2.7.4 Laboratory : Nutrition Chemistry

Member :	Professor	Tohru Fushiki, Dr. Agric. Sci.
	Associate Professor	Kazuo Inoue, Dr. Agric. Sci.
	Assistant Professor	Satoshi Tsuzuki, Dr. Agric. Sci.
	Assistant Professor	Shigenobu Matsumura, Dr. Agric. Sci.
	Doctor's program	2
	Master's Program	13
	Undergraduate	3
	Post-Doctoral fellow	2

A. Research Activities (2009.4-2010.3)

A-1. Main Subjects

a) Palatability of foods; Nutrition, Physiology and Brain science

It is important conception in the field of research of food science that new food resources are palatable and acceptable in human. To get this final goal, new foods are required to have a good sensitive nature, a good nutritional property, safety and many other good properties. We want to eat delicious foods. It can not be coped with a close food crisis that the development of food resources are accepted only by starving people. In this point of view, we studied what properties of food resources have high acceptability in human. Especially, we study on fat taste and the traditional “umami” taste by the analyses of interaction mechanisms on tongue of experimental animals.

b) Control of gastrointestinal epithelial turnover and the regulation by food components, and regulatory mechanism of gastrointestinal hormone secretion

The mucosal surface of the intestine comprises epithelial monolayer cells that are critical for the absorption of nutrients and defense. Aging epithelial cells must be rapidly replaced by younger cells for the maintenance of these functions. However, details of the underlying mechanism governing the rapid turnover of intestinal epithelial cells have remained unknown. We found a novel enzyme, designated membrane-type serine protease 1 (MT-SP1), and suggested that this enzyme is involved in the control of intestinal epithelial turnover under physiological conditions. Furthermore, we found that the activities of MT-SP1 and granzyme A (GrA), which is likely to induce apoptosis of abnormal intestinal epithelial cells, are

regulated by food components. Our studies have revealed that some food components can regulate the turnover of the intestinal epithelium.

c) Development of special foods to increase endurance capacity.

Long-distance runners have broken many world records in recent years. Because they apparently ingested special foods to increase their endurance capacity, these exogenous substances and their effects on endurance capacity have been brought into the light. We devised an adjustable-current swimming pool for the evaluation of endurance capacity of mice. Our apparatus provides for the reliable and reproducible evaluation of the endurance capacity of mice. By using our apparatus, we studied the detecting and mechanism of the effects of dietary differences and drug pretreatment on the endurance capacity. In addition, we investigate the relation to central fatigue induced by brain TGF-beta with endurance capacity in order to clarify whether food stuff that has effects on endurance capacity also modifies the manifestation of tiredness.

d) Mechanisms of manifestation of central fatigue and TGF-beta in brain

Intracerebroventricular administration of cerebrospinal fluid (CSF) from exercise-fatigued rats elicited the decrease in spontaneous motor activity of sedentary mice, as though they were exhausted. There was no such effect in the CSF from sedentary rats. Those mice administered the CSF form fatigued-rats seemed to occur the feeling of fatigue and lose their willingness to move.

We thought that the substance which involved in this phenomena was the factor that cause the feeling of fatigue. With various experiments we clarified that transforming growth factor-beta (TGF-β) was the responsible substance, because 1) the concentration of active TGF-β in CSF from fatigued-rats increased, 2) treatment of CSF from fatigued-rats with anti-TGF-β antibody eliminated the effect of decreasing spontaneous motor activity of mice, 3) elevating exercise load on rats increased both the concentration of active TGF-β in CSF and the inhibitory effect on spontaneous motor activity on mice, and 4) purified TGF-β dose-dependently depressed the spontaneous motor activity of mice. These results strongly suggested that active TGF-β in the brain elicited the manifestation of central fatigue and depression in willingness to move.

In addition, we showed the administration of TGF-β into the brain could augment the ratio of utilization of fatty acid in whole body and the preference for sweet taste. These indicated that active TGF-β in the brain not only caused feeling of fatigue, but affected to peripheral tissues (via autonomic nervous system) and involved in the mechanisms which changed metabolic state to the one during/after exercise.

e) Mechanism of induction of Rewarding effect of dietary fat

Fatty food are palatable and we are often attracted by such a high caloric or high fat foods. In addtion, dietary fat has a rewarding effedt. It is thought that the rewarding effect of fatty foods might be derived from two factors. One is orosensory palatable stimulus of fat and another is a factor that produces the feeling of satiation in the postingestive process. We are now investigating the mechanism that induces rewarding effect of fat during postingestive processes by behavioral and physiological experiments.

A-2.Publications and presentations

a) Publications

Original Papers

- Miyake Y, Tsuzuki S, Mochida S, Fushiki T, and Inouye K. The role of asparagine-linked glycosylation site on the catalytic domain of matriptase in its zymogen activation. Biochim Biophys Acta 1804: 156-165, 2010.
- Miyake Y, Tsuzuki S, Fushiki T, and Inouye K. Matriptase does not require hepatocyte growth factor activator inhibitor type-1 for activation in an epithelial cell expression model. Biosci Biotechnol Biochem 74: 848-850, 2010.
- Matsumura S, Yoneda T, Aki S, Eguchi A, Manabe Y, Tsuzuki S, Inoue K, and Fushiki T. Intragastric infusion of glucose enhances the rewarding effect of sorbitol fatty acid ester ingestion as measured by conditioned place preference in mice. Physiol Behav 99: 509-514, 2010.
- Matsumura S, Eguchi A, Kitabayashi N, Tanida M, Shen J, Horii Y, Nagai K, Tsuzuki S, Inoue K, and Fushiki T. Effect of an intraduodenal injection of fat on the activities of the adrenal efferent sympathetic nerve and the gastric efferent parasympathetic nerve in urethane-anesthetized rats. Neurosci Res, 2010.
- Inouye K, Yasumoto M, Tsuzuki S, Mochida S, and Fushiki T. The optimal activity of a pseudozymogen form of recombinant matriptase under the mildly acidic pH and low ionic strength conditions. J Biochem 147: 485-492, 2010.
- Yoneda T, Saitou K, Asano H, Mizushige T, Matsumura S, Eguchi A, Manabe Y, Tsuzuki S, Inoue K, and Fushiki T. Assessing palatability of long-chain fatty acids from the licking behavior of BALB/c mice. Physiol Behav 96: 735-741, 2009.
- Yoneda T, Saitou K, Asano H, Mizushige T, Matsumura S, Eguchi A, Manabe Y, Tsuzuki S, Inoue K, and Fushiki T. Assessing palatability of long-chain fatty acids from the licking behavior of BALB/c mice. Physiol Behav, 2009.
- Tsuzuki S, Miyake Y, Inouye K, and Fushiki T. The occurrence of matriptase C-terminal fragments on the apical and basolateral sides of Madin-Darby canine kidney

epithelial cells. Biosci Biotechnol Biochem 73: 2538-2540, 2009.
- Saitou K, Yoneda T, Mizushige T, Asano H, Okamura M, Matsumura S, Eguchi A, Manabe Y, Tsuzuki S, Inoue K, and Fushiki T. Contribution of gustation to the palatability of linoleic acid. Physiol Behav 96: 142-148, 2009.
- Murai N, Miyake Y, Tsuzuki S, Inouye K, and Fushiki T. Involvement of the cytoplasmic juxtamembrane region of matriptase in its exclusive localization to the basolateral membrane domain of Madin-Darby canine kidney epithelial cells. Cytotechnology 59: 169-176, 2009.
- Mizushige T, Saitoh K, Manabe Y, Nishizuka T, Taka Y, Eguchi A, Yoneda T, Matsumura S, Tsuzuki S, Inoue K, and Fushiki T. Preference for dietary fat induced by release of beta-endorphin in rats. Life Sci 84: 760-765, 2009.
- Miyake Y, Yasumoto M, Tsuzuki S, Fushiki T, and Inouye K. Activation of a membrane-bound serine protease matriptase on the cell surface. J Biochem 146: 273-282, 2009.
- Miyake Y, Tsuzuki S, Yasumoto M, Fushiki T, and Inouye K. Requirement of the activity of hepatocyte growth factor activator inhibitor type 1 for the extracellular appearance of a transmembrane serine protease matriptase in monkey kidney COS-1 cells. Cytotechnology, 2009.
- Matsumura S, Eguchi A, Mizushige T, Kitabayashi N, Tsuzuki S, Inoue K, and Fushiki T. Colocalization of GPR120 with phospholipase-Cbeta2 and alpha-gustducin in the taste bud cells in mice. Neurosci Lett 450: 186-190, 2009.
- Masamoto Y, Kawabata F, and Fushiki T. Intragastric administration of TRPV1, TRPV3, TRPM8, and TRPA1 agonists modulates autonomic thermoregulation in different manners in mice. Biosci Biotechnol Biochem 73: 1021-1027, 2009.
- Kojima K, Tsuzuki S, Fushiki T, and Inouye K. The activity of a type II transmembrane serine protease, matriptase, is dependent solely on the catalytic domain. Biosci Biotechnol Biochem 73: 454-456, 2009.
- Kojima K, Tsuzuki S, Fushiki T, and Inouye K. Role of the stem domain of matriptase in the interaction with its physiological inhibitor, hepatocyte growth factor activator inhibitor type I. J Biochem 145: 783-790, 2009.
- Kawabata F, Inoue N, Masamoto Y, Matsumura S, Kimura W, Kadowaki M, Higashi T, Tominaga M, Inoue K, and Fushiki T. Non-pungent capsaicin analogs (capsinoids) increase metabolic rate and enhance thermogenesis via gastrointestinal TRPV1 in mice. Biosci Biotechnol Biochem 73: 2690-2697, 2009.
- Ishihara K, Yamada A, Mita Y, Goto A, Ishimi T, Mabuchi H, Inoue K, Fushiki T, and Yasumoto K. Improved swimming pool achieves higher reproducibility and sensitivity to

effect of food components as ergogenic AIDS. J Nutr Sci Vitaminol (Tokyo) 55: 301-308, 2009.

- Hotta Y, Nakamura H, Konishi M, Murata Y, Takagi H, Matsumura S, Inoue K, Fushiki T, and Itoh N. Fibroblast growth factor 21 regulates lipolysis in white adipose tissue but is not required for ketogenesis and triglyceride clearance in liver. Endocrinology 150: 4625-4633, 2009.

- Fukatsu Y, Noguchi T, Hosooka T, Ogura T, Kotani K, Abe T, Shibakusa T, Inoue K, Sakai M, Tobimatsu K, Inagaki K, Yoshioka T, Matsuo M, Nakae J, Matsuki Y, Hiramatsu R, Kaku K, Okamura H, Fushiki T, and Kasuga M. Muscle-specific overexpression of heparin-binding epidermal growth factor-like growth factor increases peripheral glucose disposal and insulin sensitivity. Endocrinology 150: 2683-2691, 2009.

- Mochida S, Tsuzuki S, Yasumoto M, Inouye K, Fushiki T: Secreted expression of pseudozymogen forms of recombinant matriptase in Pichia pastoris. Enzyme Microb. Tech. 45 (4) 288–294 (2009)

Reviews

- Tohru Fushiki, Strategic studies of diets for health based on dietary preference and energy expenditure, J. Jpn. Soc. Nutr. Food Sci., 63, 61-68, 2010 (in Japanese)

- Manabe Y, Matsumura S, and Fushiki T. Preference for High-fat food in Animals in Animals Fat detection; taste texture postingestive effects、 (eds　Montmayeur & Coutre) CRC Press 243-264 (2009)

- Matsumura and Fushiki, Reception of fatty acid in oral cavity, Kagaku to Seibutsu, 48, 114-120 (2010), (in Japanese)

- Kazuo Inoue, Metabolism of lipids and fatty acids during exercise and sports, Rinsho Sports Igaku, 26(supple), 36-44, 2010 (in Japanese)

b) Conference and seminar papers presented

- Annual meeting of Japan Society for Bioscience, Biotechnology, and Agrochemistry (7 papers)

- Annual meeting of Japanese Society of Nutrition and Food Science (5 papers)

- Annual meeting of the Japanese Association for the Study of Taste and Smell (5 papers)

- Annual meeting of Japan Society for Spice Research (2 papers)

- AChemS 2009 Annual Meeting XXXI : 1 Presentation

- The 3rd international siymposium on physiology and pharmacology of

thermoregulation,: 1 Presentation

- 11th annual meeting of Australasian Association for Chemosensory Science: 1 Presentation
- 19th International congress of nutrition: 1 presentation

A-3.Off-campus activities

Membership in academic societies

- Fushiki, Tohru, D.Agric.Sci : Japanese Society of Nutrition and Food Science (Councilor), Japan Society for Bioscience, Biotechnology, and Agrochemistry (Councilor of Kansai branch), Japanese Society of Biochemistry (Councilor), Japan Society of Spice Study (President), Japanese Association for the Study of Taste and Smell(Councilor)
- Inoue, Kazuo. Dr. Agric. Sci. : Japan Society for Bioscience, Biotechnology, and Agrochemistry (Councilor of Kansai branch)

Research grants

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

- Scientific Research (B) : Inoue, Kazuo : Establishment of the evaluation system for central fatigue and the development of preparative basis for food which aims the control of fatigue
- Scientific Research (C) : Tsuzuki, Satoshi : Elucidation of the role for granzyme A, a binding molecule of monitor peptide, in the peptide-mediated CCK release

2.Other Research Grants

- Grant from Bio-Oriented Technology research Program for Promotion of Basic research Activities for Innovative Biosciences：Fushiki, Tohru：Construction of basics for development of highly preferable and low energy density oil by elucidatoin of chemical reception of lipids in oral cavity and its information processing in brain
- Grant from Ryoshoku kenkyu-kai：Fushiki, Tohru：Establishment of profile palate element method for evaluation of food palatability for elderly people and its application to dairy products

A-4.International cooperation and overseas activities

Membership in academic societies

- Fushiki, Tohru, Dr. Agric. Sci.: American society for nutrition (regular member), American pancreatic association (regular member)
- Inoue, Kazuo, Dr. Agric. Sci.: American society for neuroscience (regular member)

International meetings(country,roles)

- Fushiki, Tohru, Dr. Agric. Sci.：Korean international society for nutrition and food (Korea, keynote lecture)

B.Educational Activities(2009.4-2010.3)

B-1.On-campus teaching

a) Courses given

- Undergraduate level： Nutrition Chemistry (Fushiki), Taste and Preference (Fushiki) Laboratory course in food and nutrition chemistry (Inoue, Tsuzuki, Matsumura), Introduction to foreign literature in food science and biotechnology II (Inoue, Hashimoto), Basic course in information processing (Inoue, Hashimoto)
- Graduate level： Nutrition Chemistry (Advanced course) (Fushiki, Inoue), Laboratory Course in Nutrition Chemistry (Fushiki, Inoue)

B-2.Off-campus teaching etc.

Part-time lecturer

- Kazuo Inoue: Nara wemen's unversity, Department of Food Science and Nutrition, Advence course in molecular food science

Open lectures, etc.

- Tohru Fushiki: Annual meeting of research association of school lunch, Japan research association of school lunch, special lecture
- Tohru Fushiki: Cultural open lecture of Kurashiki Sakuyou university, Kurashiki Sakuyou universituy, lecturere

B-3.Overseas teaching

Lectures and seminars

- Fushiki, Tohru, Dr. Agric. Sci.

Importance of the Traditional Umami Taste in Asian Foods(lecturer) : Kasetsart University(Thai)

Importance of the Traditional Umami Taste in Asian Foods(lecturer) : Koeran society for food and nutrition(Korea)

C.Other Remarks

- Fushiki, Tohru : Division of evaluation of livestock products for facilitaion of use of recycle feed (Ecofeed), (committee member), Japan society for the promotion of science, Committee of grant-in-aid for scientific research, (member), Japan society for the promotion of science, Committee of global COE program, (member), Ajinomoto foundation for scholarship, (director), Uragami promotion foundation for food and culture, (director), Academy of Japanese cuisine, (director), Foundation of Sugiyama Reserch Institute for Industrial Chemistry, (director), Japanese association of enzyme application, (councilor), Fuji Protein committee for research promotion, (councilor), Division of sensory evaluation of flavor, Japanese general center of meat consumption, (committee member), Kyoto central wholesale market, Committee for fullfillment strategy of foothold of food, (member)