TECHNISCHE UNIVERSITÄT DRESDEN

EH&D Endothelium in Health & Disease International PhD Program Dresden

# Call for PhD students 2016

The international PhD Program "Endothelium in Health and Disease" of the Medical Faculty Carl Gustav Carus, TU Dresden, Germany, in collaboration with the German Academic Exchange Service (DAAD) opens a call for 2 PhD positions in cutting-edge research on the regulatory functions of the vascular endothelium in health and disease. We are looking for highly motivated and talented students with a passion for science. Candidates must demonstrate an excellent performance in their previous academic education. Candidates from developing countries are encouraged to apply.

Requirements:

- MSc, MD or equivalent degree in Physiology, Biochemistry, Biomedicine, Biology or related sciences
- Excellent English language skills and the ambition to work in a dynamic international environment

Required application materials:

- Motivation letter describing the applicant's work experience and research goals; please indicate your favorite research project (A or B), the project's description is below
- Resume/CV showing the applicant's background, professional skills, a list of publications and oral and poster presentations as well as additional achievements (scholarships, awards etc.)
- Transcripts including all undergraduate level certificates and university degrees. All documents, which are not in German, must be accompanied by a legally certified English translation.
- Addresses of at least two potential referees

We offer a top-level research environment, a comprehensive educational and mentoring program, courses in cutting-edge methods and soft skills.

Application deadline for the next term: June 25, 2015

Please send your application as one pdf-file via e-mail to:

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**Description of the PhD project**

**Title: Nox4, endothelial function and atherosclerosis**

**Introduction:**

Atherosclerosis is an inflammatory disease of the vessel wall which can lead to heart attack and stroke. The role of reactive oxygen species in the pathogenesis of atherosclerosis is not well-understood (Müller & Morawietz 2009). Initial studies supported a proatherosclerotic role of the superoxide anion producing NADPH oxidase (Nox) 2 complex (Rueckschloss et al. 2001). The role of other Nox isoforms in atherosclerosis is less clear (Drummond & Sobey 2014). We could show that Nox4 is the major Nox isoform in endothelial cells and regulated by laminar shear stress (Goettsch et al. 2011). This isoform mainly produces H2O2 and might mediate protective mechanism in the vessel wall. The impact of Nox4 on atherosclerosis is currently not known. Therefore, we want to study the impact of Nox4 knockout on atherosclerosis in a mouse model with high-fat diet. In addition, we want to analyze the impact of obesity and coronary artery disease on structure and function of arterial vessels of patients undergoing coronary artery bypass grafting.

Our lab is interested in the regulation of Nox isoforms Nox2 and Nox4 in endothelial cells for many years (Rueckschloss et al. 2001, Müller & Morawietz 2009). Fine particulate matter and high-fat diet regulated oxidative stress and endothelial function in mouse models (Kampfrath et al. 2011). Furthermore, we could show a downregulation of Nox2 by therapy with statins and AT1 receptor blockers in arterial vessels of patients with coronary artery disease (Rueckschloss et al. 2001, Müller & Morawietz 2009). Recently, we started working with Nox4 knockout mice. In the last months we have generated a novel model with genetic deletion of Nox4 in a proatherogenic LDL receptor knockout background and started to analyze the impact of high-fat diet on endothelial function and atherosclerosis.

**Working plan:**

This project will be divided in 3 parts. In the first part of the proposal, we want to use the novel model to study the impact of Nox4 on atherosclerosis. C57BL/6 (wild-type), LDL receptor (LDLR) knockout, Nox4 knockout and Nox4/LDLR double knockout mice will be fed a high-fat diet (60 % kcal from fat) of 20 weeks. In these mice, we will analyze the formation of atherosclerotic plaques in serial sections of the aortic arch. In the second part, we will analyze in these mice the arterial expression of pro- and anti-atherosclerotic and -inflammatory genes and the impact on endothelial function. In this way, we want to analyze the impact of Nox4 and high-fat diet on endothelial function and atherosclerosis. In the third part, we want to study the impact of obesity and coronary artery disease on endothelial function in internal mammary arteries of patients undergoing coronary artery bypass grafting surgery. The specimens are kindly provided by the Department of Cardiac Surgery, University Heart Center Dresden (Prof. Matschke).

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The vascular function in human vessels will be assessed in the lab of Andreas Deußen using a Mulvany myograph. In addition, we would like to analyze the expression of Nox2, Nox4, pro- and anti-atherosclerotic and inflammatory genes and to perform histological examinations of human arteries. Changes in gene expression, vascular function and structure are likely to occur in vessels from patients with severe coronary artery disease. These data will supplement experimental data from project part 1 and 2 and should lead to additional publications.

In summary, we aim to get in this project a better understanding of the role of Nox4 in atherosclerosis.

**References:**

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