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Review Article

Stem Cells: A Life Insurance Policy at Birth?

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A B S T R A C T

Stem cell research offers unprecedented opportunities for developing new medical therapies for debilitating diseases. These cells have the remarkable potential either to remain a stem cell or differentiate and transform into another cell type. Most of the research work up till now has been focused on two kinds of stem cells embryonic stem cells and non-embryonic "somatic" or "adult" stem cells. In recent years, umbilical cord which contains both hematopoeitic stem cells and mesenchymal stem cells have proven useful in treating different types of health problems. These stem cells can differentiate into different cell types and are less prone to rejection. The collection of cord blood is a non-invasive, painless and less expensive procedure. There are a number of public and private umbilical cord stem cell banks which cryopreserve these stem cells for future use. These stem cells act as a biological insurance which can be stored for personal use or donated to others. Umbilical cord stem cells are a potential and promising therapeutic tool

Introduction

Stem cell's ability to differentiate into different cell types makes it a highly promising candidate for human regenerative medicine. Stem cell research offers unprecedented opportunities for developing new medical therapies for neurodegenerative (Ali and Bahbahani, 2010), heart disease (Mosca RS, 2012), diabetes (David, 2009), cancer (Krtolica, 2005) and other such debilitating diseases. Stem cells differ from the other cells in plasticity, homing (travel to the site of tissue damage) and engraftment (transplanted cells reproducing in the host). The beauty of stem cells is that they can keep dividing indefinitely for renewing themselves or can produce specialized cells, for example- muscle cell, RBC or brain cell etc. They can be categorised by their potential of differentiation into totipotent, pluripotent and unipotent cells. Fertilized egg or zygote is the 'Mother Stem Cell'. It is totipotent i.e., it has the potential to differentiate and can give rise to a fully functional organism. The fertilized egg divides and its multiplying cells continue to be totipotent till the morula stage. After few more divisions it reaches the uterus and before its implantation, the early embryo acquires another category of stem cells called the Embryonic stem cells (ES). They

are derived from the inner cell mass of a blastocyte. These stem cells are considered to be pluripotent which are capable of giving rise to any type of cell and tissue. By the time an embryo becomes a foetus, second category of stem cells come into existence i.e., Adult stem cells. These cells are undifferentiated and are also called as Somatic stem cells. Organs have its own resident stem cells which are few but they bear the responsibility of regenerating an organ's entire population of specialized cells for example the testis form only sperm cells. Adult stem cells constantly divide and regenerate all the cell types of the organ from which they originate indicating their capability to regenerate the entire organ.

The third category of stem cells which are isolated nine months after fertilization are the Umbilical cord stem cells which are a heterogenous population of Hematopoietic stem cells (HSC) and Mesenchymal stem cells (Dominici *et al*, 2006 & Uccelli *et al*, 2008). HSCs can differentiate into different types of blood cells like RBC, WBC and platelets (Fig. 1) whereas MSCs differentiate into hepatocytes, neural, cardiac muscles, bone, cartilage and connective tissue (Uccelli *et al*, 2008).

Umbilical cord stem cells are lately gaining popularity as a therapeutic tool since it is not unethical, easily available, non-invasive and has low risk of infection. After delivery the umbilical cord is detached from the new born and few ounces of blood is collected. This blood is a life insurance and acts as a biocurrency which can be encashed later . The collected stem cells are processed and cryopreserved for future use in transplantations. Cells taken from the umbilical cord blood show lower risk of graft-versus-host diseases as compared to bone marrow transplantations (Ringden *et al*, 2008). Another advantage of using these cells is their abilty to produce induced pluripotent stem cells (Takenaka *et al*, 2010).

Thus a tissue which was earlier considered a biological waste has now become a treasure trove of immense medical value. Its accessibility and it's potential to differentiate makes it a promising candidate of stem cell research and for clinical applications (McGuckin and Forraz 2008).

Materials and Methods

Stem cells in treatment of Major Diseases

Nervous System Diseases: Many nervous system diseases result from the degeneration of nerve cells. Mature nerve cells cannot divide to replace those that are lost. In Parkinson`s disease, nerve cells that make the chemical dopamine degenerate. In Alzheimer's disease, cells that are responsible for the production of certain neurotransmitters are affected due to the formation of plaques in the brain. In amyotrophic lateral sclerosis, the degeneration of the upper and lower motor neurons take place (Ali & Bahbahani, 2010). In spinal cord injury, brain trauma and even stroke, many different types of cells are affected. Perhaps, the only hope for treating such individuals comes from potential to create new nerve tissue restoring function from pluripotent stem cells. Recently neurologists from All India Institute of Medical Sciences (AllMS) injected stem cells taken from patient's bone marrow of hip bone, back into his antecubital vein and found that 60 % of stroke patients who suffer partial paralysis were able to recover (Kounteya Sinha, 2009).

Umbilical cord stem cells show high potential for neural differentiation. The mononuclear fraction of umbilical cord

blood containing pluripotent stem cells along with mesenchymal cells have been reported to cure the neurodegenerative diseases (Lim *et al*, 2008). By manipulating the signals which transcription factors send to the cells, Ali *et al* (2014) was able to promote cell differentiation and maturation. They could produce nerve cells that were significantly more mature and therefore more useful as a model for neurodegenerative diseases i.e., Alzheimer's.

Ischemic Heart Diseases & Cardiomyopathy

Leading cause of heart failure and death in developed countries is Myocardial infarction. The lack of resident stem cells in the heart has led to an intensive search for alternative sources of cardiomyocyte progenitors. Embryonic stem cells have been shown to differentiate into cardiomyocytes that can form stable intracardiac grafts (Kathyjo A. *et al*, 2001). Heart attack patients can be injected with stem cells and damaged heart muscles can be repaired. Chow *et al*, (2013) showed that human Umbilical cord blood stem cells could heal damaged muscle and blood vessels in mice with peripheral vascular disease.

Primary Immunodeficiency Diseases

There are more than 70 different forms of congenital and inherited deficiencies of the immune system that have been recognized such as Severe Combined Immunodeficiency Disease (SCID), Wiskott- Aldrich syndrome (Slatter *et al*, 2006) and the Autoimmune disease - Lupus erythematosus. These diseases are characterized by an unusual susceptibility to infection and often associated with anemia, arthritis, diarrhea and selected malignancies. However, the transplantation of Umbilical cord stem cells resulted in restoration of immune functions. Umbilical cord-derived mesenchymal stem cells have also shown to regulate thymic epithelial cell development and function in mice (Liu *et al*, 2014).

Cancer

Cancer is a disease which results from uncontrolled proliferation of cells leading to malignant growth or tumor. Till date, the only treatment for such patients is radiation & chemotherapy which kill the cancerous cells in the body. Unfortunately, such procedures also kill many normal cells, including the healthy stem cells that are present in the bone marrow. Stem cell transplant can save the lives of patients suffering from cancer who have no alternative options available to them. To restore these damaged cells, the patient receives a transplant infusion of immature stem cells, which travel to the bone marrow and over time these cells begin to produce new blood cells (Castro-ManrrezaMarta *et al*, 2014).

Umbilical cord blood containing haematopoetic stem cells is popularly used in restoring blood cells, bone marrow and immune functions after radiation or chemotherapy. Recently scientists have used cord stem cells which are transfected with genes that generate cancer fighting cytokines thus inhibiting further proliferation of the cancerous cells. The stem cells from human umbilical cord have been reported to prolong the life of mouse models with prostate cancer as well as leukaemia and other types of cancer (Steenblock and Anthony, 2006).

Diseases of Bone & Cartilage

Stem cells, once appropriately differentiated

could correct many diseases and degenerative conditions in which bone or cartilage cells are either deficient in numbers or defective in function. The stem cells hold a promise for the treatment of genetic disorders such as Osteogenesis imperfecta and Chondrodysplasia. Stem cells could be cultivated and introduced into damaged areas of joint cartilage in cases of osteoarthritis or into large gaps in bone from fractures and surgeries. Mesenchymal stem cells have been used in the successful repair of bone fractures (Watson *et al*, 2014).

Spinal Cord Injury

Stem cells have a therapeutic use to restore the motor skills lost from acute spinal cord tissue damage. The stem cells derived from umbilical cord tissue are both administered intravenously and also injected intrathecally (into the spinal fluid). Intrathecal injection enables the stem cells to bypass the blood-brain barrier and migrate to the injury site within the spinal canal. Patients are treated by injecting the stem cells directly into the damaged area or into cerebrospinal fluid for the treatment of spinal cord injury. (Ning *et al*, 2013).

Type 1 Diabetes in Children

Type I diabetes is an autoimmune disease characterized by destruction of insulin producing cells in the pancreas. Current efforts are focused on the transplantation of human islets which are obtained from the pancreas. However, treatment is severely hampered by the limited availability of donated pancreas for transplantation as also due to the toxicity of immunosuppressive drugs required to prevent graft rejection.

In recent years, however pluripotent stem cells rich umbilical cord blood have proven useful in treating Type I diabetes. The pluripotent stem cells have the capacity to reprogramme hostile immune response of the host to tolerate pancreatic beta cells and to regenerate these cells, thus reversing Type I diabetes. Improvements in cryopreservation techniques and the expansion of umbilical cord blood cells prior to therapeutic infusion gives a high success rate in curing Type I diabetes (David B. 2009).

The process of stem cell treatment is relatively simple. Stem cells are extracted from embryo, umbilical cord blood or bone marrow (Butler and Menitove, 2011). They are replicated in cell culture. These new cells are then transplanted to repair the damaged tissue of the patient. Umbilical cord blood stem cells are a viable option to treat the diseases for which the current modes of therapy are inadequate.

List of few Umbilical Cord Blood Bank's

There are hundred Cord Blood Stem Cell Banks all over the world of which seventy five are public banks. Some of the popular banks are as follows:

1)*Histostem Ltd.,* (Korea) serves as the largest public blood bank in the world and stores 55,000 umbilical cord blood units of stem cells.
2)*Cryo Cell International* (United States of America) is the largest and oldest cord blood bank of the world.
3)*Cryo-Save* (Belgium) is the Europe's largest stem cell company & recently opened its facility in Bangalore.
4)*Life Cell International* (India) is the country's first and largest cord blood bank (2004).
5)*Cord Life India* has opened its facility in Calcutta.
6)*Jeevan Blood Bank & Research* (India) opened public stem cell bank in Chennai.

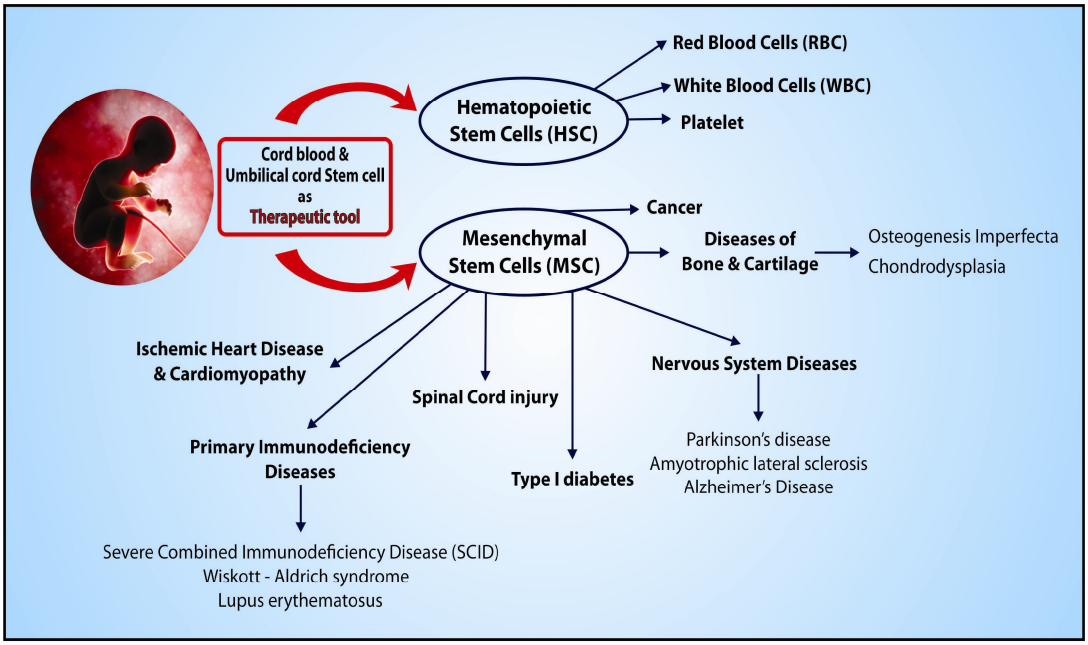

Fig. 1: Umbilical cord stem cells - A potential therapeutic tool

Stem Cell Research Centres in India

1)Stem cell experimental therapy in NICID-IN centre for regenerative medicine, India.
2)Saneron stem cell centre in Chennai.
3)Natural Centre for Biological Sciences, Bangalore.
4)Reliance Life Sciences, Bangalore.
5)Bharat Biotech International Ltd. Hyderabad.
6)National Brain Research Centre (NBRC), New Delhi.
7)L.V. Prasad Eye institute, Hyderabad.
8)A large scale DBT -funded multicentric study on stem cell has been started in AIIMS (Delhi), PAL (Chandigarh), SGPGI (Lucknow), AFMC (Pune) and Army R & R Hospital (De1hi).

Ethical Policy Concerns

Innovative research and new technologies derived from such research generally raise ethical and policy concerns. Ideally, scientists should communicate the results of their research in ways that will be readily understood by a diverse audience, and participate in public discussions related to stem cell research.

Umbilical cords are generally discarded after the birth of a baby & the cells derived from these do not present the same ethical dilemma as those from embryos. Realizing the potential health benefits of stem cell technology it will require a large and substantial investment in research. The government is the only realistic source for such an infusion of funds. For those who are challenged by serious diseases that could, in the future be relieved by therapies gained through stem cell research, public funding holds the greatest promise. Without the stimulus of public funding, new life saving treatments could be substantially delayed.

Since the first umbilical cord blood cell transplantation in 1988, stem cell based research has progressed dramatically and has contributed significantly to

regenerative medicine. Due to their abundant supply, immunological immaturity and high plasticity they have shown overwhelmingly positive response in clinical trials for neural degenerative, heart diseases, cancer and spinal cord injuries. Clinical applications of stem cell are expanding at such a rapid pace that it is wise to invest in stem cell storage for family's future health. Thus in summary, we review the history of umbilical cord blood cells and its status of banking in India and abroad along with its potential use in the treatment of human diseases.

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