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In vitro actions of bisphenol A in human placenta

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Bisphenol A (BPA) is an endocrine active chemical present in polycarbonate plastics. BPA has been detected in human placental tissues at a concentration that could potentially regulate expression of genes responsible for placental functions/development. In an *ex vivo* perfused placental perfusion model we have reported that BPA at environmentally relevant concentrations rapidly transferred from maternal to fetal compartment. The objectives of this study were to investigate whether BPA at environmentally relevant concentrations could affect expression of estrogen-responsive genes and cytokine production in human placental tissues. Villous and chorio-decidual explants were isolated from term placentae and treated with environmentally relevant concentrations of BPA (1 to 1000000 pM) for 24 hours. Explants and media were then collected and gene expression and cytokine production were investigated using real-time PCR and ELISA, respectively. mRNA expressions of estrogen receptor – α, - β (ER– α, - β), estrogen related receptor– γ (ERR-γ), artemin, aromatase and insulin like growth factor-1 (IGF-1) were investigated. In villous explants, BPA at 10 nM concentration down regulated ER-α, -β, artemin and IGF-1 and at 1pM concentration up regulated aromatase while in chorio-decidulal explants BPA at 10 nM concentration down regulated ER-α, ERR-γ and BPA at 100pm and 1pM up regulated artemin and IGF-1 mRNAs respectively. BPA exposure also showed a trend towards increased IL-1β and decreased IL-10 production in villous explants suggesting the possibility for a shift in the TH1/TH2 cytokine production by term placenta.

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Benzene and styrene metabolism: Influence of genetic polymorphisms of detoxification enzymes on the urinary excretion of occupational exposure biomarkers

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Susceptibility to chemicals may derive from genetic or acquired characteristics. Toxic chemicals once adsorbed are bio-transformed to compounds that may be more toxic than the original or converted into non-toxic metabolites that are excreted through the urine (detoxification). Genetic polymorphisms of xenobiotic metabolizing enzymes may lead to relevant shifts in the balance of bioactivation and detoxification pathways. The aim of this work was to evaluate the influence of the polymorphisms of CYP2E1, GSTs and mEH enzymes in the detoxification pathways of 2 occupational toxicants, benzene and styrene; determining the excretion variability of the urinary metabolites used as exposure biomarkers: This variability can significantly affect the biological monitoring studies for exposure assessment. In benzene exposed workers a strong influence of GSTT1 polymorphism on the excretion of S-phenyl mercapturic acid was found, reducing the conjugation rate of benzene epoxide with GSH in null subjects of about 50% with respect to the GSTT1 positive genotype for the same benzene exposure. To a lesser extent a similar effect is seen for GSTA1 mutant and GSTM1 null genotypes. In styrene exposed workers the CYP2E1*5B and CYP2E1*6 heterozygote alleles reduce the excretion of mandelic and phenyl glyoxylic acids to about 20% with respect to the wild type genotype, in the 7.5% and 13.8% of the population respectively, and the slow EPHX1 allele (codon 113) of 35% in the 17.8% of the population. A significant correlation also exists between the predicted activity profile of mEH and the excretion levels of styrene metabolites.

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