Module Number 3d Protein Pathology in Neurodegenerative Diseases and Mental Brain Disorders Module type: compulsory elective Language: English Group Size: 3 students Study semester: 1 Availability: winter semester Duration: 1 semester

Workload: Credits: Contact time: Independent study:

420 hrs 14CP 124 hrs 296 hrs

1 Courses

- a) Lecture 2 PPW
- b) Practical course 9 PPW

2 Intended learning outcomes

After completion of this module students

- (1) will have a solid understanding of two of the most common and devastating brain diseases, the neurodegenerative disorder Alzheimer's disease and the mental illness schizophrenia,
- (2) will be familiar with the neuropathology and the clinical symptoms of these diseases, diagnostic methods, molecular disease mechanisms, and therapeutic options,
- (3) will be able to explain the concept of protein pathology (misfolding and aggregation), which is fundamentally important in both neurodegenerative and a subset of mental disorders,
- (4) will be able to ask scientific questions about brain diseases and will learn how to translate these questions into experiments,
- (5) will be able to work independently and accurately with laboratory equipment,
- (6) will be able to apply basic methods to express, detect, and analyze cellular proteins,
- (7) will be able to analyse and document experimental results according to good scientific practise standards,
- (8) will be able to present and discuss experimental results and scientific context.

3 Content

The supervision of the module will be shared equally by the Korth and Weggen research groups.

Lectures:

Mental disorders (Korth lab): introduction into mental disorders, genes, and biological modelling; recombinant proteins for biological use; DISC1 protein and the dopaminergic system; pathological protein multimers and conformers in neuroscience; physiological and pathological role of α -synuclein; proteostasis and the neuroscience of aging; insoluble proteins in mental illness; experimental theory and the importance of using controls.

Neurodegenerative diseases (Weggen lab): introduction to neurodegenerative disorders and Alzheimer's disease; genetics and molecular pathogenesis, therapy and prevention; the intramembrane protease γ -secretase as a therapeutic target in Alzheimer's disease; the role of glia cells in the disease; familial Alzheimer's disease.

Practical course:

The Korth and Weggen labs belong to the Department of Neuropathology, and the students will practise a variety of experimental methods focussed on protein analysis in its facilities, and they will intensely interact with the research group members in the supervision of experiments, data analysis and documentation.

Weggen lab (days 1-8)

Exp1 – Pharmacological manipulation of amyloid-β peptide generation Experimental methods: sterile culturing of different eukaryotic cell lines, pharmacological manipulation of cells; extraction and quantification of cellular proteins, SDS-PAGE and Western blotting; ELISA analysis of secreted proteins, fluorescence microscopy Exp2 – Cellular uptake and degradation of amyloid-β peptides by monocytic cells Experimental methods: culturing of human monocytes and differentiation into macrophages; quantification of cellular protein uptake (phagocytosis assay); quantitative real-time PCR

Korth lab (days 9-15)

Exp 1 - Expression of a bioactive recombinant protein in E. coli.

Experimental methods: culturing, transformation and lysis of bacterial cells; chromatographic purification of recombinantly expressed proteins; measuring concentration and purity of proteins by Nanodrop, BCA, and SDS-PAGE.

Exp 2 –Investigating dopamine uptake and its pharmacological manipulation in vitro Experimental methods: sterile culturing of human neuroblastoma cells; pharmacological manipulation of cultured cells; fluorescence measurements, kinetic analysis

Exp 3 – Visualizing the dopamine system of the brain in wild type and transgenic rats.

Experimental methods: Cryo sectioning of rat brains; fixation of tissues; immunostaining and microscopy; quantification of anatomical changes (cell counting)

Final presentation:

At the last day of the module (day 16), the students will give a scientific presentation and will defend and discuss the results of the practical course within the scientific context.

4 Teaching methods

Lectures, interactive questionnaires, practical course with demonstrations and hands-on guidance (everybody will have hands-on experience), oral presentation, supervised protocol writing and data analysis

5 Prerequisites

Formal: Successful completion of module 1.

With regards to content: basic knowledge of neurobiology

6 **Examination type:** cumulative examination

Written exam (70% of total grade)

Oral presentation of the practical course (30% of total grade)

7 Requirements for award of credit points

Regular participation in the practical training. Final presentation of experiment results. Successful participation in the written examination. Delivery of written summary of the practical course.

8 Module applicability (in other study courses)

Master Biology

9 Assessment

The mark given will contribute to the final grade in proper relation to its credits.

10 Module convenors and main lectures

<u>Prof. Dr. Carsten Korth, Prof. Dr. Sascha Weggen</u>, Dr. Andreas Müller-Schiffmann, Dr. Svenja Trossbach, Dr. Sarah Tschirner, Rita Marreiros, Isabella Ogorek

11 Further information

The regular participation in the lecture is strongly recommended. The content of the lectures is prerequisite for the practicals and the seminars.