

## Journal Article



## Notch activation promotes cell proliferation and the formation of neural stem cell-like colonies in human glioma cells

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**Xue-Ping Zhang<sup>1, 2</sup>, Gang Zheng<sup>2</sup>, Lian Zou<sup>1</sup>, Hui-Ling Liu<sup>3</sup>, Li-Hong Hou<sup>1</sup>, Peng Zhou<sup>1</sup>, Dan-Dan Yin<sup>1</sup>, Qi-Jun Zheng<sup>1</sup>, Liang Liang<sup>1</sup>, Su-Zhen Zhang<sup>1</sup>, Lei Feng<sup>1</sup>, Li-Bo Yao<sup>1</sup>, An-Gang Yang<sup>1</sup>, Hua Han<sup>1</sup> ✉ and Jing-Yuan Chen<sup>2</sup> ✉**

- (1) Department of Medical Genetics and Developmental Biology, State Key Laboratory of Cancer Biology, Fourth Military Medical University, Chang-Le Xi Street #17, Xian, 710032, P. R. China
- (2) Department of Occupational and Environmental Health, Faculty of Military Preventive Medicine, Fourth Military Medical University, Xian, 710032, P. R. China
- (3) Department of Neurobiology, Fourth Military Medical University, Xian, 710032, P. R. China

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**Abstract** Since Notch signaling plays a critical role in stem cells and oncogenesis, we hypothesized that Notch signaling might play roles in cancer stem cells and cancer cells with a stem cell phenotype. In this study, we accessed potential functions of the Notch pathway in the formation of cancer stem cells using human glioma. Using RT-PCR, we found that most human astroglomas of different grades expressed moderate to high level of Notch receptors and ligands. mRNA of Hes5 but not Hes1, both of which are major downstream molecules of the Notch pathway, was also detected. In human glioma cell lines BT325, U251, SHG-44, and U87, mRNA encoding different types of Notch receptors were detected, but active form of Notch1 (NIC) was only detected in SHG-44 and U87 by Western blot. Interestingly, proliferation of these two glioma cell lines appeared faster than that of the other two lines in which NIC was not detected. We have over-expressed NIC of Notch1 in SHG-44 cells by constitutive transfection to evaluate the effects of Notch signaling on glioma cells. Our results showed that over-expression of NIC in SHG-44 cells promoted the growth and the colony-forming activity of SHG-44 cells. Interestingly, over-expression of NIC increased the formation neurosphere-like colonies in the presence of growth factors. These colonies expressed nestin, and could be induced to cells expressing neuron-, astrocyte-, or oligodendrocyte-specific markers, consistent with phenotypes of neural stem cells. These data suggest that Notch signaling promote the formation of cancer stem cell-like cells in human glioma.

**Keywords** Notch - Human glioma cells - Cancer stem cells

Xue-Ping Zhang, Gang Zheng and Lian Zou are contributed equally to this study.

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✉ **Hua Han (Corresponding author)**  
Email: huahan@fmmu.edu.cn

✉ **Jing-Yuan Chen (Corresponding author)**  
Email: jy\_chen@fmmu.edu.cn

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