PHTHALATE EXPOSURE AND BREAST-CANCER RISK ACCORDING TO PPARγ AND PPARGC1B GENOTYPES

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Background and Aims: Some phthalic acid diesters (phthalates) have recently been associated with breast cancer (BC). In this study we evaluated if that association is modified according to PPARγ and PPARGC1B genotypes.

Methods: 208 BC cases were age-matched with 220 population controls from the north of Mexico. Urine concentrations of nine phthalate metabolites were determined by isotope dilution/high-performance liquid chromatography and mass spectrometry. Genotyping of variant Pro12Ala (rs1801281) of the PPARγ gene and variants Ala203Pro (rs7732671) and Val279Ile (rs17572019) of the PPARGC1B gene were carried out by traditional PCR with TaqMan probes.

Results: The three polymorphisms under study were in Hardy-Weinberg equilibrium, with a minor allele frequency of 0.11, 0.14, and 0.14 for the Pro12Ala, Ala203Pro, and Val279Ile variants respectively. Only the association between the higher levels of urinary mono-(2-ethylhexyl) phthalate (MEHP) concentration with BC was modified after the stratification by the PPARγ gene Pro12Ala polymorphism alleles (for G carriers: OR=0.59 CI95%=0.25-1.39; for C carriers: OR=1.50 CI95%=1.08-2.08); and the association between the mono-iso-butyl phthalate (MiBP) with BC in women with higher urinary concentrations was modified after the stratification by the PPARGC1B gene Ala203Pro polymorphism alleles (for C carriers OR=1.12 CI95%=0.55-2.27; for G carriers OR=0.67 CI95%=0.44-1.01).

Conclusions: Our results suggest the presence of a gene-environment interaction influencing BC risk that could be determined by the magnitude of exposure.

Keywords: breast cancer, phthalates, urinary metabolites, PPARγ, PPARGC1B, gene-environment interaction.