

Mechanisms of Inhaled Multiwalled Carbon Nanotube Immune Suppression

Supporting/Contributing Agency: U.S. EPA

In 2007, Dr. Jacob McDonald and colleagues published the first manuscript on inhaled multiwalled carbon nanotube (MWCNT) biocompatibility. Dr. McDonald identified the need for inhalation exposures using nanomaterials after seeing that other groups were using an artificial mode of pulmonary exposure by depositing bolus suspensions of carbon-based nanomaterials directly into the lung. The novel inhalation exposure system developed by Dr. McDonald allowed his staff to conduct highly relevant studies to identify possible inhalation hazards associated with inhaling MWCNT. These studies specifically targeted modeling occupational exposure scenarios and showed that little pulmonary damage results from aerosolized MWCNT; however, systemic immune function was compromised following inhaled particle concentrations of $1\text{mg}/\text{m}^3$ for 6 hours per day for 14 consecutive days (Mitchell et al. 2007).

Since then, Dr. McDonald's group has identified a novel signaling cascade from the lung to the systemic immune cell milieu (Mitchell et al. 2009). The cascade is initiated by the release of an immunomodulatory cytokine called Transforming Growth Factor beta (TGF-beta). TGF-beta then activates the cyclooxygenase pathway. The cyclooxygenase pathway results in the synthesis of prostaglandins which are known T cell suppressors. These known T cell suppressors can also activate another cytokine called Interleukin 10 (IL-10) which parallels the activity of the prostaglandins in promoting immunosuppression. This hypothesis is outlined in the figure to the left. This work shows that MWCNT, upon inhalation, can cause systemic effects that require the attention of those in the regulatory community. The systemic immune system may be uniquely sensitive to nanoparticle inhalation exposure.

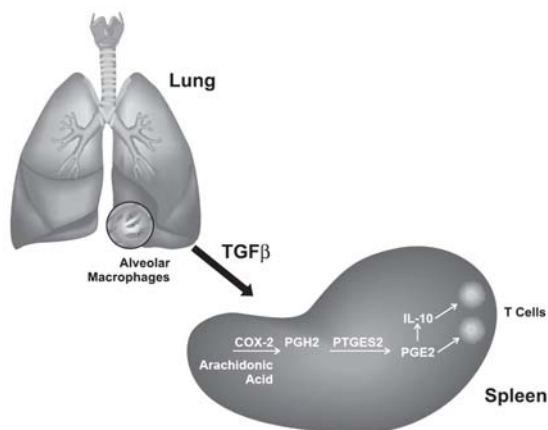


Figure 4.x. *Caption.*

References/Publications

- Mitchell, L.A., Gao, J., Vander Wal., R, Gigliotti, A., Burchiel, S.W., McDonald, J.D. (2007). *Toxicological Sciences* 100(1) 203-214.
- Mitchell, L.A., Lauer, F.T., Burchiel, S.W., McDonald, J.D. (2009). *Nature Nanotechnology*, In Review.