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REVOLUTIONIZING TOXICITY TESTING FOR PREDICTING DEVELOPMENTAL OUTCOMES

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Characterizing risk from environmental chemical exposure currently requires extensive animal testing; however, alternative approaches are being researched to increase throughput of chemicals screened, decrease reliance on animal testing, and improve accuracy in predicting adverse outcomes. Newer in vitro and in silico approaches focus on predictive modeling of adverse outcome pathways (AOPs) using computational and high-throughput screening (HTS) data for thousands of chemicals and hundreds of HTS assays in EPA's ToxCast inventory. Virtual Tissue Models (VTMs) integrate empirical data with knowledge of embryological processes to simulate normal dynamic biological tissue structures relevant to specific AOPs. These VTMs built for developmental processes simulate multiscale disruptions in the system and provide a quantitative spatio-temporal prediction of how chemicals might impact embryo-fetal development. This approach is being used to evaluate chemical effects on development, such as disruption of blood vessel formation (angiodysplasia), palatal fusion (cleft palate), limb outgrowth (ectrodactyly), and urethral fusion (hypospadias). Applications of these computational approaches toward chemical prioritization, early lifestage exposure considerations, and hypothesis generation and mechanistic understanding will lead to sustainable solutions for predictive modeling of developmental toxicity. *This work was funded by the US EPA under its Chemical Safety for Sustainability Research Program but does not reflect US EPA policy.*