Regenerative Medicine: Recent Advances and Potential Applications

Dharmendra Kumar* and Bikash Chandra Sarkhelb

*Teaching Associate, bProfessor, Animal Biotechnology Centre, Nanaji Deshmukh Veterinary Science University, Jabalpur, Madhya Pradesh, India.

Abstract

Regenerative medicine is interdisciplinary approach to treat the diseases by creating living and functional tissues to repair or replace tissue or organ which have lost their function. Regenerative medicine empowers researchers to grow tissues and organs in the laboratory and safely implant them when the body cannot heal itself. Importantly, regenerative medicine has the potential to solve the problem of the shortage of organs available for donation compared to the number of patients that require life-saving organ transplantation, as well as solve the problem of organ transplant rejection, since the organ's cells will match that of the patient. It refers to a group of biomedical approaches to clinical therapies that may involve the use of stem cells. Regenerative medicine acts by a combination of several technological approaches including the use of soluble molecules, stem cell transplantation, tissue engineering etc. Some of the examples of regenerative medicines include; the injection of stem cells or progenitor cells (cell therapies); the induction of regeneration by biologically active molecules; and the transplantation of in vitro grown organs and tissues (Tissue engineering).

Keywords: Stem cells, Regenerative medicine, Tissue engineering, Cell therapy.

1. Introduction

"Regenerative Medicine is an emerging interdisciplinary field of research and clinical applications focused on the repair, replacement or regeneration of cells, tissues or organs to restore impaired function resulting from any cause, including congenital defects, disease, trauma and aging". It uses a combination of several technological approaches including the use of soluble molecules, gene therapy, stem cell transplantation, tissue engineering and the reprogramming of cell and tissue types, that moves it beyond traditional transplantation and replacement therapies (Weissman, 2000).

The promising field of regenerative medicine is working to restore structure and function of damaged tissues and organs (Daar and Greenwood, 2007). Regenerative medicine has the potential to solve the problem of the shortage of organs available for donation compared to the number of patients that require life-saving organ transplantation. Clinical procedures that aim to repair damaged tissue or organs, most often by using tissue engineered scaffolds and stem cells to replace cells and tissues damaged by aging and by disease. Scientists work with this powerful technology to create new body parts from a patient’s own cells and tissues. The success of these efforts will eliminate the concept of tissue rejection. The goal of regenerative medicine is to one day capable of maintaining the body in such a way there will be no need to replace whole organs.

2. Thrust Areas of Regenerative Medicine

2.1 Medical Devices and Artificial Organs

According to the FDA a medical device is defined, in part, as any health care product that does not achieve its primary intended purposes by chemical action or by being metabolized. Regenerative medicines works to replace damaged or diseased tissue with synthetic devices (fully artificial organs) or synthetic and cellular components (biohybrid organs). For example, In the case of spina bifida, a birth defect, patients fail to control the urinary bladder that resulted in inability to urinate at will, or even to regulate the build up of urine, could cause back up into the kidneys, creating life-threatening damage. Now, Regenerative medicines made possible to create laboratory grown urinary bladder from their own cells.

2.2 Cell Therapies
Cell therapy is one of the most promising techniques for repair of damaged or destroyed tissue of highly variable targets e.g., Hormonal dysfunction, such as diabetes and growth hormone deficiency, neurodegenerative diseases, such as Parkinson's, Alzheimer's and Huntington's; and cardiovascular lesions, such as myocardial infarction, peripheral vascular ischaemia; as well as lesions in the cornea, skeletal muscle, skin, joints and bones etc. The objective of cell therapy is to restore the lost function rather than produce a new organ, which may cause duplicity and undesirable effects. Several resources of cells can be used to restore the damaged tissue, such as resident stem cells, multipotent adult progenitor cells, embryonic stem cells, and induced pluripotent stem cells (Takashaki and Yamanka, 2006). Some cell therapies have been established and approved for clinical use, such as artificial skin derived from keratinocytes, derived from chondrocyte, cells of the corneal limbus or pancreatic islet transplantation. These therapies have had good results, although the scarcity of the starting material may represent a serious limitation.

2.3 Tissue Engineering

Tissue engineering is the branch of regenerative medicine which uses the cells, biological factors and biomaterials, alone or in combination, with the goal of restoring normal tissue structure and functions. In some of the cases with widespread fibrosis and scar tissue, cell-based therapies may fail, due to the lack of a blood supply and/or the lack of a microenvironment of receptors and biological mediators to provide the “niche” for attracting and supporting cell differentiation, proliferation and function. In fracture cases, in vitro engineered joint that will completely integrate in vivo and provide the recipient with lifelike function is an often cited tissue engineering goal. However, in clinincle practice, the involvement of multiple biological and technical barriers as well as the incomplete understanding of the developmental biology of bone, cartilage and soft tissues. (Fisher and Mauck, 2013) are the limiting factors in tissue engineering. The use of scaffolds along with the cells to restore the normal tissue structure and functions increases the success rates. The scaffolds can be injectable, noninjectable, simple, complex, biological or synthetic in nature. The ideal scaffold has sufficient strength to protect cells from compression and shearing forces, while still having injury site anchoring potential and porosity to allow nutrient and differentiation factors to diffuse through it. The scaffold must also degrade at a rate that optimizes cellular growth and tissue regeneration.

2.4 Stem Cell Therapy

Stem cell treatments are a type of cell therapy that introduces new cells into damaged tissue in order to treat a disease or injury. All stem cells, regardless of their source, have three general properties: they are capable of dividing and renewing themselves for long periods; they are unspecialized; and they can choose to become one of many different types of cells present in the body based on signals from their environments. The internal signals are controlled by a cell’s genes, which are interspersed across long strands of DNA, and carry coded instructions for all the structures and functions of a cell. The external signals for cell differentiation include chemicals secreted by other cells, physical contact with neighboring cells, and certain molecules in the microenvironment. Some of the issues regarding stem cells remain unanswered: (1) Are the internal and external signals for cell differentiation similar for all kinds of stem cells? (2) What are the specific sets of signals that promote differentiation into specific cell types? Apart from embryonic stem cells, the adult stem cells can also be used for cell-based therapies. Many adult tissues contain stem cells which can make identical copies of themselves for long periods of time (self renewal). Adult stem cells typically generate the cell types of the tissue in which they reside, for example a blood-forming adult stem cell in the bone marrow differentiates into many types of blood cells such as red blood cells, white blood cells, and platelets. A number of experiments over the last several years have raised the possibility that stem cells from one tissue may be able to give rise to cell types of a completely different tissue, a phenomenon known as plasticity. Stem cell plasticity has the ability of differentiating blood cells into neurons and hematopoietic stem cells into heart muscle etc.

3. Examples of Regenerative Medicine

3.1 Bio Artificial Liver

The bio artificial liver system employs a hollow-fiber bioreactor cartridge that is loaded with hepatocytes. The hollow fibers act as an immunization barrier, serving to prevent direct contact of patient blood flowing on the interior of the fibers with the hepatocytes on the exterior of the fibers (Alison et al., 2009).

3.2 Heart Damage

Several clinical trials targeting heart disease have concluded that adult stem cell therapy is safe and effective, and is equally efficient in chronic as well as recent infarcts. The stem cells works to generate the heart muscle cells through multiple actions viz., it may
stimulate the regeneration of blood vessels and secrete growth factors to repopulate the heart tissue (Strauer et al., 2009).

3.3 Haematopoiesis (Blood Cell Formation)

Research using both hematopoietic adult stem cells and embryonic stem cells has contributed great insight into possible mechanisms and methods of treatment for Hematopathology (Giarratana et al., 2005). In diseases of haematopoietic cells, the immune rejection by the recipient aggravate the conditions and reduce the chance of success of transplantation treatment. The haematopoietic cells derived by stem cells of the patient could maximize the success rates of transplantation by low risk of immune rejection.

3.4 Bio Hybrid Lung

The bio hybrid lung consists of artificial alveolar capillary modules which are developed by propagating the endothelial cells into a micro fabric or scaffold (Sueblinvong and Weiss, 2009).

3.5 Tissue Engineered Ear

Vacanti et al. (1991) developed a tissue engineered ear by growth of new cartilage in the shape of a human ear. The polymer biodegradable porous matrices were seeded with living chondrocytes isolated from a freshly sacrificed calf’s shoulder and implanted subcutaneously on the dorsum of athymic rats. This resulted in the formation of new cartilage in the shape of a human ear of approximately the same dimensions as the original implants.

3.6 Brain Damage

Stem cells may also be used to treat brain degeneration, such as Parkinson's and Alzheimer's disease. The neural stem cells can be sourced from healthy adult brains, which can act as progenitor cells divide to regenerate the brain cells.

3.7 Spinal Cord Injury

The spinal cord injury can be treated successfully by transplanting the stem cells viz., embryonic and adult stem cells to a patient. In case of human, embryonic stem cells, human blastocyst stem cells into neural stem cells, then into the beginnings of motor neurons, and finally into spinal motor neuron cells were successfully used (Chen et al., 2001).

3.8 Diabetes

Diabetes patients lose the function of their insulin producing beta cells of their pancreas. The degenerated beta cells can be repopulate using embryonic stem cells. In Human, embryonic stem cells
are stimulated to form insulin-producing cells that can be transplanted into the patient (McCall et al., 2009).

3.9 Cancer
In case of leukemia and lymphoma, adult stem cells derived from bone marrow and umbilical cord are used as an alternative or in association to chemotherapy with more efficacy. During chemotherapy, the chemical agents disrupt the associated growing cell and haematopoitic cells of bone marrow in addition to leukemia or neoplastic cells (Wang et al., 2009).

3.10 Deafness
There has been success in re-growing cochlea hair cells with the use of stem cells (Boer et al., 2009).

3.11 Blindness and Vision Impairment
In a report, retinal stem cells were successfully transplanted into damaged eyes to restore vision. The stem cells stimulate the renewal and repairing the retinal cells that leads to restore the vision (Pribila et al., 2008).

3.12 Baldness
Hair follicles also contain stem cells, and researchers predict research on these follicle stem cells may lead to successes in treating baldness through "hair multiplication", also known as "hair cloning". This treatment is expected to work through taking stem cells from existing follicles, multiplying them in cultures, and implanting the new follicles into the scalp (Busuttil, 2007).

3.13 Missing Teeth
Stem cells can also be used to regrow the teeth by differentiation into tooth bud in the lab which on implantation in the gums, will give rise to a new tooth similarly as original adult teeth. It is expected to take two months to grow. The tooth bud fuses with the jawbone and releases chemicals that encourage nerve and blood vessels to connect with it (Yen and Sharpe, 2008).

3.14 Wound Healing
Stem cells are used to stimulate the growth of tissues. Normally a 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. 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 (Jettanacheawchankit et al., 2009).

4. Stem Cell Use in Animals
The stem cell researches are currently conducted in veterinary science to treat range of diseases and injuries such as myocardial infarction, stroke, tendon and ligament damage, osteoarthritis, osteochondrosis and muscular dystrophy. The advancement of veterinary medicine in terms of stem cell therapy not only give benefits to animals but also contributes the human medicine. Companion animals may be superior models than typical mouse models for human disease. Veterinary research has developed regenerative treatment models, particularly involving mesenchymal stem cells: Veterinary applications of stem cell therapy as a means of regenerating new tissue includes the injuries or defects affecting bone, cartilage, ligaments and/or tendons (Taylor et al., 2007) as the mesenchymal stem cells can differentiate into osteoblast, chondrocytes and adipocytes bone (as well as muscle, tendons and possibly other tissues). By using a humanized sickle cell anemia mouse model, Hanna et al. (2007) showed that mice can be rescued after transplantation with hematopoietic progenitors obtained in vitro from autologous induced pluripotent stem cells. There is scientific evidence supporting the medicinal properties of stem cells by following means:

1. Have 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 remodeling over scar formation,
4. Inhibiting apoptosis, and
5. Differentiating into bone, cartilage, tendon, and ligament tissue (Richardson et al., 2008).

5. Conclusions and Future Prospects of Regenerative Medicines
Taking an outlook to the future, regenerative medicine will be able to improve the quality of life for individuals, by providing healthy, functional tissues and organs. Insulin-producing pancreatic islets could be regenerated in the body or grown in the laboratory, tissue-engineered heart muscle may be available to repair human hearts damaged by myocardial infarction. Even new approaches to revitalizing used-up body parts by removing the cells from an organ and infusing new cells to integrate into the existing matrix and restore full functionality. Regenerative medicine promises to fulfill the shortage of organ donar, to treat spinal cord injuries and to replace the weakened hearts. A possible future with regenerative medicine, which has the potential to offer a faster and more complete recovery with significantly fewer side effects or risk of complications.
References