45.4% of grade 3 IDH-mutant, 1p/19q-codeleted oligodendroglioma(5/11). In a subset of cases analyzed by targeted NGS, robust signaling pathway activity was identified in 38%(11/29) at the protein level while genetic alterations predicted to activate the pathway were present in only 17.2% (5/29). Our results demonstrate robust PI3K/AKT/mTOR signaling activity in a significant fraction of IDH-mutant diffuse glioma, an association with increasing tumor grade in oligodendroglioma, and an increase at recurrence in both oligodendroglioma and astrocytoma. Overall, our data suggest that quantitative evaluation of phosphoproteins may be a sensitive method to detect PI3K/AKT/mTOR pathway activity and may be useful for patient stratification.

BIOM-39. ESTABLISHMENT OF A CONNECTIVITY SIGNATURE FOR GLIOMAS

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Recent studies have demonstrated extensive cell-to-cell connectivity between tumor cells of gliomas with considerable relevance for tumor progression and therapy resistance. Tumor microtubes (TMs) are neurite-like tumor cell extensions that build these tumor cell networks. Measuring the extent of connectivity in individual tumors has been challenging and depended on anatomical parameters that are difficult to evaluate in patient samples. We performed bulk and single-cell (sc)RNA sequencing of connected vs. unconnected tumor cells from patient-derived xenograft tumors using a newly developed technology that exploits SR101 dye transfer within tumor cell networks. scRNA sequencing was performed with 17 human glioblastoma tumor samples. Three diffuse glioma cohorts from The Cancer Genome Atlas (n = 648), the Chinese Glioma Genome Atlas (n = 668) and the NCT Neuro Master Match (n = 38, IDH-wildtype only) were used to assess clinical properties. A connectivity signature both from bulk and scRNA sequencing data of xenografted primary glioblastoma tumor cells was established. Comparative analysis showed better performance and higher biological relevance of the single-cell derived signature that involves 71 genes. Most of the genes are related to neurogenesis and neural tube development, including several previously recognized TM-relevant genes. Highest connectivity was observed in astrocytic-like and mesenchymal-like tumor cells. Induction of connectivity *in vitro* was accompanied with increase of the connectivity signature. The connectivity signature was higher in astrocytic as compared to oligodendrocytic gliomas, and highest in IDH-wildtype gliomas. In accordance, connectivity correlated strongly with dismal survival in all three glioma cohorts. The connectivity signature established here is biologically plausible and associates with prognostically relevant glioma subtypes. It provides the first proof-of-principle that tumor cell connectivity is relevant for the clinical course of patients with gliomas, and at the same time serves as a robust biomarker that can be used for future studies, including prospective clinical trials.

BIOM-40. ANALYSIS OF SERUM MIRNA IN GLIOBLASTOMA PATIENTS: TARGETED ENRICHMENT OF EXTRACELLULAR VESICLES ENHANCES SPECIFICITY FOR PROGNOSTIC SIGNATURE

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Glioblastoma is a devastating disease, for which biomarkers allowing a prediction of prognosis are urgently needed. microRNAs have been described as potentially valuable biomarkers in cancer. Here, we studied a panel of microRNAs in extracellular vesicles (EV) from the serum of glioblastoma patients and also in total serum without prior EV separation, and evaluated their correlation with the survival of these patients. Our study included 55 patients in total, 26 (47.3%) of which were treated within the multicenter Phase III CeTeG/NOA-09 trial and 29 (52.7%) in the Division of Clinical Neurooncology of the University Hospital of Bonn, as well as 10 healthy volunteers (HV). Blood was drawn from patients during the adjuvant chemotherapeutic treatment. A panel of 15 microRNAs was studied by quantitative real-time PCR in EV that were separated by size-exclusion chromatography, followed by CDxx* immunoprecipitation (SEC+CDxx*), and compared with those from total serum of glioblastoma patients and HV. Comparing SEC+CDxx* to total serum, we found evidence for enrichment of miR-21-3p and miR-106a-5p and, conversely, lower levels of miR-15b-3p in SEC+CDxx* EV. miR-15b-3p and miR-21-3p were upregulated in serum of glioblastoma patients compared to healthy subjects. Significant correlation with survival of the patients was found for levels of miR-15b-3p in total serum and miR-15b-3p, miR-21-3p, miR-106a-5p and miR-328-3p in SEC+CDxx* EV. Combining miR-15b-3p in serum or miR-106a-5p in SEC+CDxx* EV with any one of the other three microRNAs in SEC+CDxx* EV allowed for a prognostic stratification of glioblastoma patients. We have thus identified four microRNAs whose levels, in combination, can predict the prognosis for these patients. *=Cluster of Differentiation xx (CDxx); Molecule cannot be specifically mentioned due to pending patent.

BIOM-41. GENETIC MARKERS CORRELATED WITH PROGRESSION-FREE SURVIVAL TIMES IN GLIOBLASTOMA PATIENTS UNDERGOING TREATMENT WITH TUMOR TREATING FIELDS

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INTRODUCTION: Despite advances in surgical approaches, followed by chemo-radiotherapy protocols, the overall prognosis for patients with glioblastoma remains poor. Clinical trials have demonstrated that the use of low intensity alternating electric fields, known as Tumor Treating Fields (TTFields), via the Optune™ device extends overall survival times when combined with standard chemotherapy. However, the response to TTFields varies across patients, and it is currently unclear why some patients show increased time to tumor progression with TTFields treatment while others do not. One possible answer lies in the biological diversity of the tumors themselves. Genetic alterations are known to impact survival times and chemotherapy sensitivity in glioblastoma, suggesting that certain markers may also predict responsiveness to TTFields. Here, we compare the genetic profile of primary glioblastoma tumors with progression times in patients receiving TTFields treatment. METHODS: Patients with primary glioblastoma who chose treatment with the Optune™ device were prospectively enrolled and a sample from their primary tumor resection was sent for FoundationONE CDx™ testing. Genetic alteration results, including mutation burden and copy number alterations, were then compared with clinical data and tumor progression times. RESULTS: Mutations and/or copy number changes in genes that regulate cell growth/proliferation, apoptosis, and interactions with DNA were among the most common alterations observed in our cohort. For patients that recurred within 12 months, we found a common pattern of alterations that includes CDKN2A/2B co-deletion, MTAP deletion, and PIK3 mutations. This pattern was not observed in patients that recurred after 12 months. CONCLUSION: The identification of genetic markers that predict treatment responsiveness may help direct patients toward optimal treatment options. Ongoing work is aimed at expanding our sample size, correlating these genetic markers with overall patient survival, and determining if this pattern of expression is specifically related to TTFields treatment response.

BIOM-42. ASSOCIATION OF NEUTROPHIL-LYMPHOCYTE RATIO WITH GLIOMA GRADING AND SURVIVAL

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INTRODUCTION: Gliomas are the most common primary central nervous system tumor. Inflammatory responses are thought to play an important role in cancer progression. Neutrophil-lymphocyte ratio (NLR) is