Integrating demographic, clinical, and environmental exposure information to identify genomic biomarkers associated with subtypes of childhood asthma

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Childhood asthma is a multifactorial disease with a disturbingly high incidence in urbanized areas. The pathogenesis of asthma is poorly understood due to the complex relationship between genetic susceptibility and modulating environmental factors. The Mechanistic Indicators of Childhood Asthma study (MICA) has collected multiple types of clinical, demographic, exposure, and gene expression data in order to examine the interplay between environmental and genetic factors affecting asthma in a case/control cohort of children (aged 9-12 years). Oligonucleotide microarrays were used to measure gene expression from blood samples. Here, we hypothesize that asthmatic subtypes can be identified by considering gene expression data in the context of clinical measures of asthma severity/symptomology and biomarkers of environmental exposure. As a first step toward identifying subtypes, we applied an unbiased (i.e. without knowledge of asthma status) analysis to assess the association between gene expression data and information on clinical, demographic, and environmental exposure indicators gathered for 195 children. For subsequent analyses, we select only gene expression probe sets that are significantly correlated with at least one of the demographic, clinical, or exposure indicators. This filtering method prevents us from selecting only genes whose expression is associated with broadly-defined, imperfect asthma diagnoses. Statistical techniques amenable to handling disease outcome subtypes are then used to model the association of gene expression biomarkers with various definitions of asthma. Examination of the genes differentiating asthma subtypes in the context of demographic, clinical, and environmental exposures highlights mechanistic genomic etiologies underlying the disease. These include subtypes of asthma characterized by patterns of gene expression associated with immune over-stimulation and household allergy exposures, as well as combinations of genomic biomarkers with demographic factors such as gender. It is hoped that studies such as this may shed light on genes contributing to asthma pathology and environmental factors modulating the expression of those genes. Better understanding of the mechanistic underpinnings of varied asthma subtypes may lead to more personalized diagnosis, management, and treatment of the disease.

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