

## SUMMARY

### **ROLE OF TRANSIENT RECEPTOR POTENTIAL VANILLOID-1 (TRPV1) IN THE REGULATION OF BIOLOGICAL PROCESSES OF HUMAN SEBOCYTES AND DENDRITIC CELLS**

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In our previous studies, we have identified the *in situ* expression of TRPV1 on sebaceous glands and epidermal dendritic (Langerhans) cells of human skin. The aim of the current study was to investigate the role of TRPV1 in biology of human sebaceous gland derived SZ95 sebocytes and monocyte-derived dendritic cells *in vitro*. Like the human sebaceous glands, SZ95 sebocytes also expressed TRPV1. Moreover, the TRPV1 activator capsaicin inhibited both the basal and arachidonic acid induced lipid synthesis (but did not influence the viability of the cells). The specific role of TRPV1 in mediating these effects was evidenced by using both the specific antagonist I-RTX and the RNAi technique. Results of the experiments carried out in decreased  $Ca^{2+}$  containing medium suggested that the TRPV1 took part in the effect of capsaicin as a functional  $Ca^{2+}$  channel. In addition, activation of TRPV1 altered the expression of transcription factors regulating lipid synthesis as well as the production of selected cytokines. Following long-term treatment, low concentrations of capsaicin increased the proliferation rate of SZ95 sebocytes acting via TRPV1, whereas high doses decreased the viability of the cells independently of TRPV1. TRPV1 was also identified on human monocytes and monocyte-derived dendritic cells where the expression of TRPV1 was increased during dendritic differentiation induced by GM-CSF and IL-4. In addition, TRPV1 expressed by dendritic cells was found to operate as a functional  $Ca^{2+}$  channel. Dendritic differentiation was inhibited by capsaicin in a TRPV1-dependent manner: capsaicin suppressed both the expression of differentiation markers characteristic for immature dendritic cells and the phagocytosis of the cells. Moreover, stimulation of TRPV1 on differentiated, immature dendritic cells did not induce the maturation, but decreased the internalization of *E. coli* bioparticules. Maturation of dendritic cells, induced by pro-inflammatory cytokines, was inhibited by the activation of TRPV1: capsaicin suppressed the expression of markers indicating maturation and inhibited the transcription and release of proinflammatory cytokines. In parallel, the production of the anti-inflammatory cytokine IL-10 was increased by capsaicin. Our results suggest that activation of TRPV1 suppresses the lipid synthesis/differentiation of sebocytes and have an anti-inflammatory effect on dendritic cells. These data argue for the potential role of TRPV1 to influence immune processes of the human skin as well as of certain dermatoses with altered lipid homeostasis (e.g. acne vulgaris).

Keywords: Transient receptor potential vanilloid-1 (TRPV1), Sebocytes, Dendritic cells

Kulcsszavak: transient receptor potential vanilloid-1 (TRPV1), szebociták, dendritikus sejtek