Dietary induction of pruritic atopic skin in C57BL/6 mice

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[Background] Atopic dermatitis (AD) is a common chronic skin disease. Itch is a cardinal symptom of AD and has a considerable impact on the quality of life. In AD, itch is often exacerbated under certain circumstances, such as contact with wool, intake of alcohol, and during nocturnal sleep. The increased tendency to itch can contribute to the chronicity of itch and scratching. However, despite its clinical importance, the molecular basis of itch in AD is still poorly understood. We have previously shown that HR-1 hairless mice fed a special diet containing no polyunsaturated fatty acids and no starch develop AD-like pruritic skin inflammation (Fujii et al., *Exp., Dermatol.*, 24, 18-113, 2015). However, this mouse strain is thought not to be suitable for the kinds of detailed genetic studies requiring inbred or genetically altered mice. Therefore, in the present study we examined whether such pruritic conditions are reproduced in C57BL/6 (B6) mice, a strain widely used for genetic studies.

[Methods] Four-week old, B6 mice were fed the special diet. Skin conductance and transepidermal water loss (TEWL) were measured using Corneometer® and Tewameter®, respectively. Hindlimb scratching was detected and analyzed using an automatic measuring system, MicroAct®. Touch-evoked scratching (alloknesis) was assessed using 0.7 mN von Frey filaments applied to the shaved back skin.

[Results] From 10 weeks after the start of feeding, special diet-fed B6 mice exhibited decreased skin conductance and increased TEWL, indicating a decreased skin hydration and impaired skin barrier function, respectively. Histological examination showed epidermal hyperplasia and an increase in dermal mast cells in special diet-fed mice, as in AD patients. Special diet-fed mice showed an increase in spontaneous scratching as well as alloknesis. Furthermore, certain hypnotic drugs, such as ethanol and phenobarbital, markedly enhanced scratching in special diet-fed mice, but not normal ones. Although phenotypic differences among B6 substrains have been reported especially with respect to pain sensitivity, there was no significant difference in itch-associated scratching responses between substrains (B6N and B6J) and between male and female mice.

[Conclusions] This diet-induced itch model would be useful for investigating the molecular mechanisms of chronic itch, especially in AD.