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STEM CELL THERAPY FOR HUMAN DISEASES

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ABSTRACT

Stem cells are human body's master cells with ability to grow into more than 200 cell types. They are unspecialized cells which retain the ability to divide and can became highly specialized. They contribute to the bodies and ability to renew and maintain cells. They move to target areas and transform into any type of tissues. For example muscles or nerves. And it's also replace damaged cells. Now a days we can extract this cells, grow artificially it is used to transplant them into the body to treat neurodegenerative disease. The research helps to prevent or treat diseases and injuries in two ways. One is cell-based therapies and pharmaceutical development, which includes drug testing and drug delivery.

KEYWORDS: Stem cell; Progenitor cells; Neurodegenerative; Pharmaceutical development.

INTRODUCTION

Our bodies are made up of trillions of cells. These cells in an early stage, called as embryonic stem cells. Embryonic stem cells can develop into three types of Cells. That is called ectodermal, endodermal and mesodermal stem cells. These three types of stem cells then go on to form 200 different types of cells. It forms all the organs and tissues in the body, such as the bones, kidney, liver, blood and brain. After birth, embryonic stem cells are no longer present in the body. The stem cells present in the bone marrow is called hematopoietic stem cells, which are the mother cells of the cells in the blood.[1]

In this 21st century, we still do not have proper treatments for many diseases like diabetes, Parkinson's disease, Alzheimer's disease etc. The stem cell is some light of hope for the treatment of these incurable diseases. The functions of embryonic stem cells in the cardiac cells are used as cardiac progenitor cells to synthesis an organ like heart. It helps in the production of bone cells and natural killer cells (NK cells). It helps in drug discovery to synthesis new chemicals. And treating genetic disorder like DMD (Duchene muscular dystrophy), Hemophilia. It is also used for prenatal diagnosis of genetic disorders. Development of β – cells of pancreas to treat the diabetic patients who are deficient in insulin production. Stem cells will be an important therapeutic option in future medicine.

Classification of stem cell

Stem cell classification based on their origin. Stem cells can be classified, based on their origin, into four different groups.

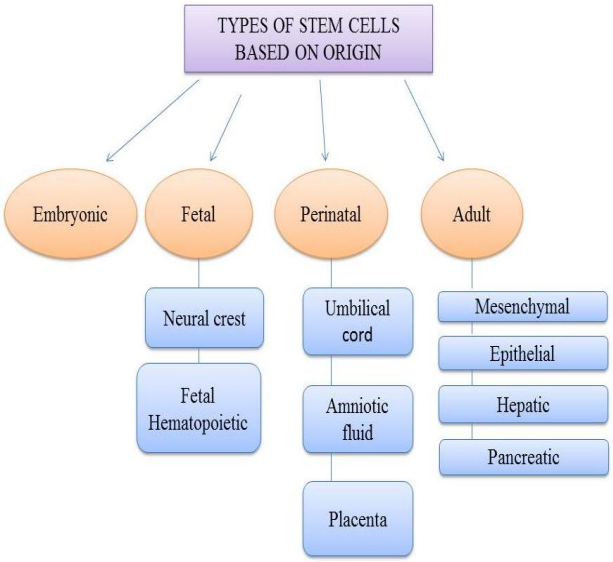

Fig. 1. Types of stem cells based on origin.

Totipotent

Totipotent stem cells are one of the most important stem cells types. Because they have the potential to develop into any cell found in the human body. The zygote

divides numerous times and forms the cells that will eventually constitute the human body This cells are called totipotent stem cells. In most animals, the only true totipotent stem cell is the fertilized egg and its immediate descendants. A totipotent stem cell can potentially generate a complete organism.[2]

Pluripotent

Pluripotent cells can give rise to all tissues of the body plus many of the cells that support the pregnancy but are unable to produce a new individual on their own.[4] They are diploid and Karyotype normal cell which can be propagated indefinitely in the primitive embryonic state. These cells can differentiate spontaneously at high frequency under a range of conditions into multiple cell types representative of all three embryonic germ layer, *in vitro and in vivo.*[5] An important additional criterion for pluripotentiality is the demonstration that the stem cell line may be cloned from a single cell.[3]

Multipotent

Multipotent cell gives rise to multiple cell types. Once stem cells are confined in a certain tissue, they become "adult stem cells" [6]. In other words, they undergo asymmetric self-renewing cell divisions but have less self-renewal ability, in part because of lack of high levels of telomerase. In addition, the array of differentiated cells that can be generated from adult stem cells is more limited, and these cells generate daughter cells that can differentiate into cells of the tissue of origin but not into another cell type.[7,8]

Oligopotent

Oligopotent cell gives rise to differentiate into a few cell types. It is a degree of potency. Examples of oligopotent stem cells are the lymphoid or myeloid stem cells.

Unipotent

Unipotent cells are self-renewing and forms mature cells of a single type. For example gamete forming cells in males are unipotent cells.

Embryonic stem cells

Embryonic stem cells (ESCs) which are derived from the inner cell mass of pre-implantation embryo possess the capability of unlimited self-renewal and expansion.[9,10,11] ESCs are also pluripotent cells that they have the ability to differentiate into all cell types of the organism under specific culturing condition in vitro.[12]

Fetal stem cell

Fetal stem cells are cell types isolated from fetal tissues and can differentiate into the various organ systems of the body. These fetal stem cells have greater plasticity and a higher capacity for replication compared to adult stem cells.[13] Fetal stem cells can be divided into neural crest stem cells, fetal hematopoietic stem cells, and fetal mesenchymal stem cells.[14]

Neural crest stem cell (NSCs)

Neural crest cells are a transient stem cell-like population that form in the dorsal neural plate border during Neurulation [15] and then they migrate to their target sites during development, where they can differentiate into variety of cell types such as sensory neurons, glia, melanocytes, adrenal medulla, and cranial cartilage/bones.[16,17]

Fetal hematopoietic stem cell (HSCs)

Like other stem cells, hematopoietic stem cells collected from fetal blood have the capacity of self-renewal and proliferation, but at a higher rate (shorter doubling time) compared to they found in cord blood or adult bone marrow-derived stem cells.[13] The most common hematopoietic system lineages such as myeloid, lymphoid, and erythroid.[24,25] It helps to maintaining the blood system through hematopoiesis throughout the lifetime of an organism.[26]

Perinatal stem cells

Perinatal (infant) stem cells can be easily obtained at birth from extra-embryonic structures such as amniotic fluid (AF),[18] umbilical cords (UC).[19] and placenta membranes.[20,21]

Umbilical cord stem cells (UCSC)

Umbilical cord stem cell is the most abundant source of stem cells, particularly hematopoietic and mesenchymal stem cells.[22]

Amniotic fluid stem cells

Amniotic fluid contains multiple cell types, mainly with mesenchymal properties including self-renewal and differentiation potential.[23] Amniotic fluid derived mesenchymal stem cells can be collected during pregnancy via amniocentesis or at the end of gestation.[20]

Placenta-derived stem cells

The human placenta has been recognized as a rich source of stem cells based on the expression of pluripotency markers. This cell up to ten times as many stem cells can be harvested from a placenta as from cord blood.

Adult stem cells (ASCs)

Adult stem cells are stored in the body and help to replace dead or damaged cells in the specific tissue.

Mesenchymal stem cells (MSCs)

MSCs are defines as Multipotent cell with the capacity for self-renewal.[27] MSCs have been isolated from almost all mesodermal layers of mesenchymal tissues including circulating blood,[28] adult and fetal bone marrow (BM), spleen, cartilage, muscle tendons.[29] adipose tissues.[30] periosteal,[31] synovial fluid,[32] and thymus.

Epithelial stem cell
Epithelial stem cells which have the capacity of self-renewal and differentiation.[30,31] Epithelial stem cells mostly reside in intestine and epidermis both of which are typical epithelial tissues.[32]

Hepatic stem cell
Hepatic stem cells can give rise to cords of potential hepatic progenitor cells, and ultimately differentiate into hepatocytes and biliary epithelial cells [36]. Bone marrow also contains a population of stem cells with hepatic potential which may contribute to hepatocyte regeneration when it becomes reprogrammed for liver recovery [37].

Pancreatic stem cell
Pancreatic stem cells or progenitor cells are multipotent stem cells which have the ability to differentiate into the lineage and specific progenitors are responsible for the developing pancreas.

Different stages of stem cell
Differentiation
Cells remain unspecialized and later divide to give rise to specialized cells eye, bone, nerve, muscles, etc. It is a process were unspecialized cell acquired the cellular traits which allows to perform specialized function. It is made up of several stages like primary and secondary differentiation followed by terminal differentiation which leads to the final stage of differentiation cells.

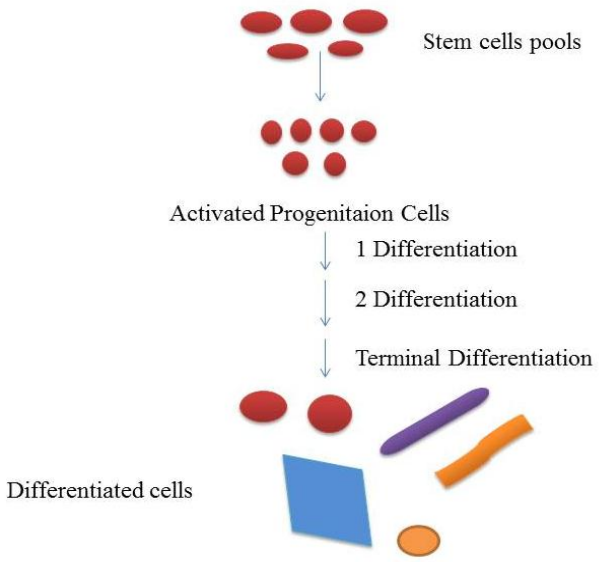

Fig. 2: Stage of differentiation cells.

Maturation
Cells in bone marrow (haemopoitic cells) can be used which easily get differentiated and matured in various cell types and stages. In our culture dish, the cells which are grown undergo different stages of growth both physically and physiology to attains next stage of life. This happens over a span of minutes to days.

During maturation the small cell undergoes changes in gene expression plasma cell which limits the cell types and moves through a closer cell type which is more defined.

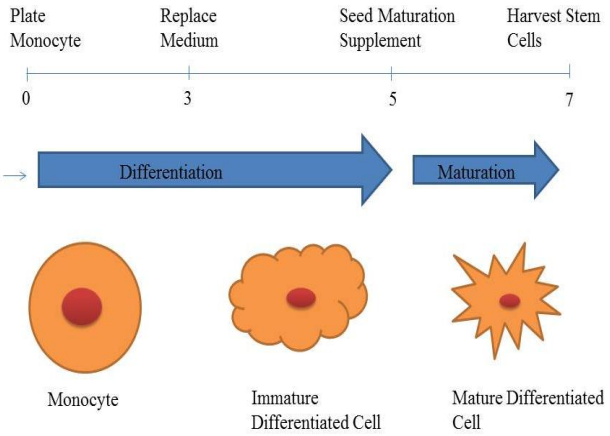

Fig. 3: Differentiated and matured in various cell types and stages.

Proliferation
The stem cell proliferates by multiplying themselves to increase the number. This process involves in sequential pattern of changes in the gene expression which leads to division of cells resulting in numerous quality. It is step wise process which brings about change in the genetic expression leading to change in the gene product. Many transection points occur between the cycles of the cells which can be mapped in order to study the pattern of cell proliferation.

Pluripotency
It is a self-replicating in nature which is divided from embryonic stem cell. Developed into three main germ layer. It is called as a master stem cell. It has ability to divide and give rise to various type of tissue for genes. Ectoderm gives rise to respiratory system, gastro intestinal system, endocrine, live and pancreas. Mesoderm gives rise to bone, connective tissue and circulatory system.

Types of plunipotent
- Induced pluripotent stem cell (ips)
- Embryonic pluripotent stem cell (EPS)
- Somatic nuclear transfer

Induced pluripotent stem cell
Ordinary skin cells are reprogramming to convertor them into pluripotent cells by introducing the specific genes which can now function as stem cell. For the first time it was used in Therapeutic application in Boston's children hospital in US to cure Neurodegenerative disorder 2008.

Embryonic pluripotent stem cell
Embryonic pluripotent stem cell other wise called "True cells" which are made from unused embryos.

Fertilization under *in vitro* condition produced several fertilized cells or embryo which is used as embryonic stem cells. However, this technique is unsuccessful because genetic match is impossible.

Somatic nuclear transfer

Somatic nuclear transfer is a transfer of nuclear from somatic cells to other cell. In case it may be can egg cell. It is a process of introduction into the nuclear of another cell which later reprograms to produce pluripotent cells.

Self-renewable and self-maintenance

Self- renewable takes place by cell cycle and cell division which produce several cells of same types. However, self-renewable may also concentrate on producing undifferentiated cell which further get differentiated into specialized cells. This process of maintaining self-renewable or differentiation is determined by cell cycle.

The percentage of self - renewable of cells is always proportional to the cell population. It is used mainly to regenerate death cells, tumors cell. Self – renewable or self - maintenance it's dependent on cell signal transduction pathways which are influence by environmental factor and metabolic process within the body.

Application of stem cell therapy

A number of stem cell therapies exist, but most are at experimental stages, costly or controversial.

Eye disease

The retina is an important tissue at the back of the eye that senses light and sends visual information to the brain. Eye diseases such as glaucoma and macular degeneration are characterized by damage to retina cells, which can eventually lead to vision loss and blindness. Stem cells might be useful for this because they can trigger to turn into any type of cell. This therapy used to replace or preserve damaged retina cells.

Symptoms

- Blurry vision
- Squinting the eye
- Severe headaches
- Difficult to see
- Swelling of the optic nerves.

Current usage

Myopia

The most common name for myopia is nearsightedness. This is the disorder that can be associated with the long eye ball or too much of corneal curvature, so that the gleams of the light entering into the eyes are not properly focused. This type of condition is very common in school kids and teenagers and can be well cured by stem cellular eye treatment.

Macular degeneration

Age related Macular Degeneration is the leading cause of vision loss and blindness affecting millions of people by the age of 50 years and above. And it's also lead disease in the arena of regenerative medicine in 2012, when the short-term results were published of two patients who underwent subretinal transplantation of human embryonic stem cell (ESC)–derived retinal pigment epithelium (RPE) cells [38]. It was the first description of a pluripotent stem cell derivative transplanted into any human being; follow-up data showed the safety of the intervention[39,40,41].

Macular Degeneration is commonly caused by the retinal damage of the eye due to which there can be severely impaired vision loss. The most important factor that may significantly increase the risk of AMD is the age. Additionally, some other factors are as well responsible of increasing the chances of developing the disease such as: Gender, Genes, Smoking, Sunlight, and Eating Habit.

Surgical technique was the only available option a treatment of AMD, till the discovery of stem cells. Stem cell technology has changed the approach as the only available non-surgical method that can reverse the damage and stop the progression of the AMD. The worldwide ongoing research has the promising candidates to effortlessly replace degenerated or damaged RPE layer in to fresh cells, which is believed to halt or reverse the version loss associated with the AMD.

Retinopathy

Retinal diseases other than the major ocular diseases discussed above also cause problems. These diseases include retinal detachment and retinal vascular complications. Retinal detachment is a medical condition in which the retina separates from the back of the eye [44]. One in 10,000 people faces this problem per year. Retinopathy or Retinitis Pigmentosa is the most common condition that is progressive, degenerative disorder affecting the retina of the eye. It particularly affects the light sensitive cells of the retain known as strong rods. They are capable of sending the info to the brain regarding every minuscule detail of your visualization via the assistance of optic nerves. Retinitis Pigmentosa is characterized by the vicissitudes in the pigment owing to the resultant degeneration of optic nerves. This in turn is connected with thinning of retinal blood vessels as the demand of blood supply lowers significantly. The prevalence of this disorder is related with the genetic deficiently. Retinopathy stem cell treatment in India is considered benefitting procedure optimum results.

Glaucoma

Glaucoma is the most common neurodegenerative disease in the inner part of retina. A increase of glaucoma 79.6 million in 2020 worldwide, from 60.5 million in 2010[42]. Glaucoma is a condition that damages the optic nerve and often occurs due to the increased

pressure in the eye. A recent study conducted by a research team from the National Eye Institute (NEI), part of the National Institutes of Health found stem cell secretion can help to protect the cells in the retina, the light – sensitive tissue in the black of the eye.

Eye injuries

The treatment uses mesenchymal stem cell that can differentiate into far, bone or cartilage, but which also produce an abundance of anti-inflammatory factors that have been shown to speed healing and reduce scaring in experimental models of eye injury.

Optic nerve

The optic nerve can lead to various pathologies due to intraorbital, intracranial, intrinsic, or systemic disorders. Optic nerve diseases could also lead to life- and vision-threatening conditions [43]. Optic nerve damage is any kind of injury or damage to the optic nerve, including trauma, inflammation, and disease [45]. It is also called optic nerve atrophy or optic neuropathy. Vision lost due to optic nerve atrophy cannot be recovered if the cause can be found earlier; further vision loss and blindness may be prevented. Currently there is no treatment option for optic nerve damage patients but after many clinical and experimental studies it has been proved that stem cells transplantation via "retro bulbar and intravitreous" can again regenerate retinal ganglion cells and their axons in the optic nerve.

Cancer disease

Cancer stem cells can be defined as cells in the tumor growth. Normal stem cells are characterized by Capability of self-renewal, strict control on stem cell numbers and ability to divide and differentiate to generate all functional elements of that particular tissue [46] Compared to normal stem cells, the cancer stem cells are no control on the cell numbers. Cancer stem cells form very small numbers in whole tumor growth and responsible for the growth of the tumor cells.

As previously stated, the cancer stem cell arose from the observation of similarities between the self-renewal mechanisms of stem cells and those of cancer cells. The general concept of cancer stem cell hypothesis could have fundamental and profound implications for cancer therapy.[47]

Differentiation therapy

Although crucial for the understanding of cancer development, anticancer approaches aimed at killing cancer stem cells may not be relevant in all clinical settings. Glioblastoma is the most aggressive cancer that begins within the brain. However, there is no evidence that they may be responsible for tumor recurrence following therapy, because glioblastomamultiform does not respond to therapy. Here, therapy fails because it does not even affect proliferating cells.[48] Thus, targeting proliferating cells is the first step required to control cancer because these progeny cells will have enough divisions to kill a patient. Targeting cancer stem cells must therefore be a secondary objective in some clinical settings such as pancreatic, brain and lung tumors.[47]

Elimination therapy

This is another way to increase the efficacy of cancer therapy is to eliminate cancer stem cells. This can be achieved using different approaches: transplantation of allogeneic haematopoietic stem cells with graft versus leukemia/tumor effect, targeted therapies against self-renewal signalling pathways and the cell cycle, modulation of chemoresistance mechanisms or tackling other specific properties of cancer stem cells.[47]

Clinical uses of stem cells used in cancer

Breast cancer

Over the past decades, millions of women have died of breast cancer (BC) as a result of late diagnosis, disease relapse.[49] and the development of resistance to endocrine and chemotherapeutic treatment regimens.[50]

Ovarian cancer

Ovarian cancer (OC) is a malignant growth arising from different parts of the ovary in females. Frequently, ovarian cancer begins within the outer lining of the ovary. However, the fallopian tube or egg cells have also been described as an origination point of Ovarian cancer.

Currently, there are several treatment options such as surgery, which is sufficient for malignant tumors that are well differentiated, and chemotherapy for the most aggressive tumors that are confined to the ovary.

Lung cancer

Lung cancer is described by uncontrolled cell growth arising from epithelial cells within the lung tissue. The most common lung carcinoma is called small-cell lung carcinoma (SCLC). Chemotherapy and radiotherapy are the common treatment options. Many of the most common lung diseases in Europe, such as lung cancer and chronic obstructive pulmonary disease (COPD), are caused by changes that occur in the cells that make up the lungs.

Lung stem cells are important for initial lung development in fetuses. Although rare in abundance, lung stem cells in adults are important for repairing damage to lungs and replacing the specialized cells that make up the lung, which naturally die and need to be replaced.

Regenerative medical applications

1. Can be found in large quantities (millions to billions of cells).
2. Can be Easily obtainable, with minimal discomfort to the patients via a minimally invasive procedure.
3. Can be differentiated along multiple cell lineage pathways in a controllable and reproducible manner.
4. Can be transplantable safely and effectively.

5. Can be manufactured in accordance with current Good Manufacturing Practice guidelines.
6. Stem cells could allow scientists to test new drugs using human cell line which could speed up new drug development. It would allow quicker and safer development of new drugs.

CONCLUSION

In summery the stem cell-based therapy improving the people lives who suffer for different types of disease. The development of new remedies for treating and preventing the problems of eye and cancer disease in this research area. Stem cell-based therapy is not only general remedy for this disease, it will producing a new biological elements help to treat the different types of disorder apart from this. Currently the research and studies about the stem cell therapy are rapidly expending and gaining the popularity of regenerative medicine. It will be helpful for the future development to treat the disease. Stem cells can create miracles and give hope to the hopeless.

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