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Cancer stem cells: A brief overview

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The haematopoietic system is organized as a hierarchy in which the majority of cells are mature and therefore need to be continuously replenished from a small pool of immature progenitors - the stem cells (1). Stem cells are endowed with two distinctive properties – first is the property of self renewal i.e. the ability to go through numerous cycles of cell division while maintaining the undifferentiated state, and second is the property of obligatory asymmetric replication i.e. a stem cell divides into one father cell that is identical to the original stem cell, and another daughter cell that is differentiated (2,3). It is the property of self renewal along with extensive potential to proliferate that has relevance in oncogenesis (1,2).

There are three kinds of stem cells: embryonal, germinal and somatic or adult stem cells. Embryonal stem cells are derived from the first five or six divisions of the fertilized egg. Their progeny gives rise to all of the adult organs. Germinal stem cells in the adult produce egg and sperm and are responsible for reproduction. Somatic or adult stem cells have limited potential to differentiate into various lineages, and they produce cells that differentiate into mature functioning cells. It is now well recognized that the adult progenitor cells of one tissue may be able to differentiate into mature cells of another tissue type.

Cancer stem cells (CSCs) are cancer cells of normal stem cells and have the ability to give rise to all cell types found in a particular cancer. It has been postulated that cancer stem cells arise by mutation from normal stem cells (1,2).

The concept of cancer stem cells has been around since the 1800's, however, the first conclusive evidence for CSCs was published in 1997 in Nature Medicine. Bonnet and Dick isolated a subpopulation of leukaemic cells that expressed a specific surface marker CD34, but lacked the CD38 marker. The authors established that the $CD34^{+}/CD38^{-}$ subpopulation was capable of initiating tumors in NOD/SCID mice that was histologically similar to the donor.

Cancer stem cells have recently been identified in several solid tumors, including breast cancer, brain cancer, colon cancer, ovary, pancreas, etc. [1-4]. The origin of cancer stem cells is still an area of ongoing research. A normal stem cell may be transformed into a cancer stem cell through dysregulation of the proliferation and differentiation pathways controlling it. The various pathways shared by stem cells can be BIM -1 pathway which appears to be active in pediatric brain tumors, Notch pathway involving the haematopoeitic, neural and mammary stem cells and the sonic hedgehog pathway [3-4].

The identification of cancer stem cells in various tumors has evolved therapeutic concepts with emphasis on targeting the cancer stem cells. It is very important to identify the source of stem cells for successful treatment. If the current treatments of cancer do not properly destroy enough cancer stem cells, the tumor will reappear. The existence of CSCs has several implications in terms of future cancer treatment and therapies. These include disease identification, selective drug targets, prevention of metastasis, and development of new intervention strategies.

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Normal somatic stem cells are naturally resistant to chemotherapeutic agents through various pumps present in them. CSCs that have mutated from normal stem cells may also express proteins that would increase their resistance towards chemotherapeutic agents. These surviving CSCs then repopulate the tumor, causing relapse. By selectively targeting CSCs, it would be possible to treat patients with aggressive, non-resectable tumors, as well as preventing the tumor from metastasizing. A number of studies have investigated the possibility of identifying specific markers that may distinguish CSCs from the bulk of the tumor.

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