

Representing Chemical-Induced Liver Injury for Multiscale Tissue Modeling

Novel biologically-based computational paradigms are vital for improving the accuracy, reducing animal testing and the cost for assessing the risk of environmental chemicals. The US EPA Virtual Liver Project is aimed at simulating the risk of toxic effects from environmental chemicals *in silico*. A multiscale computational model of hepatic biology will enable the simulation of normal and pathologic tissue responses in humans through the interplay between dynamic molecular and cellular pathways perturbed by long-term exposure to environmental chemicals. To develop a quantitative multiscale tissue model a semantic approach is being used to organize complex mode of action (MoA) and mechanistic information from literature, databases, and high-throughput biological studies. The project is currently focusing on the MoA for non-genotoxic cancer: persistent nuclear receptor activation leading to hepatocyte hyperplasia, and long-term exposure leading to neoplastic injury. This presentation will provide an overview of the knowledgebased approach for representing MoA information in rodents and its extrapolation/translation to humans.

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