NEW HORIZONS

Regenerative Medicine: A Novel Therapeutic Approach

Rashmi Sharma*, Ruchi Khajuria†, Annil Mahajan**

Gene therapy has shown encouraging results in treating various diseases, but the safety of gene delivery by means of viral vectors has become a matter of increasing public concern. Viral vectors have disadvantages of limited packaging capacity, unknown long term physiological effects because of co-transfer of extra-viral sequences, risk of immunological activation and regeneration of wild type of virus. However, the concept of regenerative medicine using stem cells may serve as a novel vehicle for carrying genes into tissues and to develop alternative therapeutic strategies to treat the diseased body organs as in case of heart failure, insulin dependent diabetes mellitus, myocardial ischemic disease, hepatic cirrhosis, renal failure etc. Advances in stem cell biology have made it possible for organ regeneration to become a reality. Stem cells are a population of immature precursor cells capable of self-renewal and provision of denovo and / or replacement cells for many tissues(1). Stem cells used in regenerative medicine are classified as embryonic or adult. At present, the regeneration of neurons, blood cells, vascular endothelial cells, cardio-myocytes, pigment cells, osteoblasts and islet cells is feasible and are being develped.

Current Status of Embryonic Stem Cells and Adult Stem Cells

Embryonic stem cells are derived from mammalian embryos in the blastocyst stage and have the ability to generate any terminally differentiated cell in the body; whereas adult stem cells are the part of tissue –specific cells of the postnatal organism into which they are committed to differentiate-Table-1 (2).

Although embryonic stem cells represent a very attractive tool from the viewpoint of tissue regeneration, they are associated with drawbacks like, rejection reactions due to allogeneic transplantation and risk of development of malignant tumor or teratoma (3). Rejection reactions are common in organs with rich blood flow. However, embryonic stem cells are presumed to be superior for the regeneration of nerve cells in the central nervous system in patients with parkinson's disease, as lymphocytes cannot cross the blood brain barrier (3). Adult stem cells also have the potential to differentiate into tissue derived from any germ layer depending upon the availability of various growth factors, biological substances or chemical substances e.g adult stem cells can differentiate into osteoblasts in presence of dexamethasone, ascorbic acid and Beta-glycerophosphite in the culture medium and chondroblasts in presence of insulin, transferrin, proline and sodium

Table1. Adult stem cells and their potential to differentiate into various tissues (2)

Cell Type	Cells Produced
Hematopoietic stem cells	Bone marrow and blood lymphohematopoietic cells
Mesenchymal stem cells	Bone, cartilage, tendon, adipose tissue, muscle,marrow stroma, neural cells
Hepatic stem cells	Hepatocytes, ductular cells
Neuronal stem cells	Neurons, astrocytes, oligodendro-cytes
Pancreatic stem cells	Beta cells
Skeletal-muscle stem cells	Skeletal- muscle fibers
Keratinocytes stem cells	Epidermis and hair follicles
Epithelial stem cells	Lungs, Intestine mucous and ciliated cells, type I and type II peumocytes, enterocytes, goblet cells, enteroendocrine cells.

From *Postgraduate Deptts. of Pharmacology &Therapeutics,† Pathology & **General Medicine Govt. Medical College, Jammu.
Correspondece to: Dr. Rashmi Sharma, Senior Demonstrator PG Deptt. of Pharmacology &Therapeutics, Govt. Medical College, Jammu.

pyruvate (3). 5-azacytidine, a demethylating agent of DNA can be used to induce stem cells to differentitate into various directions through the random activation of transcription factors (3). Another method is to infuse stem cells directly into the target organ to cause tissue regeneration. Local environment in the tissue "niche" generated by paracrine cytokines, growth factors, tissue-specific cell adhesion factors and extracellular matrix is responsible for induction of stem cells to differentiate into specific tissue (3). Adult stem cells have advantage of collection from bone marrow without organ loss, HLA-compatible transplantation due to availability of bone marrow bank system, lack of ethical issues related to embryonic stem cells, no post transplantation rejection and no need for immunosuppressive drug therapy (if bone marrow of the same patient is used) (3). However, small number of adult stem cells (one in several hundred thousand marrow cells) and difficulty in induction of adult stem cells to differentiate into specific tissue are the major limitations in the success of regenerative medicine using adult stem cells (3). Moreover, target cells obtained by using stem cells should possess a form consistent with the purpose when transplanted into patient's body e.g vascular smooth muscle cells should take form of a blood vessel. Thus, the cells should be placed on the scaffold (made up of high-molecular weight compounds that can dissolve slowly in the body) and incubated to achieve the form of blood vessel (3).

Routes of Cell Administration (1,4)

Selection of appropriate route of cell administration to the damaged organ is an essential prerequisite for the success of regenerative medicine. Cell delivery by intra-coronary catheterization technique by Maulana Azad Medical College, New Delhi has enabled them to obtain US patent for a technique which enables the regeneration of damaged organ and tissues (5). Beyond doubts regenerative medicine is expected to play a leading role in 21st century medicine and represents a novel therapeutic approach. However, the integration of studies from various scientific fields like molecular biology, developmental biology, embryology, anatomy, tissue engineering and material science seems necessary for success in this field and make it therapeutic possibility.

References

1. Perin EC, Geng Y J, Willerson J T. Adult stem cell therapy in perspective. *Circulation* 2003; 107: 935-38.
2. Medical progress: Adult stem cells for tissue repair- A new therapeutic concept. *N Engl J Med* 2003; 349: 570-82.
3. Fukuda K. Stem cell transplantation as a mode of regenerative medicine. *JMAJ* 2003; J46(8): 333-38.
4. Strauer B E, Kornowski R. Stem cell therapy in perspective. *Circulation* 2003; 107: 929-34.
5. Matapurkar B C, India, US international patent no.6227202, Assignee: Maulana Azad Medical Colledge,8th May 2001 with effect from 1996 (*available at web site usp. to gov*).