Session: Cutting-edge strategies for utilizing molecular information as the basis for cross-species extrapolation

Title: Cross-species extrapolation of an adverse outcome pathway for ecdysteroid receptor activation

Authors: Carlie A. LaLone, Daniel L. Villeneuve, Gerald T. Ankley, Ingebrigt Sylte, Tore Høgåsen, and Knut Erik Tollefsen

University of Minnesota; Water Resources Center; College of Food, Agricultural and Natural Resource Sciences; 1985 Buford Avenue, St. Paul, MN 55108 USA
LaLone.Carlie@epa.gov

U.S. Environmental Protection Agency, Office of Research and Development, National Health and Environmental Effects Research Laboratory, Mid-Continent Ecology Division; 6201 Congdon Blvd., Duluth, MN 55804, USA
Villeneuve.Dan@epa.gov
Ankley.Gerald@epa.gov

Universitetet I Tromsø, The Arctic University of Norway; Postboks 6050 Langnes 9037 Tromsø, Norway
ingebrigt.sylte@uit.no

Norwegian Institute for Water Research (NIVA), Gaustadalléen 21, N-0349 OSLO, Norway
tore.hogaasen@niva.no
knut.erik.tollefsen@niva.no

Different invertebrate nuclear receptors serve as targets for a variety of environmental contaminants. One of these is the ecdysteroid receptor (EcR). Due to the important role of this nuclear receptor in regulating development and reproduction in invertebrates, particularly during the molting process, literature mining and focused toxicity studies are underway to construct an adverse outcome pathway (AOP) for EcR activation leading to developmental and reproductive dysfunction, and mortality using the cladoceran, *Daphnia magna*, as a model species. A key element of this AOP development activity is defining the taxonomic domain of applicability beyond cladocerans. To efficiently address this component, the Sequence Alignment to Predict Across Species Susceptibility (SeqAPASS) tool allows for a streamlined evaluation of protein conservation across species through examination of primary amino acid sequence (including ortholog detection), the ligand binding domain, and individual residue alignments to predict relative intrinsic susceptibility. The individual amino acid residue alignments for EcR were conducted using information obtained from homology models and molecular docking studies. SeqAPASS results provide evidence of EcR conservation across branchiopoda, insecta, chilopoda, arachnida, malacostraca, and maxillopoda organism classes, therefore aiding in defining the taxonomic domain of the putative AOP. *The contents of this abstract neither constitute nor reflect official US EPA policy.*