

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 **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 **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