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1: [Int J Oncol](#). 2009 Mar;34(3):717-27.



### **Cancer stem cells from human glioma cell line are resistant to Fas-induced apoptosis.**

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Glioblastoma is the most common primary brain tumor, characterized by its resistance to treatments. To define efficient therapy, the origin of tumor-forming cells needs to be elucidated in order to search for new therapeutic pathways. The objective of this study was to determine the different cell populations constituting a human glioblastoma cell line, U-87 MG and their sensitivity to apoptosis induced through the activation of Fas, a membranous death receptor. By a cell sorting method, the sedimentation field flow fractionation, two major cell subpopulations were identified, a most differentiated cell fraction, containing large and adherent cells, sensitive to Fas-induced apoptosis and another one, characterized by small cells forming aggregates, expressing CD133, a marker of stem cells and more resistant to Fas-activated apoptosis. By using a selective method of culture, adapted for neural stem cell cultures, we have verified that the U-87 MG cell line contained cancer stem cells similar to the immature ones obtained by the cell sorting method. Interestingly, while these tumor stem cells, expressing CD133, were resistant to Fas-induced apoptosis, monomeric form of Fas protein was detected predominantly in these cells. In contrast, the most mature cells, responsive to Fas-activated apoptosis, collected in another cell fraction, contained oligomeric aggregates of Fas protein, a pre-signalling form of the Fas receptor, essential for the initiation of apoptosis through its activation. These results suggest that these immature stem cells in glioma could be an important factor of resistance to chemotherapy requiring apoptosis through Fas signalling system. Indeed, future strategies of treatment, inducing differentiation of these stem cells need to be considered to enhance therapeutic efficiency.

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