Stem cells: An "Aladdin's lamp": An Overview

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Summary

Stem cell therapy is emerging as a potentially revolutionary new way to treat disease and injury, with wide-ranging medical benefits. It aims to repair damaged and diseased body-parts with healthy new cells provided by stem cell transplants. Disease and disorders with no therapies or at best, partially effective ones are the lure of the pursuit of stem cell research. Recently a plethora of work has been done in this field in world around including India. However, Stem cell research presents many ethical and scientific questions as well as future challenges. Nevertheless, stem cell therapy, a prologue to an era of medical discovery of cell-based therapies that will one day restore function to those whose lives are now challenged every day, is still at the beginning of the road.

Keywords- Stem cell, adult stem cell, stem cell therapy, embryonal stem cell, pluripotent stem cells.

Introduction

Stem cells have the remarkable potential to develop into many different cell types in the body during early life and growth. In addition, in many tissues they serve as a sort of internal repair system, dividing essentially without limit to replenish other cells as long as the person or animal is still alive. When a stem cell divides, each new cell has the potential either to remain a stem cell or become another type of cell with a more specialized function, such as a muscle cell, a red blood cell, or a brain cell. Stem cells are distinguished from other cell types by two important characteristics. First, they are unspecialized cells capable of renewing themselves through cell division, sometimes after long periods of inactivity. Second, under certain physiologic or experimental conditions, they can be induced to become tissue- or organ-specific cells with special functions. In some organs, such as the gut and bone marrow, stem cells regularly divide to repair and replace worn out or damaged tissues. In other organs, however, such as the pancreas and the heart, stem cells only divide under special conditions.

Until recently, scientists primarily worked with two kinds of stem cells from animals and humans: embryonic stem cells and non-embryonic "somatic" or "adult" stem cells**.** The functions and characteristics of these cells will be explained in this document. Scientists discovered ways to derive embryonic stem cells from early mouse embryos nearly 30 years ago, in 1981. The detailed study of the biology of mouse stem cells led to the discovery, in 1998, of a method to derive stem cells from human embryos and grow the cells in the laboratory. These cells are called human embryonic stem cells. The embryos used in these studies were created for reproductive purposes through *in vitro* fertilization procedures. When they were no longer needed for that purpose, they were donated for research with the informed consent of the donor. In 2006, researchers made another breakthrough by identifying conditions that would allow some specialized adult cells to be "reprogrammed" genetically to assume a stem cell-like state. This new type of stem cell, called induced pluripotent stem cells (iPSCs)**,** will be discussed in a later section of this document. Stem cells are important for living organisms for many reasons. In the 3- to 5-day-old embryo, called a blastocyst, the inner cells give rise to the entire body of the organism, including all of the many specialized cell types and organs such as the heart, lung, skin, sperm, eggs and other tissues. In some adult tissues, such as bone marrow, muscle, and brain, discrete populations of adult stem cells generate replacements for cells that are lost through normal wear and tear, injury, or disease. Given their unique regenerative abilities, stem cells offer new potentials for treating diseases such as diabetes, and heart disease. However, much work remains to be done in the laboratory and the clinic to understand how to use these cells for cell-based therapies to treat disease, which is also referred to as regenerative or reparative medicine [1-3].

Source of Stem Cells

1) Embryonal stem cell.

2) Adult stem cell.

Embryonic Stem Cells

As their name suggests they are derived from embryos (blastocyst) that develop from eggs that have been fertilized in vitro—in an in vitro fertilization clinic— and then donated for research purposes with informed consent of the donors[4,5]. Growing embryonic stem cells in the laboratory Growing cells in the laboratory is known as cell culture. Human embryonic stem cells are isolated by transferring the inner cell mass into a plastic laboratory culture dish that contains a nutrient broth known as culture medium. The cells divide and spread over the surface of the dish. Over the course of several days, the cells of the inner cell mass proliferate and begin to crowd the culture dish. When this occurs, they are removed gently and plated into several fresh culture dishes. Embryonic stem cells that have proliferated in cell culture for six or more months without differentiating, are pluripotent and appear genetically normal are referred to as embryonic stem cell line [6].

Adult Stem Cells

An adult stem cell is an undifferentiated cell found among differentiated cells in a tissue or organ, can renew itself and can differentiate to yield the major specialized cell types of the tissue or organ. The primary roles of adult stem cells in a living organism are to maintain and repair the tissue in which they are found. In the 1960s, researchers discovered that the bone marrow

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, was discovered a few years later. Stromal cells are a mixed cell population that generates bone, cartilage, fat and fibrous connective tissue.

It was not until the 1990s that scientists agreed that the adult brain does contain stem cells that are able to generate the brain's three major cell types—astrocytes and oligodendrocytes, which are non-neuronal cells and neurons, or nerve cells[7, 8].

Functionally classification of stem cell [9] –

- *Totipotent*- stem cells are cells that can give rise to a fully functional organism as well as to every cell type of the body. Such cells can construct a complete, viable, organism. These cells are produced from the fusion of an egg and sperm cell. Cells produced by the first few divisions of the fertilized egg are also totipotent.
- *Pluripotent*- stem cells are capable of giving rise to virtually any tissue type, but not to a functioning organism. The descendants of totipotent cells and can differentiate into nearly all cells, i.e. cells derived from any of the three germ layers.
- *Multipotent*- stem cells are more differentiated cells (that is, their possible lineages are less plastic/more determined) and thus can give rise only to a limited number of tissues. For example, a specific type of multipotent stem cell called a mesenchymal stem cell has been shown to produce bone, muscle, cartilage, fat, and other connective tissues.
- *Oligopotent*- stem cells can differentiate into only a few cells, such as lymphoid or myeloid stem cells.
- *Unipotent*- cells can produce only one cell type, their own, but have the property of self-renewal which distinguishes them from non-stem cells (e.g. muscle stem cells).

History-

Key research events-

- **1908** - The term "stem cell" was proposed for scientific use by the Russian histologist Alexander Maksimov (1874–1928) at congress of hematologic society in Berlin. It postulated existence of hematopoietic stem cells.
- **1960s** - Joseph Altman and Gopal Das present scientific evidence of adult neurogenesis, ongoing stem cell activity in the brain; like André Gernez, their reports contradict Cajal's "no new neurons" dogma and are largely ignored.
- **1963** - McCulloch and Till illustrate the presence of self-renewing cells in mouse bone marrow.
- **1968** - Bone marrow transplant between two siblings successfully treats SCID.
- **1978** - Hematopoietic stem cells are discovered in human cord blood.
- **1981** - Mouse embryonic stem cells are derived from the inner cell mass by scientists Martin Evans, Matthew Kaufman, and Gail R. Martin. Gail Martin is attributed for coining the term "Embryonic Stem Cell".
- **1992** - Neural stem cells are cultured *in vitro* as neurospheres.
- **1997** - Leukemia is shown to originate from a hematopoietic stem cell, the first direct evidence for cancer stem cells [10-12].
- **1998** - James Thomson and coworkers derive the first human embryonic stem cell line at the University of Wisconsin–Madison.

- **2000s** - Several reports of adult stem cell plasticity are published.
- **2001** - Scientists at Advanced Cell Technology clone first early (four- to six-cell stage) human embryos for the purpose of generating embryonic stem cells.
- **2003** - Dr. Songtao Shi of NIH discovers new source of adult stem cells in children's primary teeth.
- **2004–2005** - Korean researcher Hwang Woo-Suk claims to have created several human embryonic stem cell lines from unfertilised human oocytes. The lines were later shown to be fabricated.
- **2005** - Researchers at Kingston University in England claim to have discovered a third category of stem cell, dubbed cord-blood-derived embryonic-like stem cells (CBEs), derived from umbilical cord blood. The group claims these cells are able to differentiate into more types of tissue than adult stem cells.
- **2005** - Researchers at UC Irvine's Reeve-Irvine Research Center are able to partially restore the ability of mice with paralyzed spines to walk through the injection of human neural stem cells.
- **August 2006** - Rat Induced pluripotent stem cells: the journal Cell publishes Kazutoshi Takahashi and Shinya Yamanaka.
- **October 2006** - Scientists at Newcastle University in England create the first ever artificial liver cells using umbilical cord blood stem cells.
- **January 2007** - Scientists at Wake Forest University led by Dr. Anthony Atala and Harvard University report discovery of a new type of stem cell in amniotic fluid. This may potentially provide an alternative to embryonic stem cells for use in research and therapy.
- **June 2007** - Research reported by three different groups shows that normal skin cells can be reprogrammed to an embryonic state in mice. In the same month, scientist Shoukhrat Mitalipov reports the first successful creation of a primate stem cell line through somatic cell nuclear transfer.
- **October 2007** - Mario Capecchi, Martin Evans, and Oliver Smithies win the 2007 Nobel Prize for Physiology or Medicine for their work on embryonic stem cells from mice using gene targeting strategies producing genetically engineered mice (known as knockout mice) for gene research.
- **November 2007** - Human induced pluripotent stem cells: Two similar papers released by their respective journals prior to formal publication: in Cell by Kazutoshi Takahashi and Shinya Yamanaka, "Induction of pluripotent stem cells from adult human fibroblasts by defined factors", and in *Science* by Junying Yu, et al., from the research group of James Thomson, "Induced pluripotent stem cell lines derived from human somatic cells":pluripotent stem cells generated from mature human fibroblasts. It is possible now to produce a stem cell from almost any other human cell instead of using embryos as needed previously, albeit the risk of tumorigenesis due to c-myc and retroviral gene transfer remains to be determined. [13,14]
- **January 2008** - Robert Lanza and colleagues at Advanced Cell Technology and UCSF create the first human embryonic stem cells without destruction of the embryo.
- **January 2008** - Development of human cloned blastocysts following somatic cell nuclear transfer with adult fibroblasts.
- **February 2008** - Generation of pluripotent stem cells from adult mouse liver and stomach: these iPS cells seem to be more similar to embryonic stem cells than the

previous developed iPS cells and not tumorigenic, moreover genes that are required for iPS cells do not need to be inserted into specific sites, which encourage the development of non-viral reprogramming techniques.

- **March 2008**-The first published study of successful cartilage regeneration in the human knee using autologous adult mesenchymal stem cells is published by clinicians from Regenerative Sciences.
- **October 2008** - Sabine Conrad and colleagues at Tübingen, Germany generate pluripotent stem cells from spermatogonial cells of adult human testis by culturing the cells in vitro under leukemia inhibitory factor (LIF) supplementation.
- **30 October 2008** - Embryonic-like stem cells from a single human hair.
- **1 March 2009** - Andras Nagy, Keisuke Kaji, *et al.* discover a way to produce embryonic-like stem cells from normal adult cells by using a novel "wrapping" procedure to deliver specific genes to adult cells to reprogram them into stem cells without the risks of using a virus to make the change. The use of electroporation is said to allow for the temporary insertion of genes into the cell.
- **28 May 2009** Kim *et al.* announced that they had devised a way to manipulate skin cells to create patient specific "induced pluripotent stem cells" (iPS), claiming it to be the 'ultimate stem cell solution'.[15-19]

Development of stem cells grown in the laboratory

Growing cells in the laboratory is known as cell culture. Human embryonic stem cells are isolated by transferring the inner cell mass into a plastic laboratory culture dish that contains a nutrient broth known as culture medium. The cells divide and spread over the surface of the dish. The inner surface of the culture dish is typically coated with mouse embryonic skin cells that have been treated so they will not divide. This coating layer of cells is called a feeder layer. The reason for having the mouse cells in the bottom of the culture dish is to give the inner cell mass cells a sticky surface to which they can attach. Also, the feeder cells release nutrients into the culture medium. Recently, scientists have begun to devise ways of growing embryonic stem cells without the mouse feeder cells. This is a significant scientific advancement because of the risk that viruses or other macromolecules in the mouse cells may be transmitted to the human cells. Over the course of several days, the cells of the inner cell mass proliferate and begin to crowd the culture dish. When this occurs, they are removed gently and plated into several fresh culture dishes. The process of replating the cells is repeated many times and for many months, and is called sub culturing. Each cycle of sub culturing the cells is referred to as a passage. After six months or more, the original 30 cells of the inner cell mass yield millions of embryonic stem cells. Embryonic stem cells that have proliferated in cell culture for six or more months without differentiating, are pluripotent, and appear genetically normal are referred to as an embryonic stem cell line. Once cell lines are established, or even before that stage, batches of them can be frozen and shipped to other laboratories for further culture and experimentation [20].

Laboratory tests are used to identify embryonic stem cells

At various points during the process of generating embryonic stem cell lines, scientists test the cells to see whether they exhibit the fundamental properties that make them embryonic stem cells. This process is called characterization. As yet, scientists who study human embryonic stem cells have not agreed on a standard battery of tests that measure the cells' fundamental properties. Also, scientists acknowledge that many of the tests they do use may not be good indicators of the

cells' most important biological properties and functions. Nevertheless, laboratories that grow human embryonic stem cell lines use several kinds of tests. These tests include: [21]

- Growing and sub culturing the stem cells for many months. This ensures that the cells are capable of long-term self-renewal. Scientists inspect the cultures through a microscope to see that the cells look healthy and remain undifferentiated.
- Using specific techniques to determine the presence of surface markers that are found only on undifferentiated cells. Another important test is for the presence of a protein called *Oct-4*, which undifferentiated cells typically make. *Oct-4* is a transcription factor, meaning that it helps turn genes on and off at the right time, which is an important part of the processes of cell differentiation and embryonic development.
- Examining the chromosomes under a microscope. This is a method to assess whether the chromosomes are damaged or if the number of chromosomes has changed. It does not detect genetic mutations in the cells.
- Determining whether the cells can be subcultured after freezing, thawing, and replating.
- Testing whether the human embryonic stem cells are pluripotent by 1) allowing the cells to differentiate spontaneously in cell culture; 2) manipulating the cells so they will differentiate to form specific cell types; or 3) injecting the cells into an immunosuppressed mouse to test for the formation of a benign tumor called a teratoma. Teratomas typically contain a mixture of many differentiated or partly differentiated cell types—indications that the embryonic stem cells are capable of differentiating into multiple cell types.

Therapeutic Potential uses of Human Stem Cells "Aladdin's Lamp"

Truly speaking stem cells are no less than "**aladdin's lamp**" which promises to cure most of the diseases that plague the mankind today.

Stem Cell used in cancer Chemotherapy

Chemotherapy aimed at rapidly dividing cancer cells inevitably hits another target—rapidly dividing hematopoietic cells. Doctors may give cancer patients an autologous stem cell transplant to replace the cells destroyed by chemotherapy. One of the most important issues in stem cell biology understands the mechanisms that regulate self-renewal. Self-renewal is crucial to stem cell function, because it is required by many types of stem cells to persist for the life time of the animal. Moreover, whereas stem cells from different organs may vary in their developmental potential, all stem cells must self-renew and regulate the relative balance between self-renewal and differentiation. Understanding the regulation of normal stem cell self-renewal is also fundamental to understanding the regulation of cancer cell proliferation, because cancer can be considered to be a disease of unregulated self-renewal. Because normal stem cells and cancer cells share the ability to self renew, it seems reasonable to propose that newly arising cancer cells appropriate the machinery for self-renewing cell division that is normally expressed in stem cells [22]. Evidence shows that many pathways that are classically associated with cancer may also regulate normal stem cell development. For example, the prevention of apoptosis by enforced expression of the oncogene bcl-2 results in increased numbers of HSCs *in vivo*, suggesting that cell death has a role in regulating the homeostasis of HSCs. If the signalling pathways that normally regulate stem cell self-renewal lead to tumorigenesis when dysregulated, then are stem cells themselves the target of transformation in certain types of cancer. There are two reasons to think that this may be the case. First, because stem cells have the machinery for self-renewal already activated, maintaining this activation may be simpler than turning it on de novo in a

more differentiated cell; that is, fewer mutations may be required to maintain self-renewal than to activate it ectopically. Second, by self-renewing, stem cells often persist for long periods of time, instead of dying after short periods of time like many mature cells in highly proliferative tissues. This means that there is a much greater opportunity for mutations to accumulate in individual stem cells than in most mature cell types [23, 24].

Stem Cells and Diabetes [25, 26]

For decades, diabetes researchers have been searching for ways to replace the insulin-producing cells of the pancreas that are destroyed by a patient's own immune system. Recently, hope for a permanent cure of diabetes has appeared, namely, the transplantation of islets isolated from donor pancreata into the livers of diabetic patients some promising results have already been obtained with embryonic stem cells (ES cells) of both rodent and human origin [27]. However, the potential use of ES cells for the treatment of diseases in humans is beclouded in controversy because of the ethical issues. In theory, embryonic stem cells could be cultivated and coaxed into developing into the insulin-producing islet cells of the pancreas. It is concluded that stem cells offer the greatest potential for the development of an abundant source of pancreatic islets, although specific obstacles must be overcome before this can become a reality [28]. The promising source of islet progenitor stem cells lies in the cells that line the pancreatic ducts. Some investigators believe that multipotent stem cells are intermingled with mature, differentiated duct cells, while others are of the opinion that the duct cells can undergo differentiation, or reversal to a less mature type of cell, which can then differentiate into an insulin-producing islet cell. Bonner Weir *et al*. reported that when ductal cells isolated from adult human pancreatic tissue were cultured, they could be induced to differentiate into clusters that contained both ductal and endocrine cells. In a month's time in culture, the cells secreted low amounts of insulin when exposed to low concentrations of glucose, and higher amounts of insulin when exposed to higher concentrations of glucose [29].

Stem cell used in nervous system diseases

Stem cell therapy offers exciting potential for ambitious cellular replacement to treat diseases such as Parkinson's disease, Alzheimer's disease or even replacement of the cell death that follows thromboembolic stroke. Longer-term safety and efficacy results should enhance our understanding of cell implantation therapy for the treatment of stroke. The much debated stem cell research has led to findings that stem cells can be used to create neurons that are destroyed in the brain as a result of Alzheimer's disease [30]. Parkinson's disease (PD) is caused by a progressive degeneration and loss of dopamine (DA)-producing neurons, which leads to tremor, rigidity, and hypokinesia (abnormally decreased mobility). It is thought that PD may be the first disease to be amenable to treatment using stem cell transplantation. Factors that support this notion include the knowledge of the specific cell type (DA neurons) needed to relieve the symptoms of the disease. In addition, several laboratories have been successful in developing methods to induce embryonic stem cells to differentiate into cells with many of the functions of DA neurons. In a recent study, scientists directed mouse embryonic stem cells to differentiate into DA neurons by introducing the gene Nurr1. When transplanted into the brains of a rat model of PD, these stem cell-derived DA neurons reinnervated the brains of the rat. Regarding human stem cell therapy, scientists are developing a number of 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. Parkinson model released dopamine and improved motor function [31].

Stem cell used in Bone Marrow Transplantation

Another use of allogeneic bone marrow transplants is in the treatment of hereditary blood disorders, such as different types of inherited anemia and inborn errors of metabolism. The blood disorders include aplastic anemia, betathalassemia, Blackfan-Diamond syndrome, globoid cell leukodystrophy, sickle-cell anemia, severe combined immunodeficiency, X-linked lymphoproliferative syndrome and Wiskott-Aldrich syndrome. Inborn errors of metabolism that are treated with bone marrow transplants include: Hunter's syndrome, Hurler's syndrome, Lesch Nyhan syndrome and osteopetrosis. In place of gene transfer, bone marrow stem cell has been studied whether causing angiogenesis or vasculogenesis. Angiogenesis, which means development from capillary endothelial cells, has been considered as a main cause to increase blood vessels in the adults [32]. On the other hand, angioblast or endothelial progenitor cells (EPC), which differentiates to the endothelial cells, enhances vasculogenesis in the embryogenic stage. These cells surround hematopoietic cells and form a blood island, then develop to blood vessels in the embryo. The advantages using bone marrow monocytes are that infection or immune reaction can not occur different from the technique using gene transfer. The disadvantage is necessity to collect bone marrow blood with a volume of 500 to 600ml under general anesthesia. The EPC and angioblast also exists in the peripheral blood, so they could be collected by using apheresis. However, the numbers of these cells are much lower than in the bone marrow and the efficacy of collection is less. To investigate the effects to human ischemic limb by bone marrow monocyte injection, Japan Trial for Therapeutic Angiogenesis Using Cell Transplantation (J-TACT) started since 2000. Our institute also started therapeutic angiogenesis to use bone marrow monocytes since 2004, independently [33].

Stem Cells Repair a Damaged Heart

Recent interest has focused on myocardial regeneration with stem-cell transplantation as a possible treatment option to reverse the deleterious hemodynamic and neurohormonal effects that occur after myocardial infarction and can lead to congestive heart failure. Recently the BOOST trial (Bone marrow transfer to enhance ST-elevation infarct regeneration) has confirmed an increase in global LVEF by 6.7% in 6 months follow up study [34]. Similar studies have been conducted recently in India at AIIMS. Future randomized clinical trials will establish the magnitude of the benefit and the effects on arrhythmias after stem-cell therapy [35]. Myoblast transplantation for cardiac repair has generated beneficial results in both animals and humans; however, poor viability and poor engraftment of myoblasts after implantation in vivo limit their regeneration capacity. Because cardiac tissue has a limited ability to regenerate after myocardial injury, many patients diagnosed with certain myocardial diseases develop heart failure. As an alternative to heart transplantation, cellular cardiomyoplasty the transplantation of exogenous cells into heart tissue—has been investigated as a way to regenerate diseased myocardium and improve the performance of failing hearts. Researchers have used various types of cells to investigate cardiac repair. In particular, many research groups have reported that mononucleated skeletal muscle-derived cells (i.e., myoblasts and satellite cells) can engraft in the heart and improve cardiac performance. Indeed, some myoblast and satellite cell populations are currently being investigated in clinical trials for cardiac repair. Skeletal myoblasts are attractive for clinical use because they can be readily harvested, expanded in vitro, and transplanted in an autologous manner [36, 37].

Spinal Cord Disorders

Advances in stem cell research have led to several transplantation strategies that promote axonal regrowth and partial functional recovery in spinal cord injury. Christopher Reeve Paralysis Foundation (CRPF) funds research to treat or cure paralysis resulting from spinal cord injury or other CNS disorders. CPRF supports a Research Consortium, focus on stem cells, making a lot of progress degeneration, glaucoma and corneal disorders [38]. Currently a paucity of literature reporting human clinical trials involving stem cell transplantation for spinal cord injury [39].

Stem cell used in wound healing

The field of epidermal stem cells has dramatically advanced in the last decade, leading to a better understanding of the molecular factors, signalling pathways and cellular events that identify and characterize stem cells, thus revealing their immense potential for therapeutic use. Furthermore, multipotent epidermal stem cells present the major advantage of easy accessibility with the discovery of their specific location within the bulge of the hair follicle. This review focuses on the most recent findings on epidermal stem cells, and their potential role in initial epidermal commitment, differentiation and wound healing processes in the skin. The differentiation of keratinocytes and subsequent generation of a protective cornified layer are processes that must be accomplished continuously, thus requiring the contribution of the primary stem cells (SCs) for the renewing epidermis. Additionally, in mammals, the epidermis gives rise to a specialized, derived structure, the hair follicle. The recent advances in biotechnology, such as genomics, proteomics, in vivo epidermal targeting, GFP labelling and adeno- and retro-viral gene transfers, will allow for much better understanding of SC biology [40, 41].

Stem Cell Therapy for HIV

The hematopoietic stem cell has long been hypothesized to be a target of human immunodeficiency virus type-1 (HIV) infection that limits the potential for compensatory immune cell production. Effects of HIV on stem cell physiology, however, appear to be indirect, as stem cells are highly resistant to HIV infection. Despite the presence of surface receptors for HIV, the hematopoietic stem cell is not infectible with HIV and can serve as a resource for cellular therapies for AIDS [42].

Stem Cell for Retinal Degeneration

Induced pluripotent stem (iPS) cells are an innovative technology that turns somatic cells into embryonic stem (ES)-like cells with pluripotent potential via the exogenous expression of several key genes. It can be used as an unlimited source for cell differentiation or tissue engineering, either of which is a promising therapy for human degenerative diseases. Induced pluripotent cells are both an unlimited source for retinal regeneration and an expectant tool for pharma projects and developmental or disease modeling [43].

Recent Trends and Future Prospects of Stem Cell

To establish India in an advantageous position in this fast developing global stem cell market, we need to have a strategy in place. The Indian Council of Medical Research (ICMR) and the Department of Biotechnology (DBT), New Delhi have plans for a national stem cell initiative to prioritize research funding, focus on clinical applications and promote 'stem cell city clusters' in India. The National Task Force on Stem Cell Research established in April 2005, is taking these plans forward. To look at the advances in stem cell research around the world, the current

regulatory scene in our country and the potential of stem cells in the future, a national seminar was organized on advances in stem cell research. There were 94 participants from different institutions of India. Stem cell research is an emerging field of interdisciplinary research with clinical implications focused on repair, replacement or regeneration of cells to salvage impaired organ function. Gurunath Kilara (Gokula–Curie Cancer Centre, Bangalore) spoke on the stem cell perspective and prospects and called for a national agenda on stem cell research that can help in therapeutics. They are effective in tissue repair, spinal cord injury, heart damage, Parkinson's disease and autoimmune diseases. Stem cells, application and banking'. Available source of stem cells for banking are umbilical cord blood (UCB) – haematopoietic stem cell banking, umbilical cord – mesenchymal stem cells, bone marrow – haematopoietic stem cells. UCB stem cells are an easily accessible source. However, they are available only at the time of birth. Stem cells need to be banked for later autologous or allogeneic use. These banks are similar to blood banks. Cord blood stem cells are collected from consenting donors and banked. These banks have large sample numbers, since human leukocyte antigen matches are difficult in small numbers. These need to be regulated more stringently compared to autologous banks.

In August 2006, Professor Shinya Yamanaka of Kyoto University succeeded in generating cells with pluripotent differentiation potential in mice by inserting just four genes (*Oct3/4, Klf4, Sox2, c-Myc*) into their mature skin cells, and named them induced pluripotent stem cells (iPS cells). The four genes required to induce pluripotency are called Yamanaka factors [45]. Human iPS cells were produced by inserting the same four genes (*Oct3/4, Klf4, Sox2, c-Myc*) used for murine iPS cells. Their method was simple and required no special equipment or technique, and was thus highly versatile. In addition, Prof. Yamanaka reported that insertion of only three genes (*Oct3/4. Klf4. Sox2*) could achieve iPS cells making the method safer without the use of carcinogenic c-Myc gene. Moreover, the initial method using retrovirus vectors, a possible carcinogen, is now improved with the use of plasmid vectors with less carcinogenic risks. Plasmid vectors, with their ability to insert genes without damaging the genes of the targeting cells, are believed to be safer than retrovirus. Recently, a group from Max Plank Institute for Molecular Biomedicine in Germany succeeded in producing murine iPS cells by inserting only one gene, *Oct 4,* with some chemical agents [45].

Transplantation therapies are likely to begin from commercial development of adult tissue banks as they represent a more convenient and ethically less contentious source than embryonic or fetal tissues. The first stem cell products on the market are likely to be mesenchymal stem cells from bone marrow, currently under development for bone and cartilage repair. Blood, particularly from cord or placenta, is a rich source of stem cells that can be developed for a range of conditions. Initially, most products will be autologous, i.e. donor-specific, since they avoid rejection problems as well as most of the regulatory hurdles. However, product pricing will be a deterrent to widespread application. The real value in stem cells will lie in the development of allogeneic products, i.e. available to use with a wide range of patients and probably arising from the more plastic embryonic or fetal sources. Here the regulatory hurdles will be considerably higher, particularly where it is indicated that transplants will be in internal organs such as liver, heart and brain in which the fate of the cells is essentially invisible. If successfully developed, these products will be widely used and would represent real value in reducing the long-term cost of hospital and social care [46].

Clinton recently overturned this law, and new clinical trials involving transplantation for Parkinson's are currently under way in the USA. A similar ruling banning the use of fertilized eggs for research and the generation of ES cells has been in place in the USA for some time.

Ironically, it was an American lab which published the first data showing that human ES cells could be grown in culture, which highlights one of the major problems when government attempts to restrict science. Industry simply stepped in and provided the funding required doing the research. There is a danger here that companies will end up in the role of God, rather than society, which is surely less acceptable. There is certainly money in both reproduction and immortality – not to mention restoring function following disease, which will drive companies to pursue this type of research.

Stem Cell- Indian Perspective

A lost science?

In Adi parva, one of the chapters of Mahabharata, it is said that Kauravas were created from pinda [a ball of flesh] which Gandhari delivered after two years of pregnancy. It was then handed over to the sage Dwapayan, which was then divided into one hundred parts and treated with herbs and ghee. The pieces were then covered with cloth and kept in a chamber to cool for two years; out of which the Kauravas were born." There cannot be any other explanation for this….. The ancient sages of India must have perfected the art of regenerating entire human beings from cells. In fact Mahabharata clearly describes the various stages of processing pieces of flesh, which is in fact closely comparable to modern techniques of harvesting and processing embryonic stem cells.[sans the sophistication!]. Perhaps stem cell research was altogether a lost science of ancient India.

Recently the Ruby Hall Medical Research Centre, a subsidiary of Pune-based Ruby Hall Clinic and Denmark based biotechnology company Mesibo are soon to form a 49:51 joint venture with an aim to establish India's largest cord blood storage facility at Pune. These measures got a pat on the back when NIH announced its interest in funding research in stem cells in the country. Recently contribution from the Indian researchers in the field of stem cell therapy has been recognized worldwide [47].

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