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Environmental exposure induced Epigenetic Transgenerational Inheritance of Neurological Disease: Generational Disease Etiology

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Transgenerational effects of environmental exposures of abnormal nutrition, stress, or toxicants significantly amplify the biological impacts and health hazards of these exposures. One of the most sensitive periods to exposure is during fetal gonadal sex determination when the germ line is undergoing epigenetic programming and DNA re-methylation occurs. Previous studies have shown that toxicants (e.g. glyphosate) can cause an increase in adult onset disease such as kidney, prostate, ovary and infertility disease, cancers, obesity and behavior abnormalities. Interestingly, this effect is transgenerational (F1, F2, F3 and further generations) and due to a permanent (imprinted) altered epimutation of the germline. The transgenerational epigenetic mechanism appears to involve the actions of an environmental exposure at the time of sex determination to permanently alter the epigenetic (e.g. DNA methylation) programming of the germ line that then alters the transcriptomes of developing organs to induce disease susceptibility and development transgenerationally. In addition to DNA methylation, alterations in sperm ncRNAs and histone retention have also been observed. A variety of different environmental compounds have been shown to induce this epigenetic transgenerational inheritance of disease including: fungicide vinclozolin, plastics BPA and phthalates, pesticides, DDT, dioxin, hydrocarbons and herbicides like atrazine and glyphosate. Interestingly, exposure specific epigenetic alterations were observed between the specific exposures. Recently we have identified in human's epigenetic biomarkers for parental germ cell transmission of offspring disease states such as infertility, autism and arthritis. The suggestion that environmental exposures and toxicants can reprogram the germ line to induce epigenetic transgenerational inheritance of disease (e.g., neurological abnormalities), is a new paradigm in disease etiology, and indicates generational disease etiology needs to be assessed in the future.

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