

CSC-RUB PhD Project Proposal

Title: Screening of pharmaceuticals for their neuroprotective properties after hypoxia.

Sector of research: Neuroscience, neuroimmunology, medicine, basic research

Degree awarded: PhD in Neuroscience

Keywords: Hypoxia, Stroke, brain damage, neuroimmunity, central nervous system (CNS) damage, neuroregeneration, reperfusion damage, cardiac arrest, arrhythmia

Supervisor of PhD project:

Prof. Dr. Carsten Theiss, Faculty of Medicine – Department of Cytology

Research focus of supervisor:

The scientific focus is on the study of the cytoskeleton in relation to neuronal and glial transport mechanisms and its functions in developmental processes and neuronal plasticity.

In addition, we are interested in the effects of cytoskeletal (re)organisation on neurodegenerative diseases, glioblastoma tumour biology, amyotrophic lateral sclerosis, schizophrenia and traumatic brain injury.

Publications:

Tjaden J, Eickhoff A, Stahlke S, Gehmeyr J, Vorgerd M, Theis V, Matschke V, Theiss C (2021) Expression pattern of T-type Ca²⁺ channels in cerebellar Purkinje cells after VEGF treatment. *Cells*. IF: 6.600

Gehmeyr J, Maghnouj A, Tjaden J, Vorgerd M, Hahn S, Matschke V, Theis V, Theiss C (2021) Disabling VEGF-Response of Purkinje Cells by Downregulation of KDR via miRNA-204-5p. *Int J Mol Sci.*, 22(4), 2173. IF: 5.923

Wolters A, Reuther J, Gude P, Weber T, Theiss C, Vogelsang H, Matschke V (2021) Teriflunomide provides protective properties after oxygen-glucose-deprivation in hippocampal and cerebellar slice cultures. *Neural regeneration research*. 2021, Nov;16(11):2243-2249. doi: 10.4103/1673-5374.310689. IF: 5.135

Brüne M, Theiss C (2020) Commentary on: “Host-parasite interaction associated with major mental illness”. Why we need integrative explanations based on evolutionary theory. *Molecular Psychiatry*, 25(1): 2-3. IF: 12.384.

Krcek R, Matschke V, Theis V, Adamietz IA, Bühler H, Theiss C (2017) Vascular Endothelial Growth Factor, Irradiation, and Axitinib Have Diverse Effects on Motility and Proliferation of Glioblastoma Multiforme Cells. *Front. Oncol.*, <https://doi.org/10.3389/fonc.2017.00182>. IF: 6.244

H-index: 22, no. of publications of the last 5 years: 35

Summary of research plan

Background: Cerebral hypoxia and subsequent reoxygenation are key components of several diseases, including traumatic brain injury, acute respiratory distress syndrome, obstructive sleep apnea, high-altitude cerebral oedema, and acute altitude sickness, as well as cardiac arrest and ischemic stroke. The latter two diseases are the most common cause of death or permanent impairment worldwide. The degree of disability is highly dependent on the time to intervention. Safe drugs for rapid intervention would therefore be desirable.

Study objective: In this project, different drugs will be investigated for their positive effect after hypoxic damage to the brain. The focus is in on two effects, (i) a possible therapeutic treatment and also (ii) preventive properties. For this purpose, *in vivo* as well as *in vitro* methods are used. The compounds will first be analyzed in cerebral slice cultures under hypoxic conditions before the effects found will be verified *in vivo* in a newly established minimally invasive animal model for hypoxia and cardiac arrhythmia.

Expected Results: We will investigate compounds with immunomodulatory, immunosuppressive, antioxidant and other mechanistic properties. For example, we have studied the drug teriflunomide, which is approved for the treatment of multiple sclerosis, one of the most common multifactorial neurodegenerative diseases in young adults. First encouraging results from this work on neuroprotection after hypoxia in slice cultures of rat brains could already be published by our group. Further studies based on these results will be continued and published soon.

Methods: Brain slice cultures, animal research (rats), hypoxia, histology, immunohistochemistry, confocal laser scanning microscopy, electron microscopy, biomolecular methods, flow cytometry

Candidate Requirements: Scientific degree in medicine, biology or related field; team player; independent thinking; highly motivated; Good English language skills; first animal experimental experience preferred.

Motivation for CSC application: We offer the applicant the opportunity to further expand her/his skills in a modern laboratory. In addition to the PhD, a close collaboration with the Research School of the Ruhr-University Bochum is recommended in order to develop interdisciplinary skills beyond the methods offered by the laboratory. In our department, the applicant works on a cutting-edge topic with direct clinical relevance. There is the possibility to learn histological methods in close connection with modern imaging techniques (confocal laser scanning microscopy, electron microscopy). But also animal experimental work as well as molecular biological and protein biochemical methods such as real-time PCR, Western blot and flow cytometric (FACs) analysis are to be learned. In terms of methods, the applicant has a very broad spectrum at her/his disposal, which can be covered by our laboratory and the support of scientific cooperations.