**Supplementary Table 2**

Models of skin disorders using differentiation of human iPSCs.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Cell of origin** | **Disease** | **Reprogramming approach** | **Cell outcome** | **Proteins expressed** | **Research outcome** | **Reference (s)** |
| Patient-derived human iPSCs from peripheral blood mononuclear cells  | Psoriasis (PsO) | Sendai virus transduction | KCsa derived from PsO-iPSCs  | P63, K1, K14, K18, K19, LOR, IVL, LAM | These findings suggest that the pathogenesis of psoriasis is likely influenced by the genetic alterations of KCs. | (Ali et al., 2020) |
| Patient-derived human iPSCs from primary fibroblasts | Recessive dystrophic epidermolysis bullosa (RDEB) | Retroviral transduction | KCs derived from RDEB-iPSCs; 3D skin equivalents | p63, DSG3, K1, K5, K14, COL7A1, Laminin 5, Loricrin | Functional KC differentiation for effective iPSC-based therapy for epidermal diseases.  | (Itoh et al., 2011) |
| Patient-derived human iPSCs from primary fibroblasts COL7A1 gene-corrected by CRISPR-Cas9 | Recessive dystrophic epidermolysis bullosa (RDEB) | Integration-free episomal vector | 3D human skin equivalents consisting of KCs and fibroblasts | K14, K10, loricrin | Demonstration of the feasibility of an iPSC-based gene correction strategy for the treatment of patients with RDEB (engraftment on mice) | (Jacków et al., 2019) |
| Patient-derived human iPSCs | Congenital ichthyosis | Lentiviral transduction | Basal KC-like cells | p63, K5, K14, K18, K10, IVL | Basal KC differentiation from human iPSCs established from ichthyosis patients  | (Lima Cunha et al., 2021) |
| Patient-derived human iPSCs from peripheral blood mononuclear cells  | Scleroderma (systemic fibrosis) | Sendai virus transduction | Skin organoid (dermal fibroblasts and KCs) | P63, K5, K14 | Drug screening of anti-fibrotic effect of raloxifene and bazedoxifene as potentially effective treatment of systemic sclerosis. | (Kim et al., 2022) |
| Human iPSCs | COVID-19 | - | Skin organoid (includes epidermis and dermis, cartilage and subcutaneous fat, and hair follicles) | P63, K14, K5, K10, K1, involucrin, ITGB1, DSG1, DSG2, laminin, COL4, nidogen, aggrecan, COL2A1 | SARS-CoV-2 can attack hair follicle and neurons in the skin. Potential platform for research on SARS-CoV-2 infection mechanisms and COVID-19 drug screening strategies (inflicted skin).  | (Ma et al., 2022) |
| Patient-derived human iPSCs from oral fibroblasts | Gorlin syndrome (GS) | Sendai virus transduction | KCs derived from GS-iPSCs | K14, ITGB4, p63 | GS keratinocyte model. Resistance of GS KCs to apoptosis with a remarkable increase in BCL2 caused by UV, which may contribute to basal cell carcinomas. | (Morita et al., 2021) |
| Primary cells and human iPSCs from fibroblasts | Recessive dystrophic epidermolysis bullosa (RDEB) | Sendai virus transduction | Primary fibroblasts and fibroblast-derived MSCsb (both fibroblasts COLJA1 gene-corrected with DNA cleavage followed by HDR applying an adenine base editor | - | Potential of adenine base editors to correct COLJA1 gene mutations as a promising strategy for autologous RDEB cell therapy. | (Osborn et al., 2020) |
| Patient-derived human iPSCs from primary dermal fibroblasts | Ectrodactyly, ectodermal dysplasia, and cleft lip/palate (EEC) syndrome | Lentiviral transduction | Mature KCs and corneal-epithelial development (two somatic mutations) | p63, K14, K18 | APR-246/PRIMA-1MET, a small compound, reverted corneal epithelial lineage commitment and reinstated normal p63-related signaling pathway.  | (Shalom-Feuerstein et al., 2013) |
| Patient-derived human iPSCs from primary fibroblasts(Gene edited with CRISPR-Cas9 and TALENs) | Dominant dystrophic epidermolysis bullosa (DDEB) | Integration-free episomal vector | KCs and dermal fibroblasts | p63, K14, and COL7 (KCs) | COL1, COL3, and COL7 (fibroblasts) | Knocking out of the COL7A1 mutant allele in DDEB via mutation site-specific mutagenesis NHEJ using CRISPR/Cas9 and TALENs. Differentiated KCs and fibroblasts could be potential sources of DDEB therapies. | (Shinkuma et al., 2016) |
| Patient-derived human iPSCs from amniotic fluid cells (trisomy 21 and rescued disomy 21) | Down syndrome  | Integration-free episomal vector | KCs; 3D human skin equivalents (KCs + dermal fibroblasts) | K10, K14, p63, IVL, loricrin (expressed in trisomy rescued disomy 21) | Impairment in keratinocyticdifferentiation in trisomy 21 iPSCs. In contrast, trisomy-rescued disomy 21 iPSC-derived KCs with an extended life capable of generating 3D skin with dermal fibroblast. | (Tanuma-Takahashi et al., 2021) |
| Patient-derived human iPSCs from fibroblasts(Gene edited with CRISPR-Cas9, COL7A1) | Recessive dystrophic epidermolysis bullosa (RDEB) | Sendai virus transduction | KCs, MSCs, and haematopoietic cells | K5, K14, p63 (KCs) | Corrected fibroblasts of RDEB-causing mutations as iPSC sources for KC differentiation with potential application in cell therapies.  | (Webber et al., 2016) |

a KC: keratinocyte;  b MSC: mesenchymal stem cell

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