

BACKGROUND INFORMATION

Gene selection is guided by the OECD Adverse Outcome Pathway (AOP) Framework as well as our team's collective experiences, knowledge, and leadership in the scientific and regulatory fields. We favor genes that:

- A) Represent key toxicity pathway nodes that are related to apical measures of regulatory concern;
- B) Respond to key contaminants found in target sector activities (e.g., oil and gas, mining, wastewater);
- C) End-users (especially regulators) are familiar with to help ensure that results can guide decision-making

THE PROCESS OF GENE SELECTION

#1 - Toxicology Approach

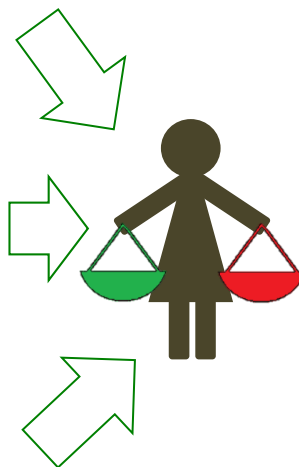
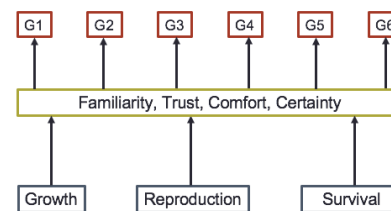
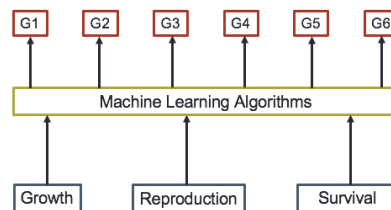
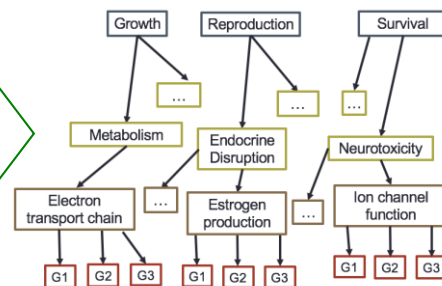
- Use data we generate from our exposure studies*
- Reviewed datasets within the group & literature
- Reviewed Reactome Pathway Database, Comparative Toxicogenomics Database, Pathcards, Qiagen, and the AOP-Wiki
- Organized genes into 3 levels: primary-(growth, reproduction, survival), secondary (biological processes), and tertiary (toxicity pathways)

#2 – Bioinformatics Approach

- Curate information from toxicogenomics databases (e.g., TG-Gates Open, Comparative Toxicogenomics Database, LINCS L1000) → Toxmine.ca knowledge base
- Machine learning to select genes that best predict apical measures linked to survival, growth, reproduction

#3 – Regulatory Approach

- Continual engagement with Canadian regulators through meetings, interviews, exchanges
- Systematic polling of gene lists to rank and prioritize



TAKE AWAY

Evidence-based, expert-guided gene list will be developed using multiple scientific approaches that mutually reinforce one another. The gene list will have high predictive power, founded on biological understanding, and be trusted by end-users.

References

Reactome.org
 CTDbase.org
 AOPWiki.org
 Pathcards.genecards.org
 Sabiosciences.com/PCRRarrayplate

Notes

Briefing note 5.1 was developed for the Genome Canada-funded project "EcoToxChip: A Toxicogenomics Tool for Chemical Prioritization and Environmental Management"
 www.ecotoxchip.ca / @ecotoxchip
 Project Leads: Nil Basu (McGill University), Doug Crump (Environment & Climate Change Canada), Markus Hecker (University of Saskatchewan)