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

4429

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

https://doi.org/10.1017/cts.2020.343 Published online by Cambridge University Press

pediatric glioblastoma (GBM) DNAm data [58 female & 91 male IDH wt samples; ages 0.1–21 yrs;], we found 7,371 differentially methylated cytosines (DMCs) at FDR≤0.05. Of the DMCs, 289 had DNAm differences between male and female samples ≥10%. The majority of probes (68%) were in CpG islands, shelves, or shores. We also found 4 differentially methylated regions (DMRs) between sexes (FWER≤0.1). In the adult GBM DNAm samples [32 F & 32 M IDH wt samples; ages 22–75 yrs], we found only 117 DMCs at FDR≤0.05, and no DMRs. In the RNAseq dataset [68 F & 54 M pHGG samples, ages 0.08–30.6 yrs], we found 383 differentially expressed genes (at FDR≤0.05), and 16 of them (4%) overlapped a DMC. DISCUSSION/SIGNIFICANCE OF IMPACT: Our findings demonstrate that pHGG exhibits sex-specific methylome differences. Interestingly, this difference is greater in the pediatric population as compared to adults. The pHGG transcriptome also differs by sex, which may be related to differential DNAm in a minority of cases.

4485

Silicone Implant Shells Increase the Rate of Proliferation of Patient-Derived BIA-ALCL Cells but Not Primary T Cells in an Engineered Biomimetic Breast Platform

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OBJECTIVES/GOALS: We use a tissue engineered, biomimetic, 3D model to study the pathogenesis of breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) by comparing the effect of silicone implant shell on proliferation of patient-derived BIA-ALCL to its precursor T cells within the breast microenvironment. METHODS/STUDY POPULATION: Patient-derived breast tissue was processed for component adipocytes, ductal organoids, and stromal vascular fraction. These were suspended within 50 µl of 0.3% type I collagen matrix to which was added 200,000 cells/mL of either patient-derived BIA-ALCL cells or T progenitor cells. These were then plated into 6mm wells. As a control, both BIA-ALCL cells and T progenitor cells were suspended within type I collagen alone at the same seeding density without breast components. Before plating, wells were lined circumferentially with either textured, smooth, or no implant shell. These were 1cm by 2cm pieces dissected from the whole implant. Wells were imaged using confocal microscopy over 8 days. RESULTS/ANTICIPATED RESULTS: Unstimulated T progenitor cell count showed no significant increase in any of the conditions tested. The change in cell count over 8 days was 3.85% in each condition ($p = 0.3352$). A Tukey's multiple comparison test comparing each condition revealed no significant increase in cell count over 8 days for all six conditions. Notably, our previous studies have shown proliferation of BIA-ALCL cells to be significantly more robust in the biomimetic platform compared to collagen-only groups, regardless of implant shell type ($p < 0.01$). BIA-ALCL cells grew nearly 30% faster in textured and smooth shell biomimetic groups compared to biomimetic wells lacking implant shell. DISCUSSION/SIGNIFICANCE OF IMPACT: Towards elucidating BIA-ALCL's etiopathology, we show that silicone implant shell has a significant effect on proliferation of BIA-ALCL cells, but not their precursor T cells. If breast implant silicone shell is not a sufficient stimulus for T cell proliferation, co-stimulatory factors are required.

4385

The Pain and Social Experiences Project: Understanding the role of interpersonal trauma in pain

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OBJECTIVES/GOALS: Traumatic interpersonal experiences are associated with higher rates of chronic pain, increased pain severity and poorer functioning. The objective of this ongoing project is to obtain prevalence rates for various forms of interpersonal trauma among individuals with chronic pain, and to explore the potential mediating effect of heightened sensory and social sensitivity on the experience of pain. METHODS/STUDY POPULATION: Patients at Michigan Medicine between the ages of 18 and 65 complete an online survey. Patients are being recruited through a tertiary-care, outpatient pain clinic, as well as through an online health research portal. We aim to recruit 700 participants; we currently have 59.6% of our goal ($n = 417$). Participants also have the option to be included in a registry from which we can recruit for future studies. Approximately 85% of our participants have agreed to be in the registry. RESULTS/ANTICIPATED RESULTS: Preliminary data show that, of the 263 (63.4%) participants for whom data on chronic pain is available, 167 (63.5%) report chronic or persistent pain over the previous 3 months. Of these, 54% reported some form of childhood abuse or neglect. Approximately 41% reported four or more adverse childhood experiences. Additionally, of the 122 participants (73%) who were in a current romantic relationship, 20% reported some form of physical violence victimization from their romantic partner. We anticipate that interpersonal trauma will be associated with poorer perceptions of social relationships, higher sensory sensitivity, and higher perceived stress. DISCUSSION/SIGNIFICANCE OF IMPACT: The PASE Project parent study will be used to better understand prevalence rates for various forms of interpersonal trauma in our chronic pain population. Future analyses and studies will explore alternative pathways linking interpersonal trauma to the experience of pain through sensory and social sensitivity, which will inform interventions aimed at reducing pain among patients with a history of trauma.

4168

Understanding ECM-Based Drug Resistivity in Breast Cancer

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OBJECTIVES/GOALS: Cell-cell (CC) and cell-matrix interactions (CM) are known to affect drug sensitivity of cancer cells, but are not effectively recapitulated using 2D platforms. This research aims to determine how cell and matrix interactions confer drug resistivity in 3 distinct culturing models: 2D (no CM/limited CC), 3D spheroids (CC) and 3D fibronectin (both). METHODS/STUDY POPULATION: We examined four breast cancer cell types. The cells were derived from a nonmetastatic primary tumor (HMLE-E2) or overt bone-metastasis (BM). Transglutaminase 2 (TGM2), a matrix crosslinking protein, is overexpressed in metastatic bone tumors and may play a key role in matrix-conferred drug resistivity. In a

https://doi.org/10.1017/cts.2020.343 Published online by Cambridge University Press