Synopsis of Original Research Paper

Development of a method for induction of iPS cell-derived cranial dermal stem cells

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The dermal layer's structural integrity, maintained by collagen/elastin networks produced by dermal fibroblasts, is fundamental to skin youthfulness. However, the rarity of dermal stem cells and ethical challenges in obtaining facial-specific samples from healthy donors have severely constrained anti-aging research. This study bridges these gaps through an innovative integration of developmental biology and stem cell technology. Building upon recent advances in neural crest cells (NCCs) induction from iPSCs, we established a robust protocol to generate craniofacial-specific mesenchymal cells from human iPSCs via NCCs. Our xeno-free 3D induction system achieves the induction of HOX-negative (craniofacial) NCCs highly efficiently, overcoming the variability and line-dependency of conventional 2D methods. These cells faithfully recapitulate patterning of mandibular arch through EDN1-dependent mechanisms, forming spatially organized structures with distal DLX2+/DLX5+/HAND2+ domains and proximal DLX2+/DLX5-/HAND2- domains. The resulting maxillary organoids demonstrate physiologically relevant features including intramembranous ossification and functional SOST+ osteocyte networks by day 38.

This research creates new opportunities to develop targeted anti-aging interventions. The cells serve as ideal substrates for testing next-generation compounds, from small-molecule to biologics addressing fibroblast senescence. Furthermore, the platform's adaptability allows future incorporation of epithelial components to model complete skin organoids, potentially revolutionizing both cosmetic safety testing and regenerative therapies for craniofacial reconstruction.