a DEN rat model. METHODS/STUDY POPULATION: Liver fibrotic changes were induced in 34 Wistar male rats by oral administration of Diethylnitrosamine (DEN) for 12 weeks. 22 rats were imaged with B-mode ultrasound at 3 different time points (baseline, 10 weeks and 13 weeks) for monitoring liver texture changes. Texture features studied included tissue echointensity (liver brightness normalized to kidney brightness) and tissue heterogeneity. 12 rats were imaged with photoacoustic imaging at 4 time points (baseline, 5 wks, 10 wks, and 13 wks) to look at changes in tissue oxygenation. Hemoglobin oxygen saturation (sO2A) and hemoglobin concentration (HbT) in the right and left lobes of the liver were measured. 8 rats were used as controls. Liver tissue samples were obtained following 13 weeks from DEN start time for METAVIR histopathology staging of fibrosis. RESULTS/ANTICIPATED RESULTS: Texture features studied showed an increase with time in DEN rats. Normalized echointensity increased from 0.28 ± 0.06 at baseline to 0.46 ± 0.10 at 10 weeks ($p < 0.0005$) and 0.53 ± 0.15 at 13 weeks in DEN rats ($p < 0.0005$). In the control rats, echointensity remained at an average of 0.25 ± 0.05 ($p = 0.31$). Tissue heterogeneity increased over time in the DEN-exposed rats from a baseline of 208.7 ± 58.3 to 344.6 ± 52.9 at 10 weeks ($p < 0.0005$) and 376.8 ± 54.9 at 13 weeks ($p = 0.06$) however it stayed constant at 225.7 ± 37.6 in control rats ($p = 0.58$). The quantitative analyses of the photoacoustic signals showed that blood oxygen saturation significantly increased with time. At 5 weeks sO2AvT increased by 53.83 % (± 0.25), and HbT by 35.31 % (± 0.07). Following 10 weeks of DEN; sO2AvT by 92.04 % (± 0.29), and HbT by 55.24 % (± 0.1). All increases were significant $p < 0.05$. In the 13th week, however, the values of all of these parameters were lower than those in the 10th week, however, the decrease was statistically insignificant. DISCUSSION/SIGNIFICANCE OF IMPACT: Quantitative features from B-mode ultrasound and photoacoustic imaging consistently increased over time corresponding to hepatic damage, inflammation and fibrosis progressed. The use of this hybrid imaging method in clinical practice can help meet the significant need for noninvasive assessment of liver fibrosis.

4167

Peri-transplant Lung Microbiome Reveal Oral Bacteria, Pepsin And Inflammatory Markers Co-associate With Primary Graft Dysfunction, Implicating Aspiration As A Potential Contributor

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OBJECTIVES/GOALS: Primary graft dysfunction (PGD) is acute lung injury in the first three days after lung transplant. Patients that experience PGD have increased mortality and an increased risk of chronic lung allograft dysfunction. The pathogenesis is thought to be an ischemia-reperfusion injury but is incompletely understood and there are no specific therapies. We investigated the role of the microbiome in PGD and associations with inflammation and markers of aspiration. METHODS/STUDY POPULATION: We collected airway lavage samples from lung transplant donors before procurement and recipients after reperfusion. We extracted DNA, amplified the bacterial 16S rRNA gene, and sequenced on the Illumina MiSeq platform. QIIME2 and Deblur were used for bioinformatic analysis. R packages were used for downstream analysis and visualizations. The host response was quantified using the Milipore 41-plex Luminex and an ELISA for pepsin. Clinical data was collected by the Penn Lung Transplant Outcomes Group. PGD was assessed by degree of hypoxemia and chest X-ray findings in the 72 hours after transplant. RESULTS/ANTICIPATED RESULTS: There was no significant difference in alpha diversity (Shannon index, $p = 0.51$), biomass (via comparison of 16S amplicon PicoGreen, $p = 0.6$), or beta diversity (Weighted UniFrac, $p = 0.472$, PERMANOVA) between subjects with PGD grade 3 ($n = 36$) and those that did not ($n = 96$). On taxonomic analysis, we found an enrichment of Prevotella in donor and recipient lungs that went on to develop PGD ($p = 0.05$). To follow up this finding we measured immune response and pepsin concentrations in recipient lungs. We found elevated levels in 35/41 cytokines measured in subjects that developed PGD as well as an elevation in pepsin and a correlation between pepsin concentration and Prevotella relative abundance (Figure 1). Additionally, Prevotella relative abundance had statistically significant positive correlations with multiple cytokines such as IL-6 (Pearson's = 0.26, $p = 0.009$) and eotaxin (Pearson's = 0.24, $p = 0.016$). DISCUSSION/SIGNIFICANCE OF IMPACT: There is an enrichment of oral anerobes in lung allografts that eventually develop PGD. This is associated with elevated levels of pepsin and markers of inflammation. These lines of evidence suggest aspiration contributes to priming the allograft for PGD.

4106

Personalizing Care For Colorectal Cancer: Identifying Novel Opportunities

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OBJECTIVES/GOALS: This project seeks to understand how personalized medicine can optimize care for patients with colorectal cancer. It identifies opportunities for personalized medicine to improve clinical outcomes, and uses cost-effectiveness analysis to assess the clinical and financial impact of this approach. METHODS/STUDY POPULATION: This project uses two methods to understand the impact of personalized medicine. First, this project has used SEER-Medicare data in conjunction with Clinical Pharmacogenetics Implementation Consortium guidelines to identify medications used by patients with colorectal cancer that can be impacted by genetic variants. This data will then be combined with population genetic variant rates to understand the likely impact screening for a given variant will have on medication response and adverse events. Medication use frequencies and genetic variant rates are then used to populate cost-effectiveness models that simulate the clinical and financial outcomes, identifying optimal genes to screen. RESULTS/ANTICIPATED RESULTS: The first result will be a comprehensive overview of treatment patterns for patients with colorectal cancer in the United States, as well as the treatments used for disease-induced comorbidities. The second result will be the identification of genetic variants based on population rates and medication utilization that should be screened in this patient population. The final result will be a breakdown of the clinical and financial outcomes associated with implementing screening for the identified genes. Preliminary results from a two-gene cost-effectiveness analysis demonstrates that screening for variants in those genes improves both clinical and financial outcomes. DISCUSSION/SIGNIFICANCE OF IMPACT: This project demonstrates how current treatment approaches can be optimized via personalized medicine. It uses epidemiological methods to identify opportunities to integrate genetic findings from other diseases, and uses cost-

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effectiveness analysis to understand the impact of transforming care. CONFLICT OF INTEREST DESCRIPTION: Stocks-Aurinia, Syndax, Adaptimmune, Rigel pharma

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Powering precision medicine research with the efficient construction of large diverse cohorts

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OBJECTIVES/GOALS: There is an imperative need to initiate translational genetic studies of hidradenitis suppurativa (HS). Such work requires large cohorts and no HS registries exist. Precision medicine initiatives provide new resources and methods for efficiently constructing cohorts, but empirically informed best practice guidelines are needed. METHODS/STUDY POPULATION: Traditional methods for building cohorts rely on clinical encounters to identify patients and collect phenotype data. Precision medicine initiatives aim to decrease the time and cost of data collection by using alternative sources, including electronic health records (EHR) and remote collection of patient-reported data. The public's use of the Internet to obtain and exchange health-related information coupled with the success of direct-to-consumer genetic companies suggests that it is feasible to remotely ascertain research participants for genetic studies. Importantly, Internet cohorts provide an opportunity to include research participants who are disconnected from healthcare, and thus remain hidden from research that relies on EHR or clinical services. RESULTS/ANTICIPATED RESULTS: First, to conduct studies in EHR we are developing an analytic pipeline for the automated extraction of an accurate HS diagnosis using natural language processing of clinical notes. In our preliminary work we are also using ICD codes to build cohorts in two EHR systems with and without linked genetic data. Second, we have developed Internet advertising campaigns for symptom-based recruitment. Informed consent and patient-reported data is collected on-line through a series of short surveys. Patients who complete the surveys and express interest in participating in genetic studies are sent saliva collection kits and return mailing material. Finally, we have established an HS biobank that has DNA from 300 participants identified through clinical services. Enrollment is on going. DISCUSSION/SIGNIFICANCE OF IMPACT: Our goal is to assemble an HS cohort that is large enough to power genetic discoveries. Our work is generating empirical evidence for precision medicine guidelines and will improve our knowledge about HS. The methods we are developing can be applied to efficiently create new cohorts for genetic studies of other diseases across different clinical areas.

4043

Saliva microRNA for pediatric concussion assessment

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OBJECTIVES/GOALS: There is no objective, biologic tool to detect concussion or guide clinical management. We previously showed that saliva microRNA (miRNA) levels differ in children with concussion and may predict symptom duration. The purpose of this study was to validate the utility of saliva miRNA and define longitudinal trends during the recovery period. METHODS/STUDY POPULATION: We collected concussion symptom burden (SCAT-5), cognitive performance (DANA), balance measures (ClearEdge), and saliva from 150 children (7-21 years) with concussion over 5 time-points: 0-2, 3-6, 7-14, 15-29, and 30-60 days post-injury. Saliva miRNA levels within the 443 concussion samples were quantified with RNA sequencing and compared to 218 samples from age- and sex-matched controls (healthy and post-exercise participants). Non-parametric ANOVA assessed RNA levels across time-points, and between concussions/controls. Machine learning was used to build logistic regression algorithms differentiating concussions/controls, and symptomatic/recovered concussion participants. Relationships between miRNAs and concussion phenotypes were explored with Spearman's Rank correlations. RESULTS/ANTICIPATED RESULTS: Fifteen miRNAs differed across control and concussion participants (FDR < 0.05). Within concussion participants, all 15 miRNAs trended back toward control levels by 30-60 days post injury. A regression algorithm employing 6 of the 15 miRNAs differentiated control and concussion participants with an area under the curve (AUC) of 0.78 in a training set ($n = 244$) and 0.84 in a naïve test set ($n = 24$). Similarly, 6 miRNAs were able to differentiate symptomatic (SCAT-5 symptom score > 7) and asymptomatic concussion participants with an AUC of 0.73 in a training set ($n = 219$) and 0.76 in a naïve test set ($n = 44$). Furthermore, 5 miRNAs showed significant ($R > 0.3$; FDR < 0.05) associations with subjective and/or objective measures of concussion-related symptoms. DISCUSSION/SIGNIFICANCE OF IMPACT: Saliva miRNAs levels are altered in children with concussion, and display predictable longitudinal trends following injury. Saliva miRNA measurement represents a non-invasive, objective tool that could be rapidly assessed to provide biologic evidence for clinicians managing pediatric concussion. CONFLICT OF INTEREST DESCRIPTION: I serve as a paid consultant and scientific advisory board member for Quadrant Biosciences, who has funded a portion of this work and licensed the findings from the Penn State College of Medicine.

4565

Sex-Specific Differences in the Genomic Landscape of Pediatric and Adult Glioblastoma

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OBJECTIVES/GOALS: It has been previously shown that pediatric high-grade glioma (pHGG) survival is different between sexes. We set out to find out whether there are sex-specific differences in the genomic landscapes of pHGG that may underlie this sex disparity. METHODS/STUDY POPULATION: We downloaded Illumina 450k DNAm data from ArrayExpress and GeneExpressionOmnibus. The *minfi* package was used to process raw DNAm data. Sex chromosomes and CpGs that are common SNPs were removed. Surrogate variables (SVs) were estimated via the *sva* Bioconductor package. Differentially methylated CpGs were identified by fitting a multiple linear regression model for the DNAm level at each CpG, with independent variables being sex (a binary variable) and the estimated SVs. RNAseq data was downloaded from Cavatica, and differential gene expression analysis was carried out via the *DESeq2* package. RESULTS/ANTICIPATED RESULTS: In the

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