Proteome Hub - Proteomics techniques

1.0 Objective

The Proteome Hub provides several proteomics techniques to study biological mechanisms in neurological diseases.

The SyNergy Proteome Hub will provide equal access to all users. However, according to the large number of projects and samples and the limited measurement time on the available instruments, we have to apply a certain prioritization of submitted projects based on:

- Scientific relevance of the project with regard to SyNergy aims
- Required sample preparation and measurement time
- Required method optimization or test sample evaluation
- Date of sample submission
- Special urgency such as manuscript revisions

The Proteome Hub members will provide a detailed data analysis report with statistical evaluation in an excel sheet. Furthermore, we will provide support for additional data analysis such as pathway and protein cluster enrichment analyses, as well as figure and manuscript preparation.

2.1 Organisation

Location and Coordinators:

Name	Institution	Location	Mail	Phone
Stefan Lichtenthaler	DZNE Munich and TUM	CSD U1 room 133	stefan.lichtenthaler@dzne.de	089-4400 46425
Christian Behrends	LMU Munich	CSD 3rd floor, room 117	christian.behrends@mail03.med.uni-muenchen.de	089-4400 46509

2.2 Technical portfolio

LC-MS/MS Instrumentation:

- 2 Easy nLC 1200 + Q Exactive HF
- 1 Easy nLC 1000 + Q Exactive

Methods:

- Label Free Quantification (LFQ) of proteins with Data Dependent Acquisition (DDA) and Data Independent Acquisition (DIA)
- Secretome Protein Enrichment with Click Sugars (SPECS) to study protein secretion in (primary) cell cultures
- Cerebrospinal Fluid (CSF) proteomics including murine CSF samples
- Proteomics of MACS or FACS sorted cells
- Affinity purification mass spectrometry to determine protein interactomes
- Proximity labeling methods (APEX2, TurboID) to study organelles and protein-protein interactions
- Ubiquitination profiling

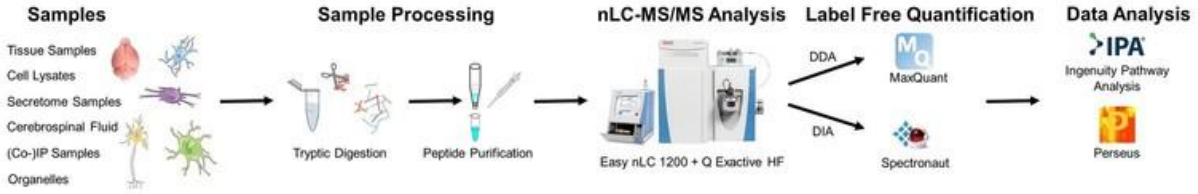

Fig.1: General proteomics workflow.

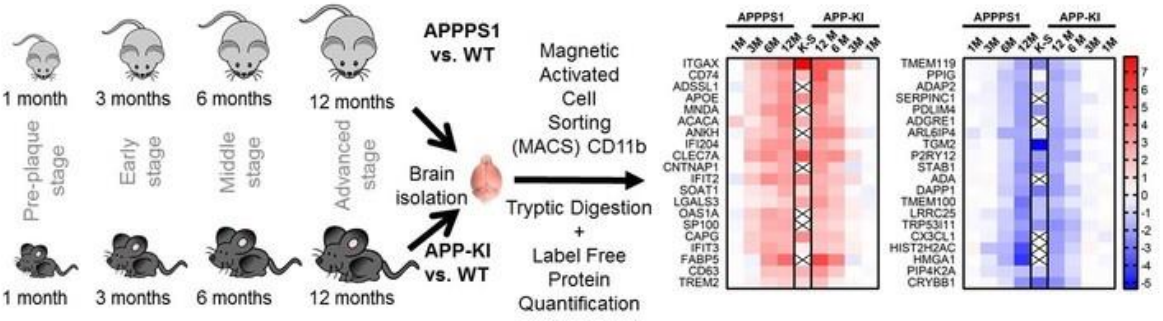

Fig.2: Proteomic analysis of MACS sorted microglia in two Alzheimer's disease mouse models.

2.3 Project request procedure

Before starting a new project, Synergy members have to provide a detailed project proposal, which will be discussed together with the members of the SyNergy Proteome Hub. Based on this proposal, the feasibility of the study will be evaluated regarding sample amount, methods, sample preparation, analysis time, but also potential limitations and discussed with the applying group. This helps to properly plan and schedule the projects. Furthermore, we want to provide advice for sample collection and submission to prevent certain pitfalls such as albumin, FCS or chemical (detergent, PEG) contaminations of samples, which can render samples useless for proteomic analyses. Additionally, some projects require initial evaluation or optimizations with test samples to achieve optimal results.

Please contact a member of the SyNergy Proteome Hub:

Research group Neuroproteomics (DZNE and TUM):

Prof. Dr. Stefan Lichtenthaler

Email: stefan.lichtenthaler@dzne.de
Phone: 089-4400 46425

Dr. Stephan Müller

Email: stephan.mueller@dzne.de
Phone: 089-4400 46437

Research Group Behrends (LMU):

Prof. Dr. Christian Behrends

Email: Christian.Behrends@mail03.med.uni-muenchen.de
Phone: 089-4400 46509

2.4 Fees

The service of the Synergy Proteome Hub is free of charge for SyNergy members within collaborative research projects.

2.5 Publications

Amin A, Badenes M, Tüshaus J, de Carvalho É, Burbridge E, Faísca P, Trávníčková K, Barros A, Carobbio S, Domingos PM, Vidal-Puig A, Moita LF, Maguire S, Střížovský K, Ortega FJ, Fernández-Real JM, **Lichtenthaler SF**, Adrain C (2023). **Semaphorin 4B is an ADAM17-cleaved adipokine that inhibits adipocyte differentiation and thermogenesis.** Mol Metab. 2023 Apr 28:101731. doi: 10.1016/j.molmet.2023.101731. Epub ahead of print. PMID: 37121509.

Bernhardt AM, Tiedt S, Teupser D, **Dichgans M**, Meyer B, Gempt J, Kuhn PH, **Simons M**, Palleis C, Weidinger E, Nübling G, Holdt L, Hönikl L, Gasperi C, Giesbertz P, Müller SA, Breimann S, **Lichtenthaler SF**, Kuster B, **Mann M**, **Imhof A**, Barth T, Hauck SM, Zetterberg H, Otto M, Weichert W, **Hemmer B**, **Levin J** (2023). **A unified classification approach rating clinical utility of protein biomarkers across neurologic diseases.** EBioMedicine. 2023 Feb 4;89:104456. doi: 10.1016/j.ebiom.2023.104456. Epub ahead of print. PMID: 36745974; PMCID: PMC9931915.

Calligaris M, Yang CY, Bonelli S, Spanò DP, Müller SA, **Lichtenthaler SF**, Troeberg L, Scilabra SD (2023). **Identification of membrane proteins regulated by ADAM15 by SUSPECS proteomics.** Front Mol Biosci. 2023 Jun 14;10:1162504. doi: 10.3389/fmolb.2023.1162504. PMID: 37388246; PMCID: PMC10304831.

Liu S, Heumüller SE, Hossinger A, Müller SA, Buravlova O, **Lichtenthaler SF**, Denner P, Vorberg IM (2023). **Reactivated endogenous retroviruses promote protein aggregate spreading.** Nat Commun. 2023 Aug 18;14(1):5034. doi: 10.1038/s41467-023-40632-z. PMID: 37596282; PMCID: PMC10439213.

Müller SA, Shmueli MD, Feng X, Tüshaus J, Schumacher N, Clark R, Smith BE, Chi A, Rose-John S, Kennedy ME, **Lichtenthaler SF** (2023). **The Alzheimer's disease-linked protease BACE1**

modulates neuronal IL-6 signaling through shedding of the receptor gp130. Mol Neurodegener. 2023 Feb 21;18(1):13. doi: 10.1186/s13024-023-00596-6. PMID: 36810097; PMCID: PMC9942414.

Nalbach K, **Schifferer M**, Bhattacharya D, Ho-Xuan H, Tseng W, Williams LA, Stolz A, **Lichtenthaler SF**, Elazar Z, **Behrends C** (2023). Spatial proteomics reveals secretory pathway disturbances caused by neuropathy-associated TECPR2. Nat Commun. 2023 Feb 16;14(1):870. doi: 10.1038/s41467-023-36553-6. PMID: 36797266; PMCID: PMC9935918.

Pratsch K, Unemura C, Ito M, **Lichtenthaler SF**, Horiguchi N, **Herms J** (2023). New Highly Selective BACE1 Inhibitors and Their Effects on Dendritic Spine Density In Vivo. Int J Mol Sci. 2023 Jul 31;24(15):12283. doi: 10.3390/ijms241512283. PMID: 37569661; PMCID: PMC10418759.

Rabinowitsch AI, Maretzky T, Weskamp G, Haxaire C, Tueshaus J, **Lichtenthaler SF**, Monette S, Blobel CP (2023). Analysis of the function of ADAM17 in iRhom2-curly-bare (cub) and Tylosis with Oesophageal Cancer (TOC) mutant mice. J Cell Sci. 2023 Jun 7:jcs.260910. doi: 10.1242/jcs.260910. Epub ahead of print. PMID: 37282854.

Tai YH, Engels D, Locatelli G, Emmanouilidis I, Fecher C, Theodorou D, Müller SA, Licht-Mayer S, Kreutzfeldt M, Wagner I, de Mello NP, Gkotzamani SN, Trovò L, Kendirli A, Aljović A, Breckwoldt MO, Naumann R, **Bareyre FM**, **Perocchi F**, Mahad D, Merkler D, **Lichtenthaler SF**, **Kerschensteiner M**, **Misgeld T** (2023). Targeting the TCA cycle can ameliorate widespread axonal energy deficiency in neuroinflammatory lesions. Nat Metab. 2023 Jul 10. doi: 10.1038/s42255-023-00838-3. Epub ahead of print. PMID: 37430025.

Werner NT, Högel P, Güner G, Stelzer W, Wozny M, Aßfalg M, **Lichtenthaler SF**, Steiner H, Langosch D (2023). Cooperation of N- and C-terminal substrate transmembrane domain segments in intramembrane proteolysis by γ-secretase. Commun Biol. 2023 Feb 15;6(1):177. doi: 10.1038/s42003-023-04470-5. PMID: 36792683; PMCID: PMC9931712.

Jülg J, **Edbauer D**, **Behrends C** (2023). C9orf72 protein quality control by UBR5-mediated heterotypic ubiquitin chains. EMBO Rep. 2023 Jun 15:e55895. doi: 10.15252/embr.202255895. Epub ahead of print. PMID: 37317656.

Tian Y, Milic J, Monasor LS, Chakraborty R, Wang S, Yuan Y, Asare Y, **Behrends C**, Tahirovic S, **Bernhagen J** (2023). The COP9 signalosome reduces neuroinflammation and attenuates ischemic neuronal stress in organotypic brain slice culture model. Cell Mol Life Sci. 2023 Aug 19;80(9):262. doi: 10.1007/s00018-023-04911-8. PMID: 37597109; PMCID: PMC10439869.