Metabonomics for MolPAGE
Discovering diabetes biomarkers

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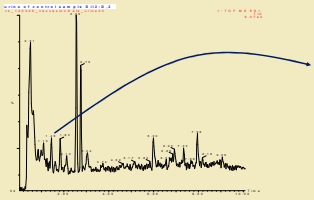
Introduction

MolPAGE (Molecular Phenotyping to Accelerate Genomic Epidemiology) is an EU consortium with almost twenty collaborating universities and companies throughout Europe. One of the aims of MolPAGE is to find early onset biomarkers for type 2 diabetes (T2DM) and cardio-vascular diseases (CVD). Novo Nordisk in Denmark and Imperial College in London are the two partners cooperating closely within the area of metabonomics. Novo Nordisk commitment in MolPAGE also covers transcriptomics.

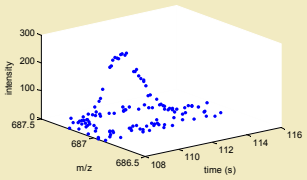
Metabonomics

Metabonomics is concerned with measuring and elucidating the metabolism in organisms. Most of the body's constituents are sooner or later metabolised and metabolites can therefore provide endpoint markers for various disease states. Any change in the bodily function will show up in the person's metabolism.

Typical samples for metabonomics analysis are blood plasma and urine. Historically, the most common analysis/experimental platform has been Nuclear Magnetic Resonance (NMR) spectroscopy. At present, mass spectrometry, often in combination with liquid chromatography (LC/MS), is rapidly gaining increased interest within metabonomics research. It is widely accepted that LC/MS can provide complementary information to that obtained with NMR. Both NMR and LC/MS will be used for analysing the MolPAGE samples in order to extract a maximum of information.



LC/MS data: total ion chromatogram of urine.

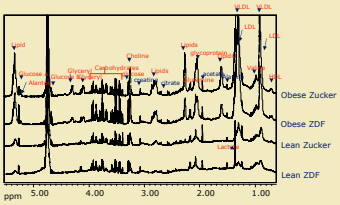


The raw data from a small time-m/z window.

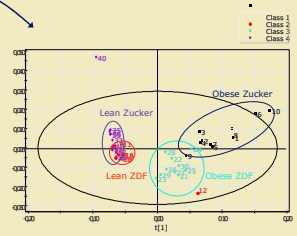
Data analysis

The instruments deliver huge amounts of data. To extract the information about potential biomarkers multivariate chemometrics tools, e.g. principal component analysis and partial least squares-discriminant analysis, are used.

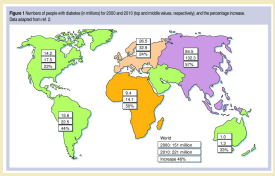
Assignments of plasma NMR spectra



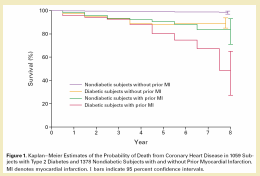
Principal component analysis allows grouping of individuals based on metabolic profiles



Background – T2DM and CVD



Zimmet et al., *Nature*, 2001



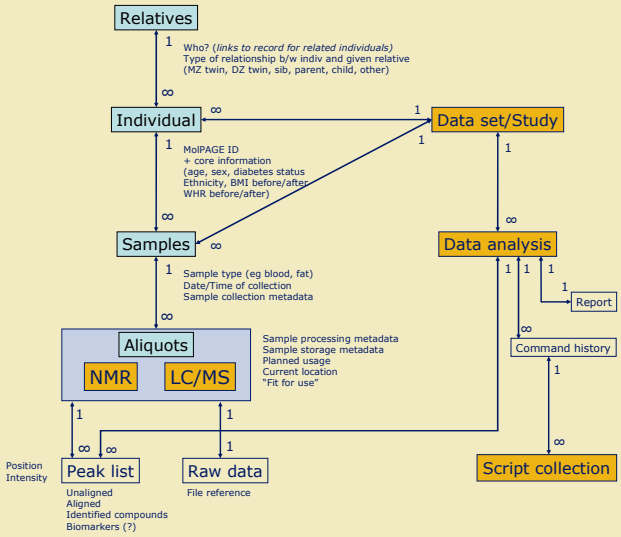
Haffner et al., *N Engl J Med.*, 1998

T2DM and CVD are major western world public health issues.

The methodology developed will have general application in human disease – including cancer and inflammatory diseases.

In-house database

To structure our knowledge and to allow for simple data retrieval and model transparency we are planning to build an in-house database for the generated MolPAGE data and information. Our hope is that MetaboMeeting 1.0 will give us both inspiration and guidelines for creating our database.



References

NMR

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Brindle et al. *Nature Med* **8**(12), 1439–1444 (2002).

LC/MS

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