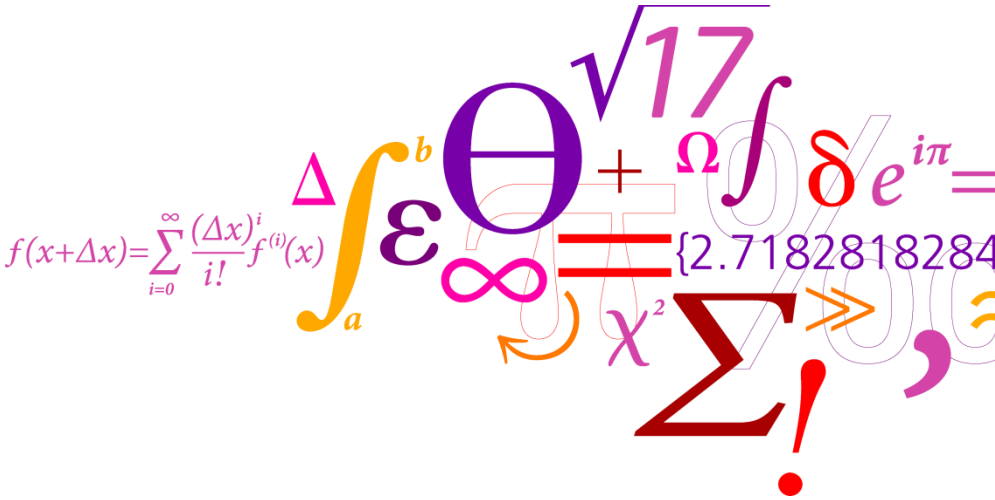
Metabolomics – A Tool for Grouping of Chemicals and Illustration of Mechanism of Action

By Kasper Skov



DTU Food
National Food Institute

Agenda

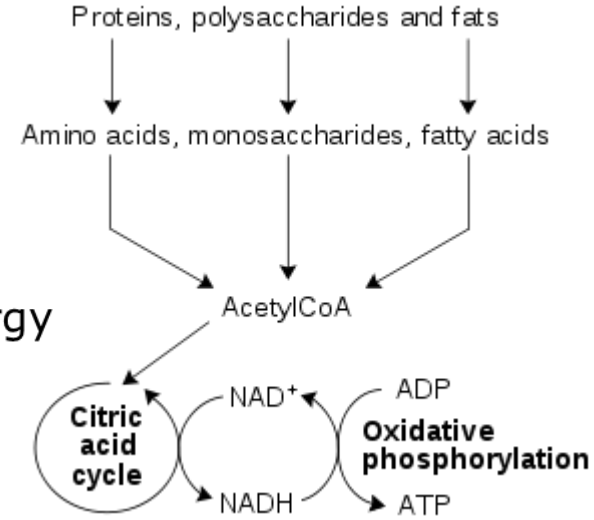
- Introduction
  - Metabolism and metabolomics
  - Mass spectrometry
  - Statistics
- Results
  - Influence of Perfluorononanoic acid (PFNA) ± mixture of EDC on rat blood metabolome
- Conclusion

Metabolomics

- Analysis of all (or as many as possible) low molecular weight metabolites in a specific biological compartment. In the present study rat blood.

Metabolism

- Food is taken up and metabolized into energy which sustains the body functions



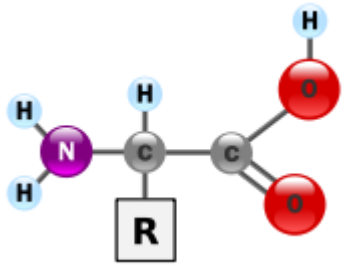
Metabolomics is the scientific study of chemical processes involving metabolites.

Specifically, metabolomics is the "systematic study of the unique chemical fingerprints that specific cellular processes leave behind", the study of their small-molecule metabolite profiles.

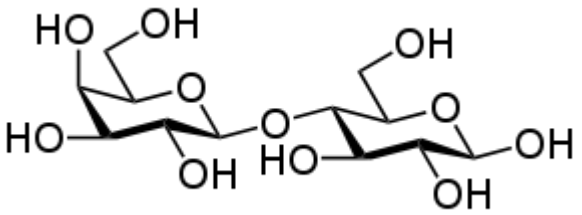
The metabolome represents the collection of all metabolites in a biological cell, tissue, organ or organism, which are the end products of cellular processes.

Wikipedia

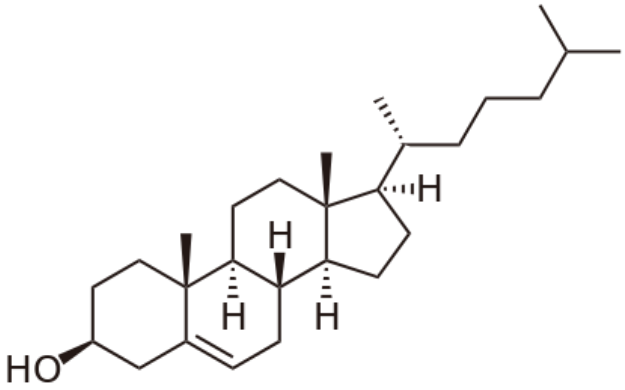
Compounds in the metabolome, examples



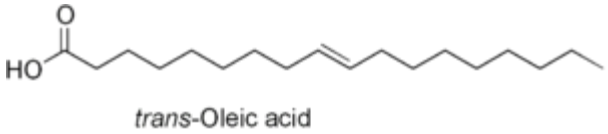
Amino acids

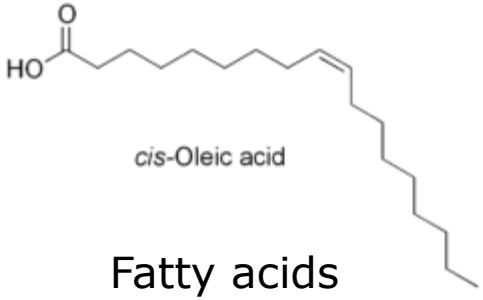


carbohydrates



cholesterol

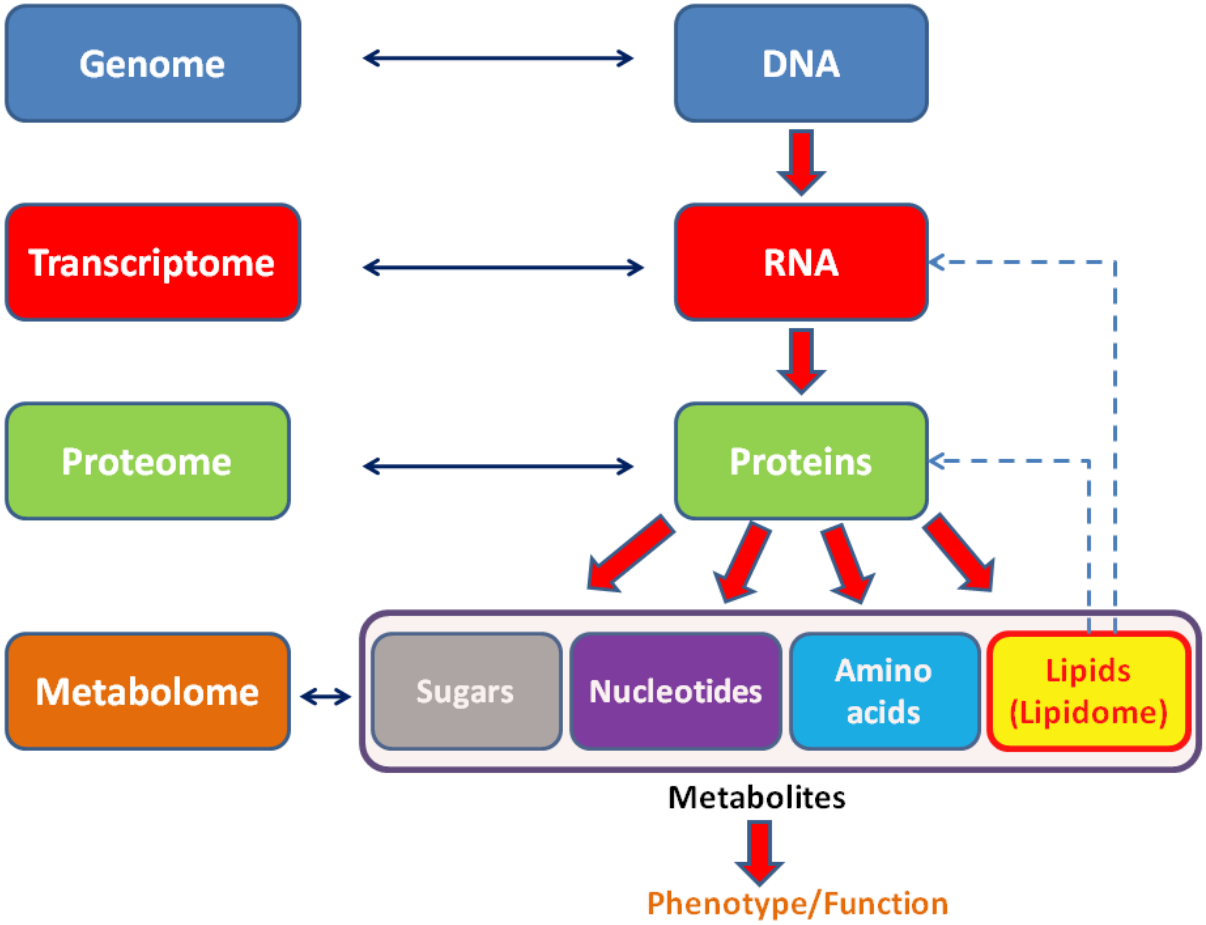




Fatty acids

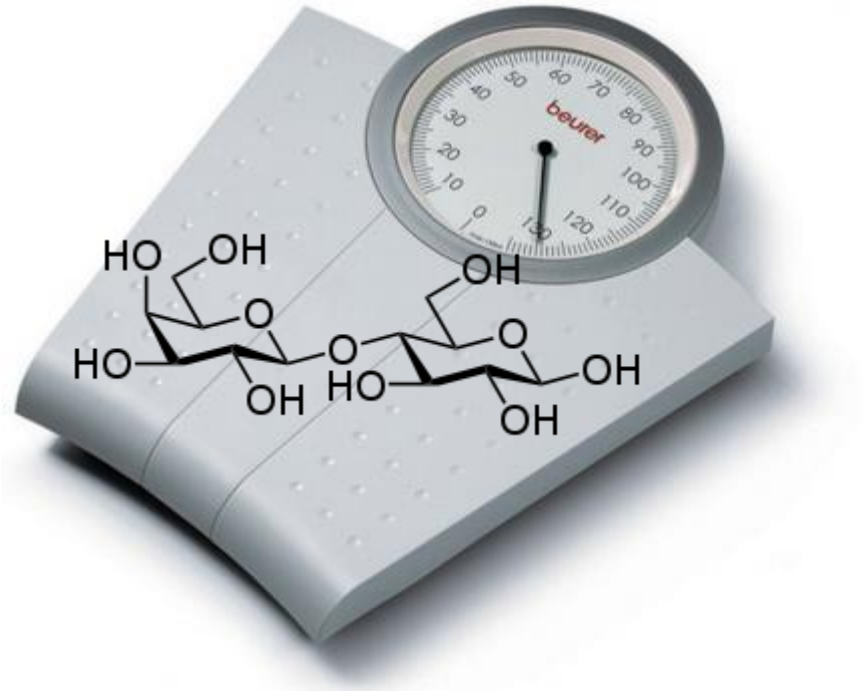
Metabolomics - relation to other omics

- Analysis of the metabolism [omics = analysis of ; metabol = metabolism]

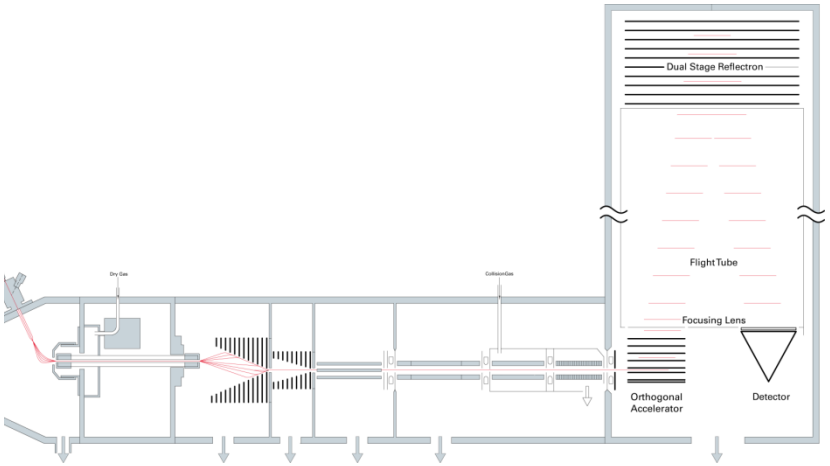


Mass spectrometry

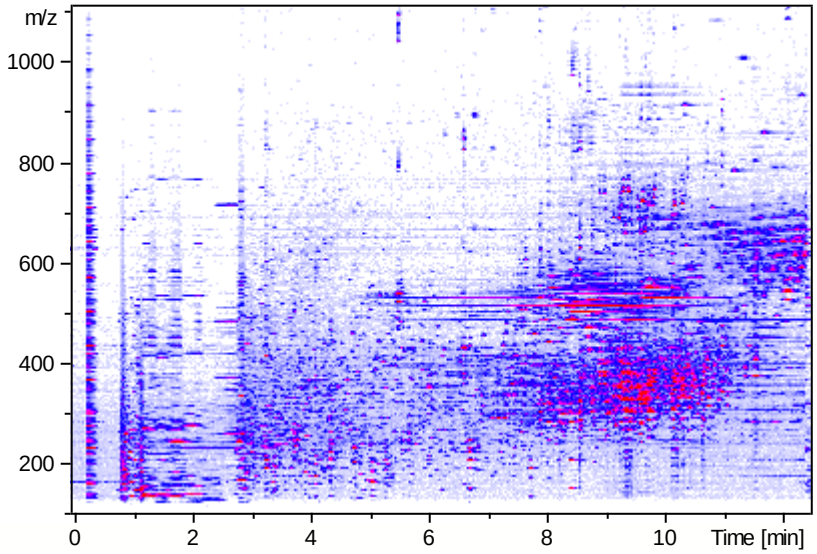
343.123488

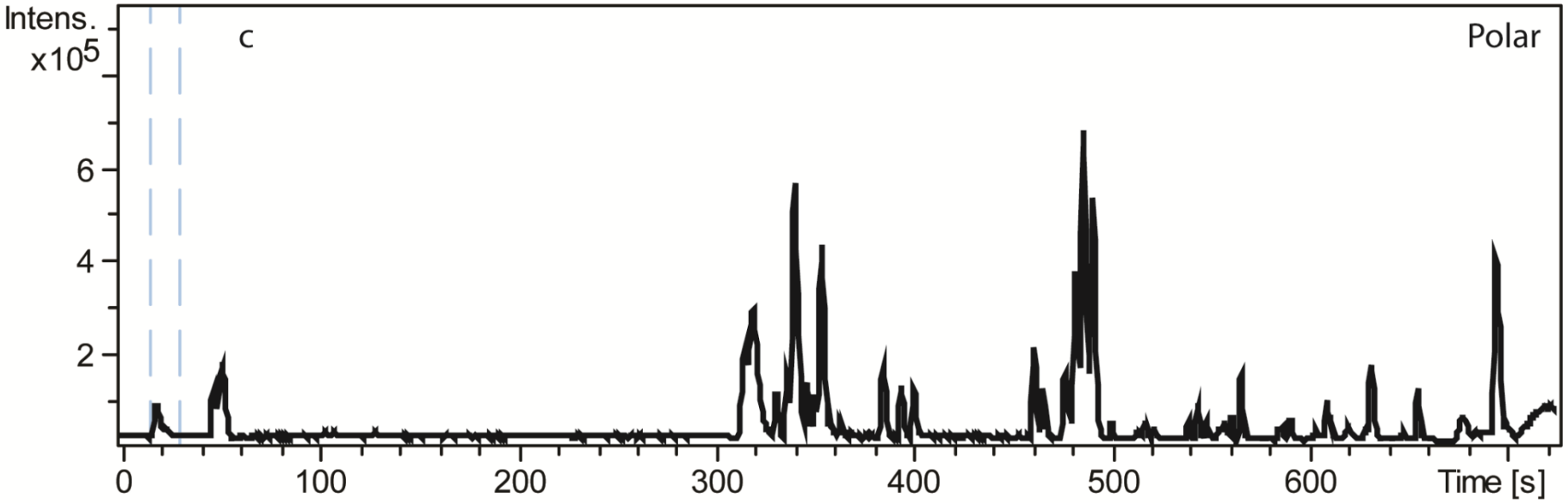


BRUKER



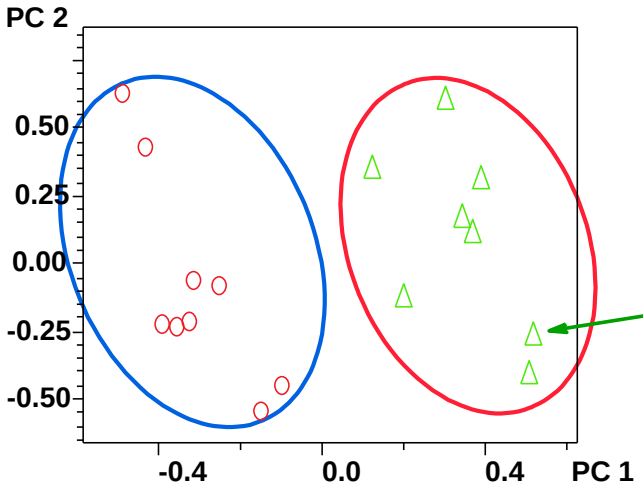
Analysis
one chromatogram from each animal





Statistics – a tool for identification

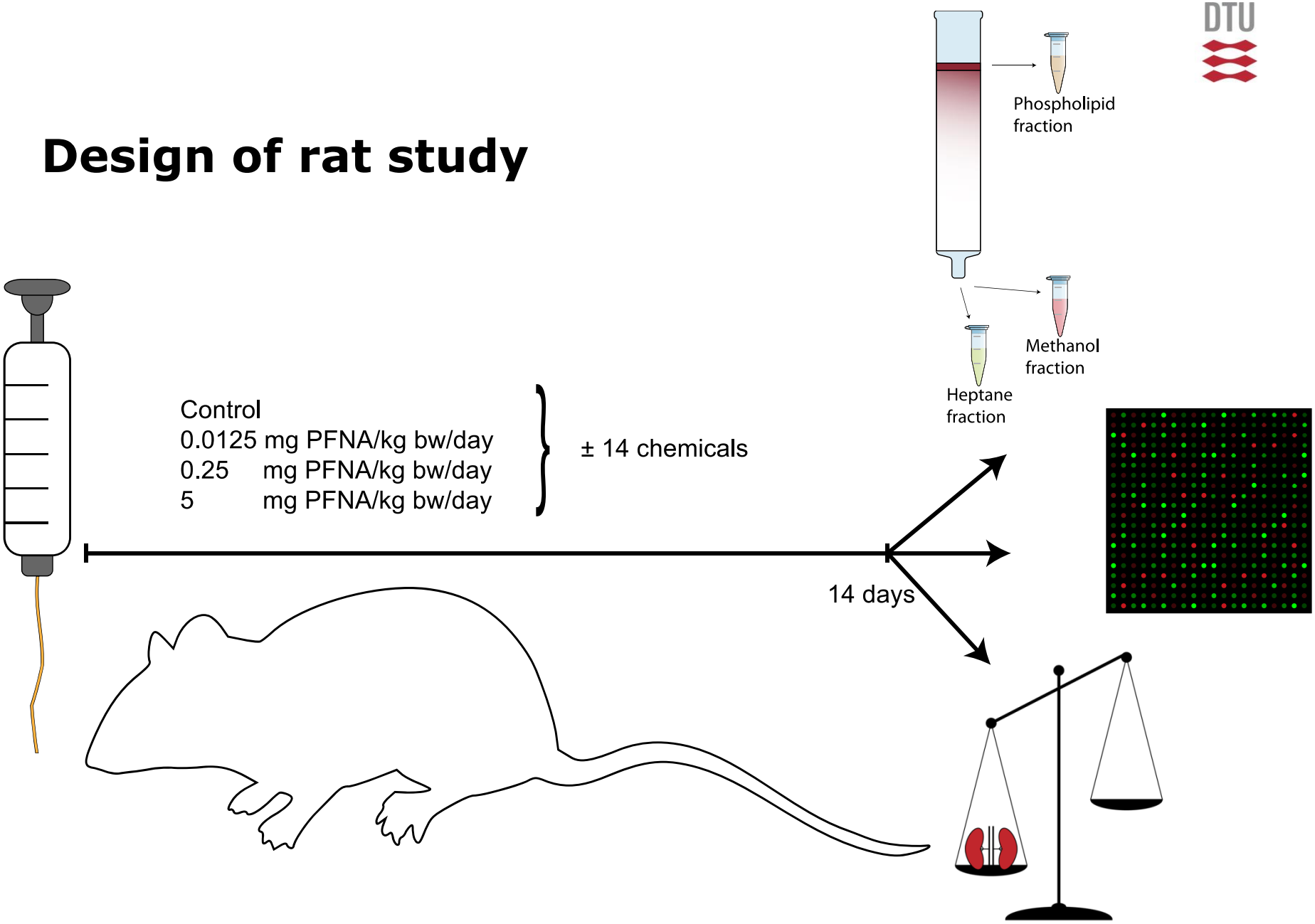
Comparison of exposed vs non-exposed animals



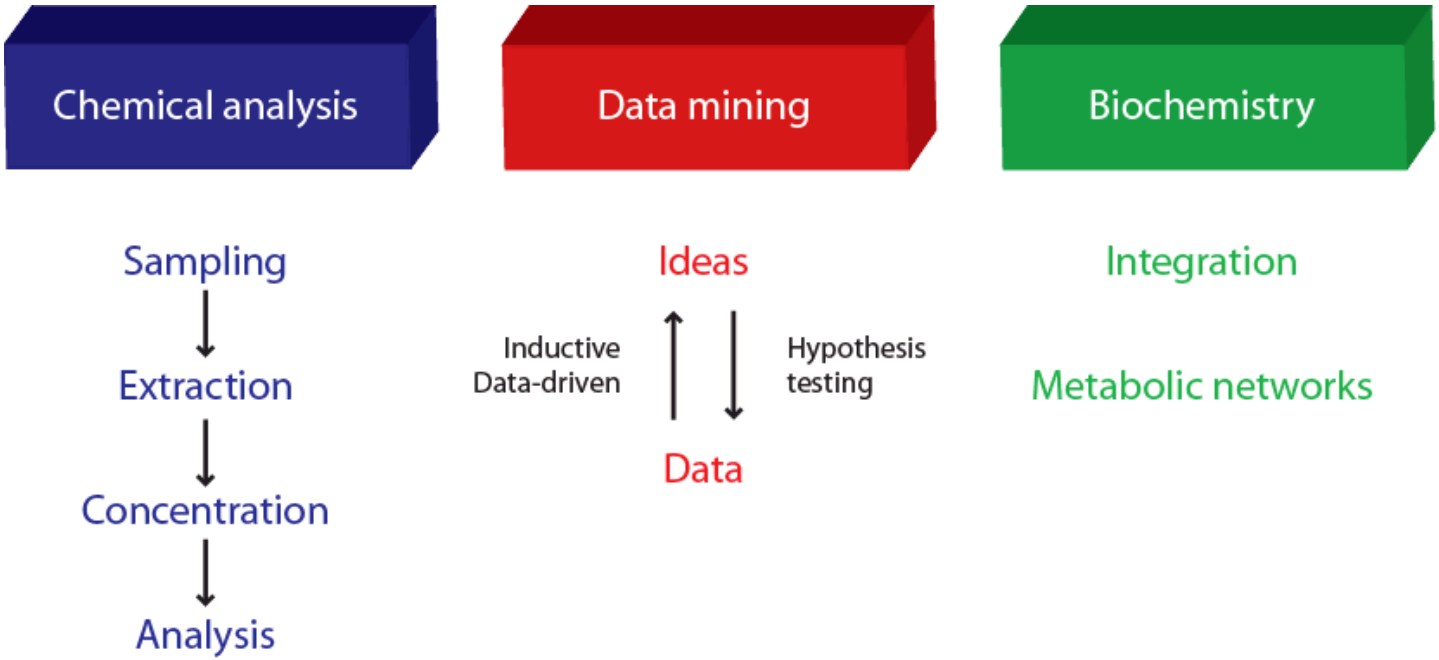
Animaldata

Scoreplot

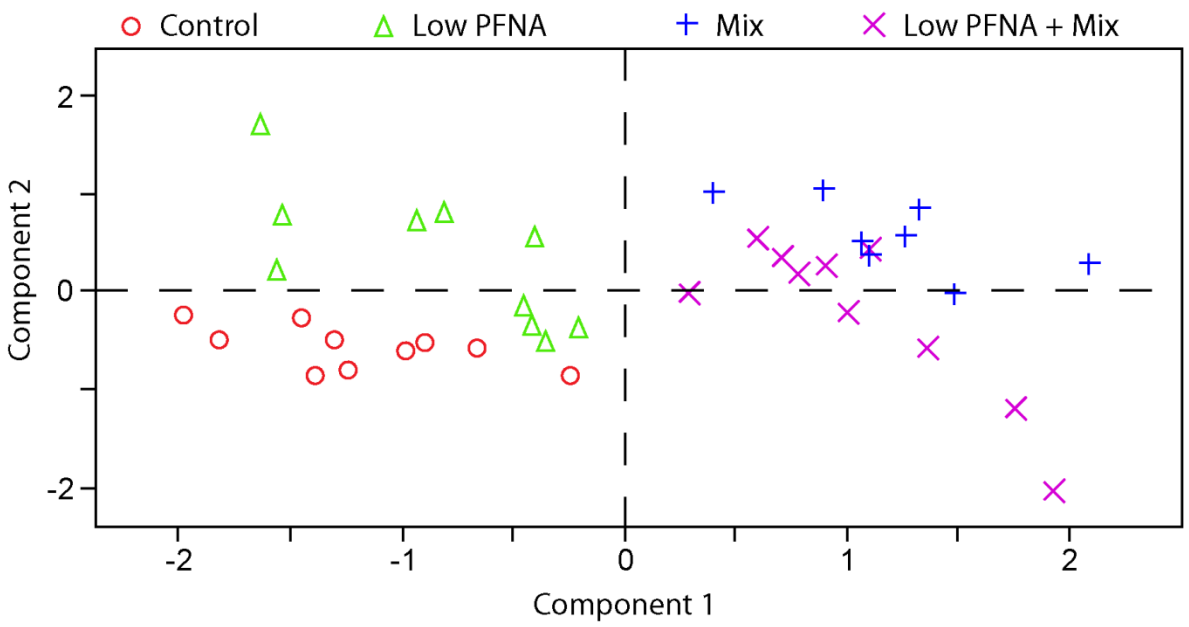
Design of rat study

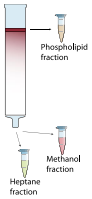


Metabolomics – workflow

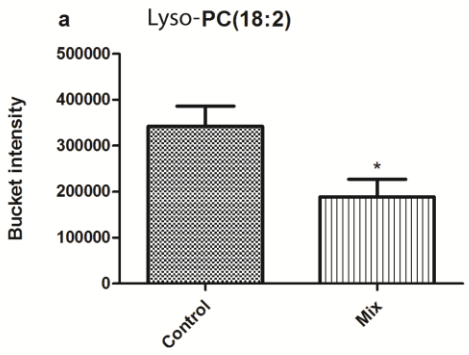


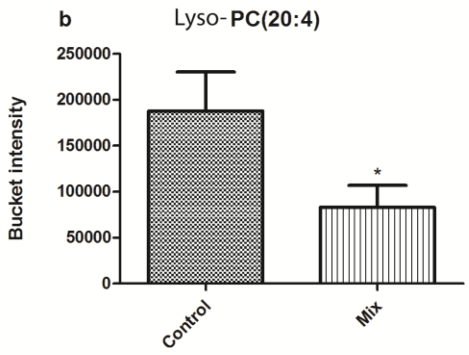
Results
PFNA
Experiment

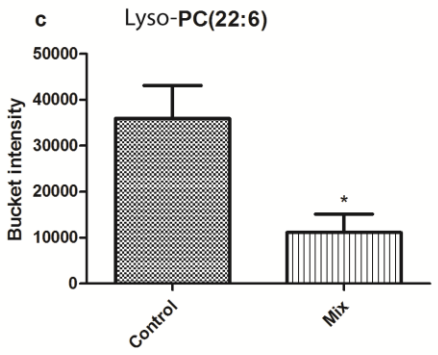


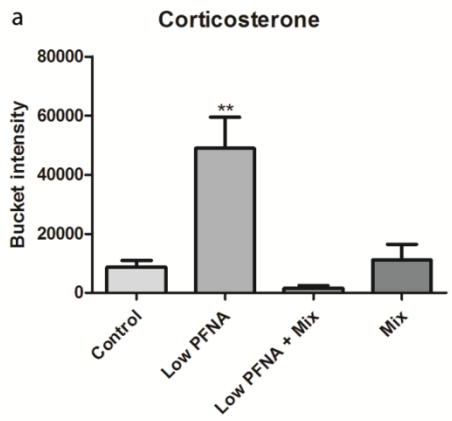


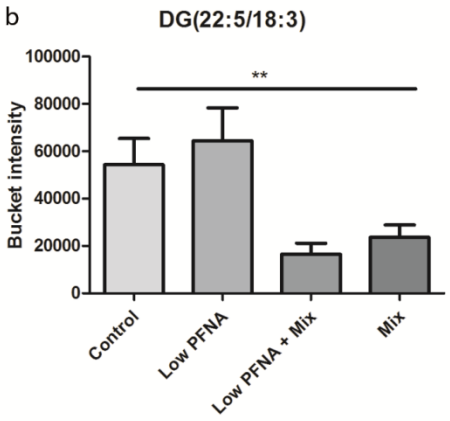
Low dose effect

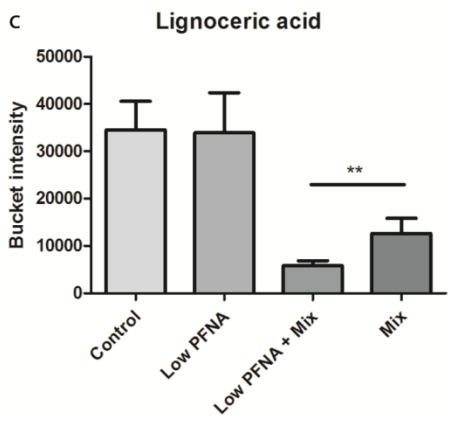








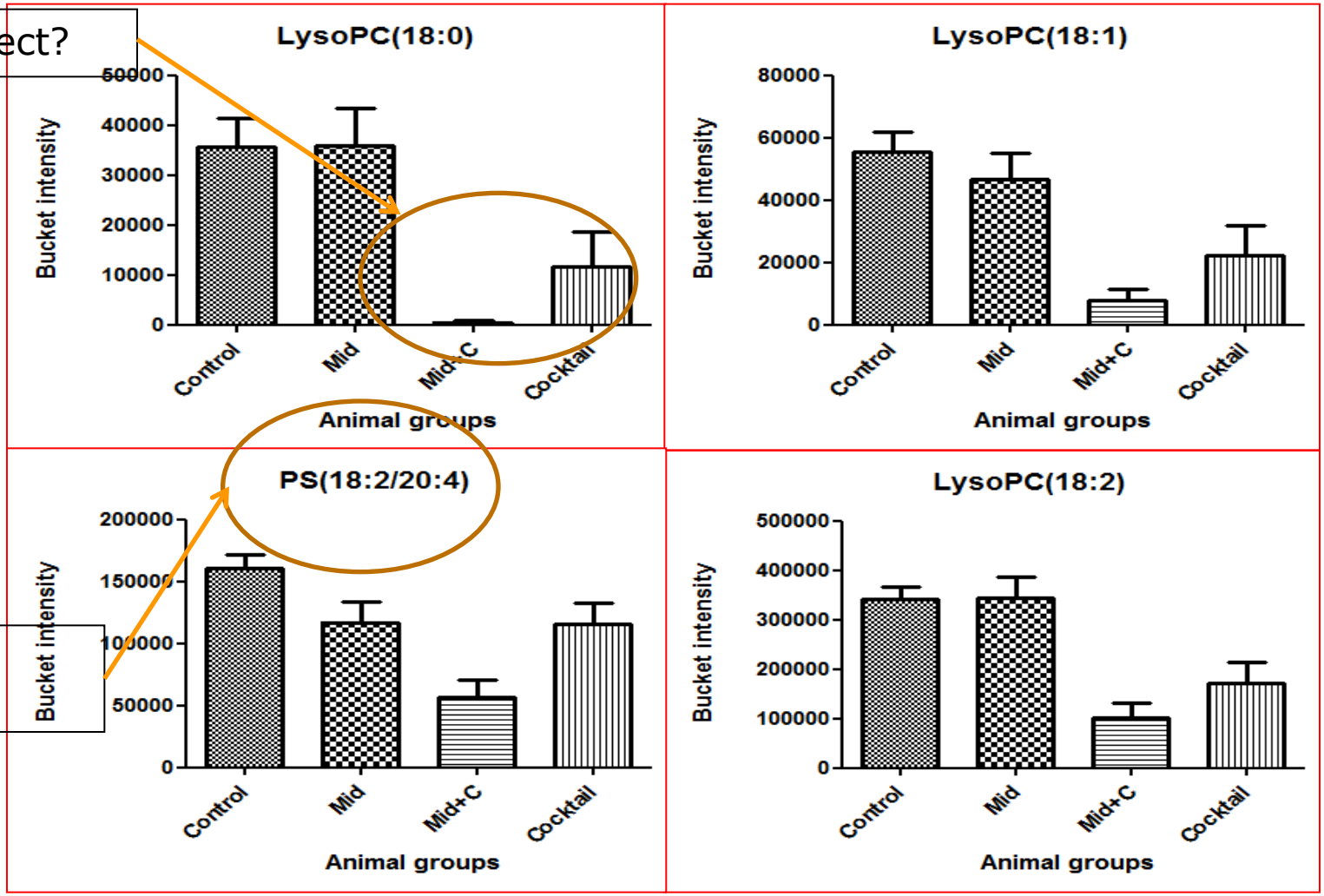




Phospholipids

Cocktail effect?

Or similar composition



Mechanisms of action for PFNA

- Decreased plasma lipid levels
- Activation of Peroxisome proliferator-activated receptor (PPAR)
- Two possible MoA
  - PPAR is activated => increased beta-oxidation, explaining the decreased levels of plasma lipids
  - The plasma lipid concentration is lower due to a response to achieve more energy to protect the body

Metabolomics

Conclusion and future perspective

- We identified changes in the metabolism even at low dose exposure
- Study how exogenous compounds effect the body metabolome.
- With a larger database of toxicity studies with metabolomic investigation. Grouping of chemicals which similar mechanism of action based on similar changes in metabolite panels.

Thanks to

- The cocktail team.
- Danish Veterinary and Food Administration
- Ministry of Food, Agriculture and Fisheries

Questions

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