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Notch signaling enhances nestin expression in gliomas.

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Recent findings suggest that Notch signaling is active in brain tumors and stem cells, and that stem cells or cells with progenitor characteristics contribute to brain tumor formation. These stem cells are marked by expression of several markers, including nestin, an intermediate filament protein. We have studied how the Notch signaling pathway affects nestin expression in brain tumors. We find that Notch receptors and ligands are expressed in vitro and in human samples of glioblastomas, the highest grade of malignant gliomas. In culture, Notch activity activates the nestin promoter. Activation of the Notch pathway also occurs in a glioblastoma multiforme mouse model induced by Kras, with translational regulation playing a role in Notch expression. Combined activation of Notch and Kras in wild-type nestin-expressing cells leads to their expansion within the subventricular zone and retention of proliferation and nestin expression. However, activation of Notch alone is unable to induce this cellular expansion. These data suggest that Notch may have a contributing role in the stem-like character of glioma cells.

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