Review Article

Review on Stem Cells: Basics Classification and Applications

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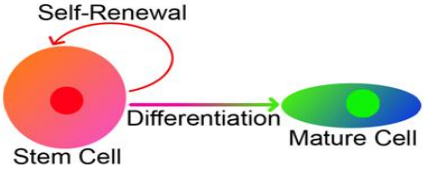
ABSTRACT

Stem cells are unspecialized cells that are capable self replication and under certain conditions are also capable of giving rise to various cell types. Stem cells responsible for the development and repair of tissues or organs in a multicellular organism. Stem cells can be categorized on two basis: (1) on basis of origin and (2) on basis of potency. In the era of rising antimicrobial resistance, stem cells emerge as an important research topic for scientists as an alternate treatment method. Research and experiment on stem cell mediated therapies hold tremendous promise due to the unique properties of stem cells. Stem cell mediated therapies show potential of providing treatment for previously untreatable illness or genetic defects. Despite the opposition faced on study of stem cells, they are nowadays becoming the norm and requirement. In this research review we will be focusing on what are stem cells, their types and future applications.

Keywords: Stem cells, potency, antimicrobial resistance, Stem cell mediated therapy, genetic defects.

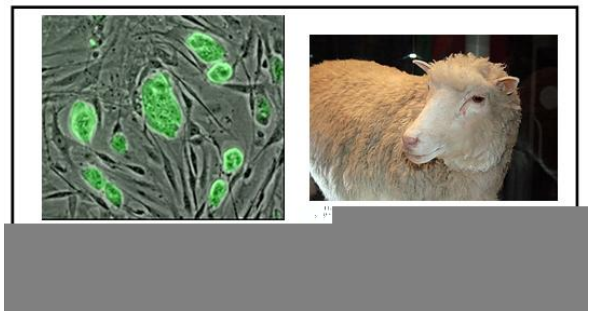
INTRODUCTION

Stem cells are defined as unspecialized clonogenic cells that are capable of self replication. Stem cells are also capable of giving rise to specialized cells through differentiation. Stem cells are found in all of us from early embryonic development to adult growth stages. Stem cells are pluripotent, hence are able to differentiate into a wide variety of specialized adult cells. Stem cells can be more accurately be defined by 3 unique properties. These properties are (a) the unspecialized nature of stem cells , one of the fundamental property of stem cell is that it is devoid of any tissue specific structures that allow it to perform specialized functions; (b) they capable of self renewal , unlike specialized cells stem cells are capable of dividing and renewing themselves for a long period of time; (c) they exhibit potency , stems cells are capable of giving rise to various specialized cells through the process of differentiation (image 1 given below). It is due to these unique properties that stem cells are studied extensively for future therapeutic developments. For decades researchers have been researching stem cells to understand their origin and development. This is done to further utilise the unique properties of stem cell to regain the totipotent ability lost by us during the course of evolution for treatment of lost or damaged organs. Hence many of the therapeutic treatments nowadays utilize stem cells. This review focuses on stem cell types, their sources, stem cell research and future aspects.



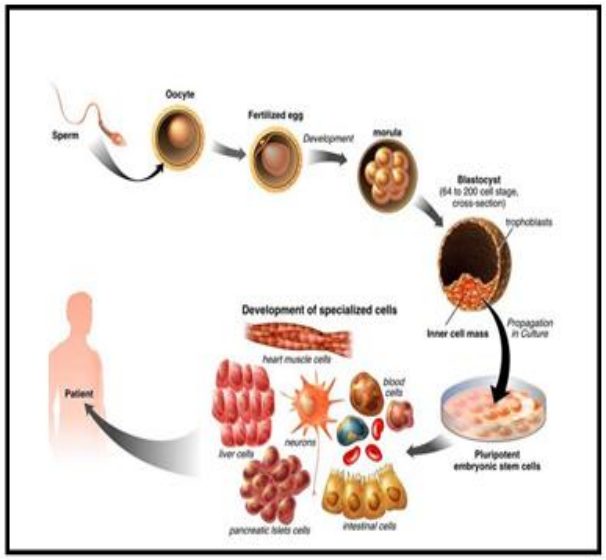
Historical Perspective

The very beginning of stem cell research had been a benign, embryonic beginning in the mid 1800s with discovery of some cells that were capable of generating other cells. In the 1900s the first real stem cells were discovered when it was found that some cells were capable to generate red blood cells. In 1908 Russian histologist Alexander Maksimov proposed the term "stem cell". The discovery of Haemopoietic stem cells in 1978 was due to the bone marrow transplant between two sibling in 1968 to successfully treat SCID.In 1981, the first in vitro stem cell line was developed from mice (image 2(a) given below).In 1988, the embryonic stem cell line was created from a hamster. In 1995, the first embryonic stem cell line was derived from a primate. In 1997, Leukaemia origin found in haemopoietic stem cell thereby indicating proof of cancer stem cells. In 1997, Ian Wilmut and his colleagues at Roslin Institute, Edinburgh created Dolly the sheep (image 2(b) given below), the first artificial animal clone speculated to be created by manipulations to embryonic stem cells.



In 1998, James Thomas and co-workers derived the first human embryonic stem cell line at the University of Madison - Wisconsin. During the same year Gearhart

from John Hopkins University derived germ cells from cells in foetal gonad tissue.Through both the sources pluripotent stem cell lines were developed (image 3 see below). Newcastle University,England scientists created the first ever artificial liver cells using umbilical cord blood stem cells in October 2006. In 2006, Shinya Yamanaka of Kyoto University,Japan discovered a way making embryonic-like cells from adult cells.His team reprogrammed ordinary adult stem cells by inserting 4 key genes forming "induced pluripotent stem cells (iPSCs)" for they won nobel prize in 2012.In 2006,Mario Capecchi, Martin Evans and Oliver Smithies won the 2007 nobel prize for their work on embryonic stem cells from mice using gene targeting strategies producing genetically engineered mice (known as "knockout mice") for gene research. In 2010, a person with spinal injury became the first to receive a medical treatment derived from human embryonic stem cells as a part of trial by Geron of Menlo Park,California a pioneering company for human embryonic stem cell therapies.In 2013, Shoukhrat Mitalipov at the Oregon National Primate Research Centre,Beaverton and his colleagues produced human embryonic stem cells from foetal cells using therapeutic cloning.In 2014, Charles Vacanti of Harvard Medical School together with Haruko Obokata at the Riken Centre for Developmental Biology in Kobe,Japan and his colleagues made a revolutionary discovery that any cell could potentially be rewound to a pre-embryonic state.In 2014, teams led by Dieter Egli of the New York Stem Cell Foundation and Young Gie Chung from CHA University, Seoul independently produced human embryonic stem cells from adult cells using therapeutic cloning.



Stem Cell

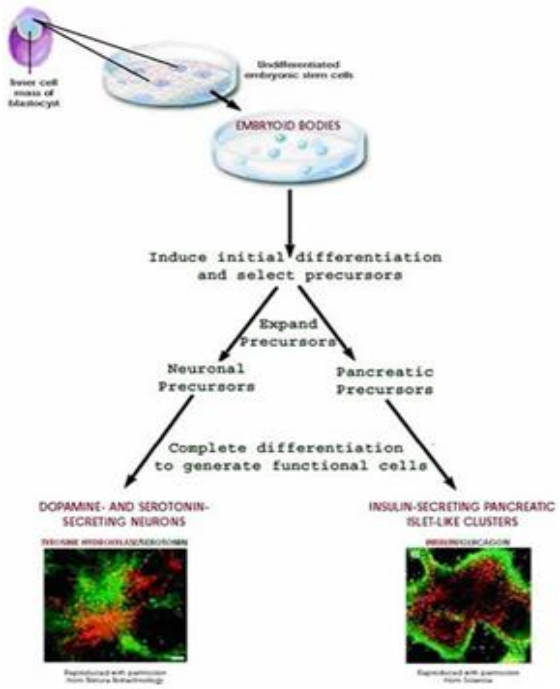
Stem cells are defined as unspecialized generic cells that are capable of self renewal and which exhibit potency that is it exhibits property of differentiation to produce serialised cells. They can be found in most multicellular organism. Stem cells are important for living organisms for various reasons. In the 3 to 5 day old embryo called blastocyst, the inner cells give rise to the entire body of the organism, including all of many specialised cell types and organs such as heart, lungs, skin, etc.(image 3 see above) . In some adult tissues such a s bone marrow, muscle, and brain,discrete populations of adult stem cells generates replacements for cells that are lost through normal wear and tear, injury, or disease. Given to their unique abilities stem cells offer new potentials for treating diseases such as diabetes, heart diseases and more. However much research is needed in the laboratories and clinic to understand how to use stem cell based therapies for disease treatment.

Classification of Stem Cell on The Basis of Their Sources

The easiest way to categorize stem cells is by dividing them into 2 types: early or embryonic and mature or adult. There is also a third type of stem cells discovered called induced pluripotent stem cells (iPSCs).

Embryonic Stem Cells

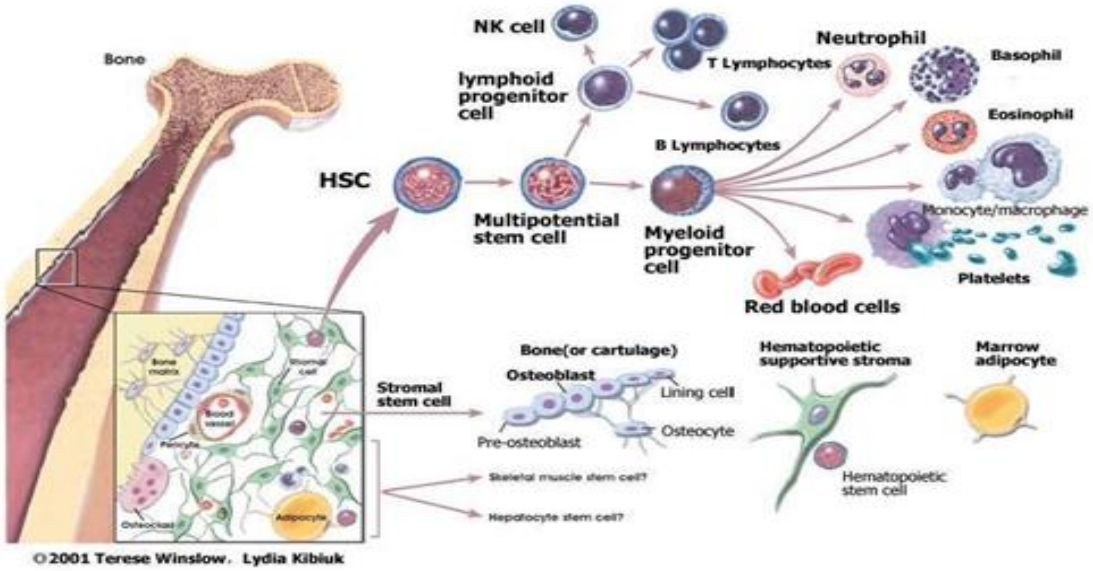
Embryonic stem cells as the name suggests are mostly derived from embryos at a developmental stage before the time of implantation would naturally occur in uterus. The embryonic stem cells are typically derived from blastocyst.A blastocyst 3-5 day old and are a hollow microscopic mass of cells. Differentiation in embryonic stem cells occurs if they are allowed to clump together to form embryoid bodies .The differentiation of embryonic stem cells are spontaneous and uncontrolled. Therefore many scientists have established some basic protocols or "recipes" for the directed differentiation of embryonic stem cells to desired specialised cells through years of experimentation by scientists (image 4 given below).



Adult Stem Cells

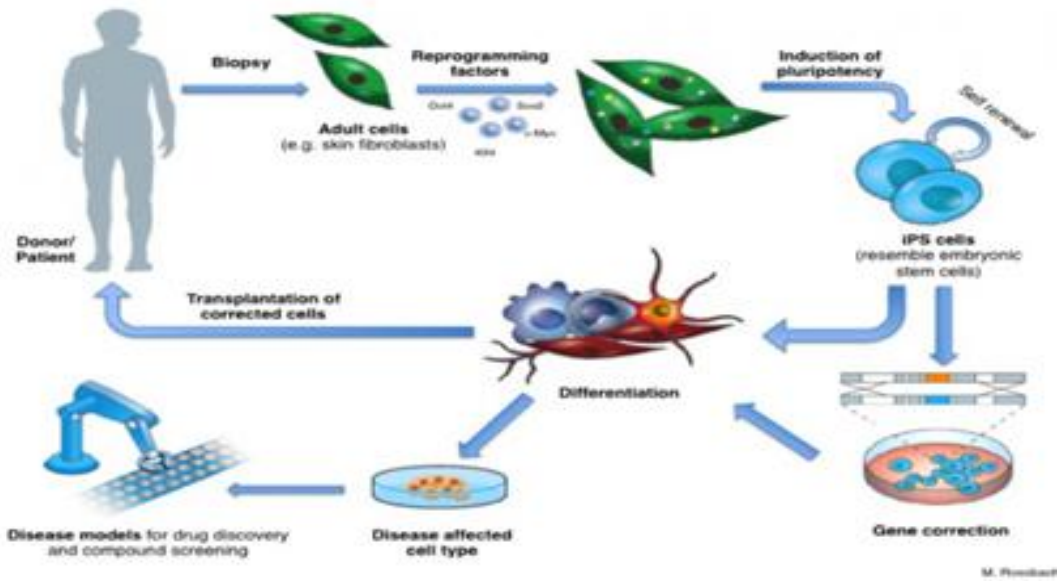
The adult stem cells are also called as "somatic stem cell" (where somatic refers to the body).These cells are thought to be undifferentiated cells found amongst

differentiated or specialized cells in a tissue or organ. Adult stem cell can differentiate to yield most specialized cells of the tissue or organ they originate from, hence differentiation in adult stem cells is highly localised.The primary role of adult stem cell in an organism is to maintain and repair tissue in which they are found. Adult stem cells appear in body after embryonic development. Adult stem cells are thought to reside in a specific area of each tissue termed as "stem cell niche".



Induced Pluripotent Stem Cells (Ipscs)

Induced pluripotent stem cells are the most recently discovered stem cell type. These stem cells were originally adult stem cells that were genetically reprogrammed to behave as embryonic stem cell-like. This is done genetically modifying the adult stem cells to express genes and factors important for maintaining the defining characteristic of embryonic stem cells.



Classification of Stem Cells Based on Potency

On the basis of their extent of differentiation stem cells are categorised into 5 main types (image 7 given below):

Totipotent

A stem cell is said to be totipotent when that stem cell can differentiate into all cell types. Zygote cell and morula formed after mitotic division in zygote cell are examples of totipotent stem cell.

Pluripotent

A stem cell with the ability to differentiate into almost all cell types but not all is said to be Pluripotent in nature. Embryonic stem cells and cells that are derived from endoderm, mesoderm and ectoderm germ layers that are found in the beginning of embryonic development.

Multipotent

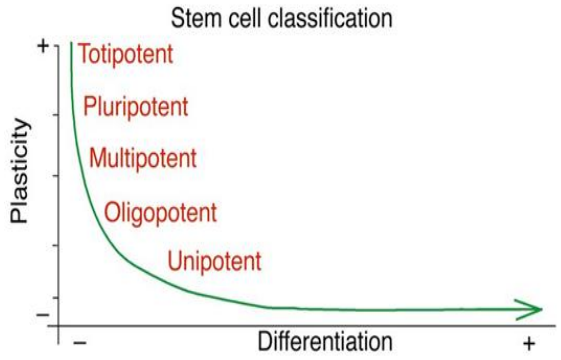
A stem cell with the ability to differentiate into a closely related family of cells. For example Hematopoietic adult stem cells can differentiate to become red blood cells, white blood cells or platelets.

Oligopotent

A stem cell with the ability to differentiate into only a few cells is termed as oligopotent in nature. For example lymphoid or myeloid adult stem cells.

Unipotent

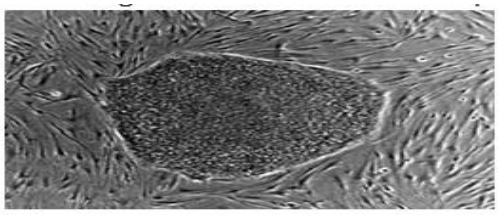
A stem cell with the ability to only produce cells of their own type but have the property of self replication required to be called a stem cell. For example muscle adult stem cells.



Stem Cell Culture

Stem cell culture is growing of stem cells in the laboratory under aseptic conditions. Human embryonic stem cells (hESCs) are generated by transferring stem cells from a preimplantation stage namely "blastocyst" of embryo into a plastic laboratory culture dish that contains nutrient broth known as "culture medium". In earlier protocol the culture dish contains an inner coating of feeder layer which consist of mouse embryonic skin layer that are treated so they would not divide and provide a sticky layer for the human embryonic stem cells (image 8 given below). The feeder cell also releases nutrients into culture medium thereby extending the shelf life of the culture. Though nowadays stem cells are cultured without feeder layer to avoid contamination of the stem cell culture via unwanted viruses or macromolecules found in mouse cells.

Sub-culturing is the process of re-plating the stem cell culture when they become crowded after a period of multiplication. The process of sub-culturing the cells is repeated many times and each cycle of sub-culturing the cells is referred to as a passage.



Stem Cell Lines

The stem cells that have been allowed to divide and propagate in a controlled culture and aseptic environment. The collection of healthy, dividing, and undifferentiated stem cells is referred to as a stem cell line. Stem cell line is generally obtained from human or animal tissues and can replicate for long periods of times in in-vitro (in laboratory) conditions.

Possible Treatments by Stem Cells

A number of stem cells therapies exist, but most are still in their experimental stage and are costly with the notable exception of bone marrow transplantation. Medical researchers anticipate that stem cells would be able to treat cancer, type I diabetes mellitus, Parkinson's disease, spinal injuries, blindness, Huntington's disease, cardiac failure, muscular damages and neurological disorders, etc..Though before stem cell therapies can be applied in a clinical setting more research is required to understand stem cell behavior upon transplantation as well as mechanism of stem cell interaction with diseased or injured microenvironment. Some of the stem cell treatments are described below (image 9 given below):

Skin replacement

Through stem cells scientists have made it possible to grow new skin using the patient's plucked hair. Skin (keratinocyte) stem cell resides in the hair follicle which can be obtained easily by plucking patient's hair. Such cells cultured to form an epidermal equivalent of the patients own skin and provides tissue for an autologous graft, bypassing the rejection of the graft.

Parkinson's treatment

Stem cells can provide dopamine -a neurotransmitter chemical lacking in Parkinson patients. The first double-blind study of fatal cell transplants for Parkinson's disease reportedly survived and released dopamine from transplanted cells and a functional improvement of clinical symptoms. However some patients developed side effects which suggested that there was over sensitization to dopamine because of its excess secretion.

Diabetes treatment

Diabetes is caused due to abnormal metabolism of insulin. Insulin is produced and secreted by structures called the islets of langerhans in the pancreas. Recently, insulin expressing cells from mouse stem cells have been generated. In addition, the cells self assemble to form structures, which closely resemble normal pancreatic islets and produce insulin. Further research is required to understand how to optimize conditions for insulin production with the aim providing a stem cell based therapy to treat diabetes and replace the constant need of insulin injections.

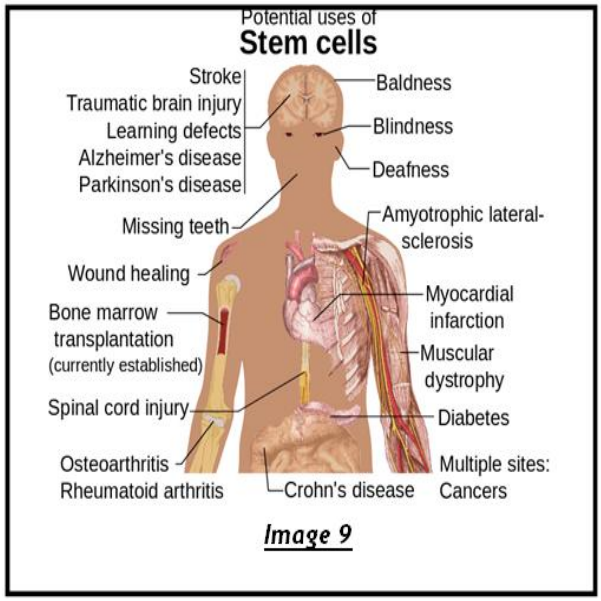


Image 9

Treatment for spinal cord injury

Adult stem cells nowadays are utilized to treat spinal cord injuries. The adult stem cells used treat spinal cord injury generally comes from two sources: the patients' own bone marrow (antilogous mesenchymal and CD34+) and human umbilical cord tissue (allergenic mesenchymal). Umbilical cords are donated by mothers after normal, healthy births. The body's immune system is unable to recognize umbilical cord derived mesenchymal stem cells as foreign therefore reduces the dangers of rejection. Umbilical cord derived mesenchymal stem cells also proliferate more efficiently than "older" cells, such those found in the fat and hence considered more "potent". These are administered to the patient in form of injections.

CONCLUSION

Through this review paper we can understand the importance of continual of stem cell research to improve and discover new methods of curing otherwise incurable diseases providing a glimmer of hope for the patients. Stem cells also play a big role in stem cell mediated therapies considering the rising threat of antimicrobial resistance as a more effective alternate treatment method.

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