Development of Transcriptomics-Based Biomarkers for Selected Endocrine Disrupting Chemicals in Zebrafish (*Danio Rerio*)

Rong-Lin Wang, David Bencic, Adam Biales, Robert Flick, Jim Lazorchak, Daniel Villeneuve, Gerald Ankley

Genome-wide transcriptional profiling by microarrays provides a powerful platform for gene expression-based biomarker discovery. After their wide acceptance in human disease diagnosis, prognosis, and drug discovery, these gene signatures are increasingly being adopted for environmental toxicology applications as well. Built upon our previous work in zebrafish of reverse-engineered transcription factor (TF) networks and their statistical linkage to various treatment conditions of endocrine disrupting chemicals (EDCs), a systematic, computationally-intensive search using genetic algorithm coupled with support vector machine was conducted for candidate gene signatures capable of distinguishing individual chemical treatment conditions from their controls. Microarray data from zebrafish brain (male, female, or combined), ovary, and testis were analyzed. The search within each tissue type was either confined to hundreds of individual TF networks significantly associated with EDCs of differing mechanisms/modes of action, or across the entire genome. In agreement with our previous findings, tissue type was found to be critical to biomarker search. Brain yielded most candidate gene signatures, followed by ovary and testis. By chemical, prochloraz had the greatest number of candidates, then flutamide, fipronil, and enthinyl estradiol. A subset of these candidates will be evaluated using an independently derived microarray dataset generated from additional EDC-exposed zebrafish samples.