

Chair

2.7.5 Laboratory : Molecular Function of Food

Member:	Professor	Kawada, Teruo, Dr. Agric. Sci.
	Assistant Professor	Takahashi, Nobuyuki, Dr. Med. Sci
	Doctor's program	5
	Master's Program	13
	Undergraduate	4
	Other	1

A. Research Activities (2010.4-2011.3)

A-1. Main Subjects

a) Genomic regulatory science on lipid metabolism and obesity

Overweight is superfluous formation of the fat, which constitutes an adipose tissue. It has been pointed out that the factor secreted from a fat cell as a key factor of a lifestyle-related diseases of recent years. Multiplication of a fat cell, specialization, and secretion of the various factor further related to development of symptoms are strongly influenced by the food ingredient to daily take. As a result of analyzing the transcriptional regulation mechanism over the target gene of PPARs (peroxisome proliferator-activated receptors), which are the master regulator of specialization of a fat cell differentiation. And then we found out that CREB-binding protein (CBP) was the indispensable factor of fat cell specialization. Furthermore, the activation factor of PPARs which promotes carbohydrate metabolism and lipid metabolism using this system was found out to natural occurring materials, especially a medicinal herb, or plants.

b) Analyses on physiological roles of brown adipocyte regulating energy consumption

Brown adipocyte is a type of cells consuming energy as heat using lipid as fuel. We investigate developmental mechanisms and functional regulation of brown adipocytes using novel methods such as in vivo imaging by MRI and fluorescence microscopy. In addition to uses of animal model, we use human adipocyte cell line. Regulations of brown adipocytes by food components will give us ways to preventing and improving obesity and its related diseases such as diabetes and atherosclerosis.

c) Basic and applied studies on energy and lipid metabolism aimed at prevention of the life-style related disease and metabolic syndrome

Initiation and progression of the life-style related disease are involved in the lipid metabolism in the various organs including gastrointestinal tract, liver and adipose tissue. For understanding and prevention of these diseases, we are performing the basic studies about lipid metabolism and adipocyte function, and applied studies about food factors regulating lipid metabolism properly. Our current research topics are 1) the screening of natural products for normalizing lipid metabolism, 2) basic and applied studies about lipoproteins in liver and small intestine, and 3) analysis of molecular mechanisms that monitor hypertrophy of adipocytes.

d) Molecular food function on the regulation of obesity-related inflammatory pathologies

Arteriosclerosis and the allergy are the familiar living body inflammations caused by food and the genetic background. The importance of the cytokines and chemokines such as tumor necrosis factor (TNF)-alpha, adiponectin, and monocyte chemoattractant protein-1 (MCP-1) in the lifestyle disease is clarified inside and outside the country in recent years. The chemokine is a super-family of the cytokine of cell migration (chemoattractant), and it is known as inflammatory mediator. In addition, the function has been found receiving the modification by various nutrients and the food factors. This research theme clarifies the realities of a chemical factor that it develops metabolic syndrome from the aspect of the cytokine and chemokine.

e) Studies on signaling network of lipid metabolism among organs/tissues.

Communication among organs/tissues is indispensable for the homeostasis. For example, nutrients derived from foods are recognized on the gastrointestinal epithelial cells so that gastrointestinal hormones are released from specific endocrine cells. The gastrointestinal hormones regulate metabolism and/or functions in other organs and tissues like the liver and adipose tissues. Disruption in such network may induce various diseases of metabolism. We are elucidating mechanism of the network composed by the liver, intestine, and adipose tissues, which are significant for systemic regulation of lipid metabolism. Our final purpose is to clarify relationship between regulation of the network and development of lipid metabolism abnormalities.

A-2.Publications and presentations

a) Publications

Books

- Takahashi N, Kawada T.

McKee "Biochemistry" Chapter 16 "Integration of metabolism" Translation

Original Papers(including book-reviews)

- Kang JH, Goto T, Han IS, Kim CS, Kawada T, Kim Y-M, Yu R.
Dietary Capsaicin reduces Obesity-induced Insulin Resistance and Hepatic Steatosis in Obese Mice fed a High-fat Diet.
Obesity (2010) 18: 780-787.

- Kim CS, Tu TH, Kawada T, Kim BS, Yu R.
The Immune Signaling Molecule 4-1BB Stimulation Reduces Adiposity, Insulin Resistance, and Hepatosteatosis in Obese Mice.
Endocrinology. (2010) 151: 4725-4735.

- Ishii N, Matsumura T, Kinoshita H, Fukuda K, Motoshima H, Senokuchi T, Nakao S, Tsutsumi A, Kim-Mitsuyama S, Kawada T, Takeya M, Miyamura N, Nishikawa T, Araki E. Nifedipine induces peroxisome proliferator-activated receptor-gamma activation in macrophages and suppresses the progression of atherosclerosis in apolipoprotein E-deficient mice.
Arterioscler Thromb Vasc Biol. (2010) 30: 1598-15605.

- Uemura T, Hirai S, Mizoguchi N, Goto T, Lee JY, Taketani K, Nakano Y, Shono J, Hoshino S, Tsuge N, Narukami T, Takahashi N, Kawada T.
Diosgenin present in fenugreek improves glucose metabolism by promoting adipocyte differentiation and inhibiting inflammation in adipose tissues.
Mol. Nutr. Food Res. (2010) 54: 1596-1608.

- Inoue, H., Takahashi, N., Okada, Y. and Konishi, M.
Volume-sensitive outwardly rectifying chloride channel in white adipocytes.
Am. J. Physiol.: Cell Physiol. (2010) 298: C900-C909.

- Nagai H, Ebisu S, Abe R, Goto T, Takahashi N, Hoshaka T, Kawada T.
Development of a novel PPARgamma ligand screening system using pinpoint fluorescence-probed protein.
Biosci. Biotechnol. Biochem. (2011) 75: 337-341.

- Kim YI, Hirai S, Takahashi H, Goto T, Ohyane C, Tsugane T, Konishi C, Fujii T, Inai S, Iijima Y, Aoki K, Shibata D, Takahashi N, Kawada T.
9-oxo-10(E),12(E)-octadecadienoic acid derived from tomato is a potent peroxisome proliferator-activated receptor α agonist to decrease triglyceride accumulation in mouse primary hepatocytes.
Mol. Nutr. Food Res. (2011) 55: 585-593.

- Fujitani Y, Aritake K, Kanaoka Y, Goto T, Takahashi N, Fujimori K, Kawada T.
Pronounced adipogenesis and increased insulin sensitivity caused by overproduction of prostaglandin D2 in vivo.
FEBS J. (2010) 277: 410-419. .

- Hirai, S.*, Uemura, T.*, Mizoguchi, N., Lee, J. Y., Taketani, K., Nakano, Y., Hoshino, S., Tsuge, N., Narukami, T., Yu, R., Takahashi, N. and Kawada, T.
Diosgenin attenuates inflammatory changes in the interaction between adipocytes and macrophages.
Mol. Nutr. Food Res. (2010) 54: 1-8. (* equal contributions) .

- Uemura T, Goto T, Kang M-S, Mizoguchi N, Hirai S, Lee, J-Y, Nakano Y, Shono J, Hoshino S, Taketani K, Tsuge N, Narukami T, Makishima M, Takahashi N, Kawada T.
Diosgenin, the Main Aglycon of Fenugreek, Inhibits LXR α Activity in HepG2 cells and Decreases Plasma and Hepatic Triglycerides in Obese, Diabetic Mice.
J. Nutr. (2011) 141: 17-23.

Reviews

- Goto T, Lee JY, Teraminami A, Takahashi N, Kawada T.
Obesity (2nd Ed.), Regulation of energy metabolism by nutritions, "Metabolic regulation in adipocytes"
Nippon Rinsho Sup (2010) 156-161.

- Hirai S, Takahashi N, Goto T, Lin S, Uemura T, Yu R, Kawada T.
Functional food targeting the regulation of obesity-induced inflammatory responses and pathologies.
Mediators Inflamm. (2010) 2010: 367838.

- Goto T, Takahashi N, Hirai S, Kawada T.

Various terpenoids derived from herbal and dietary plants function as PPAR modulators and regulate carbohydrate and lipid metabolism.

PPAR Res. (2010) 2010: 483958.

Reports,others

- Kawada T.

Preface, "Adipocytes"

The Lipid 2010 Jan.

- Kawada T.

Preface, "Adipocytes: Old knowledge and new findings"

Research for Obesity 2011 Vol. 1.

b) Conference and seminar papers presented

- Health Food Society of Taiwan (1)

- The 2010 Annual Meeting of Japan Society for the Study of Obesity (4)

- The Annual Meeting of Japan Society for Bioscience Biotechnology, and Agrochemistry (2)

- The 64th Annual Meeting of Japan Society for Nutrition and Food Science (3)

- The Satellite Symposium of 11th International Congress on Obesity(ICO2010) (4)

A-3.Off-campus activities 1

Membership in academic societies

- Kawada, Teruo, Dr. Agric. Sci. : Japan Society for the Study of Obesity (General affairs & publicity committee), Japan Society for Bioscience Biotechnology, and Agrochemistry (Kansai Branch general affairs), The Japan Endocrine Society (General affairs), Study Group on Adiposcience (General affairs)

- Takahashi, Nobuyuki, Dr. Med. Sci : Japan Society for the Study of Obesity (Councilor), The Physiological Society of Japan (Councilor), The Molecular Biology Society of Japan, Japan Society for Bioscience Biotechnology, and Agrochemistry

A-3.Off-campus activities 2

Research grants

1. Grants-in-aid for Scientific Research(KAKENHI)

- Scientific Research (S) : Kawada, Teruo, Dr. Agric. Sci. : Development Mechanism and Physiological Roles of Brown Fat Regulating Energy Expenditure

- Scientific Research (B) : Takahashi, Nobuyuki, Dr. Med. Sci : Effects of Intestinal Epithelial Lipid Metabolism on Food-derived Lipid Uptake

2.Other Research Grants

- Research and development projects for application in promoting new policy of agriculture,forestry and fisheries. : Kawada, Teruo, Dr. Agric. Sci. : Agricultural and Engineering Research for Development of High-Quality-Food Resources using Omics Approaches.

A-4.International cooperation and overseas activities 1

International joint research, overseas research surveys

- Studies on cytokine and chemokine from adipose tissue and obesity related diseases, Kawada and University of Ulsan, South Korea

- Studies on differentiation and proliferation of adipose stem cells, Kawada and INSERM, France

B.Educational Activities(2010.4-2011.3)

B-1.On-campus teaching

a) Courses given

- Undergraduate level: Molecular Function of Food (Kawada), Introduction and practice in the department of food science and biotechnology I (Kawada), Food biochemistry II (Kawada), Food Safety II (Kawada), Laboratory Course in Enzyme Chemistry and Biochemistry (Kawada and Takahashi)
- Graduate level: Advanced Course in Food and Health Science (Kawada), Seminar on Molecular Function of Food Constituents (Kawada and Takahashi), Experimental Course in Molecular Function of Food Constituents (Kawada and Takahashi)

B-3.Overseas teaching 1

International students

- International students : Undergraduate 1 (Korea) Master 3 (Korea 2, China 1) Doctoral 1 (Taiwan)