

Adverse Outcome Pathways and Extrapolation Tools to Advance the Three Rs in Ecotoxicology.

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Adverse outcome pathways (AOPs) are conceptual frameworks for identifying and organizing predictive and causal linkages between cellular-level responses and endpoints conventionally considered in ecological risk assessment (e.g., effects on survival, growth/development, and reproduction). The proposed paradigm for “Toxicity Testing in the 21st Century” advocates the use of mechanistically-based, high-throughput *in vitro* assays as a potential cost effective and scientifically-sound alternative to some whole animal hazard testing. To support the development of this approach, there is a recognized need to (1) identify and catalog common adverse outcome pathways (AOPs) and (2) based on these pathways, strategically develop appropriate batteries alternative assays. Furthermore, there is a need to develop a variety of extrapolation tools which can translate *in vitro* assay data into credible predictions of *in vivo* outcomes, preferably for a wide range of organisms. This presentation will highlight the utility of the AOP concept and discuss extrapolation tools needed to define and expand the applicability domains of mechanistic high throughput *in vitro* assay data, with specific emphasis on how these approaches can support the reduction, refinement, and/or replacement of animal use in ecotoxicology and ecological risk assessment.