Multicellular Models of Morphogenesis

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EPA's Virtual Embryo project (v-Embryo™), in collaboration with developers of CompuCell3D, aims to create computer models of morphogenesis that can be used to address the effects of chemical perturbation on embryo development at the cellular level. Such computational (*in silico*) models can help unravel complex multicellular behaviors that underlie robust development of the embryo and also inform predictive models of dysmorphogenesis from the ToxCast™ project. Several CompuCell3D prototype models are being constructed and improved, including: (1) an angiogenesis vascular development model to recapitulate spatial and temporal tumor growth and help answer questions regarding the invasiveness of different morphologies; (2) a limb-bud model to analyze patterns of cell growth and death during polarized limb outgrowth and teratogenesis; and (3) an epithelial invagination model to examine key cellular behaviors during early eye development. The simulations are based on cells acting as agents, interacting with one another and within signaling gradients established in the system. A rules-based approach is implemented whereby different cell-types in the system are programmed to respond to known components in a biological circuit. Executing the program enables self-regulating behaviors and emergent phenotypes. Preliminary analysis shows the CompuCell3D cell based models can recapitulate specific morphogenetic events from rules-based dependencies, given the appropriate starting configuration and cellular behaviors. Efforts are underway to incorporate lesions in the ToxCast HTS data and build predictive models for developmental toxicity. [This work is approved by EPA but does not reflect official Agency policy].