NEWS RELEASE

Novel 4D-Metabolomics and 4D-Lipidomics Workflows, Libraries and ML-based CCS Prediction Tools to Transform Metabolomics and Lipidomics

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- New VIP-HESI ion source boosts sensitivity in analytical flow 4D-Metabolomics, 4D-Lipidomics and small molecule quantitative screening workflows by more than 10x
- Introducing new METLIN-4D large 4D-Metabolomics CCS library for timsTOF platform
- Integration of machine integration for CCS-Predict Pro software for unknown metabolites
- New CCS-enabled 4D workflows in MetaboScape and TASQ 2022 software, including 4D-Lipidomics tools to reduce false positive identifications

BILLERICA, Mass.--(BUSINESS WIRE)-- At Bruker's virtual 4D-Metabolomics™ eXceed Symposium (**eXceed Symposia 4D-Metabolomics 2021 | Bruker**), **Bruker Corporati**on (Nasdaq: BRKR) today announced the launch of a new VIP-HESI ion source to increase sensitivity dramatically, and new integrated software tools to increase confidence in 4D-Metabolomics and 4D-Lipidomics workflows.

This press release features multimedia. View the full release here: **https://www.businesswire.com/news/home/20210621005354/en/**

timsTOF Pro 2 with VIP-HESI source (Photo: Business Wire)

The heated VIP-HESI ion source enables sensitivity gains of up to 16-fold by efficient desolvation, enabling new applications across all small molecule applications. The VIP-HESI source can be interfaced to the new timsTOF Pro 2 platform to enhance the sensitivity of 4D-Metabolomics and 4D-Lipidomics. It is also compatible with the high-performance impact II QTOF system to improve quantitative analyses of pesticides, drugs and drug metabolites in food, environmental, forensic and pharma applications where increased sensitivity allows detection of low level contaminants.

Bruker's collaborators are making major progress in 4D-Metabolomics by leveraging measured collision cross sections (CCS). The METLIN-4D library leverages the TIMS/PASEF methods to provide accurate CCS values. Professor Gary Siuzdak of Scripps has expanded the infrastructure within the established METLIN library, which generated the world's largest MS/MS spectral library for >1/2 million compounds. With the addition of METLIN-4D, CCS values measured on a timsTOF Pro system will be made available alongside the MS/MS library, adding an additional level of confidence. This allows CCS values to be utilized across the timsTOF community to increase confidence by reducing ambiguities - resulting in fewer false positive annotations.

Bruker also introduced CCS-Predict Pro, an optimized algorithm to predict CCS values across small molecule structures. CCS-Predict Pro offers large-scale CCS-enabled bioinformatics for unknown compounds. CCS-Predict Pro uses machine learning for correct identification to narrow down possible structures across small molecule workflows, including in exposomics and drug metabolite analysis.

All 4D small molecule workflows are available within the updated MetaboScape 2022 software that continues to revolutionize CCS-enabled workflows. Further advances in 4D-Lipidomics are included in MetaboScape 2022 to provide ease-of-use for lipidomics. Potential false positive identifications are shown using a novel display, in which CCS values and retention time determine whether the identification based on MS/MS fragmentation results fits the structure of the lipid. This use of orthogonal lipid characteristics allows for higher accuracy of results and the faster validation of potential lipid biomarkers.

Bruker also announced the incorporation of CCS values into TASQ 2022 to provide greater accuracy in the identification of contaminants in food and environmental samples analyzed via its quantitative TargetScreener workflow. All these tools combined allows easy adoption of 4D-Lipidomics and 4D-Metabolomics, providing more complete insights at the biological and molecular level.

A. VIP-HESI

The Vacuum Insulated Probe – Heated ESI source is a dual source with an integrated APCI probe. The VIP-HESI source is compatible with timsTOF systems and the impact II for low µL/min to mL/min LC flow rates. Significant sensitivity gains have been demonstrated with both HESI and APCI modes in positive and negative ion mode. For example, in hair analysis, sensitivity gains for drugs of abuse averaged x16, which allowed a more detailed timeline for drug usage to be created as smaller sample lengths of hair could be extracted.

Another application where gains of more than x10 have been demonstrated is in environmental and food analysis, where this improvement can simplify sample preparation or enable the earlier detection of emerging, low-level pollutants such as PFAS type molecules. Using VIP-HESI on a timsTOF system also allows isomers eluting at similar

retention times to be separated by their CCS and thus individually quantified. This powerful combination allows researchers in exposomics more detailed elucidation of compounds affecting the human exposome. Lastly, a gain of x5 was achieved for lipids in plasma in negative ion mode. This resulted in a greater number of unique lipids identified using 4D-Lipidomics for biologically important annotations.

B. Largest TIMSCCS library METLIN-4D Launch

The measurement of CCS values is the most reliable way to integrate 4D workflows for small molecules. The METLIN-4D CCS library is the first CCS library to measure CCS for more than 10,000 reference compounds and can greatly improve the identification and compound confirmation for small molecule research. All CCS values of the reference compounds were measured on a timsTOF platform in positive and negative mode. The content can be linked with the Bruker MetaoBASE Personal Library 3.0, which contains MS/MS spectra for 100,000 compounds from the METLIN compound library, giving increased confidence in compound annotation in MetaboScape 2022.

Gary Siuzdak, Professor and Director of the Center for Metabolomics and Mass Spectrometry at Scripps Research in La Jolla, CA stated: “CCS values add an orthogonal identifier for molecules. On the timsTOF platform, CCS values are acquired ‘for free’ for all analytes. We can use these CCS values to increase confidence in annotation across a broad range of compounds using the new METLIN-4D library. We will continue to add to the already acquired 10,000 CCS values and continue to expand this library.”

C. CCS-Predict Pro and MetaboScape 2022

MetaboScape 2022 is the latest release of Brukers all-in-one software solution for CCS-enabled metabolomics and lipidomics, and latest recommendations for notation of lipids are implemented. The 4D Kendrick Mass Defect analyses are complemented with an automatic outlier detection based on regression models using a dynamic cross validation. Lipids annotated by the library free rule-based annotation tool will be automatically rated by predicted CCS values calculated using a 3D hyperplane model. Dr. Lucy Woods, Bruker Business Unit Manager for Metabolomics & Lipidomics, commented: “Our 4D-Lipidomics workflows utilizing CCS prediction with Kendrick Mass Defect analyses reduce ambiguity in lipid annotation. Together, these functionalities let any laboratory easily adopt 4D-Lipidomics.”

For other small molecule structures, CCS-Predict Pro predicts CCS values to aid the annotation and reduce the number of possible candidates.

As one of the pioneers in CCS prediction using machine learning, Professor Zheng-Jiang Zhu, Director of Metabolomics Research Center at the Shanghai Institute of Organic Chemistry (SIOC), observed: "With the advent of CCS prediction, it is finally possible to make full use of CCS values in the annotation of unknown compounds. This

brings a step-change for untargeted metabolomics and lipidomics research".

Professor Zheng-Jiang Zhu is now using the timsTOF Pro platform to continue to build training sets for machine learning approaches. He continued: "The timsTOF Pro is a very versatile platform; you can do all applications on one platform. The instrument design exceeds anything else on the market."

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