Validation and application of biomarkers for postprandial hyperglycemia and related inflammation-mediated risks of metabolic diseases

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We have used nutrigenomic approach to seek biomarkers in the peripheral leukocytes for postprandial hyperglycemia and related risks of metabolic diseases such as diabetes and obesity. Microarray analysis of the genes in peripheral leukocytes in streptozotocin-treated rats showed that the gene expression of IL-1β and putative inflammatory cytokines, S100 a4/6/8/9, was induced in hyperglycemic rats. Dietary supplementation with an α-glucosidase inhibitor, miglitol, suppressed the induction of these inflammatory cytokine genes. Oral sucrose loading in rats with mild glucose intolerance led to a 2-fold increase in IL-1β gene expression in peripheral leukocytes within 3h, which was abolished by addition of miglitol to the sucrose solution. Rats with moderate insulin resistance, which was induced by high-fat diet feeding, also showed enhanced expression of the genes coding inflammatory cytokines (IL-1β, S100 a8/a9) in peripheral leukocytes. These results suggest that the gene expression of inflammatory cytokines in peripheral leukocytes is altered not only by chromic hyperglycemia but also by acute postprandial hyperglycemia.

A clinical trial in type 2 diabetes mellitus patients with hemoglobin A1c levels ranging from 6.5% to 7.9% showed that a decrease in postprandial hyperglycemia by taking miglitol for 3 months led to a significant reduction of the expression of inflammatory cytokines/cytokine-like factors, including IL-1β, TNF-α, and S100a4/6/9/10/11/12, in peripheral leukocytes. Cross-sectional studies of 310-315 Japanese men aged 40-69 years, who participated in health check-up and who were without obvious cardiovascular diseases, have demonstrated that plasma IL-1β levels are strongly associated with fasting blood glucose concentrations in healthy and preclinical non-overweight and overweight Japanese men. Stepwise multiple linear regression analysis indicated that plasma γ-GTP level is a strong (positive) explanatory factor for IL-1β̃

Our studies suggest that the transcript levels of IL-1β and S100 proteins in peripheral leukocytes are sensitive biomarkers for acute and chronic hyperglycemic history, and that plasma levels of IL-1β and γ-GTP are markers for inflammation, presumably caused by hyperglycemia and/or production of reactive oxygen species. These biomarkers may be sensitive enough to apply for clinical trials to monitor and predict the effects of functional food factors on the risk reduction of diabetes and metabolic diseases in healthy and preclinical subjects.