21st Century COE Program
Human Nutritional Science on Stress Control

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Research and educational programs

1) Psychological stress, metabolic syndrome and oxidative stress

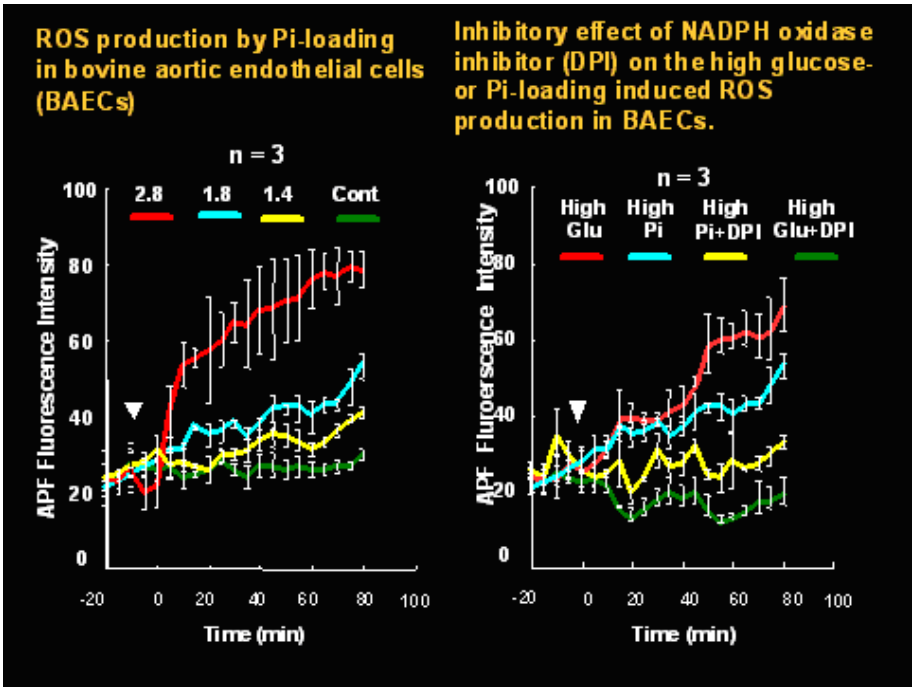
Stress, metabolic syndrome and inflammation mediated by oxidative stress

Psychological stress significantly enhances plasma catecholamine and cortisol concentrations, but does not acutely impair insulin sensitivity. Repeated psychological stress may lead to chronic alteration in cortisol and catecholamine concentrations and to insulin resistance. Furthermore, chronically elevated cortisol concentrations may favour the development of abdominal obesity and of the metabolic syndrome. People who are stressed over long periods tend to look haggard, and it is commonly thought that psychological stress leads to premature aging and the earlier onset of diseases of aging. Psychological stress is associated with increased oxidant production and oxidative damage, and thus long-term exposure to psychological stressors may enhance the risk of many diseases. The oxidative stress associated with psychological and/or emotional stress might be an appropriate target for assessing the preventive potentiality of food supplements.

2) Hyperglycemia, hyperphosphatemia and oxidative stress

Hyperglycemia can increase oxidative stress through several pathways. A major mechanism appears to be the hyperglycemia-induced intracellular reactive oxygen species (ROS) and resulting in an increased production of superoxide. Chronic hyperglycemia and advanced glycation end products increase oxidative stress in the endothelial cells, resulting in lower NO availability, DNA damage and lipid oxidation, and eventually cause endothelial dysfunction. Oxidative stress is widely invoked as a pathogenic mechanism for

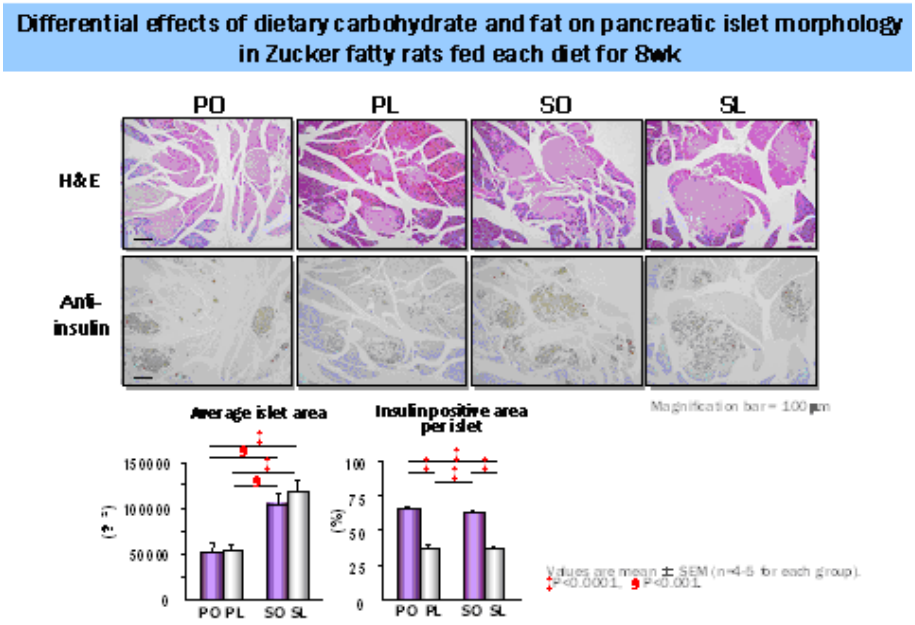
atherosclerosis. Among the sequelae of hyperglycemia, oxidative stress has been suggested as a potential mechanism for accelerated atherosclerosis. Therefore, strategies to reduce postprandial hyperglycemia and hyperinsulinemia represent an important approach to improveing glycemic control in patients with type 2 diabetes mellitus and may even prevent the deterioration of glucose metabolism in impaired glucose tolerance and the subsequent progression to diabetes. Both metabolic and epidemiologic evidence suggest that replacing high-glycemic-index forms of carbohydrate with low-glycemic-index carbohydrates could reduce the risk of type 2 diabetes.
An elevation of extracellular phosphate increased the production of ROS in bovine aortic endothelial cells, suggesting that hyperphosphatemia may be involved in endothelial dysfunction and insulin resistance resulting from oxidative stress. Thus, postprandial hyperphosphatemia might be a risk factor for CVD and mortality even in individuals without ESRD. Impairment of the counter-regulation between phosphate metabolism and FGF23/Klotho signaling may play a part in various aging-related diseases and short lifespan by reducing oxidative stress and other adverse effects. Therefore, control of dietary phosphorus intake is the most effective way to manage hyperphosphatemia.
Hyperglycemia and hyperphosphatemia enhance production of reactive oxygen species (ROS). Therefore, control of glucose and phosphate levels might be an important way to prevent cardio-vascular disease and psychological stress.



3) Combined effects of different types of dietary carbohydrates and fats on the etiology of obesity and its complication

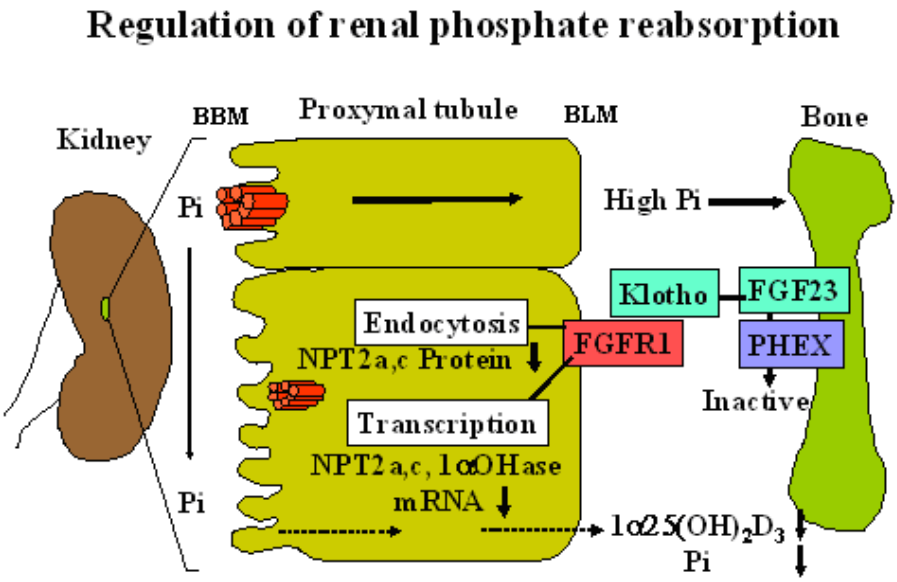
Rats were fed an isocaloric diet containing various combinations of carbohydrates [palatinose (P), an insulin-sparing sucrose analogue, and sucrose (S)] and fatty acids [oleic acid (O) and linoleic acid (L)]. After 8 wk, palatinose feeding (PO and PL) led to significant reductions in visceral fat mass, adipocyte cell size, hyperglycemia, and hyperlipidemia compared with sucrose feeding (SO and SL); pancreatic islet hypertrophy was also prevented by palatinose feeding. Linoleic-acid-fed rats (PL and SL) exhibited reduced

insulin-immunoreactive staining of the pancreatic islets, enhanced macrophage infiltration in adipose tissue, and an elevated plasma tumor necrosis factor-a concentration when compared with oleic-acid-fed rats (PO and SO). In conclusion, a diet containing palatinose and oleic acid may prevent diet-induced metabolic abnormalities.



4) Regulation of renal phosphate reabsorption

Phosphate reabsorption in the kidney plays a critical role in the regulation of Pi homeostasis. Phosphate homeostasis is regulated by variety factors such as parathyroid hormone, vitamin D, FGF23, dietary phosphate, thyroid hormone etc. through controlling renal phosphate reabsorption. Type IIa and IIc sodium-dependent phosphate transporter (NaPi-IIa and IIc) perform the most of renal phosphate reabsorption and are strictly regulated by above factors. These factors regulate the activities of both sodium-dependent phosphate transporters by changing the amount of their proteins on renal tubular cell surface via transcriptional regulation and subcellular localization. Recently, these transporters form a functional macromolecular complex with adaptor proteins and/or signal transduction molecules on the cell surface. Our goal in this study is elucidation of the molecular mechanisms of the regulation of these transporters by molecular and cellular biology techniques using mouse, rat, cell line models.



5) Education program and support

Special programs for educational purposes are provided. As a part of the stress and nutrition educational program, a new graduate school lecture/seminar series “stress, mind and nutrition” targeted towards graduate students/young researchers are set up. As for educational program of functional food development and human nutrition, world-renowned researchers both from Japanese research institutions and from abroad were invited. The effects of ginsenoside, Cordyceps sinensis, quercetin, collagen tripeptide, Bitter melon, viscous foods, barley are under investigations using molecular and biochemical techniques in animal and human studies. It is quite sure these programs will stimulate and encourage young researchers to become active facilitators in the combined research field, and at the same time, will expose them to different sciences and allow them to grow as true members of the international scientists in an age of globalization.

These research and educational programs were achieved by the collaboration with 4 staffs, 2 postdoctoral fellows, 29 postgraduate and 9 undergraduate students. These were also supported by grants Initiatives for Attractive Education in Graduate School, University of Tokushima, Japan, 21st Century COE program, Human Nutritional Science and Stress Control, Tokushima, Japan, and Grants-in-Aid for Scientific Research and Knowledge Cluster Intiative from the Ministry of Education, Culture, Sports Science, and Technology in Japan, The Ministry of Agriculture, Forestry and Fisheries in Japan.

6) Publications

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