

**Project 1.5. The role of VPS10P domain receptors in phenotypic polarization of astrocytes and microglia in the diseased brain.**

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**Background:**

Astrocytes and microglia have key impact on the progression of brain diseases. In response to pathological changes in the brain, glial cells undergo activation and secrete biologically active proteins that control immune response, stimulate angiogenesis or rebuild the extracellular matrix. Activated glial cells undergo phenotypic polarization, i.e. they acquire various properties depending on the type of stimulus which is crucial for pathogenesis of brain disorders.

Our data indicate that the activity of VPS10P domain (VPS10P-D) sorting receptors may contribute to different glial cell functions associated with phenotype polarization. VPS10P-D receptors, which include SorLA, sortilin, SorCS1, SorCS2 and SorCS3, are present in the brain where they contribute to the proper sorting of proteins in neurons. We expect that VPS10P-D receptors may also perform similar functions in astrocytes and microglia, thereby contributing to the secretion of proteins crucial for the disease progression.

In frame of this project, we will identify mechanisms that control the transcription of genes encoding VPS10P-D receptors in course of phenotypic polarization of microglia and astrocytes. Next, we will apply mass spectrometry based methods to identify new ligands for VPS10P-D receptors in astrocyte and microglia. We will then examine the molecular mechanisms of sorting these new ligands by VPS10P-D receptors. We will finally verify the significance of these newly discovered mechanisms for the course of brain diseases in *in vivo* models.

The PhD candidate will work with primary glial cultures. (S)he will use biochemical and molecular methods and microscopy. (S)he will work with murine models of brain diseases (ischemic stroke and/or glioma) and use transgenic mouse lines with modified expression of VPS10P-D receptors. The project will be carried out in collaboration with IPI PAN and Max Delbrueck Center in Berlin, where short research stays of the PhD candidate are planned.

**Aim:**

The aim of the project is to determine the importance of VPS10P-D receptors for glia function in various activation states and, in consequence, for the course of brain diseases. We plan to explore mechanisms controlling the level of VPS10P-D receptors in astrocytes and microglia and to uncover new proteins sorted by these receptors and secreted by activated glial cells. Finally, we will examine the importance of these processes for the pathogenesis of brain diseases such as gliomas, Alzheimer's disease or ischemic stroke.

**Requirements:**

- education: MSc in biology, biotechnology, pharmacy, veterinary sciences or similar
- professional experience: experience in laboratory work
- skills: reading and analyzing scientific publications, preparing presentations, good English;
- ability to work with cell cultures and/or practical knowledge of laboratory techniques such as western blot, qPCR;

- experience in work with laboratory animals will be an asset
- competencies: motivation for scientific work, interest in cellular and molecular biology, good organization of work, creativity, ability to work as a part of a team and also independently, flexibility;
- good, written and spoken, communication skills; manual skills