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Stem cells – Current concepts and Future applications

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"Stem cells (SC) are precursor, cells capable of self-proliferation and differentiation". SC have the potential to develop into many different cell types. [1].

Based on the cell type/tissue of origin, SC are classified into 3 types.

1) *Somatic Stem Cells (SSCs)* are self-renewable population of cells which are present in all tissues. They are described as "multipotent."
2) *Embryonic Stem Cells (ESCs)* are derived from pre-implantation embryos before differentiation of trophoectoderm and inner cell mass, capable of giving rise to the entire organism and extra embryonic tissues. They are described as "pluripotent".
3) *Induced Pluripotent Stem Cells (iPSCs)* are capable of differentiation into ectodermal, mesodermal and endodermal cells. These are adult cells that are "reprogrammed," to become pluripotent.

Successful culture of human embryonic stem cells was achieved just over a decade ago. Several clinical trials have been carried out using stem cells in a variety of clinical indications but most of these have been Phase I or Phase II trials.

Current therapies &Applications in Medicine:

Human SC are currently being used to test new drugs. Cancer cell lines, for example, are used to screen potential anti-tumor drugs.

The most important potential application of SC is for cell-based therapies. Donated organs and tissues are often used to replace ailing or destroyed tissue, SC directed to differentiate into specific cell types, offer the possibility of a renewable source of replacement cells and tissues to treat diseases including Alzheimer's disease, spinal cord injury, stroke, burns, heart disease, diabetes, osteoarthritis, and rheumatoid arthritis. It may become possible to generate healthy heart muscle cells in the laboratory and then transplant those cells into patients with chronic heart disease [2]. Bone-marrow have been used to treat cancer patients with conditions such as leukaemia and lymphoma; this is the only form of stem cell therapy that is widely practiced.

Neurodegenerative diseases such as in Parkinson's and Alzheimer's disease stem cells have raised a new hope. A clinical trial in Scotland in 2013, SC were injected into the brains of stroke patients. SC may lead to successes in treating baldness (Aeron Potter of the University of California-Science) and tooth regeneration technology. Heller has reported success in re-growing cochlea hair cells with the use of embryonic stem cells in cases of Deafness. Since 2003, researchers have successfully transplanted corneal stem cells into damaged eyes to restore vision.

In recent experiments, scientists have been able to coax embryonic stem cell to turn into beta cells in the lab. In Cartilage injury, a possible method for tissue regeneration in wound healing is to place adult SC "seeds" inside a tissue bed "soil" in a wound bed and allow the stem cells to stimulate differentiation in the tissue bed cells. Culture of human embryonic stem cells in mitotically inactivated porcine ovarian fibroblasts causes differentiation into germ cells. In 2012, oogonial stem cells were isolated from human ovaries and demonstrated to be capable of forming mature oocytes. These cells have the potential to treat infertility.

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Recently scientists have been investigating an alternative approach to treating HIV-1/AIDS, based on the creation of a disease-resistant immune system through transplantation of autologous, gene-modified (HIV-1-resistant) hematopoietic stem and progenitor cells (GM-HSPC). The use of stem cells for the treatment of liver disease in both humans and animals has been the focus of considerable interest. Mesenchymal stem cells are currently under clinical trials as a possible treatment for graft versus host disease and graft rejection. Clinical trials are underway to explore the low immunogenic properties of stem cells and their possible use for treatment of problems with an overactive immune system seen with allergies and autoimmune disorders [3].

Embryonic stem cell controversy: There is widespread controversy over the use of human embryonic stem cells often requiring the destruction of the blastocyst. There is other stem cell research that does not involve the destruction of a human embryo involving adult stem cells, amniotic stem cells and induced pluripotent stem cells [4].

Creating Pluripotent Stem Cells: Scientists have found a way to create stem cells by using various reprogramming techniques in the laboratory. In 2007 the announcement that Japanese researcher Shinya Yamanaka had created pluripotent stem cells using skin cells and not embryos. These stem cells are called "induced pluripotent stem cells" (also known as iPS and iPSC) and are created from adult (non-pluripotent) cells. In 2009, a Canadian-Scottish research team led by Andras Nagy was the first of several teams to announce a method to create iPS cells without the use of retroviruses.

Somatic Cell Nuclear Transfer- (SCNT): Another way to create stem cells is by taking a human oocyte and replacing original nuclear DNA with a nuclear DNA of a donor cell. When that oocyte is stimulated it becomes a blastocyst with the same genetic make-up as the donor. This potentially enables researchers or clinicians to create genetically identical tissue for tissue replacement. The use of cloning techniques to create genetically identical embryos that are then implanted in a woman who gives birth to a genetically identical child, is called "reproductive cloning." There are ethical arguments against using SCNT to create embryos for research [5].

In March 2005, UN's General Assembly adopted resolution 59/280, containing in its annex the text of the UN Declaration on Human Cloning. The field of stem cell research is still young. There is no conclusive proof of safety or therapeutic efficacy of SC in any condition yet. Unfortunately, some clinicians have started exploiting helpless patients by offering unproven stem cell treatments prematurely. Such fraudulent practices need to be stopped urgently, while ensuring that scientifically designed and responsible research on stem cells is not hindered. In 2007, the ICMR and the Department of Biotechnology jointly released Guidelines for SC Research and Therapy, which now need to be revised to reflect new scientific and clinical findings that have significantly changed the scope of SC research and possible translation [6]. The 2013 World SC Report addresses the regulatory challenges in bringing cutting edge SC research into mainstream medicine.

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