CSC-Tübingen PhD Scholarship Program

2023 application round prospective PhD positions at Tübingen University

**Faculty:** Faculty of Science

**Institute / Section / Subject:** Institute of Pharmacy / Experimental Pharmacology

**Supervising Professor(s):** Prof. Dr. rer. nat. Robert Lukowski

**About the Supervisor(s):** Robert Lukowski (RL) is a pharmacologist with long-standing interest and experience in second messenger and ion channel biology. Specifically, his laboratory has worked on the regulation and function of Ca^{2+}/Na^{+}-activated K^{+} channels as well as on 3',5'-cyclic guanosine monophosphate (cGMP) pathway modulation in animal models of disease and their utility in drug discovery applications. His present research focuses on the application of highly versatile biosensors to image the actions of potassium-selective ion channels / transporters, which are frequently targeted by cGMP (and by other "second messengers" such as Na^{+} and Ca^{+}). Such live-cell monitoring approaches can significantly improve our understanding of the domain- and cell type-selective impact of different K^{+} / cGMP pools and / or individual channels / transporters on metabolic and cardiac disease states and on malignant behaviors in cancer cells. RL acts as training coordinator and speaker of ICEPHA’s graduate program and as Vice-Speaker of the recently established Research Training Group entitled "cGMP: From Bedside to Bench" (GRK2381). To learn more about RL, his research, and co-workers follow the link to the Experimental Pharmacology group at the Institute of Pharmacy.

**Specification:** Understanding, monitoring, and perturbing cardiac cGMP signals in heart failure (HF) with preserved ejection fraction (HFpEF)

**Topic Description:** A recently developed mouse model resembling clinical features of HFpEF, a condition lacking a specific therapy, enables innovative research on this common type of HF (doi:10.1038/s41586-019-1100-z). We will apply this model to relevant mouse mutants carrying cell-specific ablations of different components of the cGMP pathway. Further, we will utilize available and newly developed cGMP-modulating agents as well as genetically encoded cGMP scavengers to perturb (amplify or dampen) the detrimental / beneficial signaling events thereby gaining insights into the cell-specific action of those agents as well as their regulatory effects on cGMP-dependent signaling events on cardiac disease mechanisms. These studies are important because discrepant roles were previously reported for non-/cardiomyocyte cGMP in mouse models of cardiac hypertrophy induced by aortic banding, angiotensin II or isoprenaline infusion, which more closely resemble HF with reduced ejection fraction (HFrEF) (doi: 10.1038/nm1175.; doi:
The major aim of the project is to identify disease-relevant cGMP signals (or pools) in distinct cardiac cells and to assess whether and how cGMP generators / effectors contribute to HFpEF (versus HFrEF) outcomes and/or related cardiac disorders.

**Degree:** Dr. rer. nat. (at the Faculty of Science) or alternatively PhD in Experimental Medicine (at the Medical Faculty).

**Required Degrees:** Applications from graduates that hold a top-ranked master’s degree in Molecular Medicine or Cardiology, Biochemistry, Cell biology or Pharmaceutical Sciences as well as graduates of related and equivalent courses of studies are welcome. A strong interest in the molecular functions, dynamics, and pathophysiological relevance of cardiac diseases modifiers, and in mouse transgenesis is clearly preferred.

**Language Requirements:** Fellows will need to plan, conduct, and troubleshoot experimental approaches to solve scientific problems, as well as to critically evaluate and effectively present and communicate their research findings. In order to meet these criteria an applicant must be able to show proof of proficiency in English on at least C1 level. Basic knowledge of German language at the point of entry is very helpful but not a must.

**Notes:** none