X-Species DILI Validation Consortium

X-Species DILI Testing in 3D Liver Microtissues as Decision-enabling Drug Development Tool for First in Human Studies

This pre-competitive consortium, organized and led by InSphero, aims to bring together representatives from pharmaceutical companies engaged and invested in the development of cross-species drug testing and validation strategies for rapid, reliable drug-induced liver injury (DILI) screening and prediction. Together, we will evaluate methods for recapitulating DILI-specific *in vivo* effects observed in animal models and patients using *in vitro* human and animal liver spheroid models and a comprehensive DILI compound library. Results will be submitted for publication in a high-profile scientific journal and for consideration as a special interest group topic at an upcoming Society of Toxicology annual meeting.

Our Vision

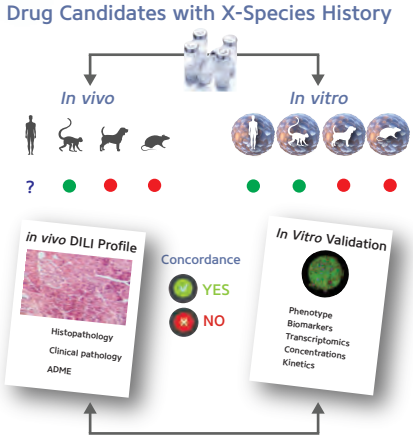
We seek for the characterization of 3D liver microtissue as decision-enabling drug development tool for first in human studies. We will identify models and methodologies that bridge the gap between human and animal *in vivo* and *in vitro* responses to a wide range of compounds and therapeutics.

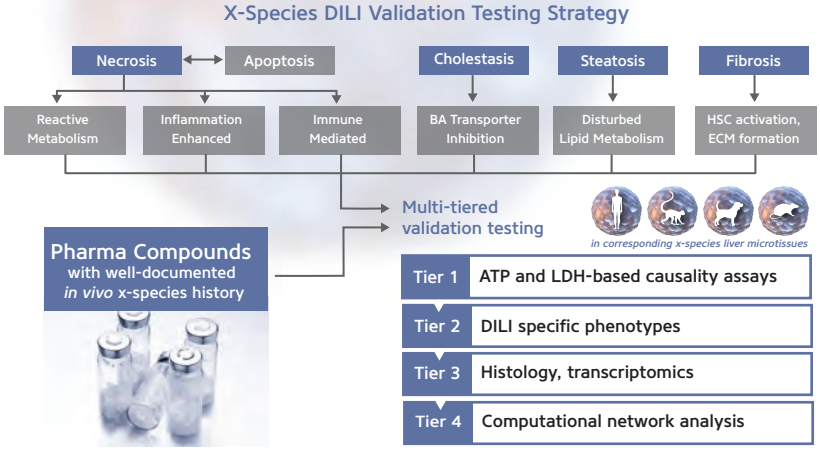
Our DILI Compound Library

Each participating pharma member will provide up to five DILI compounds for 3D *in vitro* mechanistic investigations. These compounds should come from failed or halted drug programs with well-documented preclinical DILI-specific *in vivo* profiles in the most common regulatory animal models (e.g., rat, dog, and cynomolgus monkey). Ideally, these compounds should express differential DILI across one or more species. Each selected compound will be representative of one specific drug-induced pathology, spanning necrosis, apoptosis, cholestasis, steatosis, inflammation, and fibrosis. The chemical structure and therapeutic target of test compounds will be blinded and not revealed in any consortium publications.

Our DILI Validation Strategy

InSphero will employ a multi-tiered, cross species DILI validation strategy to compare the documented *in vivo* response to the *in vitro* response in 3D liver microtissues derived from the corresponding preclinical animal models. Each type of drug-induced liver pathology will be investigated *in vitro* by the specific underlying DILI mechanism or biomarker. Analytical approaches will include histology and morphology as well as cellular, biochemical, and molecular methods. The validation criterion will be recapitulation of the documented *in vivo* DILI effect by mechanism in the relevant *in vitro* liver microtissue.





Join the Consortium

To learn more about this exclusive opportunity and explore how you can contribute to this critical study, contact Professor Armin Wolf, PhD, directly at armin.wolf@insphero.com

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