

## CSC-RUB PhD Project Proposal

**Title:** Deciphering common mechanisms in neurodegenerative diseases

**Sector of research:** Neuroscience

**Degree awarded:** PhD in Neuroscience

**Keywords:** neurodegenerative diseases, proteomics, protein chemistry, mass spectrometry, bioinformatics

**Supervisor of PhD project:** Prof. Dr. Katrin Marcus & PD Dr. Martin Eisenacher, Medizinisches Proteom-Center (MPC) & Center for Protein Diagnostics (ProDi) , Medical faculty, Ruhr-University Bochum

### Research focus of supervisor:

Our research focus lies on the elucidation of pathomechanisms and the identification of biomarkers in a variety of neurodegenerative and neuromuscular diseases, such as Alzheimer's or Parkinson's disease and Myopathies. To do so, we apply state-of-the-art proteomic techniques and related bioinformatics methodology. Our institute is equipped with five high end mass spectrometers and several add-on devices to study the composition of proteins and lipids in complex samples. For data storage and bioinformatics as well as statistics analysis high-end hardware such as hundreds of TeraByte redundant disc systems and high-performance servers with virtualization and cloud functionality are available. We further focus on functional studies in suitable cell culture systems, mimicking neurodegenerative diseases to verify or patient-derived results.

### Publications:

1. MaCPepDB: a database to quickly access all tryptic peptides of the UniProtKB (2021) Uszkoreit J, Winkelhardt, D, Barkovits K, Wulf M, Roocke S, **Marcus K, Eisenacher M**, J Proteome Res, 20(4), 2145-2150
2. Proteomic Characterization of Synaptosomes from Human Substantia Nigra Indicates Altered Mitochondrial Translation in Parkinson's Disease (2020) Plum S, Eggers B, Helling S, Stepath M, Theiss C, Leite REP, Molina M, Grinberg LT, Riederer P, Gerlach M, May C, **Marcus K**, Cells, 9(12), 2580
3. Advanced Fiber Type-Specific Protein Profiles Derived from Adult Murine Skeletal Muscle (2021) Eggers B, Schork K, Turewicz M, Barkovits K, **Eisenacher M**, Schröder R, Clemen C, **Marcus K**, Proteomes, 9(2), 28
4. CalibraCurve: A Tool for Calibration of Targeted MS-Based Measurements (2020) Kohl M, Stepath M, Bracht T, Megger DA, Sitek B, **Marcus K, Eisenacher M**, Proteomics, 20(11), e1900143.
5. A metastable subproteome underlies inclusion formation in muscle proteinopathies, Ciryam P, Antalek M, Cid F, Tartaglia GG, Dobson CM, Guettsches AK, Eggers B, Vorgerd M, **Marcus K**, Kley RA, Morimoto RI, Vendruscolo M, Weihl CC (2019) Acta Neuropathol Commun. 7(1), 197

### H-Index and No of publications (2016-2021)

Prof. K. Marcus: H-Index: 13, No of Publications: 88

PD Dr. M. Eisenacher: H-Index: 15, No of Publications: 56

### Summary of research plan

**Background:** Neurodegenerative diseases are one of the most common health threats in late age stages. They are often accompanied with an abnormal aggregation of proteins, such as A $\beta$  plaques in Alzheimer's disease (AD), Lewy bodies in Parkinson's disease (PD) or TDP-43 aggregation in Amyotrophic Lateral Sclerosis (ALS). Nevertheless, common mechanisms between diseases, potentially revealing similar patterns of protein aggregation are not known so far. Our first literature screens in combination with own results point to at least similar pathomechanisms in AD, PD and ALS. Therefore, with this project we want to get deeper insights into these (potentially) common disease mechanisms.

**Study objective:** The goal of this study is to retrospectively analyse proteomic samples (tissue and body fluids) of patients, harboring a neurodegenerative disease (e.g. Parkinson's disease, Alzheimer's disease, Amyotrophic Lateral Sclerosis). The aforementioned samples were already measured at MPC and shall be used to identify common proteomic patterns among the different diseases. In a next step, the candidate shall re-analyse proteomic datasets based on neurodegeneration from different research groups, deposited in public repositories undermining the derived results. Proteins displaying common patterns between the different disorders shall further be verified by targeted mass spectrometry (PRM) in patient tissue and body fluids. Further functional analysis using suitable model systems for different neurodegenerative and neuromuscular diseases e.g. neuronal and muscle cell lines shall be used for an in-depth characterization of the previously identified common mechanisms in neurodegeneration.

**Expected Results:** The ultimate goal of the proposed project is to identify common factors in neurodegeneration, a topic, which has not been addressed widely so far and shall lay the basis for functional analyses in cell culture systems. The results are expected to have a high impact in understanding neurodegeneration in general and shall lead to several publications.

**Methods:** Bioinformatic tools (MaxQuant, Perseus, R-Studio, KNIME), mass Spectrometry, Proteomics, SDS-PAGE, Western Blot, cell culture, immunohistochemistry

**Candidate Requirements:** We welcome applications from students of biology, biochemistry, chemistry, biotechnology, bioinformatics or a related field of study with a keen interest in medical research and cutting-edge bioanalytical methods. Preferable are experiences in one or more of the following fields: instrumental analytics, mass spectrometry, proteomics, HPLC, cell culture techniques, basic knowledge in R and R-Studio. Besides creativity, a strong ability for problem solving combined with an enthusiasm for scientific research is highly desirable. Teamwork and good communication skills, fluent English as well as the ability to work in an interdisciplinary field of research are necessary.

**Motivation for CSC application:** The MPC is embedded into the Protein Diagnostics Center at the Ruhr-University Bochum. We are one of the leading institutes in Europe for proteomic analysis and are equipped with high end and state-of-the-art equipment, e.g. including five mass spectrometers, 100s of TeraByte data storage and high-performance servers with virtualization and cloud functionality. Furthermore, the MPC has a bioinformatics group, supporting and facilitating the analysis of large proteomic datasets and developing tools for individual research questions. The MPC cooperates with several national and international groups in the field of neurodegeneration and bioinformatics and is closely affiliated to the University Hospital. A PhD candidate will have the opportunity to enrol in the RUB Research School, which offers a variety of funding options to broaden their scientific horizon and to participate in conferences and summer schools.