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A novel endocrine disrupting systems of Di-n-butyl phthalate (DBP) via PPAR subfamilies.

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Di-n-butyl phthalate (DBP) is a known endocrine disruptor and peroxisome prolifelator and has a reproductive toxicity with an unknown mechanism. Peroxisome Proliferators have a large number of biological activities, from metabolism to cell differentiation, mediated by nuclear receptor PPAR. The purpose of this study is to clarify the involvement of PPARs in PP-derived endocrine disruption. We found that exposure to DBP and PPAR agonists of rats to DBP and PPAR agonists significantly altered estardiol metabolism and that this alteration was sex-dependent. The protein levels of CYP2C11, a male specific Cytochrome P450 isoform, was significantly decreased by the presence of DBP or PPAR-alpha agonist. . In contrast the expression of the same enzyme was dramatically increased in female rats. The change may explain the differential alteration of rates of estradiol hydroxylation in male and female rats. The degree of alteration in estrogen biosynthesis measured in the testis and ovaries was found to be sex-dependent. The aromatase (CYP19) mRNA was completely abolished in a PPAR-delta agonist treated female rats. The alteration of PPAR activity was shown to cause a disruption in estrogen homeostasis.