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INHIBITORY EFFECTS OF DYNORPHIN-A ON SPINALLY ADMINISTERED BETA-ENDORPHIN- AND GRP-INDUCED SCRATCHING IN NONHUMAN PRIMATES

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Endogenous opioid peptides have been implicated in itch (pruritus) in patients with diverse systemic diseases. In addition, recent studies suggest that gastrin-releasing peptide (GRP) and its receptor (GRPR) are involved in the neurotransmission of itch and they are up-regulated in patients with chronic skin disease. The aim of the study was to characterize the magnitude and duration of scratching responses elicited by spinal beta-endorphin and GRP, and to investigate effects of antagonists and kappa opioid receptor-preferring peptide dynorphin-A on these endogenous ligand-induced scratching in monkeys. After intrathecal administration, both beta-endorphin (10–100 nmol) and GRP (1–10 nmol) dose-dependently elicited similar, profound scratching responses which last for 1–2 h. When a mu opioid receptor antagonist naltrexone (30–100 nmol) was administered intrathecally, naltrexone attenuated beta-endorphin- but not GRP-induced scratching. In contrast, when a GRPR antagonist RC-3095 (30–100 nmol) was administered intrathecally, RC-3095 was effective in blocking GRP-, but not beta-endorphin-induced scratching. Furthermore, intrathecal dynorphin-A significantly attenuated both beta-endorphin- and GRP-induced scratching. These findings indicate that spinal mu opioid receptor and GRPR are two independent receptor mechanisms mediating itch and that dynorphin-A, like most kappa opioids, is able to attenuate scratching elicited by different pruritogens in primates.

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MODELING ATOPIC ITCH AND SKIN LESIONS IN DOGS: ALLERGEN CHALLENGES IN HYPERSENSITIVE DOGS OFFER OPTIMAL TRANSLATION POTENTIAL

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In spite of itch being the most common dermatological problem seen in dogs, its experimental induction has proven to be difficult in this species. While the intradermal injections of histamine, serotonin, tryptase, substance P, IL-2, or mast cell-degranulating anti-IgE antibodies all initially failed to induce itch in dogs, recent studies have shown that recombinant canine IL-31 and proteolytically active cowhage can induce pruritic manifestations in dogs. However, modeling itch with the activation of single pathways is fraught with the risk that interventions tested using these activators might not necessarily correlate with clinical efficacy in itchy dogs because of pruritogenic pathway redundancy. To alleviate this possible lack of reliable translation of experimental findings to allergic patients, more complex models have been developed, which involve dogs sensitized to clinically relevant food, fleas or house dust mite allergens; these models have the advantage of closely reproducing both clinical and immunological characteristics of spontaneously-arising canine atopic dermatitis. As a result, experimental models involving allergen challenges in hypersensitive dogs, which reproduce both itch and skin lesions, appear to offer the optimal translatable potential not only for canine, but also for human atopic pruritus and skin lesions.

PARANEOPLASTIC ITCH

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PARANEOPLASTIC ITCH

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Paraneoplastic itch is a rare symptom that sometimes complicates malignant diseases. The frequency of this symptom is unclear, epidemiological data in this field are missing. The symptom seems to appear rather rarely, which may be explained by its heterogeneous and often unclear pathophysiology. Patients with both, haematological and solid tumour malignancies can be affected. So far, there is no clear definition of paraneoplastic itch. One must assume that paraneoplastic itch, due to the insufficient data and knowledge situation, does not receive the required attention among physicians. Adding to this is the fact that it usually appears with normal skin but itch in these patients can also occur with skin lesions due to the increased frequency of e. g. adverse drug reactions in this group of patients. All this explains why treatment of paraneoplastic itch still forms a challenge. In 2012, an interdisciplinary study group of dermatologists, internal specialists and social scientists was founded, striving to elaborate a clear definition of paraneoplastic itch and to comprise updated diagnostics and treatment. A clear definition of paraneoplastic itch is supposed to offer better and more focused diagnostics, to inspire clinical studies and to optimize possibilities of treatment.

SCORING IN CLINICAL TRIALS

IL25

UPDATE ON TOOLS FOR ITCH ASSESSMENT

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No abstract is provided.

IL26

DETERMINATION OF MINIMUM CLINICALLY IMPORTANT DIFFERENCE (MCID) OF VISUAL ANALOGUE SCALE (VAS): IN WHICH DIRECTION SHOULD WE PROCEED?

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Pruritus measurement remains a challenge. Assessment of pruritus severity using VAS is frequently used in clinical trials. How-