# Constructing Adverse Outcome Pathways for Developmental Toxicities

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This talk describes how to use information from genetic mouse models linked to phenotypic outcomes and ToxCast high throughput screening (HTS) data to construct adverse outcome pathways (AOPs) for developmental toxicities. Embryonic vascular disruption is presented as one example of AOP leading to a range of adverse prenatal outcomes. This AOP was built on molecular initiating events (MIEs) corresponding to genes from critical pathways (hypoxia/growth factor signaling, chemokine networks, ECM interactions and vessel remodeling/stabilization) with evidence of abnormal embryonic vascular development in the mammalian phenotype browsers of the Mouse Genome Informatics database (http://www.informatics.jax.org/). ToxCast HTS data for 25 assays mapping to targets in the AOP were used to prioritize >1000 chemicals for their potential to disrupt vascular development. A similar approach is being used to identify key MIEs and construct an AOP for developmental immunotoxicity and to prioritize compounds for further testing based on relevant ToxCast assays. Preliminary functional validation strategies of compound hazard predictions and AOP targets in transgenic zebrafish and human cell based assays are also discussed.