

Current and future prospects of stem cells in dermatology

Ghazala Butt

Dermatology Department, King Edward Medical University/Mayo Hospital, Lahore

In this era of life there is hardly any field of medicine that is untouched by the revolution of stem cells, so is the field of dermatology in which stem cells may prove to be a new armamentarium in treating different chronic and disabling skin diseases.

Stem cells are undifferentiated biological cells that have the self-renewal potential and they possess the ability to differentiate into specialized cells under appropriate conditions. New and promising stem cells based therapies are gaining exceptional attention for different indications in skin diseases.

Broadly stem cells are classified into embryonic and adult stem cells. Stem cells can be isolated from blood, bone marrow (BM), umbilical cord and adipose tissue etc. Stem cells in the skin reside in specialized areas with specific microenvironment. These areas are known as niches, which keep signalling stem cells and also provide framework for the stem cells. In human skin five different niches have been identified in basal layer of the epidermis, bulge region of the hair follicle, in the dermis, in dermal papillae and in the base of sebaceous glands.¹

Mesenchymal stem cells (MSCs) are stem cells

that are multipotent and can differentiate into different cell types. There is another category called induced pluripotent stem cells (iPSCs). iPSCs are developed through genetic manipulation of differentiated cells.

Mesenchymal stem cells (MSCs) have been obtained from several tissues, including adipose tissue, skin, umbilical cord blood, placenta, peripheral blood, endometrium, dental pulp, dermis, amniotic fluid, as well as from tumors.² Mesenchymal stem cells have been used in many inflammatory and autoimmune skin diseases particularly those which are not responding to conventional therapies. These include severe generalized systemic sclerosis,³ systemic lupus erythematosus,⁴ chronic graft-versus-host disease with cutaneous manifestations.⁵

Immunomodulatory and antiinflammatory effects of MSCs have also been observed in treating different eczemas like atopic dermatitis, allergic dermatitis etc.³ In patients with severe plaque psoriasis, bone marrow stem cells transplantation both autologous and allogenic, showed improvement clinically.³

MSCs possess wide differentiating potential and they not only generate cells of mesodermal origin e.g. adipocytes, chondrocytes, osteocytes etc. but also of endodermal (e.g. hepatocytes) and of ectodermal origin such as melanocytes.⁶ One of the most important function of MSCs is to support repair of damaged tissues, so when

Address for correspondence

Dr. Ghazala Butt, Assistant Professor
Dermatology Department, Unit I,
King Edward Medical University/
Mayo Hospital, Lahore
Email: ghazalakashmiri@gmail.com

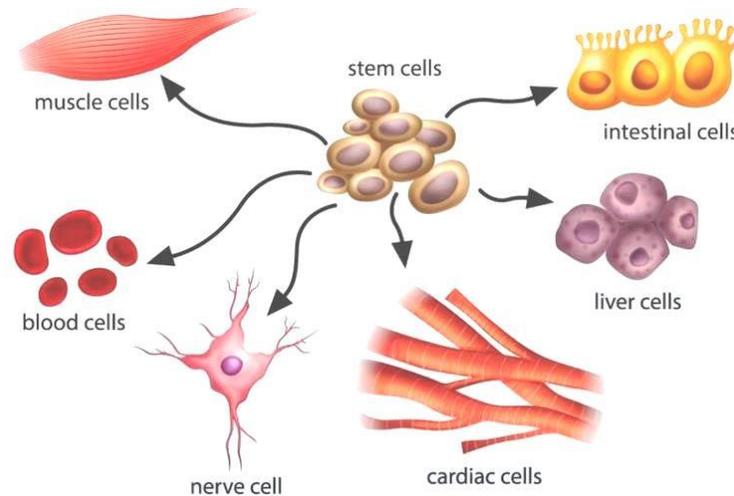


Figure 1 Human stem cell applications.

inflammation occurs, MSCs migrate towards the site of injury, differentiate into specialized cells mainly fibroblasts and release certain cytokines, chemokines and growth factors and help in regeneration of injured tissue. MSCs also modify tissue healing through proangiogenic, antifibrotic, and antiapoptotic pathways.³

The BM-MSCs are similar but somewhat different to mesenchymal stromal cells isolated from other tissues. They show plasticity with their ability to differentiate into tissues of mesodermal, endodermal, and ectodermal origin, including skin.^{7,8}

Bone marrow transplantation as one of kind of stem cells therapy initially was used in conditions like leukemias, lymphomas, other hemoglobinopathies etc. Now in many skin diseases bone marrow is used as a source of fibroblast-like cells in the dermis and their number increases in the skin after wounds.^{9,10}

Adult adipose SCs obtained via lipoaspiration, are one of the sources for iPSC.¹¹ The successful *in vitro* differentiation of both, mouse and human iPSCs into keratinocytes,¹² melanocytes,¹³ and fibroblasts¹⁴ thus opens the possibility of extending iPSC technology into

the field of dermatology. iPSC-derived fibroblasts offer a novel source of autologous cells for dermal regeneration, as fibroblasts play an important role in maintaining tissue homeostasis and wound repair by secreting certain growth factors and by making extracellular membrane proteins.¹⁵

iPSC-based therapies have also been used for inherited skin diseases e.g. junctional epidermolysis bullosa (JEB), EB simplex (EBS), ectodermal dysplasias, epidermolytic hyperkeratosis, ectrodactyly and dyskeratosis congenita etc.^{16,17} Skin biopsy cells from these patients are converted to iPSC via genetic reprogramming, genetic aberration are corrected by homologous recombination, these specific iPSC are then differentiated into specific cell type followed by transplantation into the affected patient as an autograft. Corrected iPSCs have the potential to pose an unlimited source of autologous cells of both epidermal and mesenchymal lineages for the treatment of EB and other hereditary skin diseases.¹⁸

The outer root sheath (ORS) of the hair follicle is a rich source of a type of hair follicle stem cells (HFSCs) called the melanocytes stem cells (McSCs). These HFSCs have a vast, unexplored

potential in the treatment of vitiligo as initial repigmentation often occurs around the hair follicles.

Adipose tissue-derived mesenchymal stem cells have also been used in androgenetic alopecia. Different studies are being carried out in different areas of the world including Pakistan and it is thought to be a new armamentarium in the field of regenerative medicine.

Aging is a process in which different factors play a role in causing functional and structural damage with impaired signalling. Stem cells of the aged people do not function normally. There are different underlying mechanisms, which are responsible for impaired function of stem cells in aged people, and these include defaults in DNA repair, accumulation of reactive oxygen species, dysfunctions of mitochondria and epigenetic alterations. All these are responsible for impaired stem cells functions.¹⁹ It has been found that preservation and rejuvenation of SC niches can reverse some phenotypic manifestations of aging.²⁰

Regarding safety profile, no considerable adverse events have been reported in relation to mesenchymal stem cells-based therapies, they seem to be safe and applicable for the treatment of severe, refractory immune-related diseases and other chronic skin diseases especially for severely affected patients' refractory to current first-line medications.²¹

Studies on stem cells-based therapies for different dermatological conditions are continuously increasing and application of these therapies for treating various skin diseases is also exponentially increasing. Further research is required to see the efficacy and safety of the promising stem cell-based therapies in the treatment of inherited and acquired disorders of skin.

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