Acta Derm Venereol 2003; 83: 81–82

Taylor&Francis
healthsciences

EDITORIAL: In this issue...

MMPs: They are there and they do something – also in Dermatology

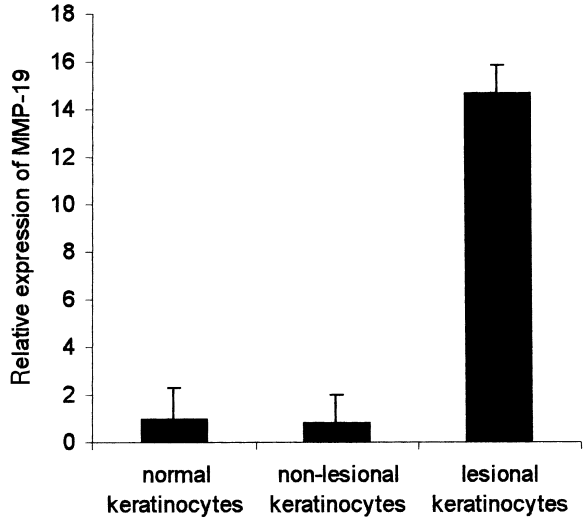
The spectrum of biological functions mediated by protein degrading enzymes, proteases, is wide indeed. Proteases and their inhibitors exert important functions inside cells, in the extracellular space, and in the blood stream. To this should be added the many proteases functioning as virulence factors of pathogenic micro-organisms. Consequently, proteases are also central actors in many pathophysiological processes, and the possibility to design specific inhibitors and modulators of their activities offers many new strategies for development of new therapeutic principles.

Proteases can be grouped into four major groups according to the catalytic mechanisms by which they are acting: the ''serine proteases'', ''cystein proteases'', ''metalloproteases'', and ''aspartate proteases'', with a serine residue, a metal ion, a cystein residue, and an aspartic acid residue being key structures of the active site enzymes belonging to the respective group. The

 ISSN 0001-5555

"matrix metalloproteases" (MMPs) is a still growing group of enzymes, today consisting of more than 20 members. Since their function is to degrade various components of the extracellular matrix in a highly regulated manner their crucial importance in normal cell biology and many pathologic processes is easily understood. MMPs have been assigned important functions in tissue remodeling cell migration, angiogenesis, and cell-cell interactions. This means that processes such as morphogenesis during embryo development, involution of the uterus and mammary glands after pregnancy and lactation, tumour invasion and spreading of malignant cells, migration of inflammatory cells and destruction of tissues by inflammation, and wound healing may all be dependent on the activities of MMPs. To this comes the recently elucidated capacity of MMPs to release and/or activate growth factors and cytokines. Given this multitude of functions it should not come as a surprise that the expression of genes coding for MMPs, as well as for their activators and inhibitors, is delicately regulated and under the influence of a vast variety of hormones, growth factors, and cytokines. The development of synthetic inhibitors, specific for the different MMPs, and the ongoing evaluation of these substances as therapeutic tools in a number of diseases, therefore seems, to say the least, a worthwhile enterprise.

With this background of demonstrated or suggested functions of MMPs, to claim the potential importance of these enzymes in dermatology is not far-fetched. Suffice it to mention psoriasis and other inflammatory conditions, blister formation, malignancies, and wound healing. This issue of *Acta Dermato-Venereologica* contains two contributions dealing with MMPs in skin biology and pathology. Suomela *et al.* (page 108) studied the expression of the recently discovered, structurally related enzymes MMP-19 and MMP-28 in psoriasis and lichen planus. For the first time MMP-19 was found to be expressed by psoriatic lesional keratinocytes *in vivo* as well as *in vitro*, but not by non-lesional psoriatic or normal keratinocytes. The expression seemed to be spatially correlated with a high proliferative rate of keratinocytes, and also with sites known to have a partially deteriorated basement membrane. In lichen planus MMP-19, too, expression was seen adjacent to basement membrane destruction. In contrast, MMP-28 was not expressed by keratinocytes in psoriasis or lichen planus. In wound healing the same group has recently shown high expression of MMP-28, also called epilysin, in proliferating keratinocytes distal from the wound edge. They suggest that total destruction of the basement membrane, as in wounds, may be needed to induce expression by keratinocytes of MMP-28.



Relative expression of MMP-19 in normal, non-lesional, and psoriatic lesional keratinocytes assessed by quantitative, real-time PCR. Fig. 3 from Suomela et al. (p. 108 in this issue).

The paper by Kobayashi *et al.* (p. 105) gives further insight into the regulation of MMP production by fibroblasts. They concentrated on MMP- 2 and MMP-9. In an *in vitro* study they show that, whereas unstimulated cultured keratinocytes secreted both these enzymes, cultured fibroblasts secreted only MMP-2 in the absence of added cytokines or growth factors. Upon addition to the culture media of TGF-β, TNF-α, or epidermal growth factor (EGF), the production of MMP-2 by fibroblasts was increased 1.5 – 2 fold. Interestingly, TGF-β and TNF-α, but not EGF, induced secretion by fibroblasts also of MMP-9.

The papers by Suomela *et al.* and by Kobayashi *et al.* both highlight the potential importance, but also the complexity, of a well regulated MMP activity and expression in the skin. We can be sure that much more is to come before the MMP field has been fully elucidated. But we should also look out for new drugs, based on knowledge generated from MMP research, of value for our patients.

Torbjörn Egelrud, MD,
Co-editor