EXPRESSION OF CARD18 /ICEBERG IN HUMAN KERATINOCYTES

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Introduction: Our recent large scale gene expression study has revealed CARD18/ICEBERG as a differentially expressed transcript in psoriatic uninvolved epidermis compared to healthy epidermis. CARD18/ICEBERG is a negative regulator of inflammasome activation, thus IL-1β maturation. It is also well-known that keratinocyte-derived IL-1β plays an important role in the pathogenesis of psoriasis. Therefore, we aimed to study the expression of CARD18/ICEBERG in differentiating human keratinocytes and in response to various psoriasis-related stress factors.
Methods: The expression of CARD18/ICEBERG mRNA was followed in spontaneously differentiating normal human keratinocytes, in keratinocytes transfected with a synthetic DNA analogue (polydA/dT) and in organotypic skin cultures incubated with T-cell lymphokines (GM-CSF, INFγ, IL-3).
Results: The CARD18/ICEBERG mRNA was expressed at low levels in proliferating keratinocytes and its expression was induced by the differentiation of the cells. Transfection of keratinocytes with a synthetic DNA analogue slightly elevated the expression of CARD18/ICEBERG mRNA. The inducibility of CARD18/ICEBERG upon T-cell lymphokine induction showed differences in psoriatic uninvolved epidermis compared to normal human epidermis. The basal expression levels were relatively high, and could not be further induced in the psoriatic uninvolved epidermis in response to T-cell lymphokines. This was in contrast to what was found in the healthy skin, where lower basal expression levels were detected, but these were inducible in response to the same treatment
Conclusions: Our results demonstrated that the mRNA expression of CARD18/ICEBERG can be induced by various psoriasis-related stress factors in human keratinocytes and we hypothesize that its high-level but uninducible expression in the uninvolved psoriatic epidermis contributes to the susceptibility to the disease.