Proteoomics in Molecular Medicine

Johan Palmfeldt, PhD, Assoc Professor

Research unit for Molecular Medicine / Molekylærmedicinsk Forskningsenhed

Olof Palmes Alle 49
Aarhus University Hospital
Department of Clinical Medicine, Aarhus University

http://clin.au.dk/forskning/core-faciliteter/mmfindex/forskning/proteomics/

E-mail: Johan.Palmfeldt@clin.au.dk

Introduction

Proteomics developed tremendiously in the recent years by the development of ever more sensitive, fast and precise mass spectrometry methods (MS). MS is the main workhorse for both identification and quantification of peptides/proteins as well as metabolites. MS can quantify thousands of proteins or characterize single proteins in detail. MS proteomics is thus a central tool in research of disease mechanisms and protein biomarker discovery.

Research unit for Molecular Medicine (RUMM)

The RUMM laboratory has extensive expertise in studying links between proteome, cellular stress and metabolism and to integrate lab data with clinical patient parameters. The research is bed-to-bench-to-bed oriented **(Fig 1).** RUMM (ca 15 employees) performs research projects within molecular mechanisms of diseases, with the focus on metabolic disorders, mitochondrial medicine and proteomics. RUMM also performs projects within chemical proteomics and characterization of single proteins.

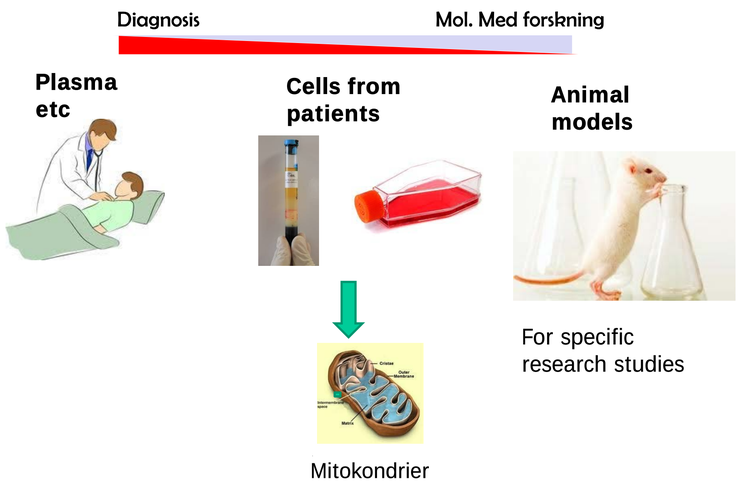


Figure 1. Different sample types are used at RUMM to perform translational molecular medicine.

Methods

RUMM is a fully equipped research unit with instrumentation for molecular biology, culturing and phenotypic characterization of cells, cellular bioenergetics (Seahorse), and proteomics.
Proteomics is performed using nano-LC/MS-MS on Q-Exactive Plus mass spectrometers (Thermo).

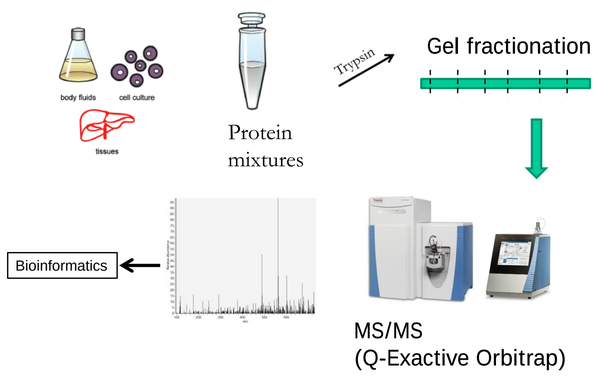
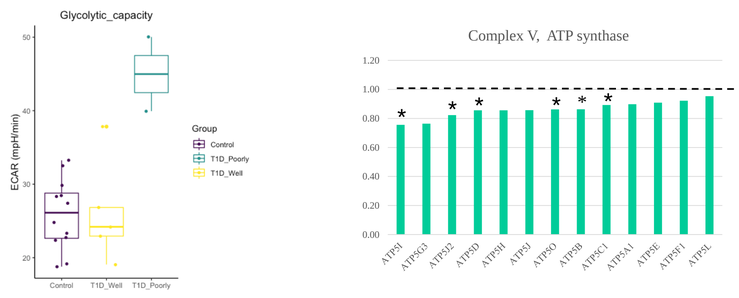


Figure 2. Example of a procedure overview going from biological sample to quantitative data of thousands of proteins.

Examples of Projects

Type 1 Diabetes

1. Circulating immune cells as biomarkers of diabetes



Bioenergetics profiling of peripheral blood mononuclear cells (PBMCs) is a minimally invasive assessment of cellular and mitochondrial function and can mirror systemic changes within the body.

We have observed alterations in bioenergetics and metabolic enzymes of PBMCs in patients with poorly controlled type 1 diabetes.

Bioenergetics and **proteomics** data will now be validated in a higher number of patients, to elucidate the exact links to disease severity.

Chemical proteomics

2. Mapping how newly synthesed drugs bind single target proteins

-Chemical modification of proteins

-Intact proteins are analyzed by state-of-the-art MS

-The novel combinations of chemical+protein is a special type of **Proteoforms**.

-Amino acid site specific information is obtained and functional effects on protein can be studied, to guide **drug development**.

Sulfide – the gasoregulator

3. Treatment of encephalopathy and cancer by targeting sulfide

Exogenous

Endogenous gasotransmitter

- Oxidative stress protection
- Neuroprotection
- Cardiovascular protection

Inherited **encephalopathy** is caused by toxic accumulation of sulfide. The disease causes death within the first decade and only alleviating treatment exists.

Sulfide regulating enzymes have also been linked to **colon cancer.**

Sulfide directed **treatment** will be performed in cell culture models and established protein biomarkers are measured to assess treatment effect.

Summary

-RUMM = Molekylærmedicinsk forskningsenhed is open for student research projects and research colloboration.

-RUMM has a friendly atmosphere with a nicely mixed staff group, and has modern laboratories next to Aarhus University Hospital.

Don't hesitate to ask for project possibilities !