
Recent review on the role of matrix metalloproteinases in biology and pathology of skin.


Recent review on the role of matrix metalloproteinases in tumor growth and invasion.


This study shows that migrating keratinocytes in dermal wounds express collagenase-1 (MMP-1), suggesting a role for this MMP in reepithelialization of wounds. Expression of MMP-1 in human epidermal keratinocytes is induced by contact to collagen.


This study shows that cleavage of native type I collagen by collagenase-1 is essential for migration of human epidermal keratinocytes on collagen.


Collagenase-3 (MMP-13) is expressed by fibroblasts in chronic human dermal ulcers, but not in normally healing wounds. In addition, MMP-13 is not expressed by migrating keratinocytes in acute or chronic wounds.

Together these3 studies provide evidence for different roles for collagenase-1 (MMP- 1)and collagenase-3 (MMP-13) in human cutaneous wound repair.

Ravanti L, Heino J, López-Otín C, Kähäri V-M. (1999) Induction of collagenase-3 (MMP-13) expression in human skin fibroblasts by three-dimensional collagen is mediated by p38 mitogen-

Collagenase-3 (MMP-13) is expressed by human skin fibroblasts only when they are cultured within collagen gel, but not when cultured in monolayer on plastic. The induction of MMP-13 expression in dermal fibroblasts is dependent on activity of p38 mitogen activated protein kinase. These results provide further evidence for entirely different regulation of the expression of collagenase-1 and collagenase-3 in human skin fibroblasts, suggesting a distinct role for them in biology and pathology.


UVB, even in doses too low to cause erythema induced expression of collagenase-1 (MMP-1), stromelysin-1 (MMP-3), and 92-kDa gelatinase (MMP-9) in normal human epidermis in vivo. Interestingly, induction of MMP-1, MMP-3, and MMP-9 by UVB was potently prevented by topical all-trans-retinoic acid without inhibition of erythema.


A single exposure to UV irradiation results in prolonged induction of collagenase-1 (MMP-1) stromelysin-1 (MMP-3) and gelatinase-B (MMP-9) expression and collagenase and gelatinase activities in human skin. This effect was inhibited by topical retinoic acid.

Together these two reports provide evidence that development of "solar scar" due to repeated exposure to sunlight may be mediated by induction of MMPs by UVB in epidermal keratinocytes.


This study shows that development of blisters in mouse skin induced by sera from patients with bullous pemphigoid is dependent on the presence of gelatinase B (MMP-9).


Development of contact hypersensitivity in mice requires the presence of stromelysin-1 (MMP-3), whereas clearance of hypersensitivity induced dermatitis is dependent on gelatinase-B (MMP-9).

Together these two papers provide new insight into the role of MMPs in cutaneous inflammation.


Collagenase-3 (MMP-13) is expressed by transformed human epidermal keratinocytes, but not by normal human epidermal keratinocytes in culture.

*Human collagenase-3 (MP-13) is specifically induced in tumor cells of squamous cell carcinomas of the head and neck, and the level of expression correlates with the invasion capacity of the tumors.*


*Human collagenase-3 is expressed by tumor cells in cutaneous squamous cell carcinomas and basal cell carcinomas, but not by keratinocytes in premalignant lesion of skin indicating that this MMP serves as a marker for keratinocyte transformation.*


*Human collagenase-3 (MMP-13) is specifically expressed by tumor cells in squamous cell carcinomas of vulva, and the expression correlates with the invasion capacity of the tumors.*

Together these 4 papers identify collagenase-3 (MMP-13) as a marker for keratinocyte transformation and invasion of squamous cell carcinomas of the head and neck and vulva.


*Expression of collagenase-3 (MMP-13), collagenase-1 (MMP-1) and gelatinase-B (MMP-9) in transformed keratinocytes and squamous cell carcinoma cells is dependent on activity of p38 mitogen activated protein kinase (MAPK). In addition, inhibition of p38 activity potently inhibits invasion of transformed keratinocytes through collagen and Matrigel.*


*Induction of collagenase-1 (MMP-1) expression in human skin fibroblasts by cytokine-activated ceramide pathway is mediated by coordinate activation of extracellular signal-regulated kinase, Jun N-terminal kinase and p38 mitogen-activated protein kinase pathways.*

Together these observations show that p38 MAPK plays an important role in the control of proteolytic activity of cells.


*Human tissue inhibitor of metalloproteinases-3 (TIMP-3) is expressed at high level in human scleroderma skin fibroblasts in vivo and in culture, suggesting a role for TIMP-3 in dermal fibrosis.*


*Tissue inhibitor of metalloproteinases-3 (TIMP-3) is expressed by stromal fibroblasts, but not tumor cells in human cutaneous squamous cell carcinomas.*


*Adenovirus-mediated expression of TIMP-3 inhibits invasion and promotes apoptosis of malignant melanoma cells in culture. This study identifies TIMP-3 as a novel secreted anti-invasive, anti-angiogenic suicide gene for cancer gene therapy.*