Clinical Diagnostics- and Imaging Mass Spectrometry Developments with an Emphasis on Lung Cancer and COPD

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Pulmonary Diseases such as Lung Cancer and Chronic Obstructive Pulmonary Disease (COPD) are currently the major leading cause of death and its prevalence is increasing. The leading cause of COPD is smoking and an estimated 600 million patients suffer from the disease. There is a lack of protein biomarker-, and imaging diagnostics today within lung disorders, such as lung cancer and COPD. These new clinical tools are expected to be used as early indicator of disease, or, as personalized indicator assays for targeted and stratified disease phenotype drug treatments in the near future. There is also a poor understanding of the mode of drug action mechanisms, by commonly used therapies, which is also true for new drugs introduced to the market. The actual targeted cells-, and proteins within disease, and the actual drug interactions are by no means understood for most medicines used in today’s therapies. These drug characteristics are needed for both efficacy-, and safety- improvements, and also requested by regulatory authorities (MHLW/FDA/EMEA).

Examples will be given from clinical studies where we have developed dedicated protein Biomarker diagnosis technologies that allows for Multiple Reaction Monitoring (MRM) multiplex quantitation methodologies. These current MRM methods was applied to biofluid and tissue applications from patients, as well as Biobanking archives. The MRM assays platforms as such are generic and can be developed and applied in principle to any set of key regulating target proteins within disease.

Compound Tissue Imaging Mass Spectrometry (CTI) is another area of fast progress where drug localization can be performed with a resolution at a single cell level. Today, we are able to optimise lung retention and correlate drug Pharmacokinetics in lung with effect and toxicity when only total concentration of drug in lung tissue homogenate can be measured.

We also realise that these developments will have business benefit of tissue imaging with the ability of localisation of unlabelled drugs and metabolites and peptides/proteins in tissue.

REFERENCES

Keyword: lung Cancer, diagnosis, biomarkers, drug treatment

PS-3

Profiling and Imaging of Peptides, Proteins and Drugs in Tissue Sections

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Neuropeptidomics is the technology approach for detailed analysis of endogenous peptides from the brain and the central nervous system. NanoLC ESI MS and MALDI imaging MS (IMS) are powerful tools utilized for profiling and imaging of a large number of neuropeptides and small proteins. A new approach using targeted sequence collections for identifying endogenous peptides from the brain has been developed. Maintaining the biochemical, molecular and structural sample integrity is essential for correct sample comparisons. We have elucidated brain neuropeptide mechanisms in experimental Parkinson’s disease. Our peptidomics approaches enabled sensitive detection, identification, and relative quantitation of a large number of endogenous neuropeptides. The analysis demonstrated several differentially expressed peptides and small proteins in the experimental model of PD. Novel peptide families affected by neurodegeneration were identified.

In the process of drug development for therapy purposes, one of the key objectives is to optimize the retention of a compound so that long effect duration can be obtained. Here we have used IMS to fine map the spatial distribution and concentration of unlabeled drugs within tissue micro-compartments. We provide evidence that compounds administered by inhaled delivery at standard pharmacological dosage can be quantitatively detected by IMS with accuracy and precision within specific organ and tissue compartments on tissue sections characterized with high definition histology. Our results highlight an important emerging technology allowing specific high resolution identification of unlabeled drugs at sites of in vivo uptake and retention.

Keyword: peptidomics, sample degradation, Parkinson’s disease, imaging mass spectrometry, drug imaging, brain, lung