

Dr. Robert Tanguay
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Rapid phenotypic screening in zebrafish: High content data for 21st century toxicology

The current paradigms used to evaluate chemical bioactivity are woefully insufficient. A major change in toxicity testing was proposed by the U.S. National Academy of Sciences Report, "Toxicity Testing in the 21st Century". Ongoing international efforts are focused on implementing high throughput *in vitro* screens, but the lack of biological complexity of these cell-based assays has limited the value of the data. A crippling limitation is that there is insufficient whole animal toxicity data to enable predictive modeling. We propose that rapid whole animal toxicity testing is needed to provide relevant phenotypic anchors. Vertebrate embryonic development is an ideal stage to explore chemical bioactivity because this enormously complex and dynamic period requires the full repertoire of molecular signaling. We have developed efficient *in vivo* phenotypic screening assays, using embryonic zebrafish, to assess chemical effects on behavior, morphology and gene expression. As a proof of concept, we obtained the EPA phase I and II Toxcast chemicals that consist of 1,078 compounds made up of pesticides, drugs, "green" chemicals, chemicals in cosmetics and other consumer products. We have successfully conducted the phenotypic screening procedure on all 1,078 compounds, and a summary of the results will be discussed.