

## S48-1 Pathological significance of histamine H1 receptor gene expression mechanism

○Hiroyuki MIZUGUCHI<sup>1</sup>, Yoshiaki KITAMURA<sup>1</sup>, Yuto KONDOH<sup>1</sup>, Wakana KURODA<sup>1</sup>, Haruka YOSHIDA<sup>1</sup>, Yuko MIYAMOTO<sup>1</sup>, Masashi HATTORI<sup>1</sup>, Takeda TAKEDA<sup>1</sup>, Hiroyuki FUKUI<sup>1</sup>

<sup>1</sup>Ins. Health Biosci. Univ. Tokushima Grad. Sch.

Therapeutics targeting disease-sensitive genes is strongly expected for the therapy of multi-factorial diseases. There is no clinical report about therapeutics for allergic disease-sensitive genes. We are focusing on the histamine H1 receptor (H1R) as a sensitive gene. H1R mediates allergy histamine signal. H1R is a rate-limiting molecule of H1R signal because the signal is increased by the increase of the receptor expression level. We discovered that the stimulation of H1R induced H1R gene expression through protein kinase c-delta activation, resulting in the receptor up-regulation. The mechanism of H1R gene expression revealed to play a key role in the receptor expression level by the studies using cultured HeLa cells and allergic rhinitis model rats. Initial treatment of antihistamines is recommended for the therapy of pollinosis. However, the mechanism of the therapy remains to be elucidated. We demonstrated that initial treatment of antihistamines to allergic rhinitis model rats resulted not only in improvements of symptoms but also in suppressing the elevation of H1R mRNA level in the nasal mucosa. Then clinical trial was achieved. When symptoms and H1R mRNA levels in nasal mucosa of pollinosis patients with and without initial treatment, both symptoms and high level of H1R mRNA were significantly improved in treated patients, compared to non-treated patients. These results strongly suggest that H1R is an allergic diseases-sensitive gene.