Review Article

Novel Prospectives of Stem Cell Therapeutics – A Clinical Approach

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ABSTRACT

Stem cell are biological cells found in all multi cellular organisms, that can divide through mitosis and differentiate into diverse specialized cell types and self renew to produce more stem cells. In mammals, there are two broad types of stem cell. Embryonic stem cells that are isolated from inner cell mass blastocytes and adults stem cell that found in various tissues. In adult organisms that stem cells and progenitor cells act as a repair system for the body replenished in adults tissues. Stem cells are culture in culture dish. Healthy potential stem cell are extracted and prepared and administered into a damaged body parts. stem cell are used to treat many Potential treatments like Brain damage, Cancer, Spinal cord injury , Heart damage , Haematopoiesis (blood cell formation) Baldness, Missing teeth, Deafness, Blindness and vision impairment, Amyotrophic lateral sclerosis, Graft vs. host disease and Cohn's disease, Neural and behavioural birth defects, Diabetes, Orthopaedics, Wound healing, Infertilit, Clinical Trials, Stem cell use in animals, Veterinary applications, Potential contributions to veterinary medicine**.**

Keywords: stem cell, embryonic stem cell, Totipotent, Pluripotent.

INTRODUCTION

Stem cells are biological cells found in all multi cellular organisms that can divide (through mitosis) and differentiate into diverse specialized cell types and can self-renew to produce more stem cells. In mammals, there are two broad types of stem cells: embryonic stem cells, which are isolated from the inner cell mass of blast cysts, and adult stem cells, which are found in various tissues. In adult organisms, stem cells and progenitor cells act as a repair system for the body, replenishing adult tissues. In a developing embryo, stem cells can differentiate into all the specialized cells (these are called Pluripotent cells), but also maintain the normal turnover of regenerative organs, such as blood, skin, or intestinal tissues[1,2]. Stem cells can now be artificially grown and transformed into specialized cell types with characteristics consistent with cells of various tissues such as muscles or nerves through cell culture. Highly plastic adult stem cells are routinely used in medical therapies. Stem cells can be taken from a variety of sources, including umbilical cord blood and bone marrow. Embryonic cell lines and autologous embryonic stem cells generated through therapeutic cloning have also been proposed as promising candidates for future therapies[1-2].

CLASSIFICATION

1. Embryonic stem cells
2. Adult stem cells.

EMBRYONIC STEM CELLS

These stem cells are derived from a four or five day old human embryo that in the blastocyst phase of development .The embryos are usually extract that been created in IVF(in vitro fertilization) clinics where several eggs are fertilized in a test tube ;but only one implanted into the woman .The sexual reproduction begins when a males sperm fertilizes a females ovum to form a single cell called as zygote the single zygote cell then begins a serious of divisions forming 2,4,8,16 cells etc. After four to six days before implantation in the uterus – this mass of cells is called a blastocyst consists of an inner cell mass (embryo blast) and outer cell mass (trophoblast).The outer cell mass becomes a part of the placenta .the inner cell mass is the group of cell that will differentiate to become all the structure of an adult organism.

ADULT STEMCELLS

Adult stem cells also called somatic cells exits throughout the body after embryonic development and are found inside different types of tissues .these stem cell have been found in tissues such as brain, bone marrow, blood, blood vessels, skeletal muscles, skin and the liver .they remain non-dividing state for years until activated by disease or tissue injury.. There are three sources of autologous adult stem cells: 1) Bone marrow, which requires extraction by harvesting, that is, drilling into bone (typically the femur or iliac crest), 2) Adipose tissue (lipid cells), which requires extraction by liposuction, and 3) Blood, which requires extraction through persist, wherein blood is drawn from the donor, (similar to a blood donation) passed through a machine that extracts the stem cells and returns other portions of the blood to the donor.

STEM CELL CULTURE

When extracting embryonic stem cell. the blastocyst stage signals when to isolate stem cell by placing the ''inner cell mass'' of blastocyst into a culture dish containing a nutrient rich broth .lacking the necessary stimulation to differentiate ,they begin to divided and replicate while maintaining their ability to become any cell type in human body .There undifferentiated cell can be stimulated to create specialized cell. Human embryonic stem cell colony either extracted from adult tissue or from a dividing zygote in a culture dish. once extracted ,scientists place the cells in a controlled culture that prohibits them from further specializing .the process of growing large numbers of embryonic stem cells has been easier growing large numbers of adult stem cells ,but progress is being made for both cell types.

PROPERTIES

The classical definition of a stem cell requires that it possess two properties:

- Self-renewal: the ability to go through numerous cycles of cell division while maintaining the undifferentiated state.
- Potency: the capacity to differentiate into specialized cell types. In the strictest sense, this requires stem cells to be either totipotent or Pluripotent to be able to give rise to any mature cell type, although multi potent or unipotent progenitor cells are sometimes referred to as stem cells .Apart from this it is being said that stem cells function is regulated in a feedback mechanism.
- Self-renewal

Two mechanisms to ensure that the stem cell population is maintained exist

1. Obligatory asymmetric replication: a stem cell divides into one father cell that is identical to the original stem cell, and another daughter cell that is differentiated
2. Stochastic differentiation: when one stem cell develops into two differentiated daughter cells, another stem cell undergoes mitosis and produces two stem cells identical to the original.

Cell potency

Potency specifies the differentiation potential (the potential to differentiate into different cell types) of the stem cell.

Totipotent

stem cells can differentiate into embryonic and extra embryonic cell types. Such cells can construct a complete, viable organism. These cells are produced from the fusion of an egg and sperm cell. Cells produced by the first few divisions of the fertilized egg are also totipotent .

Pluripotent

stem cells are the descendants of totipotent cells and can differentiate into nearly all cells i.e. cells derived from any of the three germ layers.

Multipotent

stem cells can differentiate into a number of cells, but only those of a closely related family of cells .

Oligopotent

stem cells can differentiate into only a few cells, such as lymphoid or myeloid stem cells[3-5].

Unipotent

cells can produce only one cell type, their own, but have the property of self-renewal, which distinguishes them from non-stem cells (e.g., muscle stem cells).

Induced Pluripotent

These are not adult stem cells, but rather reprogrammed cells (e.g. epithelial cells) given Pluripotent capabilities. Using genetic reprogramming with protein transcription factors, Pluripotent stem cells equivalent

to embryonic stem cells have been derived from human adult skin tissue. Shinya Yamanaka and his colleagues at Kyoto University used the transcription factors Oct3/4, Sox2, c-Myc, and Klf4 in their experiments on cells from human faces. Junying Yu, James Thomson, and their colleagues at the University of Wisconsin–Madison used a different set of factors, Oct4, Sox2, Nanog and Lin28,] and carried out their experiments using cells from human foreskin.[6]

As a result of the success of these experiments, Ian Wilmot, who helped create the first cloned animal Dolly the Sheep, has announced that he will abandon nuclear transfer as an avenue of research.

Frozen blood samples can be used as a source of induced Pluripotent stem cells, opening a new avenue for obtaining the valued cells Lineage[6-7].

Stem cell line

To ensure self-renewal, stem cells undergo two types of cell division (see *Stem cell division and differentiation* diagram)[8]. Symmetric division gives rise to two identical daughter cells both endowed with stem cell properties. Asymmetric division, on the other hand, produces only one stem cell and a progenitor cell with limited self-renewal potential. Progenitors can go through several rounds of cell division [9] before terminally differentiating into a mature cell. It is possible that the molecular distinction between symmetric and asymmetric divisions lies in differential segregation of cell membrane proteins (such as receptors) between the daughter cells[10].

How are stem cells prepared and administered

The process is as follows

step1

Before harvesting the adipose (fat)tissue it is essential that sterilised canister is used and filled with 500ml of washing solution.

Step2

In order to prepare plasma, blood is collected from the patient.

Step3

Adipose tissues is then harvested from the patient via tumescent liposuction

step4

The adipose collected is then transferred into the falcon tubes and then put into 37c shaking water bath.

Step5

These tubes are then centrifuged

Step6

after the centrifuging process, a stem cell pallet will form on the bottom of the each falcon tube using a pipette and taking extra care not the stir contains , the pallets are then carefully removed from the each tube.

Step7

The pallets are then first filtered.

Step8

by using a syringe, we collect the sample from the tube for cell counting and staining for viability.

Step9

The remaining stem cells are the activated by using daylight.

Step10

The cells are then administered back to the patient through one or more of the following modes of administration

Intravenous

Administered through a standard intra venous drip.

Injected

Administered directly into a localised area.

Stem cell treatments

Order to treat disease or injury. Many medical researchers believe that stem cell treatments have the potential to change the face of human disease and alleviate suffering. The ability of stem cells to self-renew and give rise to subsequent generations with variable degrees of differentiation capacities. Offers significant potential for generation of tissues that can potentially replace diseased and damaged areas.

Stem cell treatments are a type of intervention strategy that introduces new cells into damaged tissue in the body, with minimal risk of rejection and side effects.

Medical researchers anticipate that adult and embryonic stem cells will soon be able to treat cancer, Type 1 diabetes mellitus, Parkinson's disease, Huntington's disease, Celiac Disease, cardiac failure, muscle damage and neurological disorders, and many others. Nevertheless, before stem cell therapeutics can be applied in the clinical setting, more research is necessary to understand stem cell behaviour upon transplantation as well as the mechanisms of stem cell interaction with the diseased/injured.

Hematopoietic stem cell transplantation

Umbilical cord blood stem cells, have been used to treat cancer patients with conditions such as leukemic and lymphoma. During chemotherapy, most growing cells are killed by the cytotoxic agents. These agents, however, cannot discriminate between the leukaemia or

euplastic cells, and the hematopoietic stem cells within the bone marrow. It is this side effect of conventional chemotherapy strategies that the stem cell transplant attempts to reverse; a donor's healthy bone marrow reintroduces functional stem cells to replace the cells lost in the host's body during treatment[11].

Potential treatment

Brain damage

Stroke and traumatic brain injury lead to cell death, characterized by a loss of neurons and oligodendrocysts within the brain. Healthy adult brains contain neural stem cells which divide to maintain general stem cell numbers, or become progenitor cells. In healthy adult animals, progenitor cells migrate within the brain and function primarily to maintain neuron populations for olfaction (the sense of smell). Interestingly, in pregnancy and after injury, this system appears to be regulated by growth factors and can increase the rate at which new brain matter is formed.[citation needed] Although the reparative process appears to initiate following trauma to the brain, substantial recovery is rarely observed in adults, suggesting a lack of robustness.

Stem cells may also be used to treat brain degeneration, such as in Parkinson's and Alzheimer's disease[12-13].

Cancer

Using conventional techniques, brain cancer is difficult to treat because it spreads so rapidly. Transplanted human neural stem cells into the brain of rodents that received intracranial tumours. Within days, the cells migrated into the cancerous area and produced cytosine demines. an enzyme that converts a non-toxic pro-drug into a chemotherapeutic agent. As a result, the injected substance was able to reduce the tumours mass by 81 percent. the patient’s own lymphocytes, and stem cells injected, eventually replacing the immune system of the patient with that of the healthy donor[14].

Spinal cord injury

Transplanted Multipoten adult stem cells from umbilical cord blood to a patient suffering from a spinal cord injury and that following the procedure, she could walk on her own, without difficulty. The patient had not been able to stand up for roughly 19 years. For the unprecedented clinical test, the scientists isolated adult stem cells from umbilical cord blood and then injected them into the damaged part of the spinal cord.

Transplanted Multipoten human foetal-derived neural stem cells into paralyzed mice, resulting in locomotors improvements four months later. The observed recovery was associated with differentiation of transplanted cells into new neurons and oligodendrocysts- the latter of which forms the myelin sheath around axons of the central nervous system, thus insulating neural impulses and facilitating communication with the brain .

Differentiated human blastocyst stem cells into neural stem cells, then into pre-mature motor neurons, and finally into spinal motor neurons, the cell type that, in the human body, transmits messages from the brain to the spinal cord and subsequently mediates motor function in the periphery. The newly generated motor neurons exhibited electrical activity, the signature action of neurons[15].

Heart damage

Several clinical trials targeting heart disease have shown that adult stem cell therapy is safe, effective, and equally efficient in treating old and recent infarcts. Adult stem cell therapy for treating heart disease was commercially available in at least five continents at the last count.

Possible mechanisms of recovery include:

- ✓ Generation of heart muscle cells
- ✓ Stimulation of growth of new blood vessels to repopulate damaged heart tissue
- ✓ Secretion of growth factors

Assistance via some other mechanism

It may be possible to have adult bone marrow cells differentiate into heart muscle stem cells.

Haematopoiesis (blood cell formation)

The immune system is vulnerable to degradation upon the pathogenesis of disease, and because of the critical role that it plays in overall defence, its degradation is often fatal to the organism as a whole. Diseases of hematopoietic cells are called hematopathology. The specificity of the immune cells is what allows recognition of foreign antigens, causing further challenges in the treatment of immune disease. Identical matches between donor and recipient must be made for successful transplantation treatments, but matches are uncommon, even between first-degree relatives. Research using both hematopoietic adult stem cells and embryonic stem cells has provided insight into the possible mechanisms and methods of treatment for many of these ailments. Potential benefits to gene therapy, blood transfusion, and topical medicine.

Baldness
Hair follicles also contain stem cells, and some researchers predict research on these follicle stem cells may lead to successes in treating baldness through an activation of the stem cells progenitor cells. This treatment is expected to work by activating already existing stem cells on the scalp. Later treatments may be able to simply signal follicle stem cells to give off chemical signals to nearby follicle cells which have shrunk during the aging process, which in turn respond to these signals by regenerating and once again making healthy hair.

Missing teeth
This technology can be used to grow live teeth in human patients Stem cells taken from the patient could be coaxed in the lab into turning into a tooth bud which, when implanted in the gums, will give rise to a new tooth, and would be expected to grow within two months. It will fuse with the jawbone and release chemicals that encourage nerves and blood vessels to connect with it. The process is similar to what happens when humans grow their original adult teeth[16,17].

Deafness
Heller has reported success in re-growing cochlea hair cells with the use of embryonic stem cells.

Blindness and vision impairment
Transplanted corneal stem cells into damaged eyes to restore vision. "Sheets of retinal cells used by the team are harvested from aborted foetuses, which some people find objectionable." When these sheets are transplanted over the damaged cornea, the stem cells stimulate renewed repair, eventually restore.

Graft vs. host disease and Cohn's disease
Therapeutics using their in-development product Parochial, derived from adult bone marrow. The target disorders of this therapeutic are graft-versus-host disease and Cohn's disease**.**

Neural and behavioural birth defects
Before they die the neural stem cells succeed in inducing the host brain to produce large numbers of stem cells which repair the damage. Now developing procedures to administer the neural stem cells in the least invasive way possible - probably via blood vessels, making therapy practical and clinically feasible. Researchers also plan to work on developing methods to take cells from the patient's own body, turn them into stem cells, and then transplant them back into the patient's blood via the blood stream[18.]

Diabetes
Diabetes patients lose the function of insulin-producing beta cells within the pancreas. Human embryonic stem cells may be grown in cell culture and stimulated to form insulin-producing cells that can be transplanted into the patient[19].

Orthopaedics
Clinical case reports in the treatment of orthopaedic conditions have been reported. To date, the focus in the literature for musculoskeletal care appears to be on mesenchymal stem cells. Centavo et al. have published MRI evidence of increased cartilage and meniscus volume in individual human subjects. The results of trials that include a large number of subjects are yet to be published. However, a published safety study conducted in a group of 227 patients over a 3-4 year period shows adequate safety and minimal complications associated with mesenchymal cell transplantation mesenchymal stem cells with coverage of the treated chondral defects[20-22].

Wound healing
Stem cells can also be used to stimulate the growth of human tissues. In an adult, wounded tissue is most often replaced by scar tissue, which is characterized in the skin by disorganized collagen structure, loss of hair follicles and irregular vascular structure. In the case of wounded fetal tissue, however, wounded tissue is replaced with normal tissue through the activity of stem cells. A possible method for tissue regeneration in adults is to place adult stem cell "seeds" inside a tissue bed "soil" in a wound bed and allow the stem cells to stimulate differentiation in the tissue bed cells. This method elicits a regenerative response more similar to fetal wound-healing than adult scar tissue formation [23].

Infertility
Culture of human embryonic stem cells in mitotic ally inactivated porcine ovarian fibroblasts (POF) causes differentiation into germ cells (precursor cells of coyotes and spermatozoa), as evidenced by gene expression analysis[24].
Human embryonic stem cells have been stimulated to form Spermatozoon-like cells, yet still slightly damaged or malformed. It could potentially treat azoospermia.

Clinical Trials

Food and Drug Administration gave clearance to Gerona Corporation for the initiation of the first clinical trial of an embryonic stem cell-based therapy on humans. The trial will evaluate the drug GRNOPC1, embryonic stem cell-derived oligodendrocysts progenitor cells, on patients with acute spinal cord injury.

Stem cells use in animals

- ✓ Veterinary applications
- ✓ Potential contributions to veterinary medicine

Horses, dogs, and cats can benefit the development of stem-cell treatments in veterinary medicine and can target a wide range of injuries and diseases such as myocardial infarction, stroke, tendon and ligament damage, osteoarthritis, osteochondrosis and muscular dystrophy both in large animals, as well as humans. Companion animals can serve as clinically relevant models that closely mimic human disease[25-28].

Development of regenerative treatment models

Veterinary applications of stem cell therapy as a means of tissue regeneration have been with the use of adult-derived mesenchymal stem cells to treat animals with injuries or defects affecting bone, cartilage, ligaments and/or tendons. Because mesenchymal stem cells can differentiate into the cells that make up bone, cartilage, tendons, and ligaments (as well as muscle, fat, and possibly other tissues), the treatment of diseases affecting these tissues[29-32]. Mesenchymal stem cells are primarily derived from adipose tissue or bone marrow. Since an elevated immune response following cell transplantation may result in rejection of exogenous cells (except in the case of cells derived from a very closely genetically related individual), mesenchymal stem cells are often derived from the patient prior to injection in a process known as autologous transplantation. Surgical repair of bone fractures in dogs and sheep has demonstrated that engraftment of mesenchymal stem cells derived from a genetically different donor within the same species, termed allergenic transplantation, does not elicit an immunological response in the recipient animal and can mediate regeneration of bone tissue in major bony fractures and defects.. Stem cells can speed up bone repair in fractures/defects that would normally require extensive grafting, suggesting that mesenchymal stem cell use may provide a useful alternative to conventional grafting techniques[33-35]. Treating tendon and ligament injuries in horses using stem cells, whether derived from adipose tissue or bone-marrow, has support in the veterinary literature[34-35] While further studies are necessary to fully characterize the use of cell-based therapeutics for treatment of bone fractures, stem cells are thought to mediate repair via five primary mechanisms: 1) providing an anti-inflammatory effect, 2) homing to damaged tissues and recruiting other cells, such as endothelial progenitor cells, that are necessary for tissue growth, 3) supporting tissue remodelling over scar formation, 4) inhibiting apoptosis, and 5) differentiating into bone, cartilage, tendon, and ligament tissue.

Significance of stem cell microenvironments

The microenvironment into which stem cells are transplanted significantly alters the capacity of engrafted cells for recovery and repair . The microenvironment provides growth factors and other chemical signals that guide appropriate differentiation of transplanted cell populations and direct transplanted cells to sites of trauma or disease. Repair and recovery can then be mediated via three primary mechanisms: 1) formation and/or recruitment of new blood cells to the damaged region; 2) prevention of programmed cell death or apoptosis; and 3) suppression of inflammation. To further enrich blood supply to the damaged areas, and consequently promote tissue regeneration, platelet-rich plasma could be used in conjunction with stem cell transplantation. The efficacy of some stem cell populations may also be affected by the method of delivery; for instance, to regenerate bone, stem cells are often introduced in a scaffold where they produce the minerals necessary for generation of functional bone[36-37].

Sources of autologous (patient-derived) stem cells

Autologous stem cells intended for regenerative therapy are generally isolated either from the patient's bone marrow or from adipose tissue.. The number of stem cells transplanted into damaged tissue may alter efficacy of treatment. Stem cells derived from bone marrow aspirates, for instance, are cultured in specialized laboratories for expansion to millions of cells. Although adipose-derived tissue also requires processing prior to use, the culturing methodology for adipose-derived stem cells is not as extensive as that for bone marrow-derived cells[35,37.] While it is thought that bone-

marrow derived stem cells are preferred for bone, cartilage, ligament, and tendon repair, others believe that the less challenging collection techniques and the multi-cellular microenvironment already present in adipose-derived stem cell fractions make the latter the preferred source for autologous transplantation[38-42].

Currently available treatments for horses and dogs suffering from orthopaedic conditions

Autologous or allergenic stem cells are currently used as an adjunctive therapy in the surgical repair of some types of fractures in dogs and horses. Autologous stem cell-based treatments for ligament injury, tendon injury, osteoarthritis, osteochondrosis, and sub-chondral bone cysts have been commercially available to practicing veterinarians to treat horses since 2003 in the United States and since 2006 in the United Kingdom.. Autologous stem-cell injury and osteoarthritis in dogs, horses and dogs have been treated with autologous adipose-derived stem cells. The efficacy of these treatments has been shown in double-blind clinical trials for dogs with osteoarthritis of the hip and elbow and horses with tendon damage. The efficacy of using stem cells, whether adipose-derive.

Advantages and disadvantages of adult stem cells over embryonic stem / germ cells

Adult-derived stem cell therapies will complement, but they cannot replace, therapies that may be obtained from embryonic stem cells. Still, they do have some advantages. For example-adult stem cells offer the opportunity to utilize small samples of adult tissues, to obtain an initial culture of a patient's own cells for expansion and subsequent implantation in the same person (that is called an autologous transplant). This process avoids immune rejection by the recipient and also protects the patients from viral, bacterial or other contamination from another individual (donor) in case of allergenic transplant. With proper quality control and testing, allergenic adult stem cells may be practical as well. Autologous and allergenic transplants of hematopoietic stem cells (discussed ahead) that are isolated from mobilized peripheral blood .or form bone marrow by positive selection with antibiotics are in clinical use. Additionally, since they normally differentiate into a narrow set of cell types, directing them to a desired fate is easier.

One major disadvantage is that culturing adult stem cells in-vitro is very difficult and has not Advantages of Stem Cell Research.

Advantages of Stem Cell Research

- It provides medical benefits in the fields of therapeutic cloning and regenerative medicine.
- It provides great potential for discovering treatments and cures to a plethora of diseases including Parkinson's disease, schizophrenia, Alzheimer's disease, cancer, spinal cord injuries, diabetes and many more.
- Limbs and organs could be grown in a lab from stem cells and then used in transplants or to help treat illnesses.
- It will help scientists to learn about human growth and cell development.
- Scientists and doctors will be able to test millions of potential drugs and medicine, without the use of animals or human testers. This necessitates a process of simulating the effect the drug has on a specific population of cells. This would tell if the drug is useful or has any problems.
- Stem cell research also benefits the study of development stages that cannot be studied directly in a human embryo, which sometimes are linked with major clinical consequences such as birth defects, pregnancy-loss and infertility. A more comprehensive understanding of normal development will ultimately allow the prevention or treatment of abnormal human development.
- Another advantage of stem cell research is that it holds the key to reversing the effects of aging and prolonging our lives. Stem cell research has already found many treatments that help in slowing the aging process, and a bonus of further stem cell research is a possible 'cure' for aging altogether.
- An advantage of the usage of adult stem cells to treat disease is that a patient's own cells could be used to treat a patient. Risks would be quite reduced because patients' bodies would not reject their own cells.
- Embryonic stem cells can develop into any cell types of the body, and may then be more versatile than adult stem cells.

Disadvantages of Stem Cell Research

- The use of embryonic stem cells for research involves the destruction of blast cysts formed from laboratory-fertilized human eggs. For those people who believe that life begins at conception, the blastocyst is a human life and to destroy it is immoral and unacceptable.
- Like any other new technology, it is also completely unknown what the long-term effects of such an interference with nature could materialize.
- Embryonic stem cells may not be the solution for all ailments.
- According to a new research, stem cell therapy was used on heart disease patients. It was found that it can make their coronary arteries narrower.
- A disadvantage of most adult stem cells is that they are pre-specialized, for instance, blood stem cells make only blood, and brain stem cells make only brain cells.
- These are derived from embryos that are not a patient's own and the patient's body may reject them.

CONCLUSION

Stems cell can be used different areas. Current treatments, Potential treatments, Brain damage, Cancer, Spinal cord injury, Heart damage, Haematopoiesis (blood cell formation) Baldness, Missing teeth, Deafness, Blindness and vision impairment, Amyotrophic lateral sclerosis, Graft vs. host disease and Cohn's disease, Neural and behavioural birth defects, Diabetes, Orthopaedics, Wound healing, Infertility, Clinical Trials, Stem cell use in animals, Veterinary applications, Potential contributions to veterinary medicine, Development of regenerative treatment models, Significance of stem cell microenvironments. There is no toxic effect and adverse reactions compare to the chemotherapy, radiotherapy

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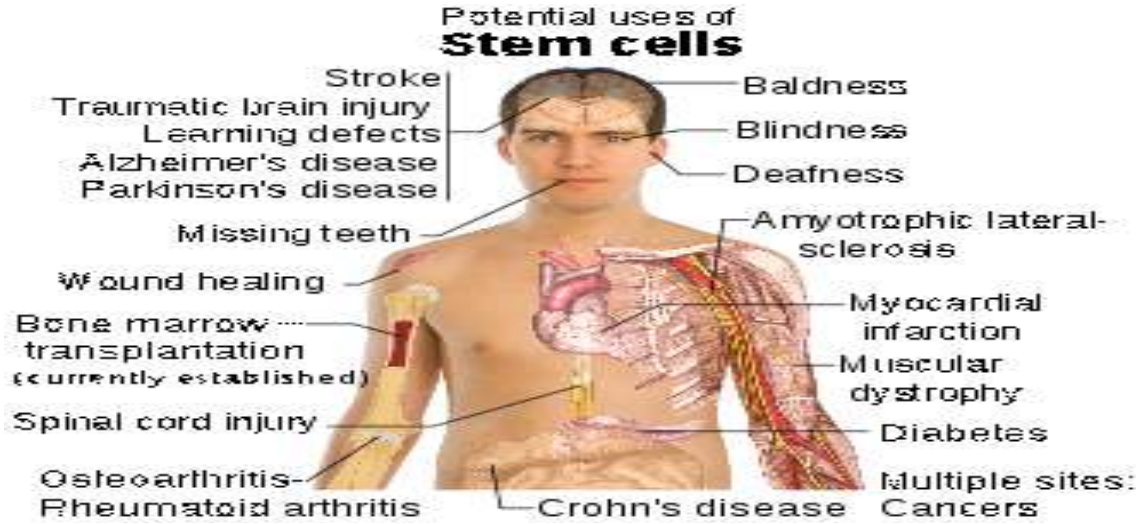

Fig. 1: Stem cell treatments

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