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Addressing family needs for social/emotional support is part of the duty of oncology care teams. This research presents a (2020) scoping review and a (2019) focus group initiated to explore pediatric neuro-oncology parent experience of social/emotional support in conjunction with developing an online peer application to address family needs. Currently, the value of online support is in the forefront of clinical conversation. The focus group queried eight parents whose children were under neuro-oncology treatment in the Northwest USA. Thematic findings include—parents want supportive peers who have (1) a personal and deep understanding of parenting a child with serious illness (they "get it"); (2) particular characteristics and skills that promote and sustain relationships, including—(a) good social skills, (b) ability to engage in "balanced" (cancer/non-cancer) conversations, (c) individual similarities (beliefs, age of children, cancer diagnosis/treatment), (d) logistic commonalities (location, availability), (e) pro-social personal characteristics (i.e. sense of humor, emotional/social flexibility), and an (f) ability to navigate and maintain social/emotional boundaries. Parents also initiated discussion about "the burden of supportive relationships" and supporting families doing "normal" activities without worrying about treatment side effects and contagions. The literature review supports finding (1) above; reveals the paucity of evidence-based supports available to this population; underscores the critical need for practitioners and researchers to develop more evidence-based supports and interventions for families of children experiencing cancer; and supports practitioners' consistently assessing parent and sibling social and emotional needs and then consistently referring or intervening when needs are identified.

TUMOR BIOLOGY (NOT FITTING A SPECIFIC DISEASE CATEGORY)

TBIO-01. SEX DIFFERENCES IN REDOX STATE UNDERLIE GLUTAMINE DEPENDENCY IN MALE GLIOBLASTOMA

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Glioblastoma (GBM) is an aggressive brain tumor in children and adults. It occurs more commonly in males, but female patients survive significantly longer. Understanding the molecular mechanisms that underlie those sex differences could support novel treatment strategies. In this regard, we found that male and female GBM patient samples differ in their metabolite abundance and that males exhibit a significantly higher abundance of amino acid metabolites. We confirmed those findings in a murine model of GBM, which has previously yielded important insights into sexual dimorphism in GBM. Furthermore, we found that male GBM cell cultures are significantly more sensitive to amino acid deprivation, which was almost entirely driven by amino acids involved in the synthesis of the antioxidant glutathione. Glutaminase 1 (GLS1) mediates the conversion from glutamine to glutamate, a crucial component of glutathione. We found that male GBM cells exhibited higher levels of GLS1, suggesting they are more dependent on glutamate. Indeed, we found that male GBM cells are more sensitive to pharmacological GLS1 inhibition with the clinical inhibitor CB-839. This correlated with significantly increased reactive oxygen species (ROS) in males compared to females. We further confirmed sex differences in redox state through pharmacological depletion of glutathione that resulted in a significant increase in ROS and cell death in male GBM. Together, these data indicate that male GBM cells are more dependent on glutamine to regulate ROS levels. This reveals novel sex-specific metabolic targets for GBM and underlines the importance of considering sex in metabolic targeting approaches.

TBIO-02. IMMUNE PROFILING OF RARE EMBRYONAL BRAIN TUMORS REVEAL EVIDENCE OF DYSREGULATED INTERFERON SIGNALLING AS A POTENTIAL DETERMINANT OF IMMUNOLOGICAL HETEROGENEITY

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Embryonal brain tumors (EBTs) remain the most common malignant pediatric brain tumors. Despite recent advances and improved understanding of the molecular biology of EBTs, clinical outcomes remain poor for rare EBTs. Previous large-scale genomic studies of rare EBTs have shed light on distinct genomic, transcriptomic and epigenomic profiles. Interestingly, these studies have revealed prominent tumor heterogeneity that provides opportunity to develop novel treatment strategies to improve patient outcomes. To examine the tumor microenvironment and identify tumor- specific biological dependencies, we performed deconvolution analysis of bulk gene expression (171 RNA-seq, 236 microarrays) and 586 methylation arrays, which revealed significant intra and inter-tumoral heterogeneity and implicated interferon (IFN)-mediated signalling as a determinant of a distinct immunological profile in rare EBTs. To further elucidate the importance of IFN signalling, we performed scRNA-seq on 20 primary samples, which provided evidence of a spectrum of IFN-immunological responses that vary from immunosuppressive to immunologically exhaustive that occur in a host dependent manner. To further validate our findings, we utilised a genetically engineered murine model of Atypical Teratoid Rhabdoid Tumor and primary xenografts in humanised mice to corroborate our in-silico profiles in vivo. Through amalgamation of our in-silico data with our in vivo data, we have identified evidence that dysregulated IFN responses represent a core element of the immunological heterogeneity present within subsets of rare EBTs. An improved understanding of the immune milieu in rare EBTs will provide avenues to develop specific onco-immune targets to address this clinical need.

TBIO-03. THE GIFT FROM A CHILD PROGRAM IS EMPOWERING POST-MORTEM TISSUE DONATION ACROSS THE UNITED STATES

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The Gift from a Child (GFAC) program was inspired by the dream of one child to donate his brain for research, recognizing the need to study tumor tissue collected at diagnosis, recurrence, and at the time of death. Founded by the Swifty Foundation in 2016, GFAC currently is comprised of five "Centers of Excellence" at institutions with expertise in pediatric neuro-oncology. Partnering with the Children's Brain Tumor Network, the program's mandate is twofold: make it possible for families to donate no matter where they live in the United States and make tissue available to scientists globally to empower discovery. In order to overcome barriers that have stifled postmortem collection in the past, GFAC has invested in Tissue Navigators - individuals at each center who coordinate all aspects of donation and communicate with families, medical providers, and laboratory scientists. In 2019 alone, GFAC coordinated 55 autopsy collections from multiple diagnosis. A key metric of the program is also capturing the global sharing and usage of each tissue sample, ensuring that tissue isn't simply "banked" but is actively being actively used to help unravel tumor biology. To date, tissue has been used for genomic and molecular data generation, preclinical model development including cell lines and PDX models, and for novel drug screening. Together with Children's Brain Tumor Network, the Gift from a Child program is helping to ensure the most precious gift that a family can make is used to accelerate the path to cures.

TBIO-05. GENOME-SCALE NUCLEOTIDE-SPECIFIC CHARACTERIZATION OF 5-HYDROXYMETHYLCYTOSINE IN PEDIATRIC CENTRAL NERVOUS SYSTEM TUMORS

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Though aberrant cytosine modifications are prevalent in cancer, nucleotide-specific 5-hydroxymethylcytosine (5hmC) modifications remain understudied, including in pediatric CNS tumors. Brain 5-hydroxymethylation is linked with development and differentiation. We measured genome-scale nucleotide-specific 5hmC in patients with diagnoses of glioma, ependymoma, and embryonal tumors under age 18 (n=36), and in non-tumor pediatric brain tissues (n=3). DNA was processed with tandem oxidative (OxBS) and bisulfite (BS) treatments followed by hybridization to the Illumina Methylation EPIC Array that interrogates over 860,000 CpG sites. We used the OxyBS R package to determine levels of 5hmC and 5mC. Mean 5hmC levels were lower in tumors (gliomas 4.1%, ependymomas 3.9%, and embryonal