

Integrated Testing Strategies for Developmental Neurotoxicity

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The potential for developmental neurotoxicity (DNT) following exposure to environmental chemicals remains a high public health priority due to concerns that recent increases in the prevalence of neurological disorders in children (e.g., ADHD, autism spectrum disorders) may in part be due to chemical effects. Thus, the need for reliable, relevant, and efficient screening tools to identify, prioritize, and evaluate chemicals for their potential to induce DNT is well recognized.

The National Toxicology Program (NTP), as part of Tox21 Phase III's effort to "Improve on Biological Coverage and Human Relevance", created a 80+ compound library of known DNTs, developmental toxicants (DTs), and adult neurotoxicants (NTs), as well as compounds of interest to the NTP with unknown DNT, DT or NT activity (e.g., flame retardants, polycyclic aromatic hydrocarbons). This library was made available to researchers interested in evaluating high throughput and/or high content cell-based and alternate animal model systems for DNT.

A workshop was conducted in September 2017 that brought together investigators from academia, industry, and the government who evaluated this library in their respective laboratories using assays that informed on some aspect of DNT. The purpose of this workshop was to discuss how different test methods could be integrated into a "battery" of medium- and high-throughput cell-based models, and alternative animal systems to prioritize compounds for further *in vivo* testing and/or to complement current regulatory DNT guideline studies. The discussion focused on the advantages and limitations of the different models as screening tools, identifying knowledge gaps, and characterizing different approaches for data analysis that could be used in comparing outcomes across disparate datasets.