primary vs. secondary patients. Preliminary results of single-gene analysis of MC tumours showed FOXM1, MYBL2, TOP2A, BIRC5 expression was higher in WHO grade III samples. Gene-expression signatures in the individual patients and gene ontology enrichment analyses are in process. CONCLUSIONS: FOXM1, MYBL2, TOP2A, BIRC5 RNA expression levels seem to rise during malignant progression across patients. Gene-expression analysis using the Nanostring technology is feasible and a potentially powerful tool to distinguish meningiomas prone to malignant transformation from truly benign meningiomas.

OTEH-4. DEEPER INSIGHT INTO INTRATUMORAL HETEROGENEITY BY MRI AND PET-GUIDED STEREOTACTIC BIOPSIES FROM GLIOBLASTOMA PATIENTS

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Glioblastoma is one of the most aggressive cancers, but the molecular evolution is still not fully understood. We used PET imaging combined with deep sequencing of glioblastoma biopsies at both the RNA and DNA levels to get a deeper insight into molecular evolution. In the clinical setting, PET imaging provides information about metabolically active tumor areas, but the molecular interpretation is unclear. Our primary objective was to perform an intratumoral spatial comparison of biopsies from potentially aggressive and less aggressive areas in glioblastomas according to PET scans. Additionally, tissue from the tumor periphery was included. We used MRI, ^{11}C-methionine(MET) PET, and ^{18}F-FDG PET was used in combination to obtain a series of neurosurgical stereotactic biopsies from tumor areas with high MET and ^{18}F-FDG uptake (hotspot), low MET and ^{18}F-FDG uptake (coldspot), as well as tumor periphery of six glioblastoma patients that were processed for whole genome, exome, and transcriptome sequencing. Differential gene expression and gene ontology analysis showed that hotspots were enriched in gene sets associated with DNA replication, cell cycle, and ligand receptor interaction. Genome and exome analysis suggested hotspots and coldspots to have similar mutational profiles. However, a limited number of hotspot-specific mutations and fusion transcripts indicated that hotspot tumor cells developed from coldspot cells and point at the potential role of hotspot driver genes in glioblastoma. Our findings reveal that hotspots in glioblastomas represent a more advanced stage of molecular evolution than coldspots.

OTEH-5. CHARACTERIZATION OF LONG-NON CODING RNA ASSOCIATED CERNA NETWORK HUB GENE INVOLVED IN GLIOBLASTOMA MULTIFORME LIPID METABOLISM

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BACKGROUND: Glioblastoma multiforme (GBM) are the major death contributor in primary brain tumour. Despite having an improved diagnostic criterion by integrating both histological and molecular features such as Isocitrate Dehydrogenase (IDH) detection, the prognosis of GBM patients still remain poor. Lipid metabolism is an essential pathway that fuel GBM aggressiveness. IDH1 one of the key enzyme that regulates it. Long non-coding RNAs (lncRNAs) act as competing endogenous RNAs (ceRNAs) in tumour initiation and progression. In parallel, miRNA-mediate ceRNA crosstalk between lncRNAs and mRNAs. In this study, we aim to investigate the IDH1 subgroup lncRNA associated ceRNA network hub gene responsible in the coordination of glioblastoma multiforme lipid metabolism using bioinformatics approach. METHODS: TCGA-GBM dataset consist of 168 GBM

RNA-seq (159 IDH1 wt and 9 IDH1 mutation) were downloaded. Differentially expressed genes (DEG) were then obtained using Limma. Gene sets related with lipid metabolism from GSEA-MSigDB were overlapped with DEG using Venn diagram to identify the DEmRNA that are related with lipid metabolism. Construction of mRNA-miRNA and lncRNA-miRNA interaction networks were performed using miRNet. The ceRNA interaction network were later combined in the Cytoscape software. Potential lncRNA hub genes were identified by CytoHubba analysis. RESULTS: From 1389 DEG, 67 genes were identified to be significant in the regulation of lipid metabolism. By analysing the lncRNA-miRNA-mRNA interaction network, candidate hub lncRNAs consists of three genes with highest connective nodes; CYTOR, LOXL1-AS1 and HOTAIR. These genes are significantly upregulated in glioma. LOXL1-AS1 serve as an excellent prognostic biomarker for both glioma and glioblastoma as the effect of high and low LOXL1-AS1 expression on patients' survival is significant (p<0.05). CONCLUSIONS: Data mining and bioinformatics approach guided the identification of the potential hub lncRNAs associated ceRNA network in GBM lipid metabolism. This allows us to uncover the novel role of lncRNA in GBM tumorigenesis.

OTEH-6. ALGORITHMIC APPROACH TO CHARACTERIZE POST-TREATMENT RECURRENT GLIOMA USING RNA SEQUENCING AND QUANTITATIVE HISTOPATHOLOGY

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INTRODUCTION: Distinguishing between tumor and treatment effect in post-treatment glioma, although crucial for clinical management, is difficult because contrast-enhancing regions are mixtures of recurrent tumor and reactive tissue, and definitive histopathological criteria do not exist. This study disentangles the marked intra-tumoral heterogeneity in the treatment-recurrent setting by developing an unsupervised framework to algorithmically categorize intraoperative MRI-localized biopsies into three clinically-relevant tissue clusters based on joint analysis of RNA sequencing and histopathological data. METHODS: A retrospective cohort of 84 MRI-localized biopsies from 37 patients with post-treatment recurrent glioblastoma underwent mRNA extraction and quantification via PLATEseq protocol. For 48 of 84 biopsies, a neighboring piece of tissue underwent quantitative histopathology based on labeling index (LI) for SOX2, CD68, NeuN, Ki67, and H&E. Correlation between LIs and gene expression for these 48 samples was performed. Genes significantly correlated (p<0.05) with ≥1 marker were used for hierarchical clustering of correlation matrix, identifying three mutually-exclusive tissue-specific gene sets. These sets were then used to perform ssGSEA to categorize each of 84 biopsies into one of three tissue types. RESULTS: Correlation analysis identified 7779 genes significantly correlated with ≥1 histopathological marker. Clustering revealed three gene sets associated with specific markers: SetA-3688 genes associated with SOX2/Ki67/H&E; SetB-2418 genes associated with CD68; SetC-1673 genes associated with NeuN. ssGSEA using these sets categorized each biopsy into one of three tissue types: 27 biopsies enriched in SetA, 28 in SetB, and 29 in SetC. CONCLUSIONS: Using MRI-localized biopsies with both RNAseq and histopathological data, this algorithmic approach allows development of three orthogonal tissue-specific gene sets that can be applied to characterize the heterogeneity in post-treatment recurrent glioma: SetA: genes correlated with SOX2/Ki67/H&E, representing recurrent tumor; SetB: genes correlated with CD68 (microglia) representing reactive tissue consistent with treatment effect; SetC: genes correlated with NeuN (neurons), representing infiltrated brain.

OTEH-7. MOLECULAR CHARACTERIZATION OF TUMOR STIFFNESS IN GLIOBLASTOMA

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