

## CSC-RUB PhD Project Proposal

**Title:** Neuroprotective and neuroregenerative effects of VEGF and progesterone

**Sector of research:** Neuroscience, growth factors / hormones, medicine, basic research

**Degree awarded:** PhD in Neuroscience

**Keywords:** neuroplasticity, neuroregeneration, brain development, central nervous system (CNS), VEGF, progesterone, miRNAs

**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  $\text{Ca}^{2+}$  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:** The neuroprotective and neuroregenerative mechanisms of action of VEGF and progesterone are investigated. We could show that VEGF positively influences somato- and dendritogenesis of neonatal neurons. Exogenous administration of progesterone also has positive effects on soma area, dendritogenesis and increased spino- and synaptogenesis in immature neurons. However, direct effects on adult neurons could not be observed with either VEGF or progesterone.

**Study objective:** The observed effects of VEGF and progesterone in the nervous system are mediated by VEGF receptor 2, the classical progesterone receptors PR-A / PR-B and the PGRMC1 receptor. Based on findings on age-dependent receptor expression, we have developed the hypothesis that post-transcriptional RNA interference (microRNA) is responsible for these effects. We assumed that microRNAs regulate the expression of the receptors for VEGF as well as progesterone.

Using appropriate profiling, we have already been able to identify microRNAs that exhibit tight coupling to these receptor mRNAs. The mechanisms of action of these identified microRNAs will now be further investigated *in vitro* and *in vivo* to modulate the neuronal plasticity of adult neurons after VEGF or progesterone administration.

**Expected Results:** This approach could potentially help in the regeneration of damaged neurons (due to stroke / ischaemia or injury).

**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.