S07-5 Increased scratching behavior and susceptibility to dermatitis in mite-infected dysfunctional CFTR-expressing mice

◯Tsuyoshi SHUTO[1,2], Yasuaki HASHIMOTO[1,2], Shota MIZUNOE[1,2], MaryAnn SUICO[1,1], Hirofumi KAI[1,2]

[1]Grad. Sch. Pharm. Sci., Kumamoto Univ., [2]Global COE "Cell Fate Regulation Research and Education Unit", Kumamoto Univ.

Cystic fibrosis transmembrane conductance regulator (CFTR) is a member of ABC transporter family and a cAMP-dependent Cl- channel at the plasma membrane of epithelial cells. CFTR is expressed in many tissues and its dysfunction causes various tissue abnormalities such as the most common lethal inherited disorder cystic fibrosis (CF). Although CFTR is expressed in human epidermis, its function in the skin is largely unexplored. In this study, $CFTR^{+/+}$ mice and $CFTR^{\Delta F508/\Delta F508}$ mice, which express WT-CFTR and most common dysfunctional mutant ΔF508-CFTR, respectively, were co-housed with mite-infected, skin-lesioned NC/Nga mice and scratching behavior and histological appearance of mouse skin were monitored to assess abnormalities. Here, we observed the significant increase of scratching behavior, skin fibrosis and expression of nerve growth factor (NGF) and protein gene product 9.5 (PGP9.5) in the skin in mite-infected $CFTR^{\Delta F508/\Delta F508}$ mice. In addition, mite-infected $CFTR^{+/+}$ mice orally administered with a chloride channel inhibitor glibenclamide had higher scratching count and increased level of NGF than vehicle-treated mice. Consistently, we observed that mite extract-infected HaCaT cells, a keratinocyte cell line, treated with CFTR inhibitor, had significantly higher level of NGF mRNA compared with DMSO-treated, mite extract-infected HaCaT cells. Our results revealed that CFTR dysfunction in the skin increases the scratching behavior and susceptibility to dermatitis in mite-infected ΔF508 CFTR mice. These results suggest that CFTR could be a potential therapeutic target for some itch-related diseases.