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REGENERATIVE MEDICINE: STEM CELL THERAPY AS AN ALTERNATIVE APPROACH FOR TREATMENT HUMAN DISEASES: REVIEW

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ABSTRACT

Regenerative medicine is a branch of medicine that will create attempts to change the course of chronic disease and restore fatigued and damaged organs in many instances. It is a tissue engineering and molecular biology branch of translational research that deals with the process of replacing, modifying or regenerating human cells, tissues or organs to restore or create normal function. Regenerative medicine It also involves the prospect of developing and safely implanting tissues and organs in the laboratory when the body cannot repair itself. Regenerative medicine refers to a group of biomedical clinical treatment strategies which may include the use of stem cells. Examples include injection of stem cells or progenitor cells (cell therapy); activation of regeneration by biologically active molecules administered alone or by secretion of infected cells (immune-modulation therapy) and by transplantation of in vitro cultured organs and tissues (tissue engineering). Stem cell therapy is the use of stem cells for treatment or prevents disease or disease. Research is underway to develop various sources for stem cells, and to apply stem cell treatments for neurodegenerative diseases and conditions, diabetes, heart disease, spinal cord injuries, retinal disease, Parkinson's disease, cancer, and other conditions.

KEYWORDS

Regenerative medicine, Embryonic stem cells, Stem cell therapy, Diabetes, Cardiovascular disease, Parkinson's disease and Cancer.

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INTRODUCTON

Regenerative medicine

Regenerative medicine is a modern field of medicine that will create attempts to alter the path of chronic illness and, in many cases, will restore exhausted and damaged organ systems[1]. The term "Regenerative Medicine" was first used in a 1992 article on hospital management by Leland Kaiser.

Kaiser's paper concludes with a series of short paragraphs on emerging technology that will have an effect[2].

Regenerative medicine is a branch of translational science of tissue engineering and molecular biology that deals with the process of replacing, restoring or regenerating human cells, tissues or organs or develops normal function[4]. The regeneration of tissues and organs provides a groundbreaking new approach to the treatment of injuries and diseases. It is a modern treatment for a new millennium. This research holds the promise of engineering damaged tissues and organs by activating the body's own repair mechanisms for the effective healing of previously irreparable tissues or organs. Regenerative medicine also includes the possibility of growth and Implanting tissues and organs safely in the laboratory because the body cannot repair itself. This would theoretically solve the problem of the lack of organs available for donation and the question of organ transplant rejection if the cells of the organ are extracted from the patient's own tissue or cells[5]. Regenerative medicine refers to a category of biomedical approaches to clinical treatment that may include the use of stem cells[6]. Examples include injection of stem cell cells or progenitor cells (cell therapy); activation of regeneration through biologically active molecules administered alone or as a secretion through infused cells (immuno-modulation therapy); and transplantation of *in vitro*-developed molecules organs and tissues (tissue engineering)[7].

Stem cells

Stem cells are the cell that has the ability to continuously divide and differentiate (develop) into various other kind of cells/tissues. When a stem cell divides, each daughter cell has the ability to either remain a stem cell or become another type of cell with more complex functions, such as a red blood cell or a brain cell. They have the ability to replace cell tissue that has been weakened or killed by severe illnesses. Moreover they can replicate themselves over and over for a very long time. They are found in multicellular organisms. In mammals, there are two large types of stem cells: embryonic stem cells, which are derived from the inner cell mass of blastocysts, and adult stem cells, which are present in various tissues. For adult humans, stem cells and progenitor cells function as a body repair mechanism that replenishes adult tissues. Within a developing embryo, the stem cells can be separated into all specialized cells - an electrode. By definition, autologous cells are obtained from one's own body, just as they can use their own blood for elective surgical procedures Adult stem cells are commonly used in medical procedures, such as bone marrow transplantation. Stem cells can now be artificially grown and transformed (differentiated) into distinct cell forms with features consistent with cells in different tissues, such as muscles or nerves. Embryonic cell lines and autologous embryonic stem cells generated through Somatic-cell nuclear transfer or dedifferentiation have also been proposed as promising candidates for future therapies[8].

Stem cell therapy through tissue repair and regeneration

Stem cell therapy requires the use of stem cells to cure or avoid a disease or condition. Bone marrow transplantation is a type of stem cell therapy that has been used for several years. No stem cell therapies other than bone marrow transplantation are commonly used. Stem cell therapy includes the use of stem cells to cure or avoid a disease or condit. Research is underway to develop different sources of stem cells and to treat neurodegenerative diseases and conditions, diabetes, heart disease, spinal cord injury, retinal disease, Parkinson's disease, cancer and other conditions[10]. The ability of scientists to isolate and cultivate embryonic stem cells, and the increasing ability of scientists to create stem cells using somatic cell nuclear transfer, and techniques to create induced pluripotent stem cells, have mounted controversy, both in relation to abortion policy and human cloning. In addition, attempts to market treatment centered on the transplantation of retained umbilical cord blood have proven controversial[11]. Engineered cells and tissues have gained much attention as an alternate method to repair or regenerate injured myocardium following myocardial infarction. A variety of candidate cell types have been transplanted into myocardial infarction animal models demonstrating their ability to boost the structural and functional capacity of the heart; for example, skeletal my oblasts, bone marrow-derived hematopoietic stem

cells, mesenchymal stem cells, endogenous cardiac stem cells, induced pluripotent stem cells, embryonic stem cells[12,13]. Clinical trials have also been ongoing to study the effects of cell transplantation in patients with myocardial infarction. The Reinfusion of Enriched Progenitor cells And Infarct Remodeling in Acute Heart Failure clinical trial investigated the effects of infused bone marrow stem cells in patient's day 4 post-myocardial infarction and reported improvement in left ventricular ejection fraction[14]. However, the Autologous Stem cell Transplantation in Acute Myocardial Infarction clinical trial reported no ventricular function improvement in stem cell transplant–treated group compared to the control group[14]. Overall, no conclusive decision on the effectiveness of adult stem cells in myocardial infarction transplantation has been made in clinical evidence. However, we are still searching for an ideal type of cell for enhanced cardiac repair and regeneration. In addition, cell transplantation has also been studied in diabetic cardiomyopathy and infracted hearts[15]. Transplanted MSCs improved cardiac function through increased angiogenesis and matrix metalloproteinase2 expression and decreased collagen and transcription of the matrix metalloproteinase9 in diabetic cardiomyopathy hearts[15]. Bone marrow stem cells were also tested for enhanced cardiac function in diabetic cardiomyopathy settings[16,17]. Transplanted diabetic bone marrow mononuclear cells and healthy bone marrow mononuclear cells into db/db mice with ischaemic myocardium. They demonstrated diabetic bone marrow mononuclear cells were unable to improve cardiac function post-myocardial infarction, whereas healthy bone marrow mononuclear cells were able to preserve fractional shortening[17]. Stem cells and "Parkinson's disease" are four terms that represent some of the most important translational work in neuroscience. The imagination of scientists has been captured by the idea that there is a single "stem" cell, a mother or a queen of all cells, capable of self-renewing and to generate all other cells in an organism. In other words, stem cells are capable of producing a number of dedicated progenitor cells and, eventually, of differentiating into mature cells. While several scientists have established various multipotent and pluripotent cell lines from a variety of sources, it is completely vital that we begin to build clinical technologies to actually use such cells in the disease. Important laboratory research in primate models should be used for Parkinson's disease to show safety and efficacy prior to human clinical trials[18].

Cells are multiplied in vitro and then immediately added to the patient to replace missing cells ("cell therapy") or implanted into 3- dimensional scaffolds ("Tissue engineering") and are distinguished differentiated to the type of cell demanded. Subsequently, the composite artificial tissue structure is inserted into a patient's tissue defect[19].

Stem cells as a future therapeutic for various human diseases

Stem cell and diabetes

Type 1 diabetes is a life-long condition characterized by the loss of islet cells found in the pancreas, known as beta cells. These cells are responsible for producing the hormone insulin, which functions to maintain a normal blood glucose level by inducing cell uptake of the molecule following a meal. (In this way, type 1 or "juvenile" diabetes is different from type 2 diabetes which is characterized by a resistance to insulin). In recent years, scientists have been searching for ways to replace the lost beta cells as a potential treatment for type 1 diabetes. Since stem cells are able to differentiate into a number of different mature cell types, this field of research has been of particular interest[20]. Diabetes mellitus is responsible for a host of conditions such as heart disease and stroke, nephropathy, retinopathy, blindness, neuropathy, gastroparesis, and periodontal disease. Cardiovascular disease (CVD) is the leading cause of morbidity and mortality in patients with diabetes, accounting for an estimated 80% of all diabetic deaths in North America[21]. Three quarters of these deaths are attributable to coronary artery diseases (CAD) leading to myocardial infarction and heart failure. Acute myocardial infarction, in the condition of diabetes, results in coagulative necrosis of the myocardium, myocyte cell loss, and infiltration of neutrophils. Cardiac myocyte cell failure in the infarcted area occurs by necrosis or apoptosis and has long been considered to be irreversible. In addition, cardiac hypertrophy is

known to be a significant mechanism for meeting increased demands under pathophysiological conditions.

Many means of restoring the cardiac function of the heart's diabetic myocardial infarction may have tremendous therapeutic potential. Latest care strategies for diabetic heart infarction and subsequent heart failure include medications (aspirin, angiotensin converting enzyme inhibitors and βblockers), angioplasty, thrombolytic therapy, ventricular aid devices and, eventually, heart transplantation[22]. However, recent advances in cell transplantation in the injured myocardium have enhanced the reality of improved cardiac function in the diseased myocardium[23,24]. In developing a possible treatment for patients with diabetes, researchers expect to develop a program that meets a number of requirements. Ideally, the stem cells will be able to replicate in culture and reproduce themselves precisely. This is, the cells are meant to be self-renewing. Stem cells should also be able to differentiate in vivo in order to create the desired type of cell. In the case of diabetes therapy, it is not clear if it is beneficial to generate only beta cells islet cells that make insulin or if other forms of pancreatic islet cells are also required. Studies by Bernat Soria and colleagues, for example, show that isolated beta cells those produced in the absence of other types of islet cells are less sensitive to changes in glucose concentrations than intact islet clusters made up of all types of islet cells. Islet cell clusters usually respond to higher-than normal glucose concentrations by releasing insulin in two phases: rapid release of high insulin concentrations and slower release of lower insulin concentrations. In this way, beta cells can fine-tune their response to glucose. Extremely high glucose concentrations may allow more insulin to be released rapidly, whereas intermediate glucose concentrations may need a rapid and slow-release insulin balance.

Insulated beta cells, as well as islet clusters with lower-than-normal levels do not release insulin in this biphasic manner from non-beta cells. Instead insulin is released in an all-or-nothing manner, with no fine-tuning for intermediate concentrations of glucose in the blood[25]. As a result, many researchers believe that it will be preferable to develop a system in which the stem or precursor cell types can be cultivated to produce all cells in the cell islet cluster In order to generate a population of cells that will be able to coordinate the release of the appropriate amount of insulin to the physiologically relevant blood glucose concentrations. Bonner-Weir and her colleagues are working with primary cell cultures duct cells and have no established cell lines that can grow indefinitely. However, the cells can be enlarged. According to the researchers, it may be possible, in principle, to do a biopsy and remove duct cells. From the patient, and then the cells in culture proliferate and give the patient back their own islets. This would work with patients with type 1 diabetes and do not have functioning beta cells, but their duct cells remain intact.

However, the autoimmune destruction would still be a problem and potentially lead to destruction of these transplanted cells[26]. Patients with type 2 diabetes may benefit from the transplantation of cells that have spread from their own duct cells because they would not need immune suppression. However, many researchers believe that if there is a genetic component to beta cell death, beta cells derived from ductal cells of the same individual would also be susceptible to autoimmune attack. The embryonic stem cells could be cultivated and coaxed into insulin-producing pancreatic islet cells. With a ready supply of cultured stem cells in hand, the theory is that a line of embryonic stem cells could be grown as needed for anyone requiring a transplant. Cells could be designed to prevent immune rejection. They could be placed in non-immunogenic material before transplantation in such a way that they would not be rejected and the patient would avoid the devastating effects of immunosuppressive drugs. There is also some evidence that differentiated cells are derived from embryonic stem cells may be less likely to cause immune rejection. While some researchers have conducted research on embryonic stem cells, other researchers have focused on insulin-producing precursor cells that naturally occur in adult and fetal tissues.

The Spain researchers reported using mouse embryonic stem cells that were engineered to allow researchers to select for cells that were differentiating into insulin-producing cells[27]. They have added DNA containing part of the insulin gene

to the embryonic cells of the mice. The insulin gene was linked to another gene that made the mice resistant to the antibiotic drug. By growing the cells in the presence of an antibiotic, only those cells that activated the insulin promoter were able to survive. The cells were cloned and then cultivated under different conditions. Cells grown in the presence of low glucose concentrations were differentiated and were able to respond to changes in glucose concentrations by increasing insulin secretion by almost sevenfold. The researchers then implanted the cells into the spleens of diabetic mice and found that symptoms of diabetes were reversed[27].

Stem cell and cardiovascular disease

Cardiovascular disease (also called heart disease) is a class of diseases that involve the heart, the blood vessels (arteries, capillaries, and veins) or both[28]. Cardiovascular disease refers to any disease that affects the cardiovascular system, principally cardiac disease, vascular diseases of the brain and kidney, and peripheral arterial disease[29].

The causes of cardiovascular disease are diverse but the most common are atherosclerosis and/or hypertension. In addition, with aging, there are a number of physiological and morphological changes that alter cardiovascular function and increase the risk of cardiovascular disease in healthy asymptomatic individuals[30].

Cardiovascular disease is the leading cause of deaths worldwide, though, cardiovascular mortality rates have declined in many high-income countries[29]. Also, cardiovascular deaths and disease have increased at a fast rate in low- and middle-income countries[31]. While cardiovascular disease typically affects older adults, the history of cardiovascular disease, especially atherosclerosis, begins in early life, making primary prevention efforts important from childhood[32]. There is also a growing focus on the prevention of atherosclerosis by improving risk factors, such as healthy eating, exercise and the prevention of smoking tobacco. Adult stem cell transplantation studies in diabetic hearts are very limited and need further study. Moreover, as per the best of our knowledge, there is no study performed on cardiomyopathy heart using embryonic stem or induced pluripotent stem cells. Embryonic stem and induced pluripotent stem cells possess many desirable traits, making them a more promising approach to attenuate the damaged myocardium. Embryonic stem cells, derived from the inner cell mass of a blastocyst, are pluripotent, undifferentiated cells.

They are capable of self-renewal and are able to differentiate into multiple cell types in the body including functional cardiomyocytes, endothelial cells, and vascular smooth muscle cells[24]. Previous studies have demonstrated the ability of embryonic stem cells transplanted into the infracted heart to engraft, differentiate into cardiomyocytes, contribute to heart regeneration, and improve heart function 23. While the molecular mechanism of myocardial repair by transplanted embryonic stem cells has yet to be explained, it remains an important area of continued study. Nevertheless, an optimized embryonic stem cell therapy holds great promise for the treatment of diabetic injured myocardium[33]. Also, induced pluripotent stem cells are reprogrammed adult cells exhibiting pluripotent cell characteristics through forced gene expression of Oct 3/4, Sox2, Klf4, and c-myc. These cells can then be directed to differentiate into specific cell types though mechanisms similar to embryonic stem cell differentiation. Fibroblast-derived induced pluripotent stem cells have recently been tested in a myocardial infarction model and demonstrated the ability to engraft into the host myocardium, differentiate into all three major heart cells such as cardiac myocytes, smooth muscle and endothelial cells, repair the ventricular wall, and restore contractile function[13].

Stem cell and Parkinson's disease

Parkinson's disease is a chronic central nervous system (CNS) condition characterized by a gradual loss of neuron in the brain that releases dopamine. Dopamine is a crucial neurotransmitter that transmits signals from dopamine neurons to the striatum of the substance Nigra pars compacta, a portion of the brain that mediates muscle regulation and coordination. Parkinson's worldwide affects about 5 million people of all races and professions, making it one of the most prevalent neurodegenerative diseases, second only to Alzheimer's. Symptoms of Parkinson's disease occur when about 80 per cent of the dopamine neurons are destroyed. This typically happens only

at 60 years of age, although cases have been recorded in people as young as 20 years of age. Similar to other neurodegenerative diseases, the vast majority of Parkinson cases occur sporadically, whereas only 10-15% of cases are familial and are linked to multiple genes that can be inherited among family members[34]. Dopaminergic neurons are the most desirable tissue types for cell replacement therapy: human embryonic Ventral mesencephalic tissue, embryonic and adult multipotent region-specific stem cells and embryonic stem cells. Recent advances in embryonic stem cell research and their implications for potential transplantation therapy for Parkinson's disease are identified. Human embryonic stem cells can be differentiated into dopaminergic neurons, and issues such as the numbers of dopaminergic neurons required for success and the risk for trachoma formation after implantation[34].

Stem cells "and Parkinson's Disease" are four words represent some of the most important translational work in neuroscience. The imagination of scientists has been captured by the idea that there is a single "stem" cell, a mother or queen of all cells, capable of self-renewing and producing all other cells in the body. In other words, stem cells are capable of generating various committed progenitor cells and ultimately differentiating into mature cells[18]. In fact, as demonstrated by[35], the donor stem cells may serve a more important mission: to protect and repair. The use of fetal-derived neural stem cells has shown significant promise in rodent models of Parkinson's disease, and the potential for tumorigenicity appears to be minimal[36,37]. In a National Institutes of Health-funded study reported in this issue of Parkinson's disease[35], have now taken the first step toward demonstrating the successful use of fetal stem cells in a primate Parkinson's model. The authors report that undifferentiated human neural stem cells (hNSCs) transplanted into severely Parkinson's 1-methyl-4-phenyl-1, 2, 3, 6-tetrahydropyridine (MPTP)-treated primates may thrive, migrate, and induce behavioral recovery of Parkinson's symptoms directly linked to decreased dopamine levels in the nigrostria system. Surprisingly, these investigators did not use neural stem cells that had been pre-differentiated into tyrosine hydroxylase- or dopamine-containing cells, and these cells also were not previously immortalized[38,39]. Some suggest that neural stem cells do not simply substitute damaged neurons, but may in fact be essential cellular factories for the supply of neuroprotective, anti-inflammatory, angiogenic and neurogenic factors to the brain, thus providing a remedial, homeostatic micro-environment[40,41]. In fact, Redmond *et al*, 35 reported that a small number of hNSC offspring spontaneously converted into "dopamine neurons" as defined by human cells with tyrosine hydroxylase and/or dopamine transporters in a monkey's brain. However, this limited number of hNSCs alone will certainly not be necessary to achieve any substantial functional change. Whoever, initial study of neural stem cells in Parkinsonian primates, the authors has made an important contribution? Through not utilizing dopamine stem cells, they offer the foundation for converting certain forms of un different stem cells into a dopamine-deficient microenvironment in primates[18].

Stem cell and cancer

Cancer, medically known as malignant neoplasm, is a large category of diseases that include unchecked cell development. In cancer, cells differentiate and expand uncontrollably, creating malignant tumors that growing invade neighboring sections of the body. Cancer may also travel to more remote areas of the body via the lymphatic system or the bloodstream. Not all cancers are cancerous; healthy cancers do not enter surrounding tissues and do not spread across the body. There are over 200 different known cancers that affect humans[42]. The causes of cancer are varied, nuanced and poorly understood. Many things are known to increase the risk of cancer, including tobacco use, dietary factors, certain infections, exposure to radiation, lack of physical activity, obesity, and environmental pollutants[43]. These factors can directly damage genes or combine with existing genetic faults within cells to cause cancerous mutations[44]. Approximately 5-10% of cancers can be traced directly to inherited genetic defects. Most diseases may be avoided from not smoking, consuming more fruits, berries and whole grains, having fewer meat and processed foods, keeping a healthier weight, exercising, reducing ultraviolet exposure, etc and refined

carbohydrates, maintaining a healthy weight, exercising, minimizing sunlight exposure, and being vaccinated against some infectious diseases[43,45].

Cancer may be diagnosed in a variety of forms, including the presence of other signs and symptoms, diagnostic procedures and medical imaging. When a suspected cancer has been identified, a clinical analysis of the tissue sample is confirmed. Cancer is typically managed with radiation, radiotherapy and surgery. The probability of recovery of the illness varies considerably based on the form and place of the cancer and the severity of the condition at the outset of therapy. Although cancer may impact people of all ages and certain forms of cancer are more frequent in children, the likelihood of contracting cancer usually rises with age. Throughout 2007, around 13 percent of all human deaths globally (7.9 million) were induced by disease. Rates are rising as more people live to an old age and as mass lifestyle changes occur in the developing world[46].

The usage of stem cells in the treatment of cancer has been problematic, with several research suggesting that stem cells cause tumors to undergo programmed cell death. However, other experiments have demonstrated that stem cells actively stimulate tumor development by causing penetration of fresh blood vessels. For both subcutaneous and lung tumors, the infusion of mesenchymal stem cells decreased cell proliferation, thus reducing the growth rate of the tumor. Part of the mode of action of stem cells therefore appears to be due to with angiogenesis, but the mechanism behind this is still unclear[47].

Stromal (mesenchymal) stem cells (MSCs), also referred to as stromal cells, are multipotent cells that are found inside the bone marrow stroma and are expected to be capable of certain organs of migrating to injured tissues and contributing to tissue regeneration[48,49]. Emerging data suggest that MSCs possess immunomodulatory and regenerative properties as they can secrete a large number of growth factors and immune active molecules[50] that can improve tissue survival and suppress the activity of various immune cells, such as alloantigen activated T and B lymphocytes[51,52].

Moreover, MSCs can secrete a large number of paracrine factors, including chemo attractants for endothelial cells, monocytes and macrophages[53]. Several recent studies have confirmed that bone marrow MSCs are moving to the tumor stromal compartment[54] and that there is a strong complex relationship between tumor cells and MSCs what has been reported during inflammation and, thus, 'tumors are wounds that never heal[55]'. Over the past several years, a significant amount of research has emerged documenting a role for MSCs in promoting epithelial-to-mesenchymal transition (ETM) and accelerating tumor growth and metastasis[54,56,57]. In addition, MSCs are being introduced into therapy for a number of clinical indications and there is a concern of possible promoting effects on tumor growth by MSCs[58]. On the other hand, several other studies reported that MSCs exert tumor suppressive effects[59].

SUMMARY

The ability of scientists to isolate and culture embryonic stem cells, and with scientists' growing ability to create stem cells using somatic cell nuclear transfer and techniques to created induced pluripotent stem cells, controversy has crept in, both related to abortion politics and to human cloning. All researchers study the possibility of the most exciting use of stem cells rests on their ability to differentiate into an enormous range of healthy functioning adult cells, thereby providing a replacement source of cells to treat serious diseases as diabetes, cardiovascular disease, Parkinson's disease and cancer disease.

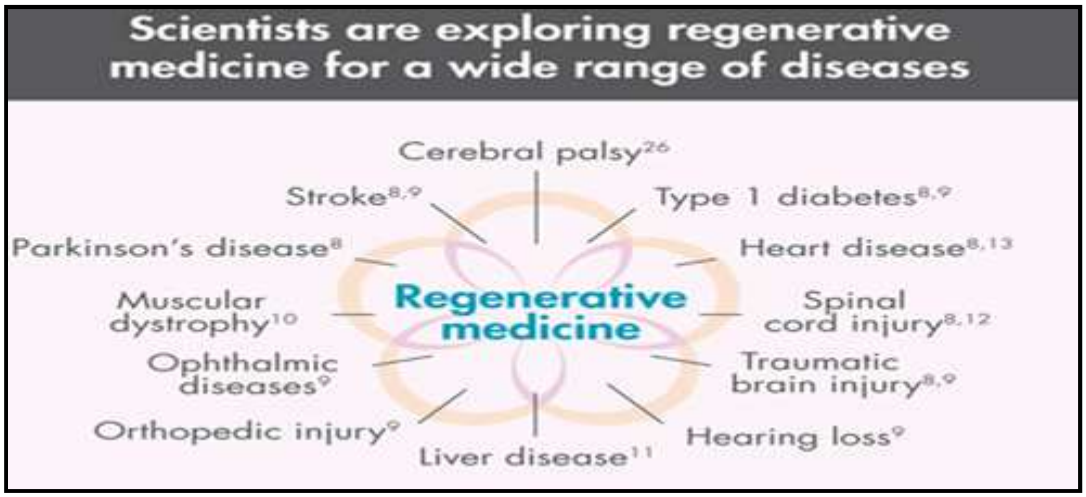

Figure No.1: Regenerative medicine is a field of research and clinical application that focuses on the process of replacing or producing normal functioning cells, organs or tissue. There are three general types of regenerative medicine that are available to people who suffer from the most common cause of chronic knee pain[3]

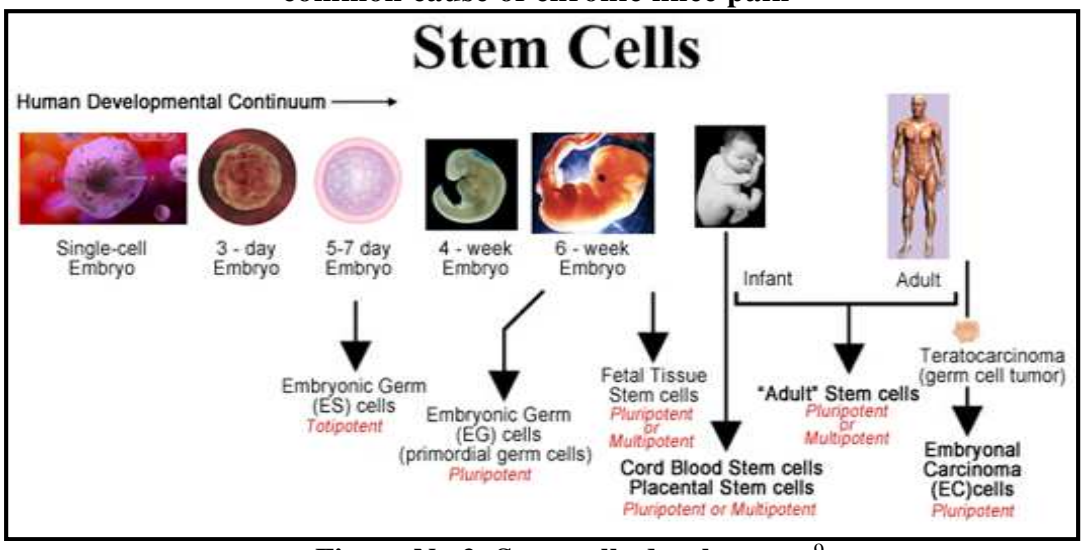

Figure No.2: Stem cells development[9]

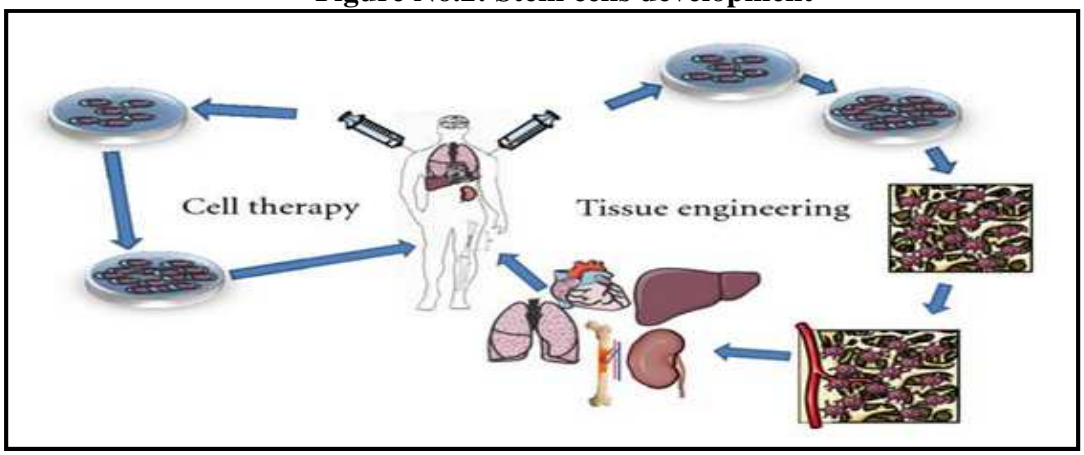

Figure No.3: The two methods for the use of stem cells in regenerative medicine. Stem cells are either rem oved from the patient (autologous transplantation) or other donors (allogenous transplantation)

CONCLUSION

Regenerative medicine is a new field of medical studies that consider a way for diseases control through own regenerative capabilities. Regenerative medicine is defined as the regeneration of lost or damaged organs through the organ transplantation as the restoration of some level of function of damaged tissues or organs. Regenerative medicine research generally focuses organ growth, self-repair and cellular therapies by regulating pluripotent stem cell and adult stem cell production and differentiation to restore the missing cells. Stem cells are special human cells that able to develop into many different cell types of cells. In addition, they also have the ability to repair damaged tissues. Stem cells are immature cells that can able to produce other blood cells that one mature and function as needed. Stem cells are divided into two main forms: embryonic stem cells and adult stem cells. The embryonic stem cells come from unused embryos resulting from an in vitro fertilization procedure used in research today. There are two types of adult stem cells. One type comes from completely developed tissues, like brain, skin, and bone marrow. There are only small numbers of stem cells in these tissues, and they are more likely to generate only certain types of cells. Example, a stem cell derived from the liver will only generate more liver cells. There are a second one called embryonic stem cells that has been manipulated in a laboratory. Stem cells act as a new therapy that became benefit to human health depending on regeneration of damaged tissue and treat various diseases such as type 1 diabetes, spinal cord injuries, chronic heart disease, Alzheimer's disease, and rheumatoid arthritis.

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CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest.

BIBLIOGRAPHY

1. Friedmann, Morvinski D, Verma I M. Dedifferentiation and reprogramming: origins of cancer stem cells, *EMBO,* 15(3), 2014, 244-253.
2. Viola J, Lal B, Grad O. The emergence of tissue engineering as a research field, *Arlington, VA: National Science Foundation,* 2003, 1-17.
3. Riggs R. Regenerative medicine: New treatments for arthritis, Healthy Living, *Knee Pain, Media, Osteoarthritis,* 8th Arthritis, 2013.
4. Tigerstrom B. How to build (and regulate) a body Part 1: Regulating tissue engineered products in Canada, *Health Law,* 19, 2011, 83-123.
5. Mason C, Dunnill P. A brief definition of regenerative medicine, *Regenerat Med,* 3(1), 2008, 1-5.
6. Riazi A M, Kwon S Y, Stanford W L. Stem cell sources for regenerative medicine, *Molecular Biol,* 482, 2009, 55-90.
7. Muneoka K, Allan C H, Yang X, Lee J, Han M. Mammalian regeneration and regenerative medicine, *Birth Defects Res C Embryo,* 84(4), 2008, 265-280.
8. Tuch B E. Stem cells-a clinical update, *Fam Physician,* 35(9), 2006, 719-721.
9. Thomson J A, Itskovitz-Eldor J, Shapiro S S, Waknitz M A, Swiergiel J J, Marshall V S, Jones J M. Blastocysts embryonic stem cell lines derived from human, *Science,* 282(5391), 1998, 1145-1147.
10. Strauer B, Steinhoff G. 10 years of intracoronary and intramyocardial bone marrow stem cell therapy of the heart: from the methodological origin to clinical practice, *Am Coll Cardiol,* 58(11), 2011, 1095-1104.
11. Karanes C, Nelson G O, Chitphakdithai P, Agura E, Ballen K K, Bolan C D, Porter D L, Uberti J P, King R J, Confer D L. Twenty years of unrelated donor hematopoietic cell transplantation for adult recipients facilitated

by the national marrow donor program, *Biol Blood Marrow Transplant,* 14(9), 2008, 8-15.
12. Menasche P. Skeletal myoblasts and cardiac repair, *Mol Cell Card,* 45(4), 2008, 545-553.
13. Nelson T J, Martinez-Fernandez A, Yamada S, Perez-Terzic C, Ikeda Y, Terzic A. Repair of acute myocardial infarction by human stemness factors induced pluripotent stem cells, *Circulation,* 120(5), 2009, 408–416.
14. Cleland J G, Freemantle N, Coletta A P, Clark A L. Clinical trials update from the American Heart Association: Repair-AMI, Astami Jelis, mega, revive-II, survive and proactive, *Eur Heart Fail,* 8(1), 2006, 105-110.
15. Zhang N, Li J, Luo R, Jiang J, Wang J A. Bone marrow mesenchymal stem cells induce angiogenesis and attenuate the remodeling of diabetic cardiomyopathy, *Exp Clin. Endocrinol. Diabet,* 116(2), 2008, 104-111.
16. Li J H, Zhang N, Wang J A. Improved anti-apoptotic and anti-remodeling potency of bone marrow mesenchymal stem cells by anoxic pre-conditioning in diabetic cardiomyopathy, *Endocrinol Invest,* 31(2), 2008, 103-110.
17. Govaert J A, Swijnenburg R J, Schrepfer S, Xie X, Van Der Bogt K E, Hoyt G, Stein W, Ransohoff K J, Robbins R C, Wu J C. Poor functional recovery after transplantation of diabetic bone marrow stem cells in ischemic myocardium, *Heart Lung Transplant,* 28(11), 2009, 1158-1165.
18. Sanberg P R. Neural stem cells for Parkinson's disease: To protect and repair, *PNAS,* 104(29), 2007, 11869-11870.
19. Ehnert S, Glanemann M, Schmitt A. The possible use of stem cells in regenerative medicine: dream or reality? *Langenbeck Archives Surgery,* 394(6), 2009, 985-997.
20. Karaoz E, Okcu A, Unal Z S. Adipose tissue-derived mesenchymal stromal cells efficiently differentiate into insulin-producing cells in pancreatic islet microenvironment both *in vitro* and *in vivo*, *Cytotherapy,* 15(5), 2013, 557-570.
21. Rahman S, Rahman T, Ismail A A, Rashid A R. Diabetes-associated macrovasculopathy: Pathophysiology and pathogenesis, *Diabetes Obes Metab,* 9(6), 2007, 767-780.
22. Woodfield S L, Lundergan C F, Reiner J S, Greenhouse S W, Thompson M A, Rohrbeck S C, Deychak Y, Simoons M L, Califf R M, Topol E J, Ross A M. Angiographic findings and outcome in diabetic patients treated with thrombolytic therapy for acute myocardial infarction: the GUSTO-I experience, *Am Coll Cardiol,* 28(7), 1996, 1661-1669.
23. Min J Y, Yang Y, Converso K L, Liu L, Huang Q, Morgan J P, Xiao Y F. Transplantation of embryonic stem cells improves cardiac function in post-infarcted rats, *Appl Physiol,* 92(1), 2002, 288-296.
24. Singla D K, Hacker T A, Ma L, Douglas P S, Sullivan R, Lyons G E, Kamp T J. Transplantation of embryonic stem cells into the infarcted mouse heart: formation of multiple cell types, *Mol Cell Cardiol,* 40(1), 2006, 195-200.
25. Soria B, Martin F, Andreu E, Sanchez-Andres J V, Nacher V, Montana E. Diminished fraction of blockable ATP-sensitive K+ channels in islets transplanted into diabetic mice, *Diabetes,* 45(12), 1996, 1755-1760.
26. Bonner-Weir S, Taneja M, Weir G C, Tatarkiewicz K, Song K H, Sharma A, O'Neil J J. *In vitro* cultivation of human islets from expanded ductal tissue, *Proc. Natl. Acad. Sci, USA,* 97(14), 2000, 7999-8004.
27. Soria B, Roche E, Berna G, Leon-Quinto T, Reig J A, Martin F. Insulin-secreting cells derived from embryonic stem cells normalize glycemia in streptozotocin induced diabetic mice, *Diabetes,* 49(2), 2000, 157-162.
28. Anthea M, Hopkins J, McLaughlin C W, Johnson S, Warner M Q, LaHart D, Wright J D. Human Biology and Health, *Englewood Cliffs, Prentice Hall, New Jersey USA,* 1st Edition, 1993, 256.
29. Kelly B B, Fuster, Valentin. Institute of Medicine; Promoting cardiovascular health in the developing world: A critical challenge to achieve global health, *Washington, D.C, National Academies Press,* 2010, 1-484.
30. Dantas A P, Jimenez-Altayo F, Vila E. Vascular aging: facts and factors, *Vascul, Physiol,* 3(325), 2012, 1-2.

31. Finegold J A, Asaria P, Francis D P. Mortality from ischaemic heart disease by country, region, and age: Statistics from World Health Organisation and United Nations, *Int Cardiol,* 168(2), 2012, 934-945.
32. McGill H C, McMahan C A, Gidding S S. Preventing heart disease in the 21st century: implications of the Pathobiological Determinants of Atherosclerosis in Youth (PDAY) study, *Circulation,* 117(9), 2008, 1216-1227.
33. Glass C E. Stem cells in the diabetic infarcted heart, *Heart Fail Rev,* 15(6), 2010, 581-588.
34. Correia A S, Anisimov S V, Li J, Brundin P. Stem cell based therapy for Parkinson's disease, *Review Art,* 37(7), 2005, 487-498.
35. Redmond D E, Bjugstad K B, Teng Y D, Ourednik V, Ourednik J, Wakeman D R, Parsons X H, Gonzalez R, Blanchard B C, Kim S U. Behavioral improvement in a primate Parkinson's model is associated with multiple homeostatic effects of human neural stem cells, *Proc Natl Acad Sci, USA,* 104(29), 2007, 12175-12180.
36. Flax J D, Aurora S, Yang C, Simonin C, Wills A M, Billinghurst L L, Jendoubi M, Sidman R L, Wolfe J H, Kim S U, Snyder E Y. Engraft able human neural stem cells respond to developmental cues, replace neurons, and express foreign genes, *Nat Biotechnol,* 16(11), 1998, 1033-1039.
37. Uchida N, Buck D W, He D, Reitsma M J, Masek M, Phan T V, Tsukamoto A S, Gage F H, Weissman I L. Direct isolation of human central nervous system stem cells, *Proc Natl Acad Sci, USA,* 97(26), 2000, 14720-14725.
38. Christophersen N S, Brundin P. Large stem cell grafts could lead to erroneous interpretations of behavioral results? *Nat Med,* 13(2), 2007, 118-119.
39. Goldman S A, Roy N S, Beal M F, Cleren C. Functional engraftment of human ES cell-derived dopaminergic neurons enriched by coculture with telomerase-immortalized midbrain astrocytes, *Nat Med,* 12(11), 2006, 1259-1268.
40. Crigler L, Robey R C, Asawachaicharn A, Gaupp D, Phinney D G. Human mesenchymal stem cell subpopulations express a variety of neuro-regulatory molecules and promote neuronal cell survival and neuritogenesis, *Exp Neurol,* 198(1), 2006, 54-64.
41. Zhang Y W, Denham J, Theis R S. Oligodendrocyte progenitor cells derived from human embryonic stem cells express neurotrophic factors, *Stem Cells Dev,* 15(6), 2006, 943-952.
42. Albini A, Sporn M B. The tumour microenvironment as a target for chemoprevention, *Nat Rev Cancer,* 7(2), 2007, 139-147.
43. Anand P, Kunnumakkara A B, Kunnumakara A B, Sundaram C, Harikumar K B, Tharakan S T, Lai O S, Sung B, Aggarwal B B. Cancer is a preventable disease that requires major lifestyle changes, *Pharm Res,* 25(9), 2008, 2097-2116.
44. Kinzler K W, Vogelstein B. The genetic basis of human cancer, *McGraw-Hill, Medical Pub. Division, New York,* 2nd Edition, 2002, 821.
45. Kushi L H, Doyle C, McCullough M. American Cancer Society Guidelines on nutrition and physical activity for cancer prevention: reducing the risk of cancer with healthy food choices and physical activity, *Cancer Clin,* 62(1), 2012, 30-67.
46. Jemal A, Bray F, Center M M, Ferlay J, Ward E, Forman D. Global cancer statistics, *Cancer Clin,* 61(2), 2011, 69-90.
47. Keramidas M, Fraipont F, Karageorgis A, Moisan A, Persoons V, Richard M, Coll J, Rome C. The dual effect of MSCs on tumour growth and tumour angiogenesis, *Stem Cell Res Therap,* 4(2), 2013, 41.
48. Wu G D, Nolta J A, Jin Y S, Barr M L, Yu H, Starnes V A, Cramer D V. Migration of mesenchymal stem cells to heart allografts during chronic rejection, *Transplantation,* 75(5), 2003, 679-685.
49. Granero-Molto F, Weis J A, Miga M I, Landis B, Myers T J, O'Rear L, Longobardi L, Jansen E D, Mortlock D P, Spagnoli A. Regenerative effects of transplanted mesenchymal stem cells in fracture healing, *Stem Cells,* 27(8), 2009, 1887-1898.
50. Kristensen L P, Chen L, Nielsen M O, Qanie

D W, Kratchmarova I, Kassem M, Andersen J S. Temporal profiling and pulsed SILAC labeling identify novel secreted proteins during ex vivo osteoblast differentiation of human stromal stem cells, *Mol Cell Proteomics,* 11(10), 2012, 989-1007.

51. Chamberlain G, Fox J, Ashton B, Middleton J. Concise review: mesenchymal stem cells: their phenotype, differentiation capacity, immunological features, and potential for homing, *Stem Cells,* 25(11), 2007, 2739-2749.
52. Phinney D G, Prockop D J. Concise review: mesenchymal stem/multipotent stromal cells: the state o.] Kinnaird T, Stabile E, Burnett M S, Lee C W, Barr S, Fuchs S, Epstein S E. Marrow-derived stromal cells express genes encoding a broad spectrum of arteriogenic cytokines and promote *in vitro* and *in vivo* arteriogenesis through paracrine mechanisms, *Circ Res,* 94(5), 2004, 678-685.
53. Karnoub A E, Dash A B, Vo A P, Sullivan A, Brooks M W, Bell G W, Richardson A L, Polyak K, Tubo R, Weinberg R A. Mesenchymal stem cells within tumour stroma promote breast cancer metastasis, *Nat,* 449(7162), 2007, 557-563.
54. Dvorak F. Tumors: wounds that do not heal, Similarities between tumor stroma generation and wound healing, *N Engl Med,* 315(26), 1986, 1650-1659.
55. Erez N, Truitt M, Olson P, Arron S T, Hanahan D. Cancer-associated fibroblasts are activated in incipient neoplasia to orchestrate tumor-promoting inflammation in an NF-kappa B-dependent manner, *Cancer Cell,* 17(2), 2010, 135-147.
56. Quante M, Tu S P, Tomita H, Gonda T, Wang S S, Takash S, Baik G H, Shibata W, Diprete B, Betz K S, Friedman R, Varro A, Tycko B, Wang T C. Bone marrow-derived myofibroblasts contribute to the mesenchymal stem cell niche and promote tumor growth, *Cancer Cell,* 19(2), 2011, 257-272.
57. Lepperdinger G, Brunauer R, Jamnig A, Laschober G, Kassem M. Controversial issue: is it safe to employ mesenchymal stem cells in cell-based therapies? *Exp Gerontol,* 43(11), 2008, 1018-1023.
58. Khakoo A Y, Pati S, Anderson S A, Reid W, Elshal M F, Rovira I I, Nguyen A T, Malide D, Combs C A, Hall G, Zhang J, Raffeld M, Rogers T B, Stetler-Stevenson W, Frank J A, Reitz M, Finkel T. Human mesenchymal stem cells exert potent antitumorigenic effects in a model of Kaposi's sarcoma, *Exp Med,* 203(5), 2006, 1235-1247.
59. Zhu Y, Sun Z, Han Q, Liao L, Wang J, Bian C, Li J, Yan X, Liu Y, Shao C, Zhao R C. Human mesenchymal stem cells inhibit cancer cell proliferation by secreting DKK-1, *Leukemia,* 23(5), 2009, 925-933.
60. Freeman M R. Sculpting the nervous system: glial control of neuronal development, *Curr Opin Neurobiol,* 16(1), 2006, 119-125.
61. Capone C, Frigerio S, Fumagalli S, Gelati M, Principato M C, Storini C, Montinaro M, Kraftsik R, Curtis M D, Parati E, Simoni M G. Neurosphere-derived cells exert a neuroprotective action by changing the ischemic microenvironment, *PLoS One,* 2(4), 2007, e373.
62. Dominici M, Le Blanc K, Mueller I, Slaper-Cortenbach I, Marini F, Krause D, Deans R, Keating A, Prockop D, Horwitz E. Minimal criteria for defining multipotent mesenchymal stromal cells, The International Society for Cellular Therapy position statement, *Cytotherap,* 8(4), 2006, 315-317.

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