Healthcare Innovations
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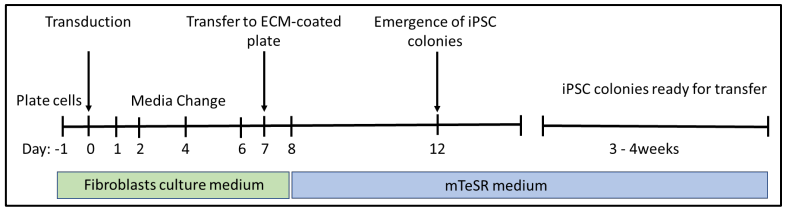
# Skin Organoid: An Advanced Tool for Human Skin Development and Reconstructive Surgery

*Abbas Shafiee [1, 2, 3], Jane Sun [2], Felicia Phua [2], Imaan Ahmed [2], Jason Brown [1, 3], Kiarash Khosrotehrani [1, 2]*

*1- Herston Biofabrication Institute, Metro North Hospital and Health Service, Brisbane, Australia; 2-UQ Diamantina Institute, Translational Research Institute, The University of Queensland, Brisbane, Australia;*
*3- Royal Brisbane and Women's Hospital, Metro North Hospital and Health Service, Brisbane, Australia.*

**Introduction**: The application of stem cells to derive functional skin for the purposes of disease modelling, study developmental pathways or regenerative medicine is a research area of great interest. Recent studies showed success in generating some skin cells/layers from human induced pluripotent stem cells (hiPSCs), but creating skin containing functional appendages, such as hair follicles and sweat glands, is still an unmet challenge in the field.

**Aim**: We aim to develop a protocol for generating skin organoids from hiPSCs.



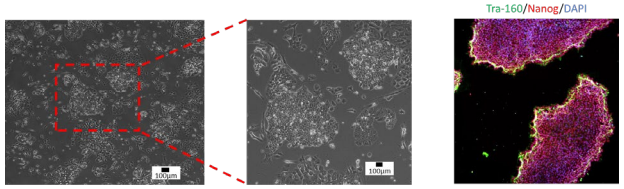




***Figure 1**: Generation of hiPSCs from human skin fibroblast cells using CytoTune 2.0 sendai reprogramming kit (Thermo Fisher). hiPSCs colonies express telomerase activity (Tra-160) and Nanog.*

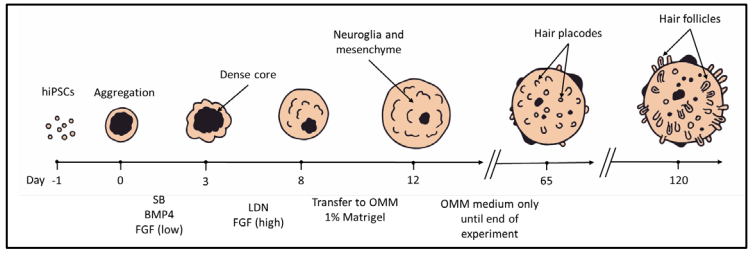



***Figure 2** : Overview of skin organoid protocol.*

**Results**: By modulating the FGF/BMP pathway in hiPSC, we could generate skin organoids that recapitulate the structure of human skin.

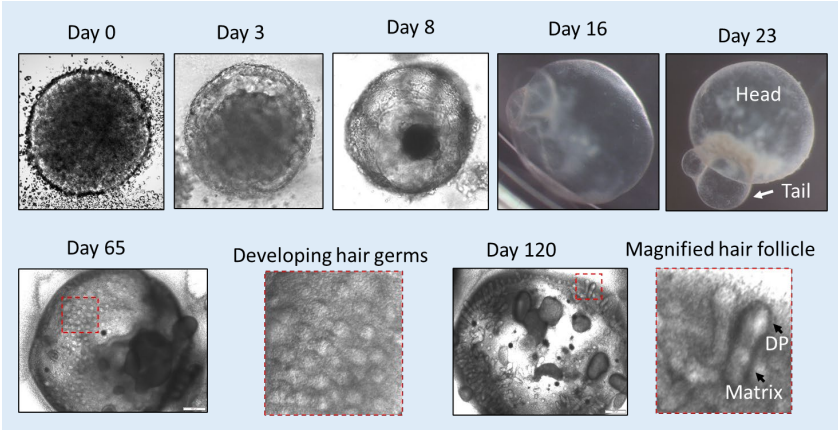



***Figure 3**: Differentiation of hiPSCs into skin organoids. By day 65 hair germs were developed and generated pigmented hair follicles by day 120 (**Figure 3**). DP: dermal papilla.*

**Results**: Immunostaining analyses demonstrated the expression of skin key markers (Keratin 14, 15 and 17, Loricrin), neural (Tuj1) and dermal papilla (Sox2).

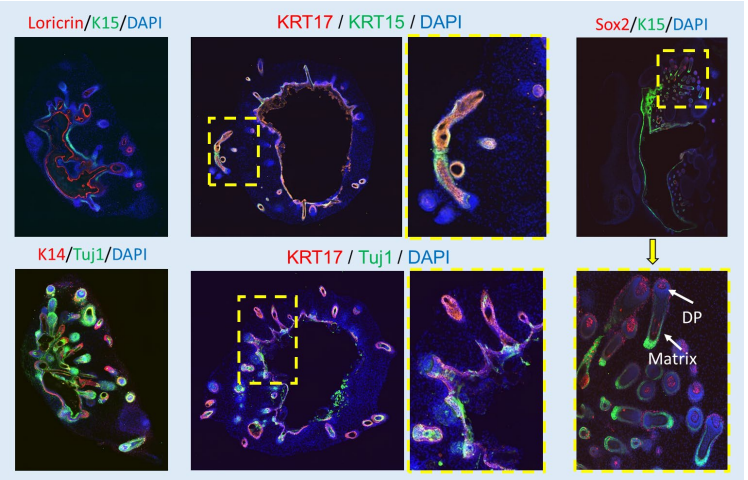



***Figure 4**: Modulation of the transforming growth factor β (TGFβ) and fibroblast growth factor (FGF) signaling pathways leads to the development of hair-bearing skin.*

**Conclusions**: Fully functional human skin organs with complete appendages were generated from human pluripotent stem cells.

**Clinical impact**: The human skin organoids generated in the current study could be utilized as an important platform to study human skin development, disease modelling and in reconstructive surgeries.