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

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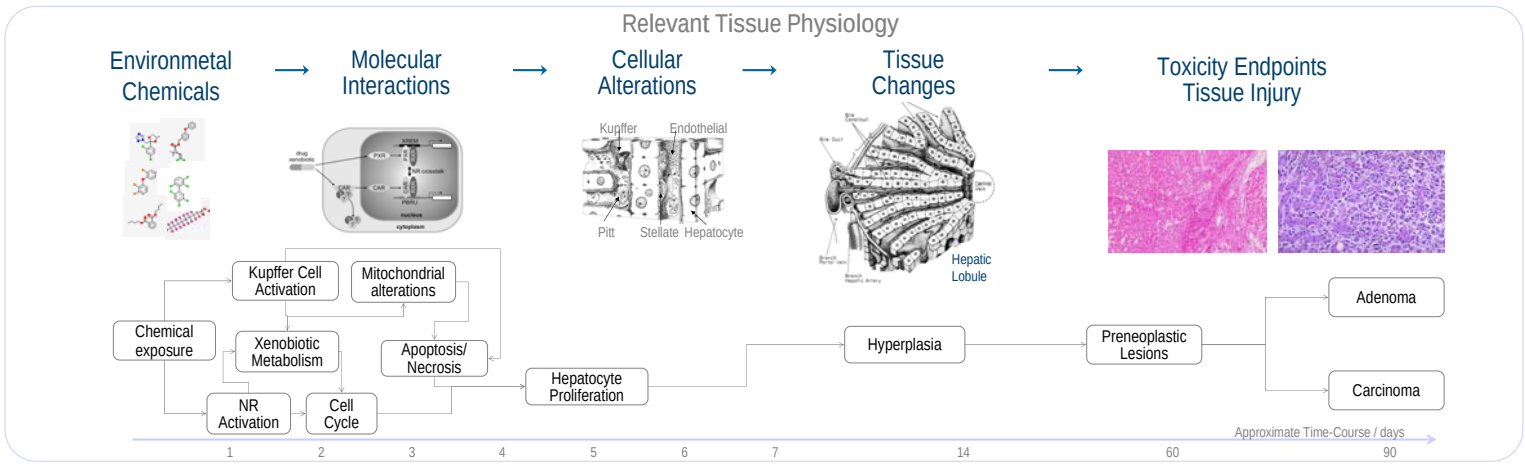
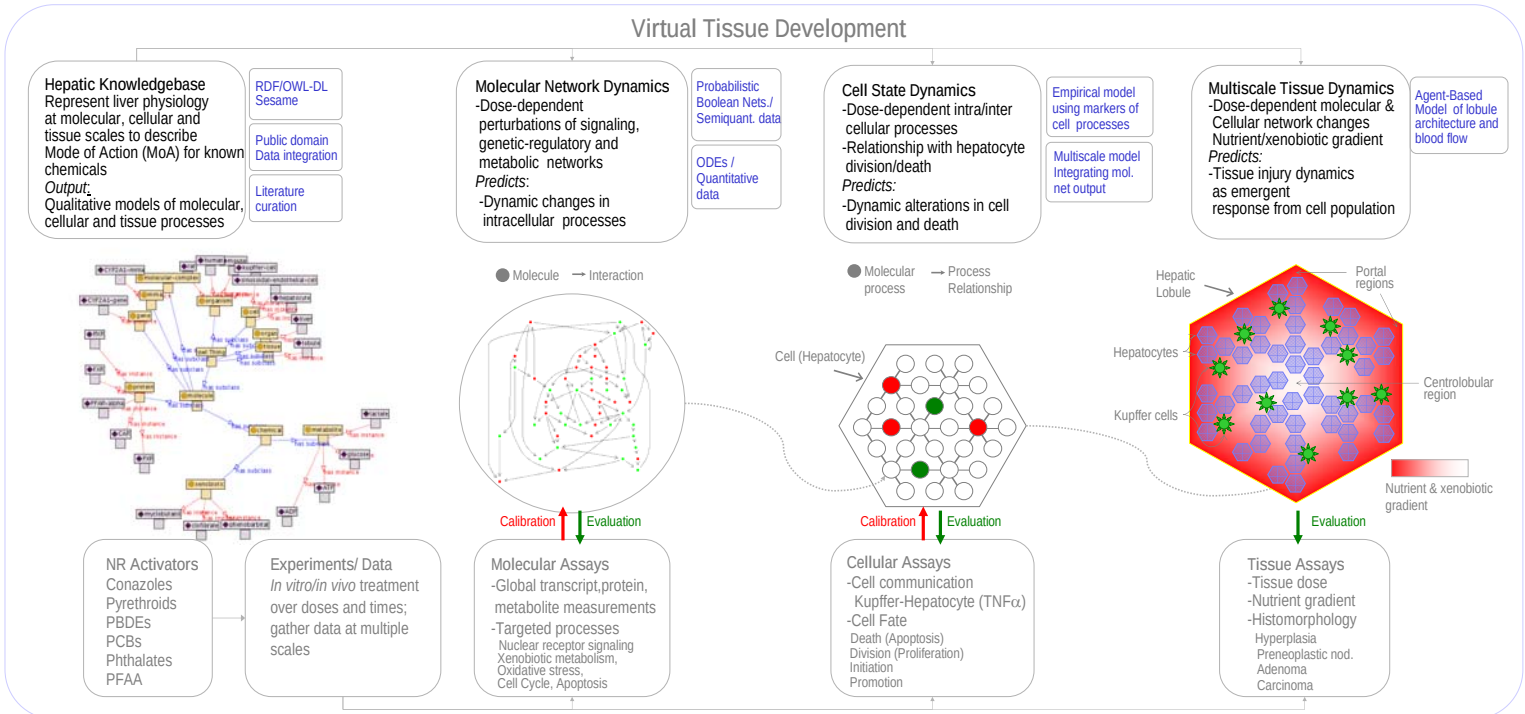
Project Summary

The objective of the Virtual Liver is to develop a biologically-based predictive model of chronic toxicity due to environmental chemicals. Our hypothesis is that chronic tissue injury is a multiscale phenomenon in which: (a) xenobiotics perturb molecular networks, which alter (b) the dynamics of cellular processes leading to discrete changes in cell state (survival/division/death), and (c) networks of cells respond to gradients of xenobiotics / nutrients producing tissue changes. We are developing a virtual tissue that (a) describes the relevant molecular and cellular processes and (b) simulates their dose-dependent chemical-induced perturbations using an agent-based approach.

Simulating Chemical-Induced Chronic Tissue Injury

Liver cancer is frequently observed in rodents due to long-term exposure to environmental chemicals. One plausible mode of toxicity includes nuclear receptor (NR) activation, cell proliferation, hyperplasia and eventually neoplastic lesions. However, assessing the dose-dependent risk of non-genotoxic rodent liver cancer to humans is challenging. The 1-2 year goal of the Virtual Liver is to model the NR-mediated molecular and cellular processes leading to hyperplasia in rodents and to evaluate their relevance in humans. In the next 3-5 years the model will be expanded to predict neoplastic lesions and other apical liver toxicity endpoints across rodents and humans.





Related Efforts

ToxCast™, vEmbryo (www.epa.org/ncct)
NIBIB/NIH (www.nibib1.nih.gov/Research/MultiScaleModeling)
IUPS Physiome Project (www.physiome.org.nz)
STEP / VHP (www.europhysiome.org)
SBML (www.sbml.org)
HepatoSys (www.systembiologie.de)

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