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Submitted

on August 07, 10:50 AM

for sot2009

Proof

CONTROL ID: 533047

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Abstract Details

PRESENTATION TYPE: Invited Presentation

KEYWORDS: embryo development, systems biology, biological pathway networks.

DATE/TIME LAST MODIFIED: August 7, 2008, 10:50 AM

DATE/TIME SUBMITTED: August 7, 2008, 10:50 AM

Abstract

TITLE: VIRTUAL TISSUE MODELS IN DEVELOPMENTAL TOXICITY RESEARCH

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ABSTRACT BODY: Prenatal exposure to drugs and chemicals may perturb, directly or indirectly, core developmental processes in the embryo (patterning, morphogenesis, proliferation and apoptosis, and cell differentiation), leading to adverse developmental outcomes. Because embryogenesis entails a genomic program that orchestrates aggregate cell behaviors across time and space, a challenge for systems biology is to integrate data and knowledge from the genomic sciences into multi-scale models of developmental toxicity that can be translated into a regulatory context. Computational models of embryonic systems can be used to improve understanding of how the core developmental processes are wired together into genetic regulatory networks (GRNs) and cellular reaction networks (CRNs), and to progressively unravel the changes in these complex systems caused by toxicant exposure. The virtual embryo project (v-Embryo™) at the US EPA aims to build, over the long-term, a working computer model of an embryo through knowledgbase and simulation of toxicity pathways that are important for development (http://www.epa.gov/ncct/v-Embryo/). In the short-term, the technology focuses on specific virtual tissue prototypes to formulate hypotheses about how mechanisms at one scale (molecular) interact to produce higher level (tissue) phenomena, thus guiding research to build quantitative dose-response models that connect to the dynamics of the subtendant GRNs and CRNs. The v-Embryo™ aligns with high-throughput screening assays and systems biology research initiatives at the National Center for Computational Toxicology (NCCT), including ACToR, ToxCast™, and the Virtual Liver. [This work has been reviewed by EPA and approved for publication but does not necessarily reflect official Agency policy].