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Publication

Mohan Manikkam, Rebecca Tracey, Carlos Guerrero-Bosagna, Michael K. Skinner (2012) Dioxin (TCDD) Induces Epigenetic Transgenerational Inheritance of Adult Onset Disease and Sperm Epimutations. PLoS ONE 7(9)e46249.

Summary

Environmental compounds can promote epigenetic transgenerational inheritance of adult-onset disease in subsequent generations following ancestral exposure during fetal gonadal sex determination. The current study examined the ability of dioxin (2,3,7,8-tetrachlorodibenzo[p]dioxin, TCDD) to promote epigenetic transgenerational inheritance of disease and DNA methylation epimutations in sperm. Gestating F0 generation females were exposed to dioxin during fetal day 8 to 14 and adult-onset disease was evaluated in F1 and F3 generation rats. The incidences of total disease and multiple disease increased in F1 and F3 generations. Prostate disease, ovarian primordial follicle loss and polycystic ovary disease were increased in F1 generation dioxin lineage. Kidney disease in males, pubertal abnormalities in females, ovarian primordial follicle loss and polycystic ovary disease were increased in F3 generation dioxin lineage animals. Analysis of the F3 generation sperm epigenome identified 50 differentially DNA methylated regions (DMR) in gene promoters. These DMR provide potential epigenetic biomarkers for transgenerational disease and ancestral environmental exposures. Observations demonstrate dioxin exposure of a gestating female promotes epigenetic transgenerational inheritance of adult onset disease and sperm epimutations.

Highlights

- One of the first reports to demonstrate the ability of Dioxin to promote the epigenetic transgenerational inheritance of disease and sperm epimutations.
- The sperm epimutations were identified that transmit this transgenerational disease development and may be used as epigenetic biomarkers of exposure and disease.
- Observations suggest that gestating females exposed to dioxin can pass on adult onset disease conditions to their great grandchildren.
- Ancestral exposure to toxicants such as dioxin may be factor in disease etiology today.