The Current Advances in the Biotechnological Application of Stem Cells

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***Abstract*—The world of medicine seems to be revolutionized with the ongoing extensive stem cell research. Stem cells are different from the normal cells present in our body. Their availability, flexibility and abundance make them different from the other type of cells. These cells can undergo many cycles of differentiation and can lead to regeneration of tissues as well as organs. These advantages of stem cells make them a good research potential. These properties are now being exploited to create stem cells based drugs and stem cell based therapy, thus leading to advances in the treatment of various diseases.**

***Index Terms*—Stem cells, embryonic stem cells, adult stem cells, applications.**

I. Introduction

The vast majority of the body's trillions of cells are differentiated, meaning they have taken on specialized properties and functions and they have lost the ability to generate cells of other types. Skin, muscle, blood, bone and the nervous system are all made up of population of differentiated cells. However, there are other cells that remain less differentiated and retain their ability to give rise to other cell types. These cells are known as stem cells. Stem cells exhibit two characteristics that are not found in most of the differentiated cells. Firstly, these cells can give rise to highly specialized cells thereby assisting the body in renewing and repairing its tissues by taking the place of cells that are lost or dead. [9]. Secondly, in the presence of proper environment these cells can undergo millions and millions of cycles resulting in development of new cells.

On the basis of their potencies these cells can be divided into various types (Table I).

There have been primarily two types of stem cells in humans and animals on which the scientists have been working. These are Embryonic stem cells (ES cells) and non embryonic "Somatic or Adult stem cells."

II. Types of Stem Cells and Their Potential in Research and Clinical Applications

A. Embryonic Stem Cells

The only cells that can demonstrate the production of almost 200 different cell types are the human embryonic stem cells. Derived from the cells of the embryo, these cells can differentiate into all cells of a human adult body. Coming primarily from the inner mass cells of blastocyst, these cells are generally pleuripotent and can grow in their undifferentiated state indefinitely. They retain their ability to grow and generate all functional adult cell types for example; ES cells can give rise to skin cells, muscle cells, heart, brain and bone cells.

TABLE I: Various Types of Stem Cells [9].

Differentiation Potential	Number of cell types	Example of stem cell	Cell types resulting from differentiation
Totipotential	All	Zygote (fertilized egg), blastomere	All cell types
Pleuripotential	All except cells of the embryonic membranes	Cultured human ES cells	Cells from all three germ layers
Multipotential	Many	Hematopoietic cells	Skeletal muscle,cardiac muscle, liver cells, all blood cells
Oligopotential	Few	Myeloid precursor	5 types of blood cells (Monocytes, macrophages, eosinophils, neutrophils, erythrocytes)
Quadripotential	4	Mesenchymal progenitor cell	Cartilage cells, fat cells, stromal cells, bone-forming cells
Tripotential	3	Glial-restricted precursor	2 types of astrocytes, oligodendrocytes
Bipotential	2	Bipotential precursor from murine fetal liver	B cells, macrophages
Unipotential	1	Mast cell precursor	Mast cells
Nullipotential	None	Terminally differentiated cell e.g. Red blood cell	No cell division

Due to their remarkable feature of retaining and developmental capacity, researchers have a high hope of producing cells and tissues that can be used in replacement and regenerative therapies. Treating disorders such as diabetics, heart attacks, blood disorders etc with the help of embryonic stem cells could revolutionize the world of medicine by providing unlimited possibilities. Also, it has been noticed over the years that there has been a decline in organ donors, cell immunocompatibility with the recipient and implant infection. In such cases embryonic stem cells can be sought to give rise to entire heart, kidney and also liver. Scientists are continuously trying to learn about instructing

Manuscript received April 3, 2012; revised July 13, 2012.
This work was supported by The University of Warwick.
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doi: 10.12720/jomb.1.1.7-10

the embryonic stem cells in culture to produce desired cell types and once grown they could themselves replace the damaged cells in the affected organs [10]

B. Adult Stem Cells

Adult stem cells are undifferentiated stem cells, which are mainly defined by their origin. Their primary role is to maintain and repair tissues in which they were found. Depending on their origin (which part of body they are from) these cells have different properties. There are many studies related to adult stem cells uses, some suggesting that they can develop into many different cell types whereas others suggesting their development only into a limited number of cell types relating to the tissues from which they originated. Adult stem cells can be characterized into Hematopoietic stem cells (found in bone marrow, provide blood cells required for fighting infections and maintain the level of blood), Mesenchymal stem cells (also found in the bone marrow. In laboratory, these cells can give rise to fat cells, cartilage, bone, tendons and ligaments, muscle cells, skin cells etc.) and Umbilical cord blood stem cells (obtained immediately after birth from the umbilical cord, rich in haemopoietic stem cells, also called as neonatal stem cells, are less mature than the stem cells of bone marrow).

Over the years, the potential use of hematopoietic stem cells for treating blood cancers, breast cancer and coronary artery disease has been exploited and scientists are showing keen interest studying the potential of producing other type of cells from these adult stem cells. They have acquired knowledge about the techniques of growing mesenchymal stem cells in large quantities. Use of cord blood cells has grown as an alternative source of hematopoietic stem cells for the treatment of cancer (leukemia). There is a huge potential in the use of umbilical cord blood stem cells for tissue repair and organ regeneration [8].

III. Applications of Stem Cells in Regenerative Medicine

The discipline of science that focuses on the combined impact of the capability of the body to self-regenerate and the power of stem cells in damaged tissues or even organs. The main focus of this discipline is the production of new tissues or organs or simply improving the function of existing ones. It has been proved that all adult tissues or organs are made up of stem cells that get impaired once a disease is caused; regenerative medicine aims at activating some kind of repair processes in the diseased organ or tissue that can thus open ways for therapies especially used for many degenerative diseases [13].

Variety of approaches like cell therapy, tissue engineering, gene therapy and biomedical engineering have given rise to various types of regenerative medicines, which will be discussed in the following section.

A. Cell Therapy

Process of injecting stem cells in the form of direct diffusion, cell fusion and nuclear programming (induced pluripotency) into an organism or a person is known as cell therapy[5].Cell therapy can be broadly classified as of two types; Autologous: Therapy using one's own cells and Allogenic: Therapy using cells from some donor.

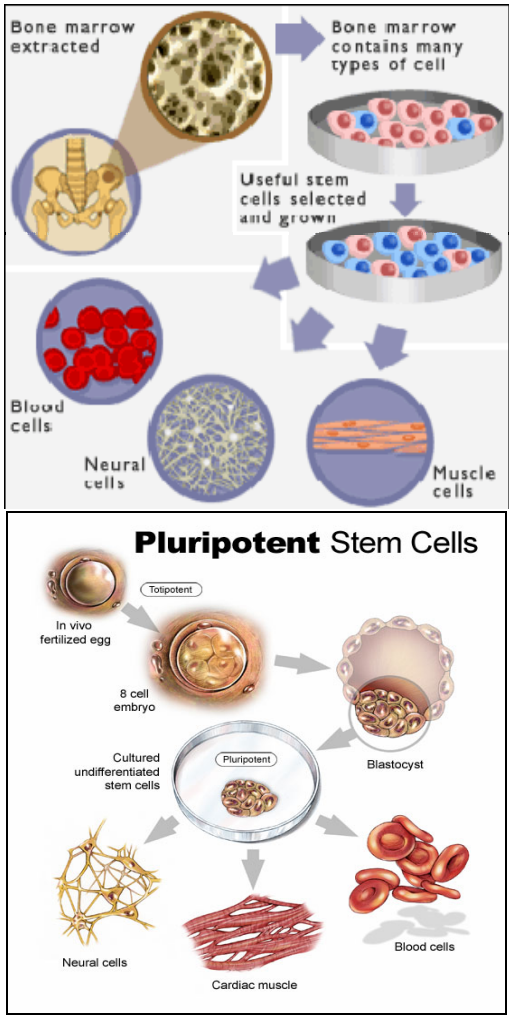

Fig. 1. Embronic stem cell culture and and Adult stem cell culture [9, 18].

Skin replacement-Whenever a hair follicle is plucked from a patient's body, so are also pluckedthe skin stem cells residing in that hair follicle. These cells when cultured can form an epidermal exactly similar to the patient's own skin thereby providing tissues for autologous growth. Scientists are studying this potential of hair follicle stem cells in clinical trials providing alternative to surgical grafts used for ulcers and burns [12].

Diseases of the nervous system- With the advance in technology, it has now been proved that neural stem cells, which are multipotent and capable of being self-renewed, can also divide in adult mammalian brain. For autologous therapy, these stem cells should be present in more accessible places than embryonic, fetal or adult brain tissue. It has been seen that dental pulp, olfactory mucosa and peridontium are good sources of neural stem cells. Brain injury models show that these cells proliferate in the neurogenic region as well as migrate towards the site of damage. Investigations on neural stem cell based therapy are still going on. This therapy has a high potential in treating diseases like Parkinson's and Alzheimer's disease (neurodegenerative disease), stroke and spinal cord injuries [2, 16].

Stem cell therapy for Diabetes Mellitus - When the pancreatic insulin producing beta cells present in the islets of

langerhans are destroyed, Diabetes mellitus is caused. Most common curative therapy for diabetes is the use of pancreas or islet cell transplants as replacements. Shortage of donor organs has led to the research of alternative ways of generation of beta cells. It has been seen that both Embryonic and adult stem cells can produce beta cells and canalso work to restore its functionality. Ductal epithelium of injured pancreas contains pancreatic stem cells that are supposed to be the next source of beta cells suitable for transplantation. Use of embryonic stem cells and reprogrammed cells holds great promise in generation of insulin secreting cells for the treatment of diabetes mellitus [2, 3].

B. Stem cells in Tissue Engineering

Tissue engineering with the help of stem cells focuses on constructing tissues or even organs on matrices or scaffolds that are usually made up of biological material. This construction follows a 3-D approach that can very well mimic various structures making the tissue (cartilage, bone, tendon etc).

With increase in life expectancy of individuals, number of aged people is increasing in the world today. With the increase in this number, there has been a continuous growth in the number of people with degenerative diseases of the skeletal system. It has been noticed that mesenchymal stem cells can give rise to various distinct tissues like bone, cartilages, fat tendon, muscle etc. The advancement in tissue engineering technique has lead to the combination of controlled growth factors with these stem cells for the development of new tissues such as cartilage and bones. As compared to normal adult organ specific cells, the proliferation capacity of pluripotent embryonic cells or multipotent stem cells is much higher; this makes stem cells as a preferred choice for tissue engineering. Particular carrier material strongly influences the quality of tissue produced by stem cells [14].Bone tissue engineering - Some features that make mesenchymal stem cells important for clinical therapies are: transduction with retroviral and other vectors is easily possible and the implants that are tissue engineered are capable of regenerating diseased and damaged tissues.Mesenchymal stem cells have a huge production in the technique of bone tissue engineering. There is a decrease in bone marrow mesenchymal cells with the growing age of a person that results in decrease in self-regenerating capacity of musculoskeletal diseases and injuries. If grown in vitro using tissue engineering these cells can be differentiated into osteoblasts.Further, they can develop into various mesenchymal lineages making them useful for repairing tissues of joints.Also, it has been seen that there is negligible self-healing potential in a damaged cartilage. Therefore, the use of stem cell therapy and tissue engineering would be a promising approach in the treatment of damaged cartilage [14].

C. Stem Cells in Gene Therapy

The use of self-renewing stem cells can eliminate the repeated administration of therapeutic cells. With the help of genetic engineering the host's own stem cells can be repaired and used for autologous transplantation. Diseases like beta thalassemia, sickle cell disease, junctional epidermolysus bullosa are being treated now. Research is now being focused on tumor specific therapy with the use of stem cells. Mesenchymal stem cells have proved to be good agents.

IV. Ethics and Regulations in Stem Cell Research

Application of human embryonic stem cells has generated a lot of interest and public debate. Religious, medical, cultural and other viewpoints have led to a widespread discourse over the use of stem cells. Life begins with the fertilization of the ovum and therefore, destruction of an embryo is thought to be equivalent to infanticide. Stem cells with nuclear transfer share the same concerns. To shun these controversies, various federal governments have had restricted access to stem cell technology. For instance, the British government had banned reproductive cloning but stem cell research and cloning to obtain useful stem cells are both permitted [4,7].

V. Conclusion and Future Prospective

The therapeutic power of stem cells in the field of regenerative medicine has a great potential for treating various diseases at early stages. Cultured stem cells have had a remarkable progress in the treatment of diseases like Parkinson's and diabetes. Once the scientists realize the full potential of stem cells and the ethical issues of embryonic stem cells (use of embryos) are worked out, a huge progress in this field would have been made. Use of stem cells would prove to be a universal cure for almost all diseases. Companies like Diarcin, Neurotech and Neuronova have already applied stem cell technology to treat chronic stroke patients and some neurodegenerative diseases [12]. Present trends have been encouraging and it is expected that there will be many breakthroughs in the coming years.

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