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Biosketch

Dr. Stevens is a Distinguished Research Fellow at Lilly Research Laboratories. For over four decades in government, academics and industry he has studied molecular and cellular responses to the metabolism and toxicity of drugs and xenobiotics. His current research focuses on application of systems biology approaches to improving drug safety assessment and elucidating mechanisms of drug toxicity. Dr. Stevens received his Ph.D. in Pharmacology from the University of Minnesota in 1980. Prior to joining Lilly Research Laboratory in 2000, he held positions at the National Institutes of Health, the Food and Drug Administration, the University of Vermont and the W. Alton Jones Cell Science Center, where he was Executive Director. He has served on a variety of national advisory committees including the HESI Board of Trustees, National Advisory General Medical Sciences at NIH, National Toxicology Program Board of Scientific Councilors (BOSC), the EPA Board of Scientific Councilors, Subcommittee on Chemical Safety for Sustainability, as well as the Boards of Directors for Argonex Pharmaceuticals, Inc., and Upstate Biotechnology, Inc. He received the Achievement Award from the Society of Toxicology in 1994 and was elected a Fellow of the American Association for the Advancement of Sciences in 1996. Dr. Stevens is recognized internationally as an expert in drug safety science and the application of systems biology approaches to drug-induces organ toxicity. He has active collaborations in Europe and was instrumental in launching the Innovative Medicine Initiative 2 (IMI2) project titled, “Translational Quantitative Systems Toxicology” (TransQST) initiated in January of 2017 and leads participation for Lilly in the IMI1 “Mechanism-Based Integrated Systems for the Prediction of Drug-Induced Liver Injury” (MIP-DILI) which wraps up activities in 2017.

Abstract 2017 III-6: Translational Quantitative Systems Toxicology (TransQST): Multi-Scale Modeling for Safety Assessment

Understanding DILI risk during drug development requires modeling across scales of complexity and across species. The TransQST project was launched in 2017 under the Innovative Medicine Initiative 2 (IMI2) umbrella of the European Union. This 5 year project brings together leading scientists from academia and the pharmaceutical sector to focus on developing next generation multi-scale models to understand whether or not preclinical safety issues identified for a drug candidate will translate across species to human. An important concept underlying the project is that systems approaches can help predict the likelihood that toxicity will translate by modeling the biology of the target organ systems and its preservation as well as the metabolism and disposition of the drug candidate. As an example,

application of network-based methods to transcriptomic data illustrates both challenges and opportunity for multi-scale models of drug-induced liver injury. Considerable work has addressed application of machine learning methods and transcriptomic data to identify gene signatures that enable 'read across' from training sets of DILI compounds to unknown compounds. An alternative approach is to model the underlying biological responses to liver injury using unsupervised methods that define gene interactions based on coalescent or intrinsic properties of the biological system, i.e. the liver. Co-expression is a coalescent property that organizes liver gene expression into modules of biological function based on perturbations caused by liver injury. By investigating the association between module perturbations and toxicity phenotypes in rat liver, underlying mechanisms of liver injury can be identified. An important future goal of the TransQST project is to apply these types of approaches to understanding the preservation of response networks across species allowing quantitative estimation of the probability that DILI risk will translate from nonclinical species to human.
http://transqst.org/