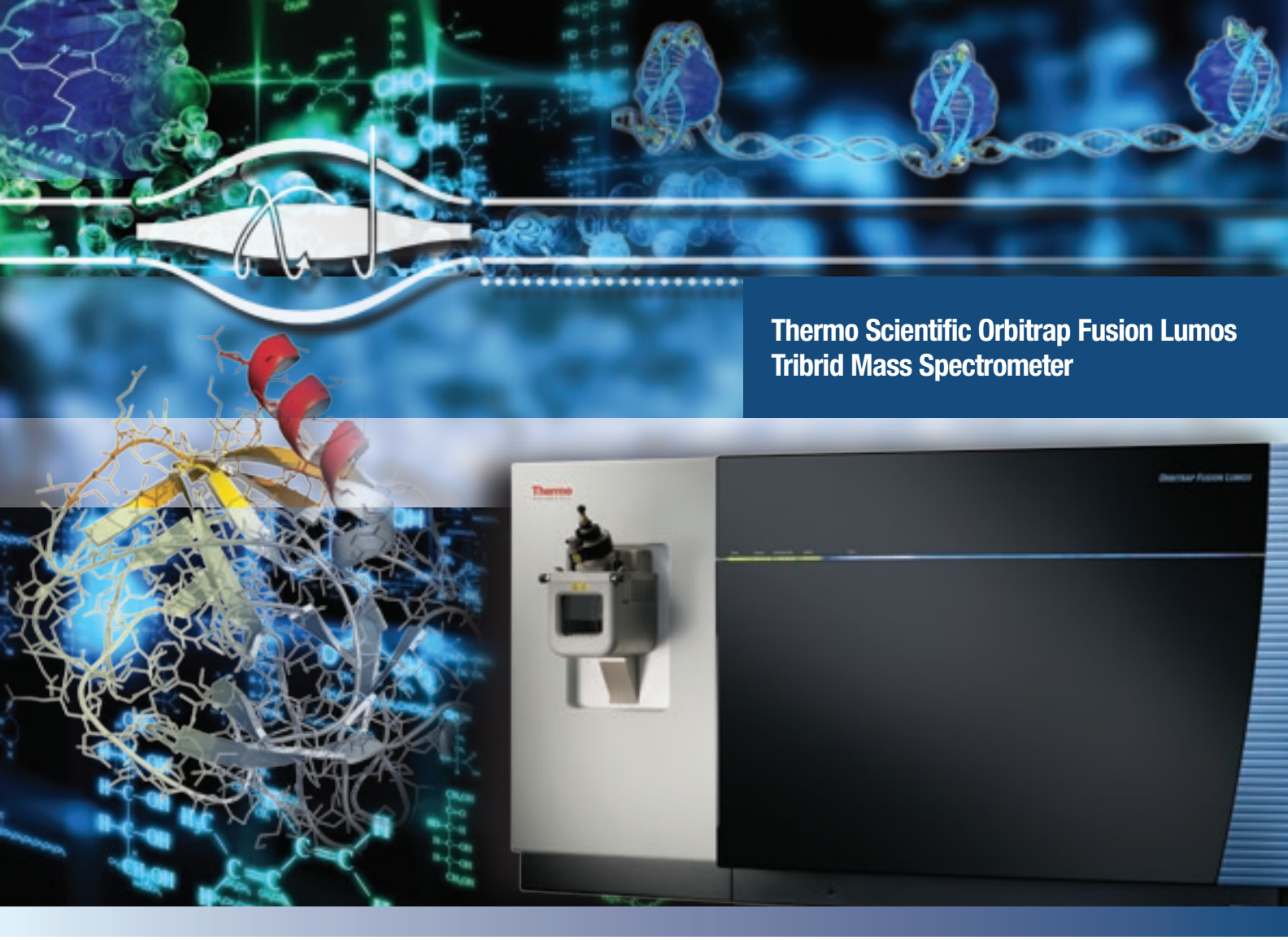


Thermo Scientific Orbitrap Fusion Lumos Tribrid Mass Spectrometer

Breakthrough Gains for Quantitative Biology

Sensitivity Transformed

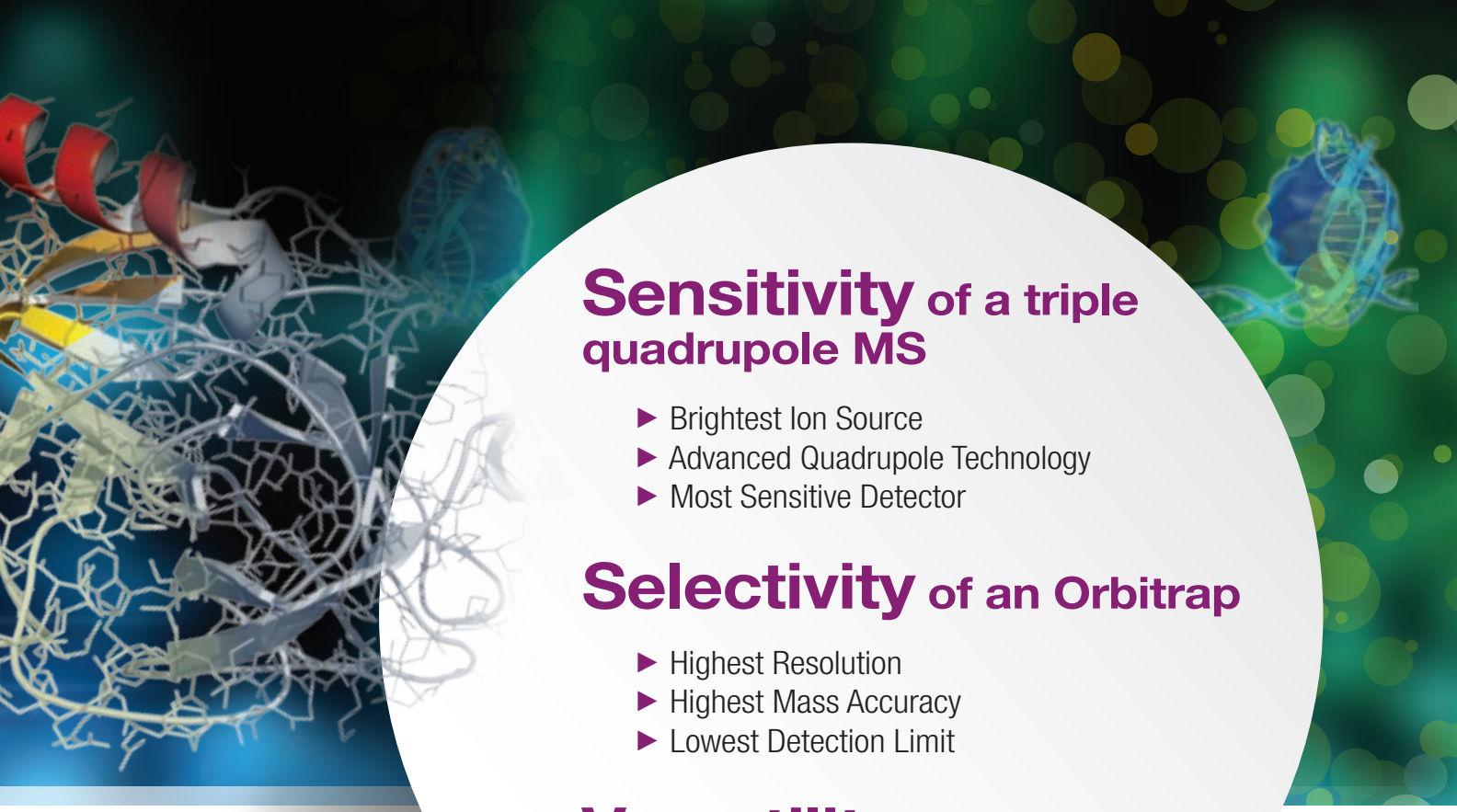
Thermo SCIENTIFIC

The Most Advanced Instrument

Built for the Most Challenging Experiments

Advancements in mass spectrometry have equipped researchers to explore new frontiers in biological science by enabling some of the most difficult analyses. These include quantifying peptides at attomole levels in complex matrices, characterizing positional isoforms of intact proteins, resolving isobaric metabolites and discerning protein structure using chemical crosslinking. The Thermo Scientific™ Orbitrap Fusion™ Lumos™ mass spectrometer is specifically designed to meet these analytical challenges and push the limits of biological research even further.

As the newest model with the innovative Tribrid architecture, the Orbitrap Fusion Lumos mass spectrometer enables unprecedented gains in biological system characterization. Incorporation of the latest technologies and groundbreaking innovations makes it the most sensitive, most selective and most versatile instrument to date.



Sensitivity of a triple quadrupole MS

- Brightest Ion Source
- Advanced Quadrupole Technology
- Most Sensitive Detector

Selectivity of an Orbitrap

- Highest Resolution
- Highest Mass Accuracy
- Lowest Detection Limit

Versatility of a Tribrid

- Four Dissociation Techniques
- Unique Tribrid Architecture
- Full Experimental Flexibility

Building upon revolutionary Tribrid architecture

The Thermo Scientific Orbitrap Fusion Lumos system is the industry-leading Tribrid mass spectrometer featuring a new atmospheric pressure interface, Advanced Quadrupole Technology, the ultra-high-field Orbitrap analyzer and the latest dual-pressure linear ion trap. The unique Tribrid architecture allows for high acquisition rates in both the Orbitrap and ion trap analyzers with full flexibility of dissociation and detection modes.

Ultra-High Field Orbitrap Analyzer

Offers resolution >500K FWHM and scan rates up to 20 Hz at 15K FWHM.

Advanced Active Ion Beam Guide

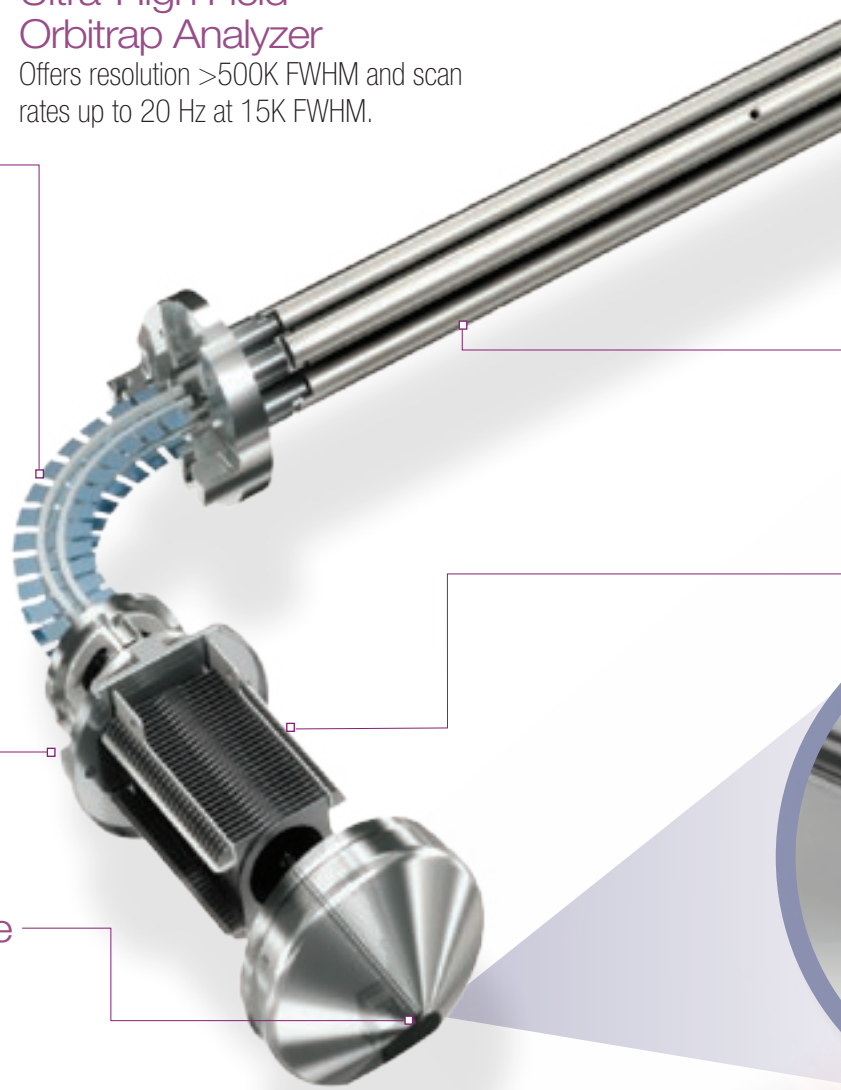
Prevents neutrals and high velocity clusters from entering mass resolving quadrupole.

EASY ETD Source

Based on Townsend discharge; reliable and easy to use.

High Capacity Transfer Tube

Increases ion flux into the mass spectrometer.

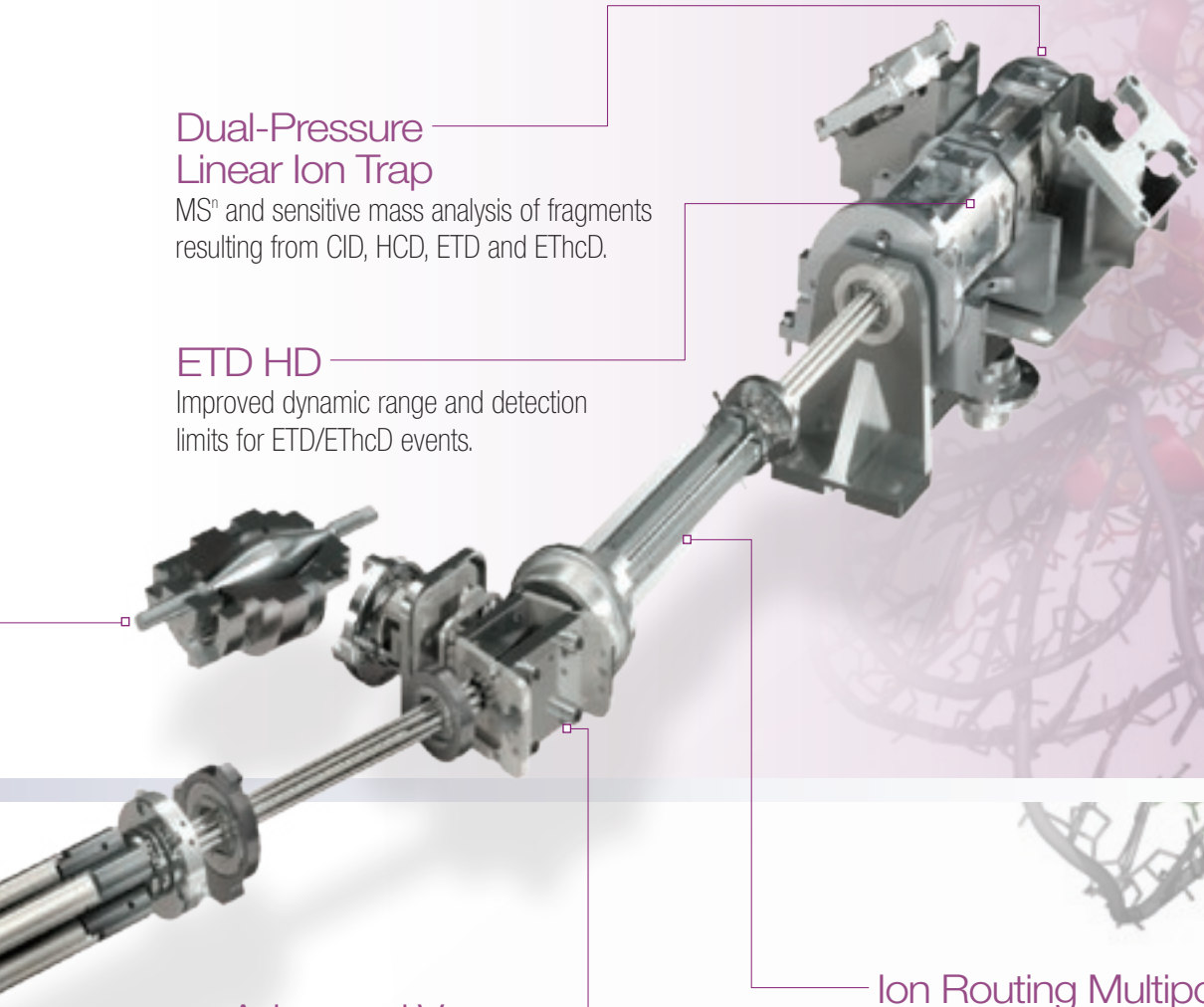


Dual-Pressure Linear Ion Trap

MS^n and sensitive mass analysis of fragments resulting from CID, HCD, ETD and EThcD.

ETD HD

Improved dynamic range and detection limits for ETD/EThcD events.



Advanced Vacuum Technology

Reduces pressure in UHV region, improving transmission to the Orbitrap analyzer.

Ion Routing Multipole

Enables parallel analysis; allows HCD at any MS^n stage.

Advanced Quadrupole Technology

Segmented design improves transmission at higher resolution; symmetric transmission across the isolation window.

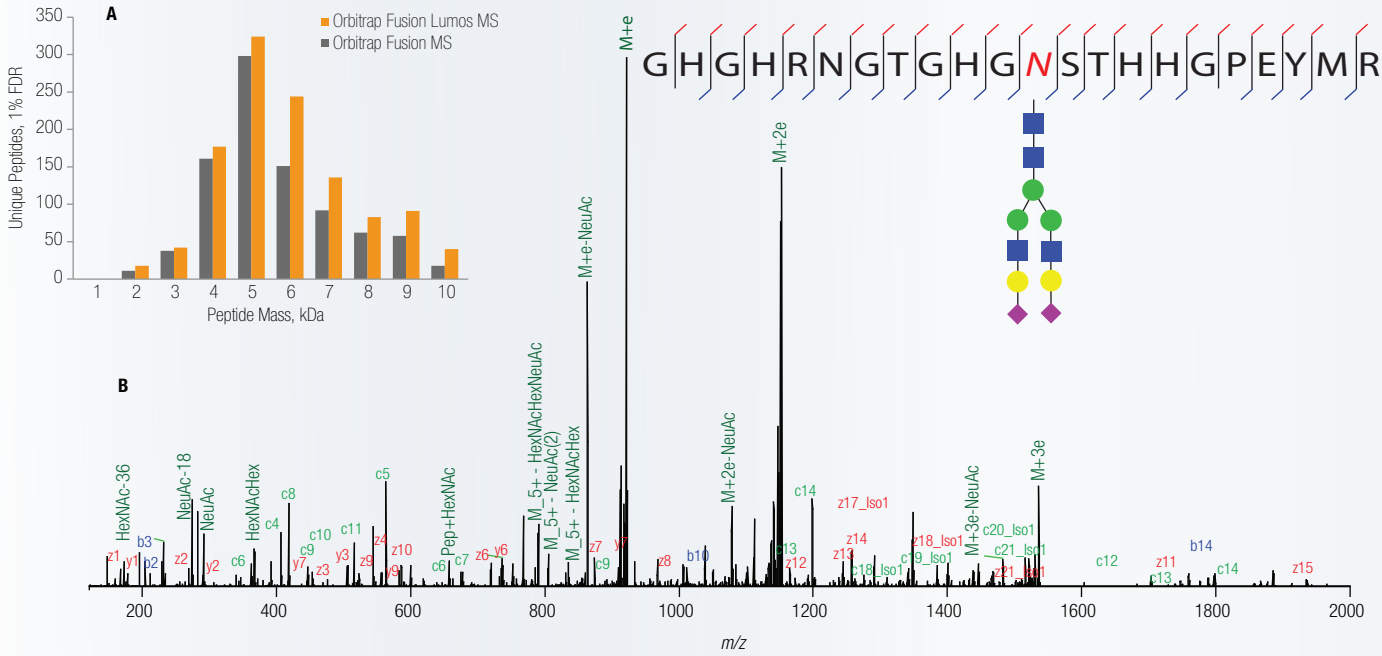
Electrodynamic Ion Funnel

Focuses ions after High Capacity Transfer Tube; broad tuning curves.

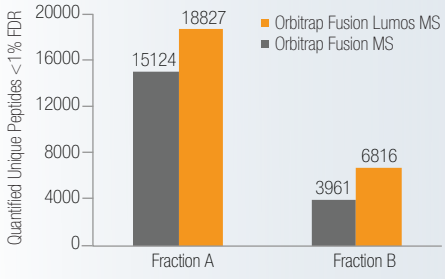
Advancing peptide quantitation and characterization

PTM analysis benefits from increased resolution and ETD HD™

Analysis of post-translational modifications (PTMs) is often central to biological research because of their roles in cellular function and disease states. The ETD/EThcD HD on the Orbitrap Fusion Lumos MS facilitates the deeper mining of challenging PTMs such as glycosylation. Backbone fragmentation provided by ETD allows for peptide sequencing and PTM site localization. EThcD provides complementary information about glycan composition while preserving the modification site. Using a combination of these techniques enables comprehensive sequencing of native sialylated glycopeptides containing multiple sites of glycosylation. The higher dynamic range of EThcD HD can benefit these analyses by improving MS/MS spectral quality, resulting in higher sequence coverage.



Glycopeptide analysis of HeLa SAX fractions on the Orbitrap Fusion MS and Orbitrap Fusion Lumos MS. A) The brighter ion source and improved ion transmission on the Orbitrap Fusion Lumos MS increase the identification of larger glycopeptides. B) An example EThcD spectrum acquired on the Orbitrap Fusion Lumos MS demonstrating extensive glycopeptide fragmentation, which provides ample information for determining peptide sequence and glycan attachment site.



Ubiquitinated peptides were enriched from HTC-116 cells treated with either DMSO or Bortezomib. Enriched peptides were labeled with TMT10plex™ reagents, fractionated using the Thermo Scientific™ Pierce™ High pH Reversed-Phase Peptide Fractionation Kit, and analyzed on either an Orbitrap Fusion MS or Orbitrap Fusion Lumos MS. The difference between the two platforms was greatest when amount of analyzed material was limited (Fraction B).

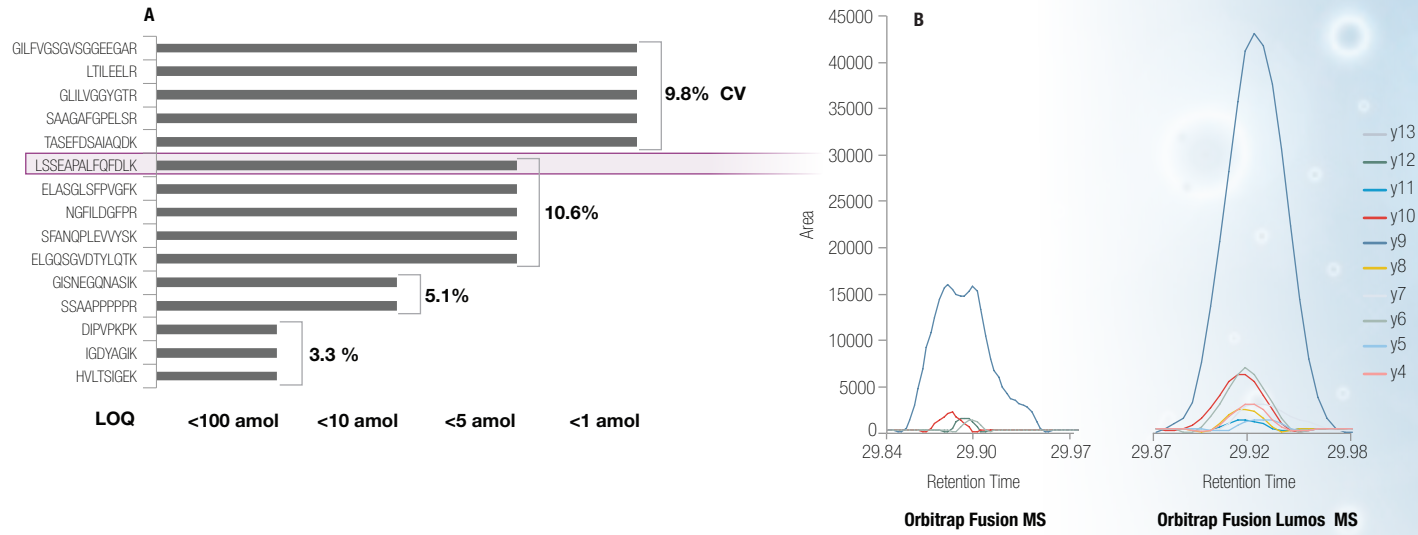
Accurate protein quantitation with TMT10plex™ reagents

Multiplexed analyses using isobaric mass tags are widely utilized for quantitative comparisons of protein and post-translational modification abundances across multiple experimental conditions. The recently introduced TMT MS^3 SPS workflow is a powerful method that enables simultaneous quantitative analysis of 10 samples, with improved accuracy achieved by reducing the co-isolation of tagged interferences. The increased sensitivity and ion transmission afforded by the brighter ion source and Advanced Quadrupole Technology of the Orbitrap Fusion Lumos MS benefit this technique further, boosting the number of quantifiable peptides present at low levels.

Data courtesy C. Rose and S. Gygi, Harvard Medical School, Cambridge, MA.

Confident low attomole limit peptide quantitation

Parallel Reaction Monitoring (PRM) (Peterson *et al.* 2012, Mol Cell Proteomics) is uniquely designed for quantifying hundreds of targeted proteins in complex matrices. Using this approach, precursor ions are isolated and fragmented, with the resulting product ions analyzed in the Orbitrap mass analyzer. This approach benefits from the brighter ion source and Advanced Quadrupole Technology of the Orbitrap Fusion Lumos MS, routinely achieving attomole-level limits of quantitation (LOQ) in matrix.

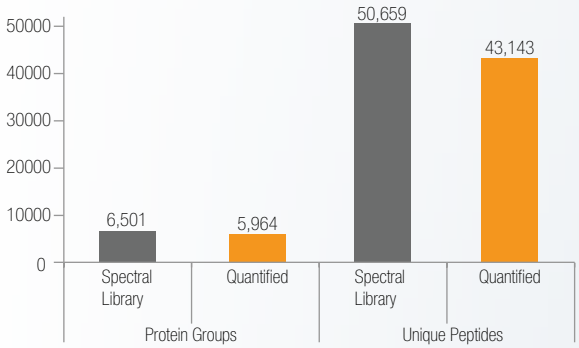


Fifteen PRTC peptides were spiked into 200 ng of HeLa digest and analyzed by LC-MS (30 min run). A) The Orbitrap Fusion Lumos MS provides accurate quantitation of all 15 PRTC peptides, some down to 1 attomole levels. Average CV% for each LOQ level is shown. Peptide quantitation is based on multiple fragment ions, as shown for the peptide LSSEAPALFQFDLK in B).

B) Orbitrap Fusion Lumos MS outperforms Orbitrap Fusion MS for high-confidence quantitation of peptides spiked into the matrix, detecting more fragment ions and with better S/N.

Data Independent Acquisition (DIA) for large-scale targeted quantitation

DIA is a powerful screening technique for comprehensive and accurate protein quantitation of biological samples. Step-wise isolation and fragmentation of all ions in a defined *m/z* window cover the targeted mass range and provide ultra-high resolution MS and MS/MS data for all components in the sample, enabling the accurate quantitation of peptides and the unique opportunity for retrospective analysis of unknowns and new targets of interest. The Orbitrap Fusion Lumos MS provides the speed, selectivity and enhanced sensitivity necessary to obtain maximum performance while maintaining high reproducibility of quantitation for low abundance analytes.

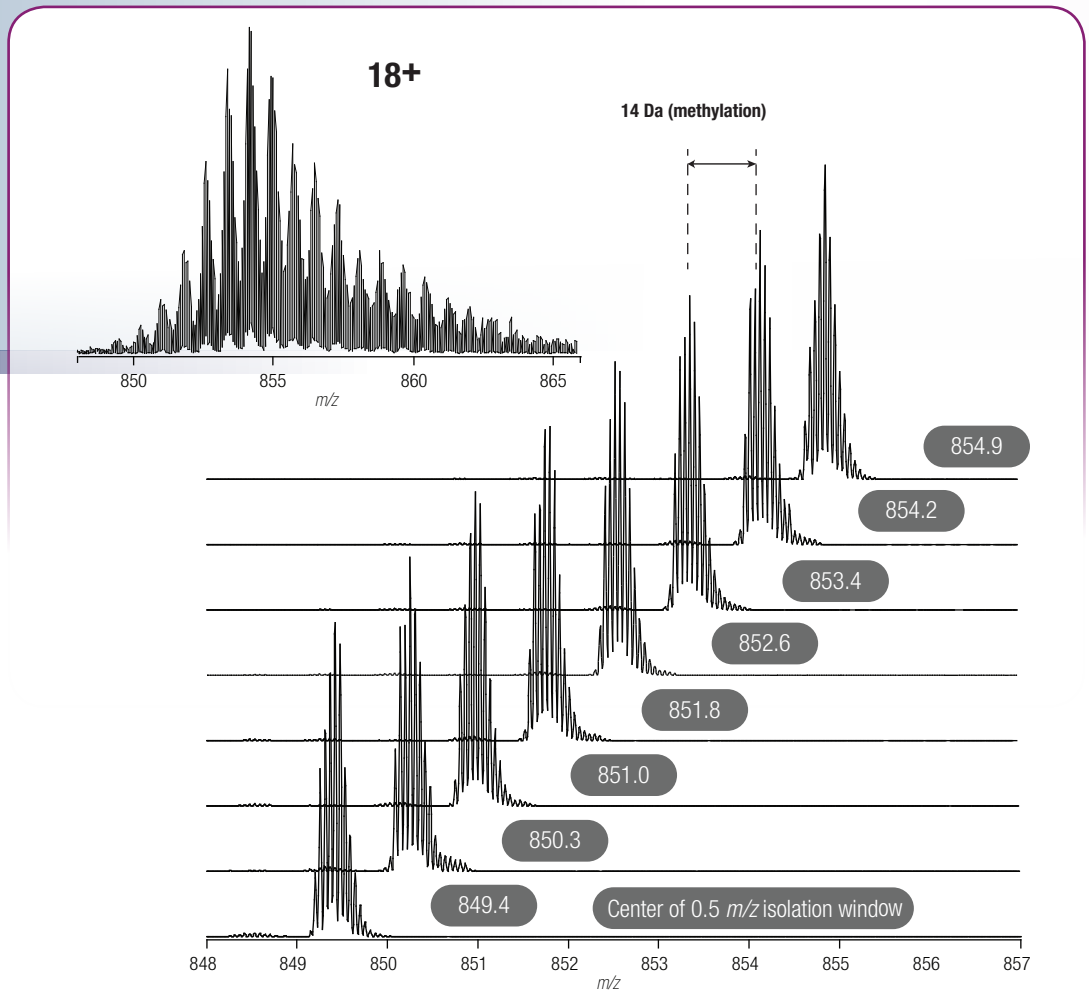


HeLa protein groups and unique peptides identified using a DIA strategy with the Orbitrap Fusion Lumos MS. Six data dependent acquisition (DDA) experiments generated an in-depth spectral library, and were followed by a DIA analysis using 15 *m/z* sequential MS^2 windows at 30,000 FWHM to survey the *m/z* 400-1000 range. The DIA analysis retrieved nearly 92% of the protein groups and over 85% of the unique peptides from the DDA library and quantified them with an average CV of 6.9% CV when using only 500 ng of HeLa digest.

New horizons in intact protein analysis

Top-down analysis of protein isoforms

Top-down mass spectrometry is commonly utilized to characterize intact proteins and their modifications. The Advanced Vacuum Technology unique to the Orbitrap Fusion Lumos MS provides optimized conditions for improved performance with intact protein analysis. The high selectivity of Advanced Quadrupole Technology allows for isolation of precursors and detection of fragments with very high resolving power in the Orbitrap analyzer. Combined, the new system most efficiently delivers the highest quality data for the characterization of protein isoforms and their post-translational modifications.



Isolation of the closely spaced methylated forms of histone H3 using a 0.5 *m/z* window. With improved ion transmission, provided by the Advanced Quadrupole Technology, it is now possible to efficiently enrich for individual isobaric protein forms for subsequent top down analysis.

Data Courtesy L. Fornelli and N. Kelleher, Northwestern University, Evanston, IL.

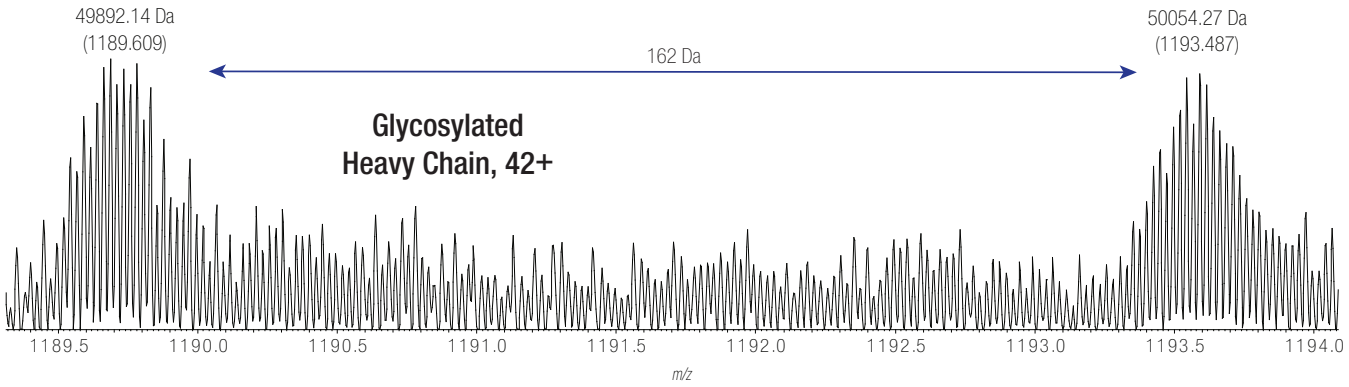
Characterization of PTMs using ETD HD

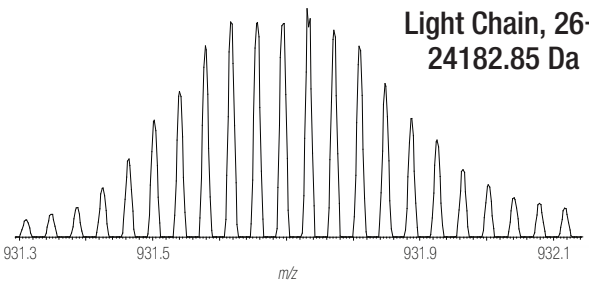
ETD HD enhances the dynamic range of ETD spectra by increasing the precursor ion storage capacity. The higher efficiency of the ETD HD experiments provides greater sequence coverage at faster acquisition rates.

Parent ion at *m/z* 854.2 was selected and fragmented with ETD HD. Improved product ion dynamic range provides higher sequence coverage and conclusively identifies the presence of two isomeric forms of histone H3, differing in the site of trimethylation (K9 vs. K27).

Comprehensive characterization of intact monoclonal antibodies

The Orbitrap Fusion Lumos mass spectrometer allows for high accuracy mass analysis of intact monoclonal antibodies with isotopic resolution of the heavy and light chains. The combination of the various fragmentation techniques, the improved detection limits and dynamic range provided by ETD HD, and Advanced Vacuum Technology results in high sequence coverage for both subunits.





CID, HCD, ETD HD
91% bond coverage

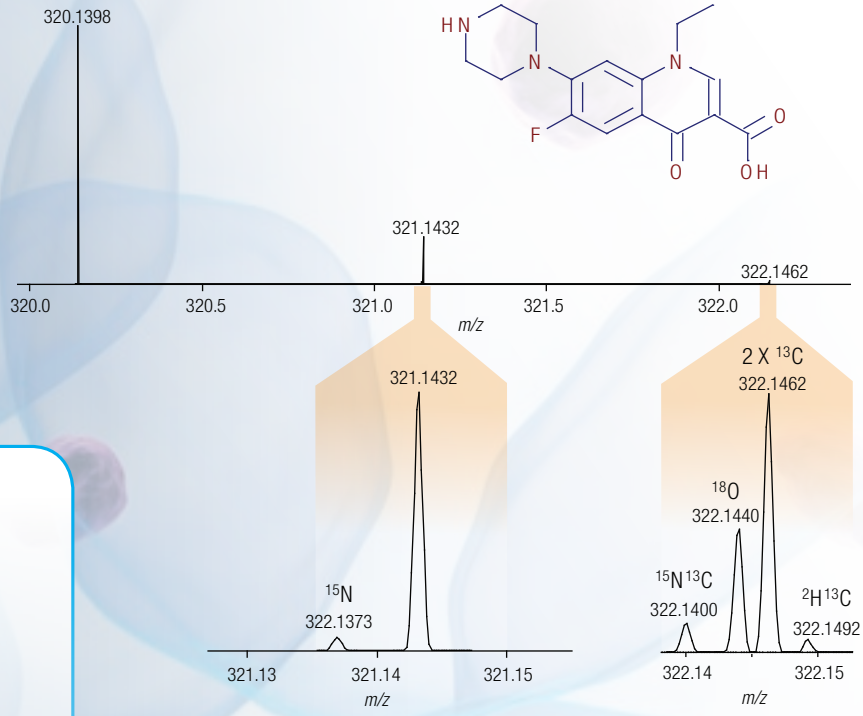
CID, HCD, ETD HD
63% bond coverage

Top down sequence verification for the light and heavy chains is achieved using a combination of fragmentation techniques. 91% bond coverage for the light chain and 63% bond coverage for the heavy chain is reported by combining results from ETD HD, CID, and HCD experiments.

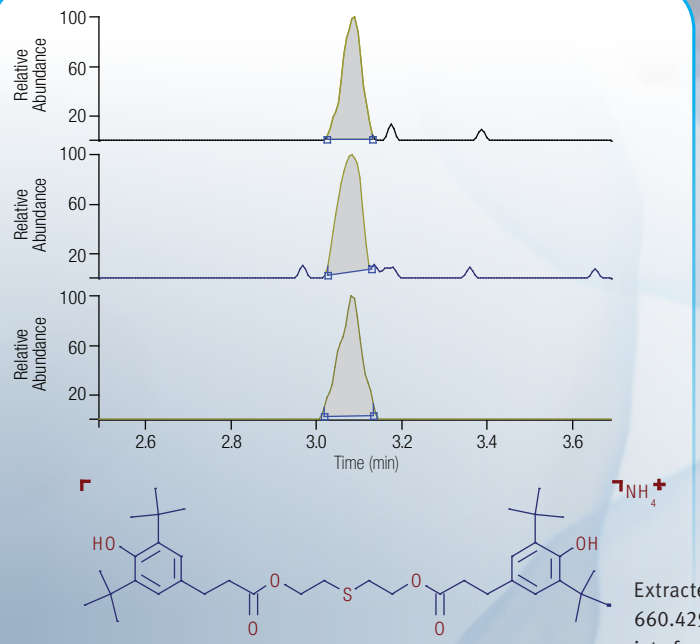
Breakthroughs in small molecule research

Resolution of isobaric interferences

The high sensitivity and high resolution of the Orbitrap Fusion Lumos MS makes it a powerful platform for the identification and quantitation of small molecules. Due to the instrument's very high resolution capabilities, fine isotopic structure can be observed, enabling the determination of highly accurate molecular formulae. This direct measurement removes the ambiguity of pattern matching estimations and is critical in cases where monoisotopic elements like fluorine or phosphorous may be present in the compound, such as in the example of norfloxacin shown below. Furthermore, the brighter source enables the Orbitrap Fusion Lumos MS to achieve far lower levels of quantitation.



High resolution MS^2 spectra of norfloxacin. The direct observations of fine isotopes of the drug are essential for determining elemental composition.

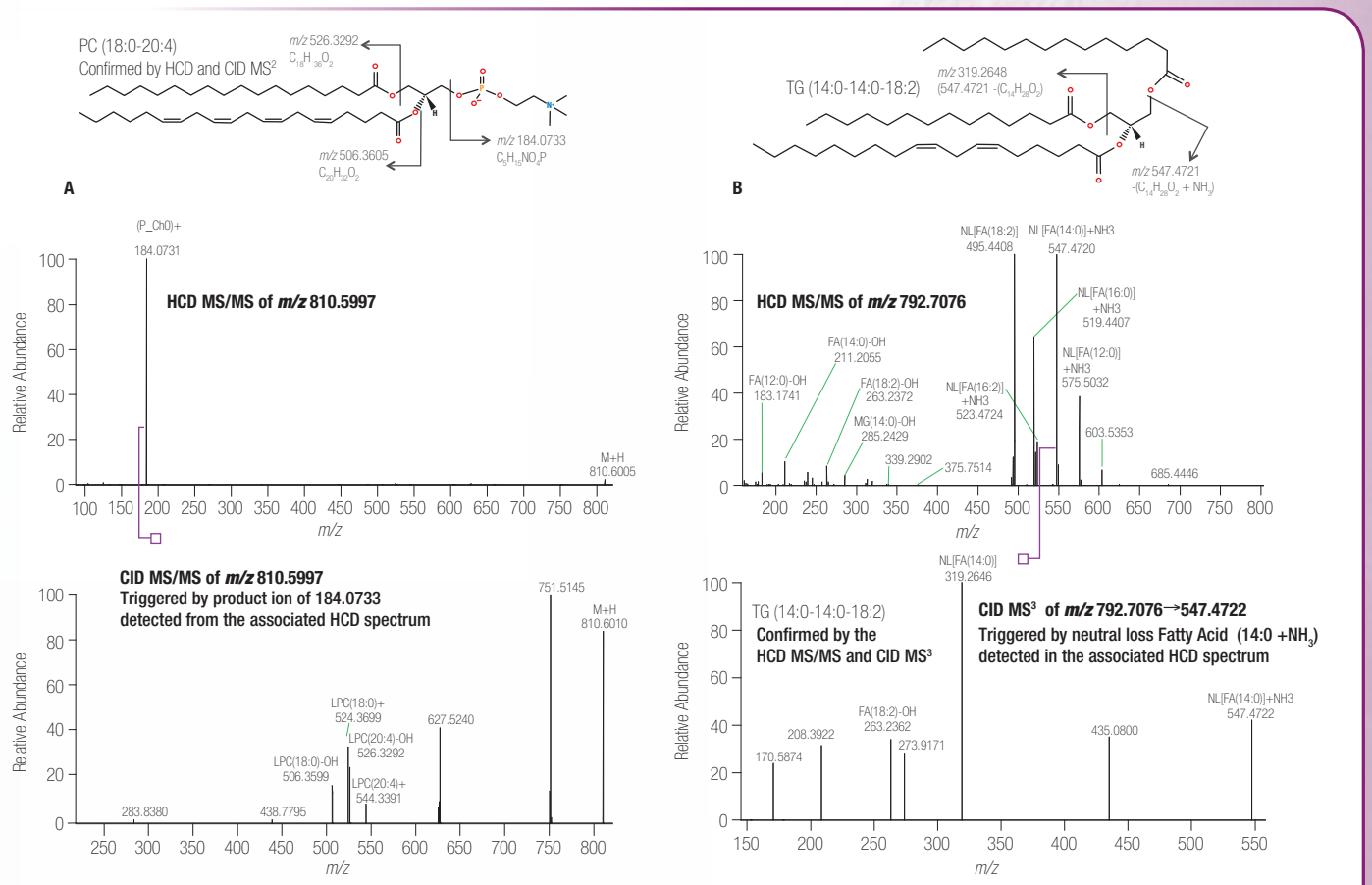


	Standard Ion Source	New Ion Source
LOQ	500 fg	100 fg

Extracted ion chromatogram of Irganox 1035 $(M+NH_4)^+$ ion at *m/z* 660.429 (100 fg on column). Irganox is a plasticizer known to leach into foods stored in plastic and must be quantified at very low levels. The Orbitrap Fusion Lumos MS operated in SIM mode was able to quantify Irganox 1035 in food simulant matrix, achieving an LOQ of 100 fg with linear dynamic range of 5 orders and <10% CV for all levels. This LOQ is 5x lower than achieved earlier on an Orbitrap instrument equipped with a standard ion source.

Comprehensive lipid profiling

HCD MS/MS is widely used to identify lipid molecular species. Previously, for specific lipid sub-classes such as phosphatidylcholine (PC), both positive and negative HCD MS/MS data were required for full characterization of the individual molecular species, significantly increasing the time needed for lipid profiling experiments. The Orbitrap Fusion Lumos MS allows intelligent acquisition of HCD MS^2, CID MS^2 and CID MS^3 to obtain complementary fragmentation information for identifying PC molecular species and co-eluting triacylglycerol (TG) isomers with a single polarity LC/MS run, yielding higher throughput, increased sensitivity and more confident analysis of lipid species.



Comprehensive profiling of: A) Phosphatidylcholine lipid species via HCD-MS^2 triggered CID MS^2 and, B) Triacylglycerol lipid species via HCD-MS^2 triggered CID MS^3.

Method development made easy

The Orbitrap Fusion Lumos Tribrid mass spectrometer includes an extensive library of templates with application-specific default settings for routine and advanced experiments in Proteomics, Glycomics and Metabolomics, allowing users to run guided methods effortlessly. The novel method editor with an intuitive drag-and-drop interface simplifies development of custom experiments without restricting access to key acquisition parameters.

Pushing the limits of science farther, faster

The newest addition to the pioneering Tribrid™ line of mass spectrometers, the Orbitrap Fusion Lumos MS expands the reach of life science researchers who are pushing the limits of quantitation and protein characterization. Incorporating the brightest ion source, the most selective quadrupole, the fastest ion trap analyzer, enhanced dissociation technologies and an ultra-high resolution Orbitrap analyzer, this instrument excels at the most challenging applications. These include analysis of low level PTMs, multiplexed relative quantitation using isobaric tags, intact protein characterization, as well as MS^n analysis and quantitation of small molecules.

The Industry's Leading Portfolio
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