Transplanting human induced pluripotent stem cell derived keratinocytes speeds deep second-degree burn wound healing

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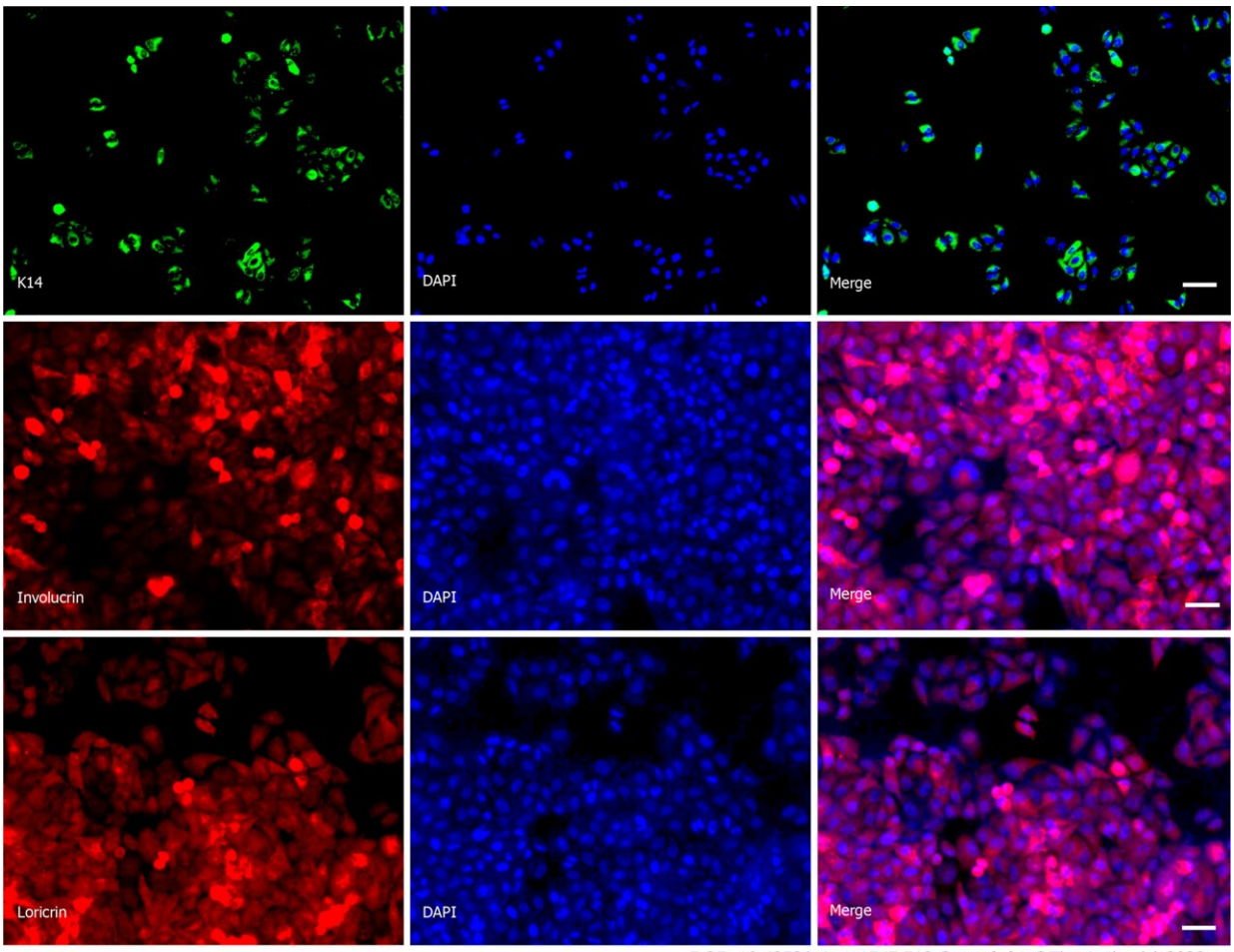

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Human induced pluripotent stem cells successfully differentiated into keratinocyte. Retinoic acid (RA) and BMP-4 were used to induce differentiation of hiPSCs into keratinocyte. The images as immunofluorescence staining of

keratinocyte marker proteins K14, involucrin and loricrin at 14 d of induced differentiation, scale bar: 25 μm. Credit: *World Journal of Stem Cells* (2023). DOI: 10.4252/wjsc.v15.i7.713

Current evidence shows that human induced pluripotent stem cells (hiPSCs) can effectively differentiate into keratinocytes (KCs), but its effect on skin burn healing has not been reported.

Recently, a research team set out to observe the effects of hiPSCs-derived KCs transplantation on skin burn healing in mice and to preliminarily reveal the underlying mechanisms.

The research is published in the *World Journal of Stem Cells*.

An analysis of differentially expressed genes in burn wounds based on GEO datasets GSE140926, and GSE27186 was established. A differentiation medium containing retinoic acid and bone morphogenetic protein 4 was applied to induce hiPSCs to differentiate into KCs. The expression of KCs marker proteins was detected using immunofluorescence staining. A model of a C57BL/6 mouse with deep cutaneous second-degree burn was created, and then phosphate buffered saline (PBS), hiPSCs-KCs, or hiPSCs-KCs with knockdown of COL7A1 were injected around the wound surface.

The wound healing, re-epithelialization, engraftment of hiPSCs-KCs into wounds, proinflammatory factor level, and the NF-κB pathway proteins were assessed by hematoxylin-eosin staining, carboxifluorescein diacetate succinimidyl ester (CFSE) fluorescence staining, enzyme linked immunosorbent assay, and Western blotting on days 3, 7, and 14 after the injection, respectively. Moreover, the effects of COL7A1 knockdown on the proliferation and migration of hiPSCs-KCs were

confirmed by immunohistochemistry, EdU, Transwell, and damage repair assays.

The researchers found that hiPSCs-KCs could express the hallmark proteins of KCs. COL7A1 was down-regulated in burn wound tissues and highly expressed in hiPSCs-KCs. Transplantation of hiPSCs-KCs into mice with burn wounds resulted in a significant decrease in wound area, an increase in wound re-epithelialization, a decrease in proinflammatory factors content, and an inhibition of NF-κB pathway activation compared to the PBS group. The in vitro assay showed that COL7A1 knockdown could rescue the inhibition of hiPSCs-KCs proliferation and migration, providing further evidence that COL7A1 speeds up burn wound healing by limiting cell proliferation and migration.

More information: Li-Jun Wu et al, Transplantation of human induced pluripotent stem cell derived keratinocytes accelerates deep second-degree burn wound healing, *World Journal of Stem Cells* (2023). DOI: 10.4252/wjsc.v15.i7.713

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