DIFFERENTIAL LUNG GENE EXPRESSION IN IMMUNOLOGICALLY-CHALLENGED RATS EXPOSED TO CONCENTRATED AIRBORNE PARTICULATES

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Asthma prevalence among children has been steadily increasing. Children residing in urbanized areas suffer disproportionately higher asthma-related morbidity and mortality. One explanation is that children living in inner cities are exposured to higher levels of environmental asthma triggers, including airborne particulate matter. To elucidate gene-environment interactions conferring differential susceptibility in metropolitan children, we first measured gene expression changes in sensitized rats exposed to concentrated airborne particulates (CAPs) [PM 2.5] in Detroit, the site of our childhood asthma clinical study. Brown Norway rats were sensitized with ovalbumin, then immunologically challenged with either saline or ovalbumin before chamber exposure to CAPs. To measure gene expression differences between saline-control and ovalbumin-challenged animals in the presence of CAPs, lung RNA was isolated and hybridized to Affymetrix R230 2.0 rat whole genome chips. Differential expression was assessed using the significance analysis of function and expression (SAFE) framework, which uses structured permutations to highlight knowledge-based gene annotative categories exhibiting unexpectedly high numbers of differentially expressed genes. The KEGG biological pathway categories demonstrating an excess of differentially expressed genes included “Cell communication,” “Metabolism of xenobiotics by cytochrome P450,” and several immunological signaling categories. Genes showing reduced expression in ovalbumin-challenged animals relative to controls included suppressor of cytokine signaling (SOCS) genes, which normally suppress the initiation of JAK-STAT inflammatory signals. Genes showing increased expression in ovalbumin-challenged animals included several members of the MAP kinase family, which promote release of asthma-associated cytokines, as well as CYP2B1, which is necessary for proper xenobiotic metabolism and has demonstrated altered expression in response to inhaled pollutants. These data will inform the analysis of pathways and gene-environment interactions relevant to asthma. (*This work was reviewed by EPA and approved for publication but does not necessarily reflect official Agency policy*.)