Analysis of molecular target sequences for explaining differences in toxic sensitivity between species

Level: Master
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Project form: Literature review / Data analysis
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The use of human and veterinary pharmaceuticals considerably increased over the past decades. While the health benefits of medication are fundamentally important, increasingly research focus on potential environmental impacts of pharmaceuticals. A range of species are unintentionally exposed to various pharmaceuticals, because of their presence in the environment. Although, concentrations of individual pharmaceuticals are often relatively low, these substances adversely affect wildlife species, which are likely to occur as consequence of specific drug target interactions. Consequently, evolutionary conserved molecular targets can be associated with an increased risk for chemical effects.

Because of high-throughput profiling technologies like transcriptomics and proteomics, but also the increasing determination of complete genomes for numerous species, more molecular information about species becomes available, which provides new opportunities in cross-species extrapolation of chemical effects. By comparing genes and proteins among species it is possible to compile data on the evolutionary conservation of drug targets and whole biological pathways. This concept is called comparative genomics. Advances in understanding the mechanistic basis for toxicological responses and identifying molecular targets in different species can provide an improvement in cross-species extrapolation.

The aim of the research project is to explore the relationships between genes/proteins involved in the metabolism of various pharmaceuticals on the one hand, and the toxicity of these substances on the other. A first step is to identify and compare genes/proteins involved in the metabolism of various pharmaceuticals in different species. The genome/toxicity relationships will be established by comparing species-specific genomic/proteomic data on metabolism with species-specific toxicity data. The ultimate idea is to use these relationships for predicting the species-specific toxicity of substances based on genomic/proteomic data.