

Neuropeptide als Sentinels der Haut

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A close crosstalk between the nerves and resident cells in the skin is now well established. Neurocutaneous interactions are involved in many physiological and pathophysiological functions including cellular development, growth, differentiation, immunity, inflammation, pruritus and wound healing.

The communication between the nervous and the immune system is mediated by different types of cutaneous nerve fibers, which release neuromediators and activate specific receptors on a variety of target cell in the skin. Cutaneous neuropeptides, neurotrophic factors and neurohormones include a large family of small peptides such as substance P (SP), calcitonin gene-related peptide (CGRP), somatostatin, vasoactive intestinal peptide (VIP), pituitary adenylate cyclase activating peptide (PACAP) or proopiomelanocortin (POMC) derived peptides for example.

Neuropeptides specifically regulate target cells by activation of high-affinity membrane receptors coupled to heterotrimeric G-proteins or by direct activation of intracellular signalling cascades. Neuropeptides are released from both, sensory or autonomic nerve fibers in the dermis as well as epidermis and thus are in close anatomic proximity to a variety of different cutaneous cell types. In addition to nerves several cutaneous cells are able to generate neuropeptides and to express neuropeptide receptors. The activity of neuropeptides is also regulated by several endopeptidases which are able to terminate neuropeptide mediated inflammation.

Moreover, neuronal proteinase activated receptors (PARs) or transient receptor potential ion channels (TRPs) are recently described structures being of crucial importance in the regulation of neurogenic inflammation. Thus, a close interaction between components of the nervous- and immune system is required to maintain tissue integrity and inflammation in the skin.

The progress in our understanding of neuroinflammation has resulted in the development of novel neuropeptide based strategies for the treatment of inflammatory and immune mediated diseases. For example targeting substance P or the respective neurokinin receptors in first clinical trials was found to be a highly effective treatment for pruritic and inflammatory skin diseases. Moreover, the antiinflammatory potential of melanocortin derived peptides are currently being investigated in first proof of concept studies.

