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Gestational exposure to BPA is associated with alterations of DNA methylation in the rat placenta in a sexually dimorphic manner.

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The long latency between exposure to endocrine disruptor chemicals (EDCs) and effects later in life leads to a need for early biomarkers of exposure that could justify the protection of pregnant women and fetuses against EDCs adverse effects.

At the interface between mother and fetus, the placenta plays a key role in fetal programming. It has been demonstrated that there is a sex-specific response of the placenta to environmental "stressors". Epigenetic has appeared to be a key mechanism for implementation of changes in gene expression in response to early life environment.

We hypothesized that changes in placental DNA methylation could provide early markers of exposure to EDCs. We aimed at studying the effect of a gestational exposure to Bisphenol A (BPA) on DNA methylation pattern in female and male rat placenta.

Pregnant rats were exposed orally to BPA (10mg/kg/d) from gestational day 6 (GD 6) to 18. Placenta obtained by cesarean section were harvested at GD 19. Male and female placenta were identified using classical PCR for SRY expression. Genome-wide DNA Microarray analysis was performed to identify genes with increased methylation following gestational exposure to BPA.

In female placenta, we identified 4 genes that exhibited hypermethylation after BPA exposure with statistical significance (adjusted p-value < 0.05): SF-1 (log Fold Change : 1,21) ; Hmx2 (log FC : 1,36) ; Tctn2 (log FC : 1,45) and Mamdc4 (log FC : 1,14). In male placenta, one gene was significantly hypermethylated: Tnks2 (log FC : 1,92).

, Using Methylation-Specific PCR after bisulfite treatment, we are currently validating the alterations of methylation of SF-1, a key factor in the development and the function of the ovaries..

In conclusion, prenatal exposure to a high dose of BPA leads to changes in placental DNA methylation pattern of specific genes in a sexually dimorphic manner. SF-1 gene appears to be a placental epigenetic target of prenatal exposure to a high dose of BPA in female placenta.