CD1 T cells in infected guinea pigs at the tissue level, demonstrating Mtb lipid immunology. As a result, we laid the groundwork for investigating whether augmenting lipid immunity in the guinea pig model will enhance immunity against tuberculosis. Fruition of such work may lead to the development of effective tuberculosis vaccines.

45698

Molecular Signatures of Cocaine Neurotoxicity in Human Brain Models[†]

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ABSTRACT IMPACT: This project will use human neuron models and bioinformatics techniques to elucidate mechanisms of cocaine neurotoxicity, which will allow treatments to be developed for minimizing or preventing neurological damage caused by cocaine abuse and overdose. OBJECTIVES/GOALS: The goals of this project are to identify genes and gene networks altered by cocaine exposure in neurons (short term), and to use these pathways to understand mechanisms of cocaine neurotoxicity for the establishment of therapeutic targets (long term). METHODS/STUDY POPULATION: To study the molecular effects of cocaine, we generated preliminary proteomics and next-generation RNA sequencing (RNAseq) data from human postmortem prefrontal cortex (Broadmann area 9 or BA9) of 12 cocaine overdose subjects and 17 controls. Future directions for this project include RNAseq analysis of neuronal nuclei sorted from human postmortem BA9 and a human induced pluripotent stem cell-derived neuron (hiPSN) model of cocaine exposure from the same postmortem subjects from whom we have brain samples. RESULTS/ANTICIPATED RESULTS: We found alterations in neuronal synaptic protein levels and gene expression, including the serotonin transporter SLC6A4, and synaptic proteins SNAP25, SYN2, SYNGR3. Pathway analysis of our results revealed alterations in specific pathways involved with neuronal function including voltage-gated calcium channels, and GABA receptor signaling. In the future, we expect to see an enhancement in neuron-specific gene expression signatures in our sorted neuronal nuclei and our hiPSN model of cocaine exposure. The hiPSN model will help elucidate which effects are due to acute versus chronic exposure of cocaine. DISCUSSION/SIGNIFICANCE OF FINDINGS: Transcriptomic signatures found with this analysis can help us understand mechanisms of cocaine neurotoxicity in human neurons. With this work and future proposed studies, we can discover targetable molecular pathways to develop drugs that can reduce or reverse cocaine-related impairment.

47149

Imaging Tools for Early Detection of Kidney Disease*

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ABSTRACT IMPACT: Chronic kidney disease (CKD) affects ~15% of the US population and the majority of patients are diagnosed too late to benefit from early intervention. We are developing a new diagnostic imaging tool (RadioCF-PET) for the kidney to enable early detection of diseases and to monitor overall kidney health.

OBJECTIVES/GOALS: Nephron mass, or the number of functioning nephrons, is a measure of the functional capacity of the kidney. RadioCF-PET may enable early detection of nephron loss in patients with or at risk of CKD before changes are clinically detectable, facilitating early interventions to improve outcomes in these patients. METHODS/STUDY POPULATION: RadioCF-PET, labeled with Cu-64, has the advantage of using sub pharmacological doses for imaging, carrying low risk and can be used with the FDA's exploratory IND (eIND) mechanism for early in human testing. We are developing the technology to be used in pre-eIND toxicology and pharmacology studies. We are also developing other aspects of translational science to propel this technology toward translation, including: market analysis, critical path to market, customer discovery, and commercialization strategy. RESULTS/ANTICIPATED RESULTS: Milestone 1: Apply technology in mouse model study and in human kidneys rejected for transplant. Anticipated Result 1: PET signal from RadioCF-PET correlates with glomerular density in healthy and diseased model male mice (R2 = 0.98). RadioCF-PET signal correlates with glomerular number in a donated human kidney (R2= 0.78). Milestone 2: Application to federal funding (STTR) and gap funding mechanisms to enable pre-eIND studies. Anticipated Result 1: Application for funding will aid to clarify and validate our market analysis and commercialization strategy. Milestone 3: Continued research and development with the technology in new studies. Other Anticipated Results: Future work with RadioCF-PET will enhance technology performance in preparation for pre-eIND studies. DISCUSSION/SIGNIFICANCE OF FINDINGS: We foresee a large clinical and commercial potential for RadioCF-PET to provide precise, early monitoring in patients at risk for or with CKD. The two biggest hurdles for clinical translation are validating safety and proving efficacy. This work targets both issues to facilitate RadioCF-PET toward clinical translation.

Clinical Epidemiology

10080

Quantifying type of dental treatment rendered for patients with special needs

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ABSTRACT IMPACT: Quantifying the types of dental procedures patients with healthcare needs receive can help understand and improve modalities of dental care to improve healthcare outcomes. OBJECTIVES/GOALS: 1. Quantify how medical complexity based on special needs diagnosis impacts dental treatment rendered 2. Comprehend how medical diagnosis of a special need can affect rate of treatment and type of treatment METHODS/STUDY POPULATION: This study consists of a chart review of all active patients in a dental school setting who have one of the following diagnoses of a special need: autism, developmental disorder, epilepsy, cerebral palsy, neuromuscular disorder, and hydrocephaly. Medical diagnoses were used to extract records and quantify the types of dental treatment rendered for these patients (preventative, restorative, and surgical), as well as the rates of appointments for this patient population. RESULTS/ANTICIPATED RESULTS: The

medical complexity of patients of this population, as defined by the number medical diagnoses, impacts the type of treatment rendered as well as how frequently these patients are seen for dental care (rate of appointments). DISCUSSION/SIGNIFICANCE OF FINDINGS: Over- or under-utilization of dental treatment modalities can impact the oral health status and outcomes for patients with special needs. The differences in types and frequency/ rate of dental treatment rendered for patients of different medical complexity can further impede their oral health and systemic health status and health outcomes.

16306

Genomic epidemiology of SARS-CoV-2 across New Mexico and the Mountain West

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ABSTRACT IMPACT: Genomic data can be used by policy and decision makers to guide, and assess the impact of, public health responses to the COVID-19 pandemic. OBJECTIVES/GOALS: Our objective is to investigate the transmission and population dynamics of SARS-CoV-2 in New Mexico and other Mountain West states using whole genome sequencing. Understanding how the virus is spreading within and between communities is vital for the design of rational, evidence-based control measures. METHODS/STUDY POPULATION: We obtained an aliquot of 500ul - 1 ml of inactivated viral transport media (VTM) from positive SARS-CoV-2 nasopharyngeal swabs as determined by qPCR from the New Mexico Department of Health, TriCore Reference Laboratory, Idaho Bureau of Laboratories, and Wyoming Public Health Laboratory. We extracted viral RNA from the VTM, and sequenced the genomes using the methodology as described by the widely adopted ARTIC amplicon tiling protocol for SARS-CoV-2. Viral genomes were then sequenced on either an Illumina MiSeq or an Oxford Nanopore Technologies (ONT) GridION. We placed these samples within the context of globally representative sequences made available via the GISAID database. Consensus sequences were aligned and added into this global dataset using the Nextstrain augur pipeline. RESULTS/ANTICIPATED RESULTS: We sequenced over 1,000 SARS-CoV-2 genomes thus far from New Mexico (n=861), Wyoming (n=213) and Idaho (n=44). We used this sequence data to infer the transmission dynamics and spread of the virus, both within states and in context of regional and international spread. We inferred at least 128 separate introductions of the virus into New Mexico and at least 29 introductions into Wyoming. The origins of these introductions are diverse, spread across multiple regions in the US and abroad. We also sequenced samples from an individual who had multiple positive tests over time. Our results suggest that this individual was re-infected with a different strain than that of the initial infection. DISCUSSION/SIGNIFICANCE OF FINDINGS: Our data show that New Mexico and other Mountain West states have continually experienced many introductions of the virus that then seed local outbreaks. By understanding the number of introductions over time, we can assess the impact of travel restrictions on transmission. Our data also supports that some individuals can be re-infected.

28835

Describing Physical Symptoms among Patients with PTSD at an Anxiety Clinic in Puerto Rico

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ABSTRACT IMPACT: Our work will provide valuable information about the associations between physical symptoms and PTSD in patients from a Spanish-speaking, evidence-based clinic. OBJECTIVES/GOALS: In this reserach study, we want to describe physical symptoms of patients with a preliminary PTSD diagnosis. We also want to explain associations between physical symptoms, and the presence, or absence of PTSD, and to evaluate findings in terms of prevention services, referrals, and alternatives for augmenting treatment-adherence. METHODS/STUDY POPULATION: This was a descriptive, secondary database analysis of the Center for the Study of Fear and Anxiety (by its Spanish acronym, CETMA). The database included information of the initial evaluation between 2012 and 2019. We aimed to describe sociodemographic and medical variables, and evaluate associations, in terms of the presence or absence of PTSD. RESULTS/ANTICIPATED RESULTS: Patients with PTSD were mostly women, single, with a completed bachelor's degree. The majority had at least one neurological, or musculoskeletal condition. Respiratory conditions were the least represented. We found significant associations between musculoskeletal, neurological, and ear/nose/throat conditions, in terms of PTSD diagnosis. DISCUSSION/SIGNIFICANCE OF FINDINGS: Puerto Rico recently experienced two hurricanes, several earthquakes, and the pandemic. Findings provide data about the interface between mental and physical symptoms of patients with PTSD. We recommend a randomized population study with mental and physical variables, for understanding possible effects of cumulative stress in Puerto Ricans.

38351

Immune-related adverse events in cancer patients receiving immune checkpoint inhibitors*

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ABSTRACT IMPACT: The existing literature describing immune-related adverse events (irAE) has predominantly focused on clinical trial populations, which may not be representative of the broader population receiving immune checkpoint inhibitors (ICI), so we sought to perform a comprehensive evaluation of irAE in a real-world population of cancer patients being treated with ICI. OBJECTIVES/GOALS: With a cohort of patients with malignancy treated with ICI, we characterized incidence, severity, timecourse of ir-AE. We sought to inform providers who prescribe ICI to recognize the clinical burden of irAE in an effort to more effectively communicate the benefits and risks of ICI with patients. METHODS/STUDY POPULATION: After obtaining approval from the institutional review board, we used a pharmacy database to identify adult cancer patients treated with an ICI between January 2014 and October 2018. We used electronic medical records to obtain