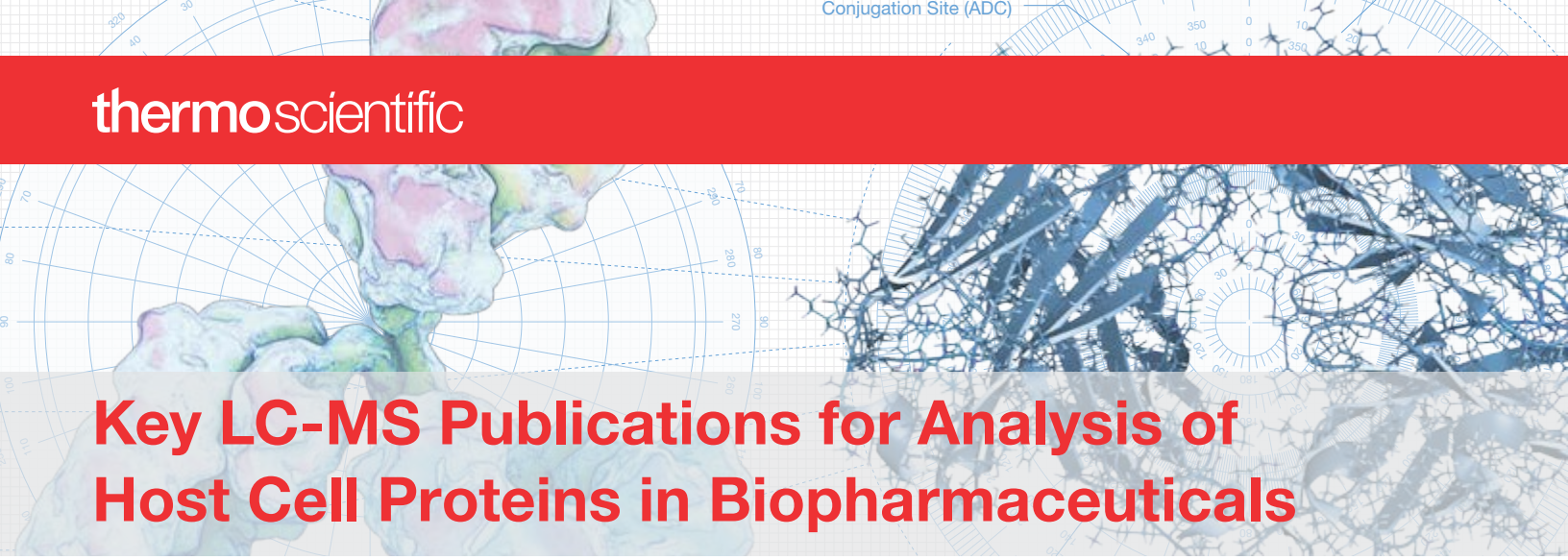

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Key LC-MS Publications for Analysis of Host Cell Proteins in Biopharmaceuticals

Key peer-reviewed publications

A Novel Sample Preparation for Shotgun Proteomics Characterization of HCPs in Antibodies

Lihua Huang, Ning Wang, Charles E. Mitchell, Tammy Brownlee, Steven R. Maple & Michael R. De Felippis. Analytical Chemistry, 2017, 89(10), 5436-5444

Key facts: Non-denaturing tryptic digestion, with and without subsequent removal of undigested biotherapeutic, performed prior to LC-MSMS using a Thermo Scientific™ Q Exactive™ Plus Hybrid Quadrupole-Orbitrap™ mass spectrometer. This methodology enabled consistent detection of spiked recombinant proteins at 0.5 ppm in preparations with mAb concentrations of 12.5 mg/mL. More proteins were identified from the NISTmAb standard with this protocol than with a traditional tryptic digest analysed using 2D-HPLC-MS.

Host Cell Protein Profiling by Targeted and Untargeted Analysis of Data Independent Acquisition Mass Spectrometry Data with Parallel Reaction Monitoring Verification.

Simion Kreimer, Yuanwei Gao, Somak Ray, Mi Jin, Zhijun Tan, Nesredin A. Mussa, Li Tao, Zhengjian Li, Alexander R. Ivanov & Barry L. Karger. Analytical Chemistry, 2017, 89(10), 5294-5302

Key facts: Data independent acquisition (DIA)-MS workflow, followed by verification and quantitation using parallel reaction monitoring (PRM), both with a Thermo Scientific™ Q Exactive™ Plus Hybrid Quadrupole-Orbitrap™ mass spectrometer. More peptides were detected when the same sample was analysed using 2D-HPLC-MS, but no additional HCP proteins were identified.

Proteomic Analysis of Host Cell Protein Dynamics in the Culture Supernatants of Antibody-Producing CHO Cells

Jin Hyoung Park, Jong Hwa Jin, Myung Sin Lim, Hyun Joo An, Jong Won Kim & Gyun Min Lee. Scientific Reports, 2017, 7(44246)

Key facts: Identification and label-free quantitation of HCPs in fed-batch culture supernatants, subsequent to Protein A purification, using LC-MSMS with a Thermo Scientific™ Q Exactive™ mass spectrometer. Analysis included GO annotation to categorise the identified HCPs and a post-processing biotherapeutic CQA assessment.

A Mass Spectrometry-based Approach to Host Cell Protein Identification and its Application in a Comparability Exercise

Veronika Reisinger, Hansjoerg Toll, Robert Ernst Mayer, Jan Visser & Florian Wolschin. Analytical Biochemistry, 2014, 463(Oct), 1-6

Key facts: A 1D-LC-MSMS approach with data dependent acquisition (DDA) on an Thermo Scientific™ LTQ Orbitrap™ mass spectrometer; utilising inclusion lists generated from HCPs present after Protein A capture, and exclusion lists from the drug product. More HCPs were detected using the drug product exclusion list than without, therefore the improvements in HCP detection outweigh the risk of excluding HCP peptides with masses corresponding to those of the drug product.

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Useful Articles and Reviews

Challenges to Industrial mAb Bioprocessing - Removal of Host Cell Proteins in CHO Cell Bioprocesses

Sarah Gilgunn & Jonathan Bones. Current Opinion in Chemical Engineering, 2018, 22, 98-106

This review outlines the up- and downstream processes that can impact the HCP profile, including co-elution of HCPs during Protein A purification. It also discusses current proteomic approaches for HCP identification and quantitation, including a focus on problematic hitch-hiker HCPs.

Recent Advancements, Challenges, and Practical Considerations in the Mass Spectrometry-based Analytics of Protein Biotherapeutics: A Viewpoint from the Biosimilar Industry

Viktor Hádaa, Attila Bagdia, Zsolt Biharia, Sarolta Baginé Timária, Ádám Fizil & Csaba Szántay Jr. Journal of Pharmaceutical and Biomedical Analysis, 2018, 161, 214-238

An extensive review of considerations for generation of accurate and reliable MS data for biopharmaceutical analyses. All aspects of protein biotherapeutic assessment are covered, including sample preparation, strategies for amino acid sequencing and challenges posed by MS-based identification of HCPs.

Identification and Quantification of Trace-Level Protein Impurities

Patrick Bennett, Hongxia (Jessica) Wang, David Horn, Zhiqi Hao & Yi Zhang. BioPharm International, 2013, 26(9)

Evaluation of a universal LC-MS assay for simultaneous identification and quantification of trace-level protein impurities in biotherapeutic products, using a Thermo Scientific™ Q Exactive™ mass spectrometer. The dynamic range detected was 5 orders of magnitude, with multiple proteins detected at 5 ppm levels.

Applications and Posters

Improving the Dynamic Range of Host Cell Proteins Analysis Using an HRAM Orbitrap Mass Spectrometer

Stephane Houel, Romain Huguet, Susan Abbatiello, David Sarracino & Jonathan Josephs. ASMS 2018, Poster

Evaluation of Factors Affecting Detection of Host Cell Proteins in Biotherapeutic Proteins Using an Orbitrap Fusion Lumos Tribrid Mass Spectrometer

Stephane Houel, Michael Blank, Romain Huguet, Seema Sharma, Martin Samonig, Vlad Zabrouskov & Jonathan Josephs. ASMS 2017, Poster

Detection and Identification of New Features as Part of Mass Spectrometry-based Quality Control

Michael Blank, Stephane Houel & Jonathan Josephs. ASMS 2017, Poster

For more information visit: **www.thermofisher.com/HCP**

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