GÖTEBORGS UNIVERSITET

Master project/ Exjobb (45-60 hp) in Environmental Toxicology / *In vitro* Toxicology

General background

In vitro experimental systems based on continuous fish cell lines have been proven to be a powerful tool to unravel molecular mechanisms and predict the toxicity of single chemical compounds with unspecific mode of action in fish. However, most continuous cell lines have the shortcoming that they have partially or completely lost tissue-specific functionalities resulting in uncertainties regarding their suitability to predict *in vivo* toxicity.

It has been demonstrated that cell lines can regain certain tissue-specific functionalities when they are grown as three-dimensional (3D) spheroidal aggregates cultures. When grown in a 3D environment cells are surrounded and interact with other cells. This intercellular connectivity assists in maintaining tissue-specific cell shape and polarity, which are required for tissue-specific functions (in liver cells these include for instance expression of xenobiotic-metabolizing enzmes, xenobitic efflux pumps etc.).

The rainbow trout liver cell line RTL-W1 belongs to the fish cell lines, which is most widely used in environmental toxicology research. It has been demonstrated to exhibit several important liver-typic functions including cytochrome P450-dependent mono-oxygenase and ABC transporters activities. Furthermore they share morphological and functional characteristics with bile preductular epithelial cells, which are considered to function as stem cells in teleost liver. It has been demonstrated that RTL-W1 aggregate cultures grown in agar show hepatocytic differentiation regaining structural and functional features of hepatocytes in their physiological environment.

The project

The objective of this degree project is to further develop a fish-cell based *in vitro* model, which better reproduce hepatotypic functions and responses that would naturally occur *in vivo*, in order to improve their predictivity and application for environmental toxicity testing. The experimental work will include the optimization of a protocol to grow 3D spheroidal aggregate cultures based on RTL-W1 cells (see Figure), the structural and functional characterization of the cultures (e.g. regarding the viability of the cells in the interior and expression of hepatocyte-specific genes/enzymes), as well as their application for toxicity testing of chemical compounds and/or engineered nanomaterials. The methods employed will include routine cell culture techniques, enzyme activity assays, gene expression analysis and microscopy analysis.

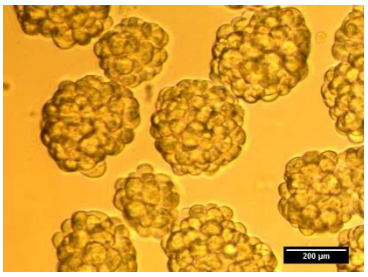

Figure. 3D spheroids

Project start

Fall 2016

Supervision

The applicant will be supervised by Assoc. Prof. Joachim Sturve and Dr. Tobias Lammel at the Zoological Institute, Department of Biological and Environmental Sciences, University of Gothenburg.

Requirements

Ideal applicants are MSc level students with a strong background and/or interest in Biology, *In vitro* Toxicology or Ecotoxicolgy and a high motivation to conduct scientific research. Previous experience in research, in particular in cell culture and molecular biology techniques is highly appreciated, but not a prerequisite. In addition, she/he should have good analytical skills, a positive and proactive attitude, and be able to work both independently and in a team. Furthermore, since we are an international research group, the applicant needs to have a high level of English in speaking, reading and writing.

Interested?

If you are interested and would like to have further information on the project and/or would like to directly apply for the position please send an email to: joachim.sturve@gu.se or tobias.lammel@gu.se