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Cancer stem cells in glioma: challenges and opportunities

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Abstract

The discovery of cancer stem cells in glioma has created a paradigm shift in our understanding of this deadly disease. Glioma stem cells exhibit sustained self-renewal and potent tumorigenic potential and differ from their more differentiated progeny in response to current therapies. Recurrent disease is likely derived from glioma stem cells or progeny reprogrammed to gain stem cell-like phenotypes, indicating that the stem cell phenotype is a crucial therapeutic target. While debate over cancer stem cell and clonal evolution models persists, important knowledge has been gained over the past decade from glioma stem cells investigation and clinical impact is expected.

Keywords

Glioma; cancer stem cells

Introduction

Malignant gliomas constitute a heterogeneous group of highly infiltrative primary brain tumors with distinct histopathological and molecular features. Each year in the United States, approximately 15,750 individuals are diagnosed with a malignant glioma and an estimated 12,740 patients succumb to this disease (1). These statistics highlight the particularly lethal nature of malignant gliomas and important need for enhanced therapeutic efficacy. Current classifications of glioma are based upon the seminal work of Bailey and Cushing, who in the 1920s named and divided glial tumors according to a putative cell type of origin and stage of cellular development (2). Likewise, efforts to provide more effective therapies continue to be driven by the studies of glioma cells of origin and underlying mechanisms of cellular development and growth. Paramount to these efforts is an evolving understanding of the cellular heterogeneity within gliomas. Thus, while the predominant cell type within an astrocytoma or oligodendroglioma may resemble an astrocyte or oligodendrocyte, respectively, each type of glioma is composed of morphologically, phenotypically and genetically heterogeneous cells.

In this review, two seemingly though not necessarily competing views of glioma heterogeneity are discussed, the stochastic and cancer stem cell models. How recent studies of microenvironmental cues, developmental signaling pathways, and treatment resistance inform our views of glioma heterogeneity, growth and therapy will also be reviewed.

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