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Human Palatal Connective Tissue Grafts: Molecular Profiles and Cell-Cell Interactions

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Objectives We have recently evaluated the molecular profiles of subepithelial connective tissue grafts (CTGs) obtained at different locations and depths in the human palate. Sixty-four grafts were assigned to four groups: anterior deep (AD), anterior superficial (AS), posterior deep (PD), and posterior superficial (PS). The data suggested strong impact of A-CTGs on epithelial cell behavior. Increased growth factor gene expression and significantly activated Erk and Akt signaling in primary human palatal fibroblasts (HPFs) derived from A-CTGs implied their involvement in cell survival, proliferation, and motility. In a follow-up study, we aim to investigate the interactions of primary HPFs, obtained from different CTG types, with oral epithelial cells.
Methods Indirect and direct co-culture systems of oral fibroblast and epithelial cells were established and cell-cell interactions were explored by using cell and molecular biology techniques.
Results Migration of primary epithelial cells as well as two immortalized epithelial cell lines was strongly ($p < 0.001$) potentiated by AD-, AS-, and PS-HPFs. In an indirect co-culture model, using transwells that allow exchange of nutrients between the two cell types but no direct contact, A-HPFs triggered prominent epithelial cell proliferation compared to P-HPFs. This finding was confirmed by experiments, in which epithelial cells were cultured in the presence of conditioned media harvested from A-HPFs. BrdU incorporation into newly-synthesized DNA as well as proliferative gene marker expression were significantly upregulated in epithelial cells cultured in A-HPF-conditioned medium. In contrast, in a co-culture model, where fibroblasts and epithelial cells were grown in direct contact, epithelial cell proliferation was not affected but expression of differentiation markers such as keratin 10, transglutaminase 1, involucrin, filaggrin and loricrin was significantly upregulated in the presence of A-HPFs.
Conclusions Our findings strongly support the suitability of A-CTGs for soft tissue augmentation in the esthetic zone, where epithelial cell migration, proliferation, and keratinization are of prime importance.