Abstract:

The connective tissue is known to have a general supportive effect for the development of the overlying epithelium; however, the more specific effects of fibroblasts and the involvement of their product, keratinocyte growth factor, on oral epithelial morphogenesis have not yet been addressed. Therefore, the purpose of this study was to investigate the effects of fibroblasts and keratinocyte growth factor on human oral epithelial morphogenesis in vitro. Reconstituted human oral epithelium was generated from primary human oral keratinocytes and fibroblasts by use of an organotypic cell culture model in a defined medium. Addition of fibroblasts to the collagen biomatrix increased total epithelial thickness from 28.0+/-5.0 microm to 66.1+/-8.6 microm (p=0.028), and basal cell proliferation from 3.6+/-0.7% to 16.6+/-1.1% (p=0.025). Presence of fibroblasts profoundly influenced the pattern of epithelial differentiation, and induced a switch in the pattern of cell death, from a predominance of spontaneous cell death in the basal cell layer (from 4.7+/-0.6% to 1.8+/-0.3%, p=0.029) to a more prevalent cell death due to terminal differentiation in the suprabasal cell layer (from 4.0+/- 0.1% to 5.4+/-0.1%, p=0.034). Keratinocyte growth factor promoted epithelial growth, but did not significantly enhance epithelial differentiation, demonstrating that fibroblasts possess additional mechanisms to keratinocyte growth factor synthesis that can modulate differentiation of reconstituted human oral epithelium.