

## Species-Specific Predictive Signatures 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 signatures that correlate with observed *in vivo* toxicity. *In vitro* profiling methods from ToxCast data consist of over 600 high-throughput screening (HTS) and high-content screening (HCS) assays, including biochemical, cell-free and cell culture assays, along with embryonic stem cells and zebrafish embryos. These data are then anchored to the publicly available ToxRefDB database, which includes *in vivo* toxicity data from 30 years worth of prenatal guideline studies of rodents and rabbits. Due to distinct developmental differences, predictive signatures of developmental toxicity were built for each species and gave cross-validation balanced accuracies over 70% when using the 309 ToxCast Phase I chemicals. 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 aid in the prioritization of 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.