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Track: Identification and prioritization of emerging contaminants

Session: Developing end-points and effects-based methodologies for characterization of emerging pollutants at relevant exposure concentrations.

Title: Novel approaches to effects-based monitoring: 21st century tools for bio-effects prediction and surveillance

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Effects-based monitoring (EBM) has been employed as a complement to chemical monitoring to help address knowledge gaps between chemical occurrence and biological effects. We have piloted several pathway-based approaches to EBM, that utilize modern bioinformatic and high throughput screening tools help establish associations between aggregate environmental exposures and biological effects. As part of our investigations, caged fathead minnows (FHM, *Pimephales promelas*) were deployed concurrently with temporally integrated water samplers. Composite water samples were analysed for 137 compounds including a variety of wastewater indicators, pharmaceuticals, and steroid hormones. Predictive tools were used to develop testable hypotheses regarding potential biological effects in caged FHM based on contaminants present in the composite samples. Specifically, information from the Comparative Toxicogenomics Database and STITCH was used to identify reported biological interactions between detected chemicals and gene/protein targets reported to be modulated by each chemical. Predicted gene/pathway interactions were compared with differentially expressed genes observed from microarray analysis of caged FHM liver. Significant ($p < 0.0001$) overlap was observed between predicted gene interactions and observed differential expression. Additionally, high-throughput in vitro assays (HTP) were used to screen environmental water extracts from two Great Lakes tributaries (n = 16 samples) for biological activity. Samples were screened for chemical interactions with over 90 different transcription factors and 48 nuclear receptors using the Attagene subset of assays employed in the US EPA ToxCast Program. The number of targets/pathways impacted varied significantly across sites. These unsupervised results were compared against targeted in vitro assays (i.e. estrogenic activity) with good agreement between specific gene interaction and in vitro activity. Chemical concentrations were also compared against potencies reported in the ToxCast database to develop a risk based prioritization of chemicals observed at each site. Both the predictive chemical-gene interaction network and bio-effects surveillance using HTP show significant promise as 21st century tools that complement classical chemical monitoring and can help direct hypothesis-driven EBM. *The contents of this abstract neither constitute, nor necessarily reflect, official US EPA policy.*