priorities using existing surveillance data and community input. METHODS/STUDY POPULATION: We used a participatory approach that included a partnership between the GP IDeA CTR Community-Engagement and Biostatistics, Epidemiology, and Research Design Cores to ensure priorities were data driven and also aligned with community-based perceptions of need. First, aggregated surveillance data across Nebraska, North Dakota, and South Dakota was presented to the GP IDeA CTR Community Advisory Board (CAB). Second, CAB members formed small groups and considered the information and generated priority health area lists. Third, small group lists were considered and discussed by the full CAB to finalize priority areas. Finally, the CAB reviewed the priorities annually thereafter. RESULTS/ANTICIPATED RESULTS: We identified priority areas for CTR that included (1) behavioral health, (2) injury prevention, (3) obesity, (4) technology to improve health care access, (5) connecting clinical/community services, and (5) addressing health disparities. These priorities align with population-based surveillance data that show lack of mental health care access, high prevalence of obesity, higher incidence of accidents, and existing racial, ethnic, and geographic health disparities. The CAB highlighted that research was also needed to improve how people can access the health innovations developed through CTR to address the other priority health issues with a goal to have an impact on population health. DISCUSSION/SIGNIFICANCE OF FINDINGS: By integrating data- and community-driven approaches we identified regional health priority areas that if addressed, can have significant impact in the GP IDeA CTR region. The priorities are listed on all GP IDeA-CTR funding announcements to encourage CTR in these areas.

93132

Relationship between Level of Response to Alcohol and Body Weight Status in Individuals across the Spectrum of Alcohol Use and Misuse

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ABSTRACT IMPACT: Improved understanding of the relationship between level of response to alcohol and body weight in the context of other contributing factors will help inform prevention and intervention efforts regarding obesity. OBJECTIVES/GOALS: We evaluated the association between level of response to alcohol and weight status across the spectrum of alcohol misuse. We hypothesized that lower level of response to alcohol would be associated with heavier weight, after controlling for obesity risk factors like food addiction, impulsivity, and low socioeconomic status. METHODS/STUDY POPULATION: Adult participants (N=587) enrolled in NIAAA's natural history study completed Self-Rating of the Effects of Alcohol (SRE), a retrospective measure of level of response to alcohol, along with Lifetime Drinking History (LDH); Yale Food Addiction (FA) Scale; Barratt Impulsiveness Scale (BIS); Delayed Discounting Task (DDT). Structured Clinical Interviews for DSM disorders were conducted to identify individuals with current alcohol use disorder (AUD). Body mass index (BMI), computed from height and weight measured during the study, and used to stratify participants into 3 groups: normal weight (N=222), overweight (N=219), or obese (N=146). RESULTS/ANTICIPATED RESULTS: SRE scores during heaviest drinking period were lowest in the heavier weight group, after accounting for FA, impulsivity, alcohol-related, and demographic variables (ê•2=238.5, p=0.002, Cox and Snell Pseudo R2=0.43). Compared to the obese group, normal weight and overweight groups had fewer FA symptoms and higher BIS cognitive complexity (p values<0.01) but similar rates of current AUD. Relative to the obese group, the normal weight group was more likely to be White, and to have lower household incomes but more education, more years of heavy drinking (LDH), and steeper delayed discounting, p values ≤0.03. The overweight group had a higher proportion of males than did the obese group, p<0.001. DISCUSSION/SIGNIFICANCE OF FINDINGS: Lower level of response during heaviest drinking period was significantly associated with current weight status, suggesting a relationship between alcohol sensitivity and BMI. Future work will explore pharmacokinetic-pharmacodynamic and additional risk factors underlying this relationship.

Mechanistic Basic to Clinical

10271

How The Kidney Reacts to Nutritional Changes?

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ABSTRACT IMPACT: Understanding the mechanism underlying the DASH diet may shed light on the physiologic process by which nutrition influences blood pressure and potentially lead the way to new therapeutics that target ion channels. OBJECTIVES/GOALS: Hypertension is a disease of the westernized world, as it stems from lifestyle habits. Lower salt consumption reduces blood pressure, yet DASH diet is much more effective, lowering blood pressure as efficiently as one anti-hypertensive drug. The precise mechanism through which DASH achieves its effect is not understood, and this is the project goal. METHODS/STUDY POPULATION: We hypothesize that exposing hypertensive volunteers to a high potassium and low sodium DASH diet will change the composition of renal ion channel in an aldosterone-dependent manner, leading to excretion of both sodium and potassium and a reduction in blood pressure. To assess how the nutritional change changes ion channel composition in the kidneys' epithelium in aldosterone-induced manner, we will monitor urine exosomes, which contain epithelial cell membranes. We designed an in-hospital nutritional studies recruiting 20 volunteers. Patients will consume carefully designed menu, and measurements will be collected daily: blood pressure, biologic samples including blood and urine electrolytes, aldosterone, and urine for exosomes. RESULTS/ANTICIPATED RESULTS: We have collected data from 5 research volunteers so far.following exposure to the high potassium diet, Aldosterone blood levels increased while blood level of both potassium and sodium was maintained within normal limits. Urinary ratio of electrolytes, sodium:potassium was reversed 5-7 days following nutritional change from 6 to 1. Both manual and automated 24-hour blood pressure measurements confirmed blood pressure reduction following nutritional change. The following illustrates the impact the diet had on a participant's 24-hour ambulatory blood pressure. Daily mean blood pressure was reduced from 120/76 mmHG to 112/68, mean awake blood pressure was reduced from 125/80 mmHG to 117/72 mmHG, and mean sleep blood pressure was reduced from 112/69 to 103/60 mmHG DISCUSSION/SIGNIFICANCE OF FINDINGS: Understanding the mechanism underlying the DASH diet may shed light on the physiologic process by which nutrition influences blood pressure and potentially lead the way to new therapeutics that target ion channels. By introducing

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our participants to a healthier lifestyle, they could maintain lower blood pressure without requiring medication.

19144

Effect of Mesalamine on Metabolic Syndrome risk factors in Ulcerative Colitis Patients: A Retrospective study

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ABSTRACT IMPACT: Currently, there are no medications to treat metabolic syndrome and our research sheds light on a potential therapeutic that could prove beneficial for this disease that affects one-third of the US population. OBJECTIVES/GOALS: Our goal was to determine the role of the GI tract in MetS, specifically how approved GI-directed medications affect metabolic parameters. Thus, we assessed the effects of mesalamine, a common therapeutic utilized to treat mild to moderate UC, on metabolic parameters in comorbid UC and MetS patients METHODS/STUDY POPULATION: This was a retrospective study with data extracted from Cerner's HealthFacts database across the United States (US). Inclusion criteria included adult patients (≥18 years old) with a diagnosis of UC and at least 3 of the 5 metabolic risk factors which included i) dyslipidemia, ii) low HDL, iii) hyperglycemia, iv) hypertension, and v) increased abdominal obesity as determined by elevated BMI. A total of 6197 patients across the US between the years of 2007 and 2017 were included. We pulled patients who had a mesalamine prescription within +/- 7 days of an encounter in which they were diagnosed with UC (index date) and the closest values to 3 and 12 months after the index date. Mean age for patients was 53.8 ±19.9, with predominance of female sex (52.9%) and white race (78.0%). RESULTS/ANTICIPATED RESULTS: There was an observed reduction in BMI, fasting glucose, and increase in HDL levels post start of mesalamine treatment along with a decrease in inflammatory markers (ESR and CRP) ($p<0.001$). DISCUSSION/SIGNIFICANCE OF FINDINGS: The GI tract contributes to numerous disorders associated with metabolic dysfunction. Our retrospective analysis revealed mesalamine treatment in comorbid UC and MetS patients improved metabolic parameters, providing evidence that targeting the GI tract in these individuals potentially improves dysregulated metabolic processes.

29120

Classification of Individuals Across the Spectrum of Problematic Opioid Use: Clinical Correlates and Longitudinal Associations with Mortality

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ABSTRACT IMPACT: A better understanding of the spectrum of problematic opioid use will lead to more targeted treatments. OBJECTIVES/GOALS: It is unclear how to approach treatment of individuals with problematic opioid use who do not clearly meet criteria for opioid use disorder (OUD). We aim to characterize clinical, demographic, and medication use at time of identification of problematic opioid use across the spectrum as well as identify predictors of poor outcomes. METHODS/STUDY POPULATION: A national sample of Veterans coded as having opioid abuse or dependence were previously categorized as (1) high likelihood of OUD, (2) limited aberrant opioid use, and (3) prescribed opioid use with no evidence of aberrant use based on chart review. We will describe how individuals in these three categories differ demographically and clinically. We will then use a trained binary logistic regression model to predict whether individuals with limited aberrant opioid use more closely resemble category (1) or (3). Cox proportional hazards models will be used to predict all-cause mortality, suicide-related mortality, opioid-overdose related mortality, and hospitalization over a three-year period using the three categories as predictors and adjusting for relevant covariates. RESULTS/ANTICIPATED RESULTS: We anticipate that Veterans with a high likelihood of OUD will be more likely to experience homelessness and have more psychiatric comorbidities (especially PTSD). We hypothesize that Veterans with prescribed opioid use and no evidence of misuse will be significantly older, more likely to have disability, medical comorbidities (ie., chronic pain, cancer), more prescriptions for non-opioid analgesics, and be prescribed higher doses of opioids. Using a trained binary logistic regression model, we predict that Veterans with limited aberrant opioid use will more closely resemble Veterans with a high likelihood of OUD. We expect that all categories of problematic opioid use will have a high risk of mortality, with a high likelihood of OUD associated with the greatest risk of premature death. DISCUSSION/SIGNIFICANCE OF FINDINGS: Identifying and better characterizing individuals with limited aberrant opioid use may be an important opportunity to intervene prior to development of severe OUD. Future research will focus on targeting interventions to this population, which may have specific needs that are separate from classic OUD or simple pain-related opioid dependence.

35336

Effect of Nuclear Soluble Adenylyl Cyclase (sAC) on Melanoma Treatment Response

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ABSTRACT IMPACT: Our data identify a novel candidate for combination strategy in melanoma treatment, and can inform clinicians in their decision-making process regarding therapeutic intervention for melanoma patients. OBJECTIVES/GOALS: Soluble adenylyl cyclase (sAC) is a novel source of cyclic AMP (cAMP). In melanoma, nuclear sAC localization has an established diagnostic utility and we newly found that nuclear sAC functions as a tumor suppressor by inhibiting Hippo pathway, which affects treatment response. Here, we examine the effect of nuclear sAC on melanoma treatment response. METHODS/STUDY POPULATION: We developed a doxycycline inducible system for increasing sAC activity only in the nucleus. We assessed whether nuclear sAC activity affects treatment response, using BRAFV600 human melanoma cell lines. Using a clonogenic assay, we examined how nuclear sAC activity affects growth inhibition in the presence of a BRAF inhibitor, vemurafenib. Our findings will be confirmed in vivo using tumor xenografts. After tumor formation in NSG mice, mice will be randomized to be fed

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