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

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