Neurobiology of Disease
Volume 25, Issue 2, February 2007, Pages 217-229

doi:10.1016/j.nbd.2006.08.022 Cite or Link Using DOI

Review

Cancer stem cells and “stemness” genes in neuro-oncology

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Received 10 August 2006; accepted 27 August 2006. Available online 1 December 2006.

Abstract

The main properties of stem cells include long-term self-renewal and the capacity to give rise to one or more types of differentiated progeny. Recently, much evidence was provided that leukemia and tumor maintenance and growth are sustained by a small proportion of cells exhibiting stem cell properties. In neural tumors, stem cells have been detected in glioblastoma, medulloblastoma and ependymoma. These observations imply that normal stem cells could be the origin of cancer stem cells; alternatively, a more differentiated progeny may revert to a “stem-like” status, and give rise to cancer stem cells. In adult brain residual stem cells are located in the hippocampus, the subventricular zone and possibly the cerebellum. However, evidence for the ability of more differentiated progeny (astroglia, oligodendroglia) to convert into “stem cells” in vitro has also been provided, thus greatly expanding the potential target of oncogenic mutations.

In the framework of the cancer stem cell hypothesis, genes originally identified as important for normal neural stem cells may be essential to support cancer stem cells as well.

Stem cell genes act in several ways: they stimulate stem cell self-replication, inhibit differentiation, control excessive replication that might lead to “exhaustion” of the stem cell pool.

Mutations in man and mouse, in spontaneous or experimental brain tumors, often target stem cell genes or genes lying in their functional pathway, the main examples being the Sonic hedgehog and the Wnt pathways. Interestingly, several stem cell genes are often overexpressed in brain tumors, even if they are not mutated. This suggests that these genes may be important for the generation of cancer stem cells from more differentiated precursors, or for cancer stem cell maintenance.

Cancer stem cells partially differentiate in vivo, and in vitro they also give rise to seemingly normal differentiated progeny, like normal stem cells: thus, their main defect, leading to cancer, may lie in the unbalance between self-replication and terminal differentiation of this minority cell population. Knowledge of extrinsic diffusible factors affecting the activity of stem cell genes may help identifying tools for inducing cancer stem cell differentiation, which might be of use in therapy.

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