

## Summer Research Internship Project Proposal

Project Topic	Toxicokinetic assessment of environmental chemicals in 3D <i>in vitro</i> liver models		
Name	Dr. Iva Sovadinová	Field	Toxicology <i>in vitro</i>
Department	RECETOX, Faculty of Science	Keywords	Toxicokinetic, <i>in vitro</i> 3D models

### Description of the Project (overview, expected outcomes, reason for research, proposed outcomes for student(s))

#### **Background:**

Non-alcoholic fatty liver disease (NAFLD) is the most common metabolic disease that afflicts 20%–30% of people globally and has a 50% prevalence in obese people. NAFLD can result in life-threatening conditions such as cirrhosis and liver cancer. Chemical exposure represents one class of environmental risk factors that might promote NAFLD. In our research group, we aim to understand the impact of different environmental chemicals to cause NAFLD. *In vitro* cultures of mammalian cells provide a valuable tool for assessing chemical effects and their links to adverse health outcomes. Especially, three-dimensional (3D) cultures, which more closely mimic *in vivo* like microenvironments, have been recognized as a successful strategy to improve the physiological relevance of liver *in vitro* models. Our research team employs these models to analyze the formation of NAFLD by exposing these 3D *in vitro* liver models to environmental chemicals. The issue is that the obtained results show just how much of the nominal concentration (the dose of the chemical added to the *in vitro* system divided by the volume of media) causes an adverse effect. However, it is known that an added chemical is partitioning within the *in vitro* system. The substance can bind, for example, to serum proteins and lipids, can sorb to plastic equipment, evaporate, transform, or metabolize. All these processes can change the nominal concentration of the added chemical on the way to the target side in the cell. Using the nominal concentration for hazard and risk assessment can lead to underestimating the hazard and risk.

#### **Project:**

In this project, we want to dive into the field of *in vitro* toxicokinetics and try to understand the distribution of different environmental chemicals in our 3D *in vitro* systems. Different extraction methods will be used to determine **1. the total concentration**  $\Rightarrow$  the concentration of a compound freely available in medium + bound to medium constituents; **2. the free concentration**  $\Rightarrow$  the concentration of an unbound compound in the exposure medium available for uptake into the cells; and **3. the intracellular concentration**  $\Rightarrow$  the concentration of a compound in the cells. The results will first help to understand the actual hazard of different chemicals to cause NAFLD better and, secondly, improve quantitative *in vitro* *in vivo* extrapolation and hazard and risk assessment in the longer term.

The internship is planned to acquire original experimental results, which could be eventually presented at an international conference and submitted for publication with the student listed as a co-author.

RECETOX, the Faculty of Science, Masaryk University, where the project will be undertaken, is internationally recognized for the research on the impact of chemical exposures on human health. RECETOX has excellent facilities and infrastructure to offer a first-rate environment for training and transferring knowledge to the student. Dr. Iva Sovadinová is an internationally recognized scientist and expert in the research and development of *in vitro* models and their use for studying health-related effects of chemicals with extensive international experience. She is co-leading the research group “Cell and Tissue Toxicology” at the RECETOX. Her students routinely travel for internships into collaborating labs, while his research group often hosts students from other Czech or international universities.

The student will be a part of the research group “Cell and Tissue Toxicology” (<http://secantox.weebly.com/>, [Twitter/@ToxCeLL](https://twitter.com/ToxCeLL)) and will be actively involved in the process of scientific inquiry and discovery. They will have wide-ranging opportunities to gain theoretical and hands-on experiences with sterile cell culturing and preparing hepatospheroids and analytical chemistry.

#### Student Requirements (prerequisites, experience, acceptable fields of study, etc.)

- A highly motivated student with an interest in toxicology, *in vitro* biomedical research and analytical chemistry
- Students from chemistry, biology and similar fields of study are welcome

#### Proposed responsibilities of the student(s)

- The student must devote full-time participation to the project (32 hours per week)
- Discuss the project progress with the supervisor and consultant daily
- Participate at the biweekly group meetings
- Present her/his project and results at the group meeting
- Write up research in the form of a scientific report

#### Additional important information (max. number of students, additional staff/faculty involved, etc.)

- Max. number of students: 1
- Supervisor: Dr. Iva Sovadinová. Consultant: MSc. Daniela Brenner