

In Vitro Insights into Chemical Carcinogenesis

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The evolution in toxicology testing to high-throughput screening (HTS) assays provides rapid, cost-effective, broad biological coverage on thousands of chemicals against hundreds of human cellular and molecular targets. Assays from the Tox21 and ToxCast HTS programs have been mapped to gene and protein level targets, which have in turn been mapped to mechanistic pathways including cancer hallmarks and characteristics of carcinogens. Probabilistic models such as Bayesian networks can incorporate this data into biologically-based frameworks and provide chemical-specific predictions based on cancer-relevant in vitro bioactivity profiles. We investigate Bayesian networks trained on data from known carcinogens, using both naïve priors and informative priors based on systematic literature review results. The goal of this model is to provide probabilities that particular chemical exposures would result in carcinogenesis or in a biological environment favorable for tumor development.