DAS METABOLOM: ERNÄHRUNGSSTATUS, METABOLISMUS, METABOLITEN

Das Metabolom

Extrinsiche Faktoren
- Ernährung (Nährstoffe und nicht-nutritive Lebensmittelinhaltsstoffe)
- Arzneimittel
- Physische Aktivität
- Darmflora
- Stress

Intrinsische Faktoren
- Körperzusammensetzung
- Stoffumsatz in den Geweben (Turnover)
- Ruheumsatz
- Alter
- Genotyp
- Gesundheitsstatus
- Reproduktiver Status
- Circadianer Rhythmus

Metabolom
Summe aller endogenen und exogenen Metaboliten
The „omics“-Cascade

**Genome**
What can happen

The genome of an organism is a complete DNA sequence of one set of chromosomes; for example, one of the two sets that a diploid individual carries in every somatic cell. The term genome can be applied specifically to mean the complete set of nuclear DNA (i.e., the "nuclear genome") but can also be applied to organelles that contain their own DNA, as with the mitochondrial genome or the chloroplast genome. Organisms is usually referred to as genomics, which distinguishes it from genetics which generally studies the properties of single genes or groups of genes.

**Transcriptome**
What appears to be happening

The transcriptome is the set of all messenger RNA (mRNA), or "transcripts", produced in one or a population of cells. Unlike the genome, which is roughly fixed for a given cell line, the transcriptome can vary with external environmental conditions. Because it includes all mRNA transcripts in the cell, the transcriptome reflects the genes that are being actively expressed at any given time.
The "omics"-Cascade

- Genome: What can happen
- Transcriptome: What appears to be happening
- Proteome: What makes it happen

The proteome is the entire complement of proteins in a given biological organism or system at a given time, i.e. the protein products of the genome. The proteome is larger than the genome in the sense that there are more proteins than genes. This is due to alternative splicing of genes and post-translational modifications like glycosylation or phosphorylation.

The "omics"-Cascade

- Genome: What has happened and is happening
- Transcriptome
- Proteome
- Metabolome
The "omics"-Cascade

The omics cascade comprises complex datasets that as an entity comprehensively describe the response of biological systems to disease, genetic, and environmental perturbations. The most powerful database will integrate data from all omic levels. However, of these databases the metabolome is the most predictive of phenotype.
The "omics"-Cascade

**Genome**
- 3 billion (3 x 10^9) base pairs, 20,000-25,000 genes

**Transcriptome**
- 1 million+ (antisense RNA-coding genes)

**Proteome**
- 1 million proteins, 2 million proteins from alternative splicing and post-translational modification

**Metabolome**
- 2500 (?) metabolites, 1200 drugs, 3500 food components

**Phenotype?**

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The "omics"-Cascade

**Genome**

- Development of nutritional strategies to optimise metabolism and phenotype

**Metabolome**

**Phenotype?**
Metabolic Profiling

- Blood sampling from individuals of different genetic background (CC/CT/TT)
- Solid phase extraction for purification
- LC-MS/MS analysis of metabolites

Metabolic Profiling

- LC-MS/MS analysis of metabolites
Metabolic Profiling

• Generation of metabolite databases
• Mass specs of different samples for metabolic profiling

Data consolidation and statistical analysis by PCA to identify profiles
Metabolic Profiling

bioinformatics
Genome sequencing
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Genotyping

Transcriptome und Proteome:
MALDI (matrix assisted laser desorption ionisation)-MS (TOF, time of flight)
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Transcriptome und Proteome:
MALDI-TOF

MALDI-TOF MS Schematic

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Transcriptome und Proteome:
MALDI-TOF

MALDI-TOF MS Schematic
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Transcriptome und Proteome:
Micro Arrays

Metabolome (Metabolomics, Metabonomics, Metabolic Fingerprinting): NMR (nuclear magnetic resonance = Kernresonanzspektrometrie, LC-MS/MS und GC-MS)

Grundidee: Bestimmung (möglichst) aller Metaboliten in Abhängigkeit von extrinsischen (Ernährung) oder intrinischen (Genetik) Faktoren und der Unterschiede zwischen den Einflussfaktoren

- Ermittlung qualitativer Unterschiede (Profiling, Fingerprinting)
- Ermittlung quantitativer Unterschiede und Identifizierung der jeweiligen Verbindungen (Metabonomics)
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Metabolome (Metabolomics, Metabonomics, Metabolic Fingerprinting): NMR (nuclear magnetic resonance = Kernresonanzspektrometrie, LC-MS/MS und GC-MS)
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Metabolome (Metabolomics, Metabonomics, Metabolic Fingerprinting): NMR (nuclear magnetic resonance = Kernresonanzspektrometrie, LC-MS/MS und GC-MS)

Bioinformatics (PCA: Principle Component Analysis)

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Metabolome LC-MS/MS und GC-MS)

LC-MS/MS: Bruker microTOF-Q (Quadrupole + TOF)
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Metabolome LC-MS/MS und GC-MS)

LC-MS/MS: Shimdazu IT-TOF (ion trap + TOF)

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Metabolome LC-MS/MS und GC-MS)

GC-MS: Agilent GC + MSD