PRURITUS

CD26/DPPIV REGULATES MECHANICAL ITCH BY ENZYMATIC DEGRADATION OF MU-OPIOID RECEPTOR LIGANDS.

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Introduction & Objectives: Innocuous touch stimuli elicit itch sensation in skin diseases such as atopic dermatitis, psoriasis and xerosis. This phenomenon is known as alloknesis (mechanical itch), while its molecular mechanism is unknown. We recently discovered involvement of CD26/DPPIV enzyme activity in the regulation of psoriatic itch. However, the role of CD26/DPPIV on alloknesis remains unclear. In this study, we investigated whether CD26/DPPIV regulates alloknesis, to clarify the regulatory mechanism of CD26/DPPIV in mechanical itch.

Materials & Methods: To quantify alloknesis, we applied innocuous mechanical stimuli using von Frey filaments to the rostral back of CD26/DPPIV knockout (CD26KO), or wild type (WT) mice 30 times at intervals of 5 s (alloknesis assay). Alloknesis score was determined as the total number of scratching responses. To quantify endomorphin-evoked itch, we counted the frequency of scratching bouts by SCLABA-real system.

Results: Alloknesis score in CD26KO mice was significantly higher than that in WT mice. When recombinant DPPIV was injected intradermally, the alloknesis score in CD26KO mice significantly decreased, while intradermal injection of mutant DPPIV with deficient enzyme activity had no effect. Mechanical itch in CD26KO mice was inhibited by intradermal injection of naloxone (mu-opioid receptor antagonist) to the level of that in WT mice. Based on these data, we focused on endomorphins (EMs, EM-1 and EM-2), endogenous ligands for mu -opioid receptor and substrates for the DPPIV enzyme. We found that each intradermal injection of EM-1 or EM-2 in WT mice induced scratching behavior which was significantly blocked by naloxone, and the frequency of scratching behavior was significantly increased in CD26KO than WT mice. Notably, EMs induced mechanical itch behavior in WT mice which was inhibited by intradermal injection of naloxone.

Conclusions: These results suggest that CD26 /DPPIV negatively regulates alloknesis (mechanical itch) through DPPIV enzymatic degradation of cutaneous EMs.