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Publication

Transgenerational Actions of Environmental Compounds on Reproductive Disease and Identification of Epigenetic Biomarkers of Ancestral Exposures (2012) Manikkam M, Guerrero-Bosagna C, Tracey R, Hague Md, Skinner MK, Plos One 2012;7(2):e31901.

Summary

The epigenetic transgenerational actions of environmental compounds and relevant mixtures were investigated with the use of pesticide, plastic, dioxin and hydrocarbon mixtures. After a transient exposure of an F0 gestating female rat during embryonic gonadal sex determination, the F1, F2 and F3 generation progeny pubertal onset and gonadal function were assessed. Transgenerational disease phenotypes observed included early onset female puberty, increased spermatogenic cell apoptosis, and decreased ovarian primordial follicle pool size. Differential DNA methylation of the F3 generation sperm promoter epigenome was examined. Epigenetic biomarkers for environmental exposures were identified that were distinct among the different exposures. Epigenetic transgenerational inheritance of disease states were induced by a variety of different classes of compounds and epigenetic biomarkers may allow for the assessment of specific ancestral environmental exposures.

Highlights

- First demonstration that number different classes of environmental toxicants can promote epigenetic transgenerational inheritance of disease.
- First demonstration that dioxin and hydrocarbon (jet fuel) and pesticide (permethrin and DEET) can promote epigenetic transgenerational inheritance which may impact populations previously exposed.
- Identified epigenetic biomarkers that were specific for exposure, suggesting ancestral exposures could be assessed with exposure specific epigenetic biomarkers.
- Identification of unique genomic feature associated with the epimutations identified, and may be used to identify future biomarkers.
- Provides further support for environmentally induced epigenetic transgenerational inheritance of adult onset disease.

Impact

Toxicology- Provides proof of concept epigenetic biomarkers may identify specific exposures that can be used to diagnose exposure, subsequent health impacts and use molecular markers for toxicological studies. This may revolutionize the field of toxicology by providing more accurate biomarkers.

Health and Disease- Demonstrates adult onset disease may in part be due to ancestral exposures mediated through epigenetic changes in the germ line (sperm). Suggests the origins of disease may be due to alterations in the epigenomes from ancestral or early life exposures. The etiology of disease will involve epimutations and altered epigenetics.

Biology- Suggests environmentally induced alterations in epigenetics will have significant impact on early development that alter adult physiology of an individual. Epigenetics and environmentally induced epimutations will have a significant role in biology.