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Alternative therapy of corneal endothelial dysfunction using skin-derived precursors

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Purpose: Explore the feasibility of differentiating skin stem cells into corneal endothelial cell-like cells (CEC-like cells) to cure corneal endothelial dysfunction.

Methods: Human skin stem cells were cocultured with corneal endothelial cells (CECs) through transwell coculture system to obtain CEC-like cells. CEC-like cells were identified by immunofluorescence, real time RT-PCR, western blotting. Dil-labeled CEC-like cells were transplanted into the rabbit's corneal endothelial dysfunction models to detect the cell function *in vivo*. Histological examination of corneas was performed to detect CEC-like cells attachment.

Results: CEC-like cells could be derived from skin stem cells and they had similar morphology and characteristic to CECs. They expressed major markers of CECs, such as Na+/K+ ATPase alpha 1, zonula occludens-1 and other functional markers. The expression levels of differentiation transcription factors FoxC1 and Pitx2 were also significantly upregulated compared with skin stem cells. CEC-like cells were transplanted into the rabbit's corneal endothelial dysfunction models, their corneal transparency and the thickness recovered while the control groups remain opaque. Histological examination showed Dil-labed CEC-like cells covered nearly full Descemet's membrane and expressed Na+/K+ ATPase in CEC-like cells injected group while almost no cells were detected on Descemet's membranes in control group.

Conclusions: This protocol enables efficient production of CEC-like cells from skin stem cells and these CEC-like cells have therapeutic effect in corneal endothelial dysfunction model. The renewable cell source and novel deriving method may lead to potential applications in cell replacement therapy for corneal endothelial dysfunction.

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