

The Virtual Liver Project: Modeling Tissue Response To Chemicals Through Multiscale Simulation

The US EPA Virtual Liver Project is aimed at simulating the risk of toxic effects from environmental chemicals *in silico*. The computational systems model of organ injury due to chronic chemical exposure is based on: (i) the dynamics of perturbed molecular pathways, (ii) their linkage with adaptive or adverse processes leading to alterations of cell state, and (iii) the integration of the molecular and cellular responses into a physiological tissue model. This is being accomplished through two strategic initiatives: (a) a knowledgebase (KB) to logically model the relevant physiologic entities and their interactions at molecular, cellular and tissue scales; and (b) a multiscale agent-based simulation to predict the dose-dependent perturbations of pathways to chronic liver injury. In the short-term the project is focusing on a subset of molecular pathways stimulated by activation of nuclear receptors leading to hepatocyte hyperplasia. With continued stimulation this pathway may lead to the development of liver tumors. The long-term vision for the project is to provide estimates for the risk of injury due to different chemicals, across genders, life-stages and populations.

This work has been reviewed by EPA and approved for presentation but does not necessarily reflect Agency views.