UPPSALA
UNIVERSITET

PhD-student position in pharmaceutical sciences within molecular pharmaceutics

Department of Pharmacy, Uppsala University

Application no later than June 30, 2013. UFV-PA 2013/1726

Starting date 1st of September 2013, or as agreed upon.

Information about the department and the research groups can be found at www.farmfak.uu.se/farm/

The PhD project will be performed in professor Per Artursson´s research group in collaboration with the Hamner Institute for Drug Safety Sciences, Research Triangle Park, North Carolina. The group takes a multidisciplinary approach and combines computational chemistry and bioinformatics with cell and molecular biology, biopharmaceutics and pharmacokinetics in order to understand how drugs are absorbed, distributed and eliminated in man. Of specific interest is to understand how these mechanisms influence drug efficacy and their adverse effects. The research group has 15+ members, most of which hold a PhD and five are PhD students. More information about the research group can be found at http://www.farmfak.uu.se/farm/lmformul-web/index.shtml

Project: A human co-culture model for prediction of drug induced liver injury

The safety assessment for pharmaceuticals includes *in vivo* repeated dose toxicity tests in laboratory animals. These in vivo studies often generate false negative and false positive results. The appearance of unexpected toxicity in man is therefore one of the major reasons for the withdrawal of a drug from the market. The liver is often a target organ in toxicology because it is responsible for the metabolism and elimination of most chemical compounds. Therefore, there is a significant need for new approaches which help classify hepatotoxic compounds earlier in drug development. This will lead to safer drugs and a more efficient drug discovery process. Such new approaches will include the development of novel human in vitro test systems, aiming at reducing the use of laboratory animals.

The overall aim of this project is to develop a new, sensitive in vitro model based on co-culture of isolated human liver cells that gives better predictions of drug induced liver injury (DILI). The PhD student will use state-of-the-art techniques to develop improved in vitro predictions of DILI and thereby contribute to reducing the need for less predictive animal experiments. The project is focused on the use of primary human liver cells that are purified and co-cultured under very specific and controlled conditions. The co-culture conditions are meant to mimic the native environments of the liver and allow

communication between different cell types and therefore allow investigation of a broad range of different mechanisms of DILI *in vitro*.

The specific aims are 1) to establish a co-culture model based on primary human hepatocytes and Kupffer cells; 2) to characterize mono- and co-cultures with regard to global proteomics and identify pathways that are activated under conditions of cellular stress; 3) to validate the model after exposure to prototypic drugs that induce DILI via different mechanisms; 4) to develop a cell-toxicokinetic model based on the generated experimental data. The project will be performed in a multidisciplinary research group in collaboration with senior researchers and other PhD students. Some experiments will be performed at the Hamner Institute for Drug Safety Sciences, Research Triangle Park, North Carolina, USA.

Qualifications: An MSc degree (or equivalent) in a relevant field is required. The ideal candidate is highly motivated with thorough education and strong interest in the research field. Previous experience with experimental setups, the wet-lab and some basic bioinformatics are beneficial. Candidates must be fluent in English.

Conditions: The PhD training comprises four years of full time research and studies. The successful candidate will receive a fellowship the first year and a PhD-student position year 2-4. The position can be combined with up to 20% of teaching assistantship, which will then prolong the position accordingly.

Information about education at the postgraduate level, admission requirements and admission decisions can be found at http://www.medfarm.uu.se/utbildning/forskarniva/ The Postgraduate Programs Committee at the Disciplinary Domain of Medicine and Pharmacy will formally approve the student's admission.

How to apply: The application should include a letter describing your research interests and motivation for PhD studies, a short description of your education, a CV, an authorized copy of your BSc/MSc degree(s), the names and contact information (address, email address, and phone number) of at least two reference persons, relevant publications (including MSc thesis).

For more information, please contact Professor Per Artursson, e-mail Per.Artursson@farmaci.uu.se, phone +46 (0)18 4714471 (office) or +46 (0) 70 4250888 (cell). The trade union representatives are Anders Grundström, Saco, phone +46 (0)18 471 5380, Carin Söderhäll, TCO/ST, phone +46 (0) 18 471 1996 and Stefan Djurström, SEKO, phone +46 (0) 18 471 3315.

Salary will be according to local guidelines at Uppsala University.

You are welcome to submit your application **no later than 30th of June 2013, UFV-PA 2013/1726**. Use the link below to access the web announcement and the application form.

PhD-student position in pharmaceutical sciences within molecular pharmaceutics