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 may influence tumor trajectory. We sought to develop signatures of cell-free miRNA in cerebrospinal fluid (CSF) and plasma of pediatric brain tumor patients as a potential tool for monitoring treatment response and detecting new diagnostic and therapeutic opportunities.

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 the stories of others in their care. This project explores the experience of pediatric neuro-oncology teams with children and young adults with pediatric brain tumors and their families, and the potential for narrative medicine to foster compassion, resilience and unity among the team.

OTHR-45. KIDS FIRST VARIANT WORKBENCH: APPLICATION TO GERMINE 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 biopsies from families with CC/SBD, and ii) establishing Kids First Data Resources, Kids First Data Repository (KFDR), 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 KFDR 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 files, visualize analysis results in multiple chart styles, display local figures, and save notebooks for sharing, further use and CavaLca 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 genomics research 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 presents a retrospective review of 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 NGS, 19 RT-qPCR, 85 NGS, 7 methylation profiling) on 100% of medulloblastoma, other embryonal tumors, and schwannoma; 90% of ependymoma; 88% of HGG; 71% of LGG/germinale/nerve tumors, and 50% of meningioma and craniopharyngioma. MAPK pathway alterations were seen in 84% of LGG/germinale/nerve tumors, with KIAA1540-BRAF fusion seen exclusively in pilocytic astrocytoma and BRAF(V600E alterations seen in diffuse LGG (75%), PINTY and PAXA. Frequent alterations seen in HGG included H3F3A-K27M, H3F3A-G34, BRAFV600E alterations seen in diffuse LGG (75%), PLNTY and PAXA. Frequent alterations seen in HGG included H3F3A-K27M, H3F3A-G34, BRAFV600E alterations seen in diffuse LGG (75%), PINTY and PAXA. Frequent alterations seen in HGG included H3F3A-K27M, H3F3A-G34, BRAFV600E alterations seen in diffuse LGG (75%), PINTY and PAXA.
fusions and p53 protein showed characteristic cyttoplasmic positivity; Patient 3 presented a new ALK-QKI fusion kinase combined with ALK mutation and focal SMARCB1 deletion. All these 3 cases received corresponding targeted therapies and have a good recovery and normal neurologic function till now. METHOD: Immunohistochemistry, fluorescent in situ hybridization and whole-transcriptome sequencing. RESULTS: Case 18 months, male, left parietal occipital lobe. Histopathology: Gliosarcoma. IHC: EML4-ALK (3+); BRAF (1+); TERT (1+); P53 (2+); MGMT (1+); Olig2(1+); MGMT (1+); CD56 (1+); Syn (1+); NSE (1+); IHC in classification algorithms significantly improves outcome prediction and risk-stratification for Group 3/4 medulloblastoma. PATIENTS and METHODS: We retrospectively evaluated published medulloblastoma transcriptomes and proteomes identifying as a potential biomarker TPD52 whose IHC prognostic value was validated across three Group 3/4 medulloblastoma clinical cohorts (n = 387) treated with conventional therapies. Risk stratification and prediction capability were computed utilizing uni- and multivariate survival analysis. Newly developed risk classifiers including TPD52 IHC were compared to state-of-the-art risk stratification schemes in terms of prediction error, area under the time-dependent receiver operating characteristic (ROC) curves and C-statistic. RESULTS: TPD52 IHC percentage positivity represents a significant independent predictor of early relapse and 5-year survival in medulloblastoma (HRs between 3.67-26.9 [95% CIs between 1.00-706.23], p = 0.05, 0.017 and 0.0038). Cross-validated survival models incorporating TPD52 IHC with clinical and molecular features (subgroup affiliation, MYC status, TERT-p15 silencing) outperformed existing risk-stratification schemes. TPD52 IHC was expressed in ~60% of patients with high-risk for Group 3/4 medulloblastoma. However, very few clinical centers have implemented TPD52 IHC as a routinely used immunohistochemistry (IHC) marker as a clinically tractable method for improvement of medulloblastoma risk-stratification. CONCLUSION: The current study adds an important asset to improve risk-stratification for Group 3/4 medulloblastoma. Integration of TPD52 IHC in classification algorithms significantly improves outcome prediction and can be clinically adopted for risk stratification on a global scale independent of advanced but technically challenging molecular profiling techniques.

Abstracts

B60: USING DNA METHYLATION PROFILING TO DEFINE TUMOR TYPE AND APPROPRIATE TREATMENT: A CASE REPORT AND REVIEW OF THE LITERATURE OF A RARE CNS CIC ALTERED SARCOMA

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The utilization of methylation profiling is increasingly becoming part of the standard evaluation for high-grade malignancies. CNS primary tumors with CIC alteration are a recently described tumor entity identified via DNA methylation profiling of primitive neuroectodermal tumors (PNET). PNETs have historically carried a poor overall prognosis; however, CNS tumors with CIC alteration have rarely been described in the literature which remains to be discussed regarding the presentation, tumor characteristics, outcomes, and ideal treatment strategy to optimize survival in these patients. We describe the case of a 2-year-old Hispanic female with a CNS primary tumor with CIC alteration. This patient initially presented with a five-week history of fatigue, headaches, and focal SMARCB1 deletion. All these 3 cases received corresponding targeted therapies and have a good recovery and normal neurologic function till now.

PATH-02

PATH-03

PATH-04

PATH-04. ARRAY-BASED GLOBAL DNA METHYLATION PROFILING OF MOUSE BRAIN TUMORS ALLOWS COMPARISON TO HUMAN TUMORS

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BACKGROUND: International consensus and the 2021 WHO classification of tumors of the CNS recognize eight molecular subgroups among Group 3/4 medulloblastoma (representing ~60% of medulloblastoma). However, very few clinical centers worldwide possess the technical capabilities to define DNA-methylation patterns or other molecular parameters of high-risk for Group 3/4 tumors. As a result, biomarker-driven risk stratification and therapy assignment constitutes a major challenge in medulloblastoma research. Here, we identify a unique immunohistochemistry (IHC) marker as a clinically tractable method for improved medulloblastoma risk-stratification. PATIENTS and METHODS: We bioinformatically analyzed published medulloblastoma transcriptomes and proteomes identifying as a potential biomarker TPD52, whose IHC prognostic value was validated across three Group 3/4 medulloblastoma clinical cohorts (n = 387) treated with conventional therapies. Risk stratification and prediction capability were computed utilizing uni- and multivariate survival analysis. Newly developed risk classifiers including TPD52 IHC were compared to state-of-the-art risk stratification schemes in terms of prediction error, area under the time-dependent receiver operating characteristic (ROC) curves and C-statistic. RESULTS: TPD52 IHC percentage positivity represents a significant independent predictor of early relapse and 5-year survival in medulloblastoma (HRs between 3.67-26.9 [95% CIs between 1.00-706.23], p = 0.05, 0.017 and 0.0038). Cross-validated survival models incorporating TPD52 IHC with clinical and molecular features (subgroup affiliation, MYC status, TERT-p15 silencing) outperformed existing risk-stratification schemes. TPD52 IHC was expressed in ~60% of patients with high-risk for Group 3/4 medulloblastoma. However, very few clinical centers have implemented TPD52 IHC as a routinely used IHC marker as a clinically tractable method for improvement of medulloblastoma risk-stratification. CONCLUSION: The current study adds an important asset to improve risk-stratification for Group 3/4 medulloblastoma. Integration of TPD52 IHC in classification algorithms significantly improves outcome prediction and can be clinically adopted for risk stratification on a global scale independent of advanced but technically challenging molecular profiling techniques.

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