

Human Pluripotent Stem Cell-Based Assay Predicts Developmental Toxicity Potential of ToxCast Chemicals

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Worldwide initiatives to screen for toxicity potential among the thousands of chemicals currently in use require inexpensive and high-throughput *in vitro* models to meet their goals. The devTOX *quickPredict platform* is an *in vitro* human pluripotent stem cell-based assay used to assess a wide range of chemicals (i.e., pharmaceutical, environmental and industrial compounds) for potential developmental toxicity affecting differing developmental lineages. The assay is being used by the United States Environmental Protection Agency (EPA) to screen the ToxCast chemical library in support of Tox21. A two tier testing strategy was employed to screen a total of 1066 chemicals in human pluripotent stem (hES) cells, guided by the AC50 (half-maximal activity concentration) across multiple cytotoxicity assays in ToxCast. To date, 347 chemicals were tested in an eight concentration dose-response in this assay. Spent media was collected to measure changes in biomarkers of developmental toxicity (ornithine and cystine) together with cell viability measurements. A preliminary analysis revealed a signal in 15-18% of all ToxCast chemicals tested based on a default threshold biomarker ratio (ORN/CYSS) ≤ 0.88 . In most of these cases the concentration producing an effect in the biomarker ratio fell below the AC50 for cell viability. Model performance (28 compound training set) showed a balanced accuracy of 82% (sensitivity 0.71, specificity 1.0). The data presented here demonstrate the utility of the assay in screening and prioritizing compounds for further testing. (Disclaimer: this abstract does not reflect EPA policy).