

At the Goethe-University Frankfurt am Main

22 PhD scholarships for Life and Natural Scientists

Within the research training group

“Translational Research Innovation – Pharma“ (TRIP)

will be available with an anticipated starting date of February 1st, 2012.

TRIP is a structured PhD programme in biomedical research. It will foster team work and comprises groups of different disciplines at the Goethe University.

At the focus of drug research at the Goethe-University, the participants of the research training group TRIP will obtain insights into translational medical research and will learn in detail the methods of their field. PhD projects will encompass research into causes, genesis and progression of the diseases as well as into prevention strategies, diagnostics and treatment.

The focus is on the following research platforms

- **Pain**
- **Multiple Sklerosis**
- **Autoimmune Diseases and**
- **Diabetes mellitus**

Further Information to the PhD projects can be found at www.zafes.de

Prerequisite for application is an outstanding degree in a relevant field. Candidates from the areas of biochemistry, biotechnology, chemistry, immunology, medicine, microbiology, molecular biology, pathophysiology, pharmacy, laboratory animal sciences and cell biology are encouraged to apply. Candidates should be highly motivated and able to work in teams across disciplines.

It is anticipated that the advertised positions will be available from February 1st, 2012.

If you are interested in one of the advertised positions, please send your complete application (Letter of motivation, CV, copies of certificates) to Dr. Torsten Arndt (t.arndt@zafes.de) or the indicated contact person(s).

Please do not send in original documents as your application will not be returned to you.

Research Platform Multiple Sklerosis

The projects here shall at different levels identify and examine new potential active substances and target molecules as well as biomarkers. A collaboration of molecular- and clinically orientated projects but also animal models is envisioned. Furthermore, test models in vitro and in vivo shall be developed which may be used for further development of drugs against MS.

PHD projects:

Effects of immune modulators on volatile biomarkers of neuronal dysfunction in the working memory of multiple sklerosis

Using structural (diffusion tensor imaging) and functional magnetic resonance tomography, anatomical and effective connectivity in the working memory network will be investigated in patients with relapsing-remitting MS while in therapy with innovative immune modulators. The investigations will be carried out in the Clinic for Neurology and the Brain Imaging Center (BIC) of the Goethe University.

Applicant profile: Physician or biologist with specific interests in neuroimaging

Academic contact: Prof. Dr. Ulf Ziemann, u.ziemann@em.uni-frankfurt.de

Effects of cannabinoid modulators on the immune cell activation and progression in the EAE mouse model of multiple sklerosis

Investigation of immune modulatory or neuroprotective effects of new substances in vitro and in vivo in mouse models of MS and analysis of potential biomarkers in patients with MS.

Applicant profile: biologist, neurobiologist or physician/medic preferred

Academic contact: Prof. Dr. Irmgard Tegeder, tegeder@em.uni-frankfurt.de

The role of ceramides in the genesis and development of multiple sklerosis

In this project, the influence of different ceramide synthases and ceramides of different chain lengths on the development of MS will be investigated using cell culture models and in vivo (EAE mouse model) .

Applicant profile: biologist, biochemist or pharmacist preferred

Academic contact: Dr. Susanne Schiffmann , susanne.schiffmann@med.uni-frankfurt.de

Development of nanoparticular carriers which can overcome the blood-brain-barrier in the therapy of MS

In the project, pharmaceutical formulations for improved transport across the blood-brain barrier will be developed.

Applicant profile: pharmacist preferred (Pharmaceutical Technology)

Academic contact: Dr. Matthias Wacker, wacker@em.uni-frankfurt.de

Target identification of the therapeutic Compound X in multiple sklerosis

In this project, the targets of a drug used in MS will be investigated by biochemical and molecular biology techniques.

Applicant profile: pharmacist or biochemist preferred

Academic contact: Prof. Dr. Dieter Steinhilber, steinhilber@em.uni-frankfurt.de

Research Platform Pain

The project team will characterise the individual reactions to pain in order to develop new strategies in the treatment of pain. Using genome-wide investigations in pain patients as well as in mouse models of pain, new target structures shall be identified and subsequently their role in pain processing shall be tested.

PHD projects:

Association of complex phenotypes and genotypes in tumour-pain patients

The project will use existing data from pain patients. In cooperation with natural scientists and computer scientists within the research platform pain, relevant genotypes and phenotypes will be determined and compared with transcriptome investigations from animal models of neuropathic pain. An analgetic therapy strategy will be deduced which comprises a new “target” or a repositioning or intelligent combination of existing drugs. At the same time a cohort of 300 tumour pain patients will be characterised prospectively in regard to their pain phenotype. The resulting complex pain phenotypes and genotypes serve as verification of clinically determined therapy strategies or of those determined in animal models. This medical PhD project will contribute to the aim of the research platform by collecting complex tumour pain phenotypes as well as the medical expertise, it is available for prospective pharmacological investigations in humans.

Applicant profile: Physicians/medics with academic interests in pain therapy, anaesthesiology and clinical pharmacology

Academic contact: Dr. Michael Zimmermann, Michael.Zimmermann@kgu.de

Association of complex pain phenotype, genome, epigenome and transcriptome data and data/knowledge generation using informatic methods of machine learning

In this PhD project, procedures for a complex description of genome, epigenome, transcriptome and pain phenotype will be developed and used for the association of molecular and clinical data, in order to establish a therapy strategy which may comprise a new “target” or a repositioning or an intelligent combination of existing drugs. The project involves the development and the application of data analysis procedures using informatics. It will also involve rule-finding in highly dimensional systems using „emergent self organizing maps“, as well as knowledge generation by data mining which will serve to verify the clinical data and data from animal models. The project will be jointly supervised with Prof. A. Ultsch, Datenbionik FB 12, Philipps-Universität Marburg, Hans-Meerwein-Straße, 35032 Marburg.

Applicant profile: computer scientist with an interest in characterisation of complex biological, clinical and pharmacological processes.

Academic contact: Prof. Dr. Jörn Lötsch, j.loetsch@em.uni-frankfurt.de

Identification of new targets in the therapy of neuropathic pain as well as tumour-associated pain

In this project, using mouse models the pain-induced transcriptional regulation for neuropathic and tumour pain will be identified in the spinal cord. Subsequently by employing molecular biology and protein biochemistry, suitable candidate genes will be characterised in regard to their location and regulation in the nociceptive system. Furthermore, the nociceptive behaviour of mice after application of test substances will be investigated to clarify the functional role of new candidates for the pain sensibilisation. Finally, so-far unknown mechanisms for pain sensibilisation in neuropathic and tumour pain will be identified in order to generate a basis for innovative pharmacological pain therapy.

Applicant profile: natural scientists with an academic interest in neurobiology and pharmacology

Academic contact: PD Dr. Dr. Achim Schmidtke, schmidtke@em.uni-frankfurt.de

Antagomire against microRNAs as new analgetics for the treatment of neuropathic pain and tumour-associated pain

Aim of the PhD project is the investigation of micro-RNA regulation in the spinal cord in mouse models for neuropathic and tumour pain. The most promising candidates from the data collection will be selected and analysed in detail in regard to their role in pain mechanisms. Subsequently, specific microRNA inhibitors (antagomires) will be used to collect information on a possible use of antagomires in the therapy of poorly treatable pain, which may serve in the future as basis for clinical studies.

Applicant profile: natural scientists with an academic interest in neurobiology and pharmacology

Academic contact: PD Dr. Ellen Niederberger, e.niederberger@em.uni-frankfurt.de

The last two projects are tightly connected. The tasks will be the investigation of mechanisms involved in pain processing. The methods used comprise a broad spectrum of experimental neuroscience, in particular molecular biology techniques, behavioural studies in animal models and fluorescence microscopy.

Research Platform Autoimmune Diseases

The importance of monocytes/macrophage systems including subpopulations of dendritic cells as target structures of innovative immune modulatory modes of actions will be investigated in mouse models of arthritis and psoriasis.

PHD projects:

Blockade of GM-CSF: evaluation of a new principle for therapy for psoriasis and psoriasis-arthritis

The influence of a blockade of proinflammatory cytokines GM-CSF in the characteristics of psoriasis and psoriasis-arthritis in mouse models will be analysed. The project is based on the hypothesis that this cytokine is of critical importance for the differentiating and effector functions of monocytes/macrophages in inflammation of skin and joints.

Applicant profile: biologist or biochemist preferred

Fachlicher Ansprechpartner: Prof. Dr. Harald Burkhardt, Harald.Burkhardt@kgu.de

Sphingosine metabolism as regulator of pDCs in chronic inflammation (RA)

Aim of the project is to investigate the influence of intra- and extracellular S1P on pDCs (cytokine production, co-stimulatory molecule expression, functional immune status) in the context of a chronic inflammation, and furthermore to follow up the (de)activation state of immune competent cells.

Applicant profile: Biologist

Academic contact: Dr. Andreas Weigert, weigert@zbc.kgu.de

Defective phagocytosis in chronic inflammation

A dysfunctional phagocytosis of apoptotic material contributes to the chronification of inflammatory processes, including RA. We assume that, due to a diminished expression/activity of Nrf2, macrophages are not any more or only to a small extent able to phagocytise. This hypothesis will be investigated mechanistically and functionally in cell culture and in animals.

Applicant profile: biologist or biochemist

Academic contact: PD Dr. Andreas von Knethen, v_knethen@zbc.kgu.de

New ligands of histamine H4 receptors

Due to the anti-inflammatory and immune modulatory effects of histamine H4 receptor ligands, new active substances which while having a high affinity show different effectivities and possibly also other pharmacological functions, are urgently needed. The design, the synthesis and the biological testing of new substances will be the focus of this PhD project.

Applicant profile: pharmacist, chemist, biochemist with experience in chemical synthesis

Pharmazeut/in, Chemiker/in, Biochemiker/in mit Syntheseerfahrung

Academic contact: Prof. Dr. Holger Stark, h.stark@zafes.de

Modulation of lysophospholipid signalling to therapeutically influence the immunological, vascular and fibrotic processes in systemic sclerosis

In this cooperation between pharmacology and rheumatology, the modulation of inflammatory/fibrotic mechanisms by lysophospholipid-dependent signalling pathways are investigated using translational research in vitro model cells and also in primary explanted cells. Besides analysis of biomaterial available from the sklerodermia-cohort, functional studies in the mouse model of bleomycin-induced fibrosis will be carried out in order to study the role of S1P in the immune mediated early phase but also in later phases of the disease.

Applicant profile: biochemist preferred (focus in immunology)

Academic contact: Prof. Dr. Heinfried H. Radeke, radeke@em.uni-frankfurt.de

Research Platform Diabetes mellitus

The research platform Diabetes mellitus aims for new diagnostics and a causal therapy for both type-1 and type-2 diabetes and the long-term implications.

PHD projects:

Design, synthesis and in vitro characterisation of modulators of the farnesoid X receptors

Aim of this project is to identify suitable modulators of the FXR and to synthesise them by organic-chemical methods. The in vitro evaluation comprises the testing using established methods such as reporter gene assays and quantitative PCR.

Applicant profile: extensive knowledge and practical experience in medicinal chemistry

Academic contact: Prof. Dr. Manfred Schubert-Zsilavecz, schubert-zsilavecz@pharmchem.uni-frankfurt.de

Design and synthesis of dual sEH/PPAR modulators

The aim of this PhD project is to design, synthesise and evaluate in vitro dual sEH/PPAR modulators with different profiles. Computer-supported drug design and modern synthesis methods will be used.

Applicant profile: chemist

Academic contact: Dr. Eugen Proschak, Proschak@pharmchem.uni-frankfurt.de

The role of soluble epoxide hydrolase in the progression of insulin sensitivity and in the prophylaxis of long-term effects of diabetes

This project focuses on 1) the elucidation of the mechanisms which control the expression and the activity of the soluble epoxide hydrolase in adipocytes and monocytes, 2) on the effects of altered amounts of fatty acids, epoxide and dioles on cellular signalling pathways and cellular metabolism, and 3) on the effects on vascular complication in metabolic syndrome when Cytochrome P450-/soluble epoxide hydrolase amounts are changed.

Applicant profile: biologist, pharmacist or physician/medic

Academic contact: Prof. Dr. Ingrid Fleming, fleming@em.uni-frankfurt.de

Interactions between adipocytes and macrophages as test platform for the investigation of (the development) of diabetes and insulin resistance

Aim is to study the influence of macrophages which are inflammatorily or antiinflammatorily polarised, on the classical insulin-signalling in human adipocytes. Also, the influence of adipokines, incl. that of adipocyte-conditioned medium, on the immune responses of human macrophages will be analysed. The knowledge of this cell-cell-communication will benefit the development of a new test system for anti-diabetics.

Applicant profile: biologist, biochemist

Academic contact: Dr. Dmitry Namgaladze, dmitry@zbc.kgu.de

Pharmacogenomics in the immune therapy of type-1 diabetes

The aim is the development of a diagnostic test procedure which highly successfully allows the prediction of an immune modulatory therapy in type-1 diabetes in order to treat the basic immune dysfunction early. Methods: cell biological and molecular genetic analysis of blood samples of patients, family members and health individuals, correlation of functional and genetic markers after immune modulation.

Applicant profile: natural scientist with experience in cell and molecular biology, and knowledge in genetic epidemiology and immunology

Academic contact: Prof. Dr. Klaus Badenhoop, badenhoop@em.uni-frankfurt.de

Therapy of type-1 diabetes mellitus in an animal model

Elements of all three PhD projects:

- Working with a virus-induced mouse model for type-1 diabetes
- Evaluation of therapies, which influence the balance between pro-inflammatory and regulatory factors in type-1 diabetes and may therefore cure type-1 diabetes
- Experiments for the activation and migration of lymphocytes using immuno-histochemistry and flow cytometry

Applicant profile: natural scientist with an academic interest in autoimmune diseases, experience in animal studies and knowledge in immunological techniques are of advantage

Academic contact: PD Dr. Urs Christen, christen@med.uni-frankfurt.de

Animal Model project A) Immune modulation by Interleukin-22 in type I diabetes mellitus

Academic contact: Prof. Dr. Heiko Mühl, H.Muehl@em.uni-frankfurt.de

Animal Model project B) ADAM10, ADAM17 and CXCL16 as therapeutic target molecules

Academic contact: PD Dr. Paul Gutwein, p.gutwein@med.uni-frankfurt.de

Animal Model project C) Combination therapy of diabetes mellitus

Academic contact: PD Dr. Urs Christen, christen@med.uni-frankfurt.de