



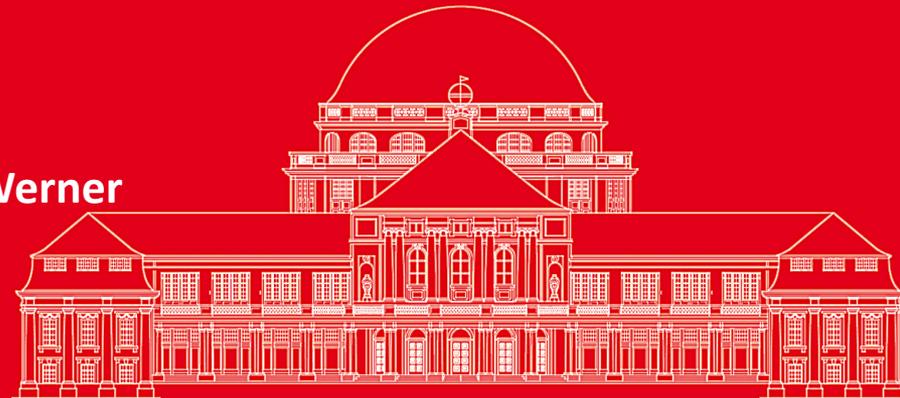
Universität Hamburg

DER FORSCHUNG | DER LEHRE | DER BILDUNG



IDENTIFIZIERUNG SOWIE QUANTIFIZIERUNG VON SCHLÜSSELMETABOLITEN DES DIABETES MELLITUS UND DES METABOLISCHEN SYNDROMS MITTELS MASSENSPEKTROMETRISCHER VERFAHREN

Philipp Werner



- 1. Diabetes:** Grundlagen, Prävalenz, Brisanz
- 2. Das Konzept**
- 3. Apparative** Möglichkeiten
- 4. analytischer Arbeitsablauf**

Metabolische Störung



World Health Organization

Kennzeichen

- Chronische **Hyperglykämie**
- Störungen des Kohlenhydrat-
Fett- und Protein**stoffwechsels**

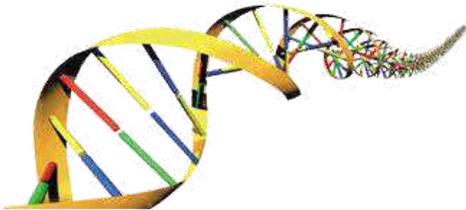
Ursachen

- Defekte Insulin**sekretion**
- Defekte Insulin**interaktion**

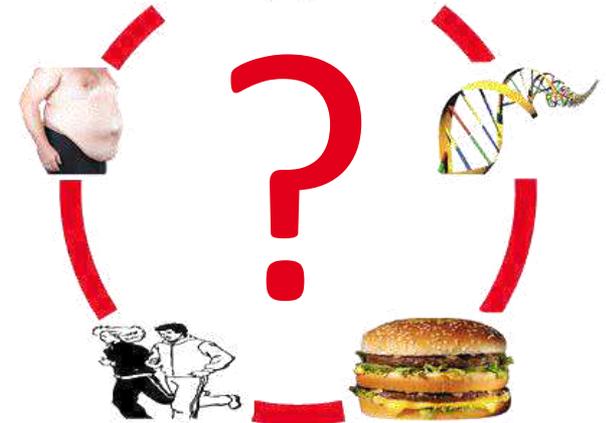
Weitere **Einteilung**

Ätiologie

Typ I



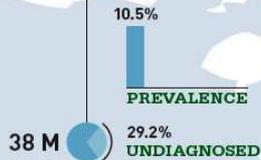
Typ II



NORTH AMERICA AND CARIBBEAN

More healthcare dollars were spent on diabetes in this region than any other

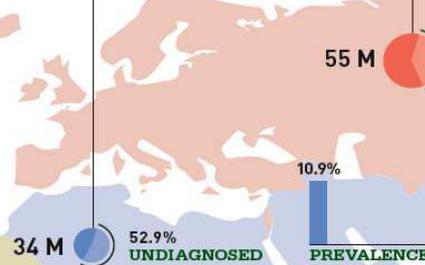
1 in 10 adults in this region has diabetes



MIDDLE EAST AND NORTH AFRICA

1 in 9 adults in this region has diabetes

More than half of people with diabetes in this region don't know they have it



EUROPE

1 out of every 3 dollars spent on diabetes healthcare was spent in this region

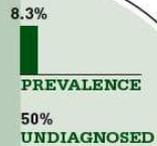
21.2 million people in this region have diabetes and don't know it



WESTERN PACIFIC

1 in 3 adults with diabetes lives in this region

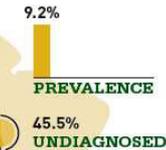
6 of the top 10 countries for diabetes prevalence are Pacific Islands



WORLD

371 M

people living with diabetes



SOUTH AND CENTRAL AMERICA

Only 5% of all healthcare dollars for diabetes were spent in this region

1 in 11 adults in this region has diabetes



AFRICA

Over the next 20 years, the number of people with diabetes in the region will almost double

This region has the highest mortality rate due to diabetes



SOUTH-EAST ASIA

1 in 5 of all undiagnosed cases of diabetes is in this region

1 in 4 deaths due to diabetes occurred in this region

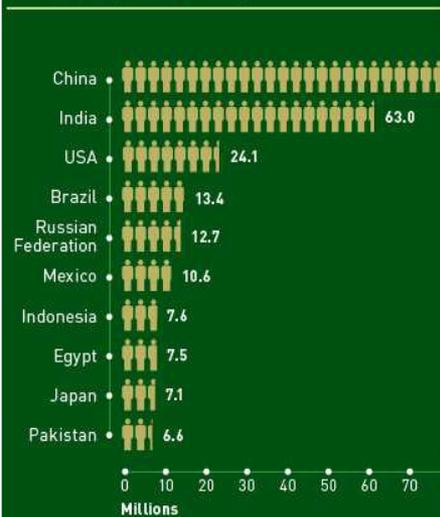
*all estimates are presented as comparative rates

NORTH AMERICA AND CARIBBEAN

More healthcare dollars were spent on diabetes in this region

More than **371 million** people have diabetes

TOP 10 COUNTRIES/TERRITORIES FOR PEOPLE WITH DIABETES (20-79 YEARS)



The number of people with diabetes is **increasing** in every country.

TOP 10 COUNTRIES/TERRITORIES FOR PREVALENCE* (%) OF DIABETES (20-79 YEARS)

| COUNTRY / TERRITORY | PREVALENCE (%) |
|----------------------------------|----------------|
| 1 Federated States of Micronesia | 63.0 |
| 2 Nauru | 24.1 |
| 3 Marshall Islands | 13.4 |
| 4 Kiribati | 12.7 |
| 5 Tuvalu | 10.6 |
| 6 Kuwait | 7.6 |
| 7 Saudi Arabia | 7.5 |
| 8 Qatar | 7.1 |
| 9 Bahrain | 6.6 |
| 10 Vanuatu | 6.6 |

*comparative prevalence

EUROPE

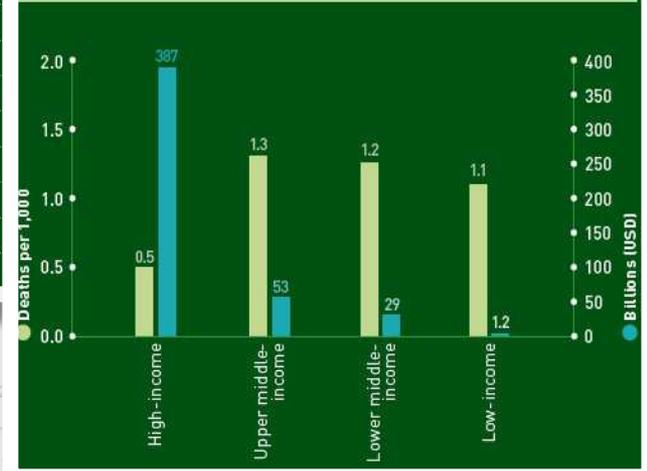
Out of every 3 dollars spent on diabetes healthcare was spent in this region
 2 million people in this region have diabetes and don't know it

WESTERN PACIFIC

1 in 3 adults with diabetes lives in this region
 6 of the top 10 countries for diabetes prevalence are Pacific Islands

4.8 million people died and **471 billion USD** were spent due to diabetes in 2012.

HEALTHCARE EXPENDITURES AND DEATHS PER 1,000 DUE TO DIABETES BY INCOME GROUP



*all estimates are presented as comparative rates

AFRICA

Over the next 10 years, the number of people with diabetes in this region will almost double
 This region has the highest mortality rate

Ausgangspunkt

- Wachsende **Gefährdung** des Menschen
- Keine Möglichkeit der **Früherkennung**
- Zu geringes Wissen über **Stoffwechsel**veränderungen während der **Ätiologie** von Diabetes Typ II Erkrankungen

Konzept



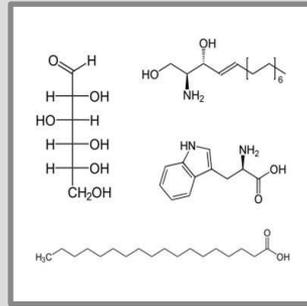
Ziel

- **Identifizierung** und relative **Quantifizierung** möglichst vieler **Metabolite** einer Plasmaprobe
- Identifizierung von **signifikanten Unterschieden** zwischen **diabetischen** und **gesunden Individuen**
- Entwicklung von schnellen **Screeningmethoden** zur **Diagnose** und **Prädiagnostik** von DM

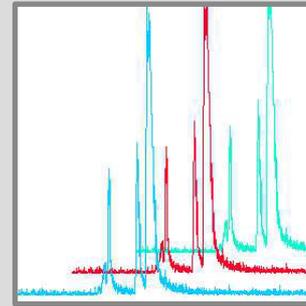
Non-targeted Metabolomics-Plattform



- Detektion von möglichst **vielen Metaboliten** in einem Analysevorgang
- Aquirieren von möglichst vielen **Identifikations-Parametern**



- Analyse von Metaboliten **verschiedenster Substanzklassen** in einem Analysevorgang



- Notwendigkeit extrem hoher **Reproduzierbarkeit**



- Möglichst weitgehende **Automatisierung** für hohes, statistisch notwendiges, Probenaufkommen
- Reduzierung der **Analysedauer**

Non-targeted Metabolomics-Plattform

Hochauflösendes

ESI-qToF-MS

- Genaue Masse, Isotopenmuster, Fragmentmuster



UHPLC

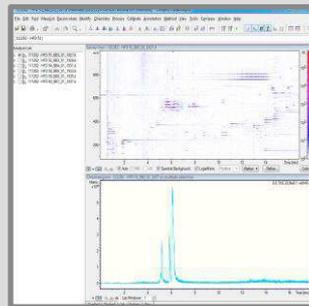
- Retentionszeit



Softwaregestützte

Datenanalyse

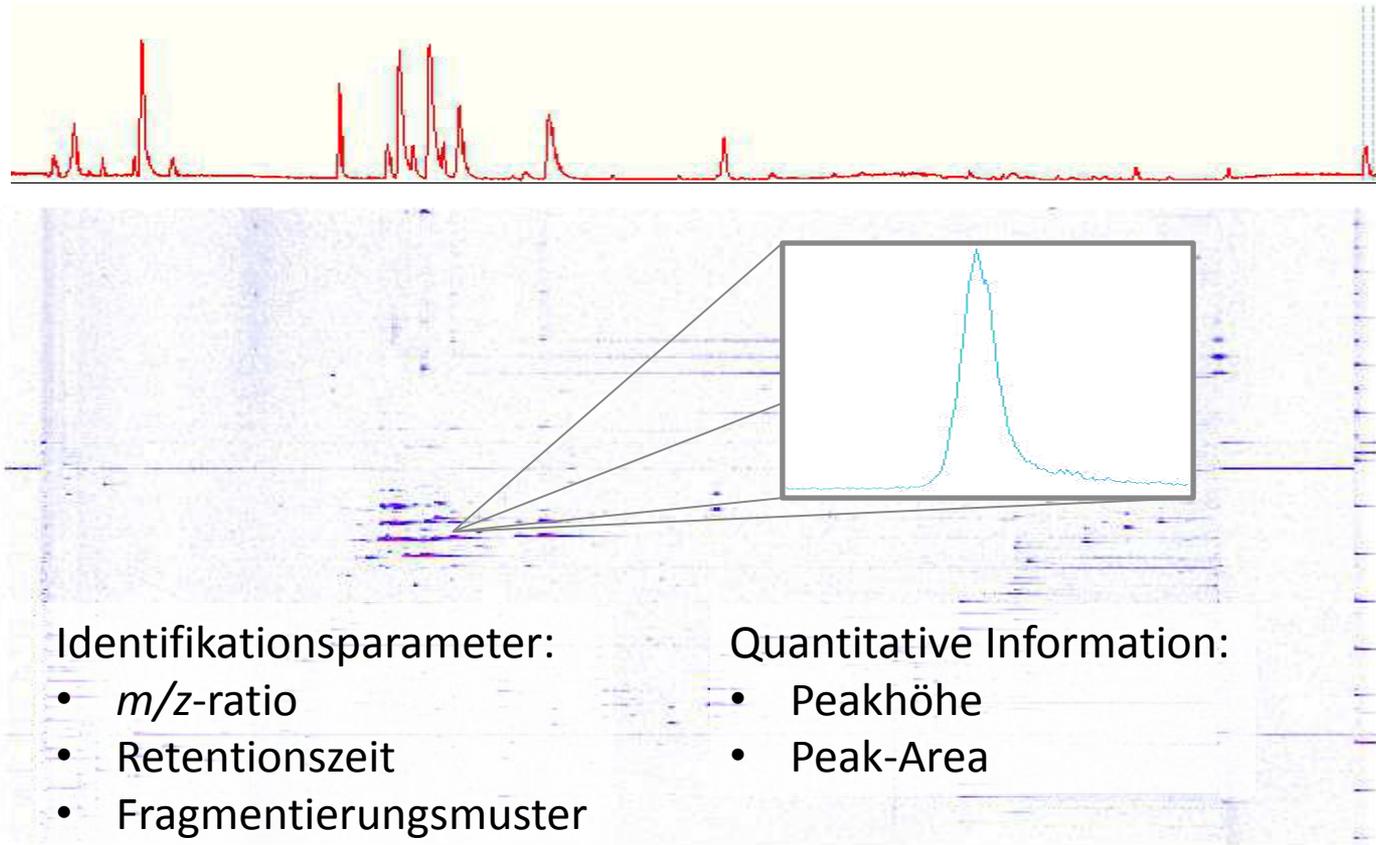
- Peak detection, quantification, statistics



Sub-2-Micron **Core-Shell**-Säulen

- Hohe Auflösung bei moderatem Druck





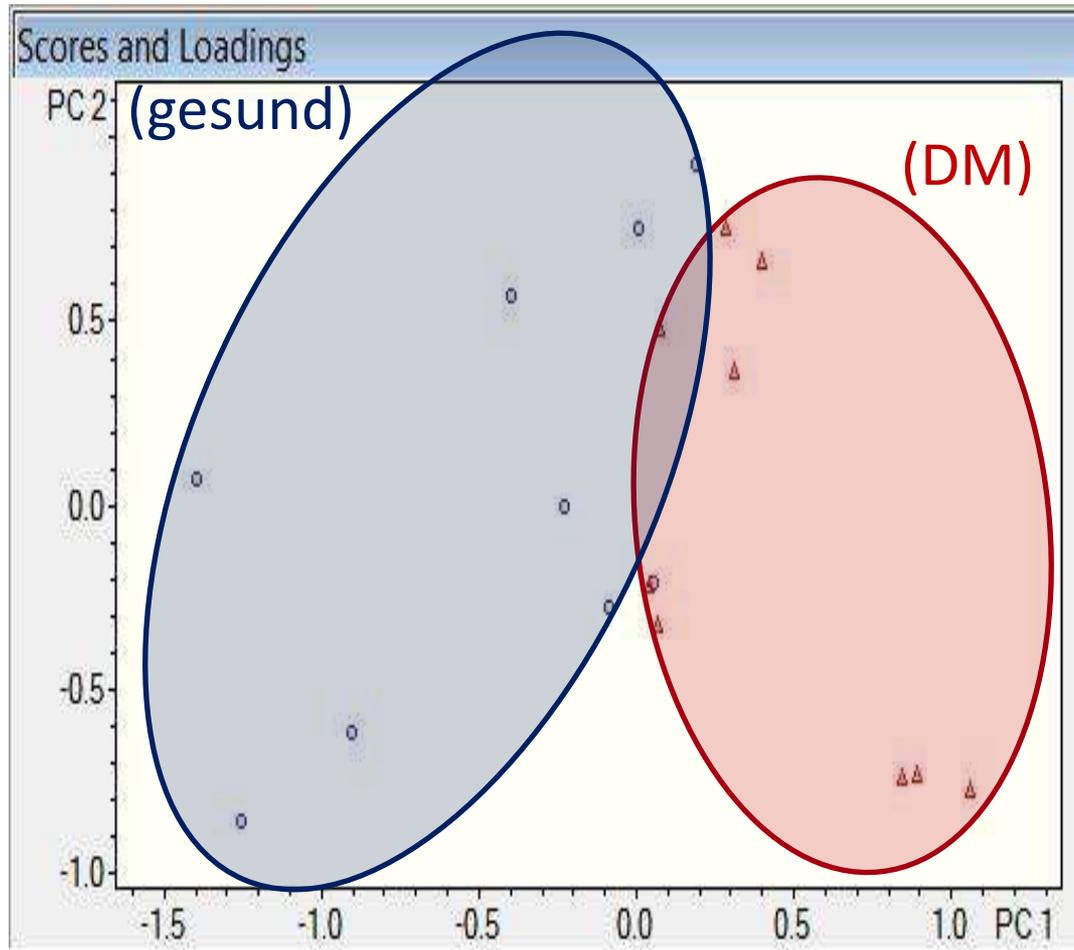
Identifikationsparameter:

- m/z -ratio
- Retentionszeit
- Fragmentierungsmuster

Quantitative Information:

- Peakhöhe
- Peak-Area

Anzahl
Variablen
=
Anzahl
Detektierter
Signale





- Die Verwendung der vorgestellten **Non-targeted metabolomics** Plattform ermöglicht in einem Analysevorgang die **Detektion und Identifizierung** von mehreren **hundert bis über tausend Metaboliten** in Blutproben.
- Durch die Analyse verschiedener **diabetischer und gesunder Proben** aus Tiermodellen können durch statistische Auswertung **potentielle Biomarker** zur Diagnose eines Diabetes Mellitus identifiziert werden.
- Durch die Analyse zeitaufgelöster Studien können potentielle Biomarker zur **Prädiagnostik** von Diabetes Mellitus identifiziert werden



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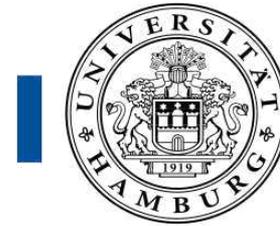
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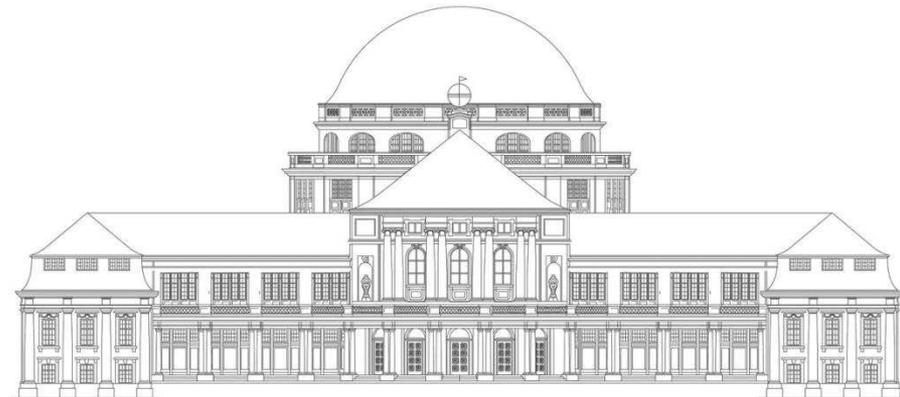
Danksagung

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Universitätsklinikum
Hamburg-Eppendorf



Quellen

1. ADA, Diagnosis and classification of diabetes mellitus. *Diabetes care* **33 Suppl 1**, S62 (Jan, 2010).
2. J. H. Faber *et al.*, Metabonomics in Diabetes Research. *J Diabetes Sci Technol* **1**, 549 (2007).
3. K. Dettmer, P. A. Aronov, B. D. Hammock, Mass Spectrometry-Based Metabolomics. *Mass Spectrom Rev* **26**, 51 (2007).
4. O. Fiehn *et al.*, The metabolomics standards initiative (MSI). *Metabolomics* **3**, 175 (2007).
5. R. C. H. De Vos *et al.*, Metabolomics: Current analytical platforms and methodologies. *Nat Protoc* **2**, 778 (2007).
6. IDF, Diabetes Atlas. 5. Edition **Brüssel**, (2012).

