



EcoToxChip: A TOXICOGENOMICS TOOL FOR CHEMICAL PRIORITIZATION AND ENVIRONMENTAL MANAGEMENT

Nil Basu¹, Doug Crump², Markus Hecker³, Jessica Head¹, Gordon Hickey¹, Natacha Hogan³, Steve Maguire¹, Jianguo Xia¹
 1-McGill University, Montreal, Canada; 2-Environment and Climate Change Canada, Ottawa; 3-University Saskatchewan, Saskatoon, Canada
 Contact: info@ecotoxchip.ca; www.ecotoxchip.ca; www.ecotoxplorer.ca

CHALLENGE

- Chemical contamination threatens the health of humans and wildlife globally
- Regulatory agencies and businesses are tasked to manage chemicals but are challenged:
 - many chemicals (e.g., 4.3K in Canada, 84K in USA, 101K in EU) need to be tested within short timeframes;
 - mandate to monitor many complex environmental samples (e.g., sediment, water, effluents);
 - testing is costly, time-consuming, and uses many animals;
 - tests on limited model species poorly predict risk in native species of concern.

Urgent worldwide demand for improved testing tools that are more efficient, affordable, flexible, predictive, and less dependent on live animal studies

OPPORTUNITY

Global paradigm shift in toxicity testing from historical whole-organism testing to mechanistic studies

Human Health:

- U.S. NRC's "Toxicity Testing in the 21st Century-Vision and Strategy"
- New approach methods (e.g., toxicogenomic tools, alternative testing strategies) and stakeholder acceptance helping to transform the field

Ecological Risk Assessment:

- Avian ToxChip qPCR array developed by Environment and Climate Change Canada researchers via commercial partnership:
 - used to screen and prioritize chemicals; study variably contaminated sites
 - embraced by Canadian regulators, environmental monitoring programs, and the scientific community

PROJECT OBJECTIVES

To develop, test, validate, and commercialize qPCR arrays (**EcoToxChips**) which consist of 384 genes covering key toxicity pathways of regulatory concern, and a data evaluation tool (**EcoToxXplorer.ca**) for the characterization, prioritization and management of environmental chemicals and complex mixtures of regulatory concern.

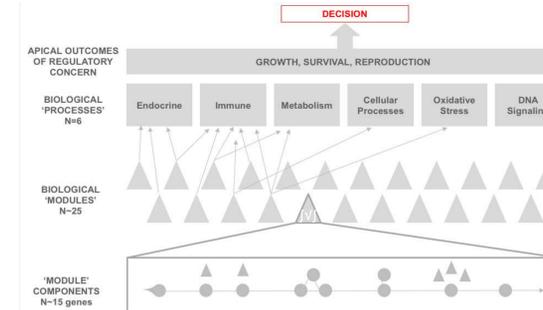
PROJECT DELIVERABLES

- EcoToxChips** for three key vertebrate model species used globally in ecological risk assessment (fathead minnow, Japanese quail, *Xenopus laevis*; fish, bird, frog);
- EcoToxChips** for three native species of commercial, recreational, and Aboriginal concern (rainbow trout, double-crested cormorant, northern leopard frog);
- EcoToxXplorer.ca** is an online data evaluation tool that provides functions to allow users to upload EcoToxChip data and interpret results; and
- Technical Guidance Document** is informed by our GE³LS (social sciences) research and will be a government-vetted resource to advise end-users on how to adopt EcoToxChips.



ECOTOXCHIP DESIGN & UPDATES

- EcoToxChip designed through design thinking steps (empathize, define, ideate, prototype, test) to maximize potential of end-user adoption of project deliverables



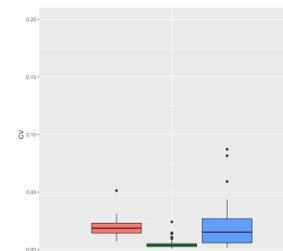
- v0.1 (alpha): internal Tier 1 tests in core project labs and Qiagen to assess technical performance
- v1.0 (beta): used in the Tier 2 validation study with core study partners (e.g., ring test, cross-platform performance)
- v2.0 (gamma): tested by a larger community of users

ECOTOXCHIP VALIDATION

Tier 1 Technical validation study (inter- & intra-lab)

- we tested 45 v0.1 JQ EcoToxChip plates (3 test sites x 3 samples x 5 replicates of each sample)
- cDNA test samples derived from individual JQ livers from control and chlorpyrifos-exposed; another cDNA sample was diluted
- each participating lab ran samples using in-house approaches
- in total, data were available from 17,280 measurement wells including measures of 361 gene targets across 16,245 wells, 16 housekeeping genes (720 wells in total across all plates) and 315 control parameters (e.g., positive PCR controls, GDC)

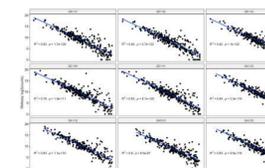
Boxplot of CV variance of housekeeping genes from 3 test labs. Inter- and intra-lab variation is less than 2.5% (median values). Similar results for the gene targets. Variance is much less than the 20% criteria noted by the MAQC program (y-axis limit).



Tier 2 Technical validation study (cross-platform)

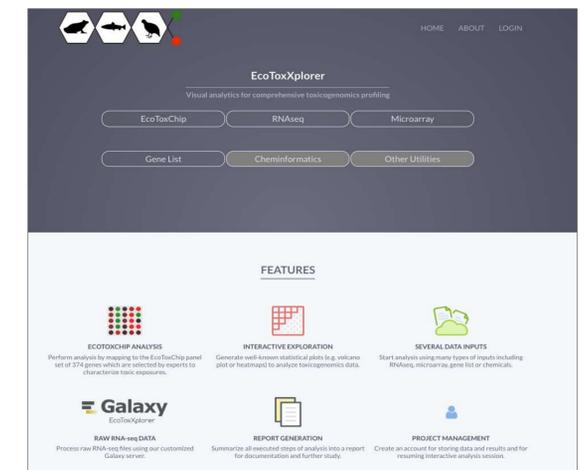
- EcoToxChip QCPR results (CT values) were compared against RNAseq counts data for n=9 v0.1 JQ EcoToxChip plates

Scatterplots demonstrate high concordance between EcoToxChip qPCR results and RNAseq counts. The overall R² is 0.81 (R=0.9) which is above the MAQC reported value of R=0.69



EcoToxXplorer.ca

Try it out! Go to www.ecotoxplorer.ca



- Data upload from diverse sources (e.g., EcoToxChip, RNAseq, microarray)
- Enter key study details (e.g., exposure and apical outcomes) as per study reporting guidance documents
- Data QC options (e.g., control wells, housekeeping genes, normalization steps, cut-offs)
- Statistical analysis modules (e.g., benchmark dose-response, mode of action, tables)
- Visualizations (e.g., heat maps, volcano plots, radar and circus plots, EcoToxModules)
- Report generation
- Create account and save work

ACKNOWLEDGEMENTS

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Research Oversight Committee: Drs. Nancy Denslow (chair), Kevin Crofton, Daniel Schlenk, Roy Suddaby, and Carole Yauk

Core Partners: Government (Environment & Climate Change Canada, US Army Corps of Engineers, US EPA) & Business (SGS AXYS, Qiagen, Shell USA)

Intro Paper: Basu N, Crump D, Head J, Hickey G, Hogan N, Maguire S, Xia J, Hecker M. 2019. EcoToxChip: A next-generation toxicogenomics tool for chemical prioritization and environmental management. *Environ Toxicol Chem.* 38(2):279-288.

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