ment represents a key risk factor for worse outcome in glioma WHO grade II. Early first-line therapy may improve outcome in such patients.

### BIOM-16. IMMUNOMIC ANALYSIS OF GLIOBLASTOMA (GBM) USING GENE EXPRESSION PROFILING

Michael Castro[1], Nilofar Badra-Azar[2], Thomas Kessler[2], Moritz Schütte[2], Bodo Lange[2], and Marie-Laure Yaspo[2]; [1]Personalized Cancer Medicine, PLLC, Los Angeles, CA, USA, [2]Alacris Theranostics GmbH, Berlin, Germany

BACKGROUND: Despite the success of immunotherapy across the spectrum of human cancer, a successful strategy has not emerged for GBM. While PD-L1 IHC and TMB have demonstrated some utility as predictors of immunotherapy benefit, responsiveness is complexly determined by factors affecting T cell trafficking, antigen presentation, other immune checkpoints, and mediators of immune exhaustion. Thus, we set out to to characterize mediators of immune resistance and their diversity in a population of GBM patients utilizing quantitative gene expression. METHODS: A set of 54 immunotherapy and checkpoint relevant genes and seven genes related to immune failure were selected from the literature. RNA gene counts for TCGA glioblastoma multiforme samples (N=163) were downloaded from https://portal.gdc.cancer.gov/. Annotation on subtypes and PFS values were obtained from PMID: 24120142. Gene expression normalization as FPKM, hierarchical clustering and box-plots were performed using R-3.6.0. Statistical differences of gene expression between subtypes were quantified using a TurkeyHSD test. RESULTS: A heatmap with hierarchical clustering for immune related genes for the TCGA GBM cohort was generated including colored annotation for the subtype and progression free survival. The graph shows a rough separation into two groups, where one group of the genes is tentatively associated with mesenchymal subtype and shorter survival and showing higher expression for most immune evasion genes. However, a heterogeneity of immune evasion signatures was identified within and across subtypes. Transcripts related to antigen presentation, EZH2, and LDHA varied significantly between GBM subtypes ($p < 0.05$). CONCLUSION: Gene expression analysis has utility to identify specific mediators of immune evasion and to inform the selection of combination therapies for discrete subsets of patients. A Bayesian approach to patient selection for specific immunotherapy strategies may enhance the likelihood of successful implementation of immunotherapy in the clinic.

### BIOM-17. BRAF MUTATION IS AN EARLY EVENT IN THE EVOLUTION OF A SUBSET OF GLIOBLASTOMAS AND IS ASSOCIATED WITH INCREASED PD-L1 EXPRESSION

Kyle Walsh[1], Joanne Xiu[2], Giselle López[1], Daniel Landi[1], Zachary Reitman[1], Sandeep Mittal[3], Andrew Brenner[4], Ekokobe Fonkem[5], Santosh Kesari[6], Surasak Phuphanich[7], Herbert Newton[8], Manjari Pandey[9], Emil Lou[10], Michael Glantz[11], Ashley Sumrall[12], Erin Dunbar[13], Macarena De La Fuente[14], W. Michael Korn[2], Mustafa Khasraw[1], and David Ashley[1]; [1]Duke University Medical Center, Durham, NC, USA, [2]Caris Life Sciences, Phoenix, AZ, USA, [3]Virginia Polytechnic Institute and State University, Roanoke, VA, USA, [4]Mays Cancer Center UT Health Science Center, San Antonio, TX, USA, [5]Barrow Neurological Institute, Phoenix, AZ, USA, [6]Translational Neurosciences and Neurotherapeutics, John Wayne Cancer Institute and Pacific Neuroscience Institute at Providence Saint John's Health Center, Santa Monica, CA, USA, [7]Cedars-Sinai, Los Angeles, CA, USA, [8]Advent Health, Orlando, FL, USA, [9]The West Cancer Center, Memphis, TN, USA, [10]University of Minnesota School of Medicine, Minneapolis, MN, USA, [11]Penn State University, State College, Hershey, PA, USA, [12]Levine Cancer Institute, Charlotte, NC, USA, [13]Piedmont Hospital, Atlanta, GA, USA, [14]Sylvester Comprehensive Cancer Center, University of Miami, Miami, FL, USA

INTRODUCTION: BRAF is a RAF-family kinase that regulates MAPK/ERK signaling. Activating *BRAF* mutations, including V600E, are common in circumscribed low-grade gliomas of childhood and young adulthood, but are uncommon in infiltrative astrocytomas, including glioblastoma. Their role in glioblastoma initiation and progression requires analysis of large datasets given the low frequency (1.0%) in TCGA IDH-wild-type glioblastomas. METHODS: Molecular profiling was done on 4679 FFPE gliomas by next-generation sequencing at Caris Life Sciences, of which 3170 underwent RNA-sequencing for gene fusion and 4603 DNA-sequencing for mutations. *MGMT* promoter methylation was tested by pyrosequencing and PD-L1 IHC was performed using the SP142 clone. RESULTS: Excluding variants of uncertain significance, *BRAF* mutations/fusions were most common in pleomorphic xanthoastrocytoma (PXA; N=12/24, 50%), glioneuronal tumors (N=6/13, 46%), pilocytic astrocytoma (PA; N=15/48, 31%), and ganglioglioma (n=5/18, 28%). *BRAF* fusions were uncommon (N=17), most frequent in PA (N=8/31, 26%) where they were associated with older age at daignosis (P=0.043), and typically involved KIAA1549 as fusion partner (70%). BRAF-mutated/fused glioblastoma patients (N=59/3126, 2%) were younger than BRAF-wild-type glioblastoma patients (54 versus 59 years, $P=3.5x10^{-3}$); more likely to be *MGMT*-unmethylated (75% versus 56%, $P=5.0x10^{-3}$); and 3x more likely to express PD-L1 (55% versus 17%, $P=2.1x10^{-10}$). In tumors harboring a V600E mutation, the variant allele frequency (VAF) was similar in glioblastoma as in PXA, PA, ganglioglioma, and glioneuronal tumors (median VAF=35%). CONCLUSIONS: *BRAF*-mutated glioblastoma were 3x more likely to express PD-L1 than *BRAF*-wild-type glioblastoma. We observed no differences in *BRAF* V600E clonality in *BRAF*-mutated glioblastoma compared to *BRAF*-mutated PXA, PA, ganglioglioma, and glioneuronal tumors, suggesting *BRAF* mutation is an initiating event in the clonal evolution of a subset of glioblastoma. There is rationale to evaluate combined *BRAF* inhibition with checkpoint inhibition in *BRAF*-mutated glioblastoma, potentially synergizing the complete response profile of the former with the durable response profile of the latter.

### BIOM-18. TUMOR LOCATION IS ASSOCIATED WITH CDKN2A STATUS IN IDH-MUTANT ASTROCYTOMAS

Jerome Graber, and Patrick Cimino; University of Washington, Seattle, WA, USA

BACKGROUND: Astrocytomas with isocitrate dehydrogenase (IDH) mutations have a better prognosis and response to therapy than matching tumors without IDH mutations. IDH-mutant tumors of any grade or histology that carry homozygous deletions in cyclin-dependent kinase inhibitor (CDKN2A) have a worse prognosis compared to tumors with intact CDKN2A. Within a retrospective cohort of IDH-mutant astrocytomas with known CDKN2A status, we examined whether there was any correlation of CDKN2A status with anatomic location. METHODS: Astrocytomas of any grade carrying IDH mutations with further molecular sequencing that included CDKN2A status were identified from a tissue database, as well as a clinical cohort of patients seen at the neuro-oncology clinic who had genomic analysis by clinical request. Imaging was reviewed for tumor location. Fisher's exact test was used to analyze differences between groups. RESULTS: Six of 35 IDH-mutant astrocytomas (17%) had CDKN2A deletions. None of the six patients with CDKN2A mutant tumors had contact with the insula, whereas 16 of 29 tumors (55%) with intact CDKN2A contacted the insula (p=0.02). The majority of tumors in both groups were located completely or partially in the frontal lobe, as is common in IDH-mutant astrocytomas, and all CDKN2A deleted tumors were in the frontal lobe. DISCUSSION: Astrocytomas with IDH mutations that also carry CDKN2A deletions have been shown to have a worse prognosis than similar grade tumors with intact CDKN2A status. This has important prognostic implications, but CDKN2A testing is not standard currently or used to stratify patients in clinical trials. Our sample size is small, but if confirmed in a larger cohort could help guide efficient testing for CDKN2A status and improve prognostication.

### BIOM-19. METABOLIC ALTERATION INDUCED BY SELECTIVE KNOCK DOWN OF GABPB1L IN U251 CELLS

Noriaki Minami[1], Vinay Ayyappan[1], Nick Stevers[2], Abigail Molloy[1], Georgios Batsios[1], Donghyun Hong[1], Anne Marie Gillespie[1], Elavarasan Subramani[1], Marina Radoul[1], Joseph Costello[3], Pavithra Viswanath[1], and Sabrina Ronen[1]; [1]Department of Radiology and Biomedical Imaging, University of California San Francisco, San Francisco, CA, USA, [2]Department of Neurological Surgery, University of California San Francisco, San Francisco, CA, USA

BACKGROUND: TERT promoter mutations that result in TERT expression are observed in over 80% of GBM and upstream inhibition of TERT expression by targeting GABPB1L is currently under investigation. In that context, non-invasive reliable biomarkers that can help detect TERT expression are needed. The aim of this research was to assess the value of magnetic resonance spectroscopy (MRS)-detectable metabolic changes as biomarkers of TERT expression in GBM. METHODS: GABPB1L knock down clones (GABPB1LKD) were established by introducing Crispr Cas9 plasmid vector targeting GABPB1L into U251 cells. Two representative clones with different knock down efficiency were chosen and compared to control cells. Tumor forming capacity was evaluated by colony formation assay and magnetic resonance imaging of orthotopically implanted tumors in mice. Cells were extracted using the dual phase extraction method and $^{1}$H-MRS data of cell extracts acquired using a Bruker 500 scanner. The data was analyzed using Mnova software. Multivariate analysis was performed using the SIMCA software. RESULTS: TERT expression was significantly reduced in GABPB1LKD compared to control cells depending on the GABPB1L knock down efficiency. Colony forming capacity was impaired in GABPB1LKD compared to control cells. *In vivo* MRI data showed significantly smaller tumor volumes in GABPB1LKD compared to control. Unbiased PCA analysis of $^{1}$H-MRS data showed separation of GABPB1LKD and control extracts and VIP scores derived from the OPLS-DA analysis, demonstrated that the common metabolites leading to separation of GABPB1LKD and control cells were aspartate, glutathione, glycerophosphocholine, glutamine, NAD(P)+, AXP. This data was confirmed by univariate analysis that revealed