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STEM CELLS: A BURGEONING FIELD OF RESEARCH IN VARIOUS THERAPIES

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ABSTRACT

Stem cell therapy holds the potential for treating damages resulting from various diseases via transplantation of cells and tissues. Pluripotency makes embryonic stem cells and these induced pluripotent stem cells ideal for use in various therapies.Therapeutic benefits from bone marrow transplantation are well established. Hematopoietic stem cells have been used for treating both haematopoietic and non-haematopoietic disorders. Hematopoietic stem cells transplantation is also used for treating number of pediatrics diseases like autism, childhood brain cancer cerebral palsy etc. In addition mesenchymal stem cells are widely for tissue repair. The safety and feasibility of these cells have been demonstrated in clinical trials.Therefore, using stem cells for treatment of injuries along with the conventional medical practice would likely accelerate the repair process and improve the quality of life of the victim. Various stem cell transplants are available and used to treat different diseases. The article enlightens the vision about the stem cells with providing an insight to various therapies.

Key words: Diabetes mellitus , cancer , neonates, infants, dwarfism.

INTRODUCTION

In victims inflicted with critical injuries/disorders like cancer, burns, loss of immune cells, fractures and renalfailure[1-5], transplantation of healthy functional cells which can repair or

replace the damage through the process of regeneration. Pluripotent human embryonic stem cells are envisioned as a viable source of cells because they can serve as an alternative source of cells from which the desired tissue can be derived,potentially endless source of versatile cells could lead to novel sources of replacement organs[6].

Stem cells have an ability to renew and can differentiate into different types of cells, therefore they are used in many transplants of normal or genetically modified stem cells, offers hope for treating thousands of lifes. 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.

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)** 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.

Types of stem cells

Adult stem cells typically generate the cell types of the tissue in which they reside. A blood-forming adult stem cell in the bone marrow—which is called a hematopoietic stem cell normally gives rise to the many types of blood cells such as red blood cells, white blood cells and platelets. The primary roles of adult stem cellsin a living organism are to maintain and repair the tissue in which they are found.

Embryonic stem cells, as their name suggests, are derived from embryos that develop from eggs that have been fertilized *in vitro—in an in vitro* fertilization. Embryonic stem cells are best suited for the generation of any cell type by directed differentiation and in sufficient numbers but their use was hampered due to ethical issues.

Stem cell therapy[7]

Known as regenerative medicine, is the replacement of diseased, dysfunctional or injured cells with stem cells or their derivatives. It's somewhat similar to the organ transplant process but uses cells instead of organs.Researchers grow stem cells in the lab. These stem cells are manipulated to make them specialize into specific types of cells, such as heart muscle cells, blood cells or nerve cells. This manipulation may involve changing the material in which the stem cells are grown or even injecting genes into the cells. The specialized cells could then be implanted into a person.

For example, if the person had heart disease, the cells could be injected into the heart muscle. The healthy, transplanted heart cells could then contribute to repairing defective heart muscle. In fact, researchers have already shown that adult bone marrow cells guided to become heart-like cells can repair heart tissue in mice, and much more research is ongoing.

Applications of stem cell therapy

Heart Tissue Regeneration[81]

Pluripotent human embryonic stem cells (hESCs) have emerged as an attractive candidate stem cell source for obtaining cardiomyocytes (CMs) because of their tremendous capacity for expansion and unquestioned potential to differentiate into CMs. Studies carried out in animal models indicate that ES-derived CMs can partially remuscularize infarcted hearts and improve contractile function; however, the effect was not sustained over long follow up periods due to their limited capacity of cell division *in vivo*. Thus, the concept of transplanting multipotent cardiovascular progenitors derived from ES cells has emerged since the progenitors retain robust proliferative ability and multipotent nature enabling repopulation of other myocardial elements also in addition to CMs. Transplantation of CMs (progenitors) seeded in biodegradable scaffold and gel based engineered constructs has met with modest success due to issues like cell penetration, nutrient and oxygen availability and inflammation triggered during scaffold degradation inversely affecting the seeded cells. Recently cell sheet based tissue engineering involving culturing cells on ‘intelligent’ polymers has been evolved. Generation of a 3-D pulsatile myocardial tissue has been achieved. However, these advances

have to be looked at with cautious optimism as many challenges need to be overcome before using these in clinical practice

Corneal Reconstruction[9]

Another area in which stem cell therapy is demonstrating rapid advancement is the field of ophthalmology.A surgical procedure known as limbal stem cell transplantation offers hope to those suffering from corneal degeneration, blindness, and other ocular diseases.The procedure involves the extraction of stem cells from the limbus, the region of the eye between the epithelial layer of the cornea and the sclera, the eye's outer layer,the cells are typically extracted from a healthy eye of the patient himself, from a family member, or from cadaveric material.Once extracted, the limbal stem cells are implanted into the patient's defective eye. The stem cells then differentiate into corneal epithelial cells which improve the health of the outermost layer of the eye.

Treatment for diabetes and diabetic ulcer:[10]

Diabetes affects 16 million people in the U.S. and is caused by the abnormal metabolism of insulin.Normally, insulin is produced and secreted by the cellular structures called the islets of Langerhans in the pancreas.Recently, insulin expressing cells from mouse stem cells have been generated. In addition, the cells self assemble to form structures, which closely resemble normal pancreatic islets and produce insulin.Future research will need to investigate how to optimise conditions for insulin production with the aim of providing a stem cell-based therapy to treat diabetes to replace the constant need for insulin injections. The diabetic ulcer, a major complication of diabetes mellitus, has remained an important clinical challenge. Not only does it affect the physical and mental health of patients, but it is also an economic burden on our society. Now, the diagnosis and classification of diabetic ulcer is guided by the Wagner classification system and the University of Texas Diabetic Wound Classification system .The standard clinical treatment of diabetic ulcer includes local wound care with dressing, virgous and repeated debridement of necrotic tissue, and offloading. Antibiotics will also be given if infection exists. However, the result is still far from satisfaction, and 14%–20% of patients with diabetic ulcer will end up with amputation. Various approaches have been developed for diabetic wound healing, but most of these approaches have centered on one facet of wound healing, such as inflammation or growth factors. Clinical and basic science studies show that these therapies can provide a comprehensive solution by addressing

multiple factors during diabetic wound healing, including cell proliferation, extracellular matrix (ECM) synthesis, growth factor release, and vascularization.

Parkinson's Disease[11]

Parkinson's disease is a disorder of the central nervous system in which the substantianigra, a part of the brain, ceases to produce dopamine, a chemical that allows for effective motion.Five Parkinson's patients received an injection of a normal protein known as glial cell line-derived neurotrophic factor.[14]The factor stimulates the adult stem cells of the brain. Within a year, the patients demonstrated a 61 percent increase in physical coordination and lessening of symptoms.

Leukemia[12]]

Leukemia is a cancer of white blood cells, or leukocytes. Like other blood cells, leukocytes are made in the bone marrow through a process that begins with multipotent adult stem cells. Mature leukocytes are released into the bloodstream, where they work to fight off infections in our bodies.Leukemia results when leukocytes begin to grow and function abnormally, becoming cancerous. These abnormal cells cannot fight off infection, and they interfere with the functions of other organs.

Successful treatment for leukemia depends on getting rid of all the abnormal leukocytes in the patient, allowing healthy ones to grow in their place. One wayto do this is through chemotherapy, which uses potent drugs to target and kill the abnormal cells. When chemotherapy alone cannot eliminate them all, physicians sometimes turn to bone marrow transplants. In a bone marrow transplant, the patient's bone marrow stem cells are replaced with those from a healthy, matching donor. To do this, all of the patient's existing bone marrow and abnormal leukocytes are first killed using a combination of chemotherapy and radiation. Next, a sample of donor bone marrow containing healthy stem cells is introduced into the patient's bloodstream. If the transplant is successful, the stem cells will migrate into the patient's bone marrow and begin producing new, healthy leukocytes to replace the abnormal cells.

Stem cell therapy prospects in children

Childhood Brain Cancer :[13]

Stem cell therapy provides a cure for children living with brain cancer. Doctors can isolate the BMP4 protein from stem cells, transplant this protein to the cancerous area, and stop the

growth of abnormal cells. This is more than simply killing the tumor. Stem cell therapy goes directly to the problem and helps the cells to once again function normally.

Autism Disorders:[14]

Autism is a group of highly complicated neurodevelopment disorders affecting 1 in every 110 children born in USA.Stem cell replacement therapy via transplantation potentially reverse brain hypo perfusion and immune dysfunction, which are considered to be two major pathophysiology mechanisms of autism. Fetal stem cells (FSC) are use in autism treatment targets the brain. In autism, areas of brain regulating memory, concentration, attention, speech etc. are damaged. Stem cell treatment improves blood and oxygen flow to the brain (improved perfusion), replaces damaged neurons and stimulates formation of the new arteries. After some time, FSC acquire properties of cells surrounding them and multiply into these cells, which results in white and gray matter restoration and, consequently, in subsidence of neurologic symptoms and improved intellectual capacity. It has been proven that mesenchymal stem cells improve immune system and terminate inflammation.

Cerebral palsy:[15]

Cerebral palsy is condition that results from injuries or abnormalities of the brain, usually in the womb but occurring anytime during 2 years after birth. It affects brain and nervous system functions such as thinking, seeing, hearing, learning and movement.Common causes are hypoxia (low oxygen levels), head injury, maternal infections such as rubella, brain bleeding, brain infection, and severe jaundice. Types of CP include: ataxic, hypotonic, spastic, dyskinetic, and mixed. Mesenchymal stem cells from umbilical cord are considered to be universal donor cells because they are not immediately recognized asforeign. The cells secrete molecules called trophic factors.Trophic factors from mesenchymal stem cells are known to stimulate repair of damaged nervous tissue in both the brain and the spinal cord. Mesechymal stem cells stimulate brain repair after stroke1 and traumatic brain injury. Because we utilize allogeneic cord tissue-derived mesenchymal stem cells, we are able to offer treatment to any qualified patient, not just those who saved their own cord blood at birth. Intrathecal injection allows the stem cells to bypass the mature blood-brain barrier efficiently and migrate throughout the central nervous system.

Tay-Sachs disease[16]

Tay-Sachs disease is caused by the absence or insufficient level of a vital enzyme called Hexosaminidase A (Hex-A). Without Hex-A, a fatty substance or lipid called GM2 ganglioside accumulates abnormally in cells, especially in the nerve cells of the brain. This ongoing accumulation, also called "substrate," causes progressive damage to the cells. To date, there is no cure or effective treatment for Tay-Sachs disease Hex-A are blocked from entering the brain by the blood. Stem cell transplantation using umbilical cord blood is an investigational procedure attempted with a small number of very young children, but to date there is not enough information for specific results about reversing or slowing damage to the central nervous system in this group with Tay-Sachs disease.

Stem cell therapy is used to induce regeneration in TAY-SSCH disease. This therapy is still in experimental stage but shown good result in few patients after using cord mesenchymalcells. Tay-Sach disease is a difficult question and lack of Hex-A is our major concern, However use of cord driven mesenchymal cells will provide healthy genes and stem cell transplantation may reset up the blood-making function, after allogenic cord stem cell transplantation.

Recent advances in stem cell therapy

Stem Cells in Treatment of Burns and Skin Ulcers[17]

Burns are injuries to tissues caused by heat, radiation, friction, electricity and chemicals. Burns injure the skin layers and they may also injure muscles and nerves. Epidermal stem cells have been used in treatment of burns and skin ulcers for decades in the basic form of skin grafts. In normal skin loss and traumatic skin loss like burns and skin ulcers epidermal stem cells are responsible for epidermal ability of regeneration. Nowadays burns and skin ulcers are very common injuries. Despite their frequency, both of these injuries are very expensive for treatment because of slow-rates of healing and possible complications.

Standard skin grafts

Skin grafting is skin transplantation to the open wound and it is used to provide coverage for wounded area. Skin grafts can be classified in autologous, allogeneic, xenogeneic and prosthetic skin grafts. In some classifications, we can find Isogeneic (transplatation between twins). Also, grafts can be classified by thickness in full-thickness grafts, split thickness grafts (these grafts are grafts with epidermis and part of the dermis) and composite grafts.

Current Use of Stem Cells in Burn Treatment

Epidermal cells can be modified both in vivo and ex vivo by viral and non-viral methods. In the first experiments with skin stem cells scientists tried to eliminate inherited genetic defects, but now these cells are used in wound healing therapy with genetically modified **keratinocytes and growth factors.** The basic concept of burns treatment with stem cells is growing them on some scaffold, and then transfer to patients wound. Replacing of the skin grafts with stem cell cultures is main goal of this method. Faster healing rates and compatibility with recipient's immune system are big achievements of stem cell technique.Main parts of stem cell production are **somatic cells** and **egg cell**. DNA from the somatic cell have to be evacuated from the somatic cell, and the rest of the cell can be discarded. Also, DNA of the egg cell is extracted and discarded. Then somatic DNA is inserted into an egg cell. The egg cell influences and reprograms the DNA from the somatic cell. This so-called embryonic cell can be induced to differentiate into skin keratinocyte under specific laboratory conditions and can be used for generating artificial skin. This is the way of creating unlimited amounts of graftable skin. In mid-1970s, a technique for serial cultivation of epidermal cells, producing the 1000- to 10000-fold area of graftable epidermis was developed. This skin grafts were very sensitive to bacterial infection, and they can be placed directly on muscle or fascia. The only problem with this technique are expenses.

Fetal skin cells in grafts

This therapy method includes fetal skin cells from aborted fetuses. Fetal cells are very potent cells for regeneration. This tissue is used for patients with deeper burns, and it was imagined that this tissue is some kind of biological bandage. During the research, scientist have discovered that fetal tissue promotes growth of the patient's own skin. This procedure starts with separation of fetal cells from the skin of aborted fetuses. Aborted fetuses skin cells divide in vitro. Then, the skin cells are allowed to grow on substrate of collagen. This procedure is used to get more than million 100cm2 grafts from a single biopsy. The patches obtained in this way were used in burn treatments, and they have not shown any complications. It took 15 days to heal the wound. There were no retraction of the skin, and not a single one rejection of the patch. Patients grafted skin was considered as almost perfect. There was a question after this method success. What happened with fetal skin stem cells? This question remains unanswered, but one thing was sure- these grafts were better than true skin grafts.

Human umbilical cord blood stem cells

These cells have property to differentiate into epithelial cells in vitro under specific conditions. This property of human umbilical cord blood stem cells is also considered as possible solution for skin-grafting.

Also, hemopoietic stem cells transplanted on the burn sites can decrease healing time.

Standard skin grafts are very good solution for extensive burns, and it will be in nearly future basic and only solution in many parts of the world.

However, considering advantages of skin stem cell tissue engineering, it is clear that this method will be the future of transplantation. The only

disadvantages of this method are currently development and big expenses of tissue production.

Reprogramming technique:[18]

The reprogramming technique allows a small percentage of cells -- often taken from the skin or blood -- to become human induced pluripotent stem cells (hiPSCs) capable of producing a wide range of other cell types. But the cell reprogramming technique is inefficient, generating mixtures in which the cells of interest make up just a small percentage of the total volume. Separating out the pluripotent stem cells is now time-consuming and requires a level of skill that could limit use of the technique and hold back the potential therapies. To solve the problem, researchers at the Georgia Institute of Technology have demonstrated a tunable process that separates cells according to the degree to which they adhere to a substrate inside a tiny microfluidic device. The adhesion properties of the hiPSCs differ significantly from those of the cells with which they are mixed, allowing the potentially-therapeutic cells to be separated to as much as 99 percent purity. The principle of the separation is based on the physical phenomenon of adhesion strength, which is controlled by the underlying biology. The separation technique, called micro stem cell high-efficiency adhesion-based recovery (μSHEAR), will allow standardization across laboratories, providing consistent results that don't depend on the skill level of the users. The μSHEAR process grew out of an understanding of how cells involved in the reprogramming process change morphologically as the process proceeds. Using a spinning disk device, the researchers tested the adhesive properties of the hiPSCs, the parental somatic cells, partially-reprogrammed cells and reprogrammed cells that had begun differentiating. For each cell type, they measured its "adhesive signature" -- the level of force required to detach the cells from a substrate that had

been coated with specific proteins. In the testing, cells from the culture were first allowed to attach to the substrate before being subjected to the flow of buffer fluid. Cells with a lower adhesive signature detached from the substrate at lower flow rates. By varying the flow rate, the researchers were able to separate specific types of cells, allowing production of stem cell cultures with purity as high as 99 percent -- from mixtures in which those cells accounted for only a few percent of the total. At different stages of reprogramming, we see differences in the molecular composition and distribution of the cellular structures that control adhesion force. Once we know the range of adhesive forces for each cell type, we can apply those narrow ranges to select the populations that come off in each range. Using inexpensive disposable cassettes, the microfluidic system could be scaled up to increase the volume of cells produced and to provide specific separations. Unlike existing labeling techniques, the new separation process works on cell colonies, avoiding the need to risk damaging cells by breaking up colonies for separation. The separation process has been tested with both reprogrammed blood and skin cells. Beyond the direct application in producing stem cells, the separation technique could also help scientists with other research in which cells need to be separated -- including potential improvements in the reprogramming technique, which won the Nobel Prize for medicine in 2012. But there are really interesting scientific questions about this process, and by isolating cells undergoing reprogramming, we may be able to make new discoveries about how the process occurs.

Current research and futuristic approach on stem cells

Sickle Cell Disease[19]

Researchers at UCLA's Eli & Edythe Broad Center of Regenerative Medicine & Stem Cell Research have successfully established the foundation for using hematopoietic (blood-producing) stem cells (HSC) from the bone marrow of patients with sickle cell disease (SCD) to treat the disease. The study was led by Dr. Donald Kohn, Professor of pediatrics and microbiology, immunology and molecular genetics in the life sciences. Kohn introduced an anti-sickling gene into the HSC to capitalize on the self-renewing potential of stem cells and create a continual source of healthy red blood cells that do not sickle. The breakthrough gene therapy technique for sickle cell disease is scheduled to begin clinical trials by early 2014. Kohn's gene therapy approach using HSC from patient's own blood is a revolutionary alternative to current SCD treatments as it creates a self-renewing normal blood cell by inserting a gene that has anti-sickling properties into HSC. This approach also does not rely on the identification of a matched donor, thus avoiding the risk of rejection of donor cells.

The anti-sickling HSC will be transplanted back into the patient's bone marrow and multiplies the corrected cells that make red blood cells without sickling."The results demonstrate that our technique of lentiviral transduction is capable of efficient transfer and consistent expression of an effective anti-sickling beta-globin gene in human SCD bone marrow progenitor cells, which improved the physiologic parameters of the resulting red blood cells. Kohn and colleagues found that in the laboratory the HSC produced new non-sickled blood cells at a rate sufficient for significant clinical improvement for patients. The new blood cells survive longer than sickled cells, which could also improve treatment outcomes. The success of this technique will allow Kohn to begin clinical trials in patients with SCD by early next year.Sickle Cell DiseaseAffecting more than 90,000 patients in the US, SCD mostly affects people of Sub-Saharan African descent. It is caused by an inherited mutation in the beta-globin gene that makes red blood cells change from their normal shape, which is round and pliable (like a plastic bag filled with corn oil), into a rigid sickle-shaped cell (like a corn flake). Normal red blood cells are able to pass easily through the tiniest blood vessels, called capillaries, carrying oxygen to organs such as the lungs, liver and kidneys. But due to their rigid structure, sickled blood cells get stuck in the capillaries and deprive the organs of oxygen, which causes organ dysfunction and failure. Current treatments include transplanting patients with donor HSC, which is a potential cure for SCD, but due to the serious risks of rejection, only a small number of patients have undergone this procedure and it is usually restricted to children with severe symptoms.

Proteins Key in Stem Cell Production Identified[20]

Researchers from the University of Toronto, the Hospital for Sick Children and Mount Sinai Hospital (with colleagues from the United States and Portugal) say they have identified certain proteins that play a key role in controlling pluripotency, which may mean a potential breakthrough in producing these cells. The findings were recently published in *Nature*. the researchers discovered the proteins using the splicing code developed a few years. "The mechanisms that control embryonic stem cell pluripotency have remained a mystery for some time. the research team found that the proteins identified by our splicing code can activate or deactivate stem cell Pluripotency.

Stem cell manipulation could bring an end to obesity[21]

Researchers at the University of East Anglia (UEA) have made a discovery in neuroscience that could offer a long-lasting solution to eating disorders such as obesity. It was previously

thought that the nerve cells in the brain associated with appetite regulation were generated entirely during an embryo's development in the womb and therefore their numbers were fixed for life. But a new study has identified a population of stem cells capable of generating new appetite-regulating neurons in the brains of young and adult rodents. Obesity has reached epidemic proportions globally. More than 1.4 billion adults worldwide are overweight and more than half a billion are obesity associated health problems include type 2 diabetes, heart disease, arthritis and cancer, and at least 2.8 million people die each year as a result of being overweight or obese.

Scientists at UEA investigated the hypothalamus section of the brain - which regulates sleep and wake cycles, energy expenditure, appetite, thirst, hormone release and many other critical biological functions. The study looked specifically at the nerve cells that regulate appetite. The researchers used "genetic fate mapping" techniques to make their discovery - a method that tracks the development of stem cells and cells derived from them, at desired time points during the life of an animal. They established that a population of brain cells called "tanycytes" behave like stem cells and add new neurons to the appetite-regulating circuitry of the mouse brain after birth and into adulthood. Lead researcher Dr Mohammad K. Hajihosseini, from UEA's school of Biological Sciences, Unlike dieting, translation of this discovery could eventually offer a permanent solution for tackling obesity.Loss or malfunctioning of neurons in the hypothalamus is the prime cause of eating disorders such as obesity. Thestudy has shown that the neural circuitry that controls appetite is not fixed in number and could possibly be manipulated numerically to tackle eating disorders. The research is published in the Journal of Neuroscience. (ANI)

EYA 1 Molecule Drives Aggressive Breast Cancer[22]

The scientists found that excess activity of this gene -- EYA1 -- also enhances development of breast cancer stem cells that promote resistance to cancer therapy, recurrence, and poor survival. Because EYA1 is an enzyme, the scientists are now working to identify a natural compound that could shut down EYA1 activity, says Richard Pestell, M.D., Ph.D., Director of Kimmel Cancer Center.

EYA1 is over-expressed in some breast cancers, but no one knew what that meant the studies have shown the enzyme drives luminal B breast tumor growth in animals and the enzyme activity is required for tumor growth. In a mouse model of aggressive breast cancer, the research team targeted a single amino acid on the EYA1 phosphatase activity. They found

that inactivating the phosphatase activity of EYA1 stopped aggressive human tumors from growing.the potential of drug treatment, is much easier to develop a drug that targets a phosphatase enzyme like EYA1, than it is to target a gene directly; Tracing how EYA1 leads to poor outcomesThe study, which was published in the May 1 issue of Cancer Research, examined 2,154 breast cancer samples for the presence of EYA1. The researchers then linked those findings to patient outcomes. They found a direct relationship between increased level of EYA1 and cyclin D1 to poor survival.

They then chose one form of breast cancer -- luminal B -- and traced the bimolecular pathway of how EYA1 with cyclin D1 increases cancer aggressiveness. Luminal B breast cancer, one of five different breast cancer subtypes, is a hormone receptor-positive form that accounts for about 20 percent of human breast cancer. It is more aggressive than luminal A tumors, a hormone receptor-positive cancer that is the most common form of breast cancer.Their work delineated a string of genes and proteins that are affected by EYA1, and they also discovered that EYA1 pushes an increase in formation of mammospheres, which are a measure of breast cancer stem cells.Within every breast cancer are breast cancer stem cells, which give rise to anti-cancer therapy resistance, recurrence and in laboratory experiments that EYA1 expression increase the number of mammospheres and other markers of breast cancer stem cells."As the EYA1 phosphatase activity drove breast cancer stem cell expansion, this activity may contribute to worse survival.

Stem cell breakthrough could lead to new bone repair therapies on nanoscale surfaces[23]

Could help people with bone fractures or osteoporosis Scientists at the University of Southampton have created a new method to generate bone cells which could lead to revolutionary bone repair therapies for people with bone fractures or those who need hip replacement surgery due to osteoporosis and osteoarthritis.The research, carried out by DrEmmajayneKingham at the University of Southampton in collaboration with the University of Glasgow and published in the journal Small, cultured human embryonic stem cells on to the surface of plastic materials and assessed their ability to change.Scientists were able to use the nanotopographical patterns on the biomedical plastic to manipulate human embryonic stem cells towards bone cells. This was done without any chemical enhancement. The materials, including the biomedical implantable material polycarbonate plastic, which is a versatile plastic used in things from bullet proof windows to CDs, offer an accessible and

cheaper way of culturing human embryonic stem cells and presents new opportunities for future medical research in this area. The use of nanotopographical patterns could enable new cell culture designs, new device designs, and could herald the development of new bone repair therapies as well as further human stem cell research. The study was funded by the Biotechnology and Biological Sciences Research Council (BBSRC). In 2011 the team successfully used plastic with embossed nanopatterns to grow and spread adult stem cells while keeping their stem cell characteristics; a process which is cheaper and easier to manufacture than previous ways of working. Dr Nikolaj Gadegaard, Institute of Molecular, Cell and Systems Biology at the University of Glasgow, says: "Our previous collaborative research showed exciting new ways to control mesenchymal stem cell - stem cells from the bone marrow of adults - growth and differentiation on nanoscale patterns. This new Southampton-led discovery shows a totally different stem cell source, embryonic, also respond in a similar manner and this really starts to open this new field of discovery up.

Stem-Cell Dental Implants Grow New Teeth Right In Your Mouth[24]

Human molar scaffolding Dr. Jeremy Mao has unveiled a technique that directs the body's stem cells into a scaffolding that will aid in the regeneration of a new tooth. Columbia University Medical Center.The loss of a tooth is a minor deformity and a major pain. Although dental implants are available, the healing process can take months on end, and implants that fail to align with the ever-growing jawbone tend to fall out. According to a study published in the latest Journal of Dental Research, a new tissue regeneration technique may allow people to simply regrow a new set of pearly whites. Dr. Jeremy Mao, has unveiled a growth factor-infused, three-dimensional scaffold with the potential to regenerate an anatomically correct tooth in just nine weeks from implantation. By using a procedure developed in the university's Tissue Engineering and Regenerative Medicine Laboratory, Dr. Mao can direct the body's own stem cells toward the scaffold, which is made of natural materials. Once the stem cells have colonized the scaffold, a tooth can grow in the socket and then merge with the surrounding tissue. Dr. Mao's technique not only eliminates the need to grow teeth in a Petri dish, but it is the first to achieve regeneration of anatomically correct teeth by using the body's own resources. Factor in the faster recovery time and the comparatively natural process of regrowth (as opposed to implantation), and you have a massively appealing dental treatment.Columbia University has already filed patent applications in regard to the technology and is seeking associates to aid in its

commercialization. In the meantime, Dr. Mao is considering the best approach for applying his technique to cost-effective clinical therapies.

Production costs, biobanks and biosecurity in cell therapy

Production costs in cell therapy are high (currently, a treatment may cost more than 40,000 dollars), mainly because drug products based on cell therapy are prepared on a low and almost individual scale, but allogeneic procedures[25]and availability of cryopreserved cell banks (biobanks) will lead cell therapy to occupy a place in the market of future pharmacology .Costs are accounted for by different items, all of them necessary, including multiple surgical procedures, maintenance of strict aseptic conditions, specific training of technical staff and maintenance of overall technical and staff support, specialized facilities, the need for producing small and highly unstable batches and, of course, design and development of the different market strategies. The question arises as to whether these costs will be compatible with at least partial funding by governments, medical insurance companies, and public and private health institutions[26].

Until widespread use of allogeneic protocols becomes established, thus overcoming the problems derived from immune rejection, and although it is not certain if allogeneic cell transplantation will ever be free from clinical complications, biobanks represent the hope for the project of cell therapy to become a reality in the future [27]. Concerning production costs, even if biobanks exist, the production of cellular therapies often require the use of cytokines, growth factors and specialized reagents which are very expensive. Stem cell banks [28] store lines of embryonic and adult human stem cells for purposes related to biomedical research. Regardless of their public (nonprofit, anonymous donation).

or private (donation limited to a client's environment) nature, stem cell banks may store cell lines from umbilical cord and placental tissue, rich in hematopoietic stem cells, or cell lines derived from various somatic tissues, either differentiated or not. There are banks of cryopreserved umbilical cord bloods throughout Europe and North America.

These were set up primarily for hematopoietic stem cell transplantation, but they are available for other clinical uses. Two of the most relevant international banks are the US National Stem Cell Bank (NSCB)[29]and the United Kingdom Stem Cell Bank [30]

The NSCB was set up at the WiCell Research Institute on September 2005 and is devoted to acquisition, characterization, and distribution of 21 embryonic stem cell lines and their subclones for use in research programs funded by the National Institute of Health (NIH), and to provide the research community with adequate technical support.

The UKSCB was created on September 2002 as an independent initiative of the Medical Research Council (MRC) and the Biological Sciences Research Council (BBSRC), and serves as a storage facility for cell lines from both adult and embryonic stem cells which are available for use in basic research and in development of therapeutic applications.

Pfizer buy the rights to a somewhat controversial cell therapy from Athersys, a biotechnology company — a sign of big pharmaceutical companies' growing interest in stem cells. Pfizer will have the rights to develop Athersys's cells to treat inflammatory bowel disease, the companies are expected to announce on .It will pay Athersys $6 million initially and up to $105 million in the future. The relatively small payment reflects that "it's really early for cell therapy and there's more research to be done," said Ruth McKernan, chief scientific officer of Pfizer Regenerative Medicine, a unit created by the company about 18 months ago to develop treatments based on stem cells.Athersys's cells, derived from human bone marrow, have not yet been tested in people with inflammatory bowel disease, a term that encompasses ulcerative colitis and Crohn's disease. But the product, called MultiStem, is in early human testing as a treatment for heart attacks and for cancer patients receiving bone marrow transplants.[31]

US Food and Drug Administration (FDA): Regulation in the United States of America

In the United States of America, restrictions are limited to research with federal funds.

No limitations exist for research with human embryonic stem cells provided the funds come from private investors or specific states. In countries such as Australia, China, India, Israel, Japan, Singapore, and South Korea, therapeutic cloning is permitted.

The FDA has developed a regulatory framework that controls both cell- and tissue-based products, based on three general areas:

i) Prevention of use of contaminated tissues or cells (e.g. AIDS or hepatitis); ii) prevention of inadequate handling or processing that may damage or contaminate those tissues or cells; and iii) clinical safety of all tissues or cells that may be processed, used for functions other than normal functions, combined with componentsother than tissues, or used for metabolic

purposes. The FDA regulation, derived from the 1997 basic document "Proposed approach to regulation of cellular and tissue-based products"[32]The FDA has recently issued updates to previous regulations referring to human cells, tissues, and all derived products [33].This regulation provides an adequate regulatory structure for the wide range of stem cell-based products which may be developed to replace or repair damaged tissue, as both basic and clinical researchers and those working in biotechnological and pharmaceutical companies which need greater understanding and information to answer many questions before submitting a tem cell-based product for clinical use.

Case studies

Case study I

Groundbreaking Surgery for Girl Born Without Windpipe[34]

Using plastic fibers and human cells, doctors have built and implanted a windpipe in a 2 ½-year-old girl — the youngest person ever to receive a bioengineered organ.The surgery, which took place on April 9 2013 here at Children's Hospital of Illinoisthe first to be performed in the United States. It was approved by the Food and Drug Administration under rules that allow experimental procedures when otherwise the patient has little hope of survival.Dr. Paolo Macchiarini, a specialist in the field of regenerative medicine who developed the windpipe and led the complex nine-hour operation, said the treatment of the Korean-Canadian toddler, Hannah Warren, made him realize that this approach to building organs may work best with children, by harnessing their natural ability to grow and heal.Hannah was born without a windpipe, or trachea — an extremely rare condition that is eventually fatal in 99 percent of cases and had lived since birth in a newborn intensive care unit in a Korean hospital, breathing through a tube inserted in her mouth. Because of other developmental problems, she cannot eat normally and cannot speak.Nearly three weeks after the surgery, the girl is acting playfully with her doctors and nurses, at one point smiling and waving goodbye to a group of visitors. Dr. Mark Holterman, a pediatric surgeon at the hospital, said that Hannah was breathing largely on her own, although through a hole in her neck, not through her mouth yet. "She's doing well," he said. "She had some complications from the surgery, but the trachea itself is doing great."The goal of regenerative medicine is to create or regrow tissues and organs to ease transplant shortages or treat conditions that do not have an effective cure. After years of scant progress, tissue engineers have begun to make advances as they have gained a better understanding of the role that stem cells — basic cells that can become tissue-specific ones — play in signaling the body to grow and repair

itself.To make Hannah's windpipe, Dr. Macchiarini's team made a half-inch diameter tube out of plastic fibers, bathed it in a solution containing stem cells taken from the child's bone marrow and incubated it in a shoebox-size device called a bioreactor.Doctors are not sure exactly what happens after implantation, but think that the stem cells signal the body to send other cells to the windpipe, which then sort out so the appropriate tissues grow on the inside and outside of the tube. Because the windpipe uses only the child's own cells, there is no need for drugs to suppress the patient's immune system to avoid rejection of the implant.

Case study II[35]

The 25-year-old, who was left paralysed by the attack, underwent treatment at SionHospital; doctors optimistic he will walk again. There is a ray of hope for 25-year-old Ahmedabad resident IrfanTheba, after he lost sensation below his hips, following his spine snapping in two places last year. He began feeling sensation in his lower limbs, following a dose of stem cell therapy at the BMC-run Sion Hospital. Irfan worked as a zookeeper at the Sakkarbag Zoo in Ahmedabad. He was attacked by a lion last year while cleaning its cage. The attack left his spine broken at two places. He underwent treatment at Rajkot where the spine was joined by a screw-and-plate technique. However, due to severe injury, Irfan lost sensation in his lower body. It was tough for the family, as Irfan had tied the knot two years ago. He also has a four-monthold daughter. "He was bedridden since he was attacked. He had bowel trouble because he had no sensation in his lower body. It was painful to see him suffer," said Irfan's father Taar Mohammad Theba, who also works at the zoo as a cleaner. The Rajkot doctors then asked Irfan and his family to approach DrAlok Sharma, a neurosurgeon attached to SionHospial, who is also an expert in stem cell therapy. "Irfan's case is unique. His spine was broken in two parts, making his a paraplegic. Getting sensation back in such cases through natural means is impossible. We then decided to treat him with stem cell therapy to see if he would recover," said Dr Sharma. Irfan was injected with stem cells that were extracted from his hipbone. After a week, he claimed he could feelsensation in his limbs. "I have a slight sensation while attending nature's call," said Irfan. "I am able to stand with the help of support as well," he added. However, Irfan may have to take another dose of stem cells after six months. Dr Sharma said that Irfan's progress may take longer than other patients because of the severity of the injury. "I have treated a patient with bullet injuries. He had walked again, so I am confident that Irfan will be on his feet in the future," said Dr. Sharma.

CONCLUSION

Stem cells pose a bright future for the therapeutic world by promising treatment options for the diseases which are considered as noncurable now a days. By virtue of funding of stem cell research, we hope to see new horizon of therapeutics in the form of organ development and replacement of lost tissue. Stem cell therapy, particularly employing MSCs, holds tremendous potential to stimulate or accelerate reparative processes and provides sufficient graftable cells for treating disaster victims suffering from critical injuries. There are also new treatments available to treat various disorders by using stem cells.Also nowadays they are used to treat obesity and cancer disorders although the research is still going on the stem cell can be used for different purpose by using sccfolds.

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ABBREVIATIONS: HSC =Hematopoietic stem cells**; HSCT=** = Hematopoietic stem cells transplantation; **MSC =** Mesenchymal stem cells**; iPSC =** induced pluripotent stem cells**; FSC =** Fetal stem cells.,**hESCs**= human embryonic stem cells, **CMs**= cardiomyocytes