

PubMed

U.S. National Library of Medicine
National Institutes of Health



Display Settings: Abstract

[Cancer Res. 2006 Aug 1;66\(15\):7445-52.](#)

Notch pathway inhibition depletes stem-like cells and blocks engraftment in embryonal brain tumors.

Fan X, Matsui W, Khaki L, Stearns D, Chun J, Li YM, Eberhart CG.

Department of Pathology, Johns Hopkins University School of Medicine, 720 Rutland Avenue, Baltimore, MD 21205, USA.

The Notch signaling pathway is required in both nonneoplastic neural stem cells and embryonal brain tumors, such as medulloblastoma, which are derived from such cells. We investigated the effects of Notch pathway inhibition on medulloblastoma growth using pharmacologic inhibitors of gamma-secretase. Notch blockade suppressed expression of the pathway target Hes1 and caused cell cycle exit, apoptosis, and differentiation in medulloblastoma cell lines. Interestingly, viable populations of better-differentiated cells continued to grow when Notch activation was inhibited but were unable to efficiently form soft-agar colonies or tumor xenografts, suggesting that a cell fraction required for tumor propagation had been depleted. It has recently been hypothesized that a small population of stem-like cells within brain tumors is required for the long-term propagation of neoplastic growth and that CD133 expression and Hoechst dye exclusion (side population) can be used to prospectively identify such tumor-forming cells. We found that Notch blockade reduced the CD133-positive cell fraction almost 5-fold and totally abolished the side population, suggesting that the loss of tumor-forming capacity could be due to the depletion of stem-like cells. Notch signaling levels were higher in the stem-like cell fraction, providing a potential mechanism for their increased sensitivity to inhibition of this pathway. We also observed that apoptotic rates following Notch blockade were almost 10-fold higher in primitive nestin-positive cells as compared with nestin-negative ones. Stem-like cells in brain tumors thus seem to be selectively vulnerable to agents inhibiting the Notch pathway.

PMID: 16885340 [PubMed - indexed for MEDLINE]

[Publication Types](#), [MeSH Terms](#), [Substances](#), [Grant Support](#)

[LinkOut - more resources](#)

You are here: [NCBI](#) > [Literature](#) > [PubMed](#)

[Write to the Help Desk](#)