24.05.2022

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The IUF – Leibniz Research Institute for Environmental Medicine investigates the molecular mechanisms through which particles, radiation and environmental chemicals harm human health. The main working areas are environmentally induced aging of the pulmonary system and the skin as well as disturbances of the nervous and immune system. Through development of novel model systems, the IUF contributes to the improvement of risk assessment and the identification of novel strategies for the prevention / therapy of environmentally induced health damage. The working group of "Alternative method development for environmental toxicity testing" led by Prof. Ellen Fritsche is looking for

A student (f/m/d) for a Master Thesis with the title:

Cross-species characterisation of the molecular and cellular effects of thyroid hormones on the development of neural progenitor cells *in vitro*.

The project: Thyroid hormones (TH), thyroxine (T4) and 3,3',5-triiodothyronine (T3) are indispensable for normal brain development and can influence numerous neurodevelopmental processes. Several studies establish TH signaling as a critical factor in regulating human brain development, and confirm the relevance of TH signaling as a target for developing adverse outcome pathways (AOPs) that link exposure to chemical endocrine disruptors to developmental neurotoxicity (DNT). It is important to be in the possession of methods that can reliably, fast and with a relatively low expenditure identify compounds that exert mode-of-actions (MoAs) via TH disruption. Here, new approach methods (NAMs) are superior to the classical animal experiments as they are faster, cheaper, are based on MoA analyses and can incorporate human data. Such NAMs can make use of *in vitro* or *in silico* tools. As *in silico* tools are fast and very cost-effective, they are the preferred vision of usage in the future, e.g. for read-across applications. Hence, *in silico* NAMs for assessing TH disruption, especially for the developing brain as the most sensitive target organ of altered TH, are warranted. *In silico* predictions are only as good as the data feeding the *in silico* model. Hence, besides *in vivo* rat models, cellular data with high human and rat relevance will tremendously help setting up such a NAMs for TH disruption. Here, *in vitro* data from both species will help with the prediction based on species extrapolation from rats to humans. A well-established *in vitro* method for brain development is the Neurosphere Assay that has been developed in the lab of Prof. Ellen Fritsche. This assay utilizes primary neural progenitor cells (NPC) from humans or rats that proliferate in culture and upon plating onto a laminin matrix cells radially migrate out of the sphere and differentiate into the main effector cells of the brain (radial glia cells, astrocytes, neurons, and oligodendrocytes). Within this project, we are using e.g. single cell RNA sequencing to investigate the cell type-specific regulation of TH-dependent genes in a species-specific context to gain understanding of TH transport and specific TH action within individual brain cell types. In addition to cellular TH actions, knowledge on TH kinetics as well as TH concentration-dependent effects on biochemical processes like ubiquitination and deiodinase-2 activity will be addressed. The aim of this master thesis is to gain understanding of the molecular and cellular effects as well as the distribution kinetics of TH in human and rat neurospheres in order to complete the superior project with the final goal of *in silico* modulation of TH transport in brain cells.

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Your profile: Our working group is looking for a motivated employee with a high level of commitment, fun at work, motivation, communication skills and team spirit. The applicant should have a completed bachelor's degree in life sciences. An additional (master) training in the field of toxicology or pharmacology is a plus. Hands on experience in cell culture is desirable. Furthermore, good knowledge of English is mandatory.

We offer: We are an interdisciplinary, international team with a pleasant working atmosphere. We offer thorough training in a highly topical, challenging area of research. The project takes place in a team with other scientists, in part from industry, with whom there will be an intensive exchange of content on project-relevant results.

Start: As early as possible.

Please address your application (short letter of motivation, CV, qualification certificates), preferably electronically to Bewerbung@IUF-Duesseldorf.de:

Prof. Ellen Fritsche
IUF – Leibniz-Institut für umweltmedizinische Forschung
c/o Personalstelle
Auf'm Hennekamp 50
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Application documents submitted by post are not returned. Documents for applicants not considered are destroyed appropriately once the procedure is complete.

Zertifikat seit 2013
audit berufundfamilie