



Progress in Stem Cell Research Opens New Avenues for Degenerative Diseases

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Editorial

Stem cells have the unique ability to divide continuously. They are found in various parts of our body, from the early stages of human development to adulthood. Stem cells are the “master” cells that transform into cells of brain, nerves, muscles, and other body parts. German biologist Ernst Haeckel coined the term stem cell to describe the fertilized egg that becomes an organism. Current stem cell research is generating strong evidences about how healthy stem cells, when under the right conditions or signals, can give rise to differentiated cells. Stem cell research is an emerging field of inter disciplinary research with clinical implications focused on repair, replacement or regeneration of cells to salvage impaired organ function. There are two broad types of stem cells, Embryonic Stem cells (ES cells) and Adult stem cells. ES cells are pluripotent stem cells derived from the inner cell mass of a blastocyst, an early-stage of embryo. Human embryos reach the blastocyst stage in 4–5 days post fertilization and isolating the embryo blast, or inner cell mass, results in destruction of the blastocyst, which raises ethical issues. Meanwhile, adult stem cells are present in various parts of tissues. Scientific interest in adult stem cells is centered on their ability to divide or self-renew indefinitely and generate all cell types of the organ from which they originate, potentially regenerating the entire organ from a few cells. Unlike for embryonic stem cells, the use of human adult stem cells in research and therapy is not considered to be controversial, as they are derived from adult tissue samples rather than human embryos designated for scientific research. Adult stem cells can be distinguished to different type’s viz., hematopoietic stem cells, mammary, intestinal, mesenchymal, endothelial, neural, olfactory, neural crest and testicular stem cells.

Stem cell therapy

Regenerative medicine is an emerging branch of medicine with the goal of restoring organ and tissue function for patients with serious injuries or chronic disease in which the body's own responses are not sufficient enough to restore functional tissue. A growing crisis in organ transplantation has driven a search for new and alternative therapies. New and current regenerative medicines use stem cells to create living and functional tissues to regenerate and repair tissue and organs in the body that are damaged due to age, disease and congenital defects. Stem cells have the power to go to these damaged areas and regenerate new cells and tissues by performing a repair and a renewal process, restoring functionality. Two key types of stem cell that are currently showing great promise to clinical applications for mankind such as, Hematopoietic Stem Cells (HSCs) and Mesenchymal Stem Cells (MSCs). HSCs found in the cord blood and peripheral blood is multipotent stem cells that have the potential to differentiate mainly into blood components such as red blood cells, white blood cells, platelets, etc. Whereas, MSCs found in the Wharton’s Jelly, bone marrow, fat tissue and tooth pulp are multi potent stem cells that have the potential to differentiate into a wide range of cells and tissues such as Fat, liver, nerve, muscle, Heart, bone and cartilage.

Hematopoietic Stem Cells (HSCs)

Hematopoietic Stem Cells (HSCs) are the stem cells that give rise to all the other blood cells through the process of hematopoiesis. They are derived from mesoderm and located in the red bone marrow, which is contained in the core of most bones. HSCs give rise to both the myeloid and lymphoid lineages of blood cells (Myeloid cells include monocyte, macrophages, neutrophils, basophils, eosinophils, erythrocytes, dendritic cells and megakaryocytes or platelets. Lymphoid cells include T cells, B cells, and natural killer cells. Hematopoietic Stem Cell Transplantation (HSCT) is the transplantation of multipotent hematopoietic stem cells, usually derived from bone marrow, peripheral blood, or umbilical cord blood, and amniotic fluid. It may be autologous (the patient's own stem cells), allogeneic (stem cells from a donor) or syngeneic (from an identical twin). It is a medical procedure in the field of hematology often performed for patients with certain cancers of

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Received Date: 24 Oct 2017

Accepted Date: 28 Dec 2017

Published Date: 03 Jan 2018

Citation:

Srivastava A. Progress in Stem Cell Research Opens New Avenues for Degenerative Diseases. *Ann Stem Cell Res Ther.* 2018; 1(1): 1005.

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the blood or bone marrow, such as multiple myeloma or leukemia.

- Acute Myeloid Leukemia (AML)
- Chronic Myeloid Leukemia (CML)
- Acute Lymphoblastic Leukemia (ALL)
- Hodgkin Lymphoma (HL) (relapsed, refractory)
- Non-Hodgkin Lymphoma (NHL) (relapsed, refractory)
- Neuroblastoma
- Ewing sarcoma
- Multiple myeloma
- Myelodysplastic syndromes
- Gliomas other solid tumors
- Thalassemia
- Sickle cell anemia
- Aplastic anemia
- Fanconi anemia
- Malignant infantile osteoporosis
- Immune deficiency syndromes
- Autoimmune diseases

Mesenchymal Stem Cells (MSCs)

Mesenchymal Stem Cells (MSCs) are an attractive source of stem cells for clinical applications, and MSCs exhibit a multilineage differentiation potential and strong capacity for immune modulation. Thus, MSCs are widely used in cell therapy, tissue engineering, and immunotherapy. Mesenchymal stem cells (MSCs) are one of the most studied and applied types of stem cells to date. These cells were first described by Friedenstein, 1966 as a cell population similar to fibroblasts, which can differentiate into multiple cell types such as osteoblasts, adipocytes, and chondrocytes. MSCs have been isolated from many tissues including bone marrow, adipose tissue, peripheral blood, Umbilical Cord Blood (UCB), umbilical cords, placenta, amniotic fluid, dental pulp and menstrual blood. Compared with other stem cell sources, UCB-MSCs have advantages such as non-invasive recovery, the abundance of MSCs, and well-known characteristics. In both pre-clinical and clinical settings, MSCs have been studied to treat a various diseases. Pre-clinically, UCB-MSCs have been used to treat

neonatal brain injury, fibro-cartilaginous embolic myelopathy, spinal cord injury, diabetic renal injury, bone loss, ischemia, hearing loss, damaged corneal endothelium, Alzheimer's disease, acute hepatic necrosis, diabetes mellitus and liver cirrhosis. Clinically, UCB-MSCs have been transplanted for treatment of autism, hereditary spinocerebellar ataxia, foot disease in patients with type 2 diabetes mellitus, and basilar artery dissection. Clinical trials on mesenchymal stem cell transplantation for engraftment of unrelated hematopoietic stem cell transplantation; treatment of steroid-refractory; articular cartilage defect treatment and hematologic malignancy treatment are the some recent investigations. About 2287 stem cell based clinical trial has been completed till date and 1451 studies are under investigation.

Induced Pluripotent Stem Cells (iPSCs)

iPSCs are adult cells that have been genetically reprogrammed to an embryonic stem cell-like state by being forced to express genes and factors important for maintaining the defining properties of embryonic stem cells. In 2006, Takahashi and Yamanaka demonstrated that by introducing four genes, Oct4, Sox2, Klf4, and cMyc, into a differentiated mouse cell, the cell could become pluripotent again. These "reprogrammed" cells were similar to mES cells. Meanwhile, Human iPSCs were first reported in 2007, it expresses stem cell markers and capable of generating cells characteristic of three germ layers (ectoderm, mesoderm, and endoderm). OCT4 is a key transcription factor for reprogramming and cell type Tran's differentiation and also plays an important role in maintaining pluripotency and self-renewal of PSCs. Methods for creating iPSCs are continuously evolving. Presence of a single transcription factor, Oct4, was enough to induce pluripotency in a certain cell type. The introduction of this factor can be done through lent virus transduction, electroporation, or the transcription factor itself. A recent report evident that Tran's differentiation of human hair follicle mesenchymal stem cells into red blood cells by OCT4. However, some risk factors in stem cell therapy are present; the major concern with the possible transplantation of ESC and iPSCs into patients is that it can form tumors including teratoma. Teratoma formation is considered a major obstacle in regards to stem-cell based regenerative medicine by the US-FDA. Once we review the available data and sketch a picture, it seems clear that for several degenerative diseases, that do not have credible answers, stem cell may provide a credible and natural treatment option. I appreciate the work of all the researchers who brought stem cell science at the present level, which has begun to open new avenues for treatment of several devastating metabolic and degenerative diseases.