

## Species-specific predictive models of developmental toxicity using the ToxCast chemical library

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EPA's ToxCast™ project is profiling the *in vitro* bioactivity of chemicals to generate predictive models that correlate with observed *in vivo* toxicity. *In vitro* profiling methods are based on ToxCast data, consisting of over 600 high-throughput screening (HTS) and high-content screening (HCS) assays, including embryonic stem cells and zebrafish embryos. The observed *in vivo* toxicity comes from 30 years worth of prenatal guideline studies of rodents and rabbits parsed into a publically available database, ToxRefDB. Due to distinct developmental differences, species specific models of developmental toxicity were built from the HTS data on the 309 ToxCast Phase I chemicals with balanced accuracies over 70%. Unique differences between the species specific models emphasized inflammatory signals in the rabbit model, and the retinoic acid receptor (RAR) and G-protein-coupled receptors (GPCRs) in the rodent model. The *in vitro* HTS profiles for 700 additional ToxCast Phase II chemicals, including failed pharmaceuticals, alternative plasticizers, and food additives are being used to validate and update the initial predictive models of developmental toxicity. These models have the potential to prioritize chemicals for further targeted toxicity testing and risk assessment, generate hypotheses about mechanistic pathways leading to adverse developmental outcomes, and reduce cost and increase throughput of chemical testing. *This abstract does not necessarily reflect US EPA policy.*