European Respiratory Society
Annual Congress 2012

Abstract Number: 2930
Publication Number: 1867

Abstract Group: 12.3. Genetics and Genomics
Keyword 1: Genetics **Keyword 2:** Epidemiology **Keyword 3:** Mutation analysis

Title: Genetic variants in Protocadherin-1, bronchial hyperresponsiveness and asthma subphenotypes in German children

Mrs. Antoaneta 6726 Toncheva toncheva.antoaneta@mh-hannover.de [1,14], Dr. Kathrin 6727 Suttner Kathrin.Suttner@lrz.tum.de [1,14], Mr. Sven 6728 Michel michel.sven@mh-hannover.de [1,14], Dr. Norman 6729 Klopp klopp@helmholtz-muenchen.de [2,3], Prof. Thomas 6730 Illig illig@helmholtz-muenchen.de [2,3], Dr. Christian 6770 Vogelberg christian.vogelberg@uniklinikum-dresden.de MD [4], Dr. Andrea 6771 von Berg vonberg@Marien-Hospital-wesel.de MD [5], Prof. Dr Albrecht 6772 Bufe albrecht.bufe@rub.de MD [6], Prof. Dr Andrea 6773 Heinzmann andrea.heinzmann@uniklinik-freiburg.de MD [7], Dr. Otto 6774 Laub sprenglaub@aol.com MD [8], Dr. Ernst 6775 Rietschel ernst.rietschel@uk-koeln.de MD [9], Prof. Dr Burkhard 6781 Simma burkhard.simma@lkhf.at MD [10], Prof. Dr Thomas 6782 Frischer thomas.frischer@meduniwien.ac.at MD [11], Dr. Jon 6783 Genuneit jon.genuneit@uni-ulm.de MD [12], Prof. Dr Erika 6784 von Mutius Erika.Von.Mutius@med.uni-muenchen.de MD [13] and Prof. Dr Michael 6787 Kabesch kabesch.michael@mh-hannover.de MD [1]. [1] Department of Pediatric Pneumology, Allergy and Neonatology, Hannover Medical School, Hannover, Germany, 30625 ; [2] Research Unit of Molecular Epidemiology, Helmholtz Zentrum Munich, Neuherberg, Germany ; [3] Hannover Unified Biobank, Hannover Medical School, Hannover, Germany, 30625 ; [4] University Children's Hospital, Technical University, Dresden, Germany ; [5] Research Institute for the Prevention of Allergic Diseases, Children's Department, Marien-Hospital, Wesel, Germany ; [6] Department of Experimental Pneumology,, Ruhr-University, Bochum, Germany ; [7] University Children's Hospital, Albert Ludwigs University, Freiburg, Germany ; [8] Kinder- und Jugendarztpraxis Laub, Kinder- und Jugendarztpraxis Laub, Rosenheim, Germany ; [9] University Children's Hospital, University of Cologne, Germany ; [10] Children's Department, University Teaching Hospital Landeskrankenhaus, Feldkirch, Austria ; [11] University Children's Hospital, University Children's Hospital, Vienna, Austria ; [12] Institute of Epidemiology and Medical Biometry, Ulm University, Ulm, Germany and [13] University Children's Hospital, Ludwig Maximilians University, Munich, Germany .

Body: Background: Recently, Protocadherin-1 (PCDH1), located on chromosome 5q31-33, in the vicinity of the cytokine gene cluster containing several known candidate genes for asthma and allergy (interleukin-4, interleukin-5, interleukin-13 and RAD50), was reported as a novel susceptibility gene for bronchial hyperresponsiveness (BHR) and asthma. Objectives: We aimed to define linkage disequilibrium (LD) between the region comprising PCDH1 and the cytokine gene cluster. Next, for a comprehensive analysis of the PCDH1 locus we conducted detailed fine mapping of the PCDH1 region and investigated effects of single nucleotide polymorphisms (SNPs) in BHR, asthma and related phenotypes. Methods: Genotype information was acquired from Illumina HumanHap300Chip genotyping, MALDI-TOF MS genotyping and

imputation. Associations were investigated in a population of at least 1,303 (651 asthmatics) from two German study populations (MAGICS and ISAAC II). Results: No relevant LD between 14 PCDH1 tagging SNPs and 98 SNPs within the cytokine cluster was detected. There were no significant associations with BHR, atopy, allergic rhinitis and atopic eczema. However, rs7719391 was associated with asthma (OR=0.85, p=0.039) and non-atopic asthma (OR=0.69, p=0.009). The exonic SNP rs3797054 previously reported to be associated with BHR and asthma, was significantly associated with non-atopic asthma (OR=0.70, p=0.019) in our study. Significant associations with non-atopic asthma were observed also for rs11167761 (OR=1.54, p=0.021), rs3935792 (OR=1.32, p=0.039), rs2974704 (OR=0.43, p=0.009). Conclusions: PCDH1 polymorphisms may specifically affect the development of non-atopic asthma in children. These authors contributed equally: Mrs. Antoaneta Toncheva, Dr. Kathrin Suttner, and Mr. Sven Michel.