European Respiratory Society
Annual Congress 2013

Abstract Number: 1729
Publication Number: P906

Abstract Group: 5.3. Allergy and Immunology
Keyword 1: Animal models **Keyword 2:** Asthma - mechanism **Keyword 3:** Immunology

Title: Over-expression of the LTC4 synthase gene in mice reproduces human aspirin-induced asthma (AIA)

Dr. Tatsuya 15842 Yokoyama mayakoyo@dokkyomed.ac.jp MD [1] and Dr. Hirokuni 15843 Hirata hirokuni@dokkyomed.ac.jp MD [1]. [1] Pulmonary Medicine and Clinical Immunology, Dokkyo Medical University, Tochigi, Japan .

Body: AIM: The pathogenesis of AIA is presumed to involve the aspirin/NSAID-induced abnormal metabolism of arachidonic acid, resulting in an increase in 5-LO metabolites, particularly LTC4. However, the role of LTC4 in the development of AIA has yet to be conclusively demonstrated. This study was to evaluate the contribution of the lipid product LTC4 secreted by the 5-LO pathway to the pathogenesis of AIA. METHODS: To evaluate antigen-induced airway inflammation, the concentrations of Th2 cytokine in BALF obtained from LTC4 synthase-transgenic (Tg) and wild-type (WT) mice after challenge with ovalbumin were measured. The ex vivo and in vivo effects of the NSAID sulpyrine were investigated in these Tg and WT mice by measuring the secretion of LTC4 from sulpyrine-treated BAL cells and the levels of LTC4 in BALF following challenge with sulpyrine. Finally, the sulpyrine-induced airway response by the administration of pranlukast, an antagonist of the cys-LT1 receptor, was analysed. RESULTS: The concentrations of IL-4, -5, and -13 in BALF from Tg mice were significantly higher than those in WT mice. Sulpyrine augmented the secretion of LTC4 in BALF and by BAL cells in Tg mice, but not in WT mice. The increased airway resistance induced by sulpyrine could be reduced by treatment with pranlukast. The secretion of LTC4 from mast cells, eosinophils was increased in the allergen-stimulated Tg mice, even in the absence of sulpyrine, as well as in BAL cells after sulpyrine. CONCLUSION: The over-expression of the LTC4 synthase in a mouse asthma model also replicates the key features of AIA. And our study supports that cys-LTs play a major role in the pathogenesis of AIA in patients with chronic asthma.