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Characteristics of the ToxCast In Vitro Datasets from Biochemical and Cellular Assays

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Measurement of perturbation of critical signaling pathways and cellular processes using in vitro assays provides a means to predict the potential for chemicals to cause injury in the intact animal. To explore the utility of such an approach, a diverse collection of 467 assays across nine different technologies was used to profile the activity of 320 bioactive compounds, having known toxicities, from the EPA's ToxCast phase I chemical library. The assays consisted of a wide variety of technologies and endpoints, both biochemical and cell-based, with the latter using both cell lines and primary cells. Assays ranged from measuring direct binding to potential toxicity targets, e.g. ligand binding to estrogen receptor-α, to downstream signaling targets, e.g. gene expression analysis, to complex cellular phenotypes, e.g. microtubule stability. Many targets or pathways were covered by two or more assays using different technologies to provide information on important differences in screening approaches. The majority of the assays target human (263) or rat (65) proteins or cells. Chemicals were tested in either concentration-response format initially or first screened at a single, fixed concentration with concentration-response screening following for any chemical defined as active. Inclusion of duplicate or triplicate samples of eight of the chemicals provided a means of evaluating the reproducibility of various assay types. Lowest Effective Concentration (LEC) or AC50s were determined for all active chemicals in each assay and comprise the data set being used for predictive modeling. *This work was reviewed by EPA and approved for publication but does not necessarily reflect official Agency policy.*