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Review Article

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STEM CELLS – AN OVERVIEW

***R. Vimalavathini**

Assistant Professor, Department of Pharmacology College of Pharmacy MTPG & RIHS Puducherry.

***Corresponding Author: R. Vimalavathini**

Assistant Professor, Department of Pharmacology College of Pharmacy MTPG & RIHS Puducherry.

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ABSTRACT

Stem cell therapy has undergone profound advancement in field of reparative medicine. Stem cells exhibit properties of self-renewal and have the potency to differentiate into wide range of adult cells. They have opened new avenues of treatment of conditions which were otherwise considered incurable. However it is still uncertain what kind of stem cells would be an ideal source for which ailment. This review focuses on the various types of stem cells and their clinical uses.

KEYWORDS: Stem cells, transplantation, clinical trials.

INTRODUCTION

Stem cells by virtue of self-renewal and differential plasticity have carved a niche for itself in modern therapeutics. In addition to therapeutic use it helps to gain insight into molecular basis of health and disease and screening of potential drugs. Different therapeutic strategies are considered when using stem cells. The first is stimulation of endogenous stem cells to induce self-repair of damaged tissues or organs. The second alternative is direct administration of stem cells so that they differentiate at the damaged or non-functional tissue sites.[1,2] They may be derived from patients own body cells (autologus), or from related or completely unrelated donors (allogenic), or from different species (xenogenic). While autologous transplants are safe allogenic transplants generally need continual immunosuppression to prevent rejection. This article focuses on types of stem cells and its clinical application.

Placental stem cell

The umbilical cord and placenta are generally discarded after birth and harvesting stem cells from them is pain and risk free for mother and child. They are safe and are less immunogenic. However the number of blood stem cells in the placenta is limited, usually only children can benefit from this type of donation and receive transplantation with a matching cord. Placental stem cells are used to cure chronic blood-related disorders such as sickle cell disease, thalasemia, and leukaemia.[3]

Umbilical cord stem cell

Cord blood obtained from new born umbilical cord is a rich source of stem cells. They exhibit low immunogenicity but has limited number of stem cells sufficient to treat children. With the advent of cord blood stem cells bank they have become a safe and feasible treatment option for allogeneic transplantation. Human umbilical cord blood cells are used to treat different haematological and genetic diseases, including lymphoid and myeloid leukaemia, Fanconi anaemia, aplastic anaemia, Hunter syndrome, Wiskott-Aldrich syndrome and thalassemia. It is being evaluated in a large number of trials for diabetes, acute liver failure, paraplegia, ataxia, multiple sclerosis, neuroblastoma, cerebral palsy, amyotrophic lateral sclerosis, multiple system atrophy, motor neuron disease, spinal cord injury and Alzheimer's disease.[4,5] Pre-clinical study proved cord blood stem cells migrated and engrafted into the cochlea of the deaf mice and holds promising hope for clinical trial in autologous infusions for childhood hearing damage. 5 Umbilical cords stem cells have also become a viable source for cartilage engineering.[6]

Embryonic stem cells

Embryonic stem cells are derived either from excess fertilised eggs or therapeutic cloning. Embryonic stem cells are pluripotent, easy to isolate, maintain diploid number of chromosomes, lacks the G1 checkpoint in the cell cycle and do not show X inactivation. The disadvantage includes immune rejection, tendency to induce tumours and ethical issues. They are used to study the specific signals and differentiation steps required in embryogenesis and tissue development and differentiation. Liable to genetic manipulation they are ideal cells for gene therapy.[7]

Adult stem cells

Adult stem cells are multi-potent and have less ethical issues. They occur in most tissues of adult and are most clinically used stem cells in clinical medicine. But their identification and isolation is difficult and their growth and differentiation in cultures are inadequate for

transplantation. In addition, they show telomere shortening and may carry the genetic abnormalities of the donor.[1]

Types of adult stem cell

1. Hematopoietic stem cells

They are obtained from bone marrow, peripheral blood, and cord blood. They are used to clinically treat multiple myeloma, non- currently evaluated in clinical trials for HIV and solid tumour treatment. 4 High doses Hodgkin's lymphoma, Hodgkin's lymphoma, β-thalassemia and sickle cell anaemia. They are being of immunosuppressant, followed by hematopoietic stem cell transplantation, have become an alternative treatment for many diseases involving the immune system such as multiple sclerosis, systemic sclerosis, rheumatoid arthritis, juvenile idiopathic arthritis, systemic lupus erythematous.[2]

2. Mesenchymal stem cells

They are derived mainly from bone marrow, other sources including peripheral blood, adipose tissue, umbilical cord blood, synovial membranes and deciduous teeth. They regulate haematopoiesis, protect and repair tissues and regulate immune reactions. Also they exhibit easy in vitro isolation and expansion and homing capacity with low immunogenicity profile. Hence these cells are also viable candidates for drug and gene delivery.[8] Diseases treated by mesenchymal stem cells include haematological diseases, autoimmune diseases, graft versus host disease, diabetes mellitus, liver diseases, kidney diseases, lung diseases, cardiovascular diseases, bone and cartilage diseases, neurological diseases and Crohn's disease.[9]

3. Adipose-derived stem cells

Adipose-derived stem cells are abundant and waste product of cosmetic liposuction. They display anti-inflammatory, anti-apoptotic, low immunogenic potential and immuno-modulatory properties that are involved in angiogenesis, healing and tissue repair processes.[1,10] Preclinical studies reveal their regenerative potential in bone, and joint cartilage, myocardial infarction, stroke and graft versus host disease. Autologous adipose-derived stem cells are being used for soft tissue engineering namely breast augmentation, for treating fistula in patients with Crohn's disease and radiotherapy-induced chronic ulcers and skin ulcer.[4]

4. Neural Stem Cells

Neural stem cells are adult stem cells located in the dentate fascia of hippocampus and the sub-ventricular area of lateral ventricles.[1] They can be sourced from foetal, neonatal or adult brain and can self-renew and differentiate to neurons, astrocytes and oligodendrocytes. Presently neurons and glial cells have successfully been generated from embryonic stem cells and mesenchymal stem cells also. Neural stem cells have entered clinical trials for amyotrophic lateral sclerosis, stroke, spinal cord injury, lysosomal storage diseases, Pelizaeus-Merzbacher disease, Lou Gehrig's disease, Parkinson[11] and Alzheimer diseases. Neural stem cells are also entering clinical trials for targeted drug therapy using 5-Fluorocytosine for the destruction of inoperable gliobastoma.[4,12]

5. Muscle Stem Cells

Regeneration of skeletal muscle during injury depends on satellite cells and side populations cells. However transplant trials of satellite cells in patients with muscular dystrophy showed minimal clinical benefits. Also isolation of these satellite cells was difficult because they are mainly found in core muscles like the diaphragm.[4] Side population cells which were easy to isolate and had homing capacity to muscles when assessed in clinical trials exhibited short term muscle regeneration ability.[4,13]

6. Liver Stem Cells

Liver stem cells consist of oval cells obtained from adult liver and hepatoblasts obtained from foetal liver. They are present in low quantity making their isolation and expansion tough. Nevertheless the potential to derive hepatic cells from non-hepatic tissues such as bone marrow, umbilical cord blood or adipose tissue has been extensively explored. Annex stem cells are easily accessible cells derived from human placental tissue, umbilical cord and cord blood and amniotic fluid showed potential to differentiate to hepatocytes in pre-clinical studies. Being pluripotent they exhibit higher differentiation and proliferation potential when compared to adult stem cells. Also they do not form teratomas in humans. Primary hepatocyte transplantation has been used for treatment of several diseases in humans, including familial hypercholesterolemia, Crigler-Najjar syndrome, urea cycle defects, acute liver failure, cirrhosis, hepatitis and liver cancer.[14]

7. Pancreatic Stem Cells

In case of type 1 diabetes mellitus functional restoration of existing β-cells, transplantation of stem cells or stem cell-derived β-like cells might provide new opportunities for treatment. Pancreatic duct cells, adult exocrine pancreatic cells were found to possess the ability to form new islets with β-like cells in vitro. Stem cells from the spleen and adult human liver cells have been demonstrated plasticity to islet cells and were able to restore normoglycemia in pre-clinical studies.[2,15]

8. Corneal Limbal Stem Cells

The limbus is the stem cell of the corneal epithelium. Corneal epithelial stem cell therapy is a hopeful option for visual disability resulting from alkali injury, Stevens–Johnson syndrome, ocular pemphigoid, keratoconjunctivitis and iatrogenic causes.[5] Both fresh and cultivated limbal tissues have been used clinically. Since collection of fresh limbal tissue is invasive cultivated limbal epithelial transplantation is widely used. Human embryonic stem cells derived retinal pigment epithelium has been used to treat age-related

macular degeneration and Stargardt's macular dystrophy. Alternatively research using periocular adipose tissue as a potential source of adult regenerative cells is being performed.[4]

9. Induced Pluripotent Stem Cells

Induced pluripotent stem cells are cells artificially reprogramed to differentiate into cells of all three germ layers. It permits safe transplantation of organ-tissue-specific adult stem cells with no immune rejection or ethical issues. Highly encouraging results have been achieved with them in lateral amyotrophic sclerosis, muscular dystrophy, Parkinson, Huntington disease, diabetes mellitus, Down syndrome, spinal muscular atrophy, haemophilia. It is used for screening drugs and toxins. However the use of viral vectors for induction can lead to tumor formation and hence their application is still limited.[1]

CONCLUSION

Stem cells manifest features that are attractive for reparative therapy. However characteristic complications such as infection, carcinogenicity, immune deficiency and mortality have limited its use. Monitoring and optimization of clinical protocols ultimately lead to safe and effective treatments.

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