intraperitoneal injections of Senexin B from day -1 to 8 and were harvested at 10 days post fracture. Control mice received vehicle injection. Calluses were analyzed through μCT and histomorphometry. RESULTS/ANTICIPATED RESULTS: At 14 days, Senexin B increased chondrogenic gene expression and improved sGAG content in hMSCs. This persisted to day 21, suggesting that Cdk8 inhibition via Senexin B promotes chondrogenesis and matrix deposition. Histomorphometric analysis reveals thatin vivotreatment with Senexin B increases cartilage content and reduces mineralization of the fracture callus compared to the Control. μCT analysis corroborates this, with distinctly less peri-cortical mineral present in Senexin B-treated calluses, and a decrease in total bone volume. These results suggest an altered progression of cartilage formation and endochondral ossification with Cdk8 inhibition. DISCUSSION/SIGNIFICANCE: Our findings reveal that increased Cdk8 is associated with poor healing in ischemic fractures. Inhibition of Cdk8 appears to increase chondrogenesis of hMSCsin vitroand in the murine fracture callusin vivo. Targeting Cdk8 offers potential to improve callus formation in impaired healing scenarios.

309

Effects of SARS-CoV-2 Variants on CD8+ T cell Epitope Diversity: Estimating Clinical Severity in the United States*

Grace Kim[1], Jacob Elnaggar[2,4], Maya Sevalia[2], Najah Nicholas[2], Mallory Varnado[2], Judy Crabtree[3] and Lucio Miele[3]
[1]LSUHSC; [2]School of Medicine, Louisiana State University Health Sciences Center, New Orleans, LA, USA; [3]Department of Genetics, LSUHSC, New Orleans, LA, USA and [4]Department of Microbiology, Immunology, and Parasitology, LSUHSC, New Orleans, LA, USA

OBJECTIVES/GOALS: Our goal was to distinguish SARS-CoV-2 CD8+ T cell epitopes of spike, membrane, and nucleocapsid products in 27 of the most frequent HLA-Aand -B alleles.We hypothesize that differences mediated by variation in SARS-CoV-2 and host HLA genetics affect the differential clinical severity and presentation of acute infection and PASC. METHODS/STUDY POPULATION: Genomic sequences of SARS-CoV-2 variants were blasted against the original Wuhan strain using Ensembl's SARS-CoV-2 browser. We examined 16 COVID variants: 2 Alpha (B.1 and B.1.1.7), 5 Delta (AY.100, AY.25, AY.3, AY.3.1, and AY.44), and 9 Omicron (BA.1, BA.1.1, BA.2, BA.4, BA.5, BQ.1, BQ.1.1, XBB.1, and XBB.1.5), sequenced from the Louisiana patient population. cDNA sequences were translated using the Expasy tool. To predict MHC-I epitope binding, we used the Immune Epitope Database and Analysis Resource, via TepiTool utilizing the IEDB recommended default prediction and the 27 most frequent HLA-A and -B alleles. In silico peptide docking was conducted on FoldX, utilizing HLA-B*15:01 structures (n= 7) from the Protein Data Bank. RESULTS/ANTICIPATED RESULTS: CD8+ epitope conservation was estimated at 87.6-96.5% in S, 92.5-99.6% in M, and 94.6-99% for N. As the virus mutated, an increasing proportion of S epitopes experienced reduced predicted binding affinity: 70% of Omicron BQ.1- XBB.1.5 S epitopes experienced decreased predicted binding, as compared to ~ 3% and ~15% in Delta AY.100-AY.44 and Omicron BA.1-BA.5 respectively. Additionally, we identified several novel candidate haplotypes that may be susceptible to severe disease, notably HLA-A*32:01, -A*26:01, -B*58:01, and -B*53:01, and relatively protected from disease, such as -A*01:01, -A*02:01,-A*31:01, -B*15:01, -B*40:01, -B*44:03, and -B*57:01. In silico analysis of COVID peptides and HLA-B*15:01, a common allotype in the United States, largely matched predicted binding patterns. DISCUSSION/SIGNIFICANCE: To elicit long term COVID-19 immunity and prevent PASC, it is important to understand the relationship between T-cells, viral variants, and HLA genetics. This project is one of the first to explore the interaction between CD8+ epitope diversity and viral genetics for the majority of the United States population.

310

Digital Physical Activity Phenotype before Cerebrovascular Disease: A Retrospective Study of Accelerometer-Measured Behavior in UK Biobank Observational Cohort*

Stephanie Zawada, Ali Ganjizadeh, Gian Marco Conte, Bart Demaerschalk and Bradley Erickson
Mayo Clinic

OBJECTIVES/GOALS: To investigate digital behavior patterns before cerebrovascular disease (CeVD), we compared accelerometer-measured physical activity (PA) phenotypes of future CeVD patients versus controls in UK Biobank. METHODS/STUDY POPULATION: Accelerometer data from 76,525 eligible participants monitored for 7-days (Jan. 2013-Dec. 2015) was classified into four categories: sedentary, light PA (LPA), moderate-to-vigorous PA (MVPA), and sleep. Covariables and diagnoses were defined using baseline data and patient records. Daily PA patterns associated with incident CeVD were compared to controls using negative binomial regression models. RESULTS/ANTICIPATED RESULTS: Adult participants with future CeVD (n = 2,163) spent 4.4% less time in MVPA (Incident Rate-Ratio (IRR) 0.956; 95% CI = 0.923-0.992; p = 0.016) compared to controls. During 0:00-5:59h (midnight to 5:59AM), future CeVD patients were less likely to sleep (IRR = 0.985; 95% CI = 0.977-0.992; p <0.001) but more likely to be sedentary (IRR = 1.189; 95% CI = 1.098-1.290; p <0.001) or in LPA (IRR = 1.108; 95% CI = 1.015-1.211; p <0.001). In subgroup analyses, decreased MVPA was observed in current/former smokers (IRR = 0.887; 95% CI = 0.819-0.963), males (IRR = 0.931; 95% CI = 0.870-0.997), and the unemployed/retired (IRR = 0.923; 95% CI = 0.856-0.998), an effect more pronounced in depressed patients (p for interaction = 0.044) and prolonged (> 2 hr/day) screen users (p for interaction = 0.018). DISCUSSION/SIGNIFICANCE: The digital phenotype of PA prior to CeVD is characterized by less sleep during 0:00-5:59h and less daily MVPA, demonstrating the utility of accelerometer data in identifying candidates for preventative intervention.

311

Democratizing access to clinical data for research: Implementation and evaluation strategies in an academic medical center and lessons learned

Riddhiman Adib, Susan Myers, Erik Benton, Aaron Cohen and Mohammad Adibuzzaman
Oregon Health & Science University

OBJECTIVES/GOALS: To facilitate data exploration at an academic medical center, we piloted self-service data science tools to provide easy access to research data and provide analytical workspace. The

https://doi.org/10.1017/cts.2024.280 Published online by Cambridge University Press