A liver digital twin for in silico testing of cellular and inter-cellular mechanisms in regeneration after drug-induced damage.

Info

PUBLIZIERT AM
2024-02-16

JOURNAL
iScience

LINK
https://www.ncbi.nlm.nih.gov/pubmed/38371522

Autoren

J. Zhao A. Ghallab R. Hassan S. Dooley J. G. Hengstler D. Drasdo

Abstract

This communication presents a mathematical mechanism-based model of the regenerating liver after drug-induced pericentral lobule damage resolving tissue microarchitecture. The consequence of alternative hypotheses about the interplay of different cell types on regeneration was simulated. Regeneration dynamics has been quantified by the size of the damage-induced dead cell area, the hepatocyte density and the spatial-temporal profile of the different cell types. We use deviations of observed trajectories from the simulated system to identify branching points, at which the systems behavior cannot be explained by the underlying set of hypotheses anymore. Our procedure reflects a successful strategy for generating a fully digital liver twin that, among others, permits to test perturbations from the molecular up to the tissue scale. The model simulations are complementing current knowledge on liver regeneration by identifying gaps in mechanistic relationships and guiding the system toward the most informative (lacking) parameters that can be experimentally addressed.