Grant application resource: Thermo Scientific Orbitrap ID-X Tribrid mass spectrometer for metabolomics, lipidomics and structural elucidation

Author
Thermo Fisher Scientific

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Goal
This document is intended to provide conclusive reasons to justify upgrading from a Thermo Scientific™ Q Exactive™ mass spectrometer series or earlier generation of Thermo Scientific™ Orbitrap™ Hybrid™ mass spectrometer series to a Thermo Scientific™ Orbitrap ID-X™ Tribrid™ mass spectrometer dedicated to significantly augment untargeted metabolite annotation and structural elucidation capabilities in untargeted metabolomics and lipidomics research.

Summary
Thermo Scientific Orbitrap Tribrid mass spectrometers are an essential tool for high-end life science research. Equipped with a quadrupole mass filter, high-field Orbitrap and linear ion trap mass analyzers, this unique hardware combination provides superior analytical performance that enables multiple modes of analysis due to the parallel isolation and detection mechanisms not available with previous generation Orbitrap Hybrid mass spectrometer series. The most difficult analyses including identification of low-abundance metabolites in human plasma, isotopomer mixture analysis, characterization
of isomeric flavonoid or lipid species in biological extracts, and obtaining high quality MS^n spectral reference libraries are fully achieved on the versatile Orbitrap ID-X Tribrid mass spectrometer. The Orbitrap ID-X Tribrid mass spectrometer is optimized for small molecules and can perform multiple fragmentation techniques (higher energy collision dissociation (HCD) in a high pressure collision cell or collisional induced dissociation (CID) in an ion trap plus stepwise MS^n) for annotating unknown metabolite structures in untargeted metabolomics and lipidomics experiments. The Orbitrap ID-X Tribrid mass spectrometer provides up to 500,000 resolution at m/z 200, high sensitivity, and rapid acquisition rates needed for obtaining high quality data for demanding applications such as isotopic tracer studies. The Orbitrap ID-X Tribrid mass spectrometer system extends the dynamic range for metabolite detection, compound annotation and quantitation needed to achieve a broad range of metabolome coverage, by combining the versatility of Tribrid architecture, selectivity of Orbitrap technology and high-quality MS^n spectra. The integration of Thermo Scientific™ AcquireX intelligent data dependent acquisition methods and the use of advanced scan filters to target specific compound classes provide unparalleled flexibility in designing experiments that meet the real-world challenges in metabolomics and lipidomics today.

Introduction
Untargeted metabolomics is a demanding application that is challenging due to: 1) a wide range of potential analytes (from very polar to non-polar molecular species), 2) the need to identify commonly present metabolites with high confidence, and 3) the need to distinguish a host of unknown compounds as unrelated chemical background or perhaps interesting metabolites. Identification of hundreds to thousands of metabolites in complex matrices such as human plasma is one of the most difficult challenges faced by metabolomics scientists. One of the main strategies employed in metabolomics is to reduce this complexity by applying several different chromatographic methods prior to analysis with a high-resolution accurate mass (HRAM) Orbitrap mass spectrometer. Unambiguous identification of metabolites requires a combination of mass spectrometric tools including high mass accuracy and precision, ultra-high resolution (isotopic fine structure), multiple dissociation techniques, and a high-resolution spectral fingerprint consisting of high-quality MS^n spectral trees. HRAM LC-MS metabolomics datasets contain many thousands of features that may be related to the biological sample or may be unrelated chemical background. Data reduction and false positives are a major roadblock in these experiments. A recent publication reported the optimized experimental conditions for a Thermo Scientific™ Orbitrap™ Fusion™ Tribrid™ mass spectrometer operated at 500,000 resolution at m/z 200 to reliably separate and measure 13C and 18O ratios in metabolites thereby substantially reducing the number of possible elemental formulas.

The Orbitrap ID-X Tribrid mass spectrometer was specifically developed with all of these analytical challenges in mind. This versatile LC-MS^n instrument is optimized to obtain the highest quality information from metabolite and lipid samples. High resolution, robust mass accuracy ensures that every full MS and MS^n scan is used effectively for obtaining comprehensive metabolite identification. Intelligent acquisition methods provide robust profiling of precious samples, deeper characterization of known and unknown compounds, and real-time interrogation of specific compound classes using highly selective scan filters.

Hardware benefits
The Orbitrap ID-X Tribrid mass spectrometer (Figure 1) has the following capabilities:

- Ultra-high resolution, consistent mass accuracy and mass precision to achieve in-depth metabolome and lipidome coverage with very high confidence
- Intelligent acquisition of high-quality LC-MS and MS^n spectra for robust detection, structure characterization and confident annotation of metabolites and lipids
- Selective and sensitive high-field Orbitrap for confident detection and quantitation
S-Lens
Optimizes ion transmission into the mass spectrometer, while minimizing in-source fragmentation

Quadrupole Mass Filter
Selects precursor ion with resolution up to 0.4 amu; Yields high ion transmission from 50 to 2000 m/z

Ultra-High-Field Orbitrap Mass Analyzer
Offers resolution up to 500,000 FWHM and MS^n scan rates up to 30 Hz

Ion-Routing Multipole
Enables parallel analysis; Allows HCD at any MS^n stage

Dual Pressure Linear Ion Trap
Sensitive MS^n mass analysis of HCD and CID fragments

Active Beam Guide
Prevents neutrals and high-velocity clusters from entering the mass resolving quadropole

Optional EASY-IC Ion Source
Generates internal calibrant ions for real-time mass calibration

S-Lens
Optimizes ion transmission into the mass spectrometer, while minimizing in-source fragmentation

Table 1. Novel features and performance benefits of the Orbitrap ID-X Tribrid mass spectrometer.

<table>
<thead>
<tr>
<th>Features</th>
<th>Benefits</th>
</tr>
</thead>
<tbody>
<tr>
<td>OptaMax NG Ion Source</td>
<td>Increased usability and robustness, and enhanced APCI performance</td>
</tr>
<tr>
<td>Streamlined mass calibration and optional internal calibration</td>
<td>Improved mass accuracy and stability across the entire mass range</td>
</tr>
<tr>
<td>Default parameters</td>
<td>Parameter settings optimized for small molecule analyses</td>
</tr>
<tr>
<td>AcquireX data acquisition mode using automatic reinjection logic</td>
<td>Automated sample profiling enables LC-MS^n analysis and comprehensive compound interrogation by sampling of blank and matrix to prioritize compounds of interest and exclude background</td>
</tr>
<tr>
<td>Templates for small molecule application-specific methods</td>
<td>Easy-to-use, pre-defined methods for metabolomics, lipidomics, metabolite annotation, and characterization of unknown compounds</td>
</tr>
<tr>
<td>MS^n library builder method</td>
<td>Enables collection of high-quality MS^n spectra for library creation (infusion and LC-MS)</td>
</tr>
<tr>
<td>Assisted collision energy</td>
<td>Provides real-time collision energy optimization for building libraries</td>
</tr>
<tr>
<td>Data-dependent HCD and CID MS^n experiments with advanced scan filters including targeted neutral losses, product ions, and isotope ratios</td>
<td>Combine untargeted profiling with data dependent experiments that are triggered only when a specific compound class is detected. Adds confidence in annotation of compound classes such as flavonoids or triacylglycerol lipids that require more sophisticated experiments for complete structural analysis</td>
</tr>
</tbody>
</table>
The Orbitrap ID-X Tribrid mass spectrometer is configured specifically for small-molecule applications. Key improvements for metabolomics and lipidomics include: 1) pre-defined method templates specifically designed for metabolites, lipids and MS^n spectral library building, 2) streamlined mass calibration procedures and, 3) intelligent acquisition methods for automating the entire acquisition workflow. Instrument specifications for the Orbitrap ID-X Tribrid mass spectrometer are summarized in Table 2.

**Top reasons for selecting the Orbitrap ID-X Tribrid mass spectrometer for metabolomics and lipidomics**

- Be more confident in metabolite annotations with high quality HCD MS^n and CID MS^n data
- Use AcquireX data acquisition methods to obtain higher LC-MS^n coverage and annotation of more real metabolites
- Obtain LC-MS^n spectra to provide more complete structure information for isomeric species

**Solution and benefits**

**Untargeted metabolomics—workflow improvements**

**Mass calibration procedure**

With the implementation of an improved and easy-to-use calibration procedure along with the use of the built-in internal calibrant option, the Orbitrap ID-X Tribrid mass spectrometer achieves mass measurements with less than 1 part-per-million (ppm) mass accuracy, as illustrated by the example of endogenous creatine from reference material NIST SRM 1950 (Figure 2, left panel). Excellent mass accuracy can be achieved for every scan across the chromatographic peak of creatine, even at low intensity, without the need of averaging several scans. Similarly, robust measurements with excellent mass accuracy were achieved for a mixture of small molecule standards, representing various endogenous metabolites ranging in molecular weight from 74–780 Da, over a period of 3 days of continuous operation (Figure 2, right panel).

### Table 2. Instrument specifications of the Orbitrap ID-X Tribrid mass spectrometer.

<table>
<thead>
<tr>
<th>Features</th>
<th>Orbitrap ID-X Tribrid mass spectrometer</th>
</tr>
</thead>
<tbody>
<tr>
<td>OptaMax Ion Source</td>
<td>Improved HESI/APCI probes for stable and robust operation</td>
</tr>
<tr>
<td>S-Lens Ion Optics</td>
<td>Stacked-ring ion guide for ion focusing and transmission</td>
</tr>
<tr>
<td>Active Beam Guide</td>
<td>Reduces noise by preventing neutrals from entering quadrupole</td>
</tr>
<tr>
<td>Quadrupole Mass Filter</td>
<td>Efficient precursor ion selection and transmission for m/z 50–2000</td>
</tr>
<tr>
<td>Ion-Routing Multipole</td>
<td>Enables parallel analysis, HCD fragmentation at any MS^n stage</td>
</tr>
<tr>
<td>Dual-Pressure Linear Ion Trap</td>
<td>Provides ion trap CID MS^n up to MS^{10} mass analysis</td>
</tr>
<tr>
<td>Optional EASY-IC Ion Source</td>
<td>Generates internal calibrant ions for real-time mass calibration</td>
</tr>
<tr>
<td>Orbitrap Mass Analyzer</td>
<td>Resolution from 7,500–500,000 FWHM at m/z 200</td>
</tr>
<tr>
<td>Scan Rate</td>
<td>Orbitrap up to 30 Hz; Ion trap up to 40 Hz</td>
</tr>
<tr>
<td>Mass Accuracy</td>
<td>&lt;3ppm RMS external calibration; &lt;1ppm RMS internal calibration</td>
</tr>
<tr>
<td>Dynamic Range</td>
<td>&gt;5,000 in a single scan</td>
</tr>
<tr>
<td>Multiplexing</td>
<td>Up to 10 different precursor ions for targeted MS^2 or SIM</td>
</tr>
<tr>
<td>Polarity Switching</td>
<td>One positive ion and one negative ion MS scan (30,000 resolution at m/z 200) in 1.1 sec</td>
</tr>
</tbody>
</table>
The value of ultra-high resolution MS data
The capability of Orbitrap ID-X Tribrid mass spectrometer to acquire full scan MS data at up to 500,000 mass resolution at m/z 200 provides clear benefits in terms of compound annotation (Figure 3). Using Compound Discoverer software, the protonated molecular ion of C₅H₁₁NO₂S (m/z 150.05844) found in human plasma is automatically grouped with the sodium adduct (m/z 172.04042) and the protonated species minus NH₃ (m/z 133.03198). The isotope fine structure at m/z 151 allows the assignment of a sulfur containing species due to the presence of the ³³S isotope. In this example, at 160,000 actual resolution the ¹⁵N and ³³S isotopes are easily separated. The accurate mass MS² spectrum matches the library spectrum of methionine and the structure of the product ions are all annotated with the expected fragment ion structures. Thus, automated data reduction and confident annotation are enabled by the use of sufficiently high resolution MS and MS² data.

AcquireX acquisition workflow
The AcquireX intelligent data acquisition workflow significantly improves the number of confident annotations using fully automated iterative exclusion and inclusion lists to obtain fewer redundant/irrelevant data dependent MSⁿ spectra.⁷ The workflow allows the user to specify different sample types that includes a solvent (experimental) blank and a pooled sample matrix, prepared from a small portion of each individual biological sample. The workflow also specifies different experimental methods—full scan MS for acquiring blank and pooled reference samples and data dependent MSⁿ for iterative sample injection. The AcquireX process is shown in Figure 4.

Figure 3. Ultra-high resolution MS and MS² data for annotation of methionine in human plasma.
The workflow consists of a fully automated sequence designed to obtain comprehensive LC-MS² analysis of a pooled sample by the iterative process described below.

• First, the AcquireX process obtains the LC-MS data for the blank and a pooled sample
• The AcquireX process creates an exclusion list from the blank and inclusion list from the sample data
• The first data dependent MS² run is acquired and the inclusion/exclusion lists are updated after the run
• On the second injection, MS² spectra are acquired for compounds remaining on the inclusion list
• This process is repeated for a user-specified number of injections

The AcquireX process is illustrated by the repeated injection of NIST SRM 1950 human plasma extract and analysis using the Orbitrap ID-X Tribrid mass spectrometer. LC-MS analysis of the solvent blank and automated data analysis generated an exclusion list of more than 4000 features (Figure 5). Similarly, LC-MS of the plasma extract generated an inclusion list with more than 5000 features. Next, the first LC-MS² acquisition and data analysis was performed and the inclusion and exclusion lists were updated prior to a second LC-MS² acquisition. As expected, with each repeated sample injection, the number of entries on the inclusion list decreased while the number of exclusion list entries increased until the maximum number of injections was reached.

During data-dependent MS², ions are selected based on abundance, without any knowledge of biological relevance or ion type. Often, irrelevant spectra, resulting from fragmentation of solvent clusters and other background ions dominate the duty cycle, limiting the capacity of the instrument to acquire informative spectra. With traditional data dependent analysis (DDA) 76% of the MS² spectra are obtained on background ions, whereas using the AcquireX process background ion MS² spectra were practically eliminated, allowing for analysis of more relevant sample components (Figure 6).

Small molecules form multiple adducts and cluster ions during electrospray ionization. Selection of highly abundant compounds, in the form of a parent ion or its accompanying isotopes and adducts, may prevent the fragmentation of metabolites of lower abundance. By populating the inclusion list with the preferred adduct ion...
for each metabolite, more compounds can be sampled by MS² in a single run. Automatically updating inclusion and exclusion lists after each injection during analysis ensures that compounds not selected for MS² will be prioritized during a subsequent injection. The number of compounds of interest that have MS² spectra acquired is compared (Figure 7) for traditional DDA vs. AcquireX process. The graphs illustrate that the iterative process is far more efficient in obtaining more MS² spectra on relevant compounds of interest.

In the traditional DDA workflow, each injection is independent of the previous one, resulting in redundant fragmentation spectra. With the AcquireX method, inclusion and exclusion lists are automatically updated after each injection, minimizing redundant fragmentation and allowing for more analytes of lower abundance to be sampled with subsequent injections. Figure 8 shows deeper interrogation of samples with subsequent injections using the AcquireX method compared to traditional DDA by acquiring: a) lower intensity precursor ions and b) fewer redundant MS² spectra.

**Figure 6.** Obtaining MS² information on compounds vs. background: AcquireX vs. traditional DDA.

**Figure 7.** Comparison of MS² on compounds of interest: traditional DDA vs. AcquireX.
The cumulative result of these improvements is that, compared to traditional DDA, the AcquireX data acquisition method obtains more MS² spectra; this significantly increases the number of mass spectral library matches (Figure 9) against mzCloud, a very high-quality, HRAM MSⁿ spectral library. The number of matches were defined as: Identity match—the precursor mass and MS² spectrum closely matches a reference compound or Similarity match—the MS² spectrum is similar to a reference compound but has a different precursor mass. After 3 injections, the total number of Identity plus Similarity matches for AcquireX data increased by more than 2-fold over the spectral matches obtained from DDA alone. A 50% increase was observed for the identity matches.

Figure 8. Deeper interrogation of samples by: a) Lower abundance precursors and b) Less redundancy.

Figure 9. AcquireX data acquisition improves mzCloud library matches vs. traditional DDA: a) Similarity plus identity match, and b) Identity match only.
**LC-MS for more confident structural annotation of isomers**

The LC-MS<sup>n</sup> capabilities of the Orbitrap ID-X Tribrid mass spectrometer for improved structure annotation are illustrated in Figure 10 by the analysis of two flavonoid isomers—Kaempferol-3-O-β-rutinoside and Luteolin 7-rutinoside<sup>3</sup>. While the LC-MS<sup>2</sup> spectra of m/z 595.1650 show the same two product ions (m/z 449 and 287, loss of one and two sugars, respectively) although with different abundances (Figure 10), the LC-MS<sup>3</sup> spectra from the m/z 287.0546 product ions are clearly different with several unique product ions for each isomer. This illustrates the concept of precursor ion fingerprinting<sup>4</sup>: the m/z 287 ion has a different sub-structure, due to the difference in the flavonoid precursors and this is reflected in the MS<sup>3</sup> spectra.

**Structure-based analysis of isomers**

There are many examples of metabolites and lipids that are amenable to a structure-based experimental approach—for example, acylcarnitine, flavonoid, phosphatidylcholine and triglyceride isomers are related to each other by common neutral losses or product ions. The LC-MS<sup>n</sup> analysis of structurally-related species such as flavonoids is enabled by a data dependent workflow that is selective for the neutral loss of sugar (Table 3) from the flavonoid core structure (Figure 11)<sup>5</sup>. The neutral losses of the various sugars observed in the fragmentation of flavonoids is provided as a pre-defined template (Structure specific MS<sup>4</sup> monosaccharide loss) in the Orbitrap ID-X Tribrid mass spectrometer method editor. For flavonoids below m/z 420, an HCD MS<sup>2</sup> experiment is performed, whereas, above m/z 420, a more selective CID MS<sup>3</sup> experiment is performed to maximize the loss of a single sugar, which in turn is the precursor ion for a CID MS<sup>3</sup> experiment. Additional sequential sugar losses lead to CID MS<sup>4</sup> and CID MS<sup>5</sup> experiments. The value of this novel workflow is that the MS<sup>n</sup> spectral tree is completely acquired, thus extensively characterizing the flavonoids in a real sample, and the MS<sup>n</sup> trees can then be searched for related flavonoid sub-structures present in a reference library.

**MS<sup>2</sup> 595.1650**

Kaempferol 3-O-β-rutinoside

**MS<sup>3</sup> 287.0546**

**MS<sup>2</sup> 595.1650**

Luteolin 7-rutinoside

**MS<sup>3</sup> 287.0546**

Figure 10. LC-MS<sup>2</sup> and MS<sup>n</sup> spectra of two isomeric flavonoids.
Lipid structure annotation using LC-dd MS² and targeted MS³ using a neutral loss scan filter

Advanced scan filters are employed during data dependent analysis to provide further characterization of specific compound classes. For example, during LC-MS analysis triglyceride (TG) lipids often elute as a mixture of isomers and thus, their MS² spectra consist of a mixture that requires additional information for annotation. Using the targeted loss trigger on the Orbitrap ID-X Trivid mass spectrometer, MS³ scans are acquired only when a characteristic loss of fatty acid and ammonia is observed during the data-dependent MS² experiment. As shown in Figure 12, the MS² spectrum of TG 48:1 is a mixture of at least two isomeric lipids. The MS³ spectra from three neutral losses gives confident annotation of TG 14:0-16:0-18:1 and TG 16:0-16:0-16:1.

Table 3. Sugar neutral losses from protonated flavonoid precursor ions.

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<tr>
<th>Saccharide</th>
<th>Neutral Loss</th>
<th>Composition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pentose (xylose, arabinose)</td>
<td>132.04226 C₅H₈O₄</td>
<td></td>
</tr>
<tr>
<td>Deoxyhexose (rhamnose)</td>
<td>146.05791 C₆H₁₀O₄</td>
<td></td>
</tr>
<tr>
<td>Hexose (glucose, galactose)</td>
<td>162.05282 C₆H₁₀O₅</td>
<td></td>
</tr>
<tr>
<td>Glucuronide</td>
<td>176.03209 C₆H₁₂O₆</td>
<td></td>
</tr>
<tr>
<td>Glucuronic acid</td>
<td>194.04265 C₆H₁₂O₇</td>
<td></td>
</tr>
</tbody>
</table>

Figure 11. Neutral loss dependent LC-MSⁿ acquisition method for flavonoids.
Figure 12. LC-MS² and targeted MS³ spectra of two isomeric triglycerides from insect larvae.

Detailed resources for the Orbitrap ID-X Tribrid mass spectrometer can be found:
thermofisher.com/orbitrapID-X
planetorbitrap.com/orbitrap-id-x#

For sole source specifications, kindly contact your local sales representative or contact us at: Grant Central.

Why choose the Orbitrap ID-X Tribrid mass spectrometer?
State-of-the-art research is the engine that drives advances in mass spectrometry innovation. Mass spectrometers must be equipped with superior performance such as higher resolution, mass accuracy, dynamic range and scan efficiency to fulfill more rigorous experimental demands and complexity. MS instruments must have the flexibility to handle qualitative and quantitative experiments while being extremely robust for high-throughput analysis. In addition, for small molecule identification the combination of features available on the Orbitrap ID-X Tribrid mass spectrometer (see Table 4 for comparison to other Orbitrap-based instruments) provides tools that offer a unique combination of multiple proven technologies for obtaining structural information (high resolution, accurate mass measurement, HCD MS² and linear ion trap MS³) along with the real-time decision-making capability to obtain more definitive characterization of metabolites, lipids and novel compounds with unknown structures. The exceptional value of the Tribrid Orbitrap-based mass spectrometers in delivering uncompromised analytical benefits while achieving superior results are well recognized by the scientific community. The Orbitrap ID-X Tribrid mass spectrometer is designed for scientists that need higher confidence in their compound structure annotations and their metabolomics studies.
<table>
<thead>
<tr>
<th>Instrument Attributes</th>
<th>Q Exactive</th>
<th>Q Exactive Plus</th>
<th>Q Exactive HF</th>
<th>Q Exactive HF-X</th>
<th>Orbitrap ID-X</th>
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<td>Mass Analyzer</td>
<td>Orbitrap</td>
<td>Orbitrap</td>
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<td>High Field</td>
<td>Tridend–ion trap and Orbitrap</td>
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<td>Top NMS²</td>
<td>Top 10 ddMS²</td>
<td>Top 10 ddMS²</td>
<td>Top 20 ddMS²</td>
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<tr>
<td>Top Speed MSⁿ</td>
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<td></td>
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<td>Yes, up to 10 precursors</td>
<td>Yes, up to 10 precursors</td>
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<td>AcquireX Intelligent Acquisition</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
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<td>Performance Features Performance Features</td>
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<td>Q Exactive Plus</td>
<td>Q Exactive HF</td>
<td>Q Exactive HF-X</td>
<td>Orbitrap ID-X</td>
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<tr>
<td>Resolution</td>
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<td>✔ ✔ ✔ (option)</td>
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<tr>
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<td>✔ ✔ ✔</td>
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<td>Application</td>
<td>Q Exactive</td>
<td>Q Exactive Plus</td>
<td>Q Exactive HF</td>
<td>Q Exactive HF-X</td>
<td>Orbitrap ID-X</td>
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<td>Untargeted Metabolomics</td>
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<td>✔ ✔</td>
<td>✔ ✔</td>
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<tr>
<td>Untargeted Lipidomics</td>
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<tr>
<td>Targeted Analysis (PRM)</td>
<td>✔ ✔</td>
<td>✔ ✔</td>
<td>✔ ✔</td>
<td>✔ ✔</td>
<td>✔ ✔</td>
</tr>
</tbody>
</table>

Table 4. Which Orbitrap system is right for my metabolomics research?

Least Fit | ✔ ✔ | ✔ ✔ | ✔ ✔ | ✔ ✔ | ✔ ✔ | ✔ ✔ | ✔ ✔ | ✔ ✔ | ✔ ✔ | ✔ ✔ | ✔ ✔ | ✔ ✔ | ✔ ✔ | ✔ ✔ | ✔ ✔ |

Best Fit
References


7. Improved Metabolome Coverage and Increased Confidence in Unknown Identification Through Novel Automated Acquisition Strategy Combining Sequential Injections and MS^n, Ioanna Ntai, Iman Mohtashemi, Jenny Berryhill, Ralf Tautenhahn, Graeme McAlister, Derek Bailey, Linda Lin, Ryo Komatsu, Caroline Ding, Seema Sharma, Tim Stratton, Vlad Zabrouskov, Amanda Souza, Andreas Huhmer, Scientific Poster #65286.

8. Flavonoid Annotation Using a Product Ion-Dependent MS^n Data Acquisition Method on a Tribrid Orbitrap Mass Spectrometer, Reiko Kiyonami, Iwao Sakane, Seema Sharma, Graeme McAlister, Caroline Ding, and Andreas Huhmer, Scientific Poster #6530.

9. New method filters for improved MS^n acquisition for small molecule and proteomics workflows, Graeme McAlister, Ioanna Ntai, Reiko Kiyonami, Romain Huguet, Caroline Ding, Iman Mohtashemi, Derek Bailey, Shannon Eliuk, Vlad Zabrouskov, Seema Sharma, Scientific Poster #65259.

10. Software Utilizing Positive and Negative Ion MS^2/MS^3 HCD and CID Spectra for Improved MS^n Lipid Identification, David A Peake, Reiko Kiyonami, Daniel Gachotte, Gavin E Reid, Yasuto Yokoi, and Andreas Hühmer, Scientific Poster #65257.

Recommended literature


https://link.springer.com/article/10.1007%2Fs13361-017-1829-2

Description: Untargeted lipidomics, infusion, PRM, MSX (multiplexed MS/MS), human plasma

MS-Based Metabolomics for the Investigation of Neuro-Metabolic Changes Associated with BDE-47 Exposure in C57BL/6 Mice, Fenfen Ji, Hemi Luan, Yingyu Huang, Zongwei Cai, Min Li, *J Anal Test* (2017) 1:233–244

https://link.springer.com/content/pdf/10.1007/s41664-017-0026-4.pdf

Description: Untargeted metabolomics, LC-MS, Quantitation, Neuro-metabolic changes


Description: Untargeted lipidomics, MS^{ALL}, liver, nano-infusion, plasma/skeletal muscle lipids, quantitation

Comprehensive Analysis of Acylcarnitine Species in db/db Mouse Using a Novel Method of High-Resolution Parallel Reaction Monitoring Reveals Widespread Metabolic Dysfunction Induced by Diabetes, Li Xiang, Juntong Wei, Xiao Yu Tian, Bei Wang, Wan Chan, Shangfu Li, Zhi Tong, Hongsong Zhang, Wei San Cheang, Qian Zhao, Hongzhi Zhao, Zhiyi Yang, Yanjun Hong, Yu Huang, and Zongwei Cai, *Anal. Chem.,* 2017, 89 (19), pp 10368–10375.


Description: Targeted metabolomics, PRM, Acylcarnitines, lipids, LC-MS^2

**Description:** Untargeted metabolomics, global metabolomics, LC-dd MS², LipidSearch


**Description:** Untargeted lipidomics, human plasma, dd MS², targeted MS³, quantitation, LC-MS, Compound Discoverer, TraceFinder

http://www.fasebj.org/content/early/2017/09/22/fj.201700657R.abstract?sid=1cb1a92d-7f74-4bac-9d8e-46cb6331a9c4

**Description:** Semi-targeted metabolomics, TraceFinder, glucose role in ammonia detoxification, mosquitoes


**Description:** Untargeted Lipidomics, Infusion, 193 nm UVPD, Lipid A, HCD and CID MS²

http://www.nature.com/nchembio/journal/vaop/ncurrent/full/nchembio.2238.html

**Description:** Untargeted Lipidomics, LC-dd MS² and targeted MS³

Vertical sleeve gastrectomy reverses diet-induced gene-regulatory changes impacting lipid metabolism, Juan Du, Jingyan Tian, Lili Ding, Candi Trac, Brian Xia, Siming Sun, Dustin E. Schones and Wendong Huang, Scientific Reports 7, 5274 (2017).
https://www.nature.com/articles/s41598-017-05349-2

**Description:** Untargeted lipidomics, LC-dd MS², LipidSearch, Vertical sleeve gastrectomy (VSG)

http://physreports.physiology.org/content/5/16/e13388.long

**Description:** Lipidomics, LC-MS, cardiolipin, cardiac fatty acid metabolism in early T2DM

http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0182819

**Description:** Untargeted metabolomics, LC-MS, human plasma, LC-dd MS² annotation, mzCloud
http://www.cell.com/cell/abstract/S0092-8674(17)30477-4

Description: Untargeted metabolomics, LC-MS, Plant metabolites

Soluble factors from stellate cells induce pancreatic cancer cell proliferation via Nrf2-activated metabolic reprogramming and ROS detoxification, Yuan Seng Wu, Chung Yeng Looi, Kavita S. Subramaniam, Atsushi Masamune and Ivy Chung, Oncotarget, 2016, 7(24) 36719-36732.

Description: Untargeted metabolomics, LC-MS, quantitation, pancreatic cancer

http://link.springer.com/article/10.1007%2Fs13361-014-1013-x

Description: Untargeted lipidomics, MSALL / targeted MS3, nano-infusion, quantitation, mouse brain tissue lipids

http://pubs.acs.org/doi/abs/10.1021/ac501451v

Description: Targeted metabolomics, LC-MS3 method development, in-source formation of pyroglutamic acid