

Peptidomics meeting ist am 6.-7. September am Royal Holoway College in London

Abstract:

DIAGNOSIS OF DISEASES BASED ON PROTEOM ANALYSIS

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We have aimed towards the definition of disease-specific biomarker polypeptides which should enable the early and non-invasive diagnosis and staging of disease and consequently the development of new therapeutic strategies.

To this end, we have developed stable capillary electrophoresis coupled mass spectrometry (CE-MS) as well as software solutions that allow the analysis and evaluation of individual samples within app. 1 hour. This technology was utilized to examine urine samples from healthy volunteers and patients with different diseases to identify disease-specific polypeptides (biomarkers). Typically, >1000 polypeptides (800 – 30000 Da) are analyzed per sample with high reproducibility.

Urine samples from >2000 healthy volunteers, patients with different renal diseases, prostate, bladder and renal cancer, or after stem cell or organ transplantation were analyzed using CE-MS. The high comparability allowed compilation of data from patients with a distinct disease and subsequent comparison to others, enabling the definition of 10-100 biomarkers specific for a given disease and consequently diagnosis and discrimination between diseases with generally >90% sensitivity and specificity. These results were further validated in several blinded studies. Several of the biomarkers were subsequently identified using CE-MS/MS sequencing.

The data enabled the generation of a human urinary polypeptide map, which holds the information on frequency and abundance of polypeptides present in urine, as well as disease-specific changes of the individual polypeptides.

The high number of disease-specific biomarkers indicated that this approach also enables the staging and evaluation of disease progression/therapy success. First results on AT-receptor blockers and antiviral substances indicate that CE-MS analysis is a powerful tool for the evaluation of therapeutic strategies.

The data also indicate that an "ideal biomarker", exclusive for one disease, does not exist. Instead, an array of well defined polypeptides that shows significant differences in distribution between disease and healthy can be defined. The combination of biomarkers to generate diagnostic patterns makes the method both more robust and specific. Spurious occurrences of peptides, absence or untypical amplitude of single peptides do not result in significant changes of the pattern. The results clearly indicate that for the thorough evaluation of a pathophysiological state, not a single biomarker should be used, but an array of distinct biomarkers that result in a specific pattern.

CE-MS analysis of urinary polypeptides in combination with appropriate software solutions, is capable of displaying an array of disease-specific changes in polypeptides at a very early state. As a consequence, this tool is certified for in-vitro diagnosis and already in clinical use for monitoring of patients and establishment of diagnosis.

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