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A Review on stem cell therapy in Cancer

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A B S T R A C T

Stem cells are the flexible cell types which can gives raise to multiple cell types. Accordingly, harnessing the potential of stem cells is considered to have great significance for therapeutic purpose. The stem cells are having certain features like unlimited proliferation potential and they share closely to cancer cells. In this review, we have addressed the developmental aspects of stem cells and cancer cells their respective biological functions in maintaining an intricate balance to decide their respective contributions to the usefulness or harmfulness in the biological system. Understanding the characteristics of cancer stem cells will help to develop novel therapies to eliminate the initiating cancer stem cell, and the relevant patents on the cancer stem cell and cancer therapy. The Markers frequently used to identify stem cells within the prostate, breast and intestine.

Keywords: Stem cell, Stem cell therapy, cancer, cell potency.

A R T I C L E I N F O

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1. Introduction

Stem cells are undifferentiated biological cells that can differentiate into specialized cells and can divide (through mitosis) to produce more stem cells. They are found in multicellular organisms. In mammals, there are two broad types of stem cells. Embryonic stem cells, which are isolated from the inner cell mass of blastocysts, and adult stem cells, which are found in various tissues. In adult organisms, stem cells and progenitor cells act as a repair system for the body, replenishing adult tissues.

Properties of stem cells:

Self-renewal: The ability to go through numerous cycles of cell division while maintaining the undifferentiated state.

Potency: The capacity to differentiate into specialized cell types. In the strictest sense, this requires stem cells to be either totipotent or pluripotent to be able to give rise to any mature cell type, although multipotent or unipotent progenitor cells are sometimes referred to as stem cells. Apart from this it is said that stem cell function is regulated in a feedback mechanism. (Muller JM, Chevrier L)

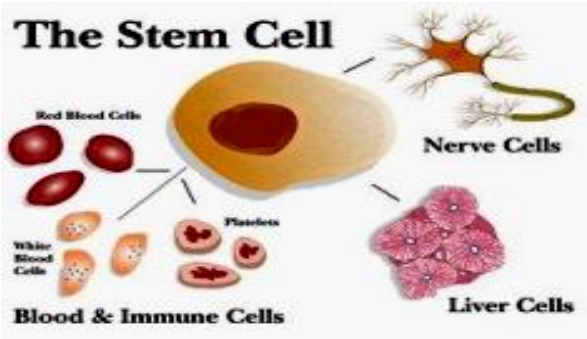

Figure 1: Structure of stem cells

Cell potency:

Potency specifies the differentiation potential of the stem cell. Totipotent stem cells can differentiate into embryonic and extra embryonic cell types. Such cells can construct a complete, viable organism. These cells are produced from the fusion of an egg and sperm cell. Cells produced by the first few divisions of the fertilized egg are also totipotent.

- Pluripotent stem cells are the descendants of totipotent cells and can differentiate into nearly all cells i.e. cells derived from any of the three germ layers.
- Multipotent stem cells can differentiate into a number of cell types, but only those of a closely related family of cells.
- Oligopotent stem cells can differentiate into only a few cell types, such as lymphoid or myeloid stem cells. (Losordo DW)

Origins of cancer:

Field theory:

Teratocarcinomas arise from normal germinal cells when these cells are placed in a tissue niche that does not enforce normal differentiation.

Chemical carcinogenesis:

Chemicals that cause cancer of the liver appear to act at various stages of the differentiation of liver lineage cells. Exposure of the skin to chemical carcinogens causes mutations in the long-term, thereby, self-renewing the mutated skin stem cells to give rise to CSCs.

Virus infections:

HPV virus infects basal stem cells of the cervix and redirects the cells from differentiation to proliferation. Another example is that of Hepatitis virus, which infects mature liver cells, stimulates proliferation and causes maturation arrest at a late stage in the liver cell lineage to give rise to liver CSCs and then hepato cellular carcinomas. (Smith LM, Nesterova A)

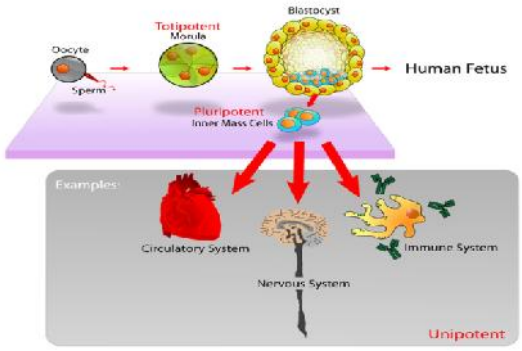

Figure 2: Embryonic stem cells originate as inner cell mass (ICM)

2. Role of stem cells in a biological system

Although stem cells occupy a small percentage of an adult tissue, they have profound biological significance. The basic biological significance of adult stem cells is to act as a reservoir of progenitor cells which can in turn act as a repair system, primarily for that particular tissue, or other tissues of that particular germline. The stem cell is an essential component of a developmental phenomenon-one of the key components of a program fundamental to organogenesis and maintenance of homeostasis throughout life. For example, neuronal stem cells help in the formation of new neurons. Adipose tissue stem cells help in the formation of adipocytes and release repair related growth factors, intestinal stem cells help in the replenishment of worn out or damaged intestinal cells. (Merchant AA, Matsui W)

Tumorigenesis:

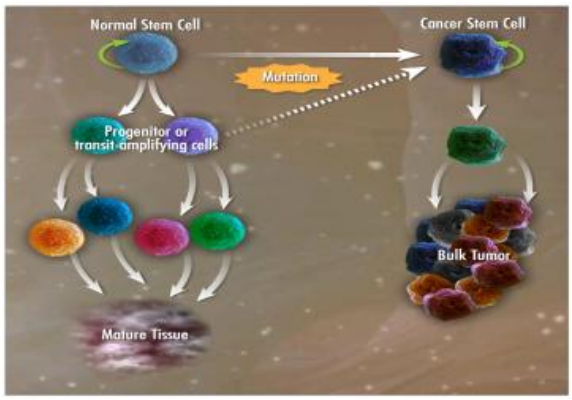

Figure 3: Stem cell development normal and cancer stem cells

Normal stem cells are undifferentiated cells in the body, they can self-renew, propagate differentiated cells, and proliferate extensively. These discoveries have fuelled interest in stem cell therapy for a wide variety of diseases, including neurological, inflammatory, and endocrine disorders. CSCs are malignant cancer cells that share the capacity of normal stem cells for self-renewal and proliferation and can differentiate into the heterogeneous population of cancer cells that comprise a malignant tumor (Marshall DJ). A common misconception is that all CSCs arise from mutated normal stem cells, but some CSCs may

arise from progenitor cells when a mutation endows these cells with the capacity for self-renewal, normally reserved to stem. A growing body of evidence suggests that CSCs are the drivers not only of tumor initiation and heterogeneity, but of treatment resistance, cancer recurrence.

Importance of stem cells: Stem cells make the 3 main types of blood cells they are red blood cells, white blood cells, and platelets.

Red blood cells (RBCs) carry oxygen away from the lungs to all of the cells in the body. They Carry carbon dioxide from the cells back to the lungs to be exhaled. A blood test called a *hematocrit,* shows how much of your blood is made up of RBCs. The normal range is about 35% to 50% for adults. People whose hematocrit is below this level have anemia.

White blood cells (WBCs) help fight infections caused by bacteria, viruses, and fungi. There are different types of WBCs.

Neutrophils are the most important type in fighting bacterial infections. The absolute neutrophil count (ANC) is a measure of the neutrophils in your blood. (Davis CG)

Lymphocytes are another type of white blood cell. There are different kinds of lymphocytes, such as T lymphocytes (T cells), B lymphocytes (B cells), and natural killer (NK) cells. Some lymphocytes make antibodies to help fight infections. The body depends on lymphocytes to recognize its own cells and reject cells that don't belong in the body, such as invading germs or cells that are transplanted from someone else.

Platelets are pieces of cells that seal damaged blood vessels and help blood to clot, both of which are important in stopping bleeding. A normal platelet count is usually between 150,000/cubic mm and 450,000/cubic mm. A person whose platelet count drops below normal is said to have *thrombocytopenia and this features are* bleed longer and have nosebleeds or bleeding gums. Spontaneous bleeding can happen if a person's platelet count drops lower than 20,000/mm3. This can be dangerous if bleeding occurs in the brain, or if blood begins to leak into the intestines or stomach. (Bapat SA)

Cancer stem cells: Cancer stem cells are cancer cells that possess characteristics associated with normal stem cells, specifically the ability to give rise to all cell types found in a particular cancer sample. They may arise from normal ASCs, from more restricted progenitor cells or even from differentiated cells. Normal stem cells are more likely to be the targets of mutants and leading to the formation of CSCs for they already possess active self-renewal pathways. It is also possible for progenitors and other differentiated cells to give rise to CSCs, though they would have to acquire more genetic mutations, especially in self-renewal genes. In cancer research experiments, tumor cells are sometimes injected into an experimental animal to establish a tumor.

3. Biomarkers based Therapy

Cancer stem cells have been identified in a growing number of hematopoietic cancer and solid tumors and are typically recognized by virtue of the expression of cell surface markers. These cells have been isolated from the bulk tumor population by the expression pattern of cell surface proteins (e.g., CD24, CD44, CD 133). The identification of markers that allow the prospective isolation of CSCs from whole tumor tissues will lead to the understanding of important biological properties of CSCs and provide the possibility to target them. (Bernards R, Rogelj S)

CD133: It is a glycosylated, 120KD protein with five transmembrane domains and two large extracellular loops. The expression of genes known to play important roles in the maintenance of cancer stem cells have been investigated in putative CD133+ CSC populations of multiple tissues. These CD133+ cells undergo multi-lineage differentiation to neurons, astrocytes, and oligodendrocytes in vitro, and can recapitulate the original tumor phenotype in vivo, unlike the CD133.

CD44 and CD 24:

It is reported as at least one characteristic of CSCs across tissues, including breast, pancreas, gastric, head and neck, ovarian and colon, whereas other markers (e.g., CD24) are not. Early results showed that invasive CD44+ prostate cells also had increased expression of Nanog, BMI1 and SHH, which is similar to CD133+ cells. The standard CD44 (CD44s) molecule is an 85- to 90-kDa transmembrane glycoprotein containing 10 standard exons and four major domains.

Stem cell transplantation:

Stem cell transplant is a procedure that replaces defective or damaged cells in patients whose normal blood cells have been affected by cancer. There are three types of stem cell transplantation:

Autologous transplant: Cells are harvested from the patient's own bone marrow before chemotherapy and are replaced after cancer treatment.

Allogeneic transplant:

Stem cells come from a donor whose tissue most closely matches the patient.

Umbilical cord blood from newborn infants is extracted from the placenta after birth and saved in special cord blood banks for future use. Stem cell transplants commonly are used to treat leukemia and lymphoma, cancers which affect the blood and lymphatic system. Transplants also can be used to help patients recover from or better tolerate cancer treatment, and to treat hereditary blood disorders such as sickle cell anemia. (Koenig M, Hoffman EP)

Finding stem cell donors

Stem cell transplant patients are matched with eligible donors by human leukocyte antigen typing. HLA are proteins that exist on the surface of most cells in the body. HLA markers help the body distinguish normal cells from foreign cells, such as cancer cells. The best match is usually a first degree relative. However, about 75% of patients do not have a suitable donor in their family and require cells from matched unrelated donors (MUD), who are located through registries such as the National Marrow Donor Program. (Croker AK)

4. Conclusion

The uses of multidisciplinary approach cancer therapy have been made in the treatment of cancer. There is increasing awareness that cancer stem cells represent a significant

challenge to effective treatment of cancer as they are resistant to current clinical drugs. The ultimate challenge in coming years will be the understanding of the stem cell programmes, particularly the control of self renewal, in an attempt to develop novel, stem cell-directed therapies. Carcinogenesis is a multi-step process related to the accumulation of genetic and epigenetic changes. At the molecular level, alterations in signalling pathways responsible for self-renewal of SCs are crucial in transformation of SCs into CSCs. While proceeding of Stem cell transplantation, we can treat the cancer stem cells.

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