formed against Gnomad3.1 (without cancer samples) using Fisher's exact test with Bonferroni adjustment. We observed 214 P-LP variants involving 190 unique individuals (21.6% of cohort). As expected, the most frequent variants were observed in *NF1, NF2,* and *TP53*(n=40 variants in 21% of individuals). *ATM*, *TSC2* and *CHEK2* variants (n=23) were observed in another 12% of individuals. An increased burden of P-LP variants was observed for 5 of these 6 genes ($p = 1.7x10^{-25}$ to $1.4x10^{-2}$, *CHEK2* $p=5.5x10^{-2}$). We also identified 5 variants in *BRCA2* (3 in high-grade glioma), 7 in REQC helicases (*BLM*, *WRN*, *REQL4*), and 16 variants in Fanconi anemia genes. Overall, cases harbored increased burden in P-LP variants in CPG genes ($p=8.8x^{-18}$) and the subset of DNA repair genes ($p=4.7x10^{-4}$). In conclusion we confirmed the association of variants in established predisposition genes while potentially identifying novel variants and genes associated in CNS tumors.

OMIC-13. THE ROLE OF COPY NUMBER ALTERATIONS IN PREDICTING SURVIVAL AND INFLUENCING TREATMENT OF CHILDHOOD BRAIN TUMORS

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Brain and central nervous system tumors are the most common form of solid tumor cancers and the second most common cancer overall among children. While many advances have been made in understanding the genomics of childhood brain tumors in recent years, the role of copy number alterations (CNAs) has not been fully characterized. Although the genomes of childhood brain tumor patients are generally considered to be relatively stable diploid genomes, analysis of a subset of pretreatment diagnostic samples from a cohort of 84 deceased patients from Washington University revealed widespread alterations, suggesting CNAs may play a larger role in the progression and prognosis of childhood brain tumors than originally thought. Follow up analysis of the entire cohort, containing a variety of tumor types that had low-pass whole genome sequencing performed, similarly showed evidence of CNAs across samples. 75 out 84 patients showed the presence of CNAs with an average of 16% of the genome being altered per sample and a median of 7%. Preliminary results examining correlations between the percentage of the genome that was copy number altered and event free survival or overall survival indicated that CNA percentage may have some prognostic value. For example, ependymoma samples showed positive correlation between alteration percentage and overall survival, while glioblastoma samples showed negative correlation. To explore copy number alteration in a larger cohort and increase statistical power, similar analyses are being performed using an additional 950 samples from the Pediatric Brain Tumor Atlas curated by The Children's Brain Tumor Network (CBTN) to determine if CNVs and CNV percentage or specific alterations can serve as prognostic markers and whether the biology of this genomic instability could inform therapeutic strategy.

OMIC-14. OPENPBTA: AN OPEN PEDIATRIC BRAIN TUMOR ATLAS

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Pediatric brain tumors comprise a heterogeneous molecular and histological landscape that challenges most current precision-medicine approaches. While recent large-scale efforts to molecularly characterize distinct histological entities have dramatically advanced the field's capacity to classify and further define molecular subtypes, developing therapeutic and less toxic molecularly-defined clinical approaches remains a challenge. To define new approaches to meet these challenges and advance scalable, shared biospecimen- and data-resources for pediatric brain tumors, the Children's Brain Tumor Network and Pacific Pediatric Neuro-Oncology Consortium, in partnership with the Alex's Lemonade Stand Foundation Childhood Cancer Data Lab, launched OpenPBTA, a global open science Pediatric Brain Tumor Atlas initiative to comprehensively define the molecular landscape of pediatric brain tumors. The initiative contains multi-modal analyses of research- and clinical-trial based DNA and RNA sequences from nearly 1,000 subjects (with 1,256 tumors) along with their longitudinal clinical data. The OpenPBTA's open science framework for analysis tests the capacity of crowd-sourced collaborative architectures to advance more rapid, iterative and integrated discovery of the underlying mechanisms of disease across pediatric brain and spinal cord tumors. Since the launch of the project, OpenPBTA has collaboratively created reproducible workflows for integrated consensus SNV, CNV, and fusion calling, enabled RNA-Seq-based classification of medulloblastoma subtypes, and more than 25 additional DNA- and RNA-based analyses. The open-science platform and associated datasets and processed results provide a continuously updated, global view of the integrated cross-disease molecular landscape of pediatric brain tumors. Such biospecimen- and clinically-linked scalable data resources provide unprecedented collaborative opportunities for precision-based, personalized therapeutic discovery and drug development with the upcoming further integration of proteomic sample data (N >300) and drug response datasets, additionally diversifying the multimodal discovery potential of crowd-sourced approaches for accelerated impact for children with brain tumors.

RARE TUMORS/OTHER

RARE-01. ASSESSING THE SYMPTOM DIAGNOSTIC INTERVAL FOR CHILDREN WITH CENTRAL NERVOUS SYSTEM TUMOURS

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Background: Diagnostic delays in pediatric neuro-oncology is a subject of distress for families and providers. We aimed to evaluate the symptom diagnostic interval (SDI) and influencing variables for children with CNS tumors. Methods: This retrospective study analyzed 210 patients diagnosed from 2001–2018 and managed at the tertiary care facility in Halifax, Canada. SDI was defined as time from first symptom until tissue diagnosis or, if not available, imaging diagnosis. Non-parametric tests were used to compare SDI between groups. Results: Median SDI was 12.4 weeks (IQR 4.3–30), longer than 7 other studies of 1308 children reporting medians of 4.5–10 weeks ($p < 0.01$). Most common tumors and their median SDI included low-grade glioma (LGG) (n=97, 46%; 17.9 weeks), medulloblastoma (n=31, 15%; 8.7 weeks), high-grade glioma (HGG) and DIPG (n=23, 11%; 5.6 weeks), and ependymoma (n=13, 6%; 13.6 weeks). The most common initial reported symptom included headache (n=63; 30%), nausea/vomiting (n=27, 18%), seizure (n=24, 12%), and visual impairment (n=13, 6.3%). Patients aged 0–3 years had a shorter SDI than patients 10 years and older (SDI 8.7 vs 14.6 weeks; $p = 0.03$). Tumor category showed longer SDI for LGG versus HGG ($p = 0.003$), DIPG ($p = 0.02$), medulloblastoma ($p = 0.03$) and other embryonal tumors ($p = 0.03$). Longer SDI was not associated with increased risk of disease progression for LGG ($p = 0.93$), medulloblastoma ($p = 0.89$), or ependymoma ($p = 0.5$). No difference in SDI was found with regard to diagnosis era, ethnicity, socioeconomic status, or distance to the tertiary care facility. Conclusion: SDI at our centre is longer than previously reported studies. SDI is linked to tumor biology and its relevance within specific tumor groups deserves further investigation given it doesn't appear to predict tumor progression/recurrence, yet families and providers feel distress when delays in diagnosis are perceived.

RARE-02. POLYAMINE PATHWAY INHIBITION IS A POTENT NOVEL THERAPEUTIC STRATEGY AGAINST DIFFUSE INTRINSIC PONTINE GLIOMA

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Diffuse intrinsic pontine glioma (DIPG) is an aggressive paediatric brainstem tumour, with a median survival of less than 1 year. Polyamines are intracellular polycations that control important aspects of cell growth and are often upregulated in cancer. Difluoromethylornithine (DFMO) is an FDA-approved inhibitor of the enzyme ornithine decarboxylase (ODC1) which is a key driver of polyamine synthesis. We investigated the efficacy of polyamine pathway inhibitors as a therapeutic strategy against DIPG.