

Toll like receptor mediated proinflammatory response to environmental respirable aerosol (carbon nanoparticles) in primary bronchial epithelial cells.

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Abstract: Humans are exposed to a diverse set of airborne antigens and toxins thereby requiring selective, rapid appropriate immune and inflammatory response to aerosols. Chronic lung diseases (CLDs) like asthma and chronic obstructive pulmonary disease (COPD) involve innate and adaptive immune responses as well as proinflammatory, inflammatory and anti-inflammatory reactions. Members of toll like receptor (TLR) family initiate both innate and adaptive immune responses following their binding of pathogen-associated molecular patterns (PAMPs) such as lipopolysaccharides (LPS) and peptidoglycans (PGN) in a highly specific manner. Thus, TLRs are currently exploited as targets for asthma and COPD drug development. Cellular expression of TLRs in the airway epithelial cells is influenced by the microenvironment (pre-existing complication in respiratory system), exposure scenarios and also in response to host defense molecules like reactive oxygen species (ROS). TLRs 1-5 and 9 are expressed in the human airway epithelium. TLR2 and TLR4 are the principal receptors involved in the recognition of various pathogens and activated in response to host molecules like ROS. Variations in TLR9 has important clinical relevance as explained by the variation of TLR response pattern among healthy, asthmatic, smokers with COPD, and smokers without COPD under the same exposure conditions. Accumulating evidence has elevated the concern on the contribution of particulate matter (PM) and ambient particle mixture (combustion derived, diesel exhaust, carbon nanoparticles) for the development of CLDs. It has been demonstrated that fine particles such as PM_{2.5} (<2.5 µm) induce CLDs among susceptible individuals. Revolution of nanotechnology and wide usage in every sphere of life resulted in nanoparticle exposure as an emerging health risk. Exposure studies in animals as well as humans with ambient dust, ultrafine carbon black particles or carbon nanoparticles (CNP) detected both pulmonary and systemic inflammation. Therefore, in the present study we sought to investigate the TLR mediated response and proinflammatory reaction on primary bronchial epithelial cells (PBEC) following CNP exposure (5ug/ml). To pursue this we are screening the transcript expression levels of 84 TLR pathway genes using RT² Profiler PCR-array (Qiagen # PAHS-018Z). Preliminary results have shown increased (≥2 fold) transcript levels of 26 TLR- pathway genes and decreased (≥2 fold) transcript levels of 12 TLR-pathway genes. Based on our initial findings we aim to perform specific mechanistic studies using PBECs cultured in the physiologically relevant air liquid interface (ALI)-3D model following aerosolized CNP exposure using the high precision PreciseInhale System.

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