Keratinocytes act as immune modulators in the effector phase of acute allergic eczematous reactions

Stefanie Foerster, Kilian Eyerich, Heidrun Behrendt, Claudia Traidl-Hoffmann

Division of Environmental Dermatology and Allergy GSF/TUM, Center for Allergy and Environment, Technical University Munich, Biedersteiner Strasse 29, 80802 Munich, Germany.

The crosstalk between T-cells and keratinocytes plays a critical role in the elicitation and maintenance of eczematous skin reactions. Most of the studies conducted to date describe effector functions of T-cells on keratinocytes such as apoptosis while the effects of keratinocytes on T-cells is not clarified. The aim of this study is to delineate modulating effects of keratinocytes on T-cell-effector functions in an allergen specific homologous *in vitro* model of acute eczema.
T-cells were isolated from PBMC of patients sensitised against Nickel. Nickel-specific T-cell lines were expanded and cloned by limiting dilution. T-cell clones were characterised with respect to surface markers and cytokine profile. Homologous keratinocytes were cultivated by using the method of suction blister. Autologous B cells were infected with the Ebstein-Barr virus (EBV) and served as antigen presenting cells (APC). Keratinocytes-T-cell-APC crosstalk studies were performed and monitored morophologically (light- and eletronmicroscopy). Furthermore the endpoints T-cell proliferation and cytokine production were analysed by Thymidine-incooporation and ELISA, respectively.
In light and electron microscopy an allergen dependent crosstalk between T-cells and keratinocytes could be demonstrated. Furthermore, keratinocytes inhibited the proliferation of 7 out of 11 nickel-specific T-cell clones; 3 clones were stimulated by keratinocytes while 1 clone reacted in a disparate manner. The induced clones showed a significantly higher production of the proinflammatory cytokine IFN-γ in the presence of keratinocytes, while this cytokine was not constantly regulated in the inhibited clones. Notably, the production of IL-10 was very strongly inhibited in the presence of keratinocytes for all clones tested; the inhibition of the TH2 cytokine IL-4 was not as strong, but still significant.
We conclude that keratinocytes modulate the effector phase of eczematous reactions by inhibiting or stimulating the proliferation of allergen specific clones and by suppressing cytokines like IL-10 and IL-4, and therefore are maintaining and driving the immune response to a Th1 dominated pattern. The further analysis of these regulatory mechanisms in allergic eczema may open new horizons for therapeutic concepts.