From Fat to Skin: A Novel Approach

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Abstract

Background: The ideal aim of skin regeneration is to find a means to replace or regenerate this complex organ with normal appearance and with complete functionality. This process can be done in-vivo or in vitro and may require cells, natural or synthetic cell-supporting scaffold materials and bioactive molecules among other components. Unfortunately, current treatments are not capable of inducing permanent satisfying replacements. Human adipose-derived stem cells (ASC) have been shown to differentiate in-vitro into both mesenchymal lineages (adipogenesis, chondrogenesis, osteogenesis, fibroblasts) and non-mesenchymal lineages (endothelium, smooth muscle, cardiomyocytes, hepatocytes and neuron-like cells), confirming their transdifferentiation ability. This versatile differentiation potential and their easy availability, places adipose-derived stem cells at the advancing front of stem cell-based therapies. We hypothesized that ASC have the capacity to transdifferentiate into keratinocyte-like cells and furthermore be able to engineer a stratified epidermis.

Methods and Results: ASC were successfully isolated from patients undergoing liposuction using Fluorescent-activated cell sorting technique (FACS). Pure populations of ASC were either co-cultured with human keratinocytes or with keratinocyte conditioned media. After a 14-day incubation period, ASC developed a polygonal cobblestone shape characteristic of human keratinocytes. Western blot and q-PCR analysis showed the presence of specific keratinocyte markers including Cytokeratin-5, Involucrin, Filaggrin and Stratifin in these keratinocyte-like cells (KLC); these markers were absent in undifferentiated ASC. To further evaluate if KLC were capable of stratification akin to human keratinocytes, ASC were seeded on top of human decellularized dermis and cultured in the presence of Epidermal Growth Factor (EGF) and 1.8mM Ca2+ concentrations. Histological analysis demonstrated a stratified structure similar to that observed in normal skin. Furthermore, immunohistochemical analysis revealed the presence of keratinocyte markers such as Involucrin, Cytokeratin-5 and Cytokeratin-10.

Conclusion: In conclusion this study demonstrates for the first time that ASC have the capacity to transdifferentiate into KLC and also to produce a stratified epidermis. This study suggests that adipose tissue is potentially a readily available and accessible source of keratinocyte-like cells, particularly for severe wounds encompassing large surface areas of the body and requiring prompt epithelialization.

References

Disclosure/Financial Support
This research was supported by the Division of Plastic Surgery at Northwestern University. Dr. Chavez-Munoz holds a Post-Doctoral Fellowship Award from the Canadian Institutes of Health Research (CIHR).
None of the authors has a financial interest in any of the products, devices, or drugs mentioned in this manuscript.