Conference title: American Society for Andrology, 2014 Annual Meeting
Session Title: Symposium on Innovations in Male Environmental Health Protection
Dates: April 4-8, 2014
Location: InterContinental Buckhead Atlanta, GA

REVOLUTION IN TOXICITY TESTING AND RISK PREDICTION FOR CHEMICALS IN THE ENVIRONMENT

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Addressing safety aspects of drugs and environmental chemicals relies extensively on animal testing; however, the quantity of chemicals needing assessment and challenges of species extrapolation require alternative approaches to traditional animal studies. 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) 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. Virtual embryo models integrate empirical data with embryological information to simulate dynamic biological tissue architectures relevant to specific AOPs. 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) among other systems. Simulations of endocrine and vascular pathways can be parameterized in this way, using in vitro data for chemical prioritization and early lifestage exposure considerations. *This work was funded by the US EPA under its Chemical Safety for Sustainability Research Program but does not reflect US EPA policy.*