Integration of gene expression, clinical, and demographic information in relation to asthma status to identify biomarkers associated with subtypes of childhood asthma

Authors: ClarLynda Williams-DeVane[1], David Reif[2], Stephen Edwards[1], Brooke Heidenfelder[3], Edward Hudgens[3], Lucas Neas[3], Elaine Hubal[2], Jane Gallagher[3]

[1]National Health and Environmental Effects Research Laboratory, US Environmental Protection Agency, Office of Research and Development, Research Triangle Park, NC USA
[2]National Center for Computational Toxicology, Office of Research and Development, US Environmental Protection Agency, Research Triangle Park, NC USA
[3]Human Studies Division, US Environmental Protection Agency, Office of Research and Development, Chapel Hill, NC, USA

ABSTRACT

Advances in biomarker development have improved our ability to detect early changes at the molecular, cellular and pre-clinical level that are often predictive of adverse health outcomes. Biomarkers for monitoring the underlying molecular mechanisms of disease are of increasing importance as risk assessment relies more substantially on mode of action. This study focuses on asthma because it is a multifactorial disease that is complicated by the complex relationship between genetic susceptibility and modulating environmental factors. The Mechanistic Indicators of Childhood Asthma (MICA) study has incorporated multiple types of clinical, demographic, exposure, and gene expression data to better understand the relationship between environmental and genetic factors affecting asthma in a case/control cohort of children from the Detroit area. Detroit and other urban areas tend to have disturbingly high incidences of childhood asthma. Oligonucleotide microarrays were used to measure gene expression from blood samples. We hypothesize that asthmatic subtypes can be described by considering gene expression data in the context of clinical measures of asthma severity and/or symptomology and biomarkers of environmental exposure coupled with knowledge of asthma status. As a first step, we assessed the association between gene expression data and information on clinical and demographic indicators for children in the MICA study in the absence of knowledge of their asthma status. For subsequent analysis, only gene expression probe sets significantly correlated with at least one of the demographic or clinical indicators are used. 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. Studies such as this may shed light on biomarkers of childhood asthma as well as interaction effects of environmental factors on these biomarkers ultimately leading to better diagnosis, management, and treatment of childhood asthma as well as better informed risk assessment.

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