European Respiratory Society
Annual Congress 2012

Abstract Number: 3079

Publication Number: P1094

Abstract Group: 7.2. Paediatric Asthma and Allergy

Keyword 1: Asthma - mechanism **Keyword 2:** Functional genomics **Keyword 3:** Animal models

Title: Alterations in ORMDL expression in experimental esthma

Dr. Michaela 9806 Schedel schedel.michaela@googlemail.com [1,2], Mr. Anthony 9807 Joetham joethama@njhealth.org [2], Prof. Dr Michael 9808 Kabesch kabesch.michael@mh-hannover.de [1] and Prof. Dr Erwin 9809 Gelfand gelfande@njhealth.org [2]. [1] Department of Pediatric Pneumology, Allergy and Neonatology, Hannover Medical School, Hannover, Germany and [2] Department of Pediatrics, National Jewish Health, Denver, United States .

Body: INTRODUCTION: A susceptibility locus on 17q21, including ORMDL3, has been identified in childhood asthma. We determined if expression of ORMDL3 and the other members of the highly conserved ORMDL family (ORMDL1-2) are altered in the lungs and tissues of mice with experimental asthma. METHODS: Intraperitoneal sensitization of C57BL/6 and Balb/c mice to ovalbumin (OVA) was carried out on days 1 and 14. Sensitized and naïve mice received aerosol challenges on days 24-26. ORMDL1-3 expression levels were analyzed in different tissues (brain, gut, heart, kidney, liver, lung, skeletal muscle, spleen, thymus) and isolated cells (lymph nodes, blood). Kinetic studies of ORMDL expression in lung, spleen, and thymus were performed 24h, 48h, and 72h after the last challenge. Gene expression data are described as relative fold-changes. RESULTS: ORMDL1-3 expression in all tissues was shown at comparable levels for both mouse strains and mRNA levels were altered only in lung and lymphoid tissues (spleen, thymus) with a peak 48h after the last challenge. In lungs of non-sensitized/challenged (n=11) vs. sensitized/challenged (n=11) C57BL/6 mice, significant decreases were observed for ORMDL1 (1.0 vs. 0.47, p=2.09E-07), ORMDL2 (1.0 vs. 0.56, p=1.12E-07), and ORMDL3 (1.0 vs. 0.50, p=2.72E-05). In parallel, significantly lower levels of ORMDL2 (1.0 vs. 0.72, p=0.01), and ORMDL3 (1.0 vs. 0.77, p=3.14E-05) were detected in spleen. In Balb/c mice similar significant effects were detectable, albeit to a lower degree. In contrast, ORMDL mRNA expression in the thymus trended upwards in sensitized and challenged mice of both strains. CONCLUSION: These data demonstrate the involvement of all members of the ORMDL family in experimental asthma.