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Incorporating hair follicle cells in artificial skin

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The pioneering clinical-histopathological work of Bishop,[1] showing the sequential healing of wounds made in his own forearm, highlighted the pivotal role of the hair follicle in the wound healing process. However, since Bishop's outstanding work in 1945, there has been little scientific production in relation to hair and wound healing until recently, when basic researchers started to uncover the biology of the so-called hair follicle–wound healing connection.[2,3]

The hair follicle is quite a complex adnexal structure and can be considered a mini-organ, *per se*, that is composed of many different types of cells that interact together and with the surrounding microenvironment: epithelial cells, mesenchymal cells from the dermal papilla and dermal sheath, several pools of epithelial, melanocyte and mesenchymal stem cells involved in hair follicle self-regeneration and pigmentation, a rich innervation and vascularization network, smooth muscle cells and resident immunocytes (mast cells, macrophages, T cells and Langerhans cells). Each of these different cell types may contribute to the healing process initiated after human skin wounding, even though it is still very incompletely understood how they do so.

In clinical practice, chronic wounds, especially chronic venous leg ulcers, entail a huge and ever-increasing healthcare challenge because of their high prevalence and costly clinical care. The fact that around 20% of venous leg ulcers do not heal in spite of standard medical care indicates the need for better therapies. One of the therapeutic alternatives for nonhealing wounds has been the use of bioengineered skin (artificial skin) composed of keratinocytes and dermal nonfollicular fibroblasts. However, it would be ideal to develop skin substitutes that contain adnexal structures (i.e. follicular cells and eccrine glands), not only because they reproduce the physiological conditions of a healthy human skin but also because of their role in stimulating wound healing.[4]

In this issue of the *BJD* Higgins *et al.*[5] report the development, *in vitro* and *in vivo*, of a skin substitute composed of follicular dermal cells obtained from the dermal sheath and dermal papilla cells of human hair follicles. In comparison with the traditional skin substitutes made from nonfollicular origin, the dermal sheath and dermal papilla cells that formed the artificial dermis showed a higher α-smooth muscle actin expression (which correlates to the cellular contractile capacity), and formed a thicker basal membrane (more intense type IV collagen expression). This study adds to previous evidence indicating that hair follicle-derived dermal cells improve bilayer skin equivalent performance in wound models[6] and complements work by other authors.[7]

Now the challenge is to perform translational work that evaluates the real efficacy of these types of skin substitutes in clinical practice.[8] The use of hair follicle punch grafts as a therapeutic tool to stimulate wound healing in chronic ulcers has been recently evaluated,[9] and compares favourably with the traditional method of split-thickness skin grafts in that follicular grafts may improve elasticity and offer a better cosmetic outcome.[10] The strategy proposed by Higgins *et al.*[5] will inspire researchers and clinicians interested in wound healing to exploit the human hair follicle and its rich cell reservoirs much more systematically for future regenerative medical purposes, which extend well beyond the skin.[11]

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Conflicts of interest

None to declare.

Mediteknia Dermatology Clinic, and Research Associate of the Medical Pathology Group, Instituto de Investigación Biosanitaria, Universidad de Las Palmas de Gran Canaria, Gran Canaria, Canary Islands, Spain
E-mail: fjimenez@clinicadelpelo.com

F. JIMENEZ

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