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Arsenic trioxide-mediated Notch pathway inhibition depletes the cancer stem-like cell population in gliomas.

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Cancer stem-like cells (CSLCs) are potential targets for treatment of glioblastoma multiforme (GBM) due to their role in tumorigenesis and recurrence. In this study, we investigated the inhibitory effect of arsenic trioxide (As(2)O(3)) on CSLCs of GBM in human glioma cell lines (U87MG, U251MG and U373MG) in vivo and in vitro. Immunofluorescence staining and flow cytometry revealed that the percentage of Nestin-positive cells in the aforementioned cell lines was diminished by 12%, 14% and 7%, respectively, after treatment with 2μM As(2)O(3). Furthermore, we used soft-agar in U87MG and tumor xenografts in nude mice to demonstrate the ability of As(2)O(3) to inhibit the formation of tumor in the three cell lines. These results indicate the negative regulation of CSLCs by As(2)O(3). In addition, a Western blot analysis revealed decreased levels of Notch1 and Hes1 proteins due to As(2)O(3) treatment. We conclude that As(2)O(3) has a remarkable inhibitory effect on CSLCs in glioma cell lines in vivo and in vitro; in addition, we determined that the mechanism of CSLC inhibition involves the deregulation of Notch activation.

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