OTHR-43. COMPOSITION OF CELL-FREE MIRNA IN CEREBROSPINAL FLUID AND PLASMA AS A MONITORING TOOL FOR PEDIATRIC BRAIN TUMORS

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Current clinical management of pediatric brain tumor patients involves non-invasive imaging studies to monitor therapeutic response and tumor progression. However, results are often inconclusive and unable to capture biological changes that presage progression on imaging. Non-invasive diagnostics, also termed liquid biopsy, have emerged for detection of cell-free cancer material but there are no such standard, clinically defined biomarkers or methods for pediatric brain tumors. Circulating miRNA presents an attractive biomarker platform given its stability in bio-fluids, selective expression in tumors and release from tumor cells into the extracellular environment. Technology development has permitted high throughput analysis of material obtained from biofluids including plasma and cerebrospinal fluid (CSF). We performed miRNA profiling across a cohort of 54 pediatric brain tumors from different histologies (low grade glioma, ependymoma, germinoma, medulloblastoma, atypical teratoid rhabdoid tumor and high-grade glioma) using CSF (33) and plasma (53) with HTG EdgeSeq platform. CSF and plasma specimens clustered independently of each other providing separate biomarker platforms. Consensus clustering performed on CSF specimens revealed clusters correlated with disease severity (tumor grade). We identified miRNA targets closely correlated with tumor grade ($p<0.001$), tumor dissemination or metastases ($p<0.001$) and survival ($p=0.001$). Similarly in plasma, through consensus clustering we identified cohorts with correlation to tumor grade. While distinct from those identified in CSF, specific plasma miRNA also correlated with clinical (tumor grade; $p<0.001$, dissemination or metastasis; $p=0.002$) and demographic (gender; $p=0.001$) features. Independently, histology-specific miRNA signature was also identified for low grade glioma, medulloblastoma and germinoma in plasma and CSF. The results present differential expression of cell-free miRNAs in plasma and CSF as biomarkers associated with diverse clinical diagnostic and prognostic measures. Further utilization of this approach provides unique platforms (plasma and/or CSF) to inform liquid biopsy-based management in the clinical setting.

OTHR-44. BUILDING NARRATIVE COMPETENCE ON THE NEURO-ONCOLOGY TEAM: A NARRATIVE MEDICINE APPROACH TO FOSTERING UNITY AND RESILIENCE FOR WORK WITH PEDIATRIC BRAIN TUMOR FAMILIES

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Narrative medicine relies on recognizing, taking in, reflecting on and responding to the stories of suffering in others. Drawing on the practice of the close reading of literature and reflection through writing, healthcare professionals gain fresh insights into their own stories and in turn connect in meaningful ways to stories of illness in their patients (Charon, 2001). The lived experience of pediatric neuro-oncology teams seesaws between hard-fought victories and stories of pain, loss, and even death. For patients who survive, many face life-long challenges that impact long-term quality of life. Learning to be an eyewitness of both beauty and pain in literature and art and writing about that witness helps teams reflect on the stories that shape them and their patients as they process the unthinkable in their work. This type of narrative competence requires what Sayantani DasGuspta refers to as narrative humility (Das Gupta, 2008). Narrative humility recognizes that stories of illness are ambiguous, contain contradictions, and belong wholly to the patient, and encourage providers to explore the role their own narrative brings to the clinician-patient relationship (Das Gupta, 2008). This narrative competence enables team members to find new ways to navigate their practice and foster team unity. Connecting to their own narrative allows them to connect to the narratives of others. They learn to be uncomfortable, to feel pain or joy, and to find power in being physically present with someone who is healed, feels marginalized, or is wounded. By listening closely to the stories of illness and loss in others and reflecting on their own stories through narrative medicine techniques, they learn to engage with the stories that define both their patients and their team dynamics. This theoretical and practical presentation explores the principles of narrative medicine and applies them to the particular experience of neuro-oncology teams.

OTHR-45. KIDS FIRST VARIANT WORKBENCH: APPLICATION TO GERMLINE GENOMIC DISCOVERIES IN THE CHILDREN'S BRAIN TUMOR NETWORK

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The Gabriella Miller Kids First Pediatric Research Program (Kids First) aims at facilitating researchers to uncover new insights into the biology of childhood cancer (CC) and structural birth defects (SBD). Kids First has two initiatives, i) whole genome sequencing of biospecimens from families with CC/SBD, and ii) establishing Kids First Data Resources. Kids First Data Resource Center developed the Kids First Data Resource Portal (KFDRP), a centralized platform to search, view, analyze, and identify currently accessible data from both Kids First and collaborative cohorts, incorporating omics and phenotypic information of 30 studies and 26,300 participants. A recently released KFDRP component is Variant WorkBench (VWB), enabling users to query, mangle, analyze and visualize genomic variants from participating cohorts, with the Children's Brain Tumor Network (CBTN) being one of the cohorts. VWB supports programming languages such as Python, Spark, SQL and R for in-depth analysis in Apache Zeppelin notebooks. In addition to variant calls and phenotypic information, VWB hosts rich external variant annotations in the public domain, such as Cancer Hotspots, COSMIC and ClinVar. Users can also load additional databases (e.g. Human Gene Mutation Database/HGMD) within a notebook, import custom datasets as temporary query tables, export analysis outputs to local drives, visualize analysis results in multiple chart styles, display local figures, and save notebooks for sharing, further use and Cavatica projects. In an effort to screen tier 1 genes (n=578) from the most recent Cancer Gene Census provided by COSMIC in CBTN, we identified ~127,500 germline variants that are both rare and damaging, or that are already cataloged in the most recent version of ClinVar/HGMD. The whole process took less than one hour which is much faster than conventional methods. VWB enables efficient genomic variant analysis and discoveries in pediatric neuro-oncology research with advanced big data technology.

OTHR-46. SINGLE INSTITUTION EXPERIENCE USING MOLECULAR ANALYSIS OF PEDIATRIC CNS TUMORS

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Molecular analysis of pediatric CNS tumors helps confirm the diagnosis, but can also guide treatment by identifying prognostic factors allowing for treatment stratification, and by unveiling active signaling pathways which can be targeted. This report is a retrospective review of the molecular analysis performed on all CNS tumors biopsied or resected at Children's Minnesota over the last 3 years to evaluate our current practices. From 2019-2021, 118 patients with newly diagnosed CNS tumors underwent surgery followed by molecular assessment (14 IHC/FISH, 85 NGS, 7 methylation profiling) on 100% of medulloblastoma, other embryonal tumors, and schwannoma; 90% of ependymoma; 88% of HGG; 71% of LGG/glioneuronal/neuronal tumors; and 50% of meningioma and craniopharygioma. MAPK pathway alterations were seen in 84% of LGG/glioneuronal/neuronal tumors, with KIAA1540-BRAF fusion seen exclusively in pilocytic astrocytoma and BRAFV600E alterations seen in diffuse LGG (75%), PLNTY and PXA. Frequent alterations seen in HGG included H3F3A-K27M, H3F3A-G34, TP53, PDGFRA, ATRX, CDKN2A/B. Common gene alterations in medulloblastoma included monosomy 6 (100%) and alteration of CTNNB1 (50%) in WNT subgroup; PTCH1 (75%) in SHH subgroup; MYC/MYCN gain (60%) or amplification (60%) in Non-WNT/SHH subgroup. Alterations in FOXR2 in CNS neuroblastoma, SMARCB1 in ATRT and C19MC in ETMR confirmed these diagnoses. Supratentorial ependymoma showed ZFTQ-RELA fusion (100%) and infratentorial ependymoma showed chromosomal copy number changes including 1q gain (40%). Meningiomas showed deletion of NF2 and SMARCB1 and craniopharyngioma had alterations in CTNNB1. Molecular analysis confirmed the diagnosis in 23% of tumors, aided with targeted treatment in 20% of patients (82% of HGG, 9% of LGG, 13% of medulloblastomas) and allowed for risk-adapted treatment in 93% of medulloblastomas. These findings indicate that identification of pathogenic variants in CNS tumors aids in the diagnosis and treatment of pediatric CNS tumors and should be considered standard practice.

PATHOLOGY/CLASSIFICATION

PATH-01. INFANT-TYPE HEMISPHERIC GLIOMA: NEW MOLECULAR ALTERATIONS AND PRECISION-MEDICINE TREATMENT

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BACKGROUND: Infant-type hemispheric glioma, harboring alterations in the receptor tyrosine kinases ALK, ROS1, NTRK and MET, is a new subtype of Pediatric-type diffuse high-grade gliomas in the 2021 WHO classification of CNS tumors. It has important clinical therapeutic value with specialized therapeutic drugs. Here, we presented 3 cases of infant-type hemispheric glioma. Patient1 with EML4-ALK fusion which often appeared in lung cancer, the other 2 patients have new molecular alterations which has not been reported before (Patient2 has both NTRK1-TP53/TP53-NTRK1