CHARACTERIZATION OF CARD18, A NOVEL NEGATIVE REGULATOR OF IL-1β IN HUMAN KERATINOCYTES AND IN PSORIASIS

Anikó Göblös [1], Judit Danis[1], Attila Bebes [1], Zsuzsanna Bata-Csörgő [1,2], Lajos Kemény [1,2], Márta Széll[2,3]

[1)] Department of Dermatology and Allergology, University of Szeged, Hungary
[2)] Dermatological Research Group of the Hungarian Academy of Sciences, University of Szeged, Hungary
[3)] Department of Medical Genetics, University of Szeged, Hungary

Psoriasis is an immune-mediated inflammatory skin disease affecting 2-3% of the population. The infiltrating immune cells and the keratinocytes both contribute to the pathogenesis of psoriasis. The IL-1β cytokine has a key role in the pathogenesis of psoriasis by mediating and initiating the infiltration of immune cells and the hyperproliferation of keratinocytes. In the psoriatic involved epidermis a higher IL-1β level can be realized which is mostly produced by the keratinocytes. Our recent large scale gene expression study has detected CARD18 (ICEBERG) as a differentially expressed transcript in psoriatic uninvolved epidermis compared to healthy epidermis. CARD18 belongs to the „CARD only protein" (COP) family and it is a negative regulator of IL-1β maturation by inhibiting inflammasome activation due direct interaction with pro-caspase1. The aims were to further characterize the CARD18 molecule in keratinocyte function and psoriasis.

Our histological staining confirmed the results of the previous microarray examination: an elevated CARD18 expression was detected in the psoriatic uninvolved epidermis compared to the healthy epidermis. The *in vitro* gene expression studies revealed low-level CARD18 mRNA expression in the proliferative state of keratinocytes that increased continuously during differentiation.

We studied the expression of some inflammasome signaling molecules (CARD18, AIM2 and caspase1 mRNA) and IL-1β secretion in keratinocytes in response to various psoriasis-related stress factors such as T-cell lymphokines, TNF-α, INF-ɣ and the synthetic DNA analogue poly(dA:dT).

In vitro keratinocytes secreted very low levels of IL-1β, whereas a significant increase was observed following inflammatory stimuli (TNF-α and INF-ɣ pretreatment, poly(dA:dT) transfection). In AIM2, CARD18 and caspase1 mRNA expression after the same treatment changes were also detected. The effects of CARD18 gene specific silencing were studied and we observed a decreased AIM2 and caspase1 mRNA expression 24 hours after silencing.

CARD18, AIM2 and caspase1 expression and IL-1β secretion can be induced by various psoriasis-related stress factors in human keratinocytes. CARD18 silencing caused a reduced inflammasome activation which we detected by a decreased IL-1β secretion, but the process remains unclear. We hypothesize that the elevated CARD18 mRNA and protein expression in the uninvolved psoriatic epidermis could contribute to the susceptibility to the disease.

Elméleti téma

Poszter