Stem the Research - Stall the Recovery

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Article summary: Stem cell is a type of cell that posses the capability of self renewal and have potential to differentiate into variety of cell types. Depending on the origin they are divided into embryonic stem cells and adult stem cells which are further divided into haematopoietic stem cell, mesenchymal stem cells, neural stem cells, mammary stem cells and intestinal Stem cells. These stem cells show potential approach for human benefits in repairing the damaged tissues while maintaining their differentiated stage.

Introduction

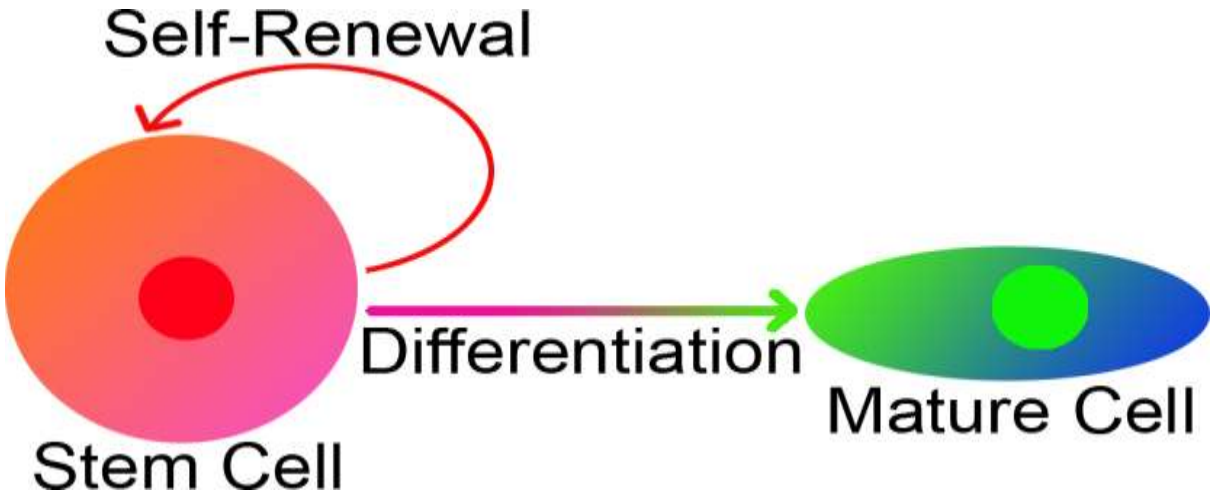
A stem cell is a cell that can both reproduce itself and generate offspring of different cell type [1].A Stem cell of a particular tissue is defined as a) undifferentiated cell i.e lacking certain tissue specific markers, b) capable of proliferation, c) able to self maintain a population, d) able to produce large number of differentiated, functional progeny, e) able to regenerate the tissue after injury, and f) flexible use of these portions [2].

Three major historical trends established the current knowledge of stem cells are [3]:

- First were studies of reproduction, or how species reproduce. Locating the organs and processes of reproduction or generation gave researchers the impetus to speculate about the causes for development.
- Second were regeneration studies. Understanding how and why certain animals regrow, damaged or injured parts generated questions about the origin of these unique features intrinsic to some animals and not to others.
- Third, the nineteenth century produced a new science called teratogeny, or study of the creation of monsters. Results of teratogenis experiments led to speculation about stem cells.

Concept of Stem cell:

The “stem cell” concept was first proposed by Till and McCulloch following their pioneering studies of the blood system regeneration *in vivo*. Ten days after transplanting limiting number of syngenic bone marrow (BM) cells into recipient mice, they observed cellular colonies that formed in the spleens of recipient mice. Analysis of these colonies revealed that a very small sub-population of the donor BM cells possessed two remarkable properties: (1) the ability to generate multiple types of myeloerythroid cells, and (2) the ability to self-replicate. These findings introduced the two defining criteria of stem cells *i.e.* multi-potency and self-renewal [4].



Properties of Stem cell:

1. Self renewal: The ability of stem cells to undergo various cell divisions while maintaining undifferentiated state. Two ways for confirmation of this property are:

a.) Obligate differentiation: When a stem cell divides, it divides into a mother cell which is undifferentiated and a daughter cell which is differentiated.

b.) Stochastic division: When one stem cell divides into two differentiated cells then another stem cell undergo mitotic division to produce two undifferentiated cells

2. Potency of Stem cell: This property specifies the potential of stem cell to differentiate into different cells. Hierarchy of stem cell includes : Totipotent cells-fertilised egg which are able to form embryo and trophoblast of placenta, Pluripotent cells- Inner cell mass of blastocyst, able to differentiate into almost all cells that arise from the three germ layers, but not the embryo because they are unable to give rise to the placenta and supporting tissues [3], Multipotent stem cells able to form specific cell lineages, Lineage committed- these are unipotent stem cells which are able to form cell type of their own.

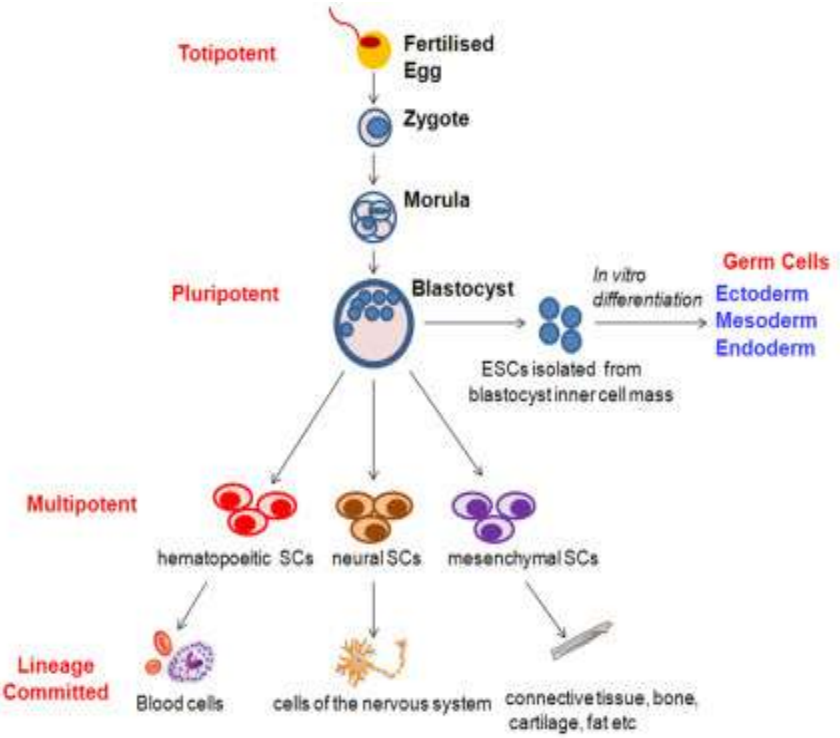


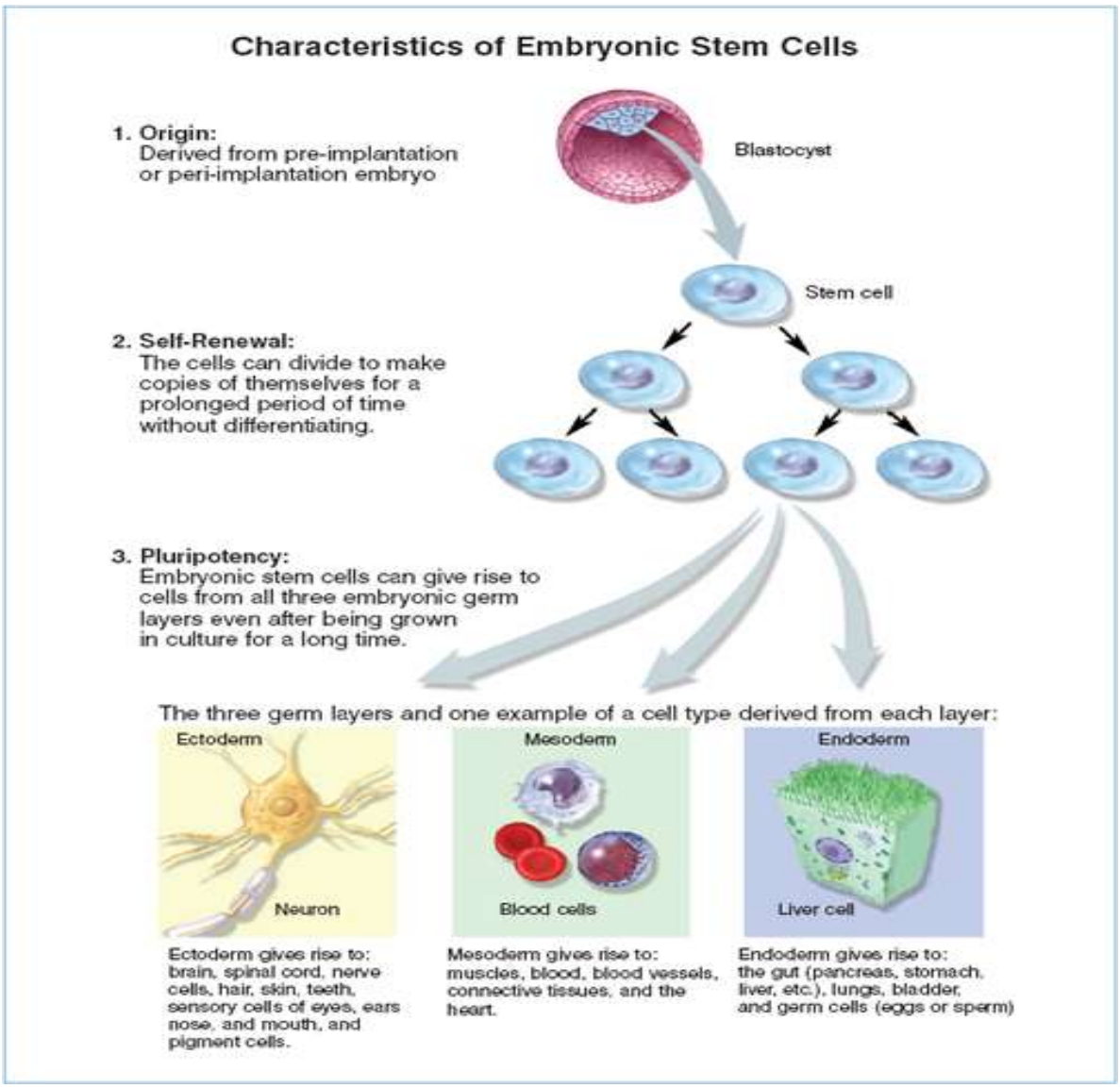
Figure1: Potency of Stem cells

Types of Stem Cell:

1.) Embryonic stem cell

Embryonic stem (ES) cells, which are derived from the inner cell mass of mammalian blastocyst, have the ability to grow indefinitely while maintaining pluripotency and the ability to differentiate into cells of all three germ layers [5]. These cells are derived from totipotent cells of the early mammalian embryo and are capable of unlimited, undifferentiated proliferation in vitro. The term “ES cell” was introduced to distinguish these embryo-derived Pluripotent cells from teratocarcinoma-derived pluripotent embryonic carcinoma (EC) cells [6]. Despite the importance of ESCs in developmental biology and their potential impact on tissue replacement therapy, the molecular mechanism underlying ESC self-renewal is poorly understood.[7] Human ES cells might be used to treat a host of diseases, such as Parkinson's disease, spinal cord injury, and diabetes. However, there are ethical difficulties regarding the use of human embryos, as well as the problem of tissue rejection following transplantation in patients. One way to circumvent these issues is the generation of pluripotent cells directly from the patients' own cells.

Several transcription factors, including Oct3/4[8], Sox2 [9]and Nanog [10], function in the maintenance of pluripotency in both early embryos and ES cells. Several genes that are frequently up regulated in tumors, such as *Stat3* [11] *E-Ras* ([12] c-*myc* (22), *Klf4* [13], and β-*catenin* [14, 15], have been shown to contribute to the long-term maintenance of the ES cell phenotype and the rapid proliferation of ES cells in culture.



2. Adult Stem Cell:

Tissue-specific stem cells, which are sometimes referred to as "adult" or "somatic" stem cells, are already somewhat specialized and can produce some or all of the mature cell types found within the particular tissue or organ in which they reside. Because of their ability to generate multiple, organ-specific, cell types, they are described as "multipotent". [16]

ASCs are postnatal derivatives of ESCs located throughout the body. ASCs maintain co-expression of at least three of the four transcription factors characteristic of ESCs (OCT4, KLF4, and SOX2) and show high expression of ABC transporters and alkaline phosphatase. ASCs have been described in many different organs, but it is not yet known how many markers are common to all ASCs or which are organ specific. One area of debate is whether populations of ASCs each expressing different sets of genes may coexist in the same organ. [17]

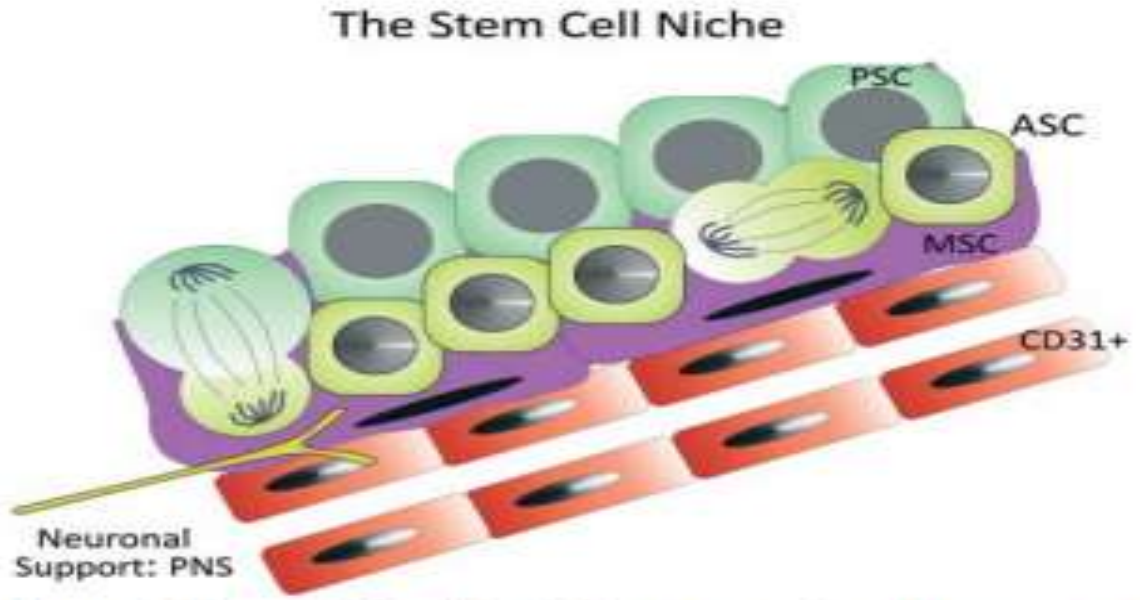


Figure 2 The adult SC niche. ASCs are organized in a compact structure supported by MSCs and receiving specific nervous (sympathetic) and vascular support. ASCs maintain a basal slow proliferative rate that neutrally drives the cells either to remain in the niche or become converted into progenitors and leave the niche. Randomly occurring factors such as proximity to cytokines might decide ASC fate through symmetric or asymmetric divisions.

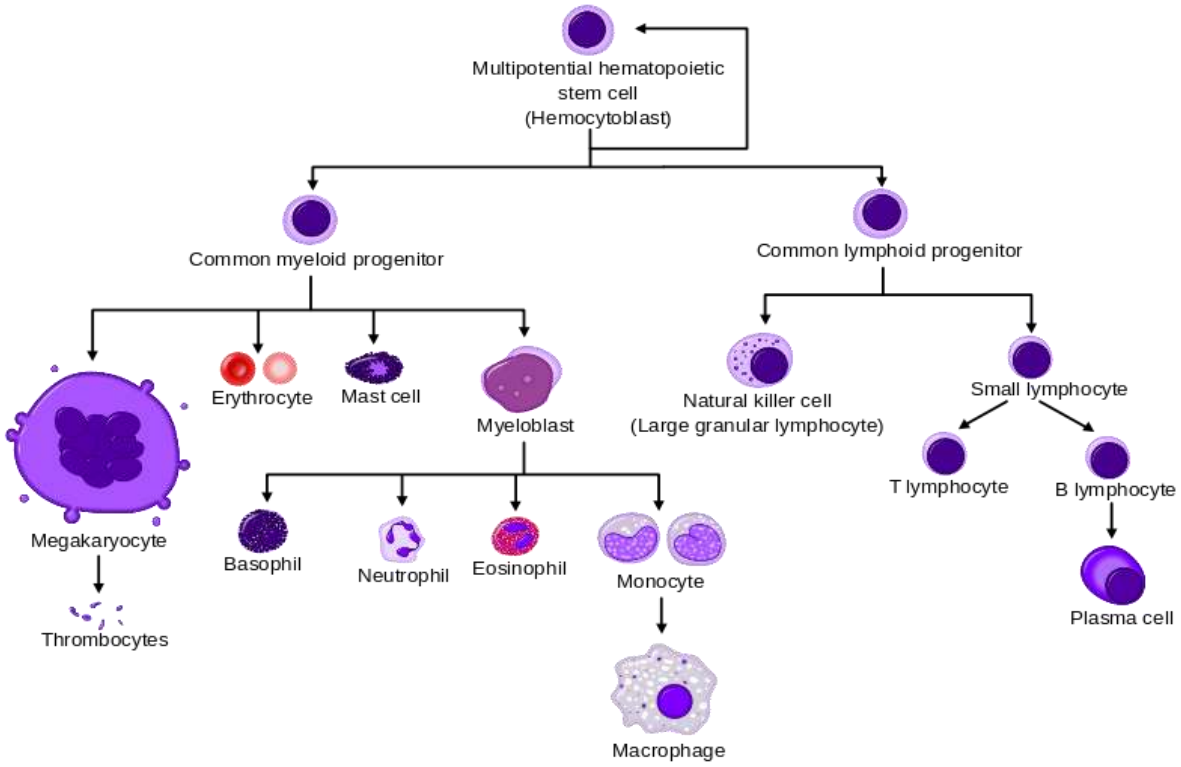
Journal of Molecular Endocrinology (2012) **49**, R89–R111

Types of Adult Stem Cell:

1. Haematopoietic stem cell:

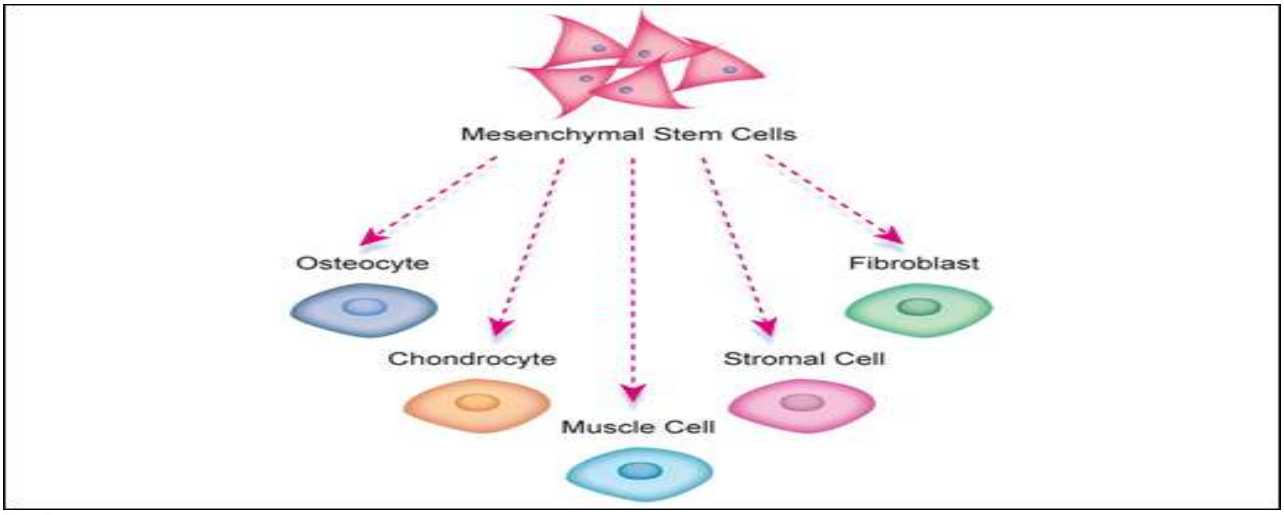
   A hematopoietic stem cell is defined as having the ability to give rise to all lineages of mature blood cells [2]. The mammalian blood system, containing more than ten distinct mature cell types, stands on

one specific cell type, hematopoietic stem cell (HSC). Within the system, only HSC possess the ability of both multi-potency and self-renewal [4].



2. Mesenchymal Stem Cell:

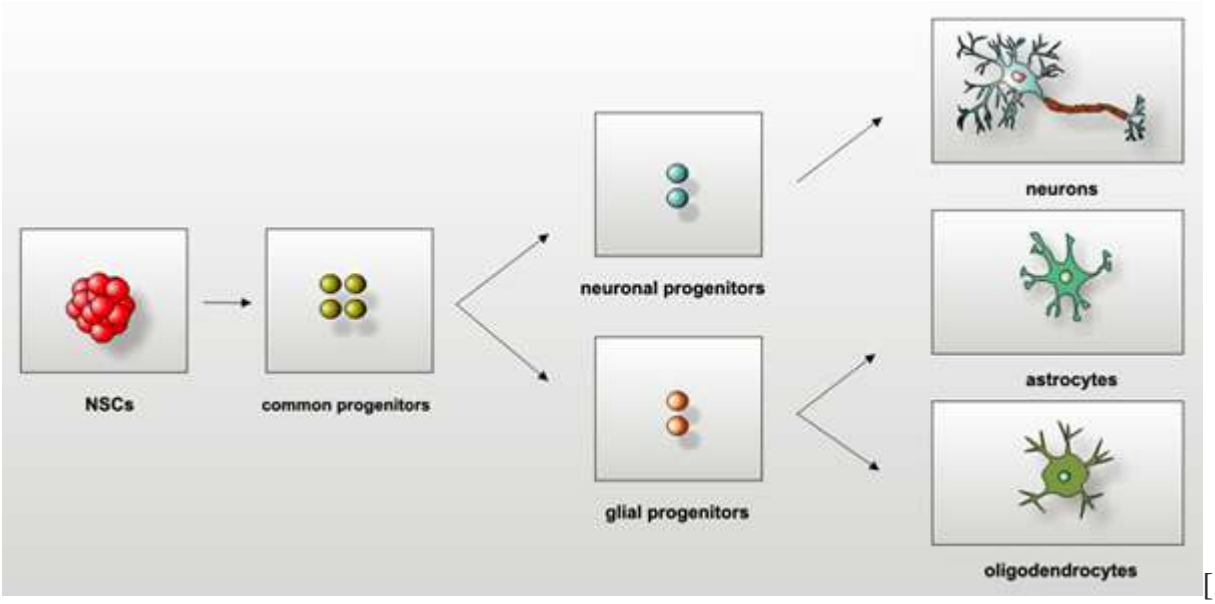
Bone and cartilage formation in the embryo and repair and turnover in the adult involve the progeny of a small number of cells called mesenchymal stem cells. These cells divide, and their progeny become committed to a specific and distinctive phenotypic pathway, a lineage with discrete steps and, finally, end-stage cells involved with fabrication of a unique tissue type, e.g., cartilage or bone. Local cuing (extrinsic factors) and the genomic potential (intrinsic factors) interact at each lineage step to control the rate and characteristic phenotype of the cells in the emerging tissue. The study of these mesenchymal stem cells, whether isolated from embryos or adults, provides the basis for the emergence of a new therapeutic technology of self-cell repair. [18]



[19]

3. Neural stem cell:

Neural precursor cells in vertebrates can self-renew and give rise to all cell types within the nervous system. Neural stem cells also give rise to other cells in the body, including skin melanocytes and a range of mesenchymal cells in the head and neck.[20]



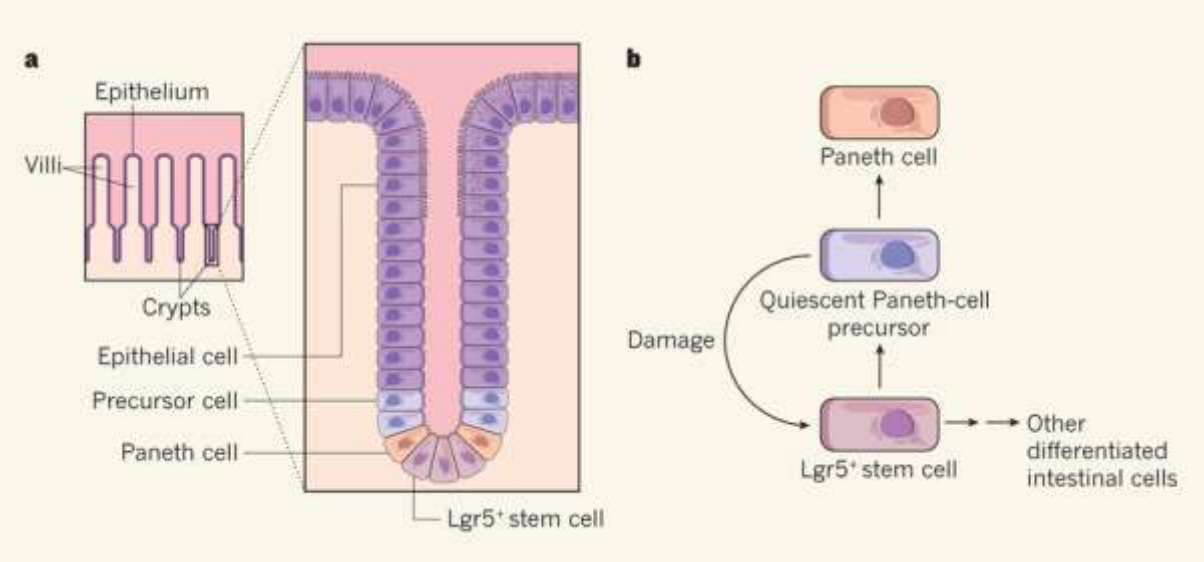
[21]

3. Mammary Stem cells:

These divide and differentiate at the time of gestation and puberty. Mammary stem cells also play a major role in treatment of carcinogenic tissues of mammary glands at the time of breast cancer.

4. Intestinal Stem Cells:

   Intestinal stem cells are present in the epithelial layer of small intestine that are regularly exposed to harsh environment. Due to this condition epithelial cell continuously shed of and intestinal stem cells differentiate and renovate the intestinal layers for proper absorption.



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