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Suppressing Glioblastoma Stem Cell Function by Aldehyde Dehydrogenase Inhibition with Chloramphenicol or Disulfiram as a New Treatment Adjunct: An Hypothesis.

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Strong expression of aldehyde dehydrogenase is a prominent feature of both normal and cancer stem cells, including the stem cell sub-population of glioblastoma. Aldehyde dehydrogenase function is used by cancer stem cells to repopulate a tumor mass after chemotherapy cytoreduction. Cancer stem cells tend to be chemotherapy compared to the non-stem cell majority cell population in several common human cancers. Such has been demonstrated specifically in glioblastoma. In normal hematopoietic stem cells with unimpaired high levels of aldehyde dehydrogenase, stem cells divide rarely and then asymmetrically to a daughter stem cell and a daughter cell on a path of differentiation or symmetrically with both daughter cells on a differentiated path. If a parallel situation obtains in glioblastoma stem cells, the migrating, far flung paucicellular extensions will be stem cell rich and use aldehyde dehydrogenase to generate the characteristic multiple metastases made up of mostly non-stem cells. With inhibition of aldehyde dehydrogenase, stem cell division to non-stem daughter cells tends to become blocked. We have three old yet potent aldehyde dehydrogenase inhibitors on the market- chloral hydrate, chloramphenicol, and disulfiram- they should be investigated as adjuncts in glioblastoma chemotherapy. If GBM stem cell function can be thwarted by potent aldehyde dehydrogenase inhibition, they will be less able to regenerate a stem cell derived tumor mass after primary resection or chemotherapy.

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