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.

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

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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.

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

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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.

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

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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

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objectives are: i) data delivery with data governance and cohort discovery under a managed self-service model and ii) data science and analytics tool for advanced users. METHODS/STUDY POPULATION: Using existing commercial frameworks, we implemented a few pilot self-service tools. The key characteristics of the tools were i) high degrees of functionality and flexibility for data access and data governance, ii) lower cost to build and maintain, and iii) long-term organizational strategic alignment with the academic medical center. We conducted a two-phase evaluation with the pilot self-service tool: functionality-based assessment, prioritizing tools for data science users, and usability-based assessment, evaluating selected tools through customized maturity models and surveys. The evaluation study targeted a focus group study with five diverse faculties and researchers in an academic medical center seeking improved access to research resources. RESULTS/ANTICIPATED RESULTS: In evaluation phase 1, we explored seven self-service tool frameworks suitable for our research data warehouse (RDW). In phase 2, we implemented the top two tools selected from phase 1, QlikView and Palantir Foundry. Although the tool built on Palantir has higher mean and individual scores for user feedback than Qlik's, there is no statistically significant difference. Both tools had steep initial learning curve. Palantir has better feedback from qualitative responses. Our study findings highlight prioritized functionalities (efficiency, flexibility, sustainability, security, and cost reduction) for data science tool users; however features and the tool itself requires long term organizational planning and investment. DISCUSSION/SIGNIFICANCE: Academic and research medical centers strongly focus on efficient pilot data access for researchers to aid hypothesis generation. Establishing a clinical research-focused self-service data tool addresses the well-established demand for research resources and offers a model for similar organizations.

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In vivo electrophysiology sex differences in the locus coeruleus of wild type F344 rats

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OBJECTIVES/GOALS: Women are twice as susceptible to ailments like anxiety, PTSD, and Alzheimer's disease compared to men. The locus coeruleus (LC), the primary source of noradrenaline for the brain is implicated in these disorders, however physiological sex differences have never been assessed in the LC. METHODS/STUDY POPULATION: To address this gap, In vivo electrophysiology under anesthesia was used to measure single unit activity of noradrenergic LC firing patterns in 4-month-old wild-type Fischer male and female rats. Recordings measured neuronal activity under basal conditions and in response to a footshock stimulation which elicits burst firing in LC neurons. Single unit activity is sorted via automatic valley seeking scan PCA, additional manual sorting is done via line and template method. Analysis is done extracting interspike interval (ISI) and firing rate of single units, additional analysis is done to quantify properties of bursting patterns (burst duration, spikes per burst, interburst interval, etc . . .). RESULTS/ANTICIPATED RESULTS: This data shows that during LC burst firing, females have longer interspike intervals compared to males, supporting the inhibitory effect of E2 on LC firing. Additionally, females have significantly different waveform patterns than males, indicating possible differences in intrinsic properties, but further supporting sexually distinct physiology of the LC . Because female rats have been estrous cycle tracked via vaginal lavage, stratification into estrus groups and further analysis may uncover differences within females. These data suggest that estrogen acts as a potent neuromodulator of noradrenergic LC neurons, providing valuable insights into the physiology of this brain region. DISCUSSION/SIGNIFICANCE: This study is the first exploration of LC physiological sex differences. This work offers insights into a critical brain region implicated in many diseases, and may pave the way for future therapeutic approaches, particularly for women, who are at a higher risk of neurological disease developing.

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Identification of novel plasma protein of Community Health Worker Program

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OBJECTIVES/GOALS: Thiswork is an evidential study that demonstrates the positive impactof integrating Community Health Workers (CHWs) and SocialDeterminants of Health on an important health outcome, notably in decreasing the 30-day unplanned hospital ED readmissions at Sinai Health Systems. METHODS/STUDY POPULATION: Using datafrom the Sinai Urban Health Institute (SUHI), we compare predictingthe readmissions of patients with and without data pertainingto Social Determinants of Health (SDoH). We thoroughly describe the data cleaning and data preprocessing, done in collaboration with experts in community health. We use a fundamental and ubiquitous classifier in Random Forest for its feature characterization capability in order to translate models results into insights and recommendations for the CHW program. RESULTS/ANTICIPATED RESULTS: We show that when patients are simply engaged byCHWs, regardless of the content of those conversations, we canincrease the predictive accuracy of our classifier by 5%. We usethis result to make recommendations for improving patient careand discuss limitations and future work. Importantly our workpoints directly to the human connection between patients andCHWs as an important feature in the readmission rate. DISCUSSION/SIGNIFICANCE: Our work shows that the predictive capabilities of the classifier increases with CHW logs and SDoH survey data, highlighting the benefit of collecting this information. This is the first step in early identification of such patients so that CHWs are focusing on and providing resources to patients who will most benefit from the program.

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Large Language Model Approaches to Understand Differences Between Guidelines and Clinician Perception of Best Practices

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OBJECTIVES/GOALS: The Clinical Implementation stage in the translational pipeline is hampered by the tension between formal evidence and clinician perceptions. For instance, when guidelines are translated into electronic clinical decision support alerts, they are often ignored. Using advances in LLMs we present a framework to quantify these discrepancies. METHODS/STUDY

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