

## **A Toxicogenomic Assessment of Primary Human Cells Exposed to Single-Walled Carbon Nanotubes**

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Engineered nanomaterials are characterized as having at least one dimension of 1 – 100 nm. Early reports show contradicting results as to the toxicity of unmodified single-walled carbon nanotubes (SWNT). Here, an in vitro toxicogenomics approach is used to assess the toxicity of these nanomaterials. Human epidermal keratinocytes (HEK) and normal human bronchial epithelial (NHBE) cells were cultured for 24 hours with cytotoxic doses of SWNT, silica (SiO<sub>2</sub>), and carbonyl iron (CI). Cells from individual treatments were harvested at each time point and snap frozen to -80° C. Total ribonucleic acid (RNA) was isolated from these cell pellets and complementary ribonucleic acid (cRNA) probes were synthesized and hybridized against gene expression microarrays. All microarray experiments were done in triplicate. To compare expression profiles from the two cell systems, only the 3,464 common unique genes were considered in this work. Gene expression profiles of significantly expressed genes (2-fold change or greater) from HEK cells were nearly 1 – 2 orders of magnitude greater than that of the NHBE cells. Using hierarchical clustering and principal components analysis (PCA), the largest variation in the gene expression values were between the skin and lung cells, regardless of nanomaterial treatment. Also, PCA showed profiles from SWNT exposure to be similar to untreated samples for both cell systems. A cytotoxic exposure with CI showed highest gene activity in the HEK cells while treatment with SiO<sub>2</sub> gave the highest activity in the NHBE cells. HEK cells treated with SWNT showed a 4-fold increase in expression for the gene that encodes for human IL-8. This is in agreement with previous citations for SWNT exposure. Two potential biomarkers (NAT10 and ZHX2) have been identified for SiO<sub>2</sub> exposure.

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