A reliability assessment of standardized human surrogate models of histaminergic and non-histaminergic itch using histamine and cowhage spicules

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We previously reported that decreased level of semaphorin 3A (Sem3A) induces epidermal hyperinnervation in AD. To defend against pathogens, skin contains antimicrobial peptides that are induced by inflammation. Reduced induction of antimicrobial peptides, including cathelicidin LL-37 and human β-defensins (hBDs), in lesional skin of AD patients was suggested to increase susceptibility to infections. Here, we investigated the effects of antimicrobial peptides, including LL-37 and hBD-1-4, on Sem3A expression in normal human epidermal keratinocytes (NHEKs). We found that treatment with LL-37, but not hBDs, enhanced Sem3A expression. This LL-37-induced Sem3A expression was completely inhibited by pertussis toxin, an inhibitor of G protein ζ subfamily of G protein α and by PD98059, an inhibitor of ERK1/2 signaling. Moreover, analysis of LL-37 receptors showed that P2X7R may be at least partly involved in LL-37-induced Sem3A expression in NHEKs. Thus, in addition to antimicrobial activity, cathelicidin LL-37 may contribute to the induction of Sem3A expression in NHEKs via certain Gi-coupled receptors and the ERK1/2 signaling pathway.

PP15
OVEREXPRESSION OF HISTIDINE DECARBOXYLASE IN THE EPIDERMIS OF PRIMATES WITH CHRONIC ITCH
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Recently, an increase in epidermal histidine decarboxylase (HDC), a key enzyme for histamine synthesis, has been shown to be involved in acute and chronic itch-related behaviors induced by topical application of anionic surfactants in mice. Moreover, HDC was up-regulated in the epidermis of atopic dermatitis patients. These findings suggest the possibility that increased HDC in the epidermis plays a role in skin conditions with chronic itch. The aim of this study was to investigate whether the expression of epidermal HDC is increased in primates with idiopathic chronic itch. The skin biopsies were collected from 8 adult female cynomolgus macaques (Macaca fascicularis) with varying degrees of idiopathic chronic itch. The skin biopsies were collected from 8 adult female cynomolgus macaques (Macaca fascicularis) with varying degrees of idiopathic chronic itch. The skin biopsies were collected from 8 adult female cynomolgus macaques (Macaca fascicularis) with varying degrees of idiopathic chronic itch. The skin biopsies were collected from 8 adult female cynomolgus macaques (Macaca fascicularis) with varying degrees of idiopathic chronic itch. The skin biopsies were collected from 8 adult female cynomolgus macaques (Macaca fascicularis) with varying degrees of idiopathic chronic itch. The skin biopsies were collected from 8 adult female cynomolgus macaques (Macaca fascicularis) with varying degrees of idiopathic chronic itch. The skin biopsies were collected from 8 adult female cynomolgus macaques (Macaca fascicularis) with varying degrees of idiopathic chronic itch.

PP16
A RELIABILITY ASSESSMENT OF STANDARDIZED HUMAN SURROGATE MODELS OF HISTAMINERGIC AND NON-HISTAMINERGIC ITCH USING HISTAMINE AND COWHAGE SPICULES
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We recently discovered in itch neurophysiology have led to an increased use of human surrogate models of both histaminergic and particularly non-histaminergic itch. However, no absolute or relative reliability assessments have been conducted for these models and methods for induction of itch using cowhage are highly variable. This study sought to standardize cowhage application and to perform a test–retest reliability-assessment for the application of both histamine and cowhage. 3 doses of cowhage (5, 15 and 25 spicules), and 1 dose of 1% histamine were applied in 4 areas on the volar forearm in 15 healthy male volunteers. All measurements were performed twice, 7.73 days (±0.73 SEM) apart. Itch- and pain-intensity were rated on a VAS. Spatial itch distribution, TEWL and blood perfusion were monitored and particularly non-histaminergic itch. However, no absolute or relative reliability assessments have been conducted for these models and methods for induction of itch using cowhage are highly variable. This study sought to standardize cowhage application and to perform a test–retest reliability-assessment for the application of both histamine and cowhage. 3 doses of cowhage (5, 15 and 25 spicules), and 1 dose of 1% histamine were applied in 4 areas on the volar forearm in 15 healthy male volunteers. All measurements were performed twice, 7.73 days (±0.73 SEM) apart. Itch- and pain-intensity were rated on a VAS. Spatial itch distribution, TEWL and blood perfusion were monitored and particularly non-histaminergic itch. However, no absolute or relative reliability assessments have been conducted for these models and methods for induction of itch using cowhage are highly variable. This study sought to standardize cowhage application and to perform a test–retest reliability-assessment for the application of both histamine and cowhage. 3 doses of cowhage (5, 15 and 25 spicules), and 1 dose of 1% histamine were applied in 4 areas on the volar forearm in 15 healthy male volunteers. All measurements were performed twice, 7.73 days (±0.73 SEM) apart. Itch- and pain-intensity were rated on a VAS. Spatial itch distribution, TEWL and blood perfusion were monitored and particularly non-histaminergic itch. However, no absolute or relative reliability assessments have been conducted for these models and methods for induction of itch using cowhage are highly variable. This study sought to standardize cowhage application and to perform a test–retest reliability-assessment for the application of both histamine and cowhage. 3 doses of cowhage (5, 15 and 25 spicules), and 1 dose of 1% histamine were applied in 4 areas on the volar forearm in 15 healthy male volunteers. All measurements were performed twice, 7.73 days (±0.73 SEM) apart. Itch- and pain-intensity were rated on a VAS. Spatial itch distribution, TEWL and blood perfusion were monitored and particularly non-histaminergic itch. However, no absolute or relative reliability assessments have been conducted for these models and methods for induction of itch using cowhage are highly variable. This study sought to standardize cowhage application and to perform a test–retest reliability-assessment for the application of both histamine and cowhage. 3 doses of cowhage (5, 15 and 25 spicules), and 1 dose of 1% histamine were applied in 4 areas on the volar forearm in 15 healthy male volunteers. All measurements were performed twice, 7.73 days (±0.73 SEM) apart. Itch- and pain-intensity were rated on a VAS. Spatial itch distribution, TEWL and blood perfusion were monitored and particularly non-histaminergic itch. However, no absolute or relative reliability assessments have been conducted for these models and methods for induction of itch using cowhage are highly variable.