

A Novel Genetic Marker for Asthma



Center for Technology Commercialization

TECHNICAL FIELD

Diagnostic: Asthma (1998-0722)

BACKGROUND

Asthma is a chronic inflammatory disorder and, in genetically susceptible individuals, this inflammation leads to increased airway responsiveness to a variety of stimuli and recurrent airway obstruction. Approximately 5% of adults and 7-10% of children in the U.S. have asthma. Roughly 50% of cases develop before the age of 10 and another 33% before the age of 40. Asthma is the fourth leading cause of morbidity and the number one cause of childhood hospitalizations in the U.S. accounting for 1.6 million emergency room visits and 10 million office visits per year. In 1998, asthma accounted for \$11.3 billion in health care costs in the U.S.

Because asthma can become progressively more severe over time, it is important to determine individuals that are susceptible to the disease at a young age. In addition, in individuals that have been diagnosed with asthma, it is clinically important to predict the severity of their disease over time. Although it is clear that both environmental and genetic influences are important in the development of asthma, the pathogenesis of this disease remains unclear.



TECHNOLOGY

Several candidate genes and loci have been linked to asthma and atopy, including IL-4, HLA complex, an adrenergic receptor and chromosomal regions such as the cytokine cluster on 5q 31-32, supporting the polygenic nature of these complex diseases. The present technology relates to the discovery that allelic variations in the IL-4 receptor gene leading to increased receptor signaling are genetic predictors of asthma. Moreover, these increased receptor-signaling mutations are also predictive of the severity of asthma in individuals having asthma. A laboratory within Cincinnati Children's Hospital Research Foundation has determined that a novel IL-4 receptor alpha chain (IL-4Ra) allele on T2-helper cells, mast cells, and basophils has been linked to susceptibility of atopy in humans. This allelic variation results from an adenine to guanine substitution at nucleotide 1902 of the IL-4 receptor cDNA, predicting a change from glutamine to arginine at position 576 in the cytoplasmic domain of the IL-4Ra. This new allele, termed the "R576" allelic variation, plays a role in the development of asthma. In addition, it has been determined that the presence of the R576 IL-4Ra allele impacts the severity of asthma in affected patients; thus, the presence of this R576 allele correlates with the severity of asthma. Specifically, an individual homozygous for the R576 allele is at greater risk for severe asthma when compared to an individual who is either heterozygous for R576 allele or possesses wild-type IL-4 receptor gene.

Currently, there are few known genetic markers for severity of asthma. Thus, this discovery has significant therapeutic potential for arming physicians with the knowledge necessary to provide patients with an individualized and highly specific treatment regime.

APPLICATIONS

1. **Gene-based test for determination of asthma susceptibility**
2. **Research tool**

ADVANTAGES

- **Standardized diagnostic tool**
- **Better manage and treat disease state**
- **Potential to develop a new therapeutic and diagnostic markets**

INVESTIGATOR

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STATUS

U.S. Patent 6,379,890
European Patent 1,137,947

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THE INVENTOR

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BACKGROUND

Dr. Khurana Hershey is the Director of the Translational Research Program in Allergy and Asthma and Professor of Pediatrics at Cincinnati Children's Hospital Medical Center and the University of Cincinnati College of Medicine.



As part of her role as Director of Center for Translational Research in Asthma and Allergy, Dr. Hershey has developed a comprehensive database of allergic children seen in allergy and asthma clinics at CCHMC. Extensive phenotypic information including clinical, demographic, and quality of life data is available for nearly 2000 children and has been entered into a comprehensive database. DNA samples are available on over 98% of these children. This registry serves as a basis for multiple projects and grants.

Dr. Hershey is an elected member of the Society for Pediatric Research and a Diplomat of the American Academy of Allergy, Asthma and Immunology. She is a recognized leader in the allergy field and serves on the Editorial Board of the Journal of Allergy and Clinical Immunology and has been asked to serve on several NIH study sections and focus groups. She is the Principal Investigator of an NIH Asthma and Allergic Diseases Cooperative Research Center. She was recently named one of the Five Leading Women in Healthcare in the Greater Cincinnati Metropolitan Area by Women's Business Cincinnati Magazine, and nominated Outstanding Woman at Cincinnati Children's Hospital Medical Center. Her other honors include being awarded the Basil O'Connor Starter Scholar Award and the Asthma and Allergy Foundation of American Investigator Award. Her research has been supported by numerous sources including the National Institutes of Health, March of Dimes and the American Heart Association.