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Integrated analysis of blood gene expression and biomarker data to define asthma endotypes in children

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Common diseases such as asthma, diabetes, and atherosclerosis result from a complex mixture of genetic and environmental factors. Much progress has been made on identifying genetic determinants for these diseases, and efforts are currently underway to better characterize environmental contributions (commonly referred to as the exposome). A better understanding of the mechanistically distinct subtypes of common complex diseases is, however, needed to make the best use of these new data streams. We evaluated methods for deriving these mechanistic subtypes using a cross-sectional study stratified *on asthmatic and non-asthmatic children* from Detroit, MI, in which a wide array of clinical and environmental biomarkers were measured along with blood gene expression. Our integrated analysis of the blood expression and clinical covariates resulted in a recursive partitioning tree that segregated study participants into purely data-driven endotypes based on their asthma status. These endotypes are consistent with previous classifications although our data suggest multiple mechanistically distinct neutrophilic subtypes. Functional characterization of the genes and associated covariates revealed a complex interaction among Th2 mediated lung inflammation, heightened systemic innate immune response, and potentially metabolic syndrome in discriminating asthma endotypes. The results from this study can be used to advance human study designs and analytical methods for investigating both genetic and environmental causes of common diseases to improve prevention, diagnosis, and treatment of these diseases. [This is an abstract or a proposed presentation and does not necessarily reflect EPA policy. Mention of trade names or commercial products does not constitute endorsement or recommendation for use.

Biography

Stephen Edwards is a Systems Biologist within the U.S. Environmental Protection Agency's National Health and Environmental Effects Research Laboratory (EPA-NHEERL) in Research Triangle Park, N.C. Dr. Edwards is developing a framework to integrate *in vitro*, lab animal, and biomarker data from target organisms to improve the scientific underpinnings of the Agency's human and ecological risk assessments. He serves as a senior advisor in the Office of Research and Development (ORD) on issues regarding the development of predictive toxicology models of disease using genomics, proteomics, and metabolomics.

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