Universität Basel

Research Project

A new high-resolution LC-MS platform for high precision and throughput quantitative biology to support life science research at the Biozentrum of the University of Basel

Third-party funded project

Project title A new high-resolution LC-MS platform for high precision and throughput quantitative biology to support life science research at the Biozentrum of the University of Basel
Principal Investigator(s) Schmidt, Alexander ;
Co-Investigator(s) Bumann, Dirk ; Hall, Michael N. ; Handschin, Christoph ; Heim, Markus H. ; Voss, Till ;
Organisation / **Research unit**
Departement Biozentrum / Proteomics (Schmidt)
Department
Project start 01.01.2020
Probable end 31.12.2020
Status Completed

Life science research is performed at many institutes and clinics at the University of Basel and encompasses areas from clinical studies to in-vitro studies with cellular systems or pathogens. Omics technologies are increasingly applied in these projects in order to gain detailed insights into biomolecular processes involved during homeostasis, regulation and perturbation of biological systems. Although genomics provides useful information on the genetic composition of a cell or organism, it is often insufficient to explain the observed biological phenotypes. These questions need to be answered by studying the protein complement (proteome) and cellular signalling by analysing post-translational modifications like phosphorylation (phosphoproteome). As outlined in this proposal, the different projects aim at a better understanding of complex processes involved in initiation and progression of diseases, including bacterial vaccination, malaria, cancer and muscle diseases, using proteomics data. Specifically, the following five projects of the proposal are described:

Project 1 attempts to establish molecular mechanisms mediating responsiveness to targeted cancer therapy by generating proteome and phosphoproteome maps from serial biopsies of hepatocellular carcinoma patients (HCC) before and during drug treatment. We then take an 'multi-omics' approach to find molecular patterns predictive for treatment success.

Project 2 focuses on the discovery of evasive signaling pathways in hepatocellular carcinoma (HCC) by quantitative proteome and phosphoproteome comparisons of patient-derived tumor organoids after Sorafenib treatment at different time points.

Project 3 employs data-independent proteomics to define cellular protein concentrations of *Staphylococcus aureus* proteins in patient abscesses and lung secretions. We will then use a reverse translational approach to find key components for urgently needed protective vaccines.

Projects 4 intends to gain novel important insights into the complex regulation of the biological program of muscle adaptation to exercise by integrating proteome, signaling and protein-protein interaction data obtained from LC-MS analyses.

Project 5ăwill employ targeted proteomics to identify components of the molecular machinery that regulates singular gene choice, an intriguing transcriptional control mechanism that facilitates antigenic variation and immune evasion of malaria parasites.ă

The proposed projects pose extremely challenging demands on protein sample analysis in terms of sensitivity, precision and throughput. Like in all clinical studies, due to the high interpatient variability, high sample numbers are required to achieve sufficient statistical power for confident target discovery and validation. Moreover, many proteins and modifications of interest are low abundant and very challenging to quantify consistently with high precision across large sample batches. After extensive evaluation, we found the Q Exactive HF-X mass spectrometer to be the only instrument on the market to have sufficient speed and sensitivity to meet these high analytical requirements. In particular, its compatibility with data-independent workflows and new on-the-fly acquisition software allows unprecedented proteome coverage in discovery and the highest sensitivity and throughput for targeted MS experiments.ă

We are convinced that the new Q Exactive HF-X is the instrument of choice to fullfil the requirements of the projects listed above, and many more to come in the future.

Keywords Mass spectrometry, hepatocellular carcinoma, proteomics, signalling pathways, infection biology, muscle training
Financed by
Swiss National Science Foundation (SNSF)

Add publication

Add documents

Specify cooperation partners