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Abstract title:

Derivation of tissue-specific functional gene sets to aid transcriptomic analysis of chemical impacts on the teleost reproductive axis.

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Oligonucleotide microarrays are a powerful tool for unsupervised analysis of chemical impacts on biological systems. However, the lack of well annotated biological pathways for many aquatic organisms, including fish, and the poor power of microarray-based analyses to detect differential expression of individual genes can limit the ability to infer and understand chemical effects based on transcriptomic data. Here we report on the supervised assembly of a series of tissue-specific functional gene sets intended to aid transcriptomic analysis of chemical impacts on the teleost reproductive axis. Preliminary supervised gene sets were identified based on a graphical systems model of the teleost brain-pituitary-gonadal (BPG) (+liver) axis. Because most microarray analyses are conducted with RNA extracted from individual tissues, tissue-specific gene sets were assembled based on current understanding of the dominant functional role of the coded protein in regulating fish reproduction. Within tissue subsets, gene sets were further organized into functional groups. For example, within ovary, specific gene subsets for steroid biosynthesis, cholesterol uptake, processing, and transport, oocyte maturation, etc. were identified. Functional subsets may be analyzed independently or lumped by tissue. Gene sets assembled based on supervised analyses were then extended by incorporating nearest neighbor genes identified from mutual information- or correlation-based transcriptional networks. The gene sets constructed as part of this work are anchored in our current understanding of important features of teleost reproduction, facilitating the ability to understand the physiological relevance of significant impacts on their expression. Additionally, because the gene sets can be used to conduct statistical analyses based on effects on the gene set collectively, rather than on the individual component genes via gene set enrichment analyses (GSEA), their application should increase the statistical power to detect changes with functional relevance. Results of this work are intended to enhance the utility of transcriptomic data for mechanistic ecotoxicology research. *The contents of this abstract neither constitute nor reflect official US EPA policy.*