Review Article:

Stem cells in health and disease

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ABSTRACT: Research on stem cells is advancing knowledge about how an organism develops from a single cell and how healthy cells replace damaged cells in adult organisms. This promising area of science is also leading scientists to investigate the possibility of cell-based therapies to treat disease, which is often referred to as regenerative or reparative medicine. Stem cells are one of the most fascinating areas of biology today. But like many expanding fields of scientific inquiry, research on stem cells raises scientific questions as rapidly as it generates new discoveries.

Key words:- Embryonic, Health, Medicine Stem cells.

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INTRODUCTION: Although the concept of a niche is an old one, it is an idea that has received a fair amount of attention recently. The niche really is a microenvironment in which the organism or the entity not only resides, but is regulated and nurtured. This comparison can be drawn for stem cells because they live, are regulated, and nurtured in a stem cell-specific microenvironment. The niche is also the place where the stem cell reproduces or self-renews. Thus, the stem cell niche is an anatomically defined space where

molecular interactions guide spatial relationships. The niche balances sustaining and constraining elements to tightly regulate stem cell number and function and has the ability to modulate these cells under conditions of physiologic change.[1]

STEM CELLS AND ITS IMPORTANCE

The term stem cell was proposed for scientific use by Russian histologist Alexander Maksimov in 1908. Stem cells are defined functionally as cells with unique capacity to self renew as well as to give rise to differentiated cells throughout the life time of the organism. [2]

Stem cells have two important characteristics that distinguish them from other types of cells.

1) They are unspecialized cells that renew themselves for long periods through cell division.

2) Secondly is that under certain physiologic or experimental conditions, they can be induced to become cells with special functions such as the beating cells of the heart muscle or the insulin-producing cells of the pancreas.

PROPERTIES OF STEM CELLS

Stem cells differ from other kinds of cells in the body. All stem cells-regardless of their source-have three general properties: they are capable of dividing and renewing themselves for long periods; they are unspecialized; and they can give rise to specialized cell types.[3, 4]

Stem cells can be broadly classified into three categories, according to their source of derivation

1. Embryonic stem cells
2. Adult stem cells
3. Cord derived embryonic like stem cells

These can also be classified according to their proliferative capacity

1. Totipotent stem cells (ability to form the embryo and the trophoblasts of the placenta)- Zygote
2. Pluripotent stem cells (ability to differentiate into almost all cells that arise from the three germ layers)- embryonic cells
3. Multipotent stem cells (capability of producing a limited range of differentiated cell)- tissue based stem cells
4. Unipotent stem cells (only able to generate one cell type)-epidermal stem

cells and spermatogonial cells of testis.

EMBRYONIC STEM CELLS

Embryonic stem cells are derived from embryos that develop from eggs that have been fertilized in vitro - in an in vitro fertilization clinic -and then donated for research purposes with informed consent of the donors and are not derived from eggs fertilized in a woman's body. [5, 6]

How are embryonic stem cells stimulated to differentiate?

As long as the embryonic stem cells in culture are grown under certain conditions, they can remain undifferentiated. But if cells are allowed to clump together to form embryoid bodies, they begin to differentiate spontaneously. They can form muscle cells, nerve cells, and many other cell types.

ADULT STEM CELLS

An adult stem cell is an undifferentiated cell found among differentiated cells in a tissue or organ, can renew itself, and can differentiate to yield the major specialized cell types of the tissue or organ. The primary roles of adult stem cells in a living organism are to maintain and repair the tissue in which they are found.

Unlike embryonic stem cells, which are defined by their origin the origin of adult stem cells in mature tissues is unknown.[7, 8]

Adult stem cell differentiation

Adult stem cells occur in many tissues and that they enter normal differentiation pathways to form the specialized cell types of the tissue in which they reside. Adult stem cells may also exhibit the ability to form specialized cell types of other tissues, which is known as Transdifferentiation or plasticity. [9]

Normal differentiation pathways of adult stem cells: In a living animal, adult stem cells can divide for a long period and can give rise to mature cell types that have characteristic shapes and specialized structures and functions of a particular tissue.

Adult stem cell plasticity and Transdifferentiation: A number of experiments have suggested that certain adult stem cell types are pluripotent. This ability to differentiate into multiple cell types is called plasticity or transdifferentiation. [10]

SIMILARITIES AND DIFFERENCES BETWEEN EMBRYONIC AND ADULT STEM CELLS

1. Embryonic stem cells can become all cell types of the body because they are pluripotent. Adult stem cells are generally limited to differentiating into different cell types of their tissue of origin.
2. Large numbers of embryonic stem cells can be relatively easily grown in culture, while adult stem cells are rare in mature tissues and methods for expanding their numbers in cell culture have not yet been worked out.
3. A potential advantage of using stem cells from an adult is that the patient's own cells could be expanded in culture and then reintroduced into the patient. The use of the patient's own adult stem cells would mean that the cells would not be rejected by the immune system. This represents a significant advantage as immune rejection is a difficult problem that can only be circumvented with immunosuppressive drugs.[11,12]
4. Embryonic stem cells from a donor introduced into a patient could cause transplant rejection. However, whether the recipient would reject donor embryonic stem cells has not been determined in human experiments.

Cord Blood Stem Cells: Cord blood stem cells are derived from umbilical cords or a placenta after a baby's birth.

STEM CELL APPLICATIONS [13]

Stem Cell Treatment of Diabetes

Stem cells potentially could be used to effectively resist immune attack as well as graft rejection. The discovery of methods to isolate and grow human Embryonic Stem cells raises hopes of doctors, researchers, and patients that a cure for type I diabetes, and perhaps type II diabetes, is within reach.

Nervous System Diseases

Nervous system diseases result from a loss or damaging of nerve cells. Scientist

Previously thought that mature nerve cells do not divide, and so there is no way to replace those neurons that are destroyed. Neurons can be induced to regrow using either ES cells to differentiate into neurons, or using adult neural stem cells (NSCs) to divide into more neurons. The most effective treatment for these health issues comes from the possibility to create new nerve tissues from pluripotent ES cells.

Adult stem cells from bone marrow also surprisingly have the potential to be useful for the treatment of nervous system

disorders due to their apparent ability to Trans-differentiate into non-blood tissues. Studies have shown that these bone marrow-derived cells are capable of changing into neuronal cells that can integrate in the brain. [14]

Neural Stem Cells to Treat Parkinson's Disease

Stem cells also offer hope to patients with Parkinson's disease, which is caused by the loss of dopamine-producing nerve cells in the brain. If stem cells can be cultivated to become these dopamine-producing nerve cells, researchers believe that they could replace the lost cells. [15]

In recent human clinical trials, fetal brain tissues were transplanted into the brains of Parkinson's disease patients, and the results showed major and long-lasting improvements in some of the patients

Neural Stem Cells to Treat Alzheimer's Disease

Sugaya and his colleagues hope to eventually show that stem cells transplanted from a patient's blood or bone marrow will be an effective treatment for Alzheimer's and other neurological diseases because they can replace cells that die from those ailments. [16]

Neural Stem Cells to Treat Stroke

Strokes cause temporary loss of blood supply to the brain which results in areas of brain tissue dying, causing the loss of certain bodily functions such as speech and motor skills. Neural stem cells offer new possibilities for brain tissue regeneration which could help stroke victims. However, there are still major limitations in delivering these cells to the brain. While NSC transplantation has been proven to improve conditions in rats with stroke damage, little reduction in lesion volume has been observed.[16]

Stem Cell Treatment of Damaged Heart Muscle

New studies have shown that stem cells might be used to treat patients who have suffered from a heart attack. By injecting bone marrow stem cells into damaged tissues of the heart, new vascular endothelium, cardio myocytes, and smooth muscle cells can be formed.

Stem Cell Treatment of Primary Immunodeficiency Diseases

Pluripotent stem cells could potentially be used in the treatment of virtually all primary immunodeficiency diseases. These diseases are characterized by a high susceptibility to infection and are often associated with anemia, arthritis, and diarrhea. However, the

transplantation of stem cells engineered with the normal gene could result in recovery of the immune function. Successful transplantation could increase the life span and quality of life for these people. [17]

Researchers from the AIDS Institute and the Institute for Stem Cell Biology and Medicine have demonstrated that human embryonic stem cells can be genetically manipulated and "coaxed" to develop into mature T-cells. T-cells are one of the body's main defenses against infection and disease, and are lowered in patients infected with HIV. The new T-cells create possibilities for a gene therapy to combat AIDS. The study suggests that it is possible to convert human embryonic stem cells into blood-forming stem cells that can differentiate into the helper T-cells that HIV specifically targets.

Stem Cell Treatment of Cancer

Stem cells can be damaged in certain cancer treatments. The cancer stem cell hypothesis is a departure from traditional models of Oncogenesis, which proposed that genetic alterations transform mature, differentiated cells into cancer cells. Cancer stem cells, however, help explain two of the most challenging and demoralizing aspects of cancer: remission and recurrence. Often, radiation or chemotherapy halts the malignancy, sometimes to the point where it can no longer be detected, yet the disease returns. Cancer stem cells may be especially resistant to eradication for two reasons.

First, current chemotherapies selectively target rapidly dividing cells, but stem cells tend to divide at a slow rate.

Second, normal stem cells congregate in niches—specific physical areas within an organ that protect stem cells.

Cancer stem cell niches have been found in the brain and proposed elsewhere, making radiation and chemotherapy treatment even more complicated. If even a small number of cancer stem cells survive an assault, they can once again give rise to full-fledged cancer as metastases result from the surviving cancer stem cells that travel through the body.

At the present time, adult bone marrow stem cells are used to treat patients following high doses chemotherapy. These treatments using stem cells may also be used for patients who have had radiation treatment for their cancer. Unfortunately, bone marrow cells are somewhat limited in their capacity to restore immune function completely, so researchers are working to develop injections of properly-differentiated stem cells that would return the complete functionality of the immune system to patients undergoing bone marrow transplantation. [18]

There are 3 types of stem cell transplants:

1. Autologous stem cell transplants
2. Allogenic stem cell transplants
3. Syngenic stem cell transplants.

Stem cells have provided new hope for many patients who suffer from a large range of diseases that currently have little or no therapeutic treatments. Advancements in this particular medical field have shown the potential of many

To realize the promise of novel cell-based therapies for such pervasive and debilitating diseases, scientists must be able to easily and reproducibly manipulate stem cells so that they possess the necessary characteristics for successful differentiation, transplantation and engraftment.

REFERENCES

1. Jackson L, Jones DR, Scotting P, Sottile V. Adult mesenchymal stem cells: Differentiation potential and therapeutic applications. Journal of Postgraduate Medicine 2007:53, 121-127.
2. Scadden DT. The stem cell niche in health and leukemic disease. Best Pract Res Clin Haematol. 2007 March; 20(1): 19–27.
3. Pittenger MF, Mackay AM, Beck SC, Jaiswal RK, Douglas R, Mosca JD et al. Multiline age potential of adult human mesenchymal stem cells. Science 1999; 284:143-7.
4. Sakaguchi Y, Sekiya I, Yagishita K, Muneta T. Comparison of human stem cells derived from various mesenchymal tissues: Superiority of synovium as a cell source. Arthritis Rheum 2005; 52:2521-9.
5. Zuk PA, Zhu M, Mizuno H, Huang J, Futrell JW, Katz AJ et al. Multiline age cells from human adipose tissue: Implications for cell-based therapies. Tissue Eng 2001;7:211-28
6. Igura K, Zhang X, Takahashi K, Mitsuru A, Yamaguchi S, Takashi TA. Isolation and characterization of mesenchymal progenitor cells from chorionic villi of human placenta. Cytotherapy 2004; 6: 543-53.
7. Halleux C, Sottile V, Gasser JA, Seuwen
8. K. Multi-lineage potential of human mesenchymal stem cells following clonal expansion. J Musculoskelet Neuronal Interact 2001; 2:71-6.
9. Friedman MS, Long MW, Hankenson KD. Osteogenic differentiation of human mesenchymal stem cells is regulated by bone morphogenetic protein-6. J Cell Biochem 2006; 98:538-54.
10. Hellmann MA, Panet H, Barhum Y, Melamed E, Offen D. Increased survival and migration of engrafted mesenchymal

bone marrow stem cells in 6-hydroxydopamine-lesioned rodents. Neurosci Lett 2006; 395:124-8.

11. Keilhoff G, Goihl A, Langnase K, Fansa H, Wolf G. Transdifferentiation of mesenchymal stem cells into Schwann cell-like myelinating cells. Eur J Cell Biol 2006; 85:11-24.
12. Halleux C, Sottile V, Gasser JA, Seuwen K. Multi-lineage potential of human mesenchymal stem cells following clonal expansion. J Musculoskelet Neuronal Interact 2001; 2:71-6.
13. Zvaifler NJ, Marinova-Mutafchieva L, Adams G, Edwards CJ, Moss J, Burger JA et al. Mesenchymal precursor cells in the blood of normal individuals. Arthritis Res 2000; 2:477-88.
14. Trounson A. New perspectives in human stem cell therapeutic research. BMC Medicine 2009, 7:29.
15. Gage FH. Mammalian neural stem cells. Science 2000; 287: 1433-8.
16. Garfinkel, Susan (2005) "Stem Cells and Parkinson's Disease." International Society for Stem Cell Research. 31 Mar. 2005.
17. Lindvall O, Kokaia Z. Stem Cells for the Treatment of Neurological Disorders 2006. Nature 441: 1094-1096.
18. Uccelli A, Moretta L, Pistoia V. Immunoregulatory function of mesenchymal stem cells. Eur J Immunol 2006; 36:2566-73.
19. Dalerba P et al. "Cancer Stem Cells: Models and Concepts," Annu. Rev. Med. 2005, 58:267-84.

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