shows a homogeneously enhancing mass with surrounding edema. The imaging differential diagnosis is broad, and includes high grade glioma and neuroinflammatory conditions. Definitive diagnosis therefore requires biopsy. Here we present a case of primary CNS lymphoma that was diagnosed as an acute demyelinating process on initial biopsy. A 68 year old female presented with gait instability and vertigo. MRI showed right cerebellar and right trigonal enhancing lesions. Biopsy revealed an acute demyelinating inflammatory process and she was diagnosed with acute disseminated encephalomyelitis. She was treated with intravenous methylprednisolone followed by oral prednisone with resulting clinical and radiographic improvement. She was re-admitted to hospital 4 months later with encephalopathy. Imaging showed a new enhancing mass in the pericallosal frontal lobes. Repeat brain biopsy showed diffuse large B-cell lymphoma. This case illustrates a highly unusual situation of biopsy-proven central demyelination preceding a primary CNS lymphoma diagnosis. It raises a number of etiopathological questions concerning the coexistence and potential causal relationships between demyelination and lymphoma. Additionally, it highlights the need for repeat biopsy if clinical and radiographic suspicion for lymphoma persists despite an alternative initial biopsy result.

PATH-61. IMMUNOHISTOCHEMICAL PHENOTYPING AND SURVIVAL ANALYSIS OF WHO GRADE II-IV GLIOMAS

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INTRODUCTION: Specific genetic mutations are linked to clinical prognosis in gliomas. There has been increasing demand to understand the association between tissue biomarker expression and survival. Using patient-derived samples, WHO grade II-IV gliomas were evaluated by the protein-staining pattern of molecular markers of interest across tumor grade, and the association between their expression and survival was investigated. METHODS: Tissue microarrays (TMA) containing duplicate 1 mm cores were generated from 78 gliomas (WHO grade II-IV) using an automated TMA system. Immunohistochemistry was performed per the manufactures recommendation to evaluate expression of: Wilms tumor 1 (WT1), platelet endothelial cell adhesion molecule (CD31), adhesion G protein-coupled receptor E5 (CD97), complement decay-accelerating factor (CD55), hypoxia inducible factor 1 subunit alpha (HIF1α), EGF-like module-containing mucin-like hormone receptor-like 3 (EMR3), integrin, and isocitrate dehydrogenase 1 (IDH1). Samples with moderate (+1) or intense (+2) staining to WT1, CD31, CD97, CD55, or HIF1α, or any staining to EMR3 or IDH1 mutation, were considered positive. RESULTS: Of the 78 tumor samples, there were 11 (14%) WHO grade II, 22 (28%) grade III, and 45 (59%) grade IV gliomas. Across grade III gliomas, anaplastic astrocytomas had significantly higher positive WT1 ($p=0.04$), CD31 ($p=0.002$) and IDH1 wild-type ($p< 0.0001$) staining. High-grade (III & IV) gliomas had significantly higher positive staining for WT1 ($p=0.013$), CD31 (0.024), integrin ($p=0.021$), and IDH1 wild type ($p=0.044$). In all gliomas, positive staining for WT1 ($p< 0.0001$), CD31 ($p=0.009$), CD97 ($p=0.024$), EMR3 ($p=0.036$), and IDH1 wild type ($p=0.0006$) were associated with worse overall survival. After adjusting for patient age, positive staining for WT1 ($p=0.003$) was associated with worse overall survival. CONCLUSION: Using immunohistochemistry, unique biomarker staining patterns were identified for WHO grade III anaplastic astrocytomas and for high-grade gliomas. Irrespective of grade, staining for WT1, CD97, CD31, EMR3, and IDH1 wild-type were associated with worse overall survival.

PATH-62. QUANTITATIVE ANALYSIS OF SEX-ASSOCIATED MGMT METHYLATION IN NEWLY DIAGNOSED GLIOBLASTOMA

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INTRO/OBJECTIVE: Glioblastoma (GBM) and MGMT have been reported to have sexual dimorphism. In multiple studies, including our own population-based cohort analysis, females had higher rates of MGMT methylation and improved methylation-associated progression-free and overall survival outcomes compared to males. MGMT methylation is assessed as a mean of five cysteine-phosphate-guanine (CpG1-5) islands (CpG methylation is highly inversely correlated with MGMT RNA expression). The primary objective of this study was to investigate differences in mean and individual CpG methylation by sex. METHODS: 155 patients who underwent first surgical intervention for newly diagnosed GBM at a single tertiary care institution between 2016 and 2018 were reviewed. Of these, 135 patients had available CpG methylation data determined by a clinically validated test using bisulfate conversion followed by PCR and pyrosequencing. MGMT was defined as methylated if the mean of CpG1-5 ≥ 12. The mean of CpG1-5 and each CpG parameter were compared by sex using the Wilcoxon signed-rank test. RESULTS: Overall (mean age 62, 34% female, 42% MGMT methylated), the median (IQR) of mean degree of methylation was 4.0% (2–33) and median CpG1-5 ranged from 3.0 to 4.5%. More females (53.3%) were MGMT methylated than males (37.1%). Females had significantly higher rates of mean methylation compared to males (14.0 vs 3.0%, $p=0.046$). Females also had higher rates of methylation at each CpG island compared to males CpG1(7.0 vs 3.0%, $p=0.15$), CpG2(8.0 vs 4.0%, $p=0.10$), CpG3(9.0 vs 4.0%, $p=0.23$), CpG4(7.0 vs 3.0%, $p=0.047$), and CpG5(6.0 vs 4.0%, $p=0.097$). CONCLUSION: Females had higher rates of mean methylation and methylation of each CpG island compared to males, although only mean and CpG4 methylation values were statistically significant given the limited sample size. Further investigation with a larger cohort is ongoing to elucidate this dimorphism and establish whether sex-specific methylation cut-offs need to be implemented into clinical practice.

PATH-63. TRANSCRIPTIONAL SIGNATURES IN HISTOLOGIC STRUCTURES WITHIN GLIOBLASTOMA TUMORS MAY PREDICT PERSONALIZED TREATMENT SENSITIVITY AND SURVIVAL

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OBJECTIVE: Personalized treatment strategies in Glioblastoma multiforme (GBM) has been hampered by intra-tumoral heterogeneity. The goals of this study were to (1) determine the impact of intra-tumoral heterogeneity on established predictive and prognostic transcriptional signatures in human GBM, and (2) develop methods to mitigate the impact of tissue heterogeneity on transcriptomic-based patient stratification. METHODS: We analyzed transcriptional profiles of GBM histological structures from the open-source Ivy Glioblastoma Atlas Project. To generate these data, infiltrative tumor, leading edge, cellular tumor [CT], perinecrotic zones, pseudopalisading cells, hyperplastic blood vessels and microvascular proliferation were microdissected from 34 newly diagnosed GBM and underwent RNA sequencing. Data from The Cancer Genome Atlas were used for validation. Principle component analysis, network analysis and gene set enrichment analysis were used to probe gene expression patterns. RESULTS: Distinct biological networks were enriched in each tumor histological structure. Classification of patients into GBM molecular subtypes varied based on the structure assessed, with many patients classified as every subtype depending on the structure analyzed. Using only CT to classify subtypes, we identified biologically unique patterns suggesting that proneural and mesenchymal tumors may be more sensitive to chemoradiotherapy and immunotherapy, respectively. Survival outcome predicted by an established multigene panel was confounded by histologic structure. Utilizing CT transcriptomics we developed a novel survival prediction gene signature that identified the highest-risk GBM patients in both CT and bulk tissue gene expression profiles. CONCLUSIONS: Histologic structures contribute to intra-tumoral heterogeneity in GBM. Using mixed-structure biopsy samples could incorrectly subtype tumors and produce invalid patient stratification. Limiting transcriptomic analysis to the CT allowed us to develop a new survival prediction gene signature that appears accurate even in mixed tissue samples. The biological patterns uncovered in the subtypes and risk-stratified groups have important implications for guiding the development of precision medicine in GBM.

PATH-64. PROSPECTIVE, BLINDED PLASMA BASED ANALYSIS FOR DIAGNOSIS OF NEWLY DIAGNOSED GLIOMA

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INTRODUCTION: In patients with newly diagnosed intracerebral lesions, gliomas are often suspected. However, other conditions such as multiple sclerosis, abscess or lymphoma are possible, as well. Furthermore, biopsy can be challenging due to eloquent and/or deep location within the brain. In this prospective, blinded study, analysis of plasma isolated cell-free DNA and exosome mRNA and miRNA from newly diagnosed glioma patients and from cancer-free volunteers was used to predict disease. METHODS: Plasma was drawn from 52 patients with newly diagnosed gliomas (28 high grade glioma (HGG), 10 low grade (LGG)) and 14 patients without documented history of cancer and recent MRI brain which was negative for brain tumor. High quality DNA and RNA was isolated and sequenced using Next Generation Sequencing and Digital Droplet PCR was used for detection and verification of trace molecular artifacts. Multianalyte processing yielded data that was harmonized and interpreted through an

Artificial Intelligence based algorithm to assess for possible glioma and to assign grade in a blinded fashion. EGFRvIII, TP53 and IDH1 mutations were also analyzed and compared to molecular testing from tumor specimens. RESULTS: 66% (25 of 38) of glioma patients were correctly diagnosed as having a malignancy. 43% of HGG and 60% of LGG patients were correctly graded. Of the 14 normal controls, 6 were concluded to be cancer-free. IDH1, EGFRvIII, and TP53 mutation had concordance of 64% (21/33), 82% (14/17) and 36% (5/14), respectively. CONCLUSIONS: Analysis of plasma cell free tumor derived DNA and RNA was relatively sensitive for detecting glioma in treatment naïve patients. In contrast, this analysis was not specific in ruling out malignancy in the normal control patients. Given this profile, in patients with newly diagnosed intracerebral lesions suspicious for glioma, this may be a useful screening test to determine the need for more invasive testing, i.e. biopsy/resection.

PATH-65. MOLECULAR SIGNATURE OF FAT1 RELATED MOLECULES IN GLIOMAS IN THE CONTEXT OF THE WHO 2016 CLASSIFICATION

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Glioblastoma (GBM, WHO grade-IV) being the most malignant and aggressive form of glioma remains a major clinical challenge, with an overall 5-year survival rate of only 9.8%. Till recently, glioma diagnosis and grading were solely dependent on the phenotypic and histological features. However, with the advancement in the understanding of the molecular biology of glioma several molecules have been identified. The importance of these molecular/genotypic features of the tumor became evident by the inclusion of these molecular features by World Health Organization (WHO) in 2016 in glioma sub-grouping. Our lab is focused on studying the role of FAT1 gene (human ortholog of *Drosophila* tumor suppressor gene, *fat)* in glioma biology and aggressiveness. We observed FAT1 gene to have an oncogenic role in glioma where it has been found to upregulate migration/invasion, inflammatory microenvironment of the tumors, HIF1α expression/activity in the tumor-cells under severe hypoxia and in regulating EMT/stemness properties of GBM-cells under hypoxia. Here, we have characterized the molecular relationship between FAT1 related molecules and known- molecular markers of glioma with the hope of identifying glioma subgroup with a molecular signature of clinical significance by (i) analyzing the expression correlation of FAT1 and FAT1 regulated pro-inflammatroy molecules like COX2, IL1b and IL6 with the known- molecular markers of glioma like p53, IDH1, MGMT, EGFR, TERT in low-grade (grade-II) and high-grade (grade-III/IV) gliomas (n=50) by real-time PCR, sequencing, immunohistochemistry and *in-silico* analysis of TCGA-GBM-data (ii) Analyzed the regulatory role of FAT1 on the above known markers by siRNA mediated knockdown of FAT1 in *in-vitro* cell-culture system and (iii) further analyzed the identified molecular signature for their correlation with the patients prognosis/survival in the follow up patients. We observed a novel molecular signature with significant correlation with patients' clinical outcome. Therapeutic targetting of FAT1 may benefit patients with high FAT1 expressing tumors.

PATH-66. THE GENOMIC LANDSCAPE OF SPINAL CORD EPENDYMOMA

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INTRODUCTION: Ependymomas are seen throughout the neural axis but spinal cord is most common in adults. A subset arises in the setting of neurofibromatosis 2, whereas most are sporadic, potentially with somatic *NF2* inactivation. The genetic drivers in *NF2* wildtype tumors are unknown, as is the spectrum of cooperating genetic alterations. METHODS: We performed targeted next-generation sequencing (NGS) to assess mutations, rearrangements, and chromosomal copy number alterations in 46 adult spinal cord ependymomas. RESULTS: The 24 females and 22 males ranged from 20–73 (median 46) years of age. Tumors were in the cervical (n=24), thoracic (n=12), and lumbar (n=10) spinal cord. Nine tumors (20%) harbored truncating *NF2* mutations with loss of the remaining wildtype allele, with frequent monosomy 13q. Thirteen NF2-wildtype tumors (28%) showed monosomy 22q with frequent monosomy 13q and trisomy 7, 9, and 12. Seventeen tumors (37%) carried a near-tetraploid genome, likely due to genomic reduplication with frequent preservation of diploidy in chromosomes 13q (77%), 14q (88%), 21q (53%) and 22q (65%). Remaining cases did not show a recurrent pattern, but one harbored focal high-level *MYCN* amplification. Three of the six recurrences were seen in the last subgroup; however, there was no significant difference for progression-free survival between four subgroups. None of the *NF2*-mutant tumors were in lumbar spinal cord, but there was no difference for tumor location or patient age between four subgroups. DISCUSSION: Biallelic *NF2* mutational inactivation characterizes only a subset of spinal cord ependymomas, and *MYCN* amplification is likely a genetic driver in a small subset of *NF2* wildtype cases. The high frequency of chromosome 22q loss even in *NF2*-wildtype tumors raises the possibility of cryptic alterations in the *NF2* gene not detected by our panel, or perhaps implicates the presence of another as yet unidentified tumor suppressor gene on chromosome 22q.

PATH-67. RECOMBINANT INTERLEUKIN-7 ENHANCES THE ANTI-TUMOR IMMUNITY OF A DENDRITIC CELL VACCINE IN A MURINE MALIGNANT GLIOMA

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BACKGROUND: Dendritic cell (DC)-based vaccines have been suggested as one of the promising immunotherapies for treating various cancers, including glioblastoma. We already developed a novel vaccination protocol with peptide-loaded DCs followed by a mixture of synthetic peptides, polyinosine- polycytidylic acid (poly-IC) and anti-CD40 antibodies (Trivax) in a melanoma mouse model. However, in a glioma mouse model, therapeutic efficacy is not as much as enough maybe due to relatively low antigenicity and blood brain barrier. MATERIAL AND METHODS: IL-7, which is one of the most important cytokines to expand and develop T cells with anti-tumor immunity, was co-administrated intravenously with Trivax in an orthotopic murine malignant glioma. RESULTS: Co-administration of the Trivax and recombinant IL-7 (Trivax7) increased the number of survivin specific T cells measured using ELISPOT assay and the population of central memory T cells, comparing with administration of Trivax. The tumor size of orthotopic mouse model in Trivax 7 group was smaller than those of Trivax only group. Finally, overall survival in Trivax 7 was longer than those of Trivax only. In addition, there was a prolonged survival of antigen-specific T cells in Trivax7 group than Trivax only group. CONCLUSION: In summary, our novel combinational immunotherapy may overcome the limitations of current cell-based cancer vaccines and could be applicable for the treatment of glioblastoma patients.

NEURO-COGNITIVE OUTCOMES

NCOG-01. NEUROCOGNITIVE FUNCTION (NCF) AND QUALITY OF LIFE (QOL) RESULTS FROM A PHASE II STUDY OF TEMOZOLOMIDE-BASED CHEMORADIOTHERAPY REGIMEN FOR HIGH RISK LOW-GRADE GLIOMAS

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BACKGROUND: RTOG 0424 reported a 73.5% 3-year overall survival (OS) rate. This secondary analysis describes changes in NCF and QOL after therapy. METHODS: Patients with HR-LGG were treated with radiation and concurrent and adjuvant temozolomide. Standardized NCF tests were performed at baseline, 6 and 12 months (mos). Rates of NCF decline were examined using the reliable change index on Hopkins Verbal Learning Test (HVLT), Trail Making Test (TMT), and Controlled Oral Word Association. Relationships between NCF and subjective cognitive concerns (MOS-Cognitive Function [MOS-CF] scale) were evaluated with Wilcoxon Rank Sum Test. QOL was assessed using FACT-Brain. Longitudinal modeling using maximum likelihood estimation evaluated predictors of change in QOL. Cox models assessed the association of baseline NCF with OS after adjusting for age, anticonvulsants, number of high risk factors, EORTC OS risk group, and tumor crossing the midline. RESULTS: From 1/2005 to 8/2009, 129 evaluable patients were accrued, and 93 (72%) completed at least one NCF/QOL measurement with completers having better neurologic function than noncompleters (p=0.04). Compliance across measures was