

The Ultra-High Performance Mass Spectrometer Brings A New World of Modality Analysis

Toray Research Center has introduced an Ultra-High Performance Mass Spectrometer, for the first time as a contract research organization laboratory in Japan. The nano-LC installed on the front enabled us to perform high-resolution and high-sensitive analyses and to respond to increasingly diversified needs in modality analysis. We introduce some examples of our new methods.

Various applications by Lumos

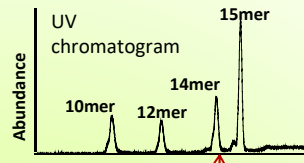
Impurity analysis of peptides and oligonucleotides
Characterization of biopharmaceuticals, such as antibody-drug conjugate:

- drug-antibody ratio (DAR), drug binding sites
- structural analysis of sugar chains / sugar binding sites
- peptide map, post-translational modifications
- position of disulfide bridges, overall amino acid sequence

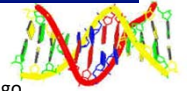
Oligonucleotide bioanalysis

Proteomics, comprehensive analysis of biomarkers

Impurity analysis of nucleic acid



Sample :
Mixture of 4 types of S-oligo

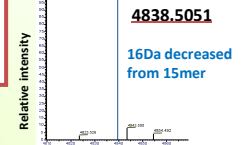


Result (molecular weight)

S-oligo	Monoisotopic molecular weight		Error (ppm)
	Measured value	Theoretical value	
15mer	4854.4852	4854.4896	-0.9
14mer	4534.4632	4534.4664	-0.7
12mer	3900.4054	3900.4081	-0.7
10mer	3210.3491	3210.3487	0.1

Errors within 1ppm

Trace elements

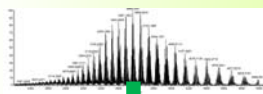


It was assumed that a part of 15mer oligo did not turned to S-oligo and remained as enzymes.

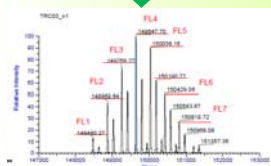
Structures of unknown elements can be also estimated from the highly accurate data.

Calculation of ADC's drug-antibody ratio

With its **ultra-high resolution**, the number of drug binding sites per antibody can be calculated through the measurement of the intact molecular weight of antibody-drug conjugates.



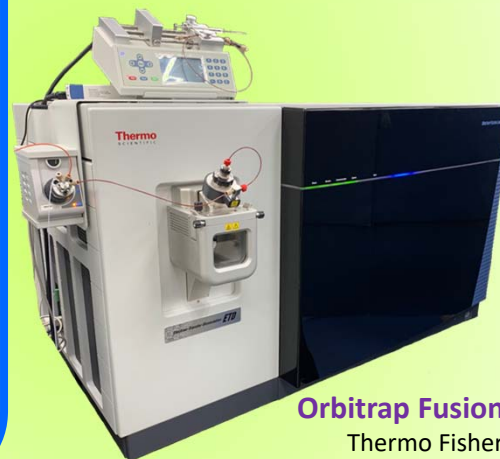
Mass spectrum of an observed ADC



Molecular weight analysis through deconvolution

Average number of drugs = 4.2

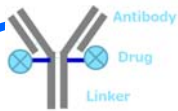
The average number of labels is calculated from the detection intensity of each drug.



Orbitrap Fusion™ Lumos™
Thermo Fisher Scientific

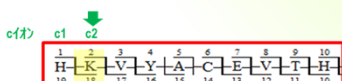


EASY-nLC™ 1200
Thermo Fisher Scientific

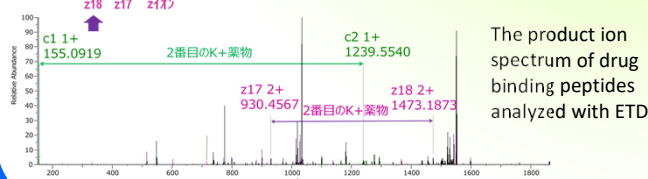


Analysis of drug binding sites of ADC

By conducting LC-MS/MS using **ETD (Electron Transfer Dissociation)**, product ions can be obtained keeping drugs bound, and the binding sites can be identified.

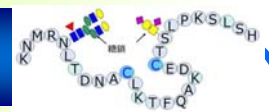


Drug binding sites can be identified directly.



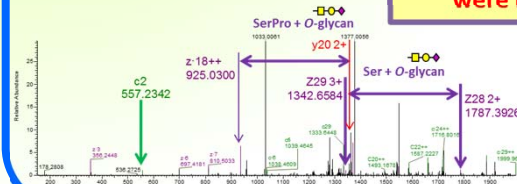
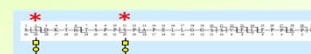
The product ion spectrum of drug binding peptides analyzed with ETD

Structural analysis of sugar chains of biopharmaceuticals



Not only the analysis of binding sites of *N-linked* sugar chain but also that of *O-linked* sugar chain, which has been difficult due to bond dissociation, is now available. Product ions can be obtained keeping drugs bound with the use of ETD.

Two binding sites of the *O-linked* sugar chain were identified.



The product ion spectrum of drug binding peptides analyzed with ETD