

Incorporating Ontologies into High-Throughput Screening Assay Annotations to Facilitate Interpretation and Increase Data Use

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In vitro high-throughput screening (HTS) assays provide valuable mechanistic information, but it is often unclear how data from these assays relate to toxicological endpoints such as developmental toxicity and endocrine disruption. We created an annotation scheme for curated HTS assays, available through the Integrated Chemical Environment (<https://ice.ntp.niehs.nih.gov/>), that can provide toxicological context to these mechanistic data to supplement biological annotations provided with HTS assays. This scheme uses controlled vocabularies within the framework of ontologies to ensure data are more findable, accessible, interoperable, and reusable (FAIR). Briefly, we evaluated technical and biological information provided by the U.S. Environmental Protection Agency's invitrodb v3.5 for Tox21/ToxCast assays and chose biological and toxicological process terms from the Open Biological and Biomedical Ontology (OBO) Foundry. We mapped assays to mechanistic target (MT) and mode of action (MOA) terms relevant to toxicological endpoints (e.g., MT terms include "histone modification", while MOA terms include "epigenetic process"). Subject matter experts curated and reviewed these terms to ensure the annotation details were consistent and appropriate. The inclusion of ontology terms produced more refined terminology, and generally increased unique annotation terms. We also established structured relationships between concepts using parent and child terminologies. The established annotations will increase interoperability across databases and aid harmonized reporting. Overall, these efforts will increase accessibility and interpretation of FAIR HTS data to identify data gaps, better inform chemical hazard assessments, and provide additional resources for investigating toxicologically relevant mechanistic assay data. This project was funded by NIEHS under Contract No. HHSN273201500010C.