



Contents lists available at ScienceDirect

International Journal of Mass Spectrometry

journal homepage: www.elsevier.com/locate/ijms

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Foreword

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Special Issue Honoring Catherine Fenselau

Igor A. Kaltashov, Richard B. van Breemen

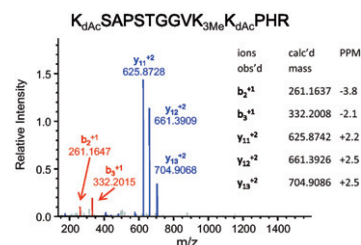
Proteomics

5–16

Analysis of histone modifications from tryptic peptides of deuterioacetylated isoforms

Elisabeth Hersman, Dwella M. Nelson, Wendell P. Griffith, Christine Jelinek, Robert J. Cotter

Nanospray LTQ/Orbitrap MS/MS spectrum of the deuterioacetylated peptide KSAPSTGGVKKPHR + 4Me, distinguished from an acetylated species by the accurate mass measurement.

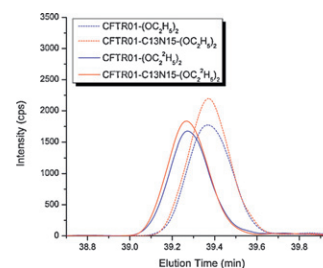


17–23

Back to deuterium: Utility of ^2H -labeled peptides for targeted quantitative proteomics

Bekim Bajrami, Vahid Farrokhi, Mengtan Zhang, Ardit Shehu, Xudong Yao

► ^2H - and $^{13}\text{C}/^{15}\text{N}$ -based peptides are comparable as quantitation standards for targeted mass spectrometry. ► Precision and accuracy for MRM-MS quantitation are not affected by the chromatographic isotope effect of ^2H -based peptides. ► Cost benefit of ^2H -based peptides allows for large-scale applications in targeted quantitative proteomics.

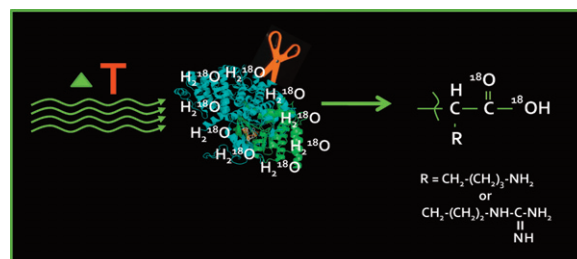


24–29

Thermally enhanced enzymatic proteolysis for rapid ^{18}O labeling in proteomics

Miquel D. Antoine, Nathan A. Hagan, Plamen A. Demirev

► We streamline protein identification protocols utilizing a microwave oven and a PCR thermocycler to accelerate enzymatic digestion. ► Performed in H_2^{18}O , rapid heating results in efficient C-terminal ^{18}O atom labeling of the proteolytic peptides. ► We investigate rates of ^{18}O incorporation as a function of tryptic peptide C-terminal amino acid type and peptide length. ► In most cases, digestion and incorporation of two ^{18}O atoms into R-terminated tryptic peptides is completed in less than five minutes.

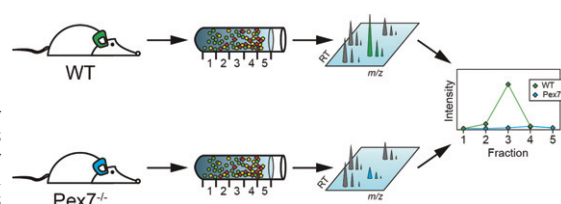


30–40

Comparative profiling of the peroxisomal proteome of wildtype and *Pex7* knockout mice by quantitative mass spectrometry

Sebastian Wiese, Thomas Gronemeyer, Pedro Brites, Rob Ofman, Christian Bunse, Christian Renz, Helmut E. Meyer, Ronald J.A. Wanders, Bettina Warscheid

► MS-based protein profiling across several density gradients enabled to comprehensively characterize peroxisomal proteomes of *Pex7*^{-/-} and WT mice. ► Comparative analysis of hundreds of protein profiles generated by label-free quantitative MS allowed to identify proteins specifically affected by the deletion of *Pex7*. ► All proteins known to contain a functional peroxisomal targeting signal 2 (PTS2) were determined to be virtually absent in high density gradient fractions of *Pex7*^{-/-} mice. ► KIAA0564 was further identified as new PTS2 candidate protein and co-localization studies of KIAA0564 fragments confirmed a peroxisomal localization. ► In addition, numerous PTS1 proteins fulfilling important functions in peroxisomal metabolism were found to be considerably increased in abundance in *Pex7*^{-/-} mice.

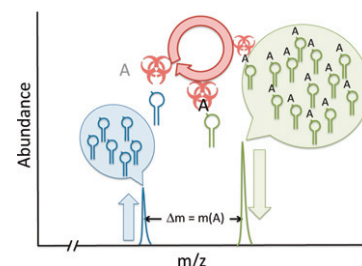


41–44

Rapid detection of ribosome inactivating protein toxins by mass-spectrometry-based functional assays

Miquel D. Antoine, Nathan A. Hagan, Jeffrey S. Lin, Andrew B. Feldman, Plamen A. Demirev

► We have developed a rapid functional assay for robust and broad-band detection of protein toxins in powders. ► The assay is based on monitoring by MALDI mass spectrometry the depurination of two DNA substrates. ► The assay is complementary to methods for intact protein toxin detection including proteomics.



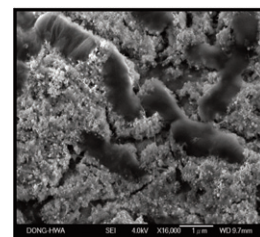
45–52

Mass spectrometric identification of pathogens in foods using a zirconium hydroxide immobilization approach

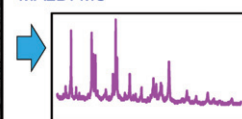
Cheng-Tung Chen, P. Muralidhar Reddy, Yuan-Ron Ma, Yen-Peng Ho

► Pathogens in milk/pudding/coffee were isolated with magnetized zirconium hydroxide. ► Captured pathogens were directly cultured and identified using MS. ► Excellent detection limit of *E. faecalis* spiked into milk (32 CFU/mL) was achieved.

E. coli immobilized on zirconium hydroxide



MALDI-MS

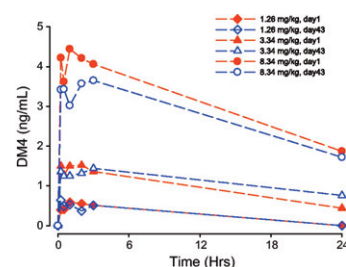


53–60

A sensitive LC–MS/MS method for the determination of free maytansinoid DM4 concentrations—Method development, validation, and application to the nonclinical studies of antitumor agent DM4 conjugated hu-anti-Cripto MAb B3F6 (B3F6-DM4) in rats and monkeys

Dong Wei, Michael Sullivan, Orlando Espinosa, Liyu Yang

► A sensitive, specific, and high throughput method was developed and validated for the quantitation of free maytansinoid DM4 in cynomolgus monkey and Sprague Dawley rat plasma using liquid chromatography-tandem mass spectrometry (LC–MS/MS). ► The quantitation range of the method was 0.500 – 100 ng/mL with a lower limit of quantitation of 0.500 ng/mL. ► The method was validated in monkey and rat plasma per FDA guidelines. The validated method was employed to monitor the free DM4 levels in plasma in the IND-enabling toxicology studies of antitumor agent DM4 conjugated hu-anti-Cripto MAb B3F6 (B3F6-DM4).



Biopolymers

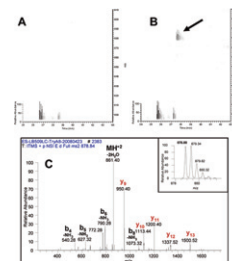
Proteins

61–69

Primary sequence determination of a monoclonal antibody against α -synuclein using a novel mass spectrometry-based approach

Eric Sousa, Stephane Olland, Heather H. Shih, Kim Marquette, Robert Martone, Zhijian Lu, Janet Paulsen, Davinder Gill, Tao He

► A novel mass spectrometry-based approach for *de novo* sequencing monoclonal antibody. ► Incorporated modification of Cys, SILAC, LC/MS/MS, and *de novo* software. ► Complete primary sequence for antibody LB509 was construed. ► Reverse-engineered antibody exhibited specific binding to α -synuclein.

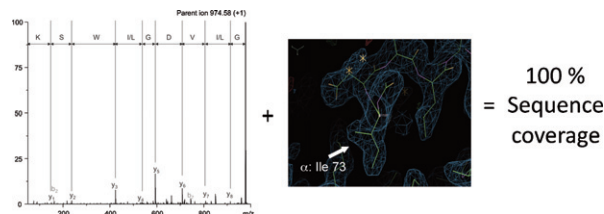


70–77

Complete sequence determination of hemoglobin from endangered feline species using a combined ESI-MS and X-ray crystallography approach

Jingshu Guo, Saurav Uppal, Lindsey M. Easthon, Timothy C. Mueser, Wendell P. Griffith

► Previously unknown sequences for Snow leopard and Amur tiger hemoglobin are presented. ► 100% sequence coverage was obtained through a combination of ESI MS and X-ray crystallography. ► The manuscript illustrates the synergy between these 2 complementary techniques. ► The incomplete sequence obtained from MS was used to aid in the solution of the crystal structures. ► Electron density maps allowed the differentiation of isomeric residues and completion of sequence.

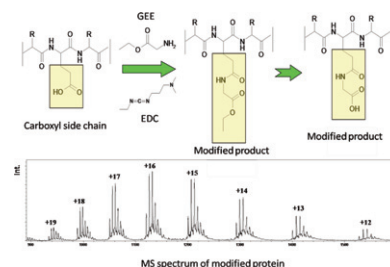


78–86

Mass spectrometry-based carboxyl footprinting of proteins: Method evaluation

Hao Zhang, Jianzhong Wen, Richard Y-C. Huang, Robert E. Blankenship, Michael L. Gross

► Carboxyl-group modification is proposed as footprint of proteins in bio settings. ► Carboxyl footprinting responds to conformation in regions with these side chains. ► This footprinting induces no major conformational change or over-labels protein. ► H/D amide exchange is a means to insure footprinting does not perturb conformation.

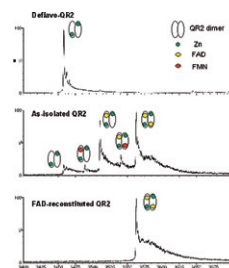


87–96

Characterization of cofactors, substrates and inhibitor binding to flavoenzyme quinone reductase 2 by automated supramolecular nano-electrospray ionization mass spectrometry

Mathias Antoine, Estelle Marcheteau, Philippe Delagrangé, Gilles Ferry, Jean A. Boutin

► Quinone reductase 2 keeps its oligomeric characteristics during mass spectrometry analyses. ► FAD stoichiometry is precisely determined by native MS. ► Native MS confirms the presence of one zinc atom per QR2 monomer. ► Native MS reveals the binding of inhibitors such as resveratrol and melatonin.

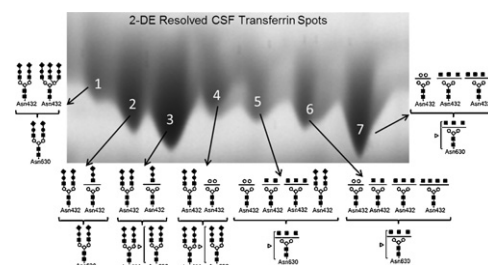


97–106

Characterization of transferrin glycopeptide structures in human cerebrospinal fluid

Kristy J. Brown, Adeline Vanderver, Eric P. Hoffman, Raphael Schiffmann, Yetrib Hathout

► Cerebrospinal fluid transferrin exists as a mixture of sialo and asialoglycoforms. ► Cerebrospinal fluid asialo-transferrin is a specific brain-type and does not normally occur in blood. ► Altered glycosylation patterns in cerebrospinal fluid transferrin is indicative of neurodegenerative diseases.

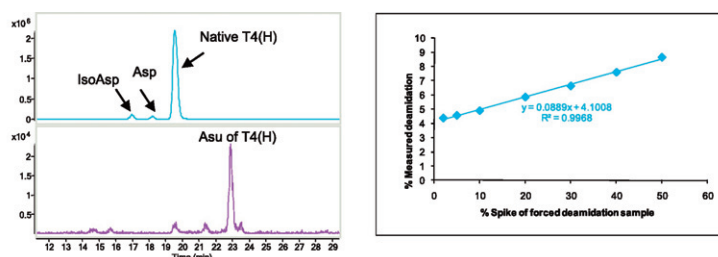


107–113

Quantification and characterization of antibody deamidation by peptide mapping with mass spectrometry

Weijie Wang, Andrea R. Meeler, Luke T. Bergerud, Mark Hesselberg, Michael Byrne, Zhuchun Wu

► A rapid peptide mapping method with MS was developed for deamidation quantification. ► The method was developed and qualified for a recombinant monoclonal antibody. ► The method is specific for multiple deamidation sites and deamidation products.



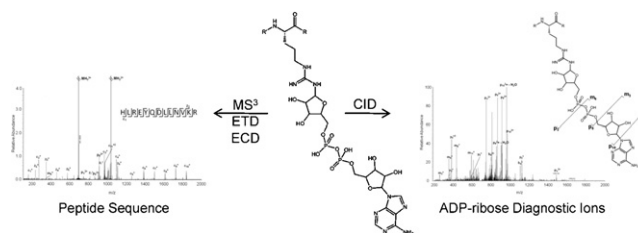
Others

114–121

A review of tandem mass spectrometry characterization of adenosine diphosphate-ribosylated peptides

Shawna M. Hengel, David R. Goodlett

► We review current tandem MS methods for identification of ADP-ribosylated peptides. ► ADP-ribosylated peptide identification is complicated by ADP-ribose fragmentation. ► A systematic nomenclature for ADP-ribosylated peptide fragments is proposed. ► Extensions from mono to poly ADP-ribosylation MS identification methods are discussed.

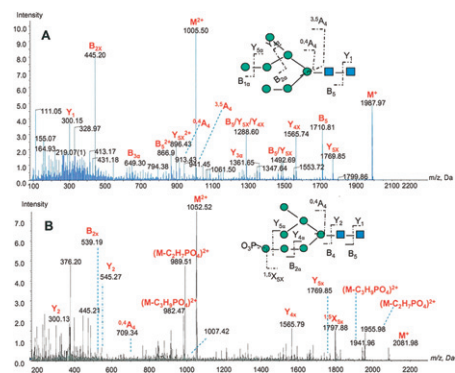


122–134

Mass spectrometry-based characterization of acidic glycans on protein therapeutics

Paul A. Salinas, May Joy C. Miller, Melanie X. Lin, Phil J. Savickas, John J. Thomas

► Several mass spectrometric techniques were required to characterize the diverse nature of phosphorylated, sialylated and sulfonated N-glycans on several therapeutic glycoproteins. ► LC-MS intact protein analysis and MALDI analysis of the total released glycans provided a qualitative assessment of the type of N-linked glycans present on each glycoprotein. ► The detailed structural characterization of the released phosphorylated glycans reveals the position of the phosphate as well as isomeric forms of the mannose residues. ► Site-specific LCMS quantitation of glycopeptides is highly dependent upon the acidic nature of the glycan(s). ► Unique sulfonated sialyl N-linked glycans were identified and characterized through HILIC-MS methods

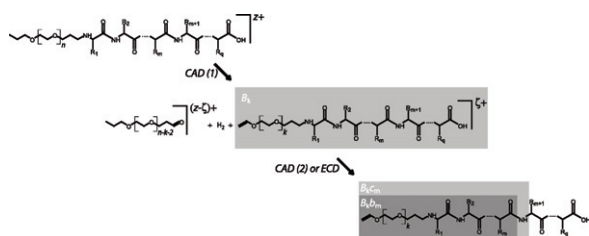


135–143

Structural characterization of protein–polymer conjugates. I. Assessing heterogeneity of a small PEGylated protein and mapping conjugation sites using ion exchange chromatography and top-down tandem mass spectrometry

Rinat R. Abzalimov, Agya Frimpong, Igor A. Kaltashov

► Characterization of PEGylated proteins is a formidable problem due to their heterogeneity. ► Quick identification of PEGylation sites is a particularly challenging task. ► Combination of ion exchange chromatography and top-down mass spectrometry shows great potential. ► The method is tested with a complex mixture of 5 kDa PEG/ubiquitin conjugates.

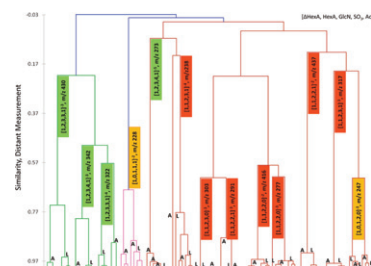


144–154

Differential characterization and classification of tissue specific glycosaminoglycans by tandem mass spectrometry and statistical methods

Nancy Leymarie, Mark E. McComb, Hicham Naimy, Gregory O. Staples, Joseph Zaia

► Statistical analysis of glycosaminoglycan tandem mass spectra. ► Hierarchical clustering to classify product ions based on tissue of origin. ► An effective means of processing glycomics tandem MS data.

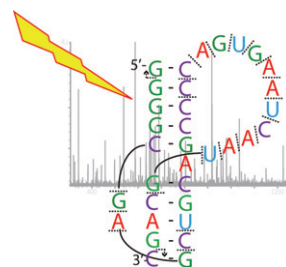


155–162

Higher-order structure of nucleic acids in the gas phase: Top-down analysis of base-pairing interactions

D. Fabris, K.A. Kellersberger, J.A. Wilhide

► Gas-phase activation can preserve intact base-pairing during MS/MS analysis of nucleic acids. ► Base-pairing interactions mask fragmentation events taking place in double-stranded regions. ► This enables the differentiation of single- versus double-stranded nucleotides by top-down MS. ► Gas-phase footprinting can support the elucidation of higher-order structure of nucleic acids.



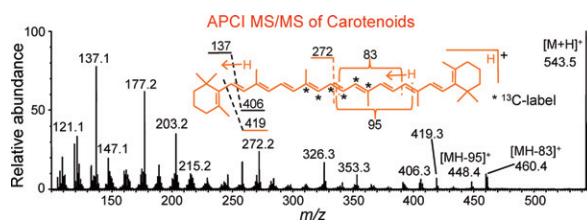
Natural Products

163–172

Atmospheric pressure chemical ionization tandem mass spectrometry of carotenoids

Richard B. van Breemen, Linlin Dong, Natasa D. Pajkovic

► Carotenoids form $[M+H]^+$ and M^- during positive and negative ion APCI, respectively. ► Positive and negative ion APCI MS/MS provide complementary structural information. ► APCI MS/MS of 12 carotenoids was used to identify characteristic fragment ions. ► Isomeric lutein and zeaxanthin could be differentiated by using APCI MS/MS. ► Isomeric lycopene, α -, β - and γ -carotene could be differentiated by APCI MS/MS.



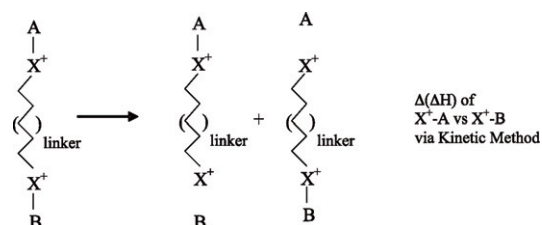
Mechanisms

173–178

The thermochemical studies of protonated amine–crown ether complexes: Extension of the kinetic method

Michael A. Zickus, Sara Koepke, Changtong Hao, Kevin Chong, Victor Ryzhov

► Modification of the kinetic method uses competitive dissociation at two different places. ► Binding order of seven crown ethers to alkylammonium and N-methyl-alkylammonium is obtained. ► Binding trends explained in terms of crown cavity size and polarizability.

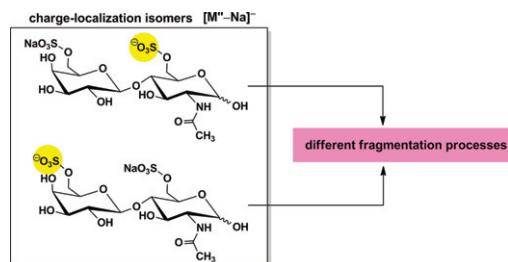


179–184

Studies on (–)ESI-MS/MS of a glycosaminoglycan disaccharide N-acetyllactosamine-6,6'-disulfate disodium salt—Charge-localization isomers

Yoko Ohashi, Masayuki Kubota, Hiroshi Hatase, Takashi Hirano, Shojiro Maki, Haruki Niwa

► Charge-localization isomers possible for a dibasic acid negative precursor ion. ► Unusual migration of sulfate anion from a sugar unit to the next unit. ► Usefulness of accurate mass measurement to determine the fragmentation path.

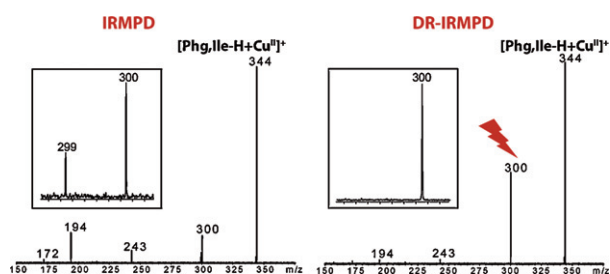


185–194

Origin of enantioselective reduction of quaternary copper D,L amino acid complexes under vibrational activation conditions

Carlos Afonso, Denis Lesage, Françoise Fournier, Valérie Mancel, Jean-Claude Tabet

► Dissociation of $[Cu^{II}(\text{Phg}, \text{AA}_1, \text{AA}_2\text{-H})]^+$ quaternary complexes involving phenylglycine yield enantioselective reduction process. ► Kinetic shift has an important role on reduction extent. ► Role of high proton affinity amino acids on the enantioselective reduction is consistent with zwitterion formation. ► Double resonance–IRMPD is very useful for mechanism elucidation.

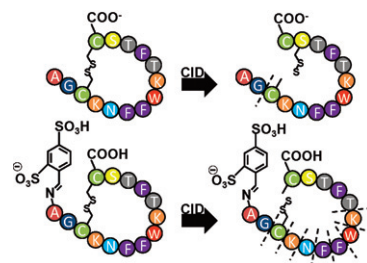


195–200

Dissociation behavior of tryptic and intramolecular disulfide-linked peptide ions modified in the gas phase via ion/ion reactions

John R. Stutzman, Kerry M. Hassell, Scott A. McLuckey

► Tryptic and disulfide-linked peptide cations are covalently modified in the gas phase via Schiff base formation at primary amines via reaction with 4-formyl-1,3-benzenedisulfonic acid (FBDSA) anions. ► Multiply protonated peptides are reduced in charge via reaction with singly deprotonated FBDSA anion whereas singly protonated peptides are inverted in charge via reaction with doubly deprotonated FBDSA. ► Collision-induced dissociation of modified peptide ions leads to fragmentation that is complementary to that noted for unmodified versions of the same peptides, which is due to charge sequestration at the highly acidic sulfonate groups of FBDSA.



Instrumentation

201–207

Paper spray ionization devices for direct, biomedical analysis using mass spectrometry

Qian Yang, He Wang, Jeffrey D. Maas, William J. Chappell, Nicholas E. Manicke, R. Graham Cooks, Zheng Ouyang

► Systematic investigation of the design factors for paper spray ionization source. ► Characterization of analyte transfer on paper media for paper spray. ► Design of disposable paper spray sample device.

