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STEM CELLS IN REGENERATIVE MEDICINE - A REVIEW

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Abstract:

Stem cells are defined as cells that have clonogenic and self-renewing capabilities and differentiate into multiple cell lineages. Stem cells are found in all of us, from the early stages of human development to the end of life. According to differentiation potential stem cells are divided into 5 types: totipotent, pluripotent, multi potent, oligopotent and unipotent. They are vital to the development, growth, maintenance and repair of our brains, bones, muscles, nerves, blood, skin and other organs. Stem cell therapy is emerging as a potentially revolutionary new way to treat disease and injury, with wide-ranging medical benefits. The face of extradentary advances in the prevention diagnosis and treatment of human diseases, devastating illness such as heart diseases, diabetes, cancer and disease of the nervous system, continue to the primer people of health, independence and wellbeing has been revived in this study. Regenerative medicine is a multidisciplinary field concerned with the replacement, repair or restoration of injured tissues. This field emerged from the need for reconstruction in children and adults in whom tissue has been damaged by diseases, trauma and congenital anomalies. Stem cell research is a promising field with an alluring potential for therapeutic intervention, and thus begs a critical understanding of the long-term consequences of stem cell replacement. Stem cells have unrestricted potential to divide and this strength is used for the regeneration and repair of cells within the body during tissue damage. Research on stem cells is advancing knowledge about how an organism develops from a single cell and how healthy cells replace damaged cells in adult organisms. This promising area of science is also leading scientists to investigate the possibility of cell-based therapies to treat disease. In our present review we tried to provide the information about stem cells and their significant role in regenerative medicine for treatment of various diseases.

Key words: *Stem cells, embryonic stem cells, adult stem cells, umbilical cord stem cells, regenerative medicine.*

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1.INTRODUCTION:

Stem cell research was launched into the limelight recently by James Thomson, a scientist at the University of Wisconsin in Madison, who successfully removed cells from spare embryos at fertility clinics and grew them in the laboratory, establishing the world's first human Embryonic Stem cell (ES cells) line. In the same year, Dr. Gearhart isolated cells from 2-4-month-old fetuses' (obtained from elective abortions with informed consent from donors who had independently decided to terminate their pregnancy). Gearhart's team established a different line of cell cultures, by collecting cells from the gonadal ridge from 9-Week-old fetuses. Embryonic Germ (EG)cells from each fetus were used to establish a separate culture line.[2]

Regenerative medicine is an emerging and rapidly evolving field of research and therapeutics to restore, maintain and improve body functions (Polak et al., 2008). Daar and Greenwood (2007) stated that regenerative medicine aims at 'repair, replacement or regeneration of cells, tissue or organs to restore impaired function'. It aids the body to form new functional tissue to replace lost or defective tissue. Ultimately, this will help to provide therapeutic treatment for conditions where current therapies are inadequate. Cell therapy and tissue engineering are part of the broader field of regenerative medicine, whose aim is the delivery of safe, effective and consistent therapies. The human body has an endogenous system of regeneration and repair through stem cells, where stem cells can be found almost in every type of tissue. This process is highly evolved through evolution, and so it is logical that restoration of function is best accomplished by these cells. Therefore, stem cells hold great promise for the future of translational medicine (NRC, 2002). Regenerative medicine is also a primer for pediatricians (Bajada et al., 2008; Julia and Polak, 2009; Vacanti, 2010; Longaker, 2010).[3]

2.TYPES OF STEM CELLS

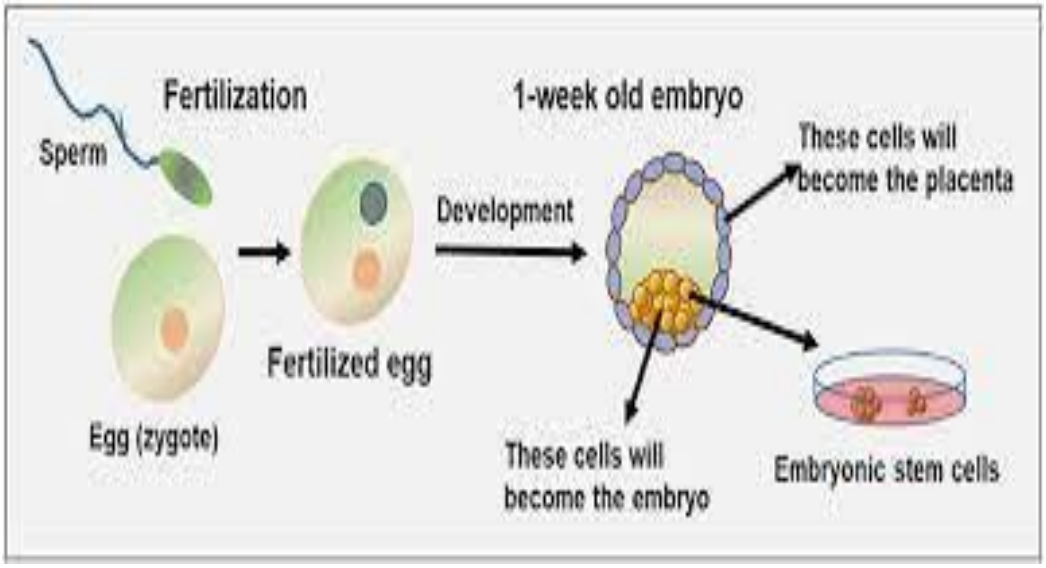
Stem cells are divided into 2 main forms. They are
a. Embryonic stem cells
b. Adult stem cells
c. Umbilical Cord Stem (UCS) cells

a. Embryonic stem cells

Pluripotent ESCs can be derived from the inner cell mass (ICM) of a 5–6-day-old blastocyst. When a blastocyst implants the ICM eventually develops into a fetus (in two months' time). The surrounding trophoblast develops into placenta.

In embryogenesis, the ICM develops into two distinct cell layers, namely the epiblast and the hypoblast. The hypoblast forms yolk sac, while the epiblast differentiates into three classical layers of the embryo; ectoderm, mesoderm and endoderm with potential of forming any tissue. ESCs were first described by Gail Martin in 1981 [4]. Thereafter, it took 17 years before the first human ESC line was established in 1998[5] at the University of Wisconsin-Madison. Since then, at least 225 human ESC lines have been created. An ESC line is defined by cell "immortality" in culture.

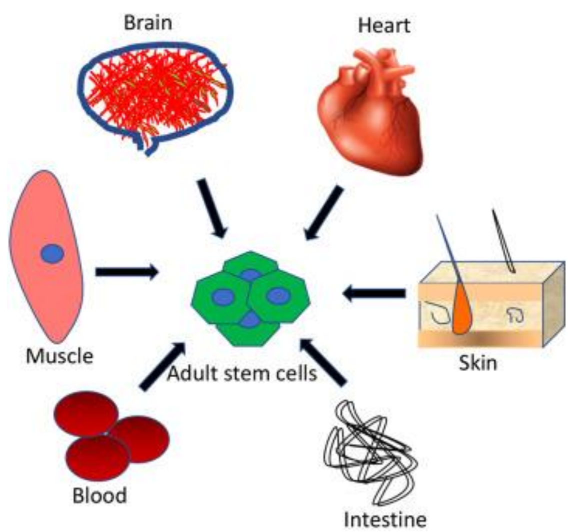
An ESC line is created by culturing the ICM on feeder layers consisting of mouse embryonic fibroblasts or human feeder cells. Recent reports showed that ESCs can be grown without the use of a feeder layer, thus avoiding the exposure to viruses and exogenous proteins [6]. Controlled differentiation into tissue committed cells is achieved by co-culture of ESCs with basic fibroblast growth factor or other cell types. Before their clinical use, ethical and scientific questions need to be resolved, e.g., the risk of teratoma formation and possible transmission of disease[7]. Eventually, these cells might be introduced for treating diabetes. In 1869, Paul Langerhans as a medical student observed for the first-time beta islet cells as microscopic islands of a different structure in the pancreas [8]. These complex mini-organs the pathological site of diabetes have always fascinated transplant and regenerative scientist not just for their complexity but also for their important clinical relevance. Soria et al. has been succeeded to introduce the human insulin gene into mouse ESCs to produce insulin and treat diabetic mice successfully [9,10].



b. Adult stem cells

Adult stem cells (also known as somatic stem cells, derived from Greek of the body) are defined as undifferentiated cells found throughout the body that divide to replenish dying cells and regenerate damaged tissues.

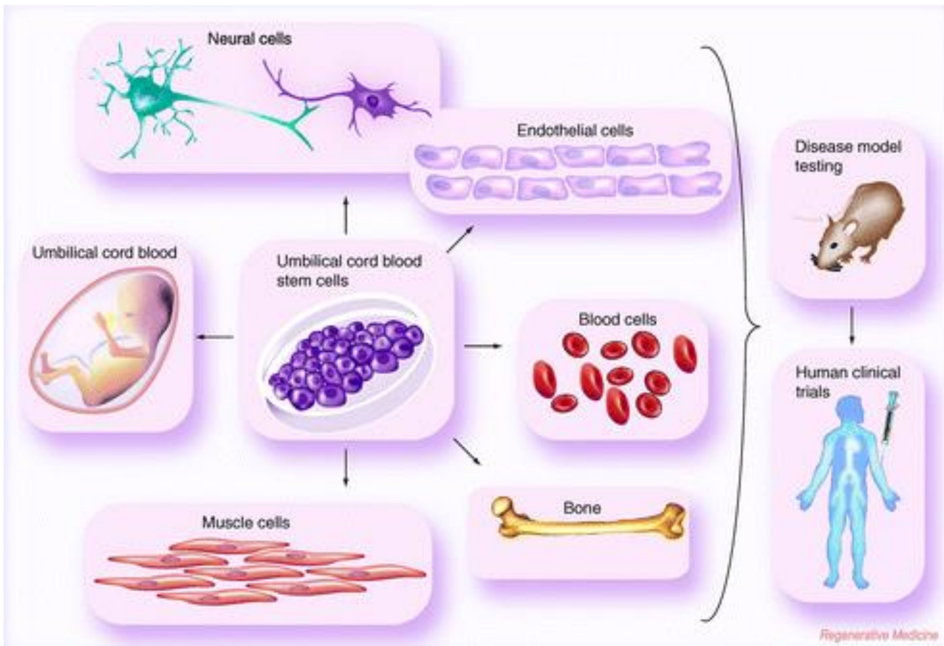
The term adult stem cells are somewhat misleading as they can be found in both children and adults. Leading as they can be found in both children and adults. There are 2 types of adult stem cells. One type comes from fully developed tissues such as the brain, skin, and bone marrow. There are only small numbers of stem cells in these tissues. They are more likely to generate only certain types of cells. For example, a stem cell that comes from the liver will only make more liver cells. The second type is induced pluripotent stem cells. These are adult stem cells that have been changed in a lab to be more like embryonic stem cells. Scientists first reported that human stem cells could be changed in this way in 2006. Induced pluripotent stem cells don't seem to be different from embryonic stem cells, but scientists have not yet found one that can develop every kind of cell and tissue.



C. Umbilical Cord Stem (UCS) Cell

The umbilical cord is the richest and purest source of stem cells. It contains two types of cells: hematopoietic stem cells (HSCs) and mesenchymal stem cells (MSCs). Each type can transform into different cells and tissues, such as white and red blood cells, nerve and muscle tissue. Collecting umbilical cord stem cells is completely non-invasive and pain-free, compared to bone marrow apheresis stem cells which require hospitalization. They are also completely ethical to collect. If you are considering stem cell banking for your baby, umbilical cord stem cells are your best option. The rich source of pure or "naïve" stem cells it contains give your baby a stronger chance of successful treatment. They are perfectly matched to the DNA of your baby and can by cryogenically frozen for 25 years or more.

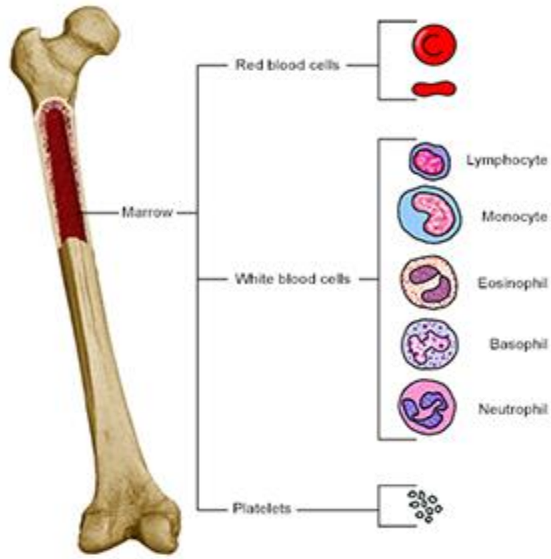
As scientific research improves, there are more discoveries being made where umbilical cord stem cells can help treat life-affecting diseases and conditions including very promising trials into treating autism. Without collecting stem cells, the umbilical cord would simply be discarded, so the sample collection process doesn't interfere at all with your birth. Thanks to the DNA link to the mother, umbilical cord stem cells have a 25% chance of being a suitable match for a sibling.



3.STEM CELL VERSUS REGENERATIVE MEDICINE

3.1 Stem cells in medicine

The only stem cells now used to treat disease are hematopoietic stem cells. These are the blood cell-forming adult stem cells found in bone marrow. Every type of blood cell in the bone marrow starts as a stem cell. Stem cells are immature cells that are able to make other blood cells that mature and function as needed. These cells are used in procedures such as bone marrow transplants. These help people with cancer make new blood cells after their own hematopoietic stem cells have been killed by radiation therapy and chemotherapy. They may also be used to treat people with conditions such as Fanconi anemia. This is a blood disorder that causes the body's bone marrow to fail. Stem cells may help your health in the future in many ways and through many new treatments. Researchers think that stem cells will be used to help create new tissue. For example, one day healthcare providers may be able to treat people with chronic heart disease. They can do this by growing healthy heart muscle cells in a lab and transplanting them into damaged hearts. Other treatments could target illnesses such as type 1 diabetes, spinal cord injuries, Alzheimer disease, and rheumatoid arthritis. New medicines could also be tested on cells made from pluripotent stem cells



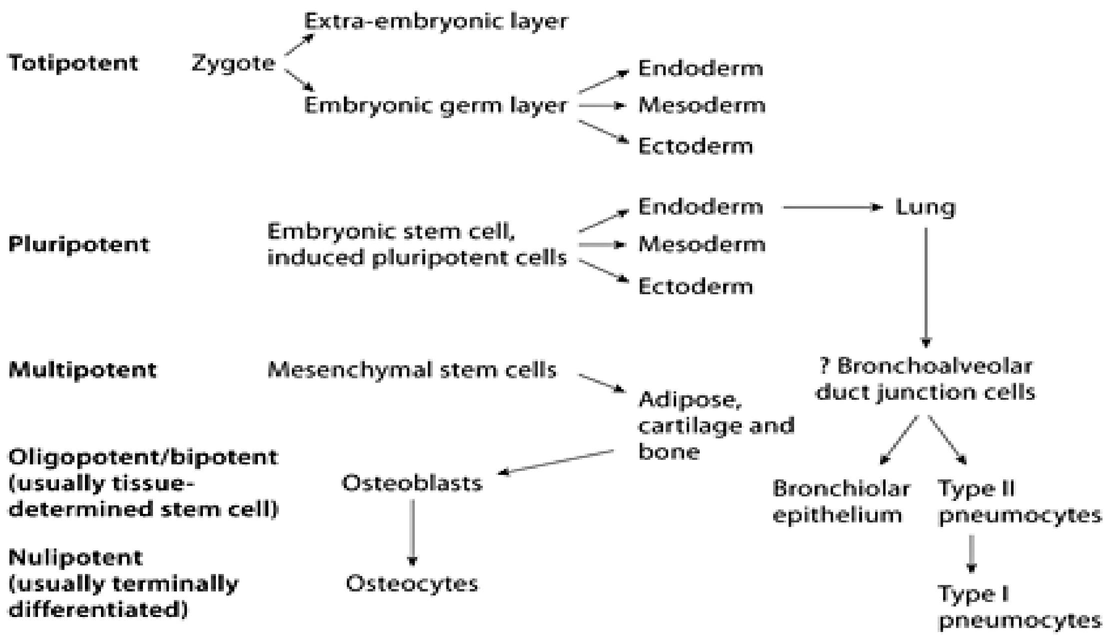
3.2 Stem cells in Regenerative Medicine

Stem cells have a capacity for self-renewal and capability of proliferation and differentiation to various cell lineages. They can be classified into embryonic stem cells (ESC) and non-embryonic stem cells (non-ESC). Mesenchymal stem cells (MSC) show great promise in several animal studies and clinical trials. ESCs have a great potential but their use is still limited due to ethical and scientific considerations.

The use of amniotic fluid derived cells, umbilical cord cells, fat and skin tissues and monocytes might be an adequate "ethically pure" alternative in future. Stem cells can improve healthcare by using and augmenting the body's own regenerative potential. Regenerative medicine aims at helping the body to form new functional tissue to replace lost or defective ones. Hopefully, this will help to provide therapeutic treatment for conditions where current therapies are inadequate. Human body has an endogenous system of regeneration through stem cells, where stem cells are found almost in every type of tissue. The idea is that restoration of function is best accomplished by these cells. Regenerative medicine comprises the use of tissue engineering and stem cell technology. This review is not meant to be exhaustive, but aims to highlight present and future applications of stem cells in this exciting new discipline. We will briefly discuss tissue engineering and stem cell technology including their different sources.

Stem Cell Classification Based on Differentiation Potential

The ability to differentiate, one of the two main characteristics of stem cells, varies between stem cells depending on their origin and their derivation. All stem cells can be categorized according to their differentiation potential into 5 groups: totipotent or omnipotent, pluripotent, multipotent, oligopotent, and unipotent[11]. The hierarchy of stem cells. Totipotent cells form embryonic and extra-embryonic tissue. Pluripotent cells form all 3 germ layers while multipotent cells generate cells limited to 1 germ layer. Bronchoalveolar duct junction cells in the lung may be multipotent while type II pneumocytes are oligopotent and differentiate into type I pneumocytes of the alveoli.



Totipotent Cells

Totipotent or omnipotent cells are the most undifferentiated cells and are found in early development. A fertilized oocyte and the cells of the first two divisions are totipotent cells, as they differentiate into both embryonic and extraembryonic tissues, thereby forming the embryo and the placenta[12].

Pluripotent Cells

Pluripotent stem cells are able to differentiate into cells that arise from the 3 germ layers – ectoderm, endoderm, and mesoderm – from which all tissues and organs develop. Pluripotent stem cells called ESCs were first derived from the inner cell mass of the blastocyst. Recently, Takahashi and Yamanaka [13]. Generated pluripotent cells by reprogramming somatic cells. These cells are called induced pluripotent stem cells (iPSCs) and share similar characteristics with ESCs. Notably, there has been no pluripotent cell population isolated from the lung.

Multipotent Cells

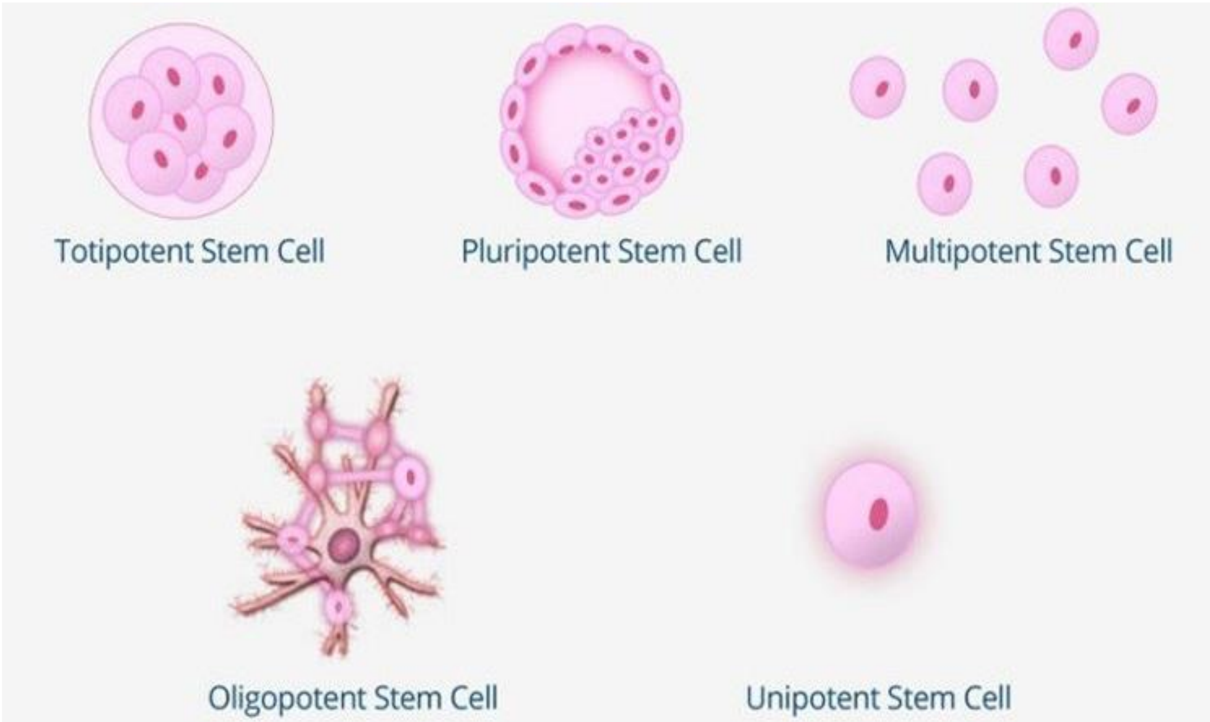
Multipotent stem cells are found in most tissues and differentiate into cells from a single germ layer [14]. Mesenchymal stem cells (MSCs) are the most recognized multipotent cell. They can be derived from a variety of tissue including bone marrow, adipose tissue, bone, Wharton's jelly, umbilical cord blood, and peripheral blood. MSCs are adherent to cell culture dishes and are characterized by specific surface cell markers. These cells can differentiate into mesoderm-derived tissue such as adipose tissue, bone, cartilage, and muscle. Recently, MSCs were differentiated into neuronal tissue which is derived from the ectoderm. This is an example of trans differentiation, i.e., when a cell from one germ layer (mesoderm) differentiates into neuronal tissue (ectoderm). Tissue-resident MSCs have been isolated from the lung; however, no other multipotent cell has been isolated to date [15].

Oligopotent Cells

Oligopotent stem cells are able to self-renew and form 2 or more lineages within a specific tissue; for example, the ocular surface of the pig, including the cornea, has been reported to contain oligopotent stem cells that generate individual colonies of corneal and conjunctival cells. Hematopoietic stem cells are a typical example of oligopotent stem cells, as they can differentiate into both myeloid and lymphoid lineages. In the lung, studies suggest that bronchoalveolar duct junction cells may give rise to bronchiolar epithelium and alveolar epithelium [16].

Unipotent Cells

Unipotent stem cells can self-renew and differentiate into only one specific cell type and form a single lineage such as muscle stem cells, giving rise to mature muscle cells and not any other cells [17,18]. In the lung, type II pneumocytes of the alveoli give rise to type I pneumocytes.



Stem Cells in Clinical Practice and Regenerative Medicine

The contribution of stem cells in modern medicine is of paramount importance, both for their broad use in basic research and for the opportunities they give us to develop new therapeutic strategies in clinical practice. Their characteristics make them valuable in a wide range of applications in biological and medical sciences [19]. For example, ESCs are excellent tools to understand human development and organogenesis. Stem cells such as iPSCs will be critical in the investigation of new and safe therapies. In addition, stem cells may be able to replace damaged tissue or even regenerate organs. IPSCs provide the opportunity to set up human models of diseases that would improve the understanding of the pathogenetic mechanisms of human diseases and would enable improvements in cell-based therapy for degenerative disorders. Cell therapy has been investigated in almost every degenerative disorder. Promising results from preclinical studies and clinical trials have already been described in several diseases, such as diabetes mellitus [20,21], chronic myeloid leukemia, cirrhosis, pulmonary fibrosis, Crohn's disease, heart failure, and disorders of the nervous system, and the immunomodulatory effects of stem cells have found their utility in several conditions characterized by predominant inflammation [22]. There are issues to consider in cell therapy and regenerative medicine. Immunodetection is still a consideration although MSCs and placental tissue as well as iPSCs circumvent the problem. The genetic stability of stem cells, especially iPSCs, remains to be elucidated. Genetic instability can give rise to tumor formation. Indeed, the plasticity and self-renewal that characterize stem cells could lead to carcinogenesis in the host tissue [23], while spontaneously occurring teratomas and related tumors could develop from the use of ESCs or iPSCs in therapeutic cell transplantation [24]. Finally, a number of ethical concerns have been raised mainly in the use of ESCs [25]. These include the ethical controversies of destroying an embryo in generating ESCs. This can now be potentially bypassed by iPSCs.

CONCLUSION:

Stem cells are an important tool for understanding both the organogenesis and the continuous regenerative capacity of the body. They could be a model for the study of pathogenetic mechanisms and could assist researchers in understanding the pathophysiology of various diseases. They also offer the possibility of developing biological models for the study of new pharmacological agents. However, the most important potential of these cells is to replace damaged tissue and even regenerate organs. Today, a large number of research protocols, preclinical studies, and clinical trials have been published. Although, several clinical studies have already reported encouraging results for the development of new therapeutic strategies in cell-based medicine, there are a number of risks and obstacles. Despite this, there is ongoing research and development that gives us great optimism about regenerative medicine.

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External Resources

a. Crossref (DOI)
b. Chemical Abstracts Service (CAS)
c. ISI Web of Science

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