJECTIVES/GOALS: Vaginal ring delivery of antiretroviral drugs may provide protection against acquisition of HIV-1 when used as pre-exposure prophylaxis. As part of a randomized placebo-controlled safety trial of a tenofovir disoproxil fumarate (TDF) intravaginal ring (IVR), we assessed product acceptability through surveys of 17 women after continuous ring use. METHODS/STUDY POPULATION: Sexually active, HIV negative women between the ages of 18 and 45 were enrolled to investigate the safety and pharmacokinetics of three months of continuous TDF IVR use. The study

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