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Peptide hormones: The sensitivity quest and sensitivity questions

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One of the critical goals in modern bioanalytical chemistry is to provide an understanding of the analytical variability between standard immunoassay and LC/MS assays methods. Measured values by the two types of analysis frequently differ by several hundred percent despite concurrent use of reference standards. The error of immuno-based assays is maximal at low analyte concentrations. To properly standardize immunoassays at low analyte concentrations (i.e. in deficiency states), it is essential to maximize the sensitivity of the LC/MS assay which can be challenging. The typical method of choice for quantitative LC/MS analysis of small molecules and tryptic digests is MRM (SRM). However, in our practice of routine quantitation of large peptide hormones/biomarkers, we have found that for trace level analytes measurement (e.g. low pg/ml), MRM does not provide satisfactory results compared to SIM. Post-translation modifications, influence of tertiary structure on electrospray ionization and especially different fragmentation pathways of peptides by collision-induced dissociation (which generates many low-abundant fragments) are common factors reducing MRM-based assay sensitivity.

We have taken an alternative approach to MRM based assays, by implementing 2D LC-LC/MS with stable isotope labeled internal standards and have achieved highly reproducible quantitation of low fmole quantities on column for large peptide/small proteins such as human insulin, glucagon, insulin C-peptide and proinsulin.

Biography

Rogatsky is a senior faculty member at Albert Einstein College of Medicine (NY, Bronx) and director of mass spectrometry at Biomarker Analytical Resource Core as part of the Harold and Muriel Block Institute for Clinical and Translational Research at Einstein and Montefiore. He has worked in the field of chromatography more than 20 years. Since 2001 his work has been within the service of the field of clinical mass spectrometry. During last 10 years (from 2004) Dr Rogatsky published 25 scientific papers in per-reviewed journals (mostly as the first author) and presented over 50 posters and lectures. Currently Dr Rogatsky serve as the Editor-in-Chief for the Journal of Chromatography and Separation Techniques (OMICS publishing group). Eduard Rogatsky completed his M.Sc (physical chemistry) in Belarus State University (former USSR) in 1990. In 1998 has completed PhD in bioanalytical chemistry (Bar-Ilan University, Israel). At the end of 1999 he started post-doctorate at Albert Einstein College of medicine and since 2001 joined faculty.

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