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Stem cells: Implications in the development of brain tumors☆

I.A. Matos Rojas[a], **D. Bertholdo**[b], **M. Castillo**[b,*]

[a] *Servicio de Radiodiagnóstico, Hospital Universitario La Paz, Madrid, Spain*
[b] *División de Neurorradiología, Hospital Universitario de la Universidad de Carolina del Norte, Chapel Hill, NC, United States*

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Abstract Stem cells are characterized by their capacity for self-renewal, for giving rise to new cells in specific tissues, and for maintaining this capacity throughout the entire life of their hosts. Stem cells are pluripotent and maintain continuous production of neurons, astrocytes, and oligodendrocytes. Stem cells in brain tumors also proliferate, undergo self-renewal, and give rise to other poorly differentiated cells. Unlike non-tumor stem cells, tumor stem cells lack the normal mechanisms that regulate proliferation and differentiation, resulting in uncontrolled production and incomplete differentiation of tumor cells. Discovering the role of tumor stem cells in the brain has given us a new perspective about the molecular pathways involved in signaling and about oncogenesis in the central nervous system; it can also help us explain the high rate of recurrence of some tumors and the diffuse nature of glioblastomas. Ideally, this perspective can be expected to lead to better treatments.

This article reviews the characteristics of non-tumor and tumor stem cells, emphasizing the importance of brain tumor stem cells in the pathogenesis of common brain tumors.

PALABRAS CLAVE
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Ependimoma

Células madre: implicaciones en el desarrollo de tumores cerebrales

Resumen Las células madre se caracterizan por su capacidad de renovarse, dar origen a nuevas células en tejidos específicos, y mantener esta capacidad a lo largo de toda la vida del anfitrión. Las células madre son pluripotenciales y mantienen una producción continua de neuronas, astrocitos y oligodendrocitos. Las células madre en los tumores cerebrales también proliferan, se renuevan y dan origen a otras células pobremente diferenciadas. La diferencia entre células madre no tumorales y tumorales reside en que estas últimas carecen de los mecanismos normales que regulan la proliferación y diferenciación, resultando en una

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* Corresponding author.
E-mail address: castillo@med.unc.edu (M. Castillo).

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producción incontrolada y en una diferenciación incompleta de células tumorales. Descubrir el papel que juegan las células madre tumorales en el cerebro nos ha proporcionado una nueva perspectiva con respecto a las vías de señal moleculares y a la oncogénesis en el sistema nervioso central, y puede ayudarnos a explicar el alto número de recurrencias en algunos tumores y la naturaleza difusa de los glioblastomas; idealmente, puede esperarse que esta perspectiva conduzca a mejores tratamientos.

Este artículo revisa las características de las células madre no tumorales y tumorales, con énfasis en la importancia que las células madre tumorales cerebrales tienen en la patogénesis de neoplasias cerebrales comunes.

Introduction

Stem cells isolated from adult humans maintain a constant production of differentiated cells in different tissues and organs thanks to their self-renewal and differentiation potential. On the other hand, cancer stem cells, with high proliferation potential and incomplete differentiation, are involved in the process of oncogenesis and chemoresistance of certain tumors such as brain tumors. Knowledge of these concepts and mechanisms is therefore necessary for their implementation in innovative diagnostic methods and new therapeutic strategies.

Stem cells

The cell is the structural, morphologic, and functional unit of all living organisms. Since organisms live longer than their differentiated cells, they need to regenerate their tissues and organs. Stem cells can replace lost cells with new cells thanks to their self-renewal potential, and are a constant source of primitive precursors of tissues and organs.

Stem cells are defined by the organ from which they derive or by the location where they are found *in vivo*.

Definition of stem cell includes three characteristics[1,2]:

- Self-renewal.
- Capacity to produce all cells of a given tissue.
- Capacity to maintain this production over a long period in the life of the host.

Stem cells can be totipotent, pluripotent, multipotent, oligopotent, and unipotent.[3] Totipotent stem cells can produce an entire organism. Totipotency is seen in zygote and during its first divisions as well as in plant meristem cells. Pluripotent cells can produce all cell lineages of the body, but cannot create an entire organism. Most stem cells belong to this category. An example of pluripotent cell is the embryonic stem cells of the inner cell mass of the blastocyst and they exist only during a short period of the embryonic development. Hematopoietic cells are multipotent; this means they can develop into multiple cell lineages to generate an entire tissue (or tissues). Cells able to form two or more cell lineages within a tissue are termed oligopotent cells, such as neural stem cells, which can generate subsets of neurons. Cells that give rise to a specific cell lineage are termed unipotent cells, such as spermatogonia. Stem cells are found in fertilized eggs, blastocyst, placental trophoblast, embryonic cells, in certain tissues such as blood tissue and specific areas of the adult nervous central system (NCS).

Neural stem cells

Neural stem cells are self-renewing, multipotent cells that continually generate neurons, astrocytes, and oligodendrocytes in the nervous system.[4] Neurogenesis is a constant process that occurs throughout life. The long-held theory that ''the brain cannot generate new neurons'' has therefore become obsolete. Interestingly, neurogenesis continues in discrete areas of the adult brain, such as the anterior portion of the subventricular zone (SVZ), subependymal zone, lining of the lateral ventricles, periventricular cerebellar zone, subgranular zone (SGZ) in the dentate gyrus of the hippocampus, and subcortical white matter[5] (Fig. 1). The SGZ is located between the lateral ventricle and the striate body and is an important source of rapidly proliferating neural stem cells, which can lead to genetic errors. The SGZ is therefore thought to be a source of cells that initiates glioblastomas and ependymomas.

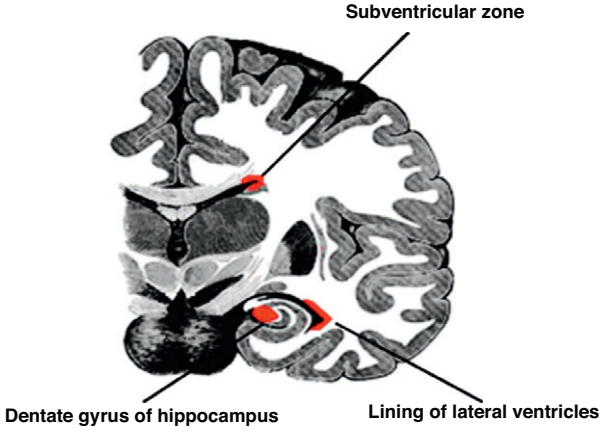

Figure 1 Neural stem cells can be found in the subventricular zone (between the caudate nucleus and lateral ventricle), subgranular zone, and lining of the lateral ventricles.