

Matrix metalloproteinase (MMP) expression in the EpiDerm-FT skin equivalent: Relevance to dermal wound healing and blistering skin diseases.

Hayden, Patrick J., Cooney, Carolyn; Stolper, Gina; Klausner, Mitchell.
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MMPs play an important role in dermal wound healing, tissue remodeling, blistering diseases, tumor invasion and metastasis. In the current work, the expression of MMPs was evaluated in a full-thickness in vitro human skin equivalent, EpiDerm-FT. Normal human epidermal keratinocytes (KC) and dermal fibroblasts (FB) were cultured to produce the highly differentiated full-thickness skin equivalents. Histologic examination of EpiDerm-FT shows a collagen dermis populated by viable FB and an epidermis of stratified KC including basal, spinous, granular and stratum corneum components. Examination of the dermal-epidermal junction by transmission electron microscopy (TEM) revealed a well-developed basement membrane. RT-PCR analysis revealed the expression of MMP1 (interstitial collagenase), MMP2 (gelatinase A), MMP-3 (stromelysin 1), MMP7 (matrilysin), MMP9 (gelatinase B), MMP10 (stromelysin 2), MMP11 (stromelysin 3), MMP13 (collagenase 3) and MMP14 (membrane-inserted) in the EpiDerm-FT model. Prior to addition of epidermal KC, contracted collagen matrices containing dermal FB expressed significant amounts of MMP1 and MMP2, but little MMP9. Following addition of the epidermal component, MMP9 expression was increased. Subsequent separation of the dermal and epidermal components prior to RT-PCR analysis revealed that the epidermal KC contributed significant amounts of MMP-1, MMP3 and MMP11. The dermal component contributed a relatively greater amount of MMP-2, MMP7, MMP9, MMP10 and MMP14. The results indicate that epidermal KC have significant influence over expression of MMPs by dermal FB. EpiDerm-FT represents an important tool for elucidation of KC-FB interactions related to MMP expression, wound healing, blistering skin diseases and matrix remodeling.

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