

these cases for PBT versus intensity-modulated radiation therapy, characterized the cyst evolution during treatment in 3 dimensions, and define an optimized protocol for treatment planning and intra-treatment monitoring.

#### RARE-07. THE LANDSCAPE OF GENOMIC ALTERATIONS IN ADAMANTINOMATOUS CRANIOPHARYNGIOMAS

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**INTRODUCTION:** Adamantinomatous craniopharyngiomas (ACPs) are characterized by activating mutations in the *CTNNB1* gene. Here we perform a comprehensive genomic analysis of 23 ACPs to define the landscape of genomic alterations in this disease. **METHODS:** We performed whole-genome sequencing of 24 ACPs and their matched normal tissues. We used Mutect 2.0 to detect mutations and indels in these samples and MutSig2CV to identify significant mutations. Copy numbers were called using the GATK4 pipeline and GISTIC 2.0 was applied to identify significant alterations. Finally, SvABA was applied to identify genome-wide structural variants and rearrangements. **RESULTS:** 18/24 (75%) of the sequenced ACPs harbored activating mutations in exon 3 of *CTNNB1* gene with an average variant allele fraction (VAF) of 0.4±0.1. These mutations have previously been shown to activate the WNT signaling pathway in these tumors. No other significantly recurrent mutations were detected in our samples. The ACPs were quiet with regard to copy number alterations and no recurrent amplifications or deletions were detected. 528 structural variations and rearrangements were detected in total in all 24 samples with an average of 22 variants per sample. Gene-Set Enrichment Analysis (GSEA) of the RNAseq data revealed upregulation of WNT/β-catenin (FDR q-value <0.25) in the *CTNNB1* mutant samples compared to *CTNNB1* WT samples. **CONCLUSION:** Our study identified previously described activating *CTNNB1* mutations in the majority of ACPs. In addition, we identified several rearrangements and structural variations in these tumors that could play an important role in the pathogenesis of the disease.

#### RARE-08. CYST FLUID CYTOKINES MAY PROMOTE EPITHELIAL-TO-MESENCHYMAL TRANSITION IN PEDIATRIC ADAMANTINOMATOUS CRANIOPHARYNGIOMA

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**BACKGROUND:** Despite poor clinical outcomes, no targeted therapies have been established for the treatment of Adamantinomatous Craniopharyngioma (ACP). The only known genetic aberration is a mutation in *CTNNB1* that results in the nuclear accumulation of beta-catenin. Nuclear beta-catenin is an established inducer of Epithelial-to-Mesenchymal Transition (EMT). ACP cyst fluid is enriched with pro-inflammatory and SASP cytokines, many of which are also directly implicated in EMT. We sought to investigate the role of EMT in ACP pathology. **METHODS:** Normal human epithelial cells were cultured and treated with ACP cyst fluid (10%) for 1, 2, 4 and 8 days. Cell morphology was monitored by live cell brightfield microscopy. The expression of EMT associated genes, ZEB1, ZEB2, SNAI-1, SLUG, TWIST, E-Cadherin, Beta-Catenin and Vimentin was determined by RT-qPCR. **RESULTS:** ACP cyst fluid treated epithelial cells were markedly transformed into long, spindle-shaped cells. ACP cyst fluid treatment resulted in the progressive up-regulation of ZEB2 over 8 days (RQ=12.0; P<0.01), the progressive up-regulation of SNAI-1 over 4 days (RQ=5.1; P<0.05) and up-regulation of Vimentin (RQ=2.2; p<0.01), identified only on Day 8. **CONCLUSION:** ACP cyst fluid can induce EMT-like changes in normal human epithelial cells. In conjunction with the frequency of beta-catenin mutation in ACP, it is possible that EMT plays a crucial role in the pathology of ACP. Understanding ACP pathology in the context of the EMT paradigm may aid the development of new targeted therapeutics.

#### RARE-09. PRESERVATION OF ENDOCRINE FUNCTION AFTER OMMAYA RESERVOIR INSERTION IN CHILDREN WITH CYSTIC CRANIOPHARYNGIOMA

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**INTRODUCTION:** Children with craniopharyngiomas (CP) can be subjected to significant morbidities caused by radical surgery and/or radiation with severe long-term consequences. Ommaya reservoir Insertion (ORI) into cystic CP represents a minimally invasive procedure that aims to preserve endocrine, hypothalamic and neurocognitive function. The purpose of this study was to determine the relevance of upfront ORI (+/- intracystic treatment) for preservation of endocrine function. **METHODS:** A retrospective chart review of children with CP treated at the Hospital for Sick Children between 01/01/2000 and 15/01/2020 was undertaken. Endocrine function was reviewed at the time of initial ORI or surgical resection and throughout the course of follow-up. Event free survival (EFS) was defined as the time to additional surgical resection or irradiation. **RESULTS:** Fifty-five patients with sufficient endocrine follow-up data were included. The median age of diagnosis was 8.3 years (range 2.1–18.0 years), 31 were males. ORI was performed as upfront treatment in 30 patients, gross total or partial resection in 24 patients and radiation in 1 patient, respectively. Endocrine function remained stable after ORI with a median EFS of 19.2 (0 – 105.3) months while the majority of patients who underwent surgical resection had documented worsened endocrine function postoperatively (median of 0; range 0 – 29.4 months) (p< 0.001). The event most commonly related to secondary endocrine deterioration was initial or delayed surgical resection. **CONCLUSIONS:** Endocrine function was preserved in patients with upfront ORI (+/- intracystic treatment). Further studies will elucidate the implications of ORI with respect to ophthalmological, vascular and neurocognitive long-term outcome.

#### RARE-10. ADAMANTINOMATOUS CRANIOPHARYNGIOMA RESIDES OUTSIDE THE BLOOD BRAIN BARRIER

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**BACKGROUND:** Adamantinomatous craniopharyngioma (ACP) is a devastating skull-base tumor believed to derive from epithelial remnants of the primordial craniopharyngeal duct (Rathke's pouch), which gives rise to the anterior pituitary gland. Genetically engineered mouse models of ACP demonstrate that perturbation of the fetal anterior pituitary can generate tumors analogous to ACP. Clinical and preclinical data indicate that IL-6 blockade may contribute to ACP tumor control, with the most common agent being the humanized monoclonal antibody, tocilizumab. This agent demonstrated poor blood-brain barrier (BBB) penetration in primates. We present findings from two children enrolled on a phase 0 clinical trial (NCT03970226) of a single dose of preoperative intravenous tocilizumab prior to resection of newly diagnosed ACP. **METHODS:** Blood samples were obtained at multiple timepoints. Serum was isolated via ficoll separation. Tumor tissue and cyst fluid were obtained 4–6 hours following the single IV dose of tocilizumab. Tissue was snap-frozen. Tumor was homogenized in RIPA buffer. Free tocilizumab in serum, cyst fluid, and tumor tissue was measured using enzyme-linked immunosorbent assay (ELISA) against a standard curve. **RESULTS:** Both patients in this trial demonstrated clinically relevant levels of tocilizumab (≥ 4µg/mL) in serum, cyst fluid, and tumor tissue, compared to undetectable levels in control samples. **CONCLUSION:** ACP resides outside BBB protection. In addition to demonstrating the feasibility of systemic delivery of tocilizumab, these findings indicate that other large molecules, including those known to have poor BBB penetration, may be systemically delivered as part of an antitumor regimen in the treatment of ACP.

#### RARE-11. QUANTITATIVE MR IMAGING FEATURES ASSOCIATED WITH UNIQUE TRANSCRIPTIONAL CHARACTERISTICS IN PEDIATRIC ADAMANTINOMATOUS CRANIOPHARYNGIOMA: A POTENTIAL GUIDE FOR THERAPY

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