Roles of signal transduction mechanisms in the regulation of cutaneous biological functions

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In our experiments, we have investigated the roles of signal transduction mechanisms in the regulation of cutaneous biological functions. We demonstrate for the first time that transient receptor potential vanillioid-1 (TRPV1) is expressed in various non-neuronal cell types of murine skin. We have also shown that expression pattern of TRPV1 (similar to our previous data on human hair follicle, HF) strongly depends on the hair cycle stage. In addition, we found that morphogenesis of HF of TRPV1-gene deficient mice exhibits a significant delay when compared to wild-type littermates. These data strongly argue for the negative role of TRPV1-coupled signaling mechanisms in regulation of HF growth.

By investigating the cannabinoid system, we have successfully identified significant amounts of the endocannabinoid anandamide (AEA) in organ-cultured human HF. In addition, AEA and the well-known exogenous cannabinoid Δ^9-THC – most probably via cannabinoid receptor-1 – were found to inhibit hair shaft elongation and matrix keratinocyte proliferation, and to induce apoptosis-driven catagen transformation. We have also shown that the intimately related endocannabinoid and vanilloid (i.e. TRPV1-coupled) systems independently (yet in an additive manner) exert their regulatory roles in HF biology.

Finally, we have investigated the regulatory role of mechano-sensitive channels (MSC) on human keratinocytes. We found that (chiefly abrupt) alterations in osmolality, creating mechanical stress stimuli, induce keratinocyte hyperproliferation and de-differentiation. Moreover, our data also suggest that these biological modulations are mediated by certain MSCs permeable to Cl^- (and regulated by the PKC system), whereas the long-term effects may also be attributed to alterations in the intracellular calcium concentration.