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Abstracts

ABSTRACTS CATEGORY CODES

ATRT – ATYPICAL TERATOID/RHABDOID TUMORS
COVD - COVID-19 AND PEDIATRIC NEURO-ONCOLOGY
DIPG - DIFFUSE MIDLINE GLIOMA/DIPG
DDEL - DRUG DELIVERY/PHARMACOKINETICS
EPCT - EARLY PHASE CLINICAL TRIALS
EPEN - EPENDYMOMA
EPID - EPIDEMIOLOGY
ETMR - ETMR AND OTHER EMBRYONAL TUMORS
GCT - GERM CELL TUMORS
HGG - HIGH GRADE GLIOMA
IMG - IMAGING
IMMU – IMMUNOTHERAPY
LINC - PEDIATRIC NEURO-ONCOLOGY IN ASIA AND OTHER LOW/MIDDLE INCOME COUNTRIES
LGG - LOW GRADE GLIOMA
MBCL - MEDULLOBLASTOMA (CLINICAL)
MBRS - MEDULLOBLASTOMA (RESEARCH)
MODL - PRECLINICAL MODELS/EXPERIMENTAL THERAPY/ DRUG DISCOVERY
NFB - NEUROFIBROMATOSIS AND OTHER PREDISPOSITION SYNDROMES
NURS – NURSING/PATIENT CARE
OTHR - OTHERS (NOT FITTING ANY OTHER CATEGORY)
PATH - PATHOLOGY/CLASSIFICATION
QOL - NEUROPSYCHOLOGY/QUALITY OF LIFE
RARE - CRANIOPHARYNGIOMA AND RARE TUMORS
RONC - RADIATION ONCOLOGY
SURG - NEUROSURGERY
SWK - SOCIAL WORK/PATIENT SUPPORT/PALLIATIVE CARE
TBIO - TUMOR BIOLOGY (NOT FITTING A SPECIFIC DISEASE CATEGORY)
THER - VIRAL/GENE THERAPY AND OTHER NOVEL THERAPIES

ATYPICAL TERATOID/RHABDOID TUMORS (ATRT)

ATRT-01. UPREGULATION OF PROTEIN SYNTHESIS AND PROTEASOME DEGRADATION CONFERS SENSITIVITY TO PROTEASOME INHIBITOR BORTEZOMIB IN MYC-ATYPICAL TERATOID/RHABDOID TUMORS

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BACKGROUND: Atypical teratoid rhabdoid tumors (ATRTs) are among the most malignant brain tumors in early childhood and remain incurable. Myc-ATRT is driven by the *Myc* oncogene, which directly controls the intracellular protein synthesis rate. Proteasome inhibitor bortezomib (BTZ) was approved by the Food and Drug Administration as a primary treatment for multiple myeloma. This study aimed to determine whether the upregulation of protein synthesis and proteasome degradation in Myc-ATRTs increases tumor cell sensitivity to BTZ. METHODS: We performed differential gene expression and gene set enrichment analysis on matched primary and recurrent patient-derived xenograft (PDX) samples from an infant with ATRT. The expressions of proteasome-encoding genes were compared among this paired model as well as between the 24 human ATRT samples and normal brain tissues. The antitumor effect of BTZ was evaluated in three human Myc-ATRT cell lines (PDX-derived tumor cell line Re1-P6, BT-12, and CHLA-266) and in the orthotopic xenograft models of Re1-P6 cell. RESULTS: Concomitant upregulation of the Myc pathway, protein synthesis, and proteasome degradation were identified in recurrent ATRTs. In ATRTs, the proteasome-encoding genes were highly expressed compared with in normal brain tissues, correlated with the malignancy of tumor cells, and were essential for tumor cell survival. BTZ inhibited proliferation and induced apoptosis through the accumulation of p53 in *in vitro* drug tests. Furthermore, BTZ inhibited tumor growth and prolonged survival in Myc-ATRT orthotopic xenograft mice. CONCLUSIONS: Our findings suggest that BTZ may be a promising targeted therapy for Myc-ATRTs.

ATRT-02. MEK/ERK SIGNALLING DEPENDENCY IN ATYPICAL TERATOID RHABDOID TUMOURS

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Atypical teratoid rhabdoid tumours (ATRTs) are high-grade malignant paediatric brain tumours with a less than one-year survival rate after diagnosis. Current treatment for ATRT, which includes high-intensive radiotherapy and chemotherapy, results in long-term side effects on ATRT patients. Hence, there is an urgent need to discover targeted therapies that could be used to treat patients with ATRT. As part of the Hudson Monash Paediatric Precision Medicine Program, we have collected 23 ATRT cell lines which we used to performed high-throughput small molecule and genetic (CRISPR) screening to identify new therapies and therapeutic targets. In parallel, we characterised the ATRT cell lines based on transcriptomic (RNA-seq) and epigenetic (methylation) signatures. An integrative multi-omic approach was then used to uncover discrete vulnerabilities in specific subsets of ATRT patients. Strikingly, these include a number of druggable dependencies, such as MEK, CDK, HDAC, and Topoisomerase, that offer a promise of rapid clinical translation. In our study, we focus on MEK dependency in a subtype of ATRT lines to further define the underlying mechanisms and biomarkers. While future studies validating the MEK/ERK signalling dependency in a wider cohort of patient models and in *in vivo* models are required, these data provide a framework for applying an integrative multi-omic approach in paediatric cancer precision medicine.

ATRT-03. IDENTIFICATION OF MICRORNA-BASED PROGNOSTIC BIOMARKERS AND CANDIDATE THERAPEUTIC AGENTS FOR ATYPICAL TERATOID/RHABDOID TUMOR

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BACKGROUND: MicroRNA (miRNA) has been found to be involved in development of many malignant pediatric brain tumors, including atypical teratoid/rhabdoid tumor (AT/RT) that is highly aggressive and carries a dismal prognosis. The current study investigated the potential value of miRNAs and pivotal genes associated with AT/RT using bioinformatics analysis, aiming to identify new prognostic biomarkers and candidate drugs for AT/RT patients. METHODS: Differentially expressed miRNAs (DEMs) and genes (DEGs) between AT/RT and normal control samples were obtained from GEO database. The target genes of DEMs were predicted via TargetScanHuman7.2 and miRDB, and then intersected with DEGs. Gene Ontology and Kyoto Encyclopedia of Genes and Genomes analyses of overlapping genes were conducted, followed by construction of protein-protein interaction network. Hub genes were determined by Cytoscape