Transcriptional profiling identifies physicochemical properties of nanomaterials that are determinants of the in vivo pulmonary response - DTU Orbit (01/06/2019)

Transcriptional profiling identifies physicochemical properties of nanomaterials that are determinants of the in vivo pulmonary response

We applied transcriptional profiling to elucidate the mechanisms associated with pulmonary responses to titanium dioxide (TiO2) nanoparticles (NPs) of different sizes and surface coatings, and to determine if these responses are modified by NP size, surface area, surface modification, and embedding in paint matrices. Adult C57BL/6 mice were exposed via single intratracheal instillations to free forms of TiO2NPs (10, 20.6, or 38 nm in diameter) with different surface coatings, or TiO2NPs embedded in paint matrices. Controls were exposed to dispersion medium devoid of NPs. TiO2NPs were characterized for size, surface area, chemical impurities, and agglomeration state in the exposure medium. Pulmonary transcriptional profiles were generated using microarrays from tissues collected one and 28 d postexposure. Property-specific pathway effects were identified. Pulmonary protein levels of specific inflammatory cytokines and chemokines were confirmed by ELISA. The data were collapsed to 659 differentially expressed genes (P ≤ 0.05; fold change ≥ 1.5). Unsupervised hierarchical clustering of these genes revealed that TiO2NPs clustered mainly by postexposure timepoint followed by particle type. A pathway-based meta-analysis showed that the combination of smaller size, large deposited surface area, and surface amidation contributes to TiO2NP gene expression response. Embedding of TiO2NP in paint dampens the overall transcriptional effects. The magnitude of the expression changes associated with pulmonary inflammation differed across all particles; however, the underlying pathway perturbations leading to inflammation were similar, suggesting a generalized mechanism-of-action for all TiO2NPs. Thus, transcriptional profiling is an effective tool to determine the property-specific biological/toxicity responses induced by nanomaterials.

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