associated with ciliogenesis. Next, we will spatially dissect the correlation between EZHIP and ependymal-like genes in primary and recurrent PFA and investigate DNA methylation, histone marks and EZHIP binding at these gene loci. CONCLUSION: Overall, our data indicate that ependymal-like cell differentiation is deregulated by EZHIP particularly in progressive PF-A ependymoma.

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EPEN-12. EZHIP IMPACTS CELLULAR DIFFERENTIATION IN POSTERIOR FOSSA GROUP A EPENDYMOMA
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BACKGROUND: High-risk ependymomas are central nervous system tumors comprising ten molecular groups with posterior fossa group A (PFA) and supratentorial ependymoma with zinc finger translocation associated (ST-ZFTA) fusions being among the most aggressive subgroups in children. Loss of H3K27 trimethylation maintained by Enhancer of Zeste homologs Inhibitory Protein (EZHIP) overexpression in PFA or ZFTA-RELA oncocfusions in ST-ZFTA ependymoma are known as important driver events. Additionally, we uncovered that high-risk ependymomas arise from undifferentiated cell populations, while more differentiated ependymal-like signatures (e.g. ciliogenic programs) are enriched in prognostically favourable subtypes. METHODS: We investigated presence of “ependymal-like” signatures by analysing mRNA expression of selected genes (RSPH1, DNAAF1, SLCA7A2, CAPS, CAPS-L) in ependymoma bulk samples (n=90). Gene expression was correlated to clinicopathological characteristics (EZHIP expression, 1q-gain/6q-loss, DNA methylation subtype). Impact on mRNA levels of ependymal-like markers was investigated upon an inducible EZHIP knockdown using lentiviral vectors in EPD210FH PFA cells. RESULTS: Ependymal-like markers were significantly lower expressed in ST-ZFTA as compared to spinal and PFB ependymoma. In PFA ependymoma two distinct groups showing either low or high expression of these ependymal-like genes were present. In detail, “ependymal-like-high” PFA were assigned to the PFA-2 subtype which was also confirmed in an independent cohort. EZHIP was strongly negative prognostic in our cohort and the expression was distinctly induced during PFA progression accompanied by increased ependymal-like signature genes. This suggests an impact of EZHIP on cell differentiation processes particularly during PFA progression. Knock-down of EZHIP in EPD210FH PFA cells increased expression of ependymal signature genes