Proper identification of the most suitable compounds having best risk/benefit ratios is a key challenge during drug development. Evaluation of drug effects and toxicity and, based on that, early decision making can be streamlined through computational approaches allowing to quantitatively analyze drug response mechanisms. Multi-scale models spanning cell, organ and body level are well suitable to integrate and analyze data obtained during drug development. Prior knowledge, mechanisms and hypotheses from experiments can be integrated in models and can be efficiently verified against targeted experiments. This improves and speeds up hypothesis testing by gaining mechanistic understanding of primary and secondary drug effects, thereby reducing the number of necessary in vitro and in vivo experiments.

The technology platform, a scalable computational environment designed for reconstructing and simulating large and complex networks, allows for e.g.
- Detailed integration of cell, organ and whole body level
- Coupling signal transduction, gene regulation and metabolic networks
- Verifying models against multiple data sets
- Handling and verifying large-scale kinetic network models
- Predicting biological processes in a whole body model time- and dose-dependently

Our modeling and simulation platform was applied to set up multi-scale models for simulating and predicting time- and dose-dependently (i) compound concentrations in blood and tissues and (ii) cellular mechanisms including toxicity in human.

This enabled us to
- Quantitatively understand intracellular mechanisms and pharmacokinetic properties of drugs
- Determine differences in the response to drugs depending on inter-individual characteristics

In summary, we demonstrate how multi-scale models in combination with a powerful modeling and simulation platform contribute to improved drug development.