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Histone H3.3G34-Mutant Interneuron Progenitors Co-opt *PDGFRA* for Gliomagenesis

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The paper explains a puzzling mutation in a particular subset of glioblastoma that spans children and adults (12 to 35 years of age). The research team assembled the largest collection of samples of this tumour-type and employed single-cell technologies to measure the levels of every gene in thousands of individual cells. They discovered new cancer-causing mutations in a gene called *PDGFRA*, which drives cell division and growth when it is activated, and showed in mouse models that it is a potent oncogene on its own. The researchers noted that close to half of the patients at diagnosis, and the vast majority at tumour recurrence, had mutations in this gene. Moreover, they revealed that the tumor originates in a specific type of neuronal stem cell and not, as previously supposed, in glial cells, and defined the mechanism linking the cell of origin with the oncogenic mutations.

The finding has therapeutic implications because *PDGFRA* is targetable by drugs that inhibit its activity, and there are, in fact, already approved drugs that target it for other cancers for which mutations in this gene are responsible, such as gastrointestinal stromal tumours. This offers hope for future work into finding targeted therapies for this particular group of deadly brain tumours.

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