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Seeing is Believing: Are Cancer Stem Cells the Loch Ness Monster of Tumor Biology?

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Abstract

Tumors are complex systems with a diversity of cell phenotypes essential to tumor initiation and maintenance. With the heterogeneity present within the neoplastic compartment as its foundation, the cancer stem cell hypothesis posits that a fraction of tumor cells has the capacity to recapitulate the parental tumor upon transplantation. Over the last decade, the cancer stem cell hypothesis has gained support and shown to be relevant in many highly lethal solid tumors. However, the cancer stem cell hypothesis is not without its controversies and critics question the validity of this hypothesis based upon comparisons to normal somatic stem cells. Cancer stem cells may have direct therapeutic relevance due to resistance to current treatment paradigms, suggesting novel multimodal therapies targeting the cancer stem cells may improve patient outcomes. In this review, we will use the most common primary brain tumor, glioblastoma multiforme, as an example to illustrate why studying cancer stem cells holds great promise for more effective therapies to highly lethal tumors. In addition, we will discuss why the abilities of self-renewal and tumor propagation are the critical defining properties of cancer stem cells. Furthermore, we will examine recent progress in defining appropriate cell surface selection markers and mouse models which explore the potential cell(s) or origin for GBMs. What remains clear is that a population of cells is present in many tumors which are resistant to conventional therapies and must be considered in the design of the next generation of cancer treatments.

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