normal or doxycycline chow for nuclear sAC induction, then subdivided to receive vehicle or vemurafenib to examine the effect of nuclear sAC activity on treatment response in vivo. We will also compare melanoma biopsies collected before and after treatment with BRAF inhibitors to assess how nuclear sAC staining affects tumor morphology in vivo. RESULTS/ANTICIPATED RESULTS: So far, nuclear sAC activity has rendered SkMel178 and M263 cell lines more susceptible to vemurafenib. Cell viability was inversely correlated both with vemurafenib and with doxycycline concentration. Cell viability after vemurafenib treatment was dramatically reduced when nuclear sAC was activated. It appears that nuclear sAC enhances the sensitivity of BRAF mutant melanomas to vemurafenib in vitro. We anticipate that xenografts of these cells in mice will be more susceptible to vemurafenib when nuclear sAC is activated. We also anticipate that positive nuclear sAC staining will correlate with a favorable response to therapy. DISCUSSION/SIGNIFICANCE OF FINDINGS: Targeted therapy with BRAF inhibitors is used in late-stage melanomas, but its use is limited as patients invariably acquire resistance. Here, we identified nuclear sAC activation as a novel candidate for combination strategy. Our data will also inform clinicians how best to integrate this biomarker into their decision-making regarding therapy.

47629

Contribution of Auditory Function to Falls Risk in Adults with Vestibulopathy

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ABSTRACT IMPACT: Findings from this study will better characterize the role of hearing loss in falls risk among patients with vestibulopathy and identify groups that are most at risk for falls. OBJECTIVES/GOALS: Vestibular dysfunction and hearing loss are independent risk factors for experiencing falls. The purpose of this study is to determine the extent, if any, to which hearing loss contributes to falls in patients with concomitant vestibular dysfunction presenting to a specialty vestibular clinic. METHODS/STUDY POPULATION: A retrospective chart review of patients ≥18 years who underwent vestibular evaluation at our institution from June 1, 2015 to October 7, 2020 will be conducted. Patients who underwent vestibular evaluation also received audiologic evaluation and degree of hearing loss will be characterized by the 4-frequency pure-tone average (0.5, 1, 2, and 4 kHz) of the better hearing ear. Falls status will be determined by the response to the following question administered at clinic-check in, 'Have you fallen in the last 90 days?' Demographics, comorbidities, and falls-associated medications will also be collected. RESULTS/ANTICIPATED RESULTS: A total of 3,265 unique patients who underwent vestibular evaluation in the study time period were identified. Patients will be categorized into discrete groups (benign paroxysmal positional vertigo, unilateral hypofunction, bilateral hypofunction, central dysfunction, and normal) based on laboratory results. Regression models will be developed to evaluate the potential association between degree of hearing loss and falls in patients with different types of vestibular dysfunction, while adjusting for demographics, comorbidities, and falls-associated medications. DISCUSSION/SIGNIFICANCE OF

FINDINGS: Findings from this study will better characterize the role of hearing loss in falls risk among patients with vestibulopathy and identify groups that are most at risk for falls. This study may potentially indicate the importance of hearing evaluation in the work-up of patients with vestibulopathy.

53746

Body Composition and Metabolic Profiles in Infants of Diabetic Mothers (IDM) as Predictors of Hunger Signaling Gene Expression

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ABSTRACT IMPACT: This study aims to advance the understanding of the biological mechanisms associated with feeding disturbances in infants born to diabetic mothers through non-invasive salivary gene expression analyses and body composition measurements at birth. OBJECTIVES/GOALS: To determine if non-invasive salivary gene expression analyses and body composition measurements at birth could elucidate biological mechanisms associated with aberrant feeding behaviors and disrupted metabolic profiles commonly seen in infants born to diabetic mothers. METHODS/STUDY POPULATION: This prospective cohort study enrolls subjects born at ≥35 weeks' gestation without a history of intrauterine growth restriction or major congenital anomalies. The diabetic cohort is defined as infants born to mothers with gestational diabetes or type 2 diabetes. The primary outcome is salivary expression of the hunger signaling genes, AMPK and NPY2R. Secondary outcomes include infant body composition measurements, obtained by skinfold measurement and/or air displacement plethysmography, and salivary expression of the adipokines, leptin, ghrelin, and adiponectin. Multiple logistic regression will be used to determine which factors are associated with AMPK and NPY2R expression. RESULTS/ANTICIPATED RESULTS: We propose that poor oral intake seen in infants of diabetic mothers may be due to alterations in the expression of hunger signaling genes (decreased expression of AMPK; increased expression of NPY2R) resulting in a diminished feeding drive in these large for gestational age infants. In addition, infant adiposity and the expression of genes involved in the adipoinsular axis will be inversely proportional to feeding volume intake. Namely, increased neonatal fat mass will be associated with increased expression of leptin and decreased expression of ghrelin and adiponectin. DISCUSSION/SIGNIFICANCE OF FINDINGS: Infants of diabetic mothers are at higher risk of poor oral feeding in the newborn period. This study aims to elucidate the link between neonatal body composition, adipoinsular axis, and hunger signaling to explain this unique feeding phenotype.

60558

Non-Suicidal Self Injury in Military Veterans with PTSD: An Ecological Momentary Assessment Study

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ABSTRACT IMPACT: This study will help determine whether ecological momentary assessment is feasible in assessing changes in negative affect and the occurrence of non-suicidal self-injury (NSSI) in military Veterans with post-traumatic stress disorder; if so it will allow for further examination of correlates of NSSI which will inform

treatment efforts. OBJECTIVES/GOALS: Given the advantages of ecological momentary assessment (EMA), and the lack of research on non-suicidal self-injury (NSSI) in military populations, the goal of the current pilot study is to determine the feasibility of using EMA to assess daily changes in post-traumatic stress disorder (PTSD) symptoms, negative affect and NSSI in veterans with PTSD. METHODS/STUDY POPULATION: Twenty military veterans with post-traumatic stress disorder (PTSD) who have engaged in non-suicidal self-injury (NSSI) in the previous 12 months will be recruited. Participants will complete assessments 4 times per day for 28 days at randomly scheduled times. Assessments will measure PTSD symptoms, negative emotions, and NSSI urges and behaviors. At the conclusion of the 28-day study period, participants will complete measures that ask about their experiences in the study, (e.g., the acceptability of the daily surveys and the accessibility of the web-based surveys). Feasibility will be determined with regard to the success of recruiting eligible participants and compliance with daily survey completion. Variability in PTSD symptoms, negative affect, and NSSI urges and behaviors also will be determined. RESULTS/ANTICIPATED RESULTS: It is anticipated that this study will successfully recruit 20 veterans with PTSD with a history of engaging in NSSI within the previous 12 months. It is also anticipated that daily survey completion rates will be approximately 90% based on previous research using EMA with veterans with PTSD and that participants will indicate satisfaction with the procedures of the study. It is anticipated that participants will demonstrate variability in PTSD symptoms, indicated by changes in the number of symptoms endorsed and the intensity of those symptoms experienced. Finally, it is anticipated that participants will demonstrate variability in negative emotions (fear, hostility, guilt, and sadness). DISCUSSION/SIGNIFICANCE OF FINDINGS: Findings from this study will support the use of EMA in a subsequent large-scale investigation examining time-varying symptoms of PTSD and negative affect as antecedents to NSSI. Information from this large-scale study will in turn be used to inform treatments that may to decrease NSSI in veterans by targeting specific symptoms and negative emotions.

63230

Quantifying Heavy Metals in Interstitial Fluid for Remote Monitoring of Chronic Exposures

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ABSTRACT IMPACT: We present a minimally-invasive approach to monitoring heavy metal exposures in geographically disperse populations; this framework may encourage and facilitate greater participation in a broad range of related clinical studies that require biosampling. OBJECTIVES/GOALS: We hypothesize that microneedle array (MA) extraction of interstitial fluid (ISF) will enable minimally-invasive quantitation of heavy metal (HM) exposure. We establish analytical parameters for ICP-MS analysis of HMs in ISF, quantify baseline HM content in ISF vs other fluids, and characterize a mixed HM exposure model. METHODS/STUDY POPULATION: Recent advances in ISF extraction and analysis suggest a minimally-invasive to monitor HM exposure longitudinally in both urban and dispersed communities. ISF can be collected with MAs and is a rich source of disease and exposure biomarkers. To refine analytical methods, Human subjects with no underlying skin disease were recruited into the IRB-approved study. Each subject had blood and urine collected. ISF was also collected using 3D-printed MA-holders. The fluids were analyzed, using ICP-MS, to quantify the levels of uranium (U), cadmium (Cd), vanadium (V), and arsenic (As). Additionally, we analyzed 2,770 subjects from the public NHANES dataset from 2018-2019. Python and Scikit-learn were used to analyze the demographics, survey responses, and metal concentrations for these individuals. RESULTS/ANTICIPATED RESULTS: While several studies have described the surface water and sediment content of toxic metals, determining biological loads remains challenging due to the need to collect blood or urine from a dispersed rural population over time. Our preliminary results suggest similar HM concentrations in ISF, compared with blood in a small unexposed population. Analysis of subjects from the NHANES public datasets suggest similar baseline blood HM concentrations in diverse subject populations with some differences in Cd depending on smoking and e-cigarette usage. Correlation maps also suggest possible synergy between different metals with cobalt and chromium showing the highest correlation. The initial results from this study have been applied to develop a mixed HM exposure model in rats for further translational testing. DISCUSSION/SIGNIFICANCE OF FINDINGS: We present a minimally-invasive HM monitoring approach. Exposure to multiple HMs is suspected to have additive or synergistic harmful health effects. We ultimately envision a wearable microneedle patch that could be mailed to individuals or distributed through community centers, worn for a few hours, and returned to a central laboratory.

76215

Implementation of Proteomics as a Diagnostic tool for Nontuberculous mycobacteria (NTM) Infection

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ABSTRACT IMPACT: Implementation of proteomics as a diagnostic tool for Nontuberculous mycobacteria (NTM) infection can provide a more accurate, efficient and cost-effective means for effectively diagnosing disease and enacting timely management decisions which can revolutionize patient care. OBJECTIVES/GOALS: Proteomic analysis is a proven diagnostic modality enabling rapid identification of microorganisms. We sought to apply proteomics to detect proteins unique to the most clinically relevant NTM. We then determined whether these unique proteomes could be used to successfully identify NTM species from in vitro cocktail preparations. METHODS/STUDY POPULATION: NTM reference strains for M. avium, m. intracellulare, m.chimaera, m. abscessus abscessus, m. abscessus massiliense and m. abscessus boletti were cultured in vitro and subjected to proteomic analysis using Liquid Chromatography tandem-Mass Spectrometry (LCMS). Tandem Mass Tag (TMT) data acquisition utilized an MS3 approach for data collection using Proteome Discoverer 2.4.
A comparative analysis of the proteome of each of these six species was performed quantitatively using LCMS. The process was repeated for three technical replicates and analyzed using the SEQUEST algorithm. Only high scoring peptides were considered utilizing a false discovery rate (FDR) of 1%. Once species-specific proteins were identified, we validated detection in individual and mixed samples of the six reference strains. RESULTS/ANTICIPATED RESULTS: The proteomic profiling of the six NTM reference strains successfully demonstrated proteins unique to each of the MAC species and MABC subspecies. Proteomic MAC species analysis produced