

## CSC-RUB PhD Project Proposal

**Title:** The gut-brain axis in an animal model of schizophrenia

**Sector of research:** Neuroscience/Psychiatry

**Degree awarded:** PhD

**Keywords:** schizophrenia, brain, gut, microbiome, microglia, rodent, immunohistochemistry, psychiatry, anxiety, behaviour, neuroinflammation, development, infection, pregnancy, neuroanatomy, neuron, cell culture, maternal immune activation, video analysis, translation, microscopy

**Supervisor of PhD project:** Jun.-Prof. Dr. Nadja Freund, LWL University Hospital, Department of Psychiatry, Psychotherapy and Preventive Medicine, Research Division Experimental and Molecular Psychiatry, e-mail: [nadja.freund@rub.de](mailto:nadja.freund@rub.de)

**Research focus of supervisor:** The aim of our work is to model psychiatric disorders in animals and to investigate the resulting changes in the brain. Numerous influences during development play a major role in the brain. In our animal model, we e.g. use maternal separation to induce early life stress or expose the developing embryo to an immune response of the mother during pregnancy. We then investigate the consequences including depressive- or schizophrenia-like behavior. Furthermore, lentiviral manipulation is used to generate our animal model for bipolar disorder. With the animal models used in our group we aim to better understand psychiatric disorders. Specific behaviors, brain regions involved and corresponding therapy options can be examined. Our goal is to contribute to the development of better treatment options, improved diagnostic criteria and early detection methods for psychiatric disorders.

**Publications:** (20 publications in the last five years; five year H-Index: 6)

1) **Juckel G**, Manitz MP, **Freund N**, Gatermann S. Impact of Poly I:C induced maternal immune activation on offspring's gut microbiome diversity - Implications for schizophrenia. *Prog Neuropsychopharmacol Biol Psychiatry*. 2021.110:110306.

2) Wegrzyn D, **Freund N**, Faissner A, **Juckel G**. Poly I:C Activated Microglia Disrupt Perineuronal Nets and Modulate Synaptic Balance in Primary Hippocampal Neurons in vitro. *Front Synaptic Neurosci*. 2021,13:637549.

3) Wegrzyn D, Manitz MP, Kostka M, **Freund N**, **Juckel G**, Faissner A. Poly I:C-induced maternal immune challenge reduces perineuronal net area and raises spontaneous network activity of hippocampal neurons in vitro. *Eur J Neurosci*. 2021, 53(12):3920-3941.

4) Mundorf A, Kubitz A, Hünten K, Matsui H, **Juckel G**, Ocklenburg S, **Freund N**. Maternal immune activation leads to atypical turning asymmetry and reduced DRD2 mRNA expression in a rat model of schizophrenia. *Behav. Brain Res.* 2021, 414:113504

5) Esshili A, Manitz MP, **Freund N**, **Juckel G**. Induction of inducible nitric oxide synthase expression in activated microglia and astrocytes following pre- and postnatal immune challenge in an animal model of schizophrenia. *Eur Neuropsychopharmacol.* 2020, 35:100-110.

**Second Supervisor of PhD project** Prof. Dr. Georg Juckel, LWL University Hospital, Department of Psychiatry, Psychotherapy and Preventive Medicine

#### Summary of research plan

**Background:** Schizophrenia is a mental disorder that affects at least over 24 million people worldwide. The exact causes of schizophrenia are not known, but various factors influence the risk to develop it. One such factor is an infection of the mother during pregnancy. Mice exposed to a maternal immune activation develop schizophrenia-like behavior but also show increased microglia cells and differences in their gut microbiome.

**Study objective:** In the proposed project we will investigate mice offspring that were exposed to maternal immune activation or not (controls). We will monitor mother-child interactions, anxiety, social behaviour, memory and sensorimotor gating deficits. In addition, we will manipulate the gut microbiome and examine the influences on behaviour as well as the brain.

**Expected Results:** We expect that manipulation of the microbiome will be able to ameliorate the effects of the exposure to the maternal immune activation. Our results will be published in international journals and hopefully lay the foundation for better treatment options for patients with schizophrenia

**Methods:** Intensive behavioural testing with modern video analysis and automated testing setups will be conducted in an animal model of schizophrenia. Brains and guts will be analysed using immunohistochemical staining, flow-cytometry and real-time PCR.

**Candidate Requirements:** Good English language skills. Team player. Experience in working with animal models. Programming skills are helpful.

**Motivation for CSC application** (max 250 words): We are a very interdisciplinary team and have regular lab meetings and journal clubs. The PhD candidate will be enrolled in a structured PhD program (IGSN) and has the possibility to attend workshops and apply for funding (to plan an event, for research stays etc.) at the RUB Research School.