Perfluoroalkylated Substances' Effect on Hepatocyte Pathology and Pharmacokinetically Relevant Drug Enzymes and Transporters

Joseph Xie, Moriah Anthony, Luigi Brunetti
Rutgers, The State University of New Jersey

Cadmium (Cd) exposure has been associated with pregnancy complications such as preterm birth and pre-eclampsia. Understanding the cellular mechanisms involved in Cd exposure can shed light on the effects of metal contaminants on placental function. We speculate that Cd could alter inflammatory signaling in the placental immune system and inform potential therapeutic targets to improve the health of pregnant women. For this purpose, we sought to investigate the relationship between cadmium accumulation in human placentas and the expression of four cytokines (Interleukin-1β, IL-1β; Interleukin-8, IL-8; Interleukin-10, IL-10; and Tumor Necrosis Factor-α, TNF-α). Healthy term human placental biospecimens (N=26) were collected at birth. Cd content was assessed using inductively coupled plasma mass spectrometry and cytokine expression was measured using enzyme-linked immunosorbent assays. The median Cd level in the human placentas was 1.9 ppb (range 0.7-6.4 ppb). Placenta samples were divided into a higher Cd content group (N=13) and a lower Cd content group (N=13) based on the median Cd concentration. Levels of pro-inflammatory cytokine expression were compared between placentas with <1.9 versus >1.9 ppb cadmium using t-tests. and no differences were observed: IL-8 (p=0.38), IL-1β (p=0.24), IL-10 (p=0.30), and TNF-α (p=0.29). In a healthy population, relationships between Cd accumulation in the placenta and enrichment of cytokines were not observed. Future studies may include placentas from pathologic pregnancies or with a greater range of Cd exposures. Overall, a comprehensive understanding of such mechanisms can contribute to improvements in maternal health. This work was supported by the SOT Intern Program, EMSOP, and NIH grants R25ES020721 and R01ES029275.