Quantification of prospective type 2 diabetes mellitus biomarkers by stable isotope dilution with bi-labeled standard glycated peptides.

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Streszczenie

Type 2 diabetes mellitus (T2DM) is a complex group of disorders, characterized by hyperglycemia, insulin resistance and insulin deficiency. In human blood, hyperglycemia ultimately results in the enhancement of glycation – a posttranslational modification formed by the interaction of protein amino groups with glucose. The resulting fructosamines (Amadori compounds) readily undergo further degradation resulting in advanced glycation end products (AGEs), known to be pro-inflammatory in humans. These compounds are highly heterogeneous and characteristic of advanced stages of the disease, whereas fructosamines are recognized markers of early diabetes stages (HbA_{1C}, glycated albumin). Recently, individual plasma protein glycation sites were proposed as promising T2DM biomarkers sensitive to short-term fluctuations of plasma glucose. However, corresponding absolute quantification strategies, applicable in regular clinical practice, are still not established. Therefore, here we propose a new analytical approach aiming at reproducible and precise quantification of multiple glycated peptides in human plasma tryptic digests. Thereby, the standard peptides comprised a ^{13}C,^{15}N-labeled lysyl residue, a dabsyl moiety for determination of standard amounts, and a cleavable linker. Known amounts of these peptides were spiked to plasma samples prior to tryptic digestion, quantification relying on stable isotope dilution. The method was demonstrated to be applicable for quantification of individual glycated sites in T2DM patients and non-diabetic controls.

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