Codon 132

Malignant gliomas have disproportionally high morbidity and mortality. Heterozygous mutations in the isocitrate dehydrogenase 1 (IDH1) gene are most common in glioma, resulting in predominantly arginine to histidine substitution at codon 132. Because IDH1 R132H requires a wild-type allele to produce (D)-2-hydroxyglutarate for epigenetic reprogramming, loss of IDH1R132H heterozygosity is associated with glioma progression in an IDH1-wildtype-like phenotype. Although previous studies have reported that transgenic IDH1R132H induces the expression of a nestin-a neural stem-cell marker, the underlying mechanism remains unclear. Furthermore, this finding seems at odds with a better outcome of IDH1R132H glioma because of a negative association of nestin with overall survival [1].

The WHO grade II diffuse astrocytomas and WHO grade III anaplastic astrocytomas are now each divided into IDH-mutant, IDH-wildtype, and NOS categories. For both grade II and III tumors, the great majority falls into the IDH-mutant category if IDH testing is available. If immunohistochemistry for mutant R132H IDH1 protein and sequencing for IDH1 codon 132 and IDH2 codon 172 gene mutations are both negative, or if sequencing for IDH1 codon 132 and IDH2 codon 172 gene mutations alone is negative, then the lesion can be diagnosed as IDH-wildtype. It is important to recognize, however, that diffuse astrocytoma, IDH-wildtype is an uncommon diagnosis and that such cases need to be carefully evaluated to avoid misdiagnosis of lower grade lesions such as gangliogliomas; moreover, anaplastic astrocytoma, IDH-wildtype is also rare, and most such tumors will feature genetic findings highly characteristic of IDH-wildtype glioblastoma.

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Tiburcio PDB, Locke MC, Bhaskara S, Chandrasekharan MB, Huang LE. The neural stem-cell marker CD24 is specifically upregulated in IDH-mutant glioma [published online ahead of print, 2020 Jul 1]. Transl Oncol. 2020;13(10):100819. doi:10.1016/j.tranon.2020.100819