WTC-LI on curated data. Random Forest (RF) out-of-bag estimated success rates were used to measure classification utility of the refined biomarker profile. Principal components analysis (PCA) was used to visualize class separation produced by the refined profile. RESULTS/ANTICIPATED RESULTS: Of the 765 metabolites detected, 580 metabolites were quantified in more than 80% of subjects/group with relative standard deviation $\geq$15%. Relevant chemokines, cytokines, and clinical biomarkers were included based on previously established clinical importance. Initial PCA explained 34.7% of the variance in the first 3 components. RF was used to identify the top 5% of biomarkers important to class separation. RF of the refined biomarker profile correctly classified cases and controls with a 96.7% estimated success rate. A PCA of the refined metabolic profile now explained 46.2% of the variance in components 1–3, demonstrating improved class separation. Differentiators between cases of WTC-LI and controls included elevated sphingolipids in cases of WTC-LI. The metabolic-inflammatory serum biomarkers MDC, Apo AI, GM-CSF, and heart rate play an important role in class separation. Phospholipids and lysolipids also appeared to differentiate cases of WTC-LI from controls. Specifically, several glycero-phosphatidylcholines (GPC) were elevated in cases of WTC-LI. DISCUSSION/SIGNIFICANCE OF IMPACT: High-dimensional data analysis on the metabolic fingerprints, serum, and clinical biomarker data of a subset of WTC-exposed 9/11 rescue workers has identified pathways associated with the loss of lung function. Sphingolipids, known to function as inflammatory signaling mediators, are thought to play important roles in lung function under both physiological and pathological conditions. Changes in sphingolipid metabolism have been linked to several pulmonary disorders, including asthma, COPD, and acute lung injury. Interestingly, a relation between sphingolipid metabolism and the metabolic-inflammatory pathway is suggested by similarities observed in PCA. Findings of elevated GPCs are similar to COPD literature. Higher levels of GPCs could correspond to elevated levels of lysophosphatidic acid (LPA), a ligand of RAGE. RAGE is a known proinflammatory mediator; LPA species have well-described roles as lipid signaling molecules, function as synthetic intermediates in other metabolic pathways, and were found to be predictive of WTC-LI. Since metabolites are more proximal markers of disease processes, metabolites could capture the complexity of past exposures and, therefore, may better inform treatment. These pathways warrant further investigation into their mechanisms and therapeutic importance.

2383

Electrical stimulation to the subcallosal cingulate and amygdala drive shifts in affective bias across patient populations

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OBJECTIVES/SPECIFIC AIMS: Deep brain stimulation is currently being evaluated as an experimental therapy for various psychiatric disorders, as well as being investigated as a method for mapping emotional brain functions. This growing area of research requires sensitive measures to quantify effects of stimulation on emotional processing. The current study examined the effects of acute stimulation to 2 limbic regions—the subcallosal cingulate (SCC) and the amygdala—on bias in the perception and evaluation of emotional facial expressions. We hypothesized that transient electrical stimulation to the limbic system would produce acute reductions in negative bias, consistent with its antidepressant effects in patients with severe depression. METHODS/STUDY POPULATION: The current study uses a novel affective bias task, developed to rapidly and covertly quantify emotional state. Over 4–6 minutes, patients rate the intensity and valence of static images of emotional facial expressions. We examined effects of electrical brain stimulation in 2 groups: patients with treatment-refractory depression undergoing SCC DBS therapy, and epilepsy patients undergoing amygdala stimulation via stereo-EEG electrodes during inpatient intracranial monitoring. DBS patients completed the task under stimulation and sham conditions during monthly visits over the first 6 months of therapy, as well as daily during a 1 week, blinded period of DBS discontinuation at the 6-month time point. Epilepsy patients completed the task under stimulation and sham conditions at a single visit. Mixed linear models and paired-samples *t*-test were used to investigate effects of stimulation as well as depression scale scores on affective bias ratings. RESULTS/ANTICIPATED RESULTS: Four SCC DBS patients showed significant effects of stimulation ($p < 0.0001$) and depressive state ($p < 0.0001$) on affective bias scores across 6 months of chronic DBS therapy, where emotional faces were perceived as less sad with stimulation ON, as well as during visits in which patients were nondepressed (typically later in the treatment course). Furthermore, 2 DBS patients showed rapid negative shifts in bias following acute blinded discontinuation of chronic stimulation, an effect which persisted over the 1-week period of discontinuation ($t_{29} = -2.58$, $p = 0.015$), in the absence of any self-reported change in mood. Likewise, 6 epilepsy patients showed significant positive shifts in affective bias with acute amygdala stimulation ($t_5 = -4.75$, $p = 0.005$). Current analyses are investigating electrophysiological, autonomic and facial motor correlates to affective bias in these patients. DISCUSSION/SIGNIFICANCE OF IMPACT: Affective bias has revealed rapid, significant changes with stimulation at 2 limbic targets—one a white matter hub and one a nuclear subcortical structure—suggesting the task's utility as an emotional outcome measure in brain stimulation studies. These stimulation-sensitive measures may provide a new metric to track treatment response to deep brain stimulation therapy for affective disorders. Future studies will determine whether affective bias can predict neuropsychiatric complications in patients undergoing stimulation mapping of brain circuitry ahead of resection surgery for epilepsy.

2392

Detecting cardiometabolic disease through breath analysis: A metabolomic approach

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OBJECTIVES/SPECIFIC AIMS: The purpose of this study is to use the baboon as a novel animal model for breath research and to identify and characterize baboon breath metabolites that reflect cardiometabolic function to inform us in the development of a noninvasive, cost-effective, and repeatable point-of-care diagnostic breath test. METHODS/STUDY POPULATION: Blood and urine was collected from control and IUGR at the approximate age of 3.5 years. Both groups were then placed on a high fat, high sugar, high salt diet for 7 weeks, after which blood, urine, and breath were collected. The breath samples were then subjected to comprehensive, 2-dimensional gas chromatography coupled with time-of-flight mass spectrometry. Using ChromaTOF software, breath VOCs were identified with at least an 80% spectral match against the National Institute of Standards and Technology (NIST) chemical reference library. The raw data were then statistically analyzed using MetaboAnalyst. We then interrogated multiple online databases to characterize and identify the role of VOCs that were present in both control and IUGR groups. RESULTS/ANTICIPATED RESULTS: Preliminary analyses of the breath VOCs indicate differences in expression between sexes and in control Versus IUGR groups. These results indicate unique "breath signatures." Further analysis of the breath VOCs reveals the presence of metabolites that are involved in β-oxidation and oxidative stress pathways. DISCUSSION/SIGNIFICANCE OF IMPACT: This breath study, a first of its kind, will develop the baboon as a superior animal model for breath biomarker research. Our observed unique "breath signatures" indicate changes in lipid metabolism and oxidative stress pathways, which we hypothesize are the early metabolic changes at the cellular level that are not yet reflected in clinical lab measures. Future directions include analyzing breath VOCs that did not meet 80% spectral match, validation using SPME technology and commercial standards, and initiating a human pilot study in clinically obese, at-risk children in collaboration with physicians at the Children's Hospital of San Antonio to develop a noninvasive, cost-effective, rapid, and repeatable point-of-care diagnostic breath test.

2399

Protective immunity to live vaccines among children with solid tumors

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OBJECTIVES/SPECIFIC AIMS: Determine whether children with solid tumors maintain intact protective immunity to live vaccines during cancer therapy and after completing cancer therapy (postTx). METHODS/STUDY POPULATION: We will perform a prospective cohort study of children with solid tumors (Hodgkin lymphoma, brain, Wilms, and germ cell tumors) followed at the Puerto Rico's University Pediatric Hospital. Protective immunity will be measured with antibody titers against live vaccines (Measles, Mumps, Rubella, and Varicella) at diagnosis, during cancer therapy, upon completion and

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3 months postTx. RESULTS/ANTICIPATED RESULTS: We hypothesize that those patients with protective immunity to live vaccines prior to cancer therapy will lose it at the end of therapy. DISCUSSION/SIGNIFICANCE OF IMPACT: Loss of protective immunity to live vaccines has been reported in patients with hematologic malignancies after cancer therapy. This lack of protective immunity, which puts patients at higher risk of acquiring vaccine preventable diseases, has been limited studied in patients with solid tumors. The Center for Diseases Control has been established that it is safe to immunize cancer survivors with live vaccines 3 months post Tx. However, no clear guidelines for revaccination have been provided for this population. Understanding the protective immunity variation against live vaccines in children with solid tumors will allow us to identify the need for revaccination with live vaccines in this vulnerable population.

2411

A pilot study: Using computational fluid dynamics to model physiologic airflow through an ovine tissue engineered tracheal graft

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OBJECTIVES/SPECIFIC AIMS: Tissue engineered tracheal grafts (TETG) could provide a life-saving cure for children with long segment airway defects. Computational fluid dynamics (CFD) is a novel and promising technique used to evaluate TETG performance. This pilot study examines the correlation of objective CFD simulations with subjective respiratory symptoms in a TETG large animal model. METHODS/STUDY POPULATION: Three-dimensional geometries of 1 TETG implanted sheep trachea were reconstructed from serial fluoroscopic images, allowing analysis with CFD simulations. Peak flow velocity (PFV) and peak wall shear stress (PWSS) across the graft as well as changes secondary to stenting were determined. CFD metrics were compared with respiratory symptoms seen on exam. RESULTS/ANTICIPATED RESULTS: Two weeks after implantation, the animal developed respiratory distress, which correlated with PFV and PWSS elevations. Although the intraluminal graft appearance changed minimally after dilation, PFV and PWSS decreased across the graft (4.5–0.8 m/s and 0.9–0.1 Pa, respectively). Long-term TETG stenting with dilation returned PFV and PWSS to baseline (0.8–0.3 m/s and 0.1–0.01 Pa, respectively), which correlated with immediate symptom resolution. DISCUSSION/SIGNIFICANCE OF IMPACT: CFD is a noninvasive modality, which allows the evaluation of airflow metrics of symptomatic TETG recipients. This diagnostic tool will permit planned interventions and graft design optimization.

2442

Alcohol reduces the ability to regulate emotion when exposed to evocative partner stimuli in individuals with a history of intimate partner violence

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OBJECTIVES/SPECIFIC AIMS: The objective of this research was to investigate the effect of alcohol and evocative stimuli on heart rate variability (HRV) in partners with a history of intimate partner violence in a placebo-controlled alcohol administration study with an emotion-regulation task. METHODS/STUDY POPULATION: In total, 17 partners (9 females, 8 males) with a history of partner violence participated in a placebo-controlled alcohol administration study with an emotion-regulation task during which HRV measures were collected. In the alcohol condition, participants were administered a mixture of 100 proof vodka and cranberry juice calculated to raise their blood alcohol concentration (BAC) to 0.08%. In the placebo condition, participants consumed a volume of juice equivalent to that consumed in the alcohol condition, but without alcohol. Alcohol and placebo conditions were counter-balanced across participants as were the presentation the blocks of evocative and neutral partner stimuli. RESULTS/ANTICIPATED RESULTS: Controlling for baseline HRV, there was a significant main effect of stimuli (evocative vs. neutral partner stimuli) on HRV in intoxicated partners, $F_{1,16} = 16.28$, $p = 0.004$. There was also a significant main effect of regulation on HRV under conditions acute alcohol intoxication, $F_{1,16} = 23.55$, $p = 0.001$. These effects tell us that intoxicated partners experienced reduced HRV when exposed to evocative stimuli from their partners. These effects also tell us that under acute alcohol intoxication, partners were less able to regulate their emotion when exposed to evocative stimuli than when they consumed a placebo beverage. DISCUSSION/SIGNIFICANCE OF IMPACT: These results suggest that increases in intimate partner violence under acute alcohol intoxication may be the result of reduce HRV. This reduction in HRV would contribute to partners' inability to response with adaptively in conflict when intoxicated. They also suggest that HRV may be an important target for intervention with partner with a history of intimate partner violence. One method may be Heart Rate Variability Biofeedback which has been shown to increase parasympathetic nervous system functioning, autonomic stability, and emotion regulation.

2477

Biofilms in wounds: Detection, individualizing treatment and monitoring response to therapy

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OBJECTIVES/SPECIFIC AIMS: The specific objectives of this project are (1) identify, test, and validate the parameters for a simplified NLOM imaging probe that will provide specific research and point-of-care information on biofilm presence, therapeutic need and response of individual wounds to treatment. (2) Identify specific proteomic and metabolomic biomarkers of (i) wound susceptibility to infection, (ii) wound response to the most commonly used antibacterial measures in wounds, and (iii) establish criteria for more effective interventions. METHODS/STUDY POPULATION: First, optimal use parameters for NLOM including illumination, field of view, focal length, linear Versus concentric image acquisition, detection and filter wavelengths were identified. Parameters for evaluation included ease and speed of imaging, ability to map diagnostic criteria. Next, using the optimised NLOM imaging modality in bacterial biofilm isolates and subsequently a rabbit ear model of biofilm wound infection, proteomic and metabolomic biomarkers of susceptibility to infection were identified. The effects of 2 standard debridement and anti-infective treatments, polyvidone-iodine solution or cetrimide 15%+ chlorhexidine gluconate 1.5% were mapped in situ for up to 10 days using the NLOM probe. RESULTS/ANTICIPATED RESULTS: Using the novel custom NLOM probe, high resolution mapping of wound biofilm infection, as well as the underlying tissue was performed throughout the onset, development, treatment, and resolution of wound biofilm infection. Specific microbiological, microstructural, oxygenation, and pH parameters were mapped at defined surface and subsurface locations and time-points. Findings included the determination that some standard antimicrobial formulations provide a supportive environment for wound infection, and that micro-channels within the biofilm and their interface with the tissues serve as an important predictor and indicator of wound infection establishment, progression, and response. DISCUSSION/SIGNIFICANCE OF IMPACT: The novel multimodality in vivo NLOM imaging approach establishes an important tool for earlier and more specific diagnosis of wound infection risk, virulence, and invasiveness along with markers of successful treatment, and a simple clinical imaging tool for improving wound infection prevention and treatment.

2485

ETV6 represses Pax5 in early B-cell development

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OBJECTIVES/SPECIFIC AIMS: The goal of this project is to determine the role of ETV6 in early B-cell development and define how germline ETV6 mutations result in predisposition to leukemia. METHODS/STUDY POPULATION: Gene expression commons were queried for expression levels of Etv6 and Pax5 at different stages of hematopoiesis. Mouse bone marrow was isolated and fractioned into cells committed to the B cell lineage via B220+ and CD43+ staining by flow cytometry and then separated into the following fractions: Fraction A (CD24low, CD19−), Fraction B (CD19+, CD24+, BP1−), and Fraction C (CD19+ CD24+ BP1+). Wild-type or germline mutant P214L ETV6 were cloned in an MiG vector and expressed in Ba/F3 cells. ChIP-PCR was performed by cross-linking proteins to DNA with 1% formaldehyde for 10 minute at room temperature, followed by cell lysis with RIPA buffer. Lysates were sonicated to shear DNA to a length of 200–1000 base pairs, then Protein A agarose beads were used to clean and immunoprecipitate chromatin. RESULTS/ANTICIPATED RESULTS: We observed that Etv6 is highly expressed in hematopoietic stem and lymphoid progenitor cells through the pre-pro-B stage (FrA), but its expression is significantly reduced in fraction B and

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