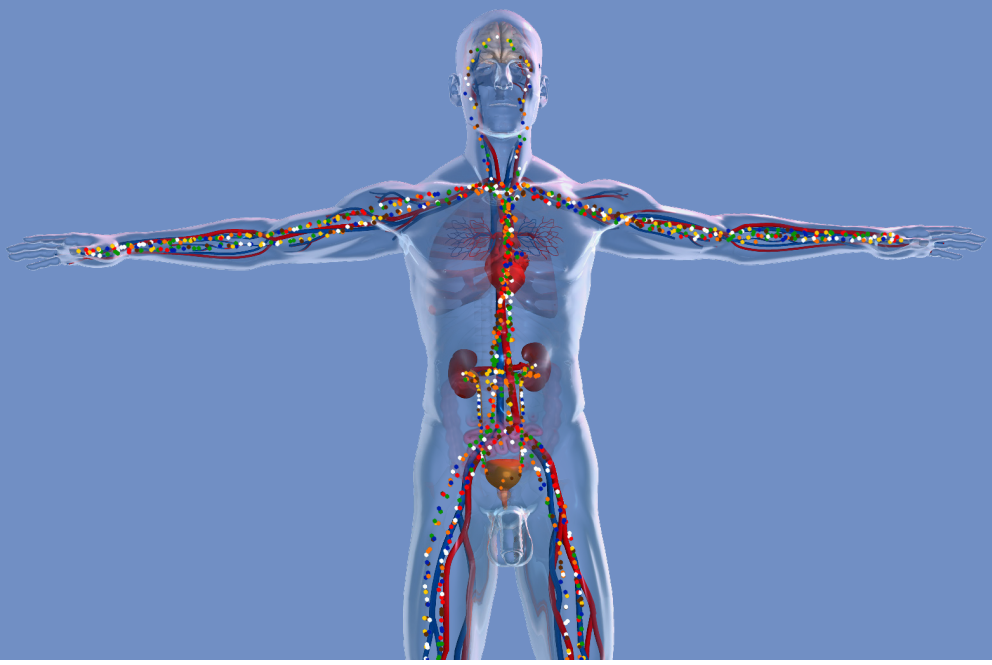
MOSAIQUES DIAGNOSTICS

CLINICAL PROTEOMICS IN DRUG DEVELOPMENT



INFORMATION

- Clinical Proteomics for early and differential diagnosis
- FDA Letter of Support
- Possibilities of a companion test in Drug Development
- Applications in Clinical Trials
- Drug Monitoring

CLINICAL PROTEOMICS FOR EARLY AND DIFFERENTIAL DIAGNOSIS

Mosaiques diagnostics provides highly innovative Clinical Proteomics services **for academic institutions** and **pharmaceutical companies**. Mosaiques revolutionary **CE-MS technology (capillary electrophoresis coupled to mass spectrometry)** helps to diagnose severe diseases at an early development stage, control efficacy of applied therapies in personalized medicine, examine efficacy of new drugs in preclinical (animal models) and clinical trials and to identify therapeutic targets.

The unique CE-MS technology displays peptides and proteins of body fluids. The generated pattern filed in a database provides a fast and authentic description of the individual health of an organism. Measurement of the proteome in combination with on-line database matching is the key to an all-in-one diagnosis for a wide spectrum of clinical applications.

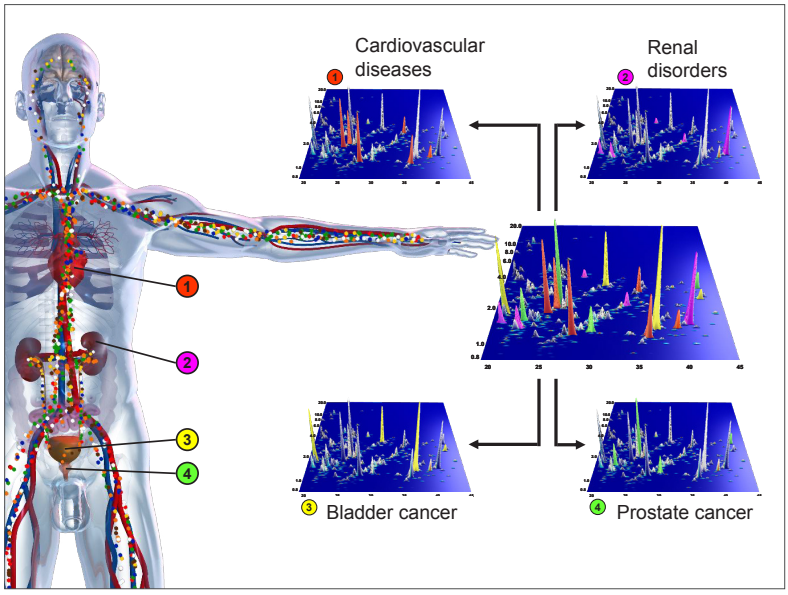


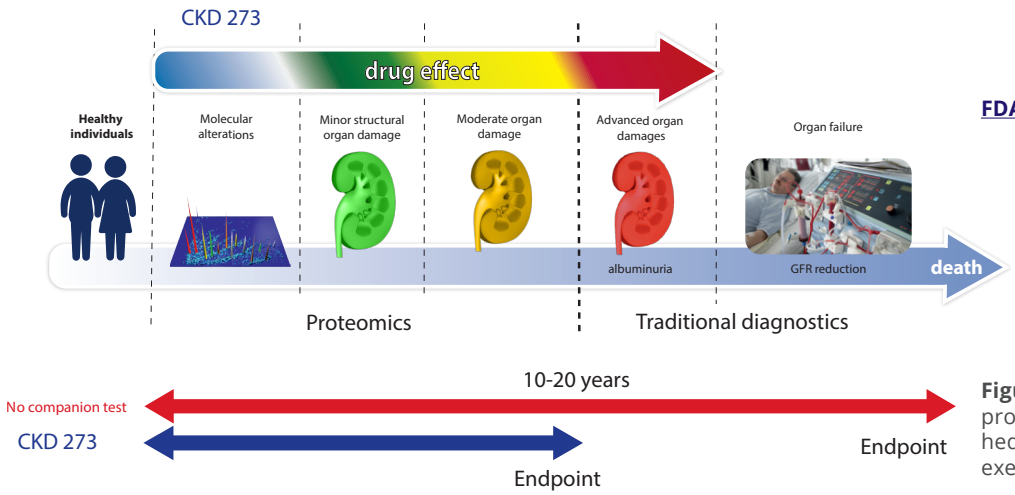
Figure 1: Changes in a distinct and defined pattern of polypeptides in body fluids will allow enormous improvements in diagnosis and therapy for many wide-spread diseases, for example neurological diseases (1), cardiovascular (2) and renal (3) diseases, bladder cancer (4) and prostate cancer (4). The polypeptide patterns distinguish patients with suffering from the disease from non-diseased population. Normalized molecular weight is plotted against normalized migration time. The mean signal intensity is given in 3D-depiction.

mosaiques diagnostics

The CE-MS technology permits adressing surrogate markers and endpoints in **(pre)clinical trials**, allowing evaluation of therapeutic strategies and new drugs on a **small number of patients** or **animal models**. Mosaiques diagnostics has successfully implemented its technology in clinical trials by order of worldwide trails, also jointly with leading pharmaceutical companies. Research projects include amongst others collaborations with the U.S. Food and Drug Administration (FDA) (Mischak et al., 2009).

FDA LETTER OF SUPPORT

CE-MS technology for diagnostic and therapeutic test applications has recently led to the first **Letter of Support by FDA (US Food and Drug Administration)** ever issued to for an MS-based Proteomics Test for Cronic Kidney Disease (June 2016). This Letter of Support was issued for **CKD273**, a biomarker for early detection of CKD and serves as an excellent demonstration of the advancement in the proteomics field.



FDA LETTER OF SUPPORT (PDF)

Figure 2: Possibilities of urinary proteomics analysis as established by Mosaiques diagnostics, exemplified by CKD273 test.

POSSIBILITIES OF A COMPANION TEST IN DRUG DEVELOPMENT

Mosaiques diagnostics developed and validated a proteome-analysis approach for clinical applications and offers the pharmaceutical industry **reliable and cost-saving** solutions for a **secure and time-saving** drug development. The benefits of the urinary proteomic analysis in the clinical trials are:

- ✓ Patient stratification in drug development, to enable earlier intervention and consequently improved survival and quality of life.
- ✓ Substantial reduction of the cost and time, while retaining power for drug assessment.
- ✓ Early assessment of therapeutic impact. Urine proteomics informs about drug response, enable prediction of best therapeutic options and may guide the personalized medicine.

DRUG MONITORING

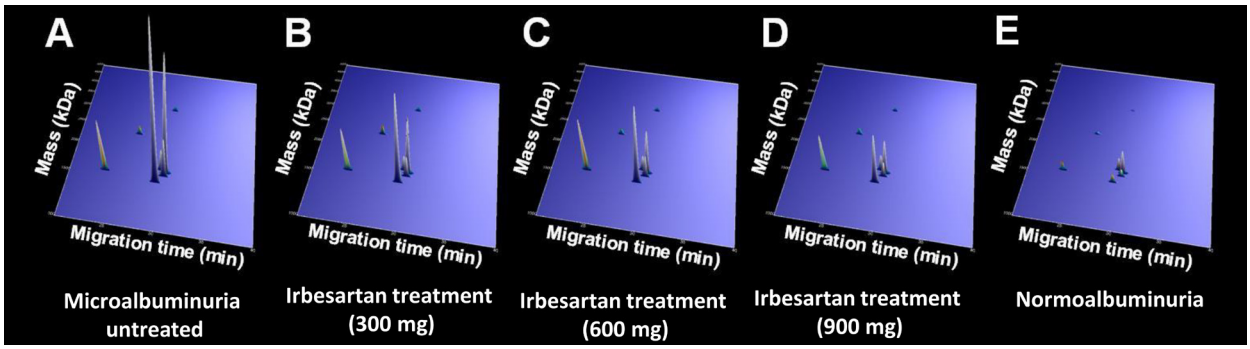


Figure 3: Irbesartan dose depending peptides. Urinary profiling using capillary electrophoresis coupled to mass spectrometry. Normalized molecular weight (1,000-5,000 Da) in logarithmic scale is plotted against normalized migration time (20-40 min). The mean signal intensity of the polypeptide peak is given in 3D-depiction. Compiled data sets of (A) microalbuminuria untreated, (B) microalbuminuria treated with 300 mg Irbesartan (C) microalbuminuria treated with 600 mg Irbesartan (D) microalbuminuria treated with 900 mg Irbesartan and (E) normoalbuminuria specimen are shown.

CKD273 MONITORS RENOPROTECTIVE EFFECTS OF IRBESARTAN

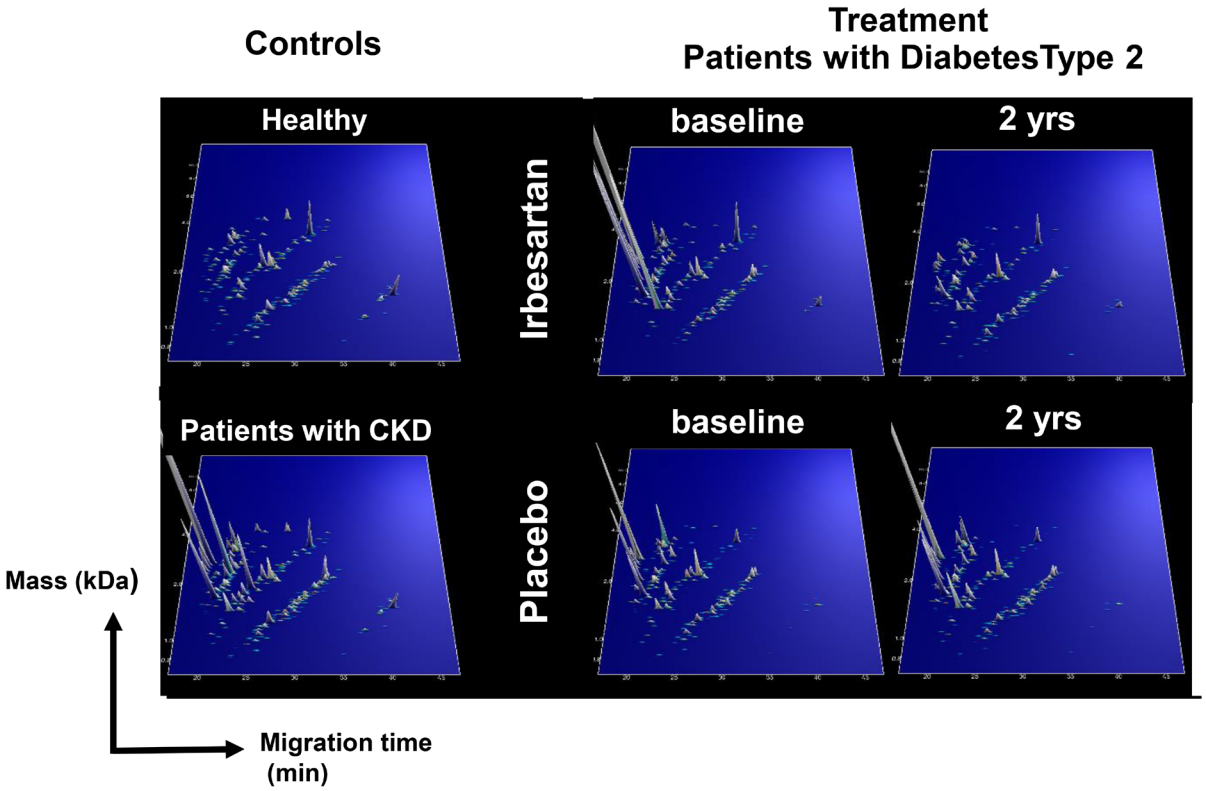


Figure 4: Peptide patterns of CKD273 marker. The compiled data sets of urine samples from patients before and after 2-year treatment of Irbesartan as well as placebo are shown. Normalized molecular mass (y-axis) is plotted against normalized CE-migration time (x-axis). The mean signal intensity is represented in 3D-depiction.
Andersen, et al. (2010)

Indications

Apart from Chronic Renal Diseases (including Diabetic Nephropathy), DiaPat GmbH, a subsidiary of mosaiques diagnostics and therapeutics AG, markets successfully new diagnostic tests in Europe for Bladder Cancer, Prostate Cancer, Cholangiocarcinoma, Coronary Artery Disease, Heart Failure, Ureteropelvic Junction Obstruction in Neonates and for early detection of Graft-versus-Host Disease, based on the CE-MS technology.

CE- MS Technology

The **stable, robust and reproducible** technology, consisting of capillary electrophoresis coupled time-of-flight mass spectrometry (**CE-TOF-MS**) and proprietary software solutions, enables fast analysis of up to 6000 polypeptides.

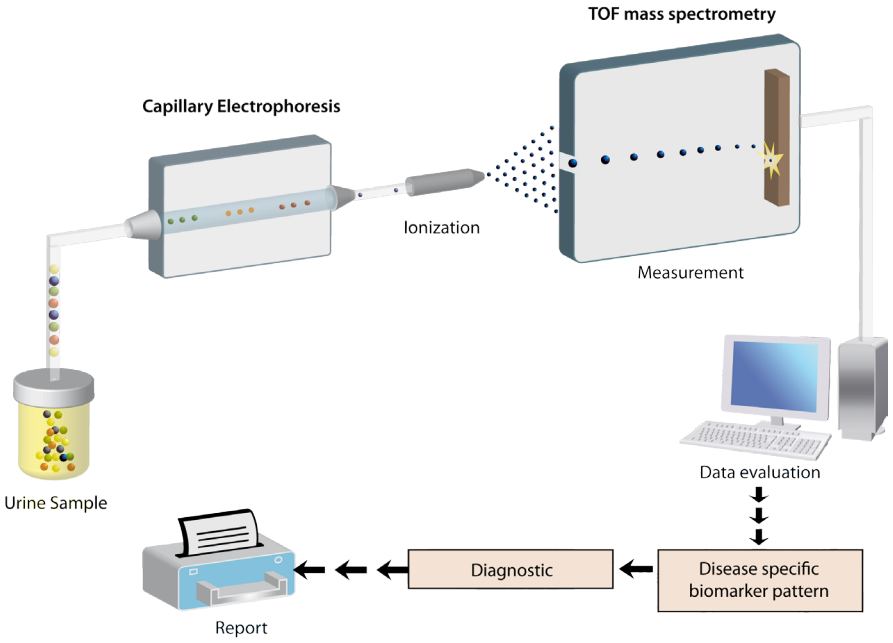


Figure 5: Schematic depiction of the technology. Urinary peptides are separated by capillary electrophoresis before their masses are detected by electro spray ionization time-of-flight mass spectrometry.

URINARY DATABASE

A database of naturally occurring human urinary peptides and proteins for use in clinical applications has been established in Mosaiques diagnostics. High resolution datasets that enable the profiling of adequate samples and recognition of sufficient features to yield robust diagnostic panels are included. The urinary database currently contains over 38.000 entries from independent samples.

WE PROVIDE

CE-MS BASED PROTEOMIC PROFILING

- Sensitive/specific biomarker discovery
- Naturally occurring sequence analysis including post-translational modifications
- Non-invasive monitoring

GLP-CONFORM QUALITY ASSURANCE PROGRAM

- Standard operating procedures
- Sample logistics internal & external audits

TECHNOLOGY RECEIVED LETTER OF SUPPORT FROM FDA AND EMPLOYED IN JOINT PROJECTS

BENEFITS OF CE-MS TECHNOLOGY IN DRUG DEVELOPMENT

- Improved assessment of drug efficacy and safety in early preclinical development: faster development at lower cost

- Multiple relevant biomarkers assessed in tissue culture, animal model and patients: higher success rate when translating into human disease

- Monitoring of drug response based on multiple biomarkers: increased reliability of results

FURTHER INFORMATION

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