SYMPOSIUM 10 - How can we integrate proteomics and metabolomics in Clinical Lab?

QUANTIFICATION OF CSF OREXIN-A AND ITS MAJOR FRAGMENT IN HYPERSOMNOLENCE DISORDERS: MOVING TOWARDS MASS SPECTROMETRY

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Introduction: Narcolepsy Type 1 (NT1) is characterized by orexin deficiency, detected via cerebrospinal fluid (CSF) Orexin-A quantification using radioimmunoassay (RIA). However, RIA has limitations, including cross-reactivity and batch variability. This study investigates CSF Orexin-A and its major fragment using liquid chromatography-mass spectrometry (LC-MS) for improved specificity.
Methods: CSF samples from 115 patients with NT1, NT2, idiopathic hypersomnia (IH), and non-specified hypersomnolence (NSH) were analyzed. RIA and LC-MS were employed to detect Orexin-A and its N-terminal fragment (QPLPDCCRQKTCSCRL). Statistical analyses assessed correlations and diagnostic value.
Results: LC-MS revealed lower CSF Orexin-A fragment concentrations than RIA-determined levels (mean difference -199.33%, $p<0.0001$), with a strong correlation ($r=0.91$). ROC analysis established an optimal LC-MS cut-off (≤0.15 pg/mL, AUC=0.98) for discriminating NT1 patients. Significant differences were observed between NT1, NT2, and other hypersomnolence groups, highlighting the diagnostic relevance of the Orexin-A fragment.
Discussion: LC-MS quantification of the Orexin-A fragment offers superior precision compared to RIA, with better classification of hypersomnolence disorders and potential clinical applications in personalized treatment approaches.

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WHAT WILL CLINICAL METABOLOMICS BRING TO THE MEDICINE OF TOMORROW ?

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Introduction

Clinical metabolomics is transforming medicine, providing a real-time biochemical snapshot of a patient's health. While genomics identifies genetic predispositions, metabolomics bridges gene expression, metabolic dysregulation, and disease manifestation. This discipline enables the characterization of pathological phenotypes, offering functional insights beyond genetics.

After 20 years of research, metabolomics has now reached a stage of maturity, making its clinical integration possible. Clinical chemists must actively adopt these technologies, mastering metabolomic profiling techniques and translating them into routine diagnostics. By doing so, they can assist in the design of clinical studies to identify novel biomarkers for disease detection, monitoring, and treatment response. Beyond conventional biomarkers, metabolomic signatures —composite metabolic patterns or fingerprints—enhance diagnostic precision and personalized therapies.

Results

To illustrate its impact, we will explore real-world applications in biomedical research. A key example is trimethylamine N-oxide (TMAO), a metabolite linked to cardiovascular disease risk. Multiple studies have validated TMAO as a predictive biomarker, offering insights into cardiovascular pathophysiology. This demonstrates how metabolomics can identify novel diagnostic and prognostic markers, paving the way for clinical adoption.

Next, we will examine metabolomic fingerprints integrated with machine learning, refining precision medicine. By leveraging supervised models, metabolomic datasets help distinguish disease subtypes, predict therapeutic responses, and personalize treatments. This data-driven approach is crucial in advancing predictive and personalized medicine.

Discussion/ Conclusion

Finally, we will address key challenges hindering clinical adoption, including protocol standardization, data reproducibility, analytical variability, and regulatory constraints.

By bridging molecular insights with clinical applications, metabolomics has the potential to redefine medicine. This presentation will offer a forward-looking perspective on how metabolomics-driven diagnostics could soon become indispensable in clinical practice, leading to more precise and personalized patient care.

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EXPLORING THE PERSPECTIVES OF INDUSTRIALIZED MASS SPECTROMETRY APPLICATIONS IN IVD

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Mass spectrometric technologies offer numerous fundamental advantages over technologies routinely used in routine clinical laboratories to date. However, conventional mass spectrometry-based measurement procedures are often highly demanding for laboratory staff, as instrument operation is complex and typically requires labor-intensive sample preparation. For these reasons, the application of mass spectrometry methods has been limited to a small number of highly specialized laboratories over the past decades.

A significant innovation for clinical laboratories is the recent introduction of the first mass spectrometry-based analyzer system, which has the potential to be integrated into fully automated laboratory workflows. The operation of this system is comparable to contemporary standard analyzer systems and no longer requires specialized expertise. Assays remain highly calibration-stable over extended periods, and instruments can be operated in a random-access mode without the need for manual sample handling. All reagents and consumables are fully ready-to-use, and the closed concept ensures that method development and validation are entirely covered by the manufacturer.

Although the current launch panels do not yet cover all potential applications, this innovative tool holds great promise for omics-based diagnostic approaches too. These include parallel detection and quantification of multiple analytes with information-rich outputs, an extremely wide range of potential analytes regardless of specific molecular features, and highest robustness and analytical reliability enabled by the unique principle of stable isotope-labeled internal standardization. Developing and implementing new assays is straightforward, as no specific reagents, such as those required for immunoassays, need to be developed.

With these significant advances in the practicality of mass spectrometry-based measurement techniques, this technology is well on its way to becoming a core component in clinical laboratories, complementing photometric techniques and immunoassays in the provision of high-quality diagnostic care.