Oncogenic signaling is dominant to cell of origin and dictates astrocytic or oligodendroglioblastoma tumor development from oligodendrocyte precursor cells.  

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Abstract  
Stem cells, believed to be the cellular origin of glioma, are able to generate gliomas, according to experimental studies. Here we investigated the potential and circumstances of more differentiated cells to generate glioma development. We and others have shown that oligodendrocyte precursor cells (OPCs) can also be the cell of origin for experimental oligodendroglial tumors. However, the question of whether OPCs have the capacity to initiate astrocytic gliomas remains unanswered. Astrocytic and oligodendroglial tumors represent the two most common groups of glioma and have been considered as distinct disease groups with putatively different origins. Here we show that mouse OPCs can give rise to both types of glioma given the right circumstances. We analyzed tumors induced by K-RAS and AKT and compared them to oligodendroglial platelet-derived growth factor B-induced tumors in Ctv-a mice with targeted deletions of Cdkn2a (p16(Ink4a-/-), p19(Arf-/-), Cdkn2a(-/-)). Our results showed that glioma can originate from OPCs through overexpression of K-RAS and AKT when combined with p19(Arf) loss, and these tumors displayed an astrocytic histology and high expression of astrocytic markers. We argue that OPCs have the potential to develop both astrocytic and oligodendroglial tumors given loss of p19(Arf), and that oncogenic signaling is dominant to cell of origin in determining glioma phenotype. Our mouse data are supported by the fact that human astrocytomas and oligodendroglialomas display a high degree of overlap in global gene expression with no clear distinctions between the two diagnoses.

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