PhD Dissertation
Department of Environmental Science and Policy
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Defense Date and Time: November 17, 2017 @ 10:00AM
Defense Location: David King Hall Room DK3006
Title: *Caenorhabditis Elegans* as a Model to Determine the Molecular Effects of Plausible Environmental Risk Factors of Breast Cancer

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ABSTRACT

Cancer is a multi-faceted disease that may involve many different tissues of various origins. Environmental factors have been identified as agents of concern for carcinogenesis, but there is little known about the molecular interactions in the cell that lead to transformation from normal to malignant. Nematodes are among the model organisms recently being utilized to expand our understanding of oncogenesis. About 60-80% of human genes have an orthologue in the genome of *C. elegans.*

This study aimed to evaluate expression (up-regulation/down-regulation) of *C. elegans'* orthologues for genes associated with breast carcinoma progression in nematodes exposed to plausible toxins and compare that to control animals in order to develop a network of molecular interactions which connect the toxin to the observed gene expression changes. We profiled the following orthologues in *C. elegans*: AIR-1, PIG-1, CUL-1, FZR-1, CPAR-1, HCP-3, HCP-4, HCP-6, KNL-1, KNL-3, JUN-1, BRC-1, BRC-2, CEP-1, MML-1, SLO-1, and SLO-2. The following potentially carcinogenic agents were studied for their impact on genetic expression: Bisphenol A, atrazine, DDT, beta-Estradiol, glyphosate, and DMSO. These toxins were diluted to 50-0.0001mM concentrations, and *C. elegans* were grown in these environments for 7 days at the LC10 concentrations of each toxin. Toxin-driven gene expression shifts were quantified using qPCR. The up-regulation of HCP-3 and BRC-1 in atrazine, the up-regulation of BRC-1 in DDT and down-regulation of CEP-1 and MML-1 in DDT, the up-regulation of HCP-3 in b-Estradiol, the down-regulation of CUL-1, FZR-1, BRC-2, CEP-1, MML-1, and PIG-1 in glyphosate, the up-regulation of HCP-3 and BRC-1 in glyphosate, and the down-regulation of JUN-1 in DMSO were evident. The connections between each toxins and each carcinogenesis-related gene responding to the toxin were analyzed using Pathway Studio. In each case, this analysis supported environmental influence studied. These results indicate that even at very small concentrations that we would expect in the natural environment, these omnipresent toxins may exert health impacts.