Foods have a variety of physiological functions

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Foods have a variety of physiological functions not only as nutrients but also signaling molecules to modify biological systems. We focus on mechanisms of adaptive change of nutritional requirement and metabolism in relation to aging and exercise, and the physiological functions of orally active short peptides derived food proteins, which act on the nervous, gastrointestinal, cardiovascular, and immune systems. By using molecular biological and pharmacological techniques on cellular, tissue and animal levels, we are elucidating the integrated interactions between food components and biological systems. These studies will contribute to prevent lifestyle-related diseases and to improve our quality of life.

Adaptive expression of dispensable amino acid-metabolic enzymes to changes in protein requirement by aging

We found that several enzyme for synthesis and degradation of dispensable amino acid (such as serine and asparagine) expresses in response to its requirement and supply from dietary protein. This suggests the physiological importance to regulate the level of dispensable amino acid. We are now focus on to clarify regulatory mechanism of gene expression of these enzymes by dietary protein.

Emotional response to food components

Excess mental stress not only exacerbates psychiatric disorders but also increases the incidence rate of lifestyle-related diseases. We have found that low-molecular-weight peptides, which are released from food proteins by enzymatic digestion, sometimes exhibits anxiolytic-like activities even after oral administration in behavior tests (Fig. 1). Among them, several bioactive peptides has potent anxiolytic-like activity comparable to anxiolytic drugs. We also elucidated their novel mode of actions. We investigate effect of bioactive peptides with anxiolytic and anti-depressive activities on glucose and lipid metabolism using type 2 diabetic mice.

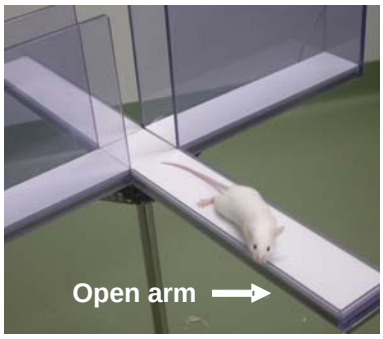

Fig. 1. Elevated plus-maze test.

Orally active functional molecules matching life stage

Anorectic drugs are developed for anti-obesity, whereas orexigenic molecules are also useful for physiological anorexia in the elderly. We have found that orally administered short peptides sometimes decrease or increase food intake in mice. We also found that central prostaglandin (PG) system, including PGD_2 and PGE_2, is important for food intake regulation in our studies on the mechanisms underlying these peptides controlling food intake (Fig. 2). In the elderly, decreases in quality of sleep, secretion of growth hormone and learning performance as well as hypertension are often elicited. To address these issues, we are researching for food stuffs improving them.

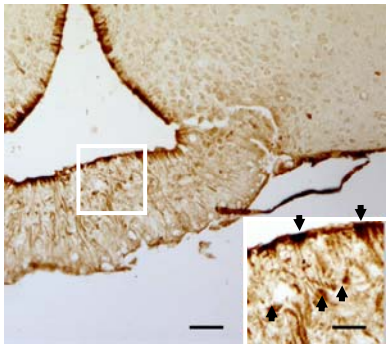

Fig. 2. Localization of prostaglandin D_2 synthase in the hypothalamus.

Keywords

bioactive peptides, lifestyle-related disease, food intake regulation, anti-diabetes, learning, anxiolytic activity, anti-hypertension, pain response, protein engineering

Recent Publications

Characterization of ovolin, an orally active tryptic peptide released from ovalbumin with anxiolytic-like activity.
Oda A, Kaneko K, Mizushige T, Lazarus M, Urade Y, Ohinata K. J Neurochem. 2012 (in press)

Complement C5a exhibits anxiolytic-like activity via the prostaglandin D_2-DP_1 receptor system coupled to adenosine A_{2A} and $GABA_A$ receptors.
Miyamoto C, Yoshida M, Yoshikawa M, Mizushige T, Ohinata K. Prostaglandins Other Lipid Mediat. 2012;98(1-2):17-22.

Lupeol supplementation improves blood pressure and lipid metabolism parameters in stroke-prone spontaneously hypertensive rats.
Ardiansyah, Yamaguchi E, Shirakawa H, Hata K, Hiwatashi K, Ohinata K, Goto T, Komai M.
Biosci Biotechnol Biochem. 2012;76(1):183-5.

Soymorphin-5, a soy-derived μ-opioid peptide, decreases glucose and triglyceride levels through activating adiponectin and PPARα systems in diabetic KKAy mice.
Yamada Y, Muraki A, Oie M, Kanegawa N, Oda A, Sawashi Y, Kaneko K, Yoshikawa M, Goto T, Takahashi N, Kawada T, Ohinata K. Am J Physiol Endocrinol Metab. 2012;302(4):E433-40.

β-Lactotensin derived from bovine β-lactoglobulin exhibits anxiolytic-like activity as an agonist for neurotensin NTS_2 receptor via activation of dopamine D_1 receptor in mice.
Hou IC, Suzuki C, Kanegawa N, Oda A, Yamada A, Yoshikawa M, Yamada D, Sekiguchi M, Wada E, Wada K, Ohinata K. J Neurochem. 201;119(4):785-90.

Zinc as an appetite stimulator - the possible role of zinc in the progression of diseases such as cachexia and sarcopenia.
Suzuki H, Asakawa A, Li JB, Tsai M, Amitani H, Ohinata K, Komai M, Inui A.
Recent Pat Food Nutr Agric. 2011;3(3):226-31.

Central PGE_2 exhibits anxiolytic-like activity via EP1 and EP4 receptors in a manner dependent on serotonin 5-HT_{1A}, dopamine D_1 and $GABA_A$ receptors.
Suzuki C, Miyamoto C, Furuyashiki T, Narumiya S, Ohinata K. FEBS Lett. 2011;585(14):2357-62.

Rapakinin, Arg-Ile-Tyr, derived from rapeseed napin, shows anti-opioid activity via the prostaglandin IP receptor followed by the cholecystokinin CCK_2 receptor in mice.
Yamada Y, Ohinata K, Lipkowski AW, Yoshikawa M. Peptides. 2011;32(2):281-5.

Antihypertensive activity of transgenic rice seed containing an 18-repeat novokinin peptide localized in the nucleolus of endosperm cells.
Wakasa Y, Zhao H, Hirose S, Yamauchi D, Yamada Y, Yang L, Ohinata K, Yoshikawa M, Takaiwa F.
Plant Biotechnol J. 2011;9(7):729-35.

Orally administered soymorphins, soy-derived opioid peptides, suppress feeding and intestinal transit via gut mu_1-receptor coupled to 5-HT_{1A}, D_2, and $GABA_B$ systems.
Kaneko K, Iwasaki M, Yoshikawa M, Ohinata K. Am J Physiol Gastrointest Liver Physiol.
2010 ;299(3):G799-805.

C-type natriuretic peptide as a new regulator of food intake and energy expenditure.
Inuzuka M, Tamura N, Yamada N, Katsuura G, Oyamada N, Taura D, Sonoyama T, Fukunaga Y, Ohinata K, Sone M, Nakao K. Endocrinology. 2010;151(8):3633-42.

Rapakinin, an anti-hypertensive peptide derived from rapeseed protein, dilates mesenteric artery of spontaneously hypertensive rats via the prostaglandin IP receptor followed by CCK_1 receptor.
Yamada Y, Iwasaki M, Usui H, Ohinata K, Marczak ED, Lipkowski AW, Yoshikawa M. Peptides. 2010; 31: 909-14.

Dipeptide Tyr-Leu (YL) exhibits anxiolytic-like activity after oral administration via activating serotonin 5-HT_{1A}, dopamine D_1 and $GABA_A$ receptors in mice.
Kanegawa N, Suzuki C, Ohinata K. FEBS Lett. 2010; 584: 599-604.

Complement C5a stimulates food intake via a prostaglandin D_2- and neuropeptide Y-dependent mechanism in mice.
Ohinata K, Takagi K, Biyajima K, Kaneko K, Miyamoto C, Asakawa A, Eguchi N, Urade Y, Inui A, Yoshikawa M. Prostaglandins Other Lipid Mediat. 2009; 90: 81-4.
β-Lactotensin derived from bovine β-lactoglobulin suppresses food intake via the CRF system followed by the CGRP system in mice.
Hou IC, Yoshikawa M, Ohinata K. Peptides. 2009; 30: 2228-32.
Orally administered novokinin, an angiotensin AT_2 receptor agonist, suppresses food intake via prostaglandin E_2-dependent mechanism in mice.
Ohinata K, Fujiwara Y, Fukumoto S, Iwai M, Horiuchi M, Yoshikawa M. Peptides. 2009; 30: 1105-8.
Orally administered zinc increases food intake via vagal stimulation in rats.
Ohinata K, Takemoto M, Kawanago M, Fushimi S, Shirakawa H, Goto T, Asakawa A, Komai M. J Nutr. 2009; 139: 611-6.
Angiotensin AT_2 receptor agonists act as anti-opioids via EP_3 receptor in mice.
Yamada Y, Ohinata K, Lipkowski AW, Yoshikawa M. Peptides. 2009; 30(4):735-9.
Accumulation of the bioactive peptides, novokinin, LPYPR and rubiscolin, in seeds of genetically modified soybean.
Nishizawa K, Kita A, Doi C, Yamada Y, Ohinata K, Yoshikawa M, Ishimoto M. Biosci Biotechnol Biochem. 2008; 72: 3301-5.
Food intake regulation by central complement system.
Ohinata K, Yoshikawa M. Adv Exp Med Biol. 2008; 632:35-46. Review.
Central prostaglandin D_2 exhibits anxiolytic-like activity via the DP_1 receptor in mice.
Zhao H, Ohinata K, Yoshikawa M.Prostaglandins Other Lipid Mediat. 2009; 88(3-4): 68-72.
Enterostatin reduces serum cholesterol levels by way of a CCK_1 receptor-dependent mechanism.
Takenaka Y, Shimano T, Mori T, Hou IC, Ohinata K, Yoshikawa M. Peptides. 2008; 29(12): 2175-8.
Central prostaglandins in food intake regulation.
Ohinata K, Yoshikawa M. Nutrition. 2008; 24(9): 798-801.
Effect of biotin ingestion on the improvement of hypertension in SHRSP
Komai M, Watanabe-Kamiyama M, Kamiyama S, Ohinata K, Horiuchi K, Furukawa Y, Shirakawa H. Nippon Yakurigaku Zasshi. 2008 Apr; 131(4): 248-51.
Central prostaglandin D_2 stimulates food intake via the neuropeptide Y system in mice.
Ohinata K, Takagi K, Biyajima K, Fujiwara Y, Fukumoto S, Eguchi N, Urade Y, Asakawa A, Fujimiya M, Inui A, Yoshikawa M. FEBS Lett. 2008; 582(5):679-84.
Angiotensin II and III suppress food intake via angiotensin AT_2 receptor and prostaglandin EP_4 receptor in mice.
Ohinata K, Fujiwara Y, Fukumoto S, Iwai M, Horiuchi M, Yoshikawa M.
FEBS Lett. 2008; 582(5): 773-7.
Anti-hypertensive activity of genetically modified soybean seeds accumulating novokinin.
Yamada Y, Nishizawa K, Yokoo M, Onishi K, Teraishi M, Utsumi S, Ishimoto M, Yoshikawa M. Peptides. 2008; 29(3): 331-7.
Hypotensive activity of novokinin, a potent analogue of ovokinin(2-7), is mediated by angiotensin AT_2 receptor and prostaglandin IP receptor.
Yamada Y, Yamauchi D, Usui H, Zhao H, Yokoo M, Ohinata K, Iwai M, Horiuchi M, Yoshikawa M. Peptides. 2008; 29(3): 412-8.
A potent hypotensive peptide, novokinin, induces relaxation by AT_2- and IP-receptor-dependent mechanism in the mesenteric artery from SHRs.
Yamada Y, Yamauchi D, Yokoo M, Ohinata K, Usui H, Yoshikawa M. Biosci Biotechnol Biochem. 2008; 72(1): 257-9.
Rubimetide (Met-Arg-Trp) derived from Rubisco exhibits anxiolytic-like activity via the DP_1 receptor in male ddY mice.
Zhao H, Ohinata K, Yoshikawa M. Peptides. 2008; 29(4): 629-32.
Met-Arg-Trp derived from Rubisco lowers blood pressure via prostaglandin D_2-dependent vasorelaxation in spontaneously hypertensive rats.
Zhao H, Ohinata K, Yoshikawa M. Peptides. 2008; 29(3): 345-9.
Enterostatin (APGPR) suppresses the analgesic activity of morphine by a CCK-dependent mechanism.
Takenaka Y, ShimanoT, Yamada Y, Yoshida M, Ohinata K, Yoshikawa M. Peptides. 2008; 29(4): 559-63.
Soymorphins, novel m opioid peptides derived from soy β-conglycinin β-subunit, have anxiolytic activities.