

Role of cutaneous prostaglandin D₂ level in the itch-scratch reaction in mice

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Itching, which elicits the reaction of scratching, is considered to be a physiological phenomenon to eliminate foreign matter from the skin surface. In addition, however, scratching can also be a skin disrupting behavior. It is, therefore, presumed that there may be some strict regulatory mechanism to suppress excessive skin disruption and maintain cutaneous homeostasis. We examined the effects of various substances in NC/Nga mice, a known animal model of atopic dermatitis, using prolonged scratching as an indicator of itching. The results revealed that while indomethacin aggravated the scratching, and prostaglandin D₂ (PGD₂) significantly suppressed it. These results suggest that PGD₂ plays a physiological inhibitory role against pruritus in the NC/Nga mice. Therefore, we investigated the relationship between scratching and the cutaneous PGD₂ production level using the mechanical scratching test. Mechanical scratching increased the skin damage and cutaneous PGD₂ levels in a scratch-count-dependent manner, suggesting the existence of a regulatory mechanism for itching, in which scratching increases the cutaneous PGD₂ production, and PGD₂, in turn, suppresses the pruritus. To investigate the relationship between scratching and the cutaneous PGD₂ levels in NC/Nga mice, the cutaneous PGD₂ levels were compared between NC/Nga mice without dermatitis and NC/Nga mice with dermatitis. The results revealed that aggravation of the scratching in the spontaneous dermatitis model was caused by a defect in the ability to produce PGD₂, which has a physiological inhibitory role against pruritus, resulting in the development of dermatitis.