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A Review on Stem cells-Therapeutic Applications

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Abstract: The zygote begins to divide 30 hours after fertilization and forms in to a hallow ball of cells, the blastocyst, which has an outer layer of cells called trophoblasts and cluster of cells in inner sphere called inner mass of cells, which are pluripotent cells capable of giving rise the three germ layers, called embryonic stem cells (ES).In addition to embryonic stem cells mammals have other type of stem cells, the adult stem cells found in issues in children and adults these stem cells are more specialized (differentiated) pluripotent stem cells. The property of stem cells to proliferate indefinitely in culture and can differentiate into any cell type has attracted the scientist's interest, given the potential applications of these cells in field of clinical medicine. In this new age of medical science, Stem cells, directed to differentiate into specific cell types,. Stem cell therapy can provide both help and hope to the patients suffering with Alzheimer's diseases, spinal cord injury, stroke, burns, heart disease, diabetes, osteoarthritis, and rheumatoid arthritis neurological disorders and also insomnia, memory problems, chronic fatigue, stress and anxiety. Stem cell therapeutic applications are also evident in cosmetology such as baldness, tooth implantation, hair growth.

The present paper briefs origin of pluropotent cells, factors involved in stem cell culture and their applications in treating diseases.

Introduction:

Totipotent cells are derived from the inner cell mass of mammalian blastocysts. These cells have the ability of pluripotency and to differentiate into cells of all three germ layers are known as *Embryonic Stem cells* (ESC).

There are two broad types of stem cells, the cells that are isolated either from embryo or from cord are *Embryonic stem cells* and the other type of stem cells are the *Multipotent stem cells* (MSC) which are adult stem cells, found in various tissues in children and adults. These stem cells are more specialized (differentiated) pluripotent stem cells.

The property of embryonic stem cells (ES):

Embryonic stem cells have the potential to proliferate indefinitely in culture and can differentiate into any cell type, have attracted scientific interest, given the scope for applications of these cells in regenerative medicine. ES cells might serve as vectors to carry and express genes in target organs in the course of gene therapy. Establishment of ES cells after transplantation has been observed in research animal disease models,. Stem cells, directed to differentiate into specific cell type, offer the possibility of a renewable source of replacement cells and tissues to treat diseases including Human ES cells might be used to treat a host of diseases such as Cerebral palsy, Mental retardation, autism, Alzheimer's diseases, spinal cord injury, stroke, burns, heart disease, diabetes, and rheumatoid arthritis(Thomson et al., 1998).its applications are recommended in cosmetology that are – face lift, hair growth on bold head, tooth eruption, eye brow shaping etc

Stem cells' tremendous therapeutic potential arises from their ability to continually self-renew and turn into any adult tissue. However, there are ethical difficulties regarding the use of human embryos, as well as the problem of tissue rejection following transplantation in patients. One way to overcome these issues is the generation of pluripotent cells directly from the patients' own cells – “The Somatic cells”.

Somatic cells can be reprogrammed by transferring their nuclear contents into oocytes (Wilmut et al., 1997) or by fusion with ES cells (Cowan et al., 2005) indicating that unfertilized eggs and ES cells contain factors that can confer pluripotency to somatic cells. The factors that play a role in the maintenance of ES cell identity also play pivotal roles in the induction of pluripotency in somatic cells.

Types of stem cells - similarities and differences:

There are a few similarities and differences have been observed between embryonic and adult stem cells, embryonic stem cells can be grown relatively easily in culture. Adult stem cells are rare in matured tissues, so isolating these cells from an adult tissue is challenging as large numbers of cells are needed for stem cell replacement therapies this is an important distinction. Scientists believe that tissues derived from embryonic and adult stem cells may differ in the likelihood of being rejected after transplantation. As it is not known whether tissues derived from embryonic stem cells would cause transplant rejection, since the phase-1 clinical trials testing the safety of cells derived from hESCs have only recently been approved by the United States Food and Drug Administration (FDA).

Use of embryonic stem cells/adult stem cells- advantages and disadvantages:

Adult stem cells and human embryonic stem cells have advantages and disadvantages regarding the potential use of cell-based regenerative therapies**.** One major difference between adult and embryonic stem cells lies in their ability to produce types of differentiated stem cells. Embryonic stem cells can become all cell types of the body because they are pluripotent**.** Adult stem cells are thought to be limited to differentiating into cell types of their tissue of origin. In adult organisms, adult stem cells (multipotent) and are generally referred to by their tissue origin (mesenchymal stem cell, adipose-derived stem cell, endothelial stem cell, dental pulp stem cell, etc.). In a developing embryo, *Embryonic Stem cells* (ESC) can not only differentiate into all the specialized cells, but also maintain the normal turnover of regenerative organs, such as blood, skin, or intestinal tissues Adult stem cells have been shown to produce bone, muscle, cartilage, fat and other connective tissues.

As adult stem cells obtained patient's own cells, currently believed less likely to initiate rejection after transplantation. This is because a patient's own cells could be expanded in culture, coaxed into assuming a specific cell type **(**differentiation**),** and then reintroduced into the patient. The use of the own adult stem cells would may not be rejected by the immune system. This represents a significant advantage, as immune rejection can be circumvented only by continuous administration of immunosuppressive drugs, and the drugs themselves may cause deleterious side effects.

Isolation of stem cells:

Researchers have succeeded in growing cells (stem cells) in the laboratory through a procedure known as cell culture**.** The Collection of Stem Cells from the Blood Stream (Peripheral Blood Stem Cells [PBSC]) involves several steps (i)Growth factors, medications are administered are drugs that stimulate blood stem cells to grow red cell and white cell and to be released into the blood stream. This process is called "mobilization. (ii)Chemotherapy with growth factors may also be used to release stem cells from the bone marrow into the bloodstream. .(iii) blood is collected for stem cells (iv) In medical language, the harvesting is called apheresis or leukapheresis **–** is a procedure whereby blood from the patient or donor passes through a special machine that separates (using a centrifuge technique) stem cells. (v) The stem cells collected and cultured.

Culturing of stem cells:

Human embryonic stem cells (hESCs) are generated by transferring the stem cells into a plastic laboratory culture dish that contains nutrient known as culture medium**.** The inner surface of the culture dish is typically coated with mouse embryonic skin cells that have been treated so they will not divide. This coating layer of cells is called a 'feeder layer'. The mouse cells in the bottom of the culture dish provide the cells a sticky surface to which they can attach. Also, the feeder cells release nutrients into the culture medium. The cells divide and spread over the surface of the dish. Once the cell line is established, the original cells yield millions of embryonic stem cells. Embryonic stem cells that have proliferated in cell culture for a prolonged period of time without differentiating are pluripotent**.** Researchers have devised ways to grow embryonic stem cells without mouse feeder cells.

Factors involved in Culture stem cells:

By combining selected factors it has been proved to generate pluripotent cells, in to induced pluripotent stem (iPS) cells, directly from mouse embryonic or adult fibroblast cultures.these transcription factors, including Oct3/4 (Niwa et al., 2000), Sox2 (Avilion et al., 2003), c-*myc* (Cartwright et al., 2005), *Klf4* (Li et al., 2005), and β-*catenin* (Sato et al., 2004), have shown to contribute to the long-term maintenance of the ES cell phenotype and the rapid proliferation of ES cells in culture, In this study, researchers have examined whether these factors could induce pluripotency in somatic cells. In addition to above factors several proteins and growth factors play a role to signal stem cell growth, both inside and outside the cell proteins called Wnt, FGF, BMP and a signaling factor heparan sulfate.

A research team at Karolinska Institutet has shown to produce human stem cells entirely without the use of other cells or substances from animals. Instead they are cultured on a matrix of a single human protein- laminin-511(is a part of human connective tissue).

Lahann and Gary Smith, an associate professor in obstetrics and gynecology in the U-M Health System, and their co-workers built a new stem cell growth matrix that is completely synthetic and doesn't contaminate the stem cells

Today, donated organs and tissues are often used to replace destroyed tissue, but there is a gross shortcoming in availability and supply of transplantable organs. Perhaps the most important application of human stem cells is the generation of cells and tissues that could be used for cell-based therapies**.** Properties of stem cells to differentiate into specific cell types offer the possibility of a renewable source of replacement to cells and tissues that aid to treat diseases.

Stem-cell transplant dosage:

Numbers of studies have been completed to determine the numbers of stem cells need to introduce in to patient. The number of stem cells is quantified by a special laboratory technique called "CD34+ cell analysis by flow cytometry." Most transplant physicians collect enough stem cells for two transplants (over 4 million CD34+ cells per kilogram body weight).

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Somatic cells can be reprogrammed by transferring their nuclear contents into oocytes (Wilmut et al., 1997) or by fusion with ES cells (Cowan et al., 2005) indicating that unfertilized eggs and ES cells contain factors that can confer pluripotency to somatic cells. The factors that play a role in the maintenance of ES cell identity also play pivotal roles in the induction of pluripotency in somatic cells.

Characteristics required by stem cell for transplantation:

For cell-based therapies of pervasive diseases, scientists must be able to manipulate stem cells necessary characteristics for successful differentiation, transplantation, and engraftment. For achieving successful cell-based treatments, extensive proliferation and to generate sufficient quantities of tissue, the following characteristics may be required: (i)Differentiate into the desired cell type(s) (ii)Survive in the recipient after transplant(iii)Avoid harming the recipient in any way(iv) Function appropriately for the duration of the recipient's life(v)Integrate into the surrounding tissue after transplant

Therapeutic applications:

Rheumatoid arthritis (RA): Mesenchymal stem cells (MSCs) have been proposed to be a useful tool for treatment of rheumatoid arthritis (RA), not only because of their multipotency but also because of their immunosuppressive effect on lymphocytes.

Alzheimer's disease, Parkinson's disease: Parkinson's – disease is caused by the progressive degeneration of dopamine receptors of brain cells. Replacing these cells is considered a promising therapeutic strategy. Loss of different types of neurons and glial cells in the brain and spinal cord leads to neurological diseases such as Alzheimer's disease and spinal cord injury. At present discovery of the therapeutic potential of stem cells offers new strategies for the treatment of neurological diseases

Type 1 Diabetes: The cells of the pancreas that normally produce insulin are destroyed by the own immune system of patients who suffer from type 1 diabetes. New studies indicate that it may be possible to direct the differentiation of human embryonic stem cells in cell culture to form insulin-producing cells that eventually could be used in transplantation therapy for persons with diabetes.

Metachromatic leukodystrophy(MLD also called Arylsulfatase “A”deficiency)**:** MLD is directly caused by a deficiency of the enzyme arylsulfatase A and without this enzyme, sulfatides destroy the myelin sheath of the nervous system. Dr.M Nieder (2002)showed significant improvements in nerve conduction velocities after hematopoietic Stem Cell infusion in four patients with MLD .

Stem Cells as Source of Cancer-Fighting T Cells- -Adult stem cells from mice converted to antigen-specific T cells - the immune cells that fight against cancer tumor cells - show promises in cancer immune therapy and may lead to a simpler, more efficient method of treating cancer.

Culturing of fully developed sperms: In the new study, Karim Nayernia(2007), at the University of Newcastle, and his team isolated mesenchymal stem cells from the bone marrow of male volunteers. The team believes it will take another three to five years of work to achieve fully developed sperm cells (Prof .Nayernia was at the University of Göttingen, Germany, published in the journal Reproduction: Gamete Biology).

Usage of stem cells in cosmetology:

(i)Stem cells- Face lift: A stem cell facelift is a cosmetic procedure that purportedly uses once own stem cells from fat removed by liposuction. Fat cells naturally contains stem cells are used for grafting, which involves removing fat cells from one area and then injecting this fat into another area to remove signs of aging - sagging skin, wrinkles, and decreased facial fullness.

(ii)Hair growth - World-renowned epidermal and hair researcher at Rockefeller University in New York City, in 2003, Elaine Fuchs and a team of scientists determined that adipose –derived stem cells in combination of WNT proteins and Noggin proteins (both are natural proteins)lead to hair re –growth. ‘Androgenic Alopecia’ characterstic horseshoe shaped male bold head. Back of head is called hair transplant donor area or nor wood stage7.Trans planting hair (whole follicular hair) is removed from donor area implanted at another required area of scalp.

(iii)Growth of eyebrows: hair is collected from donor area (back and sides of scalp) and implanted to shape eyebrow.

(iv)Tooth regeneration: Dr. Jeremy Mao has unveiled a technique that directs the body's stem cells into Human molar scaffolding that will aid in the regeneration of a new tooth. (Columbia University Medical Center).

Stem Cell therapy, is unique and innovative in their applications of regenerative medicine treatments provides hopeless patients with neurological diseases such as , Parkinson's disease, Cerebral palsy, Multiple Sclerosis and Spinal injuries, autoimmune conditions such as systemic and skin Lupus, dermatomyositis, scleroderma and others, difficult eye retina problems and diseases of Internal Organs conditions such as problems with the heart, liver or kidney.(Omar D Gonzalez M.D of *Integra Medical Center)*

To summarize, stem cells offer exciting promise for future therapies, but significant technical hurdles remain that can be overcome through years of intensive research.

DISCLAMAIRE: This is A Reviwe Article

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Top stem cell centres in the world

Stem Cell Therapy india Autism,cerebral palsy,MR,Diabetes Paraplegia,costwww.chaitanyastemcell.com

The Center for Cellular Therapy at Tel Aviv Sourasky Medical Center in Israel, led by pioneer **Dr. Shimon Slavin**, treats all blood cancers, plus several other cancers; autoimmune diseases such as MS, nerve injuries, spinal injuries and sickle cell.

Foundation Don Roberto Fernandez Vina is led by **Dr. Roberto Fernández Viña** and has two clinics: Clínica San Nicolás in **Argentina** and El Salvador Regenerative Medicine Institute in **El Salvador**.

Regenocyte Therapeutic based in Naples, Florida with a Repair Stem Cell clinic in the **Dominican Republic** for cell implantation

China Stem Cells is a conglomerate of about a dozen hospitals located throughout China that treat patients having neurological and autoimmune diseases.