

Peripubertal Serum Dioxin Concentrations and Sperm Methylation of Young Russian Adults



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Background: Animal data have demonstrated that the sperm methylome is sensitive to endocrine disrupting compounds (EDCs) at specific windows of development; however, the association of exposure to EDC in the peripubertal period with sperm DNA methylation in human or animals is unknown.

Main Questions: Are peripubertal serum dioxin concentrations associated with genome-wide profiles of DNA methylation in sperm collected in young adulthood?

Design: The Russian Children's Study is a prospective cohort of 516 boys who were enrolled at 8–9 years of age and provided semen samples at 18–19 years of age. At enrollment, serum dioxins, including the potent dioxin congener, 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD), were measured. Whole genome bisulfite sequencing of sperm was conducted to identify differentially methylated regions (DMR) between highest ($n = 4$, median serum TCDD 10.4 pg/g lipid) and lowest ($n = 4$, median serum TCDD 0.39 pg/g lipid) peripubertal TCDD groups.

Main Results: The mean methylation across all CpG sites was significantly lower in the highest peripubertal serum TCDD group compared to the lowest group ($49.1 \pm 4.9\%$ and $61.9 \pm 5.2\%$, respectively; *t*-test, $p = 0.01$). We found 52 DMRs that distinguished two serum TCDD groups. One of the top scoring networks, "Cellular Assembly and Organization, Cellular Function and Maintenance, Carbohydrate Metabolism," identified estrogen receptor alpha (ESR1) as its central regulator.

Conclusions: Findings from our limited sample size suggests that peripubertal environmental exposures are associated with sperm DNA methylation in young adults. Funds: RSF #14-45-00065, parental study - US NIH #R01 ES014370

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