Aldehyde dehydrogenase 1 positive glioblastoma cells show brain tumor stem cell capacity.

Glioblastoma (GBM) is the most aggressive primary brain tumor and is resistant to all therapeutic regimens. Relapse occurs regularly and might be caused by a poorly characterized tumor stem cell (TSC) subpopulation escaping therapy. We suggest aldehyde dehydrogenase 1 (ALDH1) as a novel stem cell marker in human GBM. Using the neurosphere formation assay as a functional method to identify brain TSCs, we show that high protein levels of ALDH1 facilitate neurosphere formation in established GBM cell lines. Even single ALDH1 positive cells give rise to colonies and neurospheres. Consequently, the inhibition of ALDH1 in vitro decreases both the number of neurospheres and their size. Cell lines without expression of ALDH1 do not form tumor spheroids under the same culturing conditions. High levels of ALDH1 seem to keep tumor cells in an undifferentiated, stem cell-like state indicated by the low expression of beta-III-tubulin. In contrast, ALDH1 inhibition induces premature cellular differentiation and reduces clonogenic capacity. Primary cell cultures obtained from fresh tumor samples approve the established GBM cell line results.