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ENVIRONMENTAL SIGNALING AS A MODEL TO INTEGRATE DIVERSE ENVIRONMENTAL FACTORS AT THE MECHANISTIC LEVEL

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Abstract: Currently, environmental determinants of disease or dysfunction are usually viewed as independent contributions to an overall process with little or no common mechanistic underpinning. The concept of environmental signaling may help integrate multiple inputs from diverse sources. Environmental signaling is built on the study primarily of endocrine disrupting chemicals (EDC), which comprise a class of environmental agents that mimic or block hormones involved in homeostasis and reproductive function in many classes of vertebrates including humans. The most prominent hormonal activity expressed among environmental chemicals is that of the female sex hormone, estrogen. Many chemicals of diverse structures have been reported to be estrogenic. Among these, the globally persistent chlorinated pesticides, like DDT and methoxychlor, and the ubiquitous component of plastics, bis-phenol A (BPA) have been of concern both for human exposure as well as documented adverse effects on reproduction and development in humans and wild life. Studies in our lab have shown that various estrogenic chemicals can alter the fate of cells via epigenetic mechanisms ranging from DNA methylation changes to altered profiles of micro-RNA production and receptor co-regulator recruitment. Recently, results from other labs have described similar alterations in the epigenome associated with heavy metals and even trauma. In this paper, we develop a mechanistic construct for integrating diverse environmental signaling inputs that have long-term functional outcomes on health and disease.

Key words: endocrine disruption, EDC, cellular signaling, human stem cells, whole genome RNA-sequencing, Epigenomics, trauma, heavy metals, chlorinated hydrocarbons, integration

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