Macrophage Heterogeneity and Cadmium Exposure in Human Placentas

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Placental macrophages protect the mother and fetus from infection by engulfing harmful bacteria and signaling with other cells. Cadmium (Cd) is a prevalent heavy metal environmental pollutant that targets the placenta and interferes with normal functioning and has been shown to disrupt immune signaling in other tissues. We sought to evaluate associations between enrichment of macrophage subpopulations in human placentas and accumulation of Cd. Healthy full-term human placentas (n=20) were collected from Robert Wood Johnson University Hospital. Cd concentrations were quantified using ICP-MS. Tissues were designated as low (N=10) or high Cd (N=10) if concentrations were below or above the median level of 2.9 ppb, respectively. Placental tissue sections were stained for macrophage markers CD14, CD68, CD163, CD206, and DC-SIGN using immunohistochemistry and imaged with GRYPHAX software. The number of positively stained cells were counted manually using ImageJ's Cell Count software and normalized to tissue area. No differences in placental weight were observed between low and high Cd exposure; however, birth weight tended to be reduced in placentas with high Cd levels (p=0.0887). Notably, the number of macrophages that stained for the scavenger receptor (CD163) was increased (44%) (p=0.0014), while enrichment of macrophages stained for the mannose receptor (CD206) was reduced (p=0.0438) in placentas with cadmium levels over 2.9 ppb. Notably, CD163 is a homeostatic receptor and increases in the placenta has been linked with obesity, preeclampsia, and gestational diabetes. By comparison, CD206 is a pathogen recognition marker, and its staining is reduced in placentas from pregnancies with spontaneous preterm birth. As a result, placentas with higher Cd levels may be more susceptible to pathogenic infections and pregnancy complications. This work was supported through the ASPET SURF Program, Rutgers Office for Research and Economic Development, and NIH grants R25ES020721 and R01ES029275.