Studies of interleukin-20 expression in human keratinocytes and psoriasis

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ABSTRACT

This PhD dissertation is based on studies carried out at the Department of Dermatology, Aarhus University Hospital, Aarhus, Denmark.

IL-20 is a member of the IL-10 family of cytokines suspected to play a role in the pathogenesis of psoriasis.

It was the aim of the present dissertation to investigate IL-20 expression in psoriatic skin and determine the mechanisms regulating IL-20 expression in the skin.

We found that IL-20 mRNA was more than 20-fold upregulated in lesional psoriatic skin and that the increased IL-20 mRNA expression decreased in parallel with improvement of the disease, clinically as well as histologically. Furthermore, it was demonstrated that normal human keratinocytes rapidly express and secrete IL-20 protein upon exposure to pro-inflammatory stimuli, such as IL-1β and UVB irradiation. It was discovered that IL-20 expression is highly dependent on the activation of the p38 MAPK and that IL-20 is a NF-κB regulated gene.

Finally, IL-20 expression was experimentally induced in non-lesional psoriatic skin using either IL-1β stimulation (ex vivo) or UVB irradiation (in vivo). These stimuli exclusively induced IL-20 mRNA expression (as determined with in situ hybridization) in the epidermal keratinocytes and release of IL-20 protein from the cultured biopsies. However, immunofluorescent stainings could not detect IL-20 protein in the keratinocytes but exclusively detected IL-20 protein in IL-20 mRNA negative, epidermal dendritic cells.

The findings of the present dissertation support, that IL-20 may play a role in the pathogenesis of psoriasis. Furthermore, it is established that keratinocytes exposed to pro-inflammatory stimuli are a rapidly inducible source of IL-20 in psoriatic skin. The fact that IL-20 protein in non-lesional psoriatic skin exposed to pro-inflammatory stimuli was detected in IL-20 mRNA negative dendritic cells indicates that these cells may be a target for keratinocyte-derived IL-20.