Proteomics and Mass Spectrometry Core Facility

Department for Biomedical Research, Murtenstr. 28, 3008 Bern

UNIVERSITÄT BERN

The core facility team

The Proteomics and Mass Spectrometry Core Facility (PMSCF) of the University of Bern consists of a small team of dedicated scientists. Our mission is to provide proteomics and mass spectrometry services to anyone in Life Science wishing to identify and quantify peptides/proteins in their samples.

Our wetlab team receives samples and prepare them. When ready, our instrument scientist injects them in the instrument, which will deliver a set of data (chromatograms, spectra etc.) that needs interpreting.

The core of the *bioinformatics* work in our group consists in **confidently identifying and quantifying peptides and proteins**, producing **visualisation of the results** and when appropriate also **differential expression between groups.** We also provide bioinformatics support for downstream analysis such as **gene set enrichment**, STRING **network integration**, feature reduction such as least absolute shrinkage and selection operator (**Lasso**) etc.

Anne-Christine is the local computational scientist and will be your main port of call and guide through your bioinformatics project in our group.

Prof. Dr. phil. nat Manfred Heller

Head of core facility

M.Sc. Sophie Braga Lagache

Senior assistant

Natasha Buchs

Lab assistant

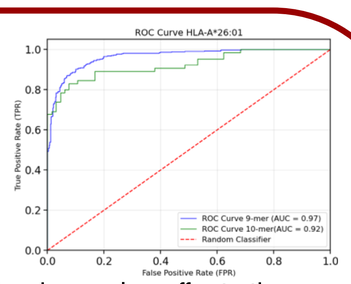
Dr. phil. nat Anne-Christine Uldry

Computational scientist

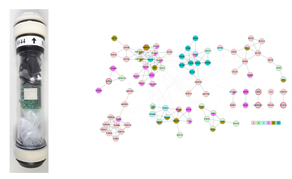
Past and present student bioinformatics projects

*) Master project 2025 (T. Schlatter): Kinase activity exploration with neural networks

*) Research project 2024 (A. Maalouf): Exploration of neural networks for peptide-MHC Class I binding prediction

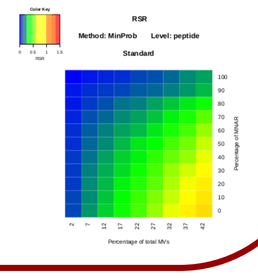


*) Blood transport study 2022 [1]: how the mode of transport of blood samples affects the proteome of circulating extracellular vesicles; proteomics coupled to acceleration sensor measurements as well as application of Lasso algorithm



*) Master project 2021 (L. Kadamala Samuel): training of neural networks in order to predict phosphatase substrates from short AA motifs

*) 4 weeks project 2020 (V. Paukku): exploring the output of a variety of gene set enrichment tools



*) Master project 2019 (M. Jornod): development of software tools (python) for the Identification of cross-linked peptides

*) 4 weeks project 2018 (M. Jornod): exploring the effect of different imputation procedures on synthetic data

Research interests

Immunopeptidomics

Alexandra joined our team end of 2022 to work on a proteogenomic project which consists in collecting cancer neoantigens and study them by mass spectrometry.

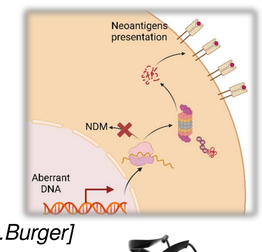
Alexandra E. Burger

PhD student

The idea is that we should be able to promote MHC-I presentation of neoantigens at the cell surface by inducing NMD inhibition, thereby potentially triggering an adequate immune response. Identifying these presenting peptides is therefore a crucial step towards a potential treatment.

Bioinformatics involved:

- Proteogenomics: using PacBio Iso-Seq + Riboseq data in order to produce a suitable protein database for the identification of neoantigens by mass spec (database search)
- *De novo* identifications to look for potential mutations and boost identifications
- Validation of presenting candidate peptides, including using *a priori* knowledge of immunopeptidomics



[A.Burger]

[Wikipedia common]

Extra-cellular vesicles

Extracellular vesicles (EVs) are lipid-bound enclosures that contain a variety of cellular components (metabolites, proteins etc.), and which the cells naturally secrete throughout their life cycle and death.

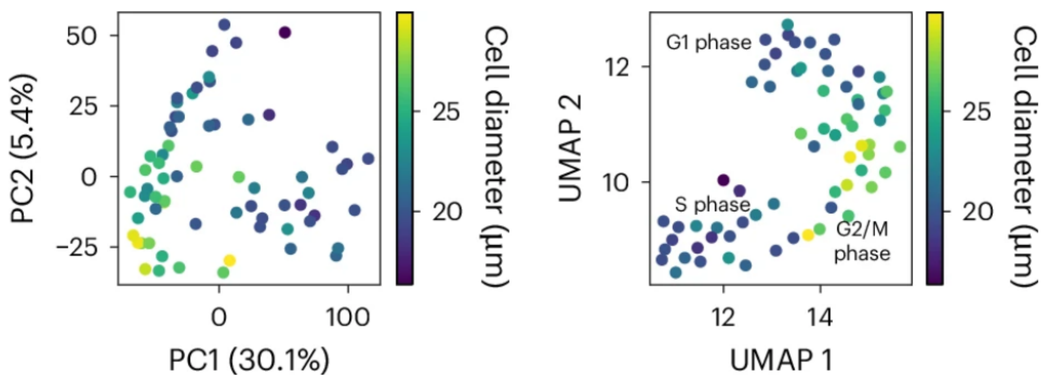
As the cells release EVs, many of them will be found circulating in the blood stream, and as such they serve as long distance messengers to all parts of the organism. EVs have indeed been shown to play roles in a variety of processes including signaling and cancer growth, and are now widely recognized as **potential disease biomarkers and treatment targets**.

Methods have been developed to collect peripheral blood or urine from donors and extract circulating EVs from it, and to analyze them by mass spectrometry.

Single cell proteomics (SCP)

SCP is a relatively new field as very low-abundance samples have long been a challenge for high-throughput mass spectrometry instruments. Advances in both sample preparation and instrumentation are however now allowing us to detect in the order of thousand of proteins per cell[3,4].

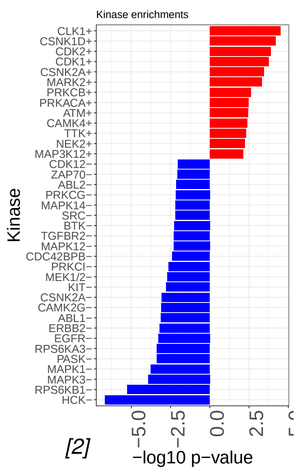
Ex from [4] (epithelial-like human lung cancer cells):



A project initiated by our core facility and involving the cell sorting core facility (FACS) and the Lung Precision Medicine group of the University of Berne will get into its stride in the autumn with the arrival of a wetlab/instrument master student. The effect of at least one drug against lung fibrosis on different cell types will be studied.

Bioinformatics involved:

- Exploration of specific issues related to PSM and protein validation in SCP
- Differential expression
- Data mining techniques (feature extractions etc)



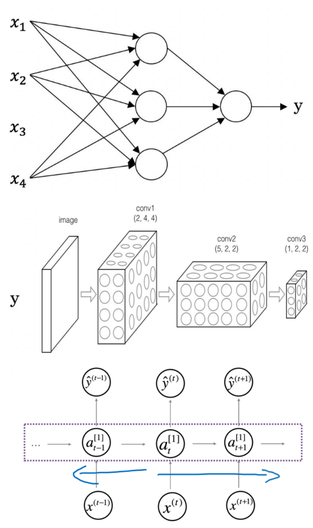
[2]

Myelodysplastic Syndromes (MDS) and Acute Myeloid Leukemias (AML)

A collaborative effort between the Hematology and Oncology department of the Inselspital and our Proteomics and Mass Spectrometry Core Facility has given us access to a number of samples from donors with documented hematological disorders. EVs have been extracted and are ready to be analyzed. The idea here is to detect features that can be ascribed to specific hematological pathologies or donor characteristics.

Bioinformatics involved:

- Differential expression
- Data mining techniques (feature extractions etc)



[Andrew Ng, Deep NN Coursera course]

Neural networks (NN) tools explorations

Realising that a number of tools used from PSM validation to kinase-substrate identification rely on NN, the group is taking a closer look at such tools in order to gauge both their power and limitations, and train their own. Some projects are undergoing (see above) and can be further developed. Alternative possibilities include phosphoproteomics and collisional cross section predictions.

Bioinformatics involved:

- Data curation
- Data organisation and partition
- NN building, training and testing
- NN validation

[1] Effect of Sample Transportation on the Proteome of Human Circulating Blood Extracellular Vesicles (2022); Uldry A *et al;* Int. J.Mol. Sci. 2022,23, 4515; doi.org/10.3390/ijms23094515

[2] Inference of kinase-signaling networks in human myeloid cell line models by Phosphoproteomics using kinase activity enrichment analysis (KAEA) (2021); Hallal *et al*; BMC Cancer 21, 789; doi.org/10.1186/s12885-021-08479-z

[3] Bennett HM, Stephenson W, Rose CM, Darmanis S. Single-cell proteomics enabled by next-generation sequencing or mass spectrometry. Nat Methods. 2023 Mar;20(3):363-374. doi: 10.1038/s41592-023-01791-5. Epub 2023 Mar 2. PMID: 36864196.

[4] Bubis, J.A., Arrey, T.N., Damoc, E. et al. Challenging the Astral mass analyzer to quantify up to 5,300 proteins per single cell at unseen accuracy to uncover cellular heterogeneity. Nat Methods 22, 510–519 (2025). https://doi.org/10.1038/s41592-024-02559-1