

About this edition:

In this edition of our quarterly Newsletter, we highlight current publications about recent developments in mass spectrometry technology and its impact on biomarker and clinical research. We also discuss peptide selection criteria for QconCATs.

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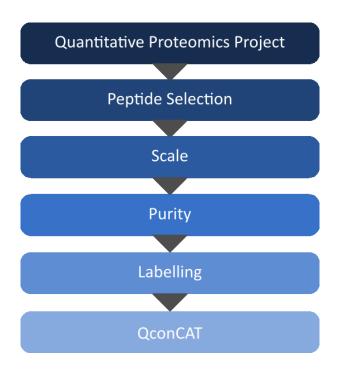
How to design the most appropriate QconCAT for your research project

Part 1: Peptide selection

QconCATs are concatenations of peptides representing the target protein. Choosing optimal peptides for quantification is a crucial step in QconCAT design.To enable absolute protein quantification, these peptides must fulfill certain biological and biochemical criteria concerning the amino acid composition, hydrophobicity, length, ionizability etc. Many of these criteria can be predicted by in silico analysis of the target proteins, based on databases (e.g. UniProt, PeptideAtlas) or based on predictive models (e.g. for trypsin cleavage). However, databases and algorithms can never tell the full story. Many factors, like the detectability of a peptide, depend on the sample preparation procedure and the exact MS system setup. An alternative approach starts with generating experimental data. Performing a shotgun or DIA analysis allows for the selection of peptides proven to be detectable and helps setting up a targeted MS method. However, these peptides may be not ideal for quantification as they could be subject to posttranslational modification (phosphorylation, oxidation, glucosylation etc).

The most efficient approach combines experimental data and *in silico* analysis, leading to selection of the most appropriate peptides for absolute quantification.

Using our in-house software for peptide evaluation, PolyQuant assists you selecting the most suitable peptides for your QconCAT.



Research focus:

Advances in mass spectrometry-based biomarker and clinical research

Mass spectrometry-based proteomics is an established technique for biomarker discovery and validation and is becoming increasingly relevant to clinical application as the detected and independently verified biomarker panels often outperform current state-of-the-art clinical assays focusing on only one biomarker.

Large clinical cohorts and machine learning are the foundation for developing a suitable biomarker panel while short gradients, new scan modes and multiplexing enable high throughput analyses for clinical routine.



MS-based proteomics of body fluids: The end of the beginning

Bader JM, Albrecht V, Mann M. Mol Cell Proteomics. 2023 May 18;100577.

In this <u>review</u>, Bader JM et al. discuss recent technological advances from sample preparation methods to measurement and data analysis and the impact on biomarker research and application in clinical diagnostics and precision medicine.

Proteomics Clinical Applications

Fast and straightforward simultaneous quantification of multiple apolipoproteins in human serum on a high-throughput LC-MS/MS platform

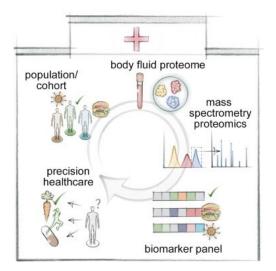
Kim H, Yang WS, An D, Lee SG, Baek JH. Proteomics Clin Appl. 2023 May;17(3):e2200056.

For diagnosis and risk assessment for developing cardiovascular diseases, apolipoproteins are considered as appropriate biomarkers. In clinical routine, immunoassays are the prevalent method for measuring apolipoproteins. As these assays have limitations in specificity, sensitivity and multiplexing, mass spectrometry can be used as complementary method.

To speed up sample preparation time for clinical routine Kim et al. developed a method detecting Apolipoproteins (ApoA1, ApoB100, ApoC3, ApoB48 and total ApoB) in human serum using stable isotope labelled (SIL) peptides as reference. Their sample preparation method reduced turnaround time to 1.5 h.

Kim et al. examined only a small number of apolipoproteins in their study. Our CVD-Kit contains the proteins examined in this study and additional proteins of interest and can be used for fast and easy parallel quantification of 47 proteins linked to cardiovascular diseases.







A multiplexed assay for quantifying immunomodulatory proteins supports correlative studies in immunotherapy clinical trials

Whiteaker JR, Zhao L, Schoenherr RM, Huang D, Lundeen RA, Voytovich U, Kennedy JJ, Ivey RG, Lin C, Murillo OD, Lorentzen TD, Colantonio S, Caceres TW, Roberts RR, Knotts JG, Reading JJ, Perry CD, Richardson CW, Garcia-Buntley SS, Bocik W, Hewitt SM, Chowdhury S, Vandermeer J, Smith SD, Gopal AK, Ramchurren N, Fling SP, Wang P, Paulovich AG. Front Oncol. 2023 May 2;13:1168710.

Immunotherapy is an efficient therapy for certain cancer patients but the same therapy can have adverse effects in other patients. To minimize patient risk, predictive and monitoring biomarkers need to be identified, allowing to select the appropriate therapy. Mass spectrometry complements other technologies and does not depend on antibodies for detection and quantification of specific proteins.

Whiteaker et al. extend a previously developed multiplexed mass spectrometry-based assay (the "IO-1" assay) for quantification of 46 immunomodulatory proteins evaluating the cancer-immunity cycle. Their new IO-2 assay uses a panel of newly developed monoclonal antibodies, configured into a novel, multiplex immuno-MRM assay. As reference for their MS analysis, they used cleavable synthetic peptides. A well designed QconCAT could help speeding up the workflow by enabling the addition of dozens of reference standards in a single pipetting step.