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Approaches for Inferring Associations between Chemical Exposures and Biological Effects for Field-exposed Organisms.

Title:

Application of Supervised and Unsupervised Tools to Direct Effects-Based Monitoring Efforts in the Great Lakes Areas of Concern: Maumee River, Ohio.

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Abstract: (2500 character limit including spaces)

Application of Unsupervised Tools to Direct Effects-Based Monitoring in the Great Lakes Areas of Concern: Maumee River, Ohio.

Effects-based approaches that employ molecular and tissue level tools to detect and characterize biological responses to contaminants can be a useful complement to chemical monitoring approaches. When the source/type of contamination is known, a predetermined, or supervised, set of assays, linked to key-events within adverse outcome pathways (AOPs), can be employed to generate weight of evidence linking biomarkers with potential hazards of regulatory concern (reproduction, mortality, development). Where complex mixtures of industrial, agricultural, and municipal contaminants are present, tools that scan a broad array of biological responses (unsupervised tools) provide a means to survey biological effects of a sample or site-specific exposure, allowing appropriate supervised assays/endpoints to be selected for subsequent monitoring. This approach was used for a series of sites within the Maumee River Great Lakes Area of Concern (AOC). Pollution in the Maumee River AOC is historical and current and stems from industrial, agricultural and municipal sources. Sites were selected to target specific sources (e.g., waste water treatment plants (WWTP), industrial, and urban outflows) and up- or down-stream gradients relative to those point sources of contaminant input. Caged fathead minnows deployed for four days at each site and water samples were collected for bioassay and chemical analyses (legacy compounds and chemicals of emerging concern). Two unsupervised approaches were employed. First, chemistry data were used to identify potential chemical-gene interactions. Second, high-throughput screening was performed, using a subset of assays utilized by US EPA Toxcast. Results were used to identify molecular pathways and targets perturbed by surface waters from the study sites. A number of endocrine-related responses were observed and targeted with supervised assays associated with reproductive AOPs. Gene expression (e.g., vtg, cyp3a), T47D estrogenicity bioassay, and plasma hormone levels showed changes in activity at the WWTP and immediate downstream sites. Other molecular targets identified included glucocorticoid receptor for which supervised assays were developed. Overall, effects-based monitoring using this unsupervised to supervised approach provides a means of understanding the biological consequences of complex contamination within an aquatic system. *The content of this abstract neither constitutes, nor necessarily reflects, US EPA views or policy.*