

Carbon black nanoparticles induce biphasic gene expression changes associated with inflammatory responses in the lungs of C57BL/6 mice following a single intratracheal instillation - DTU Orbit (08/11/2017)

Carbon black nanoparticles induce biphasic gene expression changes associated with inflammatory responses in the lungs of C57BL/6 mice following a single intratracheal instillation

Inhalation of carbon black nanoparticles (CBNPs) causes pulmonary inflammation; however, time course data to evaluate the detailed evolution of lung inflammatory responses are lacking. Here we establish a time-series of lung inflammatory response to CBNPs. Female C57BL/6 mice were intratracheally instilled with 162µg CBNPs alongside vehicle controls. Lung tissues were examined 3h, and 1, 2, 3, 4, 5, 14, and 42days (d) post-exposure. Global gene expression and pulmonary inflammation were assessed. DNA damage was evaluated in bronchoalveolar lavage (BAL) cells and lung tissue using the comet assay. Increased neutrophil influx was observed at all time-points. DNA strand breaks were increased in BAL cells 3h post-exposure, and in lung tissues 2-5d post-exposure. Approximately 2600 genes were differentially expressed (± 1.5 fold; $p \leq 0.05$) across all time-points in the lungs of exposed mice. Altered transcript levels were associated with immune-inflammatory response and acute phase response pathways, consistent with the BAL profiles and expression changes found in common respiratory infectious diseases. Genes involved in DNA repair, apoptosis, cell cycle regulation, and muscle contraction were also differentially expressed. Gene expression changes associated with inflammatory response followed a biphasic pattern, with initial changes at 3h post-exposure declining to base-levels by 3d, increasing again at 14d, and then persisting to 42d post-exposure. Thus, this single CBNP exposure that was equivalent to nine 8-h working days at the current Danish occupational exposure limit induced biphasic inflammatory response in gene expression that lasted until 42d post-exposure, raising concern over the chronic effects of CBNP exposure.

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