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Application of High-Throughput Screening and High-Content Imaging in Environmental Toxicology

Abstract Title:

Exploring the Potential Utility of High-throughput Bioassays Associated with US EPA Toxcast Program for Effects-based Monitoring and Surveillance

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Environmental monitoring and surveillance strategies are essential for identifying potential hazards of contaminant exposure to aquatic organisms. Chemical monitoring is effective for chemicals with well characterized hazards and for which sensitive analytical methods are available. Effects-based strategies provide a useful complement to chemical monitoring. Effects-based monitoring and surveillance utilizes various tools to identify the potential biological consequences to environmental contaminant exposures. Monitoring approaches use targeted assays for which a hazard of concern has been identified. However, this does not allow for identification of other targets that can be indicative of other hazards, limiting the utility of targeted approaches for open-ended surveillance purposes. High-throughput assays can provide an effective approach for screening a wider range of biological targets. To test this concept, we employed the Attagene subset of assays utilized for the US EPA Toxcast Program to screen selected environmental samples for biological activity. The Attagene assays screen for chemical interactions with different transcription factors. In the Fall of 2012, composite, ambient, water samples were collected at four locations, each with varying proximity to a wastewater treatment plant, within the St. Louis River Area of Concern, MN. Instrumental analyses were used to determine the occurrence of various wastewater indicators, human pharmaceuticals and steroid hormones in the samples and solid phase extracts, reconstituted in DMSO, and were screened in the Attagene assays. Of the 137 analytes measured by instrumental analysis, 72 of the analytes had been run in Toxcast. At any particular location, the number of analytes detected ranged from 13 to 44 and greater than half of the chemicals detected at any location had response profiles in Toxcast. The number of gene targets significantly impacted in the Attagene assays varied substantially across locations. However, all of the gene targets identified at each location could be explained by chemicals that have Toxcast response profiles. The gene targets identified using this unsupervised approach can now be used to direct future

targeted analyses to examine trends over time at these locations. The results highlight the use of high throughput assays for surveillance and identifying gene targets that can be useful for subsequent site-specific monitoring. *The contents of this abstract neither constitute, nor necessarily reflect, official US EPA policy.*