C17orf96

Chromosome 17 Open Reading Frame 96

Uncharacterized Protein C17orf96

The PFA molecular subgroup of posterior fossa ependymomas (PF-EPNs) shows poor outcomes. H3K27me3 (me3) loss by immunohistochemistry (IHC) is a surrogate marker for PFA wherein its loss is attributed to overexpression of Cxorf67/EZH2 inhibitory protein (EZHIP), C17orf96, and ATRX loss. Nambirajan et al. aimed to subgroup PF-EPNs using me3 IHC and study correlations of the molecular subgroups with other histone-related proteins, 1q gain, Tenascin C, and outcome. IHC for me3, acetyl-H3K27, H3K27M, ATRX, EZH2, EZHIP, C17orf96, Tenascin-C, and fluorescence in-situ hybridization for chromosome 1q25 locus were performed on an ambispective PF-EPN cohort (2003-2019). H3K27M-mutant gliomas were included for comparison. Among 69 patients, PFA (me3 loss) constituted 64%. EZHIP overexpression and 1q gain were exclusive to PFA seen in 72% and 19%, respectively. Tenascin C was more frequently positive in PFA (p = 0.02). H3K27M expression and ATRX loss were noted in one case of PFA-EPN each. All H3K27M-mutant gliomas (n = 8) and PFA-EPN (n = 1) were EZHIP negative. C17orf96 and acetyl-H3K27 expression did not correlate with me3 loss. H3K27me3 is a robust surrogate for PF-EPN molecular subgrouping. EZHIP overexpression was exclusive to PFA EPNs and was characteristically absent in Diffuse midline glioma H3 K27M-mutants and the rare PFA harboring H3K27M mutations representing mutually exclusive pathways leading to me3 loss [1)].

1)
Nambirajan A, Sharma A, Rajeshwari M, Boorgula MT, Doddamani R, Garg A, Suri V, Sarkar C, Sharma MC. EZH2 inhibitory protein (EZHIP/Cxorf67) expression correlates strongly with H3K27me3 loss in posterior fossa ependymomas and is mutually exclusive with H3K27M mutations. Brain Tumor Pathol. 2020 Nov 1. doi: 10.1007/s10014-020-00385-9. Epub ahead of print. Erratum in: Brain Tumor Pathol. 2021 Jan 9;: PMID: 33130928.