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EFFECTS OF MATERNAL AU-NP EXPOSURE BY INHALATION ON FOETO-PLACENTAL DEVELOPMENT AND PLACENTAL FUNCTION, IN A RABBIT MODEL

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Gold nanoparticles (Au-NP) are contained in consumer and medical products leading to an potential of workers being exposed to Au-NP among them pregnant women, but effects of Au-NP on offspring is still unclear. The aim was to evaluate the effects of maternal sub-chronic Au-NP inhalation throughout the gestation on the foeto-placental development and placental function in a rabbit model. 11 pregnant females (Au-NP) inhaled uncoated Au-NP (11.5nm) at $132 \pm 38 \mu\text{g}/\text{m}^3$ for 5 days/week, from 1-27dpc of gestation. 11 controls were exposed to clean air in the same conditions. Gestation was monitored by ultrasound. At 28dpc, maternal bronchoalveolar fluid, hematology and biochemistry, maternal and foetal biometry were analyzed using a linear model. DNA lesions were evaluated by alkaline comet assay and Au quantified by neutron activation in various maternal and male foetal tissues. Placental gene expression was explored using a customized microarray. Foetal growth was not affected, although umbilical Doppler resistance was increased at 27dpc in Au-NP. At 28dpc, maternal lymphocytes numbers were increased in bronchoalveolar fluid from Au-NP. Maternal blood mean corpuscular volume was significantly decreased in Au-NP, whereas maternal biometry and biochemistry, foetal biometry remained unchanged. At 28dpc, DNA lesions were detected in maternal bone marrow and in male, but not female, foetal kidneys. Au-NP were strongly detected in maternal lungs, liver and plasma and in the placenta, heart, lungs and kidneys of male fetuses, but not in brain. 3 genes were differentially expressed between groups. Gene Set Enrichment Analysis revealed opposite gene set enrichment profiles in Au-NP males and females compared to C. Maternal and foetal phenotypes were weakly affected by *in utero* exposure to Au-NP through maternal inhalation but DNA lesions were observed. Moreover, Au-NP were able to reach placental and foetal tissues and to affect placental gene expression in a sex-specific manner.