# Analysis of a ToxCast™ HTS Toxicity Signature

# for putative Vascular Disruptor Compounds

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## ABSTRACT

Recent studies have shown the importance of blood vessel formation during embryo development and the strong correlation to developmental toxicity. Several developmental toxicants, such as thalidomide, have been identified which specifically target the forming embryonic vasculature. In an analysis of ToxCast™ high-throughput screen (HTS) data from 467 assays and 309 chemicals a number of developmental toxicants were found to also disrupt *in vitro* assays for specific targets or cellular processes important to vasculogenesis and angiogenesis. The preliminary predictive signature built from ToxCast data for several *in vivo* developmental endpoints from EPA's ToxRefDB database includes a pro-inflammatory/anti-angiogenic chemokine signaling network, elements of the vascular endothelial growth factor (VEGF) signaling pathway, and the plasminogen activating system (PAS) of enzymes and growth factors mediating matrix remodeling and local signaling during blood vessel growth. We hypothesize that embryonic microvascular networks are targets for certain environmental compounds with teratogenic potential, and have identified a group of putative Vascular Disruptor Chemicals (pVDCs) from the ToxCast Phase I dataset.