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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