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Biosimilar assessment: Quantitation of antibody variants and pharmacokinetic studies using peptide mapping LC-MS analysis

Introduction: Peptide mapping has been widely accepted as an identity test for biotherapeutics in the QC lab. Recently, the peptide mapping based-multi attribute method (MAM) by ultrahigh performance liquid chromatography (UPLC) coupled to high resolution mass spectrometry (HRMS) have been employed for the confirmation of sequence, and the identification and quantitation of sequence variants and modifications for biosimilar development directly and simultaneously. In addition the peptide mapping technique combining multiple reaction monitoring (MRM) HRMS is gaining momentum as an alternative tool in the pharmacokinetic studies of large molecules including biosimilars. However, one common challenge for application of the technique is sample preparation due to specific structural complex and/or biological endogenous interference. The purpose of this presentation is to describe the approaches of optimization of sample preparation in peptide mapping for quantitation of antibody variants and for pharmacokinetic studies.

Case study 1: Optimization of oxidation detection for a mAb prone to be oxidized

Methods: UPLC-HRMS, tryptic digestion, stable isotope label, PinPoint software. A mAb was incubated with $H_2{}^{18}O_2$ overnight at room temperature first following by regular sample preparation for peptide mapping.

Results: The artificial oxidation formation during sample preparation and storage in autosampler was minimized. Intermediate precision was improved significant.

Conclusion: Platform peptide map MAM LC-MS method works for mAbs. Some mAbs are susceptible to oxidation formation at methionine residues. For accurate oxidation measurement, the use of isotope labelled peptide map LC-MS is essential.

Case study 2: Improvement of specificity in free and total PK assays

Methods: UPLC-MS/MS, tryptic digestion, complementarity-determining region, signature peptides, PinPoint software, immuno affinity.

Results: Specificity of the pharmacokinetic assay was obtained by using several levels of separation.

Conclusion: Reagent free LC-MS/MS approach allows suitable quantitation of total mAb for periclinical studies. Capture approach is especially useful for quantitation of free and partial free mAb in human serum.

Recent Publications

1. Marini J C, et al. (2014) White paper: systematic verification of bioanalytical similarity between a biosimilar and a reference biotherapeutics. AAPS Journal 16(6):1149-1158.
2. Islam R (2014) Bioanalytical challenges of biosimilars. Bioanalysis 6(3):349-356.
3. Iwamoto N, et al. (2016) Validated LC/MS bioanalysis of Rituximab CDR peptides using nanosurface and molecular-orientation limited (nSMOL) proteolysis. Biol. Pharm. Bull. 39(7):1187-1194.
4. Baru R (2017) Applications of targeted proteomics and mass spectrometry in Trastuzumab pharmacokinetics assessments. J Syst Biol Proteome Res 1(1):7-9.
5. Vialaret J, et al. (2018) What sample preparation should be chosen for targeted MS monoclonal antibody quantification in human serum? Bioanalysis 10(10):723-735

Biography

Jane Xiao has obtained her PhD in Analytical Chemistry at University of Wales Swansea, UK. She is a Co-Founder and Senior Director in Biologics Characterization at Axcel BioPartners. Prior to that, she served as Director at Oncobiologics, Head of a proteomics lab at Johnson & Johnson and Senior Scientist at Merck. For the last 15 years she has worked for the pharmaceutical industry leading analytical method development for protein characterization, biomarker development in early phase clinical trials, biosimilar development for similarity assessment and comparability assessment.

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