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Editorial

The New Age of Stem Cell Gene Therapy for Regenerative Medicine

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Editorial

Breakthrough discovery of induced pluripotent stem cells by Dr. Shinya Yamanaka and colleagues (Nobel Prize 2012) has paved the way for major progress in diverse areas of stem cell biology. In skin biology considerable evidences showed that skin stem cells are involved in the process of skin repair [1]. Several labs are currently focused on understanding cellular and molecular mechanisms that regulate skin biology such as wound healing, ageing and associated genetic diseases. One such life-threatening genetic disease called Junctional Epidermolysis Bullosa (JEB) is caused by mutations in three genes-LAMA3, LAMB3 or LAMC2-which encode the a3, β3 and c2 chains of laminin 332, that perturb the functions of laminin. Different forms of epidermolysis bullosa affect approximately 500,000 people worldwide and is associated with a grim survival of a few months or years [2]. In skin, laminin 332 is an essential component of the dermal-epidermal basement membrane. Laminin 332 can be regarded as a supramolecular bridge between the basal keratinocytes of the epidermis and the underlying dermis, which provides the skin integrity and resistance against external mechanical forces. The clinical symptoms of JEB are diminished dermal-epidermal adhesion resulting in skin blistering, skin fragility, thus impairing their quality of life and could lead to skin cancer. Unfortunately, there is no known cure for JEB and more than 40% of patients die before adolescence.

However, recent heroic work published in Nature (Hirsch et al, 2017) [3], showed that autologous transgenic keratinocyte cultures could regenerate an entire, fully functional epidermis on a seven-year-old child suffering from a devastating, life-threatening form of JEB [3]. A team of researchers in Ruhr-University, Germany analyzed a seven-year-old child who carried a homozygous acceptor splice site mutation (C1977-1G>A, IVS 14-1G>A) within intron 14 of LAMB3. This resulted in blisters all over the patient's body, particularly on limbs, back and flanks. The condition deteriorated severely six weeks before admission, owing to infection with *Staphylococcus aureus* and *Pseudomonas aeruginosa*. To begin with, they established primary keratinocyte cultures from a biopsy ($4cm^2$) taken from a non-blistering area of the patient. After transducing with retroviral vector expressing the full-length LAMB3 cDNA, $4cm^2$ biopsy was expanded to $8500cm^2$ transgenic epidermal grafts, enough to cover patient's entire denuded body surface. They detected limited number of long-lived stem cells, called as holoclones. Holoclones have the capacity to extensively self-renew *in vitro* and *in vivo* and produce progenitors that replenish terminally differentiated keratinocytes. After surgery, approximately 80% of the patient's total body surface area was restored by the transgenic epidermis. During the 21-month follow-up, the regenerated epidermis adhered firmly to the underlying dermis. Even after more than 20 epidermal renewing cycles, it did not form blisters, including areas where follow-up biopsies were taken. The patient's serum did not contain autoantibodies directed against the basement membrane zone.

In conclusion, transgenic epidermal stem cells can regenerate a fully functional epidermis virtually indistinguishable from a normal epidermis and demonstrated life-saving regeneration. A major unaddressed question is related to the mechanisms that control the balance of epidermal growth and differentiation. A better understanding of the complex signals, cellular interactions, and mechanisms of tissue regeneration may open new avenues for treatment. However, it is notable that during this time, the epithelium undergoes continual remodeling. The challenge now is to exploit this newfound knowledge to harness the natural potential of stem cells for the desired task at hand. The successful outcome of this study paves the way for gene therapy to treat other types genetic disorders and provides a blueprint that can be applied to other stem cell-mediated combined ex vivo cell and gene therapies. Numerous unresolved biological problems will occupy researchers for the coming decade, but their solutions will provide the molecular soil that will nurture new and improved clinical applications in regenerative medicine.

Conflicts of Interest

All author declare that they have no conflicts of interest concerning on this manuscript.

References

1. Gonzales KA, Fuchs E (2017) Skin and Its Regenerative Powers: An Alliance between Stem Cells and their Niche. Developmental Cell 43: 387-401.
2. Fine JD, Bruckner-Tuderman L, Eady RA, Bauer EA, Bauer JW, et al. (2014) Inherited epidermolysis bullosa: updated recommendations on diagnosis and classification. J Am Acad Dermatol 70: 1103-1126.
3. Hirsch T, Rothoeft T, Teig N, Bauer JW, Pellegrini G, et al. (2017) Re-generation of the entire human epidermis using transgenic stem cells. Nature 551: 327-332.