OMICS Group Conferences
Accelerating Scientific Discovery

4th International Conference on
Biomarkers & Clinical Research

July 15-17, 2013 Courtyard by Marriott Philadelphia Downtown, USA

Stabilizing proteins and peptides in human plasma sample for biomarker development

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Abstract

Proteins and peptides in serum and plasma samples contain status information of a ariety of diseases. However, these proteins and peptides are subject to proteolytic and other enzymatic degradation intrinsic to plasma sample, resulting in preanalytical variability and a barrier in translating the discovered biomarkers from batch-side research into bedside applications. Quantitation of the protein biomarkers, especially for metabolic peptides (e.g. GLP-1, GIP, Glucagon, and Oxytomodulin (OXM)) for metabolic and diabetes research, is essential in biomarker and/or drug development. One major challenge is to stabilize these peptides in blood specimens against intrinsic proteolytic activities for accurate quantitation.

Here we reported how these plasma protein and peptide biomarkers were cleaved by intrinsic proteases and peptidases and how these were stabilized in PI-based collection system starting from phlebotomy. We characterized the kinetics of digesting a peptide (e.g. FPA) as Sequential Multiple-Step Reaction (SMSR). The loss of full-length GLP-1, GIP, Glucagon and OXM peptides all were cleaved to remove the first N-terminal two residues caused by DPP IV activity. We also found the other protease and peptidase activities caused the digestions of these peptides, specifically multiple cleavage sites were found on OXM sequences. Both DPP IV and other protease activities were inhibited with our developed technology.

Biography

Jizu Yi has dedicated his carrier in basic and application research in Life Science. His research has across Protein Chemistry, Proteomics, Analytical Biochemistry, Physical Biochemistry, to their applications in pharmaceutical and biotechnological industrials. Yi is a Staff Scientist at BD Diagnostics, and his current research interests are focused on plasma protein and peptide stabilization for biomarker development, specifically in cancer and metabolic diseases.