Alterations in gene expression in normal human breast cells in response to diesel particulate extract (SRM1975) detected with DNA microarrays

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Abstract

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Diesel particulate extract (DPE) is a complex mixture containing polycyclic aromatic hydrocarbons. As such it is a major genotoxic environmental pollutant that is detrimental to human health. Alterations in gene expression in normal human mammary epithelial cells (NHMECs) in response to diesel particulate extract (SRM1975) have been investigated using DNA microarrays. The capacity for DPE to induce cytotoxicity was determined over a concentration range of 0.025 - 4 µl/ml using the MTT (3-[4, 5-dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide) assay. A dose dependent decrease in cell viability was observed with a 50% cell death occurring at a concentration of 1.5µl/ml. Transcriptional response in NHMECs was monitored after a 24h exposure to non-cytotoxic concentrations of DPE (0.1, 0.2, 0.3 and 0.4 µl/ml) using DNA oligonucleotide microarrays (U133A, Affymetrix). Of the total 22,000 genes present on the gene array, exposure to DPE altered expression of 117 to 493 genes by at least 2 fold. Several metabolism genes were induced significantly ($p \leq 0.005$) in a dose dependent manner (e.g. AKR1C1, INSIG1, NQO1), however, others had increased expression but remained similar for all doses (CYP1A1, CYP1B1, HSD17B2). Further, signal transduction genes (KRTHA4, NCOA1, SPRR2B, HBP17), immune/inflammation response genes (PTGS2, IF144, IL1R2) and apoptosis genes (ALOX15B) were all up regulated significantly compared to solvent control (DMSO). Cell cycle control genes (BIRC5, CDKN3, CTGF) and DNA replication genes (RRM2, CDC6, PFS2) were significantly ($p \leq 0.005$) down regulated. These results suggest several genes that may be useful biomarkers of DPE exposure that may be of value for monitoring workers.

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