illnesses. The small number of mentally ill patients undergoing TAVR may point to provider bias as a contributor to this high selectivity, and further evaluation would be of clinical use.

312

## Metabolomics Approach to Cellular Senescence: Characterizing the Secretory Phenotype and Metabolism of Irradiation-Induced Senescent Human Pre- Adipocytes

Zinnarky Kiani Ortiz-Correa, Ian R. Lanza
Mayo Clinic, Rochester, MN

OBJECTIVES/GOALS: The study aims to identify and measure metabolites in irradiation-induced senescent pre-adipocytes induced by the increased secretion of pro-inflammatory cytokines. Through untargeted metabolomics, we seek to understand the alterations to metabolism and mitochondrial activity that occur during irradiation-induced senescence. METHODS/STUDY POPULATION: First, commercially available human primary subcutaneous pre-adipocytes were cultured in vitro, and irradiated to induce senescence. To confirm senescence, cells were stained for beta-galactosidase, which was positive in senescent pre-adipocytes. The cells and their conditioned cultured media were then collected and frozen for untargeted metabolomics to profile metabolites. The sample analysis is currently underway and will be conducted using central carbon isotope tracing and chromatograph mass spectrometry. Principal Component Analysis, fold change analysis, and heat maps will be used to detect and report the changes in metabolite signals. Oxygen consumption rate and extracellular acidification rate measurements are in progress at present using the Agilent Seahorse XF Cell Mito Stress Test. RESULTS/ANTICIPATED RESULTS: We expect that metabolites of central carbon metabolism and oxidative phosphorylation will be upregulated. The concentrations of metabolites of pathways altered by the pro-inflammatory cytokines that have been identified to be secreted by senescent cells are expected to be altered. The metabolites measured in conditioned culture media will provide insight into the changes to the cellular microenvironment caused by senescence. Finally, we anticipate that mitochondrial function, and both aerobic and anaerobic metabolism will be altered in senescent pre-adipocytes compared to controls. Through the present study, we will achieve a better understanding the metabolic alterations that occur as part of cell senescence in pre-adipocytes. DISCUSSION/SIGNIFICANCE: Adipose tissue dysfunction due to the accumulation of senescent cells has been linked to chronic diseases such as diabetes and insulin resistance, and inflammaging. Through this study, we expect to provide new insight into the metabolic alterations of senescence and offer a backbone for prospective translational human studies and clinical trials.

313

## Microstructural changes in the brainstem regions of the auditory pathway among children with hearing loss

Iram Ahmad, Peter Moon, Kristi Ward, Taseer Din, Sara Saki, Alan Cheng, Kristen Yeom
Stanford University

OBJECTIVES/GOALS: Diffusion MRI can identify microstructural brain changes and can provide insight into neural development and to potentially prognosticate speech and language outcomes in children with SNHL. The goal of our study was to investigate MRI-based microstructural changes along the brainstem regions of the auditory pathway in pediatric patients with SNHL. METHODS/STUDY POPULATION: We reviewed cohort of pediatric patients with SNHL who obtained MRI at 3T between 2011 and 2019. We identified 16 pediatric patients (age RESULTS/ANTICIPATED RESULTS: We identified significant differences in FA values of the SON between the SNHL cohort and controls (0.377 ± 0.056 vs 0.422 ± 0.052; p=0.009). No other FA or MD values were significantly different between the two groups. Among younger children (ï‚£5 years), MD was significantly decreased in the SNHL cohort compared to controls in the IC (0.918 ± 0.051 vs 1.120 ± 0.142; p5 years), there were no significant differences in MD (1.124 ± 0.198 vs 0.997 ± 0.103; p = 0.119). There were no significant differences in MD or FA in the white matter fibers of the IC-SON tract. DISCUSSION/SIGNIFICANCE: This study is the first to assess microstructural changes in brainstem auditory pathway regions among children with SNHL. Longitudinal studies are warranted to assess the predictive value of these MRI-based findings for long-term outcomes and the efficacy of intervention.

315

## Non-invasive and quantitative surgical outcome evaluation of patients with sagittal craniosynostosis undergoing sagittal craniectomy*

Connor Elkhill[1], Jiawei Liu[2], Marius George Linguraru[3], Scott LeBeau[4], David Khechoyan[5], Brooke French[5], Antonio R. Porras[6]
[1]Computational Bioscience Program, University of Colorado Anschutz Medical Campus [2]Department of Biostatistics and Informatics, Colorado School of Public Health [3]Children's National Health System, Washington, DC [4]Plastic & Reconstructive Surgery, Children's Hospital Colorado [5]Plastic & Reconstructive Surgery Children's Hospital Colorado, University of Colorado School of Medicine [6]Department of Biostatistics and Informatics, Colorado School of Public Health, Children's Hospital Colorado

OBJECTIVES/GOALS: Craniosynostosis is the premature fusion of one or more cranial sutures that produces brain growth constraints and typically requires surgical treatment. We present an age- and sex-specific method to evaluate surgical outcomes using non-invasive 3D photogrammetry that brings objectivity to the current approach for clinical assessment. METHODS/STUDY POPULATION: First, we created standardized head anatomy representations for 2,020 patients (1,081 males, 939 females, age 3.14 ± 3.05 years) without cranial pathology from their computed tomography (CT) images based on our previous methods. We used principal component regression stratified by sex to establish age-specific normative ranges of anatomical variability and we designed a new metric called cranial shape abnormality (CSA) index that calculates the number of standard deviations from normality of a given patient's head anatomy. We calculated our CSA index in a group of 56 patients (44 male, 12 female) with sagittal craniosynostosis who underwent sagittal craniectomy from their pre- (22 ± 30 days before surgery) and post-surgical (267 ± 63 days after surgery) 3D photograms to evaluate surgical outcomes. RESULTS/ANTICIPATED RESULTS: We observed a reduction in the CSA index from 1.28 ± 0.26 before surgery to 0.87 ± 0.22 after surgery ($p < 0.001$ with a paired Wilcoxon test). The CSA index decreased in 53 of 56 patients (94.6%), who consistently

https://doi.org/10.1017/cts.2023.367 Published online by Cambridge University Press

showed head shape improvements after corrective surgery during clinical evaluation. Linear temporal regression indicates a CSA index decrease of 0.43 ± 0.05 during the first year after surgery. We found no significant correlation between a patient's age at surgery and the patient's CSA index after surgery (Pearson's correlation coefficient 0.17, p = 0.20) or the patient's change in CSA index before and after surgery (Pearson's correlation coefficient 0.22, p = 0.11), suggesting that sagittal craniectomy is equally effective for all patients who are between 85 and 331 days old at the time of surgery. DISCUSSION/SIGNIFICANCE: Our new CSA index is a sex- and age-specific metric of head shape anomalies built upon the observed statistical distributions in the normative pediatric population. Our metric can objectively evaluate pre- and post-surgical head shapes and will allow the investigation of the reported variability in surgical outcomes among patients and procedures.

317

## Omics based analysis to identify novel markers of TMZ response in Glioblastoma Multiforme

Megan R. Reed[1], Annick De Loose[2], Grace Guzman[2], A. Geoffrey Lyle[3], Katrina Learned[4], Olena M. Vaske[3], Analiz Rodriguez[2]
[1]UAMS [2]UAMS Department of Neurosurgery [3]UCSC Department Department of Molecular, Cell and Developmental Biology [4]UC Santa Cruz Genomics Institute

OBJECTIVES/GOALS: MGMT methylation status is used to predict the response to TMZ. However, a subpopulation of patients lacking MGMT methylation still respond to TMZ. We applied omics approaches and functional studies to a cohort of GBM patients to identify novel markers that may more accurately predict TMZ response. METHODS/STUDY POPULATION: We applied a combination of omics approaches and functional studies to a cohort of GBM patients to search for novel markers that would predict the response to TMZ treatment more accurately than traditional markers. Using a set of 47 primary and secondary GBM tumor samples, we employed comparative transcriptomics, whole exome sequencing, data independent acquisition (DIA) proteomics, and phosphoproteomics to look for DNA mutations and changes in gene expression and/or protein expression that correlated to response or non-response to TMZ. Subsequently, we performed functional studies and analyzed patient treatment data to validate our results. RESULTS/ANTICIPATED RESULTS: This study is in early stage, but we anticipate that our combination of methods may allow us to identify and validate at least one novel biomarker for TMZ response in patient GBM. For example, comparative transcriptomics or phosphoproteomics may identify a previously unrecognized gene or protein over/under-expression in a subset of patients. In this case we will validate findings using western blotting, IHC staining, and through siRNA of target gene/protein on patient derived GBM cells to examine if removal of this marker leads to TMZ sensitivity. We will further confirm prediction of marker correlation through comparison with matched patient treatment data. DISCUSSION/SIGNIFICANCE: The identification of improved biomarkers to predict response to TMZ treatment is a discovery that could rapidly become standard of care for GBM patients. It would ensure that all responders receive TMZ and avoid exposing nonresponders unnecessarily to TMZ and its potential side effects.

318

## Optimizing the Identification and Prediction of Statin Intolerance to Improve Statin Adherence Using Natural Language Processing and Machine Learning

Boguang Sun[1], Rui Zhang[2], Chih-Lin Chi[3], Robert Straka[4]
[1]Department of Experimental and Clinical Pharmacology, College of Pharmacy, University of Minnesota [2]Department of Surgery, University of Minnesota Medical School [3]School of Nursing, University of Minnesota [4]Department of Experimental and Clinical Pharmacology, College of Pharmacy, University of Minnesota

OBJECTIVES/GOALS: Aim1: To develop a natural language processing (NLP) algorithm to effectively identify statin associated muscle symptoms (SAMS) in patients'electronic health records (EHRs). Aim2: To develop a machine learning model based on clinical features within EHRs that predict the likelihood of SAMS occurrences. METHODS/STUDY POPULATION: A retrospective cohort of adult patients initiated on statins within the Minnesota Fairview Healthcare System EHRs from 2010 to 2020 will be analyzed. NLP-PIER (Patient Information Extraction for Research) platform will be used to search and identify patients who developed SAMS after statin initiation. Manual annotation of clinical notes will be completed to validate the accuracy of identified SAMS cases. Then, a selection of clinical features within the EHRs will be input as predictors for machine learning algorithms development. Select machine learning classifiers will be deployed to generate models for the prediction of SAMS and the best-performing model will be selected based on model performance. RESULTS/ANTICIPATED RESULTS: The expected outcomes include generation of a fine-tuned NLP algorithm that can rigorously identify SAMS occurrences within EHRs. Further, we anticipate having a practical risk model that accurately predicts patients'risks of developing SAMS when taking statins. DISCUSSION/SIGNIFICANCE: The positive and translational impact of our research will be to equip healthcare providers with such informatics tools to improve statin adherence, ultimately promoting patient optimal health and outcomes by maximizing the tolerance and thus realizing the therapeutic benefits of statins.

319

## Optimizing Urinary cell mRNA profiling of kidney allograft recipients: Development of a home processing protocol for noninvasive diagnosis of T cell mediated rejection and BK virus nephropathy

Thalia Salinas, Carol Li, Catherine Snopkowski, Gabriel Stryjniak, Divya Shankaranarayanan, Shady Albakry, Ruchuang Ding, Vijay K. Sharma, Steven P. Salvatore, Surya V. Seshan, Darshana M. Dadhania, Thangamani Muthukumar, Manikkam Suthanthiran
New York Presbyterian- Weill Cornell Medicine, New York, NY

OBJECTIVES/GOALS: Development of a user friendly home kit that enables kidney transplant recipients to process urine at home and post the lysate containing RNA to a Core Laboratory would simplify urinary cell mRNA profiling and facilitate longitudinal monitoring. We report our home processing protocol and investigation of its diagnostic performance characteristics. METHODS/STUDY POPULATION: We developed a home processing protocol (HPP) consisting of urine filtration and lysis of urinary cells, both

https://doi.org/10.1017/cts.2023.367 Published online by Cambridge University Press