UNIKLINIK KÖLN | Institut für Humangenetik | CMMC CENTER FOR MOLECULAR MEDICINE COLOGNE

The Institute of Human Genetics (University Hospital Cologne) / RG Zempel is seeking applications for

2 MSc Students (f/m/d)

ready to start in Summer 2022. We are searching for students interested in the area of

Neurodegeneration and pathomechanisms of sporadic and genetic forms Alzheimer's disease and related tauopathies

to join the laboratory "Functional Genetics of Neurodegeneration and Neurologic Disorders" under the lead of Hans Zempel, MD PhD MSc, with currently 1 technician, 4 advanced PhD students, 2 finishing Master students and 1 Bachelor student. The group is embedded in the Institute of Human Genetics (University Hospital Cologne), with roughly 50 scientists and medical doctors, joint progress reports and journal clubs together with collaborating neuroscience groups from adjacent research institutions (University Hospital, CECAD).

The applied methods in our laboratory comprise (but are not limited to) state of the art cellular neurobiology / cell biology, molecular biology / advanced genetic engineering, biochemistry, and advanced microscopy. Applicants should be enthusiastic about understanding basic disease pathomechanisms to help find treatment for currently incurable diseases. For a brief overview of current projects, see https://humangenetik.uk-koeln.de/en/research/functional-genetics-of-neurodegeneration-and-neurological-disorders-working-group/.

Your profile:

- Master student in Biology, Cellular Neuroscience or related disciplines
- Intrinsic motivation and reliability, collaborative work attitude and flexibility
- Experience in cell culture work, fluorescence microscopy, molecular cloning and practical knowledge of mass spectrometry/RNAseq or other omics-based applications are beneficial.
- Good oral and written communication skills in English
- Willing to commit 6-12 months (usually 3+6 months)

Our offer:

- A highly motivated international team of young researchers associated with the CMMC and University Hospital Cologne, with state of the art equipment and core facilities
- Close contact to principle investigators and research groups of the above mentioned institutes, fast integration to an open-minded and welcoming group and institute
- Supervised training in performing advanced laboratory work, scientific writing for publications and grants, and scientific presentations. Master students will be supported to obtain stipends and follow-up funding for a PhD
- Prospective continuation of the project as a fully funded doctoral thesis (3 years, 65% TVöD or similar stipend)
- Variety of established projects, including the projects described on the following page:

Call for applications: 2 MSc Students, RG Zempel / Functional Genetics Neurodegeneration

The applicants will work e.g. on the following projects:

Alzheimer's Disease (AD) and related tauopathies are severe dementia syndromes, there is no cure. We strive to better our understanding of the molecular disease mechanisms, to enable the development of targeted therapeutic approaches. The microtubule-associated protein TAU is a key driver of the neurodegeneration observed in Alzheimer's disease (AD) and other types of dementia/neurodegerenation syndromes. Besides its role in disease pathogenesis, TAU stabilizes neuronal microtubules and likely promotes essential functions, such as axonal growth, transport, synapse formation, and neuronal activity. Alternative splicing of the gene encoding for TAU, *MAPT*, results in the expression of six isoforms in the human brain that differ in their intracellular localization. Focusing on human neuronal models and TAU-humanized mice expressing all human isoforms is crucial for understanding AD pathomechanisms.

Project 1: Isoform-specific toxicity of TAU in AD and related tauopathies

In this project, we established a human iPSC-based neuronal model to study (isoform-specific) functions of TAU. We are currently establishing lentiviral-/AAV-based delivery of individual isoforms to characterize isoform-specific properties of TAU and investigate how TAU mediates toxicity in AD. Using live-cell imaging methods, immunofluorescence staining techniques, and *in vitro* models of AD, we will unravel the contribution of TAU and its isoforms on hallmarks of AD, such as microtubule and spine loss. In addition, we will use multi-omics approaches to discover novel drivers and modifiers of disease in a human neuronal context.

The project highly relies on cell culture work using HEK cells, iPSCs and iPSC-derived neurons but will also take advantage of primary murine neurons derived from TAU-humanized mice. Follow up projects will also focus on animal experiments; experience with animal handling (e.g., FELASA B) is beneficial but not a prerequisite. A great part of the project will also use microscopy-based analyses, such as immunofluorescence imaging, image analysis and live-cell imaging. The student will closely collaborate with a late-stage PhD student and might be able to take over the project after graduation of the PhD student.

Project 2: Intracellular TAU sorting mechanisms and TAU interactome studies

The TAU protein is mainly sorted to the axonal compartment in healthy brain neurons. We aim to unravel the mechanisms that are responsible for efficient TAU sorting under physiological conditions as this is a prerequisite for understanding the development of pathological TAU missorting. We focus on both protein-intrinsic components and cellular interactors that may contribute to the axonal localization of TAU. During the Master's thesis, the student would collaborate with an experienced PhD student to drive forward this project.

The primary cell model used for the project are human induced pluripotent stem cell (hiPSC)-derived glutamatergic neurons. Further *in vitro* neuronal models are primary mouse forebrain neurons and human SH-SY5Y-derived neurons. We use either transfection or lentiviral transduction to introduce self-engineered plasmids to the neuronal cultures. Besides plasmid introduction, the cell culture work includes e.g. maintenance tasks like seeding and passaging of hiPSCs, biotinylation assays or related time course experiments, and protein harvesting. Downstream analysis approaches include advanced fluorescence microscopy, western blots, and TurboID-based interactome studies using mass spectrometry.

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Further information & Contact

Application deadline: None. The positions are advertised until they are filled.

Candidates should submit a single PDF including a very short motivational letter (max. half a page), curriculum vitae that includes grades & honours & and lab/IT skills acquired, academic transcripts, a brief description of previous research experience if not included in the CV.

Please send your application as one single/merged, compressed PDF-file to: **hans.zempel@uk-koeln.de**.

Applications from female candidates are welcome; suitably qualified women will be given preferential consideration unless other applicants clearly demonstrate superior qualifications. We also welcome applications from disabled candidates, who will also be given preferential consideration over other applicants with comparable qualifications.