Universität Basel

Research Project

Swiss Centre for Applied Human Toxicology

Third-party funded project

Project title Swiss Centre for Applied Human Toxicology
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Organisation / Research unit
Bereich Medizinische Fächer (Klinik) / Klinische Pharmakologie
Departement Pharmazeutische Wissenschaften
Departement Pharmazeutische Wissenschaften / Molecular and Systems Toxicology (Odermatt)
Department
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Status Completed

The projects focusing on mechanisms and in vitro prediction of non-allergic idiosyncratic toxicity represent one of four core projects within the research program of the Swiss Center for Applied Human Toxicology (SCAHT). The research projects focus on the identification and characterization of risk factors for idiosyncratic toxicity.Idiosyncratic toxicity of drugs is rare and is not related to their pharmacological action. This type of toxicity can therefore so far not be predicted and is not detected by the usual screening methods during preclinical and clinical drug development. The ability to predict such adverse effects would represent a large step towards safer medicines.

The following questions will be addressed:

1. Can the concept of underlying risk factors rendering cells, animals or individuals more susceptible to drug toxicity be confirmed experimentally?

2. Can suitable human cell lines to address idiosyncratic toxicity be derived and characterized; and can these cell lines be manipulated for the introduction of such risk factors?

3. Are the methods developed suitable for high throughput screening?

The project of the Molecular and Systems Toxicology group will specifically focus on the investigation of “multiple cellular stressors” as risk factors for impaired drug metabolism and drug toxicity. We aim at establishing conditions to study effects of endoplasmic reticulum stress on xenobiotics metabolism in cultured cells and at constructing cell systems to study the impact of endoplasmic reticulum redox changes on xenobiotics metabolism and toxicity. Furthermore, the influence of various potential risk factors, including vitamins, hormones, nutrients, oxidative stress and redox changes, for drug- and environmental chemical-induced toxicity will be investigated in various cell models.

Keywords idiosyncratic toxicity, cell model, mechanism, drug, metabolism, adverse drug reaction
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