

weight before surgery, but many regain weight. Exploring perceptions of self efficacy as well as learning more about what structural and systemic barriers affect self efficacy is important to inform how to improve our approach for sustained weight loss and health behavior changes.

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### Sources of Sound Exposure in Pediatric Critical Care\*

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**OBJECTIVES/GOALS:** Sleep is critical for healing, however pediatric intensive care unit (PICU) sound is above recommended levels (i.e., 45 A-weighted decibels [dBA]). This observational study identifies sources of PICU sound and compares sources between times of high (i.e., dBA $\geq$ 45) and low (i.e., dBA < 45) levels. **METHODS/STUDY POPULATION:** The sound environment of 10 critically ill children 1 to 4 years of age was monitored via a bedside dosimeter and video camera for 48 hours, or until PICU discharge. Dosimeter and video data were uploaded to Noldus Observer XT and time synchronized. A reliable, previously published coding scheme developed to identify sound sources in the adult ICU was modified for the pediatric population. Sound sources (e.g., clinician/family/child [verbal vs. non-verbal] vocalization, patient care, medical equipment) were identified via instantaneous sampling of video data at each minute of recording. The proportion of sampling points with each sound source are compared between times of high and low sound levels, and between day (7:00-18:59) and night (19:00-6:59) shift. **RESULTS/ANTICIPATED RESULTS:** Video coding is ongoing, with high inter-rater reliability ( $\kappa = 0.99$ , SD  $\leq 0.01$ ). **DISCUSSION/SIGNIFICANCE:** Medical equipment sound is ubiquitous in the PICU. Clinicians should optimize the PICU sound environment for sleep, including minimizing equipment alarms, conversation, general activity, and screen media during child rest. Large-scale studies are needed to confirm findings from this small cohort.

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### Targeting metabolic and epigenetic programs to re-sensitize glioblastoma to chemotherapy\*

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**OBJECTIVES/GOALS:** Treatment options for glioblastoma (GBM) are limited. Prognosis remains dismal, with an 18 month on average survival rate following diagnosis due to treatment resistance and disease recurrence. The goal of this project is to investigate hallmarks of cancer progression that contribute to temozolomide (TMZ) resistance, a first line treatment for GBM. **METHODS/STUDY POPULATION:** Two signaling pathways were investigated in TMZ-sensitive and -resistant GBM cell lines and in primary and recurrent patient-derived xenograft (PDX) tumor cells by genetically and pharmacologically inhibiting methionine adenosyltransferase 2A (MAT2A) and adenosylhomocysteinase (AHCY). Cell growth and survival were assessed by measuring protein expression of proliferation, oxidative stress and cell cycle arrest markers. EPIC array analysis and targeted bisulfite sequencing were conducted to identify changes in genome-wide and specific CpG island

methylation. The Seahorse XF Analyzer measured mitochondrial respiratory capacity and oxidative metabolism. Induced pluripotent stem cell organoids were co-cultured with PDX tumor cells to determine if treatments mitigate tumor cell invasiveness. **RESULTS/ANTICIPATED RESULTS:** Compared to parental cells (PC), MAT2A gene expression was increased by 1.7-fold in acquired resistant and de novo resistant GBM cells (RC) [(transcript per million): PC, 7386  $\pm$  0.012; RC, 12925  $\pm$  0.023; n=2; p=2.10e-8]. Compared to TMZ-sensitive cells (TS), TMZ-resistant cells (TR) demonstrated a 56% increase in baseline oxygen consumption rate [(pmol/min): TS, 179  $\pm$  6.7; TR, 279  $\pm$  13; n=18; p=.0012] and 64% increase in maximal respiratory capacity [(pmol/min): TS, 403  $\pm$  29; TR, 659  $\pm$  35; n=6; p=.0012]. **DISCUSSION/SIGNIFICANCE:** MAT2A and AHCY contribute to TMZ resistance and recurrence by dysregulating methylation programs and upregulating antioxidant programs, respectively. These findings provide a foundation for developing novel combinatory therapeutic strategies and inform clinical studies intended to increase remission and reduce recurrence for GBM patients.

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### The Alabama Genomic Health Initiative: Integrating Genomic Medicine into Primary Care

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**OBJECTIVES/GOALS:** Supported by the State of Alabama, the Alabama Genomic Health Initiative (AGHI) is aimed at preventing and treating common conditions with a genetic basis. This joint UAB Medicine-HudsonAlpha Institute for Biotechnology effort provides genomic testing, interpretation, and counseling free of charge to residents in each of Alabama's 67 counties. **METHODS/STUDY POPULATION:** Launched in 2017, as a state-wide population cohort, AGHI (1.0) enrolled 6,331 Alabamians and returned individual risk of disease(s) related to the ACMG SF v2.0 medically actionable genes. In 2021, the cohort was expanded to include a primary care cohort. AGHI (2.0) has enrolled 750 primary care patients, returning individual risk of disease(s) related to the ACMG SF v3.1 gene list and pre-emptive pharmacogenetics (PGx) to guide medication therapy. Genotyping is done on the Illumina Global Diversity Array with Sanger sequencing to confirm likely pathogenic / pathogenic variants in medically actionable genes and CYP2D6 copy number variants using Taqman assays, resulting in a CLIA-grade report. Disease risk results are returned by genetic counselors and Pharmacogenetics results are returned by Pharmacists. **RESULTS/ANTICIPATED RESULTS:** We have engaged a state-wide community (>7000 participants), returning 94 disease risk genetic reports and 500 PGx reports. Disease risk reports include increased predisposition to cancers (n=38), cardiac diseases (n=33), metabolic (n=12), other (n=11). 100% of participants harbor an actionable PGx variant, 70% are on medication with PGx

guidance, 48% harbor PGx variants and are taking medications affected. In 10% of participants, pharmacists sent an active alert to the provider to consider/ recommend alternative medication. Most commonly impacted medications included antidepressants, NSAIDs, proton-pump inhibitors and tramadol. To enable the EMR integration of genomic information, we have developed an automated transfer of reports into the EMR with Genetics Reports and PGx reports viewable in Cerner. **DISCUSSION/SIGNIFICANCE:** We share our experience on pre-emptive implementation of genetic risk and pharmacogenetic actionability at a population and clinic level. Both patients and providers are actively engaged, providing feedback to refine the return of results. Real time alerts with guidance at the time of prescription are needed to ensure future actionability and value.

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### **The Effects of PTSD-Dependent Neurogenic Hypertension and Inflammation on Thoracic Aortic Aneurysm Progression\***

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**OBJECTIVES/GOALS:** Nearly all thoracic aortic aneurysm patients suffer from hypertension leading to elevated wall tension and abnormal extracellular matrix remodeling. PTSD patients have higher blood pressure both at rest and in response to stimuli. Although stress is associated with cardiovascular disease, the exact mechanism linking the two is still unknown. **METHODS/STUDY POPULATION:** Adult C57BL/6 mice underwent a PTSD induction protocol consisting of inescapable foot shock followed by single prolonged stress. The mice were assessed incrementally for their PTSD-like phenotype using specific behavioral tests chosen to assess for each of the human criteria of PTSD according to the DSM-V. Tail cuff blood pressure measurements were taken serially throughout the 16-week protocol. At terminal study, thoracic aortic diameter measurements were obtained through digital microscopy and plasma was harvested for cytokine analysis. Thoracic aortic aneurysms (TAA) were induced through periadventitial application of a calcium chloride solution on the descending thoracic aorta in BPH/2J and BPN/3J adult mice. The thoracic aortic diameter was measured at terminal study through digital microscopy. **RESULTS/ANTICIPATED RESULTS:** Using our PTSD-like mouse model we have demonstrated that PTSD-like mice have significantly higher systolic blood pressure following a reminder of the traumatic event than control mice recapitulating the human phenotype. They also had increased plasma proinflammatory cytokines and larger thoracic aortic diameters than control mice. Although the increased thoracic aortic diameter is not an aneurysm, it suggests ECM remodeling is occurring predisposing the aorta to aneurysm formation. Finally, we have shown that in neurogenic hypertensive mice, TAA formation was accelerated by 12 weeks with roughly 70% dilation at 4 weeks post-TAA induction surgery as compared to roughly a 20% dilation in control mice. **DISCUSSION/SIGNIFICANCE:** Altogether, these studies reinforce the link between stress and TAA development, and our mouse model will allow for the underlying mechanism to be elucidated. Better understanding of the mechanism linking PTSD and TAA will allow for the creation of novel therapeutics to treat PTSD symptoms while also delaying TAA progression.

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### **The Impact of Critical Social Determinants of Health on Personal Medical Decisions: Analysis of Older Americans in All of Us**

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**OBJECTIVES/GOALS:** A growing number of older adults in the United States have multiple social determinants of health (SDoH) that are barriers to effective medical care. We used generalizable machine learning methods to identify and visualize subtypes based on participant-reported SDoH profiles, and their association with delayed medical care (self-reported yes/no). **METHODS/STUDY POPULATION:** Data. All participants aged  $\geq 65$  in All of Us with complete data on 18 SDoH self-reported variables, selected through consensus by 2 experienced health services researchers, and guided by Andersen's behavioral model. Covariates included demographics, and the outcome was delayed medical care. Cases ( $n=4090$ ) consisted of participants with at least one of the 18 SDoH variables, and controls ( $n=7414$ ) consisted of participants with none of them. **Method.** (1) Used bipartite network analysis and modularity maximization to identify participant-SDoH biclusters, and visualize them through ExplodeLayout. (2) Used multivariable logistic regression (adjusted for demographics and corrected through Bonferroni) to measure the odds ratio (OR) of each participant bicluster to the outcome, compared with the controls. **RESULTS/ANTICIPATED RESULTS:** The analysis identified 7 SDoH subtypes (<https://post-img.cc/Vd7Pg4xZ>) with statistically significant modularity compared with 100 random permutations of the data (All of Us=.51, Random Mean=.38,  $z=20$ ,  $P$  **DISCUSSION/SIGNIFICANCE:** The results identified 7 distinct subtypes based on SDoH profiles and their risk for delayed medical care, highlighting the importance of addressing specific combinations of barriers, with affordability having the highest risk. Furthermore, the analytical methods used are generalizable and have been made publicly available on CRAN and All of Us.

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### **The Implications of High Expression of VISTA, a Negative Check Point Regulator, on Prognosis Across Malignant Solid Tumors: a Systematic Review and Meta-Analysis\***

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**OBJECTIVES/GOALS:** Targeting the V-domain immunoglobulin suppressor of T cell activation (VISTA) signaling pathway has been suggested as a promising approach for overcoming resistance to current immune checkpoint therapies in advanced cancer. This review will synthesize the rapidly-expanding literature on VISTA protein expression on prognosis in various cancers. **METHODS/STUDY POPULATION:** To determine the prognostic significance of high VISTA expression across treatment-naïve malignant tumors, a systematic review and meta-analysis will be performed of published