Cache Valley PM2.5 Activates Akt, Inflammatory Pathways, and Induces Genetic Damage in Human Lung Cells

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Northern Utah’s Cache Valley frequently has some of the nation’s highest concentrations of PM2.5 particulate pollution. Exposure to PM2.5 is associated with increased all-cause mortality, cardiovascular and cardiopulmonary diseases, heart attack, stroke, COPD, Alzheimer’s disease, and lung cancer. The purpose of this study was to determine the cellular responses of human lung cells (BEAS-2B) exposed to PM2.5 particulate pollution collected in Cache Valley (CVPM; (1 and 12 µg/ml; 24 hr). Parallel experiments were conducted using diesel exhaust particles (DEP) as a positive control. Exposure to CVPM resulted in genetic damage as assessed by the Comet Assay and a significant increase in the number of actively-dividing cells compared to control cells by flow cytometry (p < 0.05), with similar potency to that of DEP exposed cells. Whole-genome microarray (Affymetrix Human 2.0) identified affected genes principally related to the inflammatory and immune pathways, as well as activated serine/threonine Akt (*aka* protein kinase B or PKB)-dependent pathways. RNA sequencing with gene set enrichment pathway and clustering analysis confirmed that differentially expressed genes involved the immune response, Akt activation pathways, and MAPK activation. Subsequent qRT-PCR showed that CVPM and DEP exposure significantly increased expression of inflammatory markers including IL-6, CD40LG, and PLAG27 as well as cytochrome P450 (CYP) 1A1 in a concentration-dependent manner (p < 0.05). Treatment-related changes in expression of most genes were similar between particle types, while some genes and pathways revealed particle-specific effects, such as CYP1A1 (CVPM > DEP), and CD40LG (DEP > CVPM). Immunoblotting confirmed activation of Akt by phosphorylation of Thr308 in both CVPM and DEP exposed cells. Given the oncogenic nature and centrality of Akt and related pathways in cell division and proliferation, our data is consistent with the hypothesis that CVPM induces carcinogenesis with potency similar to that of DEP. This research is supported by the Marriner S. Eccles Charitable Foundation and by Utah State University.