Pluripotent stem cell technology: a promising remedy for hypopigmentation disorders

Abstract

Pigment cells - epidermal melanocytes play physiological role in providing defense against harmful UV rays. Defect or deficiency of melanocytes and/or melanocyte stem cells can lead to pigmentation disorder such as vitiligo. The vitiligo forms white patches on the skin on the body. It is an autoimmune disease because the pigment inducing cells are damaged. Amongst its therapies, are UV light, cosmetic cover-up and corticosteroid local application. Human epidermis has been produced in vitro from mature epidermal stem cells of donors to provide the cell remedy. Source of pluripotent stem cells, either of embryonic origin or genetic reprogramming offers a substitute for epidermal cell treatment as these cells are immortal and pluripotent - theoretically capable of providing any number of cells of any desired phenotype. Keratinocytes and melanocytes resulting from pluripotent stem cells can be used for pathological modelling of genodermatoses allowing recognition of new disease-specific pharmacological treatment. We discuss the current approaches and imminent scenario of stem cells in hypopigmentation.

Keywords: stem cell, melanocytes, vitiligo, melanin, pigmentation

Reconstruction of pigmented system using stem cell technology

Melanin production gives the skin its characteristic pigmentation and increases during sun exposure to protect the cells from the DNA-damaging effects of UV light. Melanocytes have been generated from human embryonic stem cells. The approach involves growing the stem cells in a carefully controlled manner while subjecting them to the specific chemical signals that drive the formation of melanocytes in a developing embryo. It has not been possible to generate melanocytes at different stages of development including mature, fully functional and immature precursors. How melanocytes develop ad function normally, and how failure in these processes lead to diseases, is a matter of study.

The hair follicle is a constantly renewing, where 66% of the lower follicle (travel part) totally is recovered over the hair cycle, while the staying upper lasting segment is kept up. The irregular hair cycle comprises three phases of hair follicle viz. development (anagen), trailed by a relapse stage (catagen), and a resting stage (telogen). Melanocytes show up at the onset of anagen stage where they effectively multiply and separate into developed melanocytes. Throughout catagen, the melanocytes are drained from the follicles by apoptosis. Melanocytes go missing in telogen hair follicle until melanogenesis starts in the ensuing anagen stage. Given this regenerative cycle of melanogenesis, the presence of the stem cells for follicular melanocytes has been recommended over 10years.

Pluripotent stem cell technology offers a promising approach for studying human melanocyte development and disease. Timed exposure to activators of WNT, Bone morphogenetic proteins (BMP), and Endothelin 3 (EDN3) signaling triggers the sequential induction of neural crest and melanocyte precursor fates under dual-SMAD-inhibition condition. Using a SOX10::GFP human embryonic stem cell (hESC) reporter line, it was demonstrated that the temporal onset of WNT activation is critical for human neural crest induction.
Subsequent maturation of hESC-derived melanocytes yields a pure population that matches the molecular and functional properties of adult melanocytes. Melanocytes from Hermansky-Pudlak syndrome and Chediak-Higashi syndrome patient specific induced PSCs (iPSCs) reproduced the ultrastructural features of disease-associated pigmentation defects (Figure 1).

Skin stem cells reside in the stratum basal of the epidermis, sebaceous glands, and bulge area of the hair follicles. The HFSCs continuously supply new cells to the bulb during the anagen phase. The outer root sheath (ORS) of the hair follicle is a rich source of a type of HFSCs called melanocyte stem cells (MelSCs). Hair follicle melanocytes play an important role in repigmentation of vitiliginous lesion. Migration of the precursor melanocytes in the mid portion of the hair follicle, found to be MelSCs have been implicated in the re-pigmentation following both chemical and physical stimulus. Common therapeutic modalities such as tacrolimus, phototherapy and dermabrasion act through MelSCs. Newer cellular techniques have explored the use of ORS hair follicle suspension in surgical treatment of vitiligo. Advancement of melanocyte and stem cell research have identified various cytokines, growth factors and regulations involved in proliferation and differentiation of melanoblasts, which can be used for autologous in-situ melanocyte regeneration.

Figure 1 Disease-specific melanocytes that realistically recapitulate pigmentation defects can be derived from human pluripotent stem cells using a stepwise differentiation pattern.

Figure 2 Shows that after loss of epidermal melanocytes by injuring or UV light (a) MelSCs from the stem cells area of the proximal hair follicle epithelium move into the recovering epidermis to multiply, hence creating new separated pigment producing melanocytes (b).
Conclusion

Stem cells are the master cells of the human body which can divide to produce their own copies as well as other types of cells. They are found in various parts of the human body at every stage of development - from embryo to adult. Because stem cells are so versatile, they could potentially be used to repair and replace damaged human tissues. The purpose of experimental stem cell therapy offers potential benefits like slowing down or stopping further deterioration caused by the disease, or reversing the effects of the disease. The goal of therapy in vitiligo is to regenerate the damaged colour producing cells of the skin (melanocytes) and to correct the aberrant immune system. Normally in vitiligo the body’s own immune system attacks and damages the colour producing cells of the skin, hence it is an autoimmune disease. Mesenchymal stem cells have been found to have immunomodulatory and immunosuppressive properties. Administration of mesenchymal stem cells in vitiligo prevents further damage to melanocytes and reduces disease progression. Knowledge of the melanocyte reservoir is of importance to understand the mechanism of repigmentation, which is crucial for designing newer strategies for vitiligo therapy. The possibility of skin areas without hair follicles where repigmentation occurs with a diffuse pattern suggests the existence of an amplified concept of the melanocyte reservoir that would include the intermolecular epidermis as well.

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Conflict of interest

The author declares no conflict of interest.

References