Evaluation of Compatibility of ToxCast High-Throughput/High-Content Screening Assays with Engineered Nanomaterials

K. Houck[1], A. Wang[1]

[1] U.S. Environmental Protection Agency (EPA), National Center for Computational Toxicology, RTP, North Carolina, USA.

High-throughput and high-content screens are attractive approaches for prioritizing nanomaterial hazards and informing targeted testing due to the impracticality of using traditional toxicological testing on the large numbers and varieties of nanomaterials**.** The ToxCast program at EPA has used various high-throughput assays and developed computational tools to help assess potential toxicity and identify toxicity pathways of hundreds of traditional chemicals. The ToxCast phase I data are publicly accessible (1) and used by researchers to investigate links between chemicals and diseases (2). We investigated the compatibility of ToxCast cell-based high-throughput screening assays on engineered nanomaterials, with the ultimate goals of identifying toxicity/biological pathways affected by nanomaterials and finding correlations among nanomaterial physic-chemical characteristics, testing conditions, and nanomaterial toxicities/bioactivities.

We initially evaluated 15 nanomaterials and reference materials (4 nano-Ag with different coatings, 6 CNTs, nano-Au, AgNO3, micro-Ag, micro-quartz, and dispersant for a nano-Ag) on 6 assays. These 6 assays measured cell growth kinetics, transcription factor activity, cellular toxicity phenotypes, secreted and cell surface protein profiles, and cellular signaling pathways in various cultured cells, as well as developmental toxicity in zebrafish embryos (EPA). Our preliminary results showed that, at the same mass concentration, AgNO3 was most toxic, followed by nano-Ag, while CNT, nano-Au, micro-Ag and micro-quartz were not toxic in most cell-based assays. Similarly, AgNO3 was more toxic to zebrafish embryos than nano-Ag, and no obvious dose-dependent developmental toxicity was observed for any of the materials under tested conditions. Nano-Ag, micro-Ag and AgNO3 data are consistent with other studies, while the lack of detected CNT toxicity may be due to the type of CNT used as well as limited compatibility of current assays for CNT. In terms of pathways affected, AgNO3 and nano-Ag elicited changes associated with oxidative stress/antioxidant, metal exposure, heat shock, stress, DNA damage, and apoptosis, indicating that the use of high-throughput screenings can illustrate mechanistic information. We continue testing other classes of nanomaterials, such as nano-TiO2, nano-ZnO, and nano-SeO2, and evaluating the compatibility of high-throughput/high-content screening assays with these nanomaterials. *This abstract may not necessarily reflect U.S. EPA policy.*

References

(1) http://www.epa.gov/ncct/toxcast/
(2) http://cerhr.niehs.nih.gov/evals/diabetesobesity/