Correlation of In Vitro Cytotoxicity and Acute Toxicity

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Although cytotoxicity assay data cannot currently be used to replace animal tests for predicting acute hazard classes, two in vitro cytotoxicity assays have been validated to estimate starting doses for acute oral toxicity tests in animals. To more broadly investigate the utility of cytotoxicity and other in vitro assays to predict acute lethality, high throughput screening (HTS) data from the ToxCast and Tox21 programs was used to predict LD50 values and binary toxicity categories (toxic vs. nontoxic). To further investigate the correlation of in vitro to in vivo results, we used reverse toxicokinetics to estimate equivalent administered doses from in vitro effective concentrations. These analyses confirmed that no single in vitro assay can currently predict acute systemic toxicity in rodents and prompted us to evaluate approaches that combine assay results. This work was supported with U.S. Federal funds from NIEHS/NIH/HHS under Contract HHSN273201500010C.