Thermo Scientific™ Q Exactive™ Series Hybrid Quadrupole-Orbitrap™ Mass Spectrometer for Metabolomics

Goal

This document is intended to address the technical and workflow benefits of the Thermo Scientific™ Q Exactive™ Hybrid Quadrupole-Orbitrap family of mass spectrometers (MS) with conclusive arguments to justify this range of MS systems as the ideal instruments of choice for Metabolomics applications.

Summary

The Thermo Scientific™ Q Exactive™ hybrid quadrupole-Orbitrap™ mass spectrometers are robustly engineered to provide enhanced resolution, mass accuracy, wide dynamic range, fast acquisition rates, and have emerged as exceptional MS instruments suited for metabolomics applications. The instruments deliver excellent experimental flexibility, functionalities and usability to meet the scientific and analytical demands required to accelerate Metabolomics research. Mass spectrometry based strategies for Metabolomics studies can provide both qualitative and quantitative information, enabling confident metabolite identification and monitoring of metabolite abundance levels across biologically complex and large sample sets. Multiple application workflows from metabolite biomarker discovery to large-scale quantitative metabolomics can be accomplished on the Q Exactive MS platforms. The Thermo Scientific™ Q Exactive™ MS systems allow the simplification of workflows, empowering research laboratories with the versatility to conduct various MS analyses and undertake numerous research projects, driving experimental efficiency, quality results and productivity.

Introduction

Mass spectrometry based approaches are commonly used for Metabolomics studies due to higher sensitivity and detection of a large range of metabolites. Despite the technical advancements in MS instrumentation, getting deep metabolome coverage and accurate measurements of biological significant metabolites remains an arduous task for researchers. Several analytical obstacles are encountered in the detection and reliable identification of metabolites as these molecules are structurally diverse and possess varied physiochemical properties. Comprehensive analysis of metabolites involving different analytical strategies can provide valuable insights for gaining better understanding in metabolomics studies. Capacity to perform multiple analytical techniques on a single MS platform is a highly advantageous and attractive solution as it drives experimental flexibility while offering complementary pieces of information. Mass spectrometers today have increased resolution and mass accuracy, and have emerged as a dominant tool for structural characterization in various applications beyond early drug discovery.

The ease of operating sophisticated MS tools has vastly improved and this is no exception on the Q Exactive MS systems. Apart from the hardware improvements, these instruments come with intuitive software features to promote operational usability and effective adoption of Thermo Scientific™ Orbitrap™ technology. Users can easily set optimal instrument parameters, perform

simple maintenance and calibration procedures to ensure instrument stability and tackle troubleshooting effortlessly. This reduces instrument downtime significantly and allows for increased sample stream to maximize instrument acquisition time while keeping productivity up. The user-friendly software interface has templates for easy acquisition method development and optimization to fit various experimental needs. Superior qualitative performance on the Q Exactive MS analytical platforms are a real asset for compound identification, metabolite biomarker discovery and retrospective data analysis to advance research studies. The robust and reliable quantitative aspects of the instrument line support routine, high throughput, large-scale targeted metabolomics studies, making the Q Exactive family of mass spectrometers ideal analytical instruments with great utility for any laboratory.

Hardware Benefits

The Q Exactive mass spectrometers have the following capabilities:

- High resolution and mass accuracy for attaining identification confidence suited for in depth metabolome coverage.
- Fast acquisition speeds, compatible with UHPLC flow rates, while delivering high MS and MS/MS spectral quality for sensitive detection and robust quantification of lipids and metabolites.
- Selectivity and sensitivity of both the standard and ultra-high-field Orbitrap analyzers, available on all Thermo Scientific™ Q Exactive MS platforms, to achieve more confident identification and quantitative precision.

Q Exactive MS systems are equipped with the following features:

- Advanced Active Beam Guide (AABG) – reduces background noise, ensuring system stability and robustness.
- Advance Quadrupole Technology – results in improved selectivity and transmission efficiency to achieve quantitation accuracy, especially for low abundant analytes in highly complex matrices.
- C-trap – regulates ion population followed by efficient transmission into the ultra-high-field Orbitrap mass analyzer.
- Ultra-high-field Orbitrap mass analyzer on the Q Exactive HF MS and Q Exactive HF-X MS – Highest resolution available on a benchtop mass spectrometer of 240,000 at *m/z* 200 and scan rates up to 40 Hz at 7,500 FWHM, capable of faster scan speeds and higher resolutions for both discovery and quantitation experiments.

Built on the proven, advanced, analytical, and robust performance of the first benchtop Q Exactive hybrid quadrupole-Orbitrap mass spectrometer, the most recent Q Exactive platforms (i.e.: Q Exactive HF MS, Q Exactive HF-X MS) have had key improvements made to its various hardware components that give enhanced analytical capabilities. These include:

- Ultra-high-field Orbitrap mass analyzer vs. standard Orbitrap mass analyzer (e.g.: Thermo Scientific™ Q Exactive™ Focus MS, Q Exactive MS and Thermo Scientific™ Q Exactive™ Plus MS) – Capable of achieving faster scan rates and higher resolving power with improved transient times.

Table 1. Fundamental features and performance benefits of the Q Exactive family of mass spectrometers

Features	Benefits
High resolution	High resolving power to resolve closely related masses in complex matrices and fine isotope structure for confident elemental composition prediction
Sub ppm mass accuracy	High selectivity and confidence in molecular formula determination, especially useful for unknown analysis
High spectral quality	Improved transient times to produce top quality MS/MS spectra acquisitions
Scan speed	Faster scan rates for improving metabolite identification rates and achieving quantitation accuracy
Easy to use software	Intuitive instrument control and method editor software for ease of operations and flexible analytical method creation
Experimental flexibility	SIM, AIF, DDA, PRM, DIA acquisition modes

- Advanced Active Beam Guide consists of an injection flatapole that serves as a prefilter to reduce contamination; a bent flatapole provides an axial field for optimal ion transfer and removal of neutral ions.
- Advanced Quadrupole Technology comprises of a segmented quadrupole to achieve better isolation efficiency and optimum ion transmission for narrow isolation windows, leading to greater quantitation accuracy.

Detailed product specifications for all the Thermo Scientific Q Exactive MS products can be found here.

Top Reasons for selecting the Q Exactive MS platforms for Metabolomics

- High resolution accurate mass combined with high sensitivity increases compound detection and annotation confidence for improved metabolome coverage.
- Analytical robustness for routine, high throughput applications, delivers reproducible and precise quantitative results.
- Fast scan speeds for shorter gradient times in combination with MS multiplexing capabilities drive experimental efficiency and productivity.
- High data quality guaranteed to address complex sample matrices against competing MS technologies.

Solution and Benefits

Why is Higher Resolution Necessary for My Metabolomics MS Experiments?

The Q Exactive HF MS and Q Exactive HF-X MS come equipped with a compact, ultra-high-field Orbitrap mass analyzer found only on more recently developed Orbitrap-based mass spectrometry platforms. Compared to the standard Orbitrap analyzer, this enhanced analyzer effectively doubles the operating frequency, thus increasing its resolving power and scan speed. These exceptional benefits promote better instrument productivity and added confidence in identification and quantitation experiments in less time. These MS systems can achieve 240,000 resolving power (FWHM) at *m/z* 200 (280,000 resolution at *m/z* 200 with enhanced resolution option on Q Exactive Plus MS), significantly higher than similar benchtop mass spectrometers in the current product portfolio at 140,000 resolution (FWHM) and other comparable commercial mass spectrometers available on the market.

Challenges are often encountered in MS analyses, especially in the detection and differentiation of isobaric metabolite species. Low resolution produces potential false positives in identification and lower identification rates, less abundant metabolites are not detected. MS platforms with high resolution capabilities, like the Q Exactive HF MS or Q Exactive HF-X MS, are analytical instruments of choice for metabolite characterization as metabolites of interest can be resolved from near mass isobaric ions or background ions that typically populate complex matrices. With higher resolution, we demonstrate the effect of baseline resolving two isobaric species (arginine and *N*-acetyl ornithine) with a mass difference of 65 ppm at 60,000 resolution. These two species would otherwise appear as a single peak at 15,000 resolution (Figure 1).

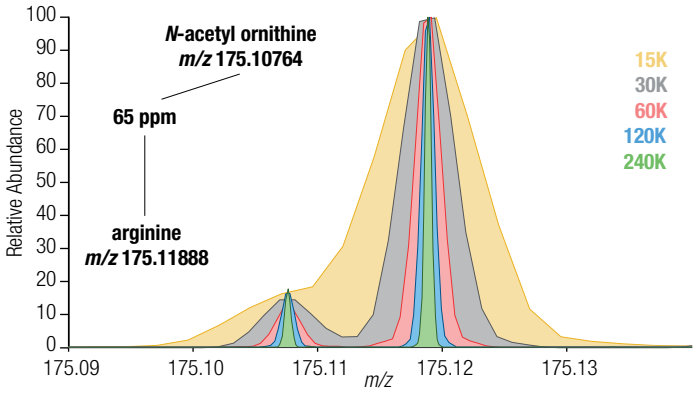

Figure 1. Increasing resolution improves detection of isobaric species arginine and *N*-acetyl ornithine which require at least a minimum of 60,000 resolving power for baseline separation.

High MS resolving power further becomes important for fine isotopic pattern determination, which leads to more confident elemental formula prediction. At higher resolution settings, MS sensitivity on the Orbitrap analyzer is not sacrificed and the mass accuracy can be maintained without the need for internal calibration or lock mass calibration procedures. These are the ideal instruments of choice as they strike the balance between achieving superior resolving power, excellent detection sensitivity and selectivity. High resolution is critical in metabolomics studies for differentiation of isobaric species and resolving matrix and background interferences, particularly for low abundant metabolites in complex samples. Furthermore, these instruments could be considered even more suitable for small molecule analysis, as higher resolution is attainable at lower *m/z* range.

Faster Scan Speeds

There is a known trade-off in scan speeds on the Orbitrap mass analyzer as we go to higher resolution settings. This phenomenon is addressed with the ultra-high-field Orbitrap analyzer, which at the same resolution on a standard Orbitrap mass analyzer, can produce the same number of scans in half the transient time. The ability to operate at faster acquisition rates at high resolutions produces faster acquisition cycles, increasing the number of compounds detected, thereby providing greater depth in analysis of a sample. More compounds are detected as shown in a NIST SRM1950 human plasma standard analyzed across increasing resolution settings on the Q Exactive HF MS (Figures 2A and 2B).[1,2] Competing mass spectrometers typically operate at 30,000 resolution, limiting the detection capability required for in-depth discovery experiments. Increasing the MS resolving power from 30,000 to 60,000, results in a 40% increase in number of metabolites detected. An additional 10% of metabolites are detected when operating at 120,000 resolution. Faster scan speeds (more scan points across a peak and improved %CVs) without decreased resolution, result in improved precision for qualitative and quantitative experiments. The quality of quantitation experiments improves with better integration specificity, thus contributing to data integrity and accuracy. This improvement in scan speeds does not sacrifice the resolution of the Orbitrap analyzer. In fact, the Q Exactive HF MS delivers a higher resolution by a factor of 1.8 times over other Q Exactive MS platforms equipped with the standard Orbitrap analyzer. Enhanced analytical performance is achieved, resulting in a 36% increase in compound detection at similar resolutions on two different MS platforms with different Orbitrap analyzers (Figure 3).

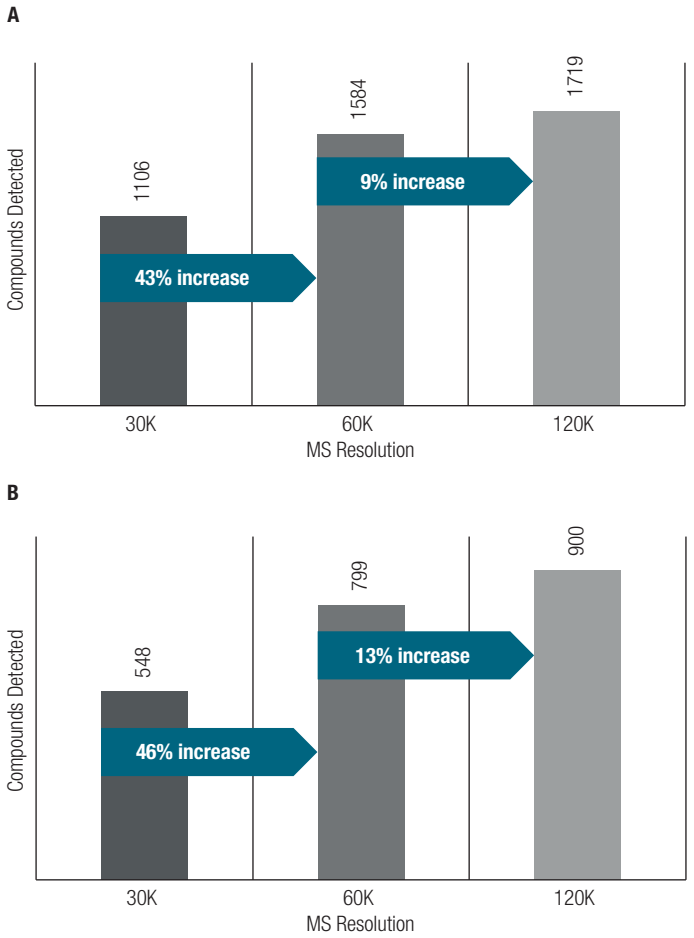

Figure 2. NIST SRM1950 human plasma standard analyzed on a Q Exactive HF MS in positive (A) and negative (B) polarity at 30K, 60K and 120K resolutions produced increased numbers of compounds detected with increasing MS resolving power.[1]

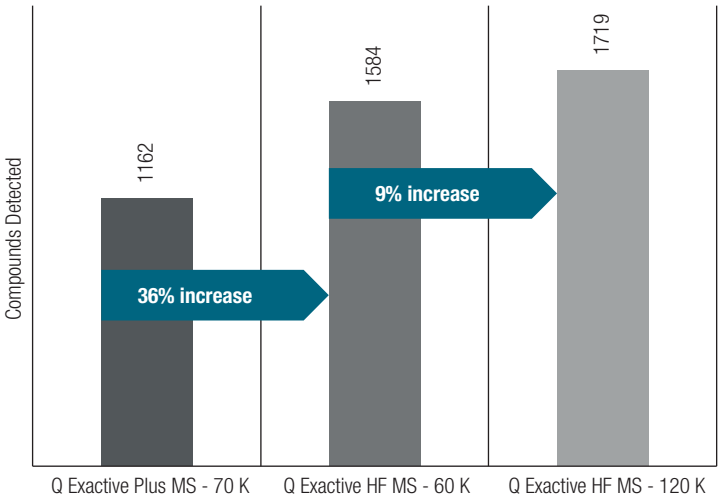

Figure 3. Human plasma reference standard analyzed on Q Exactive Plus MS at 70K resolution and Q Exactive HF MS at 60K and 120K resolutions produced improved numbers of metabolites detected at similar MS resolving power.

Why is Mass Accuracy Important?

Identification of unknown metabolites is a highly rigorous endeavor, but with the advancement in MS technologies, we now have better tools to get accurate mass assignments and achieve unambiguous determination of metabolite species in complex mixtures. The ability of higher performing MS instruments to reach lower mass tolerance ranges would better discriminate mass differences and bring greater confidence in predicting possible elemental compositions of unknowns. Significantly superior spectral quality can be obtained due to high resolution accurate mass (HRAM), thus yielding better metabolite coverage. The mass accuracy from scan-to-scan across the chromatographic peak of creatine with theoretical *m/z* 132.0768 is well maintained at sub ppm level and is instrumental for confident peak assignment of unknown compounds (Figure 4). At the MS/MS level, ensuring mass accuracy for fragment ions enables a more accurate calculation of possible empirical formulas, which increases our confidence of identifying characteristic fragments associated with the metabolite candidate (Figure 5). This fragmentation information is valuable in advancing unknown identification especially for structural annotation and matching against available compound databases and spectral libraries.

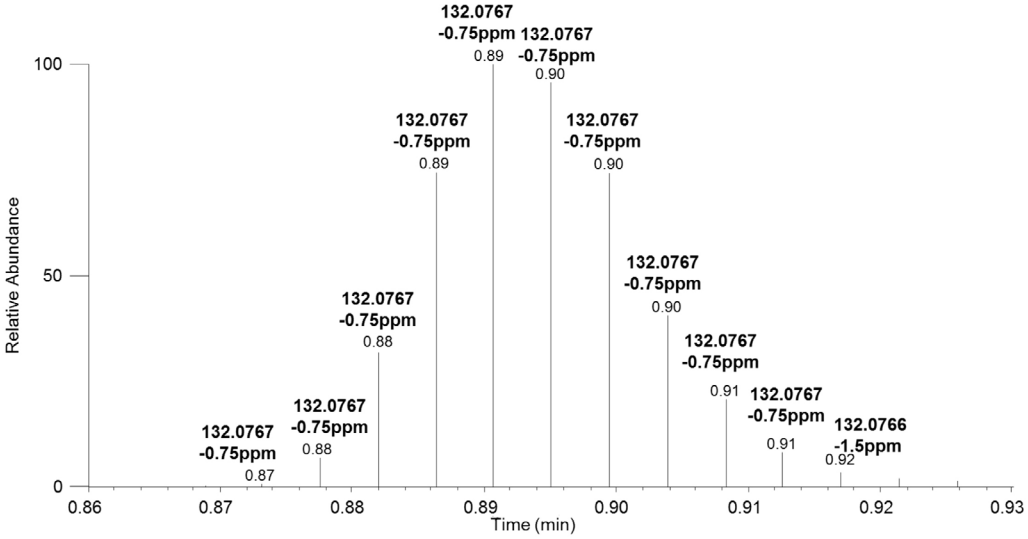

Figure 4. Excellent mass stability from scan-to-scan across the peak for creatine with theoretical *m/z* 132.0768

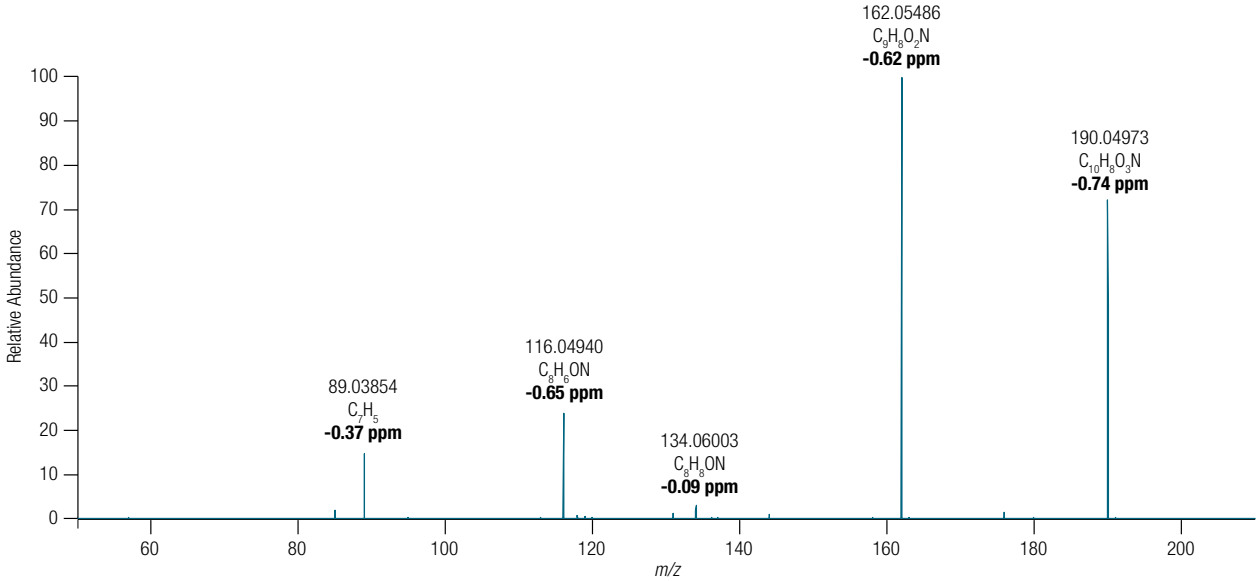

Figure 5. Excellent mass accuracy during fragmentation allows chemical formula calculation of fragment ions of kynurenic acid that can be further used for structure annotation and compound database matching.

We further demonstrate minimal fluctuation in mass accuracy of internal standards D8-valine and D4-succinate spiked in NIST SRM1950 human plasma standard, across 150 injections over a 55-hour period on the Q Exactive HF MS (Figure 6). This MS system can maintain robust mass stability after continuous injections over an extended period of analysis time, which serves to contribute towards more reliable and confident results. This is especially important when running large-scale metabolomics studies, where consistent data output must be routinely obtained. The Q Exactive HF MS can conduct both positive and negative polarity switching in a single acquisition, which comes useful in the experimental design for discovery metabolomics analysis, in cases of working with insufficient sample amounts or limited instrument analysis time. Additionally, the ability to multiplex and carry out parallel acquisition modes on the Q Exactive HF MS will produce sufficient data points to obtain excellent reproducibility and low variance. As smaller isolation mass windows are utilized in such instruments, researchers can achieve greater selectivity and improved sensitivity as well.

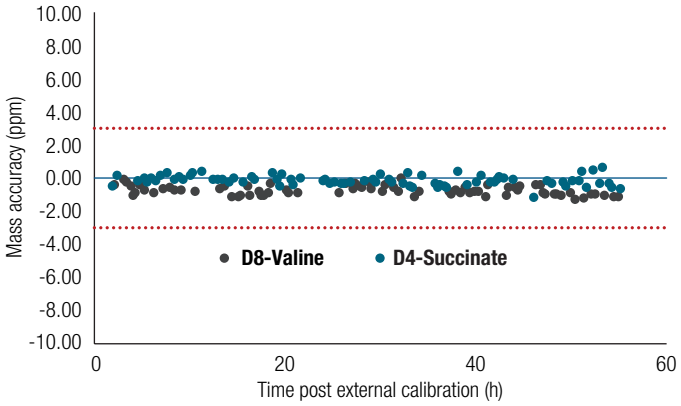

Figure 6. Mass accuracy of internal standards D8-valine and D4-succinate stable at less than 2ppm during a 55-hour analysis in both positive and negative polarity

Applying High Resolution and Accurate Mass to Stable Isotope Labeling Studies

Untargeted metabolomics studies offer an unbiased approach to understand the behavior of a biological system and give insight to important metabolites and pathways of hypothetical interest. Isotope labeling has been widely adopted in the past to derive mechanistic understanding of metabolic pathways and networks, as well as achieving functional understanding in cellular metabolism. Stable isotopic labeling is one technique used extensively in the identification, determination and quantitation of metabolites involved in metabolic pathways. As discussed, MS-based metabolite identification relies heavily on elemental composition prediction as one main approach. With high mass accuracy, researchers can significantly narrow down the number of possible chemical formulae for a detected mass. Isotopic labeling can be used further for structural identification of a potential metabolite, benefitting the interpretation of MS/MS or MS^n fragmentation spectra to achieve greater accuracy especially where multiple isomers of a metabolite may exist. Mass spectrometers with very high resolution capabilities is required in such experiments to reliably separate isotopically labeled compounds and differentiate between labeled and unlabeled metabolites based on their mass differences. Sufficient isotopic resolution would allow untargeted detection of isotopes with minimal background interference,[3] leading to better success in the discovery of novel metabolites and metabolic pathways.

An experiment evaluating the importance of high resolution to resolve isotopic labeled peaks was performed on the Q Exactive HF mass spectrometer. Isotopically labeled species of adenosine triphosphate (ATP) were extracted from a sample of MDB-MA-231 cells grown in stable isotope-labeled (SIL) [13]C6 glucose and [13]C5[15]N2 glutamine medium for 24 hours. As the MS resolution on the instrument increases, the isotopologue peaks become more defined and the ^{13}C and ^{15}N double labeled isotopic metabolites are baseline resolved at higher resolution parameter settings.[4] Without increased resolution, the isotopologues would not be well resolved and accurately identified (Figure 7). The results further emphasize that high resolution and stable mass accuracy are crucial MS performance attributes for accurate assignments of isotopic labeled species, making it possible to track metabolite isotopologues in complex samples and examining metabolic pathways (Table 2).

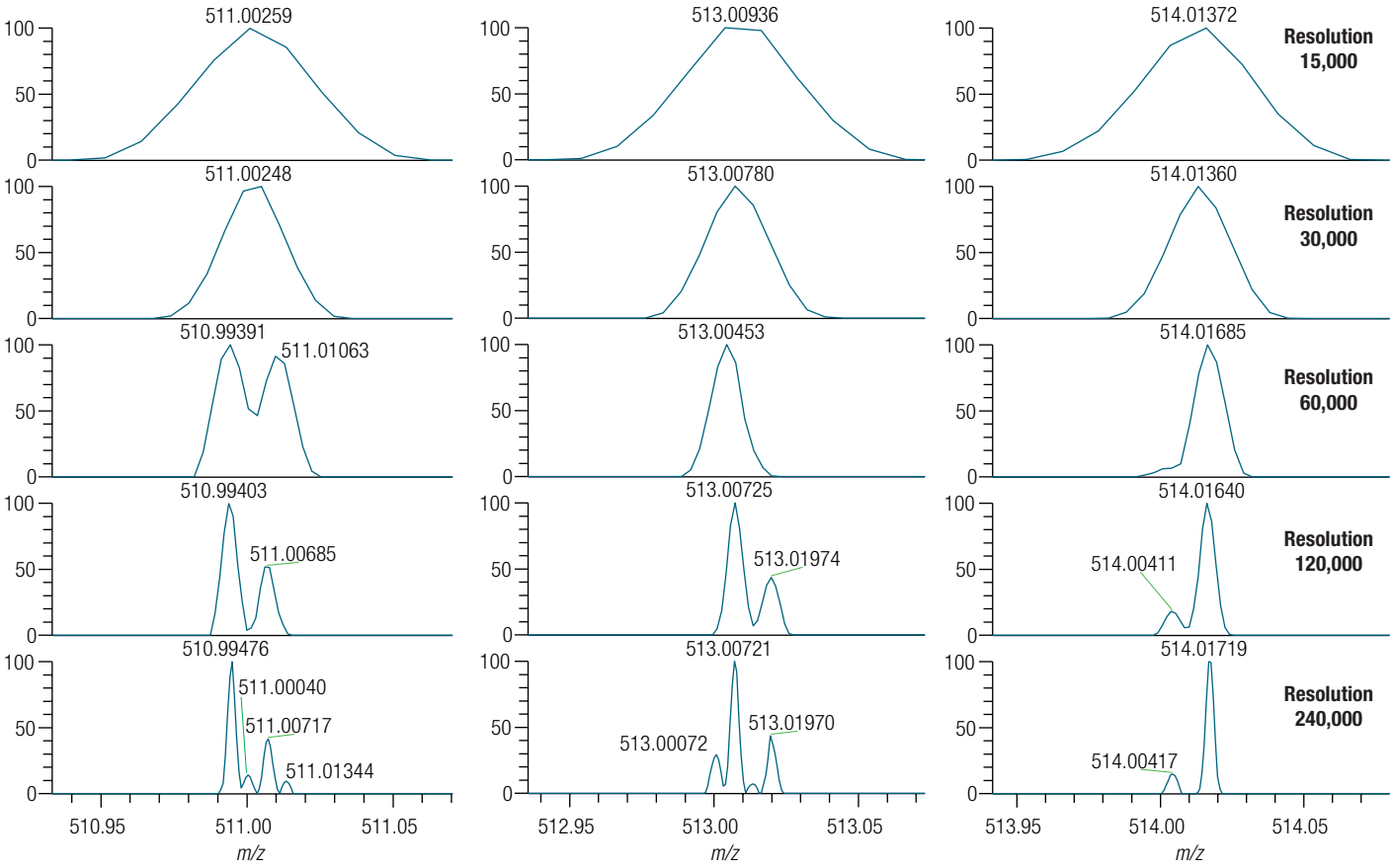

Figure 7. Increased resolution enabled the $^{13}C/^{15}N$ isotopically labeled species of ATP ($C_{10}H_{16}N_5O_{13}P_3$, *m/z* = 508.00302) to be well resolved.[4]

Table 2. Excellent mass accuracy on the Q Exactive HF MS allowed the precise assignment of isotopic labeled species of ATP.[4]

Assignment	Theoretical *m/z*	Measured *m/z*	Error (ppm)
$C_{10}H_{16}{}^{15}N_3N_2O_{13}P_3$	510.99413	510.99476	0.90
$^{13}C_1C_9H_{16}{}^{15}N_2N_3O_{13}P_3$	511.00045	511.00040	-0.10
$^{13}C_2C_8H_{16}{}^{15}N_1N_4O_{13}P_3$	511.00677	511.00717	0.78
$^{13}C_3C_7H_{16}N_5O_{13}P_3$	511.01309	511.01344	0.68
$^{13}C_2C_8H_{16}{}^{15}N_3N_2O_{13}P_3$	513.00081	513.00072	-0.17
$^{13}C_3C_7H_{16}{}^{15}N_2N_3O_{13}P_3$	513.00716	513.00721	0.10
$^{13}C_5C_5H_{16}N_5O_{13}P_3$	513.01980	513.01970	-0.29
$^{13}C_3C_7H_{16}{}^{15}N_3N_2O_{13}P_3$	514.00419	514.00417	-0.04
$^{13}C_5C_5H_{16}{}^{15}N_1N_4O_{13}P_3$	514.01683	514.01719	0.70

Targeted Metabolomics Analysis on Hybrid Quadrupole-Orbitrap MS Systems

Targeted metabolomics studies focus on the detection and accurate quantitation of a predefined set of metabolites, allowing the monitoring of important metabolites related to metabolic pathways of interest or key pathophysiological processes. Numerous publications have shown that high resolution MS instruments possess comparable quantitative performance to triple quadrupole platforms, overcoming known limitations with unit resolutions and wide *m/z* distributions. Use of high resolution MS quantitative approach offers the opportunity for obtaining targeted information and global metabolomics data in a single analysis.[5] Achieving sensitivity, specificity, reproducibility and robustness in targeted metabolomics analyses on an Orbitrap MS is no longer a limitation and challenges previous notions of inadequate quantitation capability on high resolution systems.

Ideally, when conducting targeted metabolomics experiments, we want a standardized workflow from sample preparation, quality control, analytical method and internal standards to introduce minimal variance and achieve high reproducibility. This is of high importance when working on large cohort studies that require consistent and reproducible quantitation results, and when comparing or integrating data across different centers and laboratories. Hence, the development of a standardized quantitative analytical method for accurate quantitation of metabolites and lipids in complex biological systems is in demand. Here, we introduce the Absolute*IDQ*® p400 HR kit developed on hybrid quadrupole-Orbitrap MS platforms that delivers a standardized and quality-controlled analytical method for accurate, reproducible and reliable quantitation.[6] Quantitative experiments for a validation or verification type study can be performed on Q Exactive MS systems without the need for demanding method optimization. The fast scan speeds on such instruments can accommodate UHPLC flowrates, bringing about robust quantifications.

Broad metabolite and lipid coverage provided by the kit combined with multiplexing capabilities of Q Exactive HF MS, allow quantitation of up to 408 endogenous metabolites covering 11 metabolite classes (amino acid, biogenic amines, phosphatidylcholines, acylcarnitines, lysophosphatidylcholines, diglycerides, triglycerides, sphingomyelins, ceramides, cholesteryl esters and hexoses) relevant to key pathophysiological processes. The utility of the Absolute*IDQ* p400 HR for monitoring changes in metabolite concentration in serum samples obtained from Type 2 Diabetes (T2D) study subjects and healthy controls analyzed on the Q Exactive HF mass spectrometer is demonstrated (Figure 8). For instance, increased

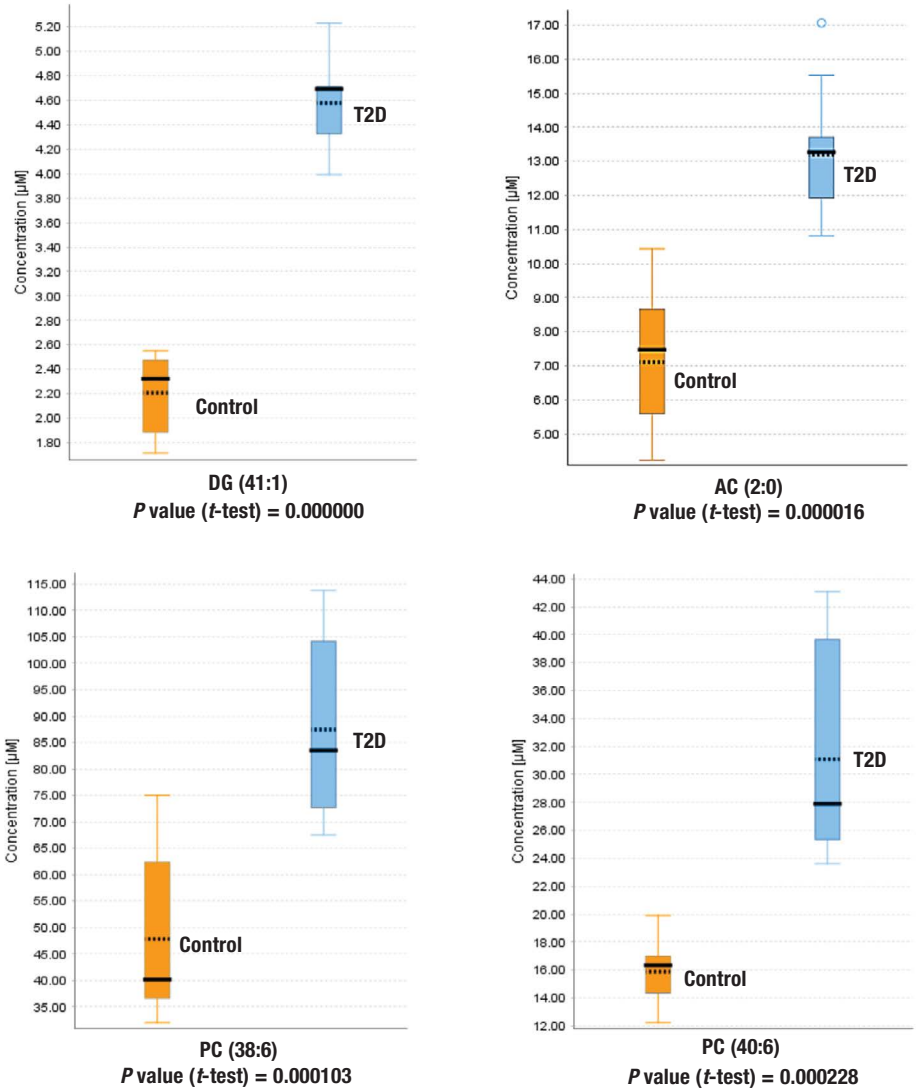

Figure 8: Monitoring changes in metabolite concentrations between samples obtained from Type 2 Diabetes study subjects and healthy controls with the Absolute*IDQ*® p400 HR and Q Exactive HF MS

concentrations of diglecyride DG (41:1), acetylcarnitine AC (2:0), phosphatidylcholine PC (38:6) and PC (40:6) were detected in the T2D serum samples compared to the control subjects. This is of significance as acetylcarnitine AC (2:0), phosphatidylcholine PC (38:6) and PC (40:6) have been previously reported to be associated with higher likelihood of T2D.[7,8,9]

The accuracy of the method, calculated based on the measured concentration versus the theoretical concentration, in LC-MS analysis is shown (Figure 9), which displays the data for the low Quality Control (QC) sample. The reproducibility of the method is demonstrated (Table 3), showing examples of measured concentrations, % RSDs of selected metabolites detected and quantified in a T2D serum sample which was extracted and analyzed in triplicate. The obtained %RSD for all analytes detected above the limit of detection (LOD) in the T2D serum sample analyzed by LC-MS and flow injection analysis (FIA)-MS is summarized (Figure 10). For 78% of all lipids and metabolites detected above LOD, the %RSD was less than 15% and overall, 88% of the analytes had %RSDs lower than 20%. These results clearly demonstrate the good reproducibility of the analytical method and low variance of the MS instrument analytical performance.

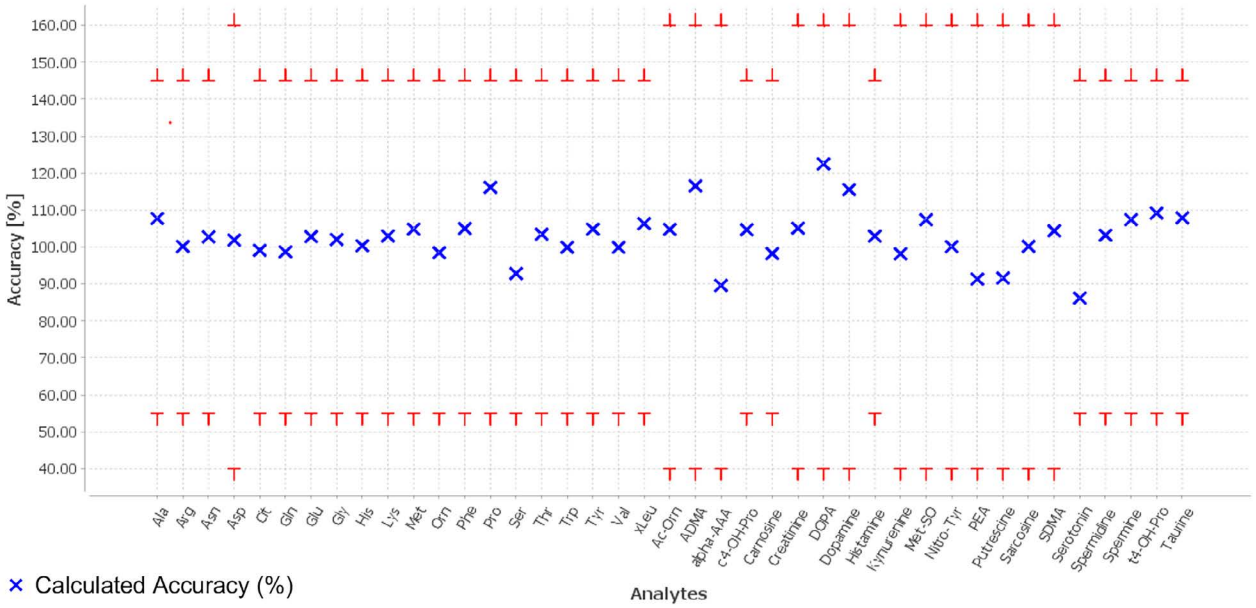

Figure 9: Calculated accuracy (%) for the low QC sample

Table 3: Measured concentration and % RSD of selected metabolites analyzed in triplicates with the Absolute*IDQ*® p400 HR and Q Exactive HF MS

	Concentration (µM) Replicate 1	Concentration (µM) Replicate 2	Concentration (µM) Replicate 3	RSD (%)
PC (38:6)	70.3	67.5	72.7	3.7
PC (40:6)	43.1	39.7	39.7	4.8
AC (2:0)	10.8	13.3	11.9	10.4
LPC (18:0)	41.2	44.9	41.4	4.9
CE (20:5)	56.1	54.7	55.0	1.3
SM (37:2)	2.24	2.16	2.32	3.6
DG (36:2)	28.5	26.7	25.6	5.4
DG (34:3)	3.41	3.52	3.28	3.5
Taurine	56.2	62.4	56.8	5.8
Glycine	258	293	270	6.5
ADMA	0.488	0.538	0.479	6.3

PC: phosphatidylcholines, LPC: Lysophosphatidylcholines , SM: Sphingomyelins, DG: Diglecyrides, CE: Ceramides, ADMA: Asymmetric dimethylarginine

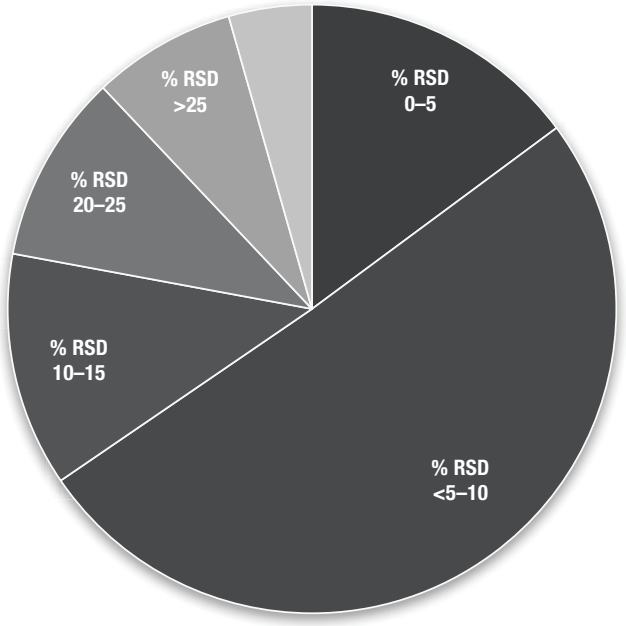

Figure 10. Observed % RSD (triplicate analysis) for all analytes detected above LOD by LC-MS and FIA-MS in a T2D serum sample. A high proportion (88%) of detected analytes had %RSD below 20%, demonstrating good reproducibility of the analytical method.

Untargeted Analysis on the Q Exactive HF-X MS

The ability to analyze highly complex, low abundant and challenging biological samples have driven the development of better MS technologies, particularly in performance attributes of faster scan speeds, increased resolution and sensitivity. Orbitrap mass analyzer-based mass spectrometers are recognized for their high resolution and accurate mass detection capabilities and are highly versatile for multiple applications, making them the ideal MS tool for addressing various analytical and workflow challenges. The Q Exactive HF-X MS is the latest advancement in the benchtop hybrid quadrupole-Orbitrap-based mass spectrometer series. This MS system has several proven hardware innovations: a high capacity transfer tube and electrodynamic ion funnel in the ion source architecture to produce increased ion transmission thereby giving higher sensitivity; optimized scan matrix and accelerated higher-energy collisional dissociation (aHCD) that enable faster MS/MS acquisitions, ensuring the delivery of high quality MS/MS spectra. The better data quality provided by these improvements potentially maximizes insights from identification experiments, bringing greater confidence to achieve comprehensive analysis of very complex samples.

To reiterate the benefits of higher resolution and fast acquisition speeds of Orbitrap mass analyzer-based instruments, a lipid identification experiment based on a SRM1950 plasma standard was carried out on both the Q Exactive HF MS and Q Exactive HF-X MS systems. On the Q Exactive HF-X MS, ion accumulation time is maximized within a shorter transient time due to reduced overhead scan times and the aHCD feature. This effectively results in 60% higher lipid identification numbers on the Q Exactive HF-X MS at the same resolution setting of 120,000 on both systems (Figure 11). The higher scan rates in combination with the improved sensitivity on the Q Exactive HF-X MS are advantageous for increased throughput while maintaining data quality. To demonstrate this, a shorter chromatographic method was implemented to determine if at least the same or increased number of identifications could be observed. The original standard 30-minute liquid chromatography (LC) method on the Q Exactive HF MS versus a 20-minute LC method on the Q Exactive HF-X MS was compared. Results show the identification of more lipid species, a 24% increase within a shorter analysis time (Figure 12). Sufficient data points across the chromatographic peak were obtained without affecting the MS/MS spectral quality. This presents a throughput and sensitivity improvement with a shortened gradient runtime and would allow the acquisition of more significant data, gaining deeper insights from your research experiments. This can benefit large-scale metabolomics studies and is valuable towards improving experimental efficiency to accommodate increasing sample quantities and issues with instrument access time, ultimately promoting laboratory productivity.

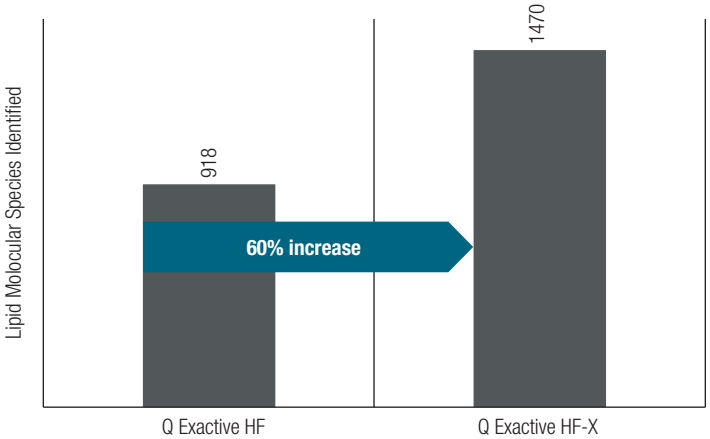

Figure 11. A 60% increase in lipid molecular species identified on the Q Exactive HF-X MS based on aligned data of two biological replicates of the SRM 1950 standard

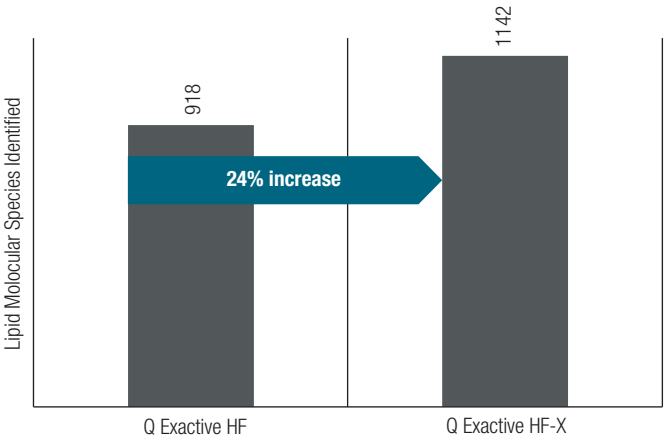

Figure 12: A 24% increase in lipid molecular species identified with the shorter gradient runtime on the Q Exactive HF-X MS from SRM 1950 standard based on aligned data of two biological replicates

Why choose Orbitrap?

Research trends and analytical needs have driven advanced mass spectrometry innovation especially in the past decade. Mass spectrometers of today must be equipped with superior performance attributes such as higher resolution, mass accuracy, dynamic range and fast scanning capabilities to fulfil rigorous experimental demands and handle extremely complex samples. In today's research, these same instruments must have the flexibility to handle qualitative and quantitative experiments, carry out a variety of analytical techniques including parallel reaction monitoring (PRM) and multiplexing, in addition to being highly robust and giving consistent instrument performance for high throughput analysis. Since its introduction in 2005, the Orbitrap technology has revolutionized mass spectrometry based research to meet various analytical challenges across multiple application fields of interest. The exceptional value of Orbitrap based MS systems in delivering uncompromised analytical benefits and achieving greater experimental possibilities have been well recognized by the scientific community. Adoption of Orbitrap technology over the years has grown exponentially with the proven increase in numbers of Nature and Science family publications (Figure 13). Furthermore, the hybrid quadrupole Orbitrap mass spectrometer (Q Exactive) has been proven to be a tremendous analytical workhorse for many labs in different applications both in academic and applied research. Compared to competing MS technologies, the high numbers of publications utilizing Orbitrap mass spectrometers is a testament to the unparalleled performance of the technology.

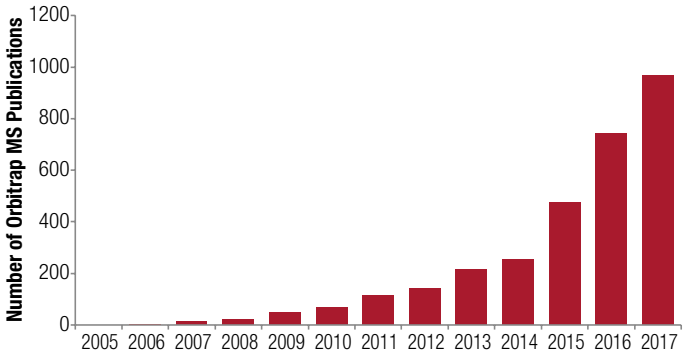

Figure 13: Rising trend in number of Orbitrap MS based research publications in Nature and Science journals since its introduction in 2005.[10]

The Q Exactive MS series has multiple products to suit your research requirements.

Table 4. Which Q Exactive hybrid quadrupole Orbitrap system is right for my research?

Instrument Attributes	Q Exactive Focus MS	Q Exactive MS	Q Exactive Plus MS	Q Exactive HF MS	Q Exactive HF-X MS
Analyzer	Orbitrap	Orbitrap	Orbitrap	Ultra-High Field Orbitrap	Ultra-High Field Orbitrap
Mass Range	*m/z* 50–2000	*m/z* 50–6000	*m/z* 50–6000	*m/z* 50– 6000	*m/z* 50–2000; *m/z* 200–4000
Maximum Resolution @ *m/z* 200	70,000	140,000	140,000; 280,000 with Enhanced Resolution option	240,000	240,000
Maximum Scan Speed	12 Hz	12 Hz	12 Hz	18 Hz	40 Hz
Top N/MS^n	Top 3 $ddMS^2$	Top 10 $ddMS^2$	Top 10 $ddMS^2$	Top 20 $ddMS^2$	Top 40 $ddMS^2$
Mass Accuracy, Internal Calibration	<1 ppm	<1 ppm	<1 ppm	<1 ppm	<1 ppm
Polarity switching	<1 sec	<1 sec	<1 sec	<1 sec	<1 sec
Multiplex	SIM only, up to 10 precursors	Yes, up to 10 precursors	Yes, up to 10 precursors	Yes, up to 10 precursors	Yes, up to 10 precursors
Intact Protein Mode	No	No	Yes	Yes	No
Biopharma Option	No	No	Yes	Yes	Yes
Collision Energy	NCE and CE	Normalized CE	Normalized CE	Normalized CE	Normalized CE
Dissociation	HCD	HCD	HCD	HCD	HCD

Table 5. Which Q Exactive Orbitrap system best suits my experimental requirements?

Performance Features	Q Exactive Focus MS	Q Exactive MS	Q Exactive Plus MS	Q Exactive HF MS	Q Exactive HF-X MS
Resolution	◔	◑	● **	◕	◕
Sensitivity	◑	◑	◕	◕	●
Speed	◑	◑	◑	◕	●
Dynamic Range	◑	◑	◑	◑	●
Mass Accuracy	●	●	●	●	●
Multiplexing	◕	●	●	●	●

**Enhanced resolution option up to 280,000

Table 6. Which Q Exactive Orbitrap system best suits my area of research?

Application	Q Exactive Focus MS	Q Exactive MS	Q Exactive Plus MS	Q Exactive HF MS	Q Exactive HF-X MS
Targeted Metabolomics	◕	◕	◕	●	●
Targeted Metabolomics (Absolute*IDQ*® p400 HR Kit)	●	●	●	●	NA
Unknown compound annotation	◕	◕	◕	●	●
Untargeted metabolite profiling	◕	◕	◕	●	●
Lipid Analysis	◕	◕	◕	●	●
Stable Isotopic Labeling Analysis	◑	◑	●	●	●

References

1. Advantage of high resolution accurate mass spectrometry for metabolite identification in untargeted metabolomics studies. Ioanna Ntai, Ralf Tautenhahn, Tim Stratton, Anastasia Kalli, Amanda Souza, Andreas Huhmer. Scientific poster. (Download)

2. NIST Standard Reference Material (SRM) 1950 Metabolites in Frozen Human Plasma. http://srm1950.nist.gov/

3. Stable isotope-labeling studines in metabolomics: new insights into structure and dynamics of metabolic networks. Achuthanunni Chokkathukalam, Dong-Hyun Kim, Michael P Barrett, Rainer Breitling, and Darren J Creek; *Bioanalysis.* **2014** February; *6*(4): 511–524

4. Metabolomic Analysis of $^{13}C/^{15}N$ Labeled Metabolites Using High Resolution Orbitrap Mass Spectrometry and Compound Discoverer Software. Anastasia Kalli, Bryson Bennett, Junhua Wang, Caroline Ding and Ralf Tautenhahn. ASMS poster. (Download)

5. From targeted quantification to untargeted metabolomics: Why LC-high-resolution-MS will become a key instrument in clinical labs. Bertrand Rochat; *TrAC Trends in Analytical Chemistry,* **2016,** *84,* Part B, pp. 151–164.

6. Biocrates Absolute*IDQ*® p400 HR Kit for broad lipid and metabolic profiling. http://www.biocrates.com/images/p400-HR_Folder_v01-2018.pdf

7. Identification of serum metabolites associated with risk of type 2 diabetes using a targeted metabolomics approach. Anna Floegel et.al. *Diabetes,* **2013,** *62,* 639–648.

8. Plasma acylcarnitine profiles suggest incomplete long-chain fatty acid oxidation and altered tricarboxylic acid cycle activity in type 2 diabetic African-American women. Adams SH et.al. *J. Nutr.* **2009,** *139:* 1073-1-82

9. Association of Metabolites with Obesity and Type 2 Diabetes Based on FTO Genotype. Yeon-Jung Kim et.al. *PLoS ONE,* **2016,** 11(6), 1–11

10. Source data – Nature Family of Journals and Science. Journals AAAS.

Recommended Publications

Q Exactive Metabolomics Literature

Novel insights into development of diabetic bladder disorder provided by metabolomic 2 analysis of the rat non-diabetic and diabetic detrusor and urothelial layer. Yi Wang, Gary G. Deng and Kelvin P. Davies. *Am J Physiol Endocrinol Metab,* **2016** Aug 1;311(2):E471-9. http://ajpendo.physiology.org/content/311/2/E471
Description: Untargeted, diabetic bladder disorder, relative quantitation, LC-MS

Untargeted Metabolomics to Ascertain Antibiotic Modes of Action. Isabel M. Vincent, David E. Ehmann, Scott D. Mills, Manos Perros, Michael P. Barretta. *Antimicrob Agents Chemother,* **2016** Mar 25;60(4):2281–91. http://aac.asm.org/content/60/4/2281.long
Description: Untargeted, antibiotic modes of action, LC-MS

Halogenated hydrocarbon solvent related cholangiocarcinoma risk: biliary excretion of glutathione conjugates of 1,2-dichloropropane evidenced by untargeted metabolomics analysis. Yu Toyoda, Tappei Takada & Hiroshi Suzuki. *Sci Rep.* **2016** Apr 18;6:24586. http://www.nature.com/articles/srep24586
Description: Untargeted metabolomics, LC-MS, relative quantitation, biliary excretion

Establishment of local searching methods for orbitrap-based high throughput metabolomics analysis. Haiping Tang, Xueying Wang, Lina Xu, Xiaorong Ran, Xiangjun Li, Ligong Chen, Xinbin Zhao, Haiteng Deng, Xiaohui Liu. *Talanta* **2016** 156-157 163–171. http://www.sciencedirect.com/science/article/pii/S0039914016302946
Description: Untargeted, LC-MS, metabolite database

Supporting Aspartate Biosynthesis Is an Essential Function of Respiration in Proliferating Cells. Lucas B. Sullivan, Dan Y. Gui, Aaron M. Hosios, Lauren N. Bush, Elizaveta Freinkman, and Matthew G. Vander Heiden. *Cell.* **2015** Jul 30;162(3):552–63. http://www.cell.com/cell/fulltext/S0092-8674(15)00854-5
Description: Untargeted, LC-MS, mitochondrial respiration, aspartate synthesis

Metabolomics and lipidomics reveal perturbation of sphingolipid metabolism by a novel anti-trypanosomal 3-(oxazolo [4,5-b]pyridine-2-yl)anilide. Daniel Stoessel, Cameron J. Nowell, Amy J. Jones, Lori Ferrins, Katherine M. Ellis, Jennifer Riley, Raphael Rahmani, Kevin D. Read, Malcolm J. McConville, Vicky M. Avery, Jonathan B. Baell, Darren J. Creek. *Metabolomics* **2016** 12:126.
http://link.springer.com/article/10.1007/s11306-016-1062-1
Description: Untargeted, LC-MS, metabolomic analysis of drug treated *Trypanosoma brucei*

In-Depth Characterization and Validation of Human Urine Metabolomes Reveal Novel Metabolic Signatures of Lower Urinary Tract Symptoms. Ling Hao, Tyler Greer, David Page, Yatao Shi, Chad M. Vezina, Jill A. Macoska, Paul C. Marker, Dale E. Bjorling, Wade Bushman, William A. Ricke & Lingjun Li. *Sci Rep.* **2016** Aug 9;6:30869.
http://www.nature.com/articles/srep30869
Description: Untargeted, LC-MS, relative quantitation, Urinary Tract Symptoms, Urine Metabolomics

Targeting One Carbon Metabolism with an Antimetabolite Disrupts Pyrimidine Homeostasis and Induces Nucleotide Overflow. Zheng Ser, Xia Gao, Christelle Johnson, Mahya Mehrmohamadi, Xiaojing Liu, Siqi Li and Jason W. Locasale. *Cell Reports* 15, 2367–2376, June 14, **2016.**
http://www.cell.com/cell-reports/abstract/S2211-1247(16)30618-0
Description: Targeted profiling, LC-MS, relative quantitation, antimetabolite therapeutic

Metabolomics-assisted proteomics identifies succinylation and SIRT5 as important regulators of cardiac function. Sushabhan Sadhukhan, Xiaojing Liu, Dongryeol Ryu, Ornella D. Nelson, John A. Stupinski, Zhi Li, Wei Chen, Sheng Zhang, Robert S. Weiss, Jason W. Locasale, Johan Auwerx and Hening Lin. *PNAS* vol. 113, no. 16, 4320-4325, **2016.**
http://www.pnas.org/content/113/16/4320.abstract
Description: Untargeted, targeted, LC-MS, cardiac function

Global metabolic analyses identify key differences in metabolite levels between polymyxin-susceptible and polymyxin-resistant *Acinetobacter baumannii.* Mohd Hafidz Mahamad Maifiah, Soon-Ee Cheah, Matthew D. Johnson, Mei-Ling Han, John D. Boyce, Visanu Thamlikitkul, Alan Forrest, Keith S. Kaye, Paul Hertzog, Anthony W. Purcell, Jiangning Song, Tony Velkov, Darren J. Creek & Jian Li. *Scientific Reports 6,* Article number: 22287 **(2016).**
http://www.nature.com/articles/srep22287
Description: Untargeted, LC-MS, relative quantitation

AMPK Is Essential to Balance Glycolysis and Mitochondrial Metabolism to Control T-ALL Cell Stress and Survival. Rigel J. Kishton, Carson E. Barnes, Amanda G. Nichols, Sivan Cohen, Valerie A. Gerriets, Peter J. Siska, Andrew N. Macintyre, Pankuri Goraksha-Hicks, Aguirre A. de Cubas, Tingyu Liu, Marc O. Warmoes, E. Dale Abel, Allen Eng Juh Yeoh, Timothy R. Gershon, W. Kimryn Rathmell, Kristy L. Richards, Jason W. Locasale. *Cell Metab.* **2016** Apr 12;23(4):649–62.
http://www.cell.com/cell-metabolism/fulltext/S1550-4131(16)30111-5
Description: Untargeted, LC-MS, relative quantitation, T-ALL, AMPK, glycolysis

Amino Acid Metabolism is Altered in Adolescents with Nonalcoholic Fatty Liver Disease—An Untargeted, High Resolution Metabolomics Study). Ran Jin, Sophia Banton, ViLinh T. Tran, Juna V. Konomi, Shuzhao Li, Dean P. Jones, and Miriam B. Vos. *J Pediatr.* **2016** May;172:14–19.e5.
http://www.jpeds.com/article/S0022-3476(16)00028-7/abstract
Description: Untargeted, LC-MS, non-alcoholic fatty liver disease (NAFLD

Phosphoenolpyruvate Is a Metabolic Checkpoint of Anti-Tumor T Cell Responses. Ping-Chih Ho, Jessica Dauz Bihuniak, Andrew N. Macintyre, Matthew Staron, Xiaojing Liu, Robert Amezquita, Yao-Chen Tsui, Guoliang Cui, Goran Micevic, Jose C. Perales, Steven H. Kleinstein, E. Dale Abel, Karl L. Insogna, Stefan Feske, Jason W. Locasale, Marcus W. Bosenberg, Jeffrey C. Rathmell, and Susan M. Kaech. *Cell.* **2015** Sep 10;162(6):1217–28.
http://www.cell.com/cell/fulltext/S0092-8674(15)01025-9
Description: Untargeted, LC-MS, Glycolytic Metabolites Analysis

Environment Impacts the Metabolic Dependencies of Ras-Driven Non-Small Cell Lung Cancer. Shawn M. Davidson, Thales Papagiannakopoulos, Benjamin A. Olenchock, Julia E. Heyman, Mark A. Keibler, Alba Luengo, Matthew R. Bauer, Abhishek K. Jha, James P. O'Brien, Kerry A. Pierce, Dan Y. Gui, Lucas B. Sullivan, Thomas M. Wasylenko, Lakshmipriya Subbaraj, Christopher R. Chin, Gregory Stephanopolous, Bryan T. Mott, Tyler Jacks, Clary B. Clish, and Matthew G. Vander Heiden. *Cell Metabolism 23,* 517–528, March 8, **2016.**
http://www.cell.com/cell-metabolism/abstract/S1550-4131(16)00041-3
Description: Untargeted, LC-MS, Metabolic Dependencies of Ras-Driven Non-Small Cell Lung Cancer

Plant-like biosynthesis of isoquinoline alkaloids in *Aspergillus fumigatus.* Joshua A Baccile, Joseph E Spraker, Henry H Le, Eileen Brandenburger, Christian Gomez, Jin Woo Bok, Juliane Macheleidt, Axel A Brakhage, Dirk Hoffmeister, Nancy P Keller and Frank C Schroeder. *Nat Chem Biol.* **2016** Jun;12(6):419–24.
http://www.nature.com/nchembio/journal/v12/n6/full/nchembio.2061.html
Description: LC-MS, fungi, natural product discovery

SHMT2 drives glioma cell survival in ischaemia but imposes a dependence on glycine clearance. Dohoon Kim, Brian P. Fiske, Kivanc Birsoy, Elizaveta Freinkman, Kenjiro Kami, Richard L. Possemato, Yakov Chudnovsky, Michael E. Pacold, Walter W. Chen, Jason R. Cantor, Laura M. Shelton, Dan Y. Gui, Manjae Kwon, Shakti H. Ramkissoon, Keith L. Ligon, Seong Woo Kang, Matija Snuderl, Matthew G. Vander Heiden and David M. Sabatini. *Nature.* **2015** Apr 16;520(7547):363-7.
http://www.nature.com/nature/journal/v520/n7547/abs/nature14363.html
Description: Untargeted metabolite profiling, LC-MS, flux experiments

Metabolic control of type 1 regulatory T cell differentiation by AHR and HIF1-α. Ivan D Mascanfroni, Maisa C Takenaka, Ada Yeste, Bonny Patel, Yan Wu, Jessica E Kenison, Shafiuddin Siddiqui, Alexandre S Basso, Leo E Otterbein, Drew M Pardoll, Fan Pan, Avner Priel, Clary B Clish, Simon C Robson & Francisco J Quintana. *Nat Med.* **2015** Jun;21(6):638–46.
http://www.nature.com/nm/journal/v21/n6/full/nm.3868.html
Description: Untargeted, LC-MS

Dipeptide species regulate p38MAPK–Smad3 signalling to maintain chronic myelogenousnleukemia stem cells. Kazuhito Naka, Yoshie Jomen, Kaori Ishihara, Junil Kim, Takahiro Ishimoto, Eun-Jin Bae, Robert P. Mohney, Steven M. Stirdivant, Hiroko Oshima, Masanobu Oshima, Dong-Wook Kim, Hiromitsu Nakauchi, Yoshihiro Takihara, Yukio Kato, Akira Ooshima & Seong-Jin Kim. *Nat Commun.* **2015** Aug 20;6:8039.
https://www.nature.com/articles/ncomms9039
Description: Untargeted, LC-MS, cancer stem cells

A three-dimensional engineered tumour for spatial snapshot analysis of cell metabolism and phenotype in hypoxic gradients. Darren Rodenhizer, Edoardo Gaude, Dan Cojocari, Radhakrishnan Mahadevan, Christian Frezza, Bradly G.Wouters and Alison P. McGuigan. *Nat Mater.* **2016** Feb;15(2):227–34.
https://www.nature.com/articles/nmat4482
Description: Tissues, biomaterials-cells, biomedical engineering

Metabolomic and proteomic analysis of serum from preterm infants with necrotising entercolitis and late-onset sepsis. Christopher J Stewart, Andrew Nelson, Achim Treumann, Tom Skeath, Stephen P Cummings, Nicholas D Embleton and Janet E Berrington. *Pediatr Res.* **2016** Mar;79(3):425–31.
https://www.nature.com/articles/pr2015235
Description: Untargeted, LC-MS, serum metabolic profiling, diagnostic markers

PGC1α drives NAD biosynthesis linking oxidative metabolism to renal protection. Mei T. Tran, Zsuzsanna K. Zsengeller, Anders H. Berg, Eliyahu V. Khankin, Manoj K. Bhasin, Wondong Kim, Clary B. Clish, Isaac E. Stillman, S. Ananth Karumanchi, Eugene P. Rhee & Samir M. Parikh. *Nature 531,* 528–532 (24 March **2016**).
http://www.nature.com/nature/journal/v531/n7595/full/nature17184.html
Description: Untargeted, LC-MS

Untargeted metabolomics analysis reveals key pathways responsible for the synergistic killing of colistin and doripenem combination against *Acinetobacter baumannii.* Mohd Hafidz Mahamad Maifiah, Darren J. Creek, Roger L. Nation, Alan Forrest, Brian T. Tsuji, Tony Velkov & Jian Li. *Scientific Reports 7,* Article number: 45527 **(2017).**
http://www.nature.com/articles/srep45527
Description: Untargeted, LC-MS

Whole-genome sequencing identifies common-to-rare variants associated with human blood metabolites. Tao Long, Michael Hicks, Hung-Chun Yu, William H Biggs, Ewen F Kirkness, Cristina Menni, Jonas Zierer, Kerrin S Small, Massimo Mangino, Helen Messier, Suzanne Brewerton, Yaron Turpaz, Brad A Perkins, Anne M Evans, Luke A D Miller, Lining Guo, C Thomas Caskey, Nicholas J Schork, Chad Garner, Tim D Spector, J Craig Venter & Amalio Telenti. *Nature Genetics 49,* 568–578 *(2017).*
http://www.nature.com/ng/journal/v49/n4/full/ng.3809.html
Description: Untargeted, LC-MS, blood metabolites

Untargeted metabolomics of colonic digests reveals kynurenine pathway metabolites, dityrosine and 3-dehydroxycarnitine as red versus white meat discriminating metabolites. Caroline Rombouts, Lieselot Y. Hemeryck, Thomas Van Hecke, Stefaan De Smet, Winnok H. De Vos & Lynn Vanhaecke. *Sci Rep. 2017* Feb 14;7:42514.
http://www.nature.com/articles/srep42514
Description: Untargeted, LC-MS

Metabolic gatekeeper function of B-lymphoid transcription factors. Lai N. Chan, Zhengshan Chen, Daniel Braas, Jae-Woong Lee, Gang Xiao, Huimin Geng, Kadriye Nehir Cosgun, Christian Hurtz, Seyedmehdi Shojaee, Valeria Cazzaniga, Hilde Schjerven, Thomas Ernst, Andreas Hochhaus, Steven M. Kornblau, Marina Konopleva, Miles A. Pufall, Giovanni Cazzaniga, Grace J. Liu, Thomas A. Milne, H. Phillip Koeffler, Theodora S. Ross, Isidro Sánchez-García, Arndt Borkhardt, Keith R. Yamamoto, Ross A. Dickins, Thomas G. Graeber & Markus Müschen. *Nature.* **2017** Feb 23;542(7642):479–483.
https://www.nature.com/articles/nature21076
Description: Untargeted, LC-MS, cancer metabolism

Shigatoxin encoding Bacteriophage φ24B modulates bacterial metabolism to raise antimicrobial tolerance. G. S. Holt, J. K. Lodge, A. J. McCarthy, A. K. Graham, G. Young, S. H. Bridge, A. K. Brown, M. Veses-Garcia, C. V. Lanyon, A. Sails, H. E. Allison & D. L. Smith. *Sci Rep.* **2017** Jan 20;7:40424.
http://www.nature.com/articles/srep40424
Description: Untargeted, LC-MS, metabolite profile

Starved epithelial cells uptake extracellular matrix for survival. Taru Muranen, Marcin P. Iwanicki, Natasha L. Curry, Julie Hwang, Cory D. DuBois, Jonathan L. Coloff, Daniel S. Hitchcock, Clary B. Clish, Joan S. Brugge & Nada Y. Kalaany. *Nat Commun.* **2017** Jan 10;8:13989.
http://www.nature.com/articles/ncomms13989
Description: Untargeted, LC-MS

The role of fatty acid β-oxidation in lymphangiogenesis. Brian W. Wong, Xingwu Wang, Annalisa Zecchin, Bernard Thienpont, Ivo Cornelissen, Joanna Kalucka, Melissa García-Caballero, Rindert Missiaen, Hongling Huang, Ulrike Brüning, Silvia Blacher, Stefan Vinckier, Jermaine Goveia, Marlen Knobloch, Hui Zhao, Cathrin Dierkes, Chenyan Shi, René Hägerling, Veronica Moral-Dardé, Sabine Wyns, Martin Lippens, Sebastian Jessberger, Sarah-Maria Fendt, Aernout Luttun, Agnès Noel, Friedemann Kiefer, Bart Ghesquière, Lieve Moons, Luc Schoonjans, Mieke Dewerchin, Guy Eelen, Diether Lambrechts & Peter Carmeliet. *Nature.* **2017** Feb 2;542(7639):49–54.
https://www.nature.com/articles/nature21028
Description: Targeted, LC-MS

An integrated multi-omics analysis of the NK603 Roundup-tolerant GM maize reveals metabolism disturbances caused by the transformation process. Robin Mesnage, Sarah Z. Agapito-Tenfen, Vinicius Vilperte, George Renney, Malcolm Ward, Gilles-Eric Séralini, Rubens O. Nodari & Michael N. Antoniou. *Scientific Reports 6,* Article number: 37855 **(2016).**
http://www.nature.com/articles/srep37855
Description: Untargeted, LC-MS, quan, GMO, plant

Systemic depletion of L-cyst(e)ine with cyst(e)inase increases reactive oxygen species and suppresses tumor growth. Shira L Cramer, Achinto Saha, Jinyun Liu, Surendar Tadi, Stefano Tiziani, Wupeng Yan, Kendra Triplett, Candice Lamb, Susan E Alters, Scott Rowlinson, Yan Jessie Zhang, Michael J Keating, Peng Huang, John DiGiovanni, George Georgiou & Everett Stone. *Nat Med.* **2017** Jan;23(1):120–127.
https://www.nature.com/articles/nm.4232
Description: Untargeted, LC-MS, cancer metabolism

Urinary Biomarkers of Whole Grain Wheat Intake Identified by Non-targeted and Targeted Metabolomics Approaches. Yingdong Zhu, Pei Wang, Wei Sha & Shengmin Sang. *Sci Rep.* **2016** Nov 2;6:36278.
http://www.nature.com/articles/srep36278
Description: Untargeted, LC-MS, Quantitation

Q Exactive Plus Literature

Validation of highly sensitive simultaneous targeted and untargeted analysis of keto-steroids by Girard P derivatization and stable isotope dilution-liquid chromatography-high resolution mass spectrometry. Alexander J. Frey, Qingqing Wang, Christine Busch, Daniel Feldman, Lisa Bottalico, Clementina A. Mesaros, Ian A. Blair, Anil Vachani, Nathaniel W. Snyder. *Steroids Volume 116,* December **2016,** Pages 60–66.
http://www.sciencedirect.com/science/article/pii/S0039128X16301556
Description: Untargeted, targeted, LC-MS, stable-isotope-labeled, steroids

Exogenous Fatty Acids Are the Preferred Source of Membrane Lipids in Proliferating Fibroblasts. Cong-Hui Yao, Ronald Fowle-Grider, Nathanial G. Mahieu, Gao-Yuan Liu, Ying-Jr Chen, Rencheng Wang, Manmilan Singh, Gregory S. Potter, Richard W. Gross, Jacob Schaefer, Stephen L. Johnson, Gary J. Patti. *Cell Chemical Biology Volume 23,* Issue 4, 21 April **2016,** Pages 483–493.
http://www.cell.com/ccbio/abstract/S2451-9456(16)30083-6
Description: Untargeted, LC-MS, Intracellular metabolites

Defining and Detecting Complex Peak Relationships in Mass Spectral Data: The Mz.unity Algorithm. Nathaniel G. Mahieu, Jonathan L. Spalding, Susan J. Gelman, and Gary J. Patti. *Anal. Chem.,* **2016,** *88* (18), pp 9037–9046.
http://pubs.acs.org/doi/abs/10.1021/acs.analchem.6b01702
Description: Untargeted, LC-MS, Software development

Integration of Molecular Networking and In-Silico MS/MS Fragmentation for Natural Products Dereplication. Pierre-Marie Allard, Tiphaine Péresse, Jonathan Bisson, Katia Gindro, Laurence Marcourt, Van Cuong Pham, Fanny Roussi, Marc Litaudon, and Jean-Luc Wolfender. *Anal. Chem.,* **2016,** *88* (6), pp 3317–3323.
http://pubs.acs.org/doi/abs/10.1021/acs.analchem.5b04804
Description: Untargeted, LC-MS, Workflow development

Targeted Isolation of Indolopyridoquinazoline Alkaloids from Conchocarpus fontanesianus Based on Molecular Networks. Rodrigo Sant'Ana Cabral, Pierre-Marie Allard, Laurence Marcourt, Maria Cláudia Marx Young, Emerson Ferreira Queiroz, and Jean-Luc Wolfender. *J. Nat. Prod.,* **2016,** *79* (9), pp 2270–2278.
http://pubs.acs.org/doi/abs/10.1021/acs.jnatprod.6b00379
Description: Untargeted, LC-MS, metabolite profiling, natural products

Anti-Candida Cassane-Type Diterpenoids from the Root Bark of Swartzia simplex. Quentin Favre-Godal, Stephane Dorsaz, Emerson F. Queiroz, Laurence Marcourt, Samad N. Ebrahimi, Pierre-Marie Allard, Francine Voinesco, Matthias Hamburger, Mahabir P. Gupta, Katia Gindro, Dominique Sanglard, and Jean-Luc Wolfender. *J. Nat. Prod.,* **2015,** *78* (12), pp 2994–3004.
http://pubs.acs.org/doi/abs/10.1021/acs.jnatprod.5b00744
Description: Untargetd, LC-MS, plant metabolites, natural products

Annotation of the Staphylococcus aureus Metabolome Using Liquid Chromatography Coupled to High-Resolution Mass Spectrometry and Application to the Study of Methicillin Resistance. Sandrine Aros-Calt, Bruno H. Muller, Samia Boudah, Céline Ducruix, Gaspard Gervasi, Christophe Junot, and François Fenaille. *J. Proteome Res.,* **2015,** *14* (11), pp 4863–4875.
http://pubs.acs.org/doi/10.1021/acs.jproteome.5b00697
Description: Untargeted, LC-MS, Staphylococcus aureus metabolome, metabolic profile

LC-quadrupole/Orbitrap high-resolution mass spectrometry enables stable isotope-resolved simultaneous quantification and ^{13}C-isotopic labeling of acyl-coenzyme A thioesters. Alexander J. Frey, Daniel R. Feldman, Sophie Trefely, Andrew J. Worth, Sankha S. Basu and Nathaniel W. Snyder. *Analytical and Bioanalytical Chemistry* May **2016,** *Volume 408,* Issue 13, pp 3651–3658.
http://link.springer.com/article/10.1007%2Fs00216-016-9448-5
Description: LC-MS, stable isotope-labeled

Evidence that 2-hydroxyglutarate is not readily metabolized in colorectal carcinoma cells. Susan J. Gelman, Nathaniel G. Mahieu, Kevin Cho, Elizabeth M. Llufrio, Timothy A. Wencewicz and Gary J. Patti. *Cancer & Metabolism* **(2015)** 3:13.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4665876/
Description: Targeted, LC-MS, SIM, colorectal carcinoma

Lactate metabolism is associated with mammalian mitochondria. Ying-Jr Chen, Nathaniel G Mahieu, Xiaojing Huang, Manmilan Singh, Peter A Crawford, Stephen L Johnson, Richard W Gross, Jacob Schaefer & Gary J Patti. *Nature Chemical Biology 12,* 937–943 **(2016).**
http://www.nature.com/nchembio/journal/v12/n11/full/nchembio.2172.html
Description: Targeted, LC-MS

Biotin starvation causes mitochondrial protein hyperacetylation and partial rescue by the SIRT3-like deacetylase Hst4p. Christian T. Madsen, Kathrine B. Sylvestersen, Clifford Young, Sara C. Larsen, Jon W. Poulsen, Marianne A. Andersen, Eva A. Palmqvist, Martin Hey-Mogensen, Per B. Jensen, Jonas T. Treebak, Michael Lisby & Michael L. Nielsen. *Nature Communications 6,* Article number: 7726 **(2015).**
http://www.nature.com/articles/ncomms8726
Description: Untargeted, LC-MS, Acetyl-CoA measurements

Metabolic control of type 1 regulatory T cell differentiation by AHR and HIF1-α. Ivan D Mascanfroni, Maisa C Takenaka, Ada Yeste, Bonny Patel, Yan Wu, Jessica E Kenison, Shafiuddin Siddiqui, Alexandre S Basso, Leo E Otterbein, Drew M Pardoll, Fan Pan, Avner Priel, Clary B Clish, Simon C Robson & Francisco. *J Quintana. Nature Medicine 21,* 638–646 **(2015)**.
http://www.nature.com/nm/journal/v21/n6/full/nm.3868.html
Description: Untargeted, LC-MS

Warpgroup: increased precision of metabolomic data processing by consensus integration bound analysis. Nathaniel G. Mahieu, Jonathan L. Spalding and Gary J. Patti. *Bioinformatics, 32*(2), **2016,** 268–275.
https://academic.oup.com/bioinformatics/article-lookup/doi/10.1093/bioinformatics/btv564
Description: Untargeted LC-MS, Software development

Addition of Alanyl-Glutamine to Dialysis Fluid Restores Peritoneal Cellular Stress Responses – A First-In-Man Trial. Klaus Kratochwill, Michael Boehm, Rebecca Herzog, Katharina Gruber, Anton Michael Lichtenauer, Lilian Kuster, Dagmar Csaicsich, Andreas Gleiss, Seth L. Alper, Christoph Aufricht, Andreas Vychytil. *PLoS One.* **2016** Oct 21;11(10):e0165045.
http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0165045
Description: LC-MS, non-targeted metabolite profiling, peritoneal effluents from 8 randomly selected patients, Transcend system

Tenofovir and adefovir down-regulate mitochondrial chaperone TRAP1 and succinate dehydrogenase subunit B to metabolically reprogram glucose metabolism and induce nephrotoxicity. Xinbin Zhao, Kun Sun, Zhou Lan, Wenxin Song, Lili Cheng, Wenna Chi, Jing Chen, Yi Huo, Lina Xu, Xiaohui Liu, Haiteng Deng, Julie A. Siegenthaler & Ligong Chen. *Sci Rep.* **2017;** 7: 46344.
https://www.nature.com/articles/srep46344
Description: Untargeted, LC-MS, Tracefinder, proteomics, metabolomics, HIV treatment, nephrotoxicity

Q Exactive HF Literature

Targeted Metabolomic Analysis of Head and Neck Cancer Cells Using High Performance Ion Chromatography Coupled with a Q Exactive HF Mass Spectrometer. Shen Hu, Junhua Wang, Eoon Hye Ji, Terri Christison, Linda Lopez, and Yingying Huang. *Anal. Chem.,* **2015,** *87* (12), pp 6371–6379.
http://pubs.acs.org/doi/abs/10.1021/acs.analchem.5b01350
Description: Targeted, LC-MS, cancer cells, absolute quantitation

Simultaneous Determination of Multiple Intracellular Primary Metabolites by Ultrahigh Performance Liquid Chromatography Coupled with a Q Exactive HF Mass Spectrometer. Nannan Qiu, Di Wu, Xia Cui, Guoliang Li, Sai Fan, Dawei Chen, Yunfeng Zhao, and Yongning Wu. *Anal. Chem.,* **2016,** *88* (19), pp 9647–9653.
http://pubs.acs.org/doi/abs/10.1021/acs.analchem.6b02417
Description: Targeted, PRM, central metabolic pathways, glycolysis pathway, tricarboxylic acid cycle (TCA), serine biosynthesis pathway (SSP), glutaminolysis pathway, and closely related biosynthetic reactions

Chronic psychological stress and high-fat high-fructose diet disrupt metabolic and inflammatory gene networks in the brain, liver, and gut and promote behavioral deficits in mice. Maria Elizabeth de Sousa Rodrigues, Mandakh Bekhbat, Madelyn C. Houser, Jianjun Chang, Douglas I. Walker, Dean P. Jones, Claudia M.P. Oller do Nascimento, Christopher J. Barnum, Malú G. Tansey. *Brain Behav Immun.* **2017** Jan;59:158–172.
http://www.sciencedirect.com/science/article/pii/S0889159116304093
Description: Untargeted, LC-MS, high resolution metabolomics, diet

Bioconcentration and Biotransformation of Amitriptyline in Gilt-Head Bream. Haizea Ziarrusta, Leire Mijangos, Urtzi Izagirre, Merle M. Plassmann, Jonathan P. Benskin, Eneritz Anakabe, Maitane Olivares, Olatz Zuloaga. *Environ. Sci. Technol.,* **2017** Feb 21;51(4):2464–2471.
http://pubs.acs.org/doi/abs/10.1021/acs.est.6b05831
Description: Untargeted, LC-MS, Compound Discoverer, fish metabolites

Effect of harvest time on some in vitro functional properties of hop polyphenols. Takako Inui, Koharu Okumura, Hiroo Matsui, Takahiro Hosoya, Shigenori Kumazawa. *Food Chem.* **2017** Jun 15;225:69–76.
http://www.sciencedirect.com/science/article/pii/S030881461730002X
Description: Untargeted, LC-MS, hop polyphenols

Simultaneous metabolomics and lipidomics analysis based on novel heart-cutting two-dimensional liquid chromatography-mass spectrometry. Shuangyuan Wang, Lina Zhou, Zhichao Wang, b, Xianzhe Shi, Guowang Xu. Analytica Chimica Acta Volume 966, 8 May **2017,** Pages 34–40.
http://www.sciencedirect.com/science/article/pii/S0003267017302817
Description: Untargeted, LC-MS

Anion-Exchange Chromatography Coupled to High-Resolution Mass Spectrometry: A Powerful Tool for Merging Targeted and Non-Targeted Metabolomics. Michaela Schwaiger, Evelyn Rampler, Gerrit Hermann, Walter Miklos, Walter Berger, and Gunda Koellensperger. *Anal. Chem.,* **2017,** *89* (14), pp 7667–7674.
http://pubs.acs.org/doi/abs/10.1021/acs.analchem.7b01624
Description: Untargeted, targeted, cancer cells, relative quantitation, absolute quantitation

Age-related changes in the metabolic profiles of rat hippocampus, medial prefrontal cortex and striatum. Lina Wati Durani, Hamizah Shahirah Hamezah, Nor Faeizah Ibrahim, Daijiro Yanagisawa, Suzana Makpol, Hanafi Ahmad Damanhuri, Ikuo Tooyama. *Biochem Biophys Res Commun.* **2017** Nov 25;493(3):1356–1363.
http://www.sciencedirect.com/science/article/pii/S0006291X1731954X
Description: Untargeted, LC-MS, brain aging metabolites, Compound Discoverer, mzcloud

Glucose Metabolism and Oxygen Availability Govern Reactivation of the Latent Human Retrovirus HTLV-1. Anurag Kulkarni, Manuel Mateus, Cyrille C. Thinnes, James S. McCullagh, Christopher J. Schofield, Graham P. Taylor and Charles R.M. Bangham. *Cell Chemical Biology 24,* 1377–1387, November 16, **2017.**
http://www.cell.com/cell-chemical-biology/abstract/S2451-9456(17)30314-8
Description: Ion chromatography, Untargeted, Relative Quantitattion, human retrovirus HTLV-1

Reverse Iontophoretic Extraction of Metabolites from Living Plants and their Identification by Ion-chromatography Coupled to High Resolution Mass Spectrometry. Maria Isabel González Sánchez, James McCullagh, Richard H. Guy and Richard G. Compton. *Phytochemical Analysis Volume 28,* Issue 3, May/June **2017,** Pages: 195–201.
http://onlinelibrary.wiley.com/doi/10.1002/pca.2660/abstract
Description: Plant metabolite identification, ion chromatography, IC-MS, untargeted

Analysis of stable isotope assisted metabolomics data acquired by high resolution mass spectrometry. X. Wei, P. K. Lorkiewicz, B. Shi, J. K. Salabei, B. G. Hill, S. Kim, C. J. McClain and X. Zhang. *Anal. Methods,* **2017,** 9, 2275–2283.
http://pubs.rsc.org/en/content/articlelanding/2017/ay/c7ay00291b#!divAbstract
Description: Stable isotope assisted metabolomics (SIAM), Untargeted, LC-MS

thermo scientific

Metabolic Pathways and Networks Associated with Tobacco Use in Military Personnel. Dean P. Jones, PhD, Douglas I. Walker, BS, Karan Uppal, PhD, Patricia Rohrbeck, DrPH, COL Timothy M. Mallon, MD, MPH, and Young-Mi Go, PhD. *J Occup Environ Med.* **2016** Aug;58(8 Suppl 1):S111–6.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4978145/
Description: Untargeted, LC-MS, Quantitation, high-resolution metabolomics (HRM)

High-Resolution Metabolomics Assessment of Military Personnel: Evaluating Analytical Strategies for Chemical Detection. Ken H. Liu; Douglas I. Walker; Karan Uppal; ViLinh Tran; Patricia Rohrbeck; Timothy M. Mallon; Dean P. Jones. *J Occup Environ Med.* **2016** Aug;58(8 Suppl 1):S53–61.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4978147/
Description: Serum metabolites detection with high-resolution MS, untargeted, LC-MS

Off-line mixed-mode liquid chromatography coupled with reversed phase high performance liquid chromatography-high resolution mass spectrometry to improve coverage in lipidomics analysis. Narváez-Rivas M, Vu N, Chen GY, Zhang Q. *Anal Chim Acta.* **2017** Feb 15;954:140–50.
https://www.sciencedirect.com/science/article/pii/S000326701631443X?via%3Dihub
Description: Confident identification of lipid species, lipid profiling

Find out more at **www.thermofisher.com/grantcentral**

ThermoFisher SCIENTIFIC

WP65227-EN 0718S