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Stem Cell Based Therapies: A Review

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ABSTRACT:

Stem cell based therapies offer the greatest hope in any area of medicine to humanity's most devastating diseases. The regenerative capabilities of stem cells present a unique opportunity to treat human illness and injury. They are endowed with the property of self-renewal and the ability to differentiate into cells that are committed to restricted developmental pathways. A wide variety of adult mammalian tissues harbors stem cells, yet "adult" stem cells may be capable of developing into only a limited number of cell types. In contrast, embryonic stem (ES) cells, derived from blastocyst-stage early mammalian embryos, have the ability to form any fully differentiated cells of the body. Stem cell research offers the hope of transplants being done without the sacrifice of another person losing an organ. Clinical trials on the use of stem cells are underway for a wide variety of conditions and there is an emphasis on the use of bone marrow, umbilical cord blood and mesenchymal stem cells. This review focuses on the different types of stem cells and their theraputic uses in treating diseases such as Parkinson's, heart diseases, brain injuries, diabetes, etc. in today's biomedical world.

Keywords: stem cell therapies, embryonic stem cells, mesenchymal stem cells, umbilical cord blood, bone marrow transplant, Parkinson's disease.

[I] INTRODUCTION:

Stem cells are one of the most fascinating areas of biology today. Stem cells have two defining characteristics: the ability for indefinite self-renewal to give rise to more stem cells, and the ability to differentiate into a variety of specialized daughter cells to perform specific functions [33]. The potential and the fundamental concept behind stem cells lies in the cellular differentiation. We can categorize cells depending on their ability to differentiate: unipotent, multipotent, pluripotent and totipotent. Stem cells, directed to differentiate into specific cell types, offer the possibility of a renewable source of replacement cells and tissues to treat diseases including Parkinson's and Alzheimer's diseases, spinal cord injury, stroke, burns, heart disease, diabetes, osteoarthritis, and rheumatoid arthritis. They constitute a promising resource in regenerative medicine for the generation of appropriate cell types in cell replacement therapy.

[II] TYPES OF STEM CELLS:

There are two types of stem cells - embryonic stem cells and adult stem cells - which are classified according to their origin and differentiation potential. Embryonic and adult stem cells have immense research opportunities for potential therapy.

2.1. Embryonic Stem Cells:

The first human embryonic stem cells (ESC) were derived from a blastocyst inner cell mass obtained from a fertilized oocyte [36], capable of infinite division and differentiation into cells of all tissues types [29]. As long as the embryonic stem cells in culture are grown under certain conditions, they can remain undifferentiated (unspecialized). But if cells are allowed to clump together to form embryoid bodies, they begin to differentiate spontaneously. They can form muscle cells, nerve cells, and many other cell types. Diseases that might be treated by transplanting cells generated from human embryonic stem cells include Parkinson's disease, diabetes, traumatic spinal cord injury, Purkinje cell degeneration, Duchenne's muscular dystrophy, heart disease, and vision and hearing loss. Their use for clinical therapy is a relatively new endeavor. Pluripotent stem cells, derived from human embryonic stem (ES) cells, have while maintaining their ability to proliferate indefinitely in culture. However, their application for therapy remains closely associated with ethical concerns related to both their origin and teratogenic potential [14,34,31,6,30]. ESC's are therefore a potentially limitless source of totipotent cells for transplant-based cell therapies.

2.2. Adult Stem Cells :

Adult, or tissue-specific, stem cells are found in the majority of fetal and adult tissues and are derived from tissues that continually replenish themselves (peripheral blood, dermis and gastrointestinal epithelium) [5]. Adult stem cells can be obtained from a number of tissues, but they generally display low proliferation rates and lineage restrictions [43,28,7,1]. They are multipotential [20] and are thought to function by replacing cells that are injured or loss. Their most common source is the bone marrow which contains at least two kinds of stem cells. One population, called hematopoietic stem cells, forms all the types of blood cells in the body. A second population, called bone marrow stromal cells. Stromal cells are a mixed cell population that generates bone, cartilage, fat, and fibrous connective tissue [32]. The use of adult stem cells in research and therapy is not as controversial as the use of embryonic stem cells.

[III] STEM CELL BASED THERAPIES:

Stem cell based therapies, encompassing collection, purification, manipulation, characterization delivery of cells for therapeutic purposes, have existed since the first successful bone marrow transplantations in 1968 [8].

3.1. Bone Marrow Stem Cell Therapy:

Extensive data from animal models indicate that bone marrow stem cells (BMC) are capable of differentiating into cells of cardiac and vascular lineages [23,37,25]. Bone marrow–derived mesenchymal stem cells, mononuclear cells, and circulating endothelial progenitor cells have all been shown to differentiate into cardiomyocytes both *in vitro* and *in vivo*. Another potential mechanism is that transplanted BMCs may secrete a variety of growth factors and cytokines [38] thereby enhancing myocyte survival following ischemic injury and facilitating the migration of resident cardiac stem cells [2] to the site of injury and their reparative activity. The finding of infarct scar size reduction with BMC therapy may signify new myocyte formation, superior preservation of existing myocytes, or both following BMC transplantation. There are evidences that bone marrow derived mononucleated cells (BM-MNC) can generate skeletal muscle. Muscle regeneration and repair are thought to be carried out by muscle-specific stem cells called satellite cells. Derivation of skeletal muscle myocytes from BM-MNC has been studied in human and in mouse models of degenerative muscle disease [39,4]. Conversion of BMC to hepatocytes has been evidenced in animal models [26] and in humans [35]. BMC can differentiate into pancreatic endocrine-cells without cell fusion [15,13] and BM-derived pancreatic islet cells are functional in a mouse model of chemically induced diabetes [13]. Several studies suggested that BM-MNC can differentiate into central nervous system (CNS) cells, including neurons, oligodendrocytes and astrocytes, both *in vivo* and *in vitro* [9].Such cell populations emerged as attractive candidates for regenerative cardiac therapy.

3.2. Embryonic Stem Cell Therapy:

In people who suffer from type I diabetes, the cells of the pancreas that normally produce insulin are destroyed by the patient's own immune system. Embryonic stem cells (ESC) can be differentiated into insulin-producing cells by manipulating culture conditions. *In vitro* differentiation of mouse ESC can generate embryoid bodies, which, after selection for nestin expressing ESC, were stimulated to differentiate towards a ß-cell-like phenotype [22]. ES cell-derived dopamine neurons have been shown to survive and function in a rat model of Parkinson's Disease [16]. The Landmark's study is the first to document the potential clinical utility of regenrating damaged heart muscle by injecting ESC–derived cardiomyocytes directly into the site of the infarct [19].

3.3. Mesenchymal Stem Cell Therapy:

Mesenchymal stem cells (MNC's) are multipotent cells with a strong capacity for self-renewal, which can be isolated from a variety of tissues, such as bone marrow, adipose tissue, umbilical cord, and UCB. MSC's have the ability to differentiate into a variety of cell types, depending on cues from their microenvironment. MSCs have been studied for use in neurologically related cell-based therapy in adult experimental animal models and in clinical trials of human brain disorders, such as Parkinson's and Huntington's disease, traumatic brain injury, and stroke [3,11,42,17].Mesenchymal progenitor cells, isolated from the dental follicle of human third-molar teeth [24] can generate periodontal ligament-like tissue [41], implying that they may be a useful for regenerative periodontal therapy. There are many strategies for producing dopamine neurons from human stem cells in the laboratory for transplantation into humans with Parkinson's disease. The successful generation of an unlimited supply of dopamine neurons could make neurotransplantation widely available for Parkinson's patients at some point in the future.

3.4. Umbilical Cord Blood Stem Cell Therapy:

Umbilical cord blood (UCB) is rich in hemapoietic stem/progenitor cells, regulatory T-lymphocytes (Tregs), monocytes, mesenchymal stem cells (MSC's), endothelial progenitor cells (EPC's), and stromal precursor cells [27] and, consequently, holds promising potential for the treatment of neurological disorders. UCB has been widely used for the treatment of various hematopoietic disorders [18,21]. Recent studies have shown that they induce regeneration in the central nervous system [10,12]. With respect to neonatal brain injury, UCB transplantation is emerging as a promising therapeutic approach for treatment of hypoxic-ischemic brain injury and ischemic stroke [40].

[IV] CONCLUSIONS:

There are many ways in which human stem cells can be used in basic research and in clinical research. It is difficult to predict which stem cells- those derived from the embryo, the fetus, or the adult- or which methods for manipulating the cells, will best meet the needs of basic research and clinical applications. It is necessary to understand the signals in a mature organism that cause a stem cell population to proliferate and remain unspecialized until the cells are needed for repair of a specific tissue. The technical hurdles between the promise of stem cells and the realization of their uses can be overcome by continued intensive stem cell research and search for more practical sources of stem cells in humans.

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