

(様式1)

社団法人日本栄養・食糧学会 研究業績

<学 会 賞>

1. 候補者

研究題目:(和)	分岐鎖アミノ酸代謝の調節機構に関する研究		
(英)	Study on regulatory mechanisms of branched-chain amino acid metabolism		
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2. 研究業績要旨(1,000字以内)

分岐鎖アミノ酸(BCAA:ロイシン、イソロイシン、バリン)は、必須アミノ酸であるため、哺乳動物の体内ではその分解系のみが存在する。この分解系(代謝系)は、ほぼ全てミトコンドリアに存在し、最初の2つのステップは3つのBCAAに共通であり、この分解系の大きな特徴を示す反応である。第一ステップは、BCAAアミノ基転移酵素による可逆的なアミノ基転移反応である。第二ステップは、分岐鎖 α -ケト酸脱水素酵素(BCKDH)複合体による不可逆的な酸化脱炭酸反応である。以下に述べる候補者等の研究により、BCKDH複合体は特異的キナーゼ(BCKDHキナーゼ(BDK))による酵素タンパク質のリン酸化により活性調節されることが明らかにされた。これらの事実より、第二ステップの酵素活性調節がBCAA代謝を調節するとされている。候補者らは、BCKDH複合体の活性調節機構に関する初期の研究において、ラット肝臓と心臓よりBDKの精製を試みた。その結果、44 kDaの単一のタンパク質が精製され、BDKが同定された。次いで、BDK遺伝子クローニングにも成功し、これはミトコンドリアのタンパク質キナーゼとして初めてクローニングされた遺伝子であった。さらに、候補者等のBDKの存在状態に関する研究において、BDKがBCKDH複合体に結合する結合型と結合していない遊離型として存在することが明らかにされ、BCKDH複合体はBDKの結合型酵素量に依存して活性調節(抑制)されることが明らかにされた。これらの生化学的研究を基礎として、候補者等は種々の栄養状態および生理状態におけるBCAA代謝調節機構を明らかにした。すなわち、高タンパク質食摂取、筋収縮活動(運動)は、BCKDH複合体からBDKを解離してその複合体を活性化し、BCAA代謝を促進すること、一方、低タンパク質食摂取は逆の機構でBCAA代謝を抑制することが判明した。このBDKによるBCKDH複合体の活性調節により、BCAA代謝の臓器特異性、BCAA代謝に対するホルモン(エストロゲンと甲状腺ホルモン)作用、および疾病(肝硬変と糖尿病)の影響を説明することができた。以上のように、候補者等のBCAA代謝におけるBDKの役割の研究により、BCAA代謝調節機構の多くの部分が明らかにされた。

3. 報文等リスト

- (1) この研究に直接関連するもの(10編以内)
1. Doisaki, M., Katano, Y., Nakano, I., Hirooka, Y., Itoh, A., Ishigami, M., Hayashi, K., Goto, H., Fujita, Y., Kadota, Y., Kitaura, Y., Bajotto, G., Kazama, S., Tamura, T., Tamura, N., Feng, G., Ishikawa, N., and Shimomura, Y. Regulation of hepatic branched-chain α -keto acid dehydrogenase kinase in a rat model for type 2 diabetes mellitus at different stages of the disease. **Biochem. Biophys. Res. Commun.** 393: 303-307, 2010.
 2. Kuzuya, T., Katano, Y., Nakano, I., Hirooka, Y., Itoh, A., Ishigami, M., Hayashi, K., Honda, T., Goto, H., Fujita, Y., Shikano, R., Muramatsu, Y., Bajotto, G., Tamura, T., Tamura, N., and Shimomura, Y. Regulation of branched-chain amino acid catabolism in rat models for spontaneous type 2 diabetes mellitus. **Biochem. Biophys. Res. Commun.** 373: 94-98, 2008.
 3. Shimomura, Y., Honda, T., Shiraki, M., Murakami, T., Sato, J., Kobayashi, H., Mawatari, K., Obayashi, M., and Harris, R.A. Branched-chain amino acid catabolism in exercise and liver disease. **J. Nutr.** 136: 250S-253S, 2006.
 4. Shimomura, Y., Yamamoto, Y., Bajotto, G., Sato, J., Murakami, T., Shimomura, N., Kobayashi, H., and Mawatari, K. Nutraceutical effects of branched-chain amino acids on skeletal muscle. **J. Nutr.** 136: 529S-532S, 2006.
 5. Honda, T., Fukuda, Y., Nakao, I., Katano, Y., Goto, H., Nagasaki, M., Sato, Y., Murakami, T., and Shimomura, Y. Effects of liver failure on branched-chain α -keto acid dehydrogenase complex in rat liver and muscle: comparison between acute and chronic liver failure. **J. Hepatol.** 40: 439-445, 2004.
 6. Obayashi, M., Shimomura, Y., Nakai, N., Jeoung, N.H., Nagasaki, M., Murakami, T., Sato, Y., and Harris, R.A. Estrogen controls branched-chain amino acid catabolism in female rats. **J. Nutr.** 134: 2628-2633, 2004.
 7. Kobayashi, R., Murakami, T., Obayashi, M., Nakai, N., Jaskiewicz, J., Fujiwara, Y., Shimomura, Y., and Harris, R.A. Clofibric acid stimulates branched-chain amino acid catabolism by three mechanisms. **Arch. Biochem. Biophys.** 407: 231-240, 2002.
 8. Obayashi, M., Sato, Y., Harris, R.A., and Shimomura, Y. Regulation of the activity of branched-chain 2-oxo acid dehydrogenase (BCODH) complex by binding BCODH kinase. **FEBS Lett.** 491: 50-54, 2001.
 9. Popov, K.M., Zhao, Y., Shimomura, Y., Kuntz, M.J., and Harris, R.A. Branched-chain α -ketoacid dehydrogenase kinase: Molecular cloning, expression, and sequence similarity with histidine protein kinases. **J. Biol. Chem.** 267: 13127-13130, 1992.
 10. Shimomura, Y., Nanaumi, N., Suzuki, M., Popov, K.M., and Harris, R.A. Purification and partial characterization of branched-chain α -ketoacid dehydrogenase kinase from rat liver and rat heart. **Arch. Biochem. Biophys.** 283: 293-299, 1990.
- (2) その他の論文(編数制限なし)
11. Matsumoto, H., Akita, K., Sakai, R., and Shimomura, Y. Analysis of branched-chain α -keto acid dehydrogenase complex activity in rat tissues using α -keto[1- 13 C]isocaproate as substrate. **Anal. Biochem.** 399: 1-6, 2010.
 12. Shimomura, Y., Inaguma, A., Watanabe, S., Yamamoto, Y., Muramatsu, Y., Bajotto, G., Sato, J., Shimomura, N., Kobayashi, H., and Mawatari, K. Branched-chain amino acid supplementation before squat exercise and delayed-onset muscle soreness. **Int. J. Sport Nutr. Exerc. Metab.** 20: 236-244, 2010.
 13. Fujimura, Y., Muramatsu, Y., Akita, K., Bajotto, G., and Shimomura, Y. Modified method for purifying rat liver branched-chain α -ketoacid dehydrogenase complex. **Biosci. Biotechnol. Biochem.** 73: 766-768, 2009.
 14. Akita, K., Fujimura, Y., Bajotto, G., and Shimomura, Y. Inhibition of branched-chain α -ketoacid dehydrogenase kinase by thiamine pyrophosphate at different potassium ionic levels. **Biosci. Biotechnol. Biochem.** 73: 1189-1191, 2009.
 15. *Shimomura, Y., Kobayashi, H., Mawatari, K., Akita, K., Inaguma, A., Watanabe, S., Bajotto, G., and Sato, J. Effects of squat exercise and branched-chain amino acid supplementation on plasma free amino acid concentrations in young women. **J. Nutr. Sci. Vitaminol.** 55: 288-291, 2009.

16. Bajotto, G., Murakami, T., Nagasaki, M., Sato, Y., and Shimomura, Y. Decreased enzyme activity and contents of hepatic branched-chain α -keto acid dehydrogenase complex subunits in a rat model for type 2 diabetes mellitus. **Metabolism** 58: 1489-1495, 2009.
17. 下村吉治, 分岐鎖アミノ酸(BCAA)代謝の調節機構. **化学と生物**, 47: 480-485, 2009.
18. *Asai, Y., Bajotto, G., Yoshizato, H., Hamada, K., Higuchi, T., and Shimomura, Y. The effects of endotoxin on plasma free amino acid concentrations in rats. **J. Nutr. Sci. Vitaminol.** 54: 460-466, 2008.
19. Nakai, N., Shimomura, Y., Tamura, T., Tamura, N., Hamada, K., Kawano, F., and Ohira, Y. Leucine-induced activation of translational initiation is partly regulated by the branched-chain α -keto acid dehydrogenase complex in C2C12 cells. **Biochem. Biophys. Res. Commun.** 343: 1244-1250, 2006.
20. Ishiguro, Y., Katano, Y., Nakano, I., Ishigami, M., Hayashi, K., Honda, T., Goto, H., Bajotto, G., Maeda, K., and Shimomura, Y. Clofibrate treatment promotes branched-chain amino acid catabolism and decreases the phosphorylation state of mTOR, eIF4E-BP1, and S6K1 in rat liver. **Life Sci.** 79: 737-743, 2006.
21. *Bajotto, G., and Shimomura, Y. Determinants of disuse-induced skeletal muscle atrophy: Exercise and nutrition countermeasures to prevent protein loss. **J. Nutr. Sci. Vitaminol.** 52: 233-247, 2006.
22. *Murakami, T., Matsuo, M., Shimizu, A., and Shimomura, Y. Dissociation of branched-chain α -keto acid dehydrogenase kinase (BDK) from branched-chain α -keto acid dehydrogenase complex (BCKDC) by BDK inhibitors. **J. Nutr. Sci. Vitaminol.** 51: 48-50, 2005.
23. Shiraki, M., Shimomura, Y., Miwa, Y., Fukushima, H., Murakami, T., Tamura, T., Tamura, N., Moriwaki, H. Activation of hepatic branched-chain α -keto acid dehydrogenase complex by tumor necrosis factor- α in rats. **Biochem. Biophys. Res. Commun.** 328: 973-978, 2005.
24. Shimomura, Y., Honda, T., Goto, H., Nonami, T., Kurokawa, T., Nagasaki, M., and Murakami, T. Effects of liver failure on the enzymes in the branched-chain amino acid catabolic pathway. **Biochem. Biophys. Res. Commun.** 313: 381-385, 2004.
25. Shimomura, Y., Murakami, T., Nakai, N., Nagasaki, N., Harris, R.A. Exercise promotes BCAA catabolism: effects of BCAA supplementation on skeletal muscle during exercise. **J. Nutr.** 134: 1583S-1587S, 2004.
26. Shimomura, Y., Murakami, T., Nagasaki, M., Honda, T., Goto, H., Kotake, K., Kurokawa, T., and Nonami, T. Regulation of branched-chain amino acid metabolism and pharmacological effects of branched-chain amino acids. **Hepatology Res.** 30S: 3-8, 2004.
27. Shimomura, Y., and Nagasaki, M. Molecular mechanisms for the effects of exercise on the regulation of glucose, fatty acid and amino acid metabolism. **Korean Journal of Exercise Nutrition** 6: 67-76, 2002.
28. Shimomura, Y., Murakami, T., Nakai, N., and Nagasaki, M. Exercise and metabolism in muscle cells: Molecular aspects of energy metabolism during exercise and adaptation to exercise training. In "Exercise, Nutrition, and Environmental Stress" Vol. 1 (Nose, H., Gisolfi, C.V., and Imaizumi, K., eds.), pp. 89-116, Cooper Publishing Group, Traverse City (MI), 2001.
29. Harris, R.A., Kobayashi, R., Murakami, T., and Shimomura, Y. Regulation of branched-chain α -keto acid dehydrogenase kinase expression in rat liver. **J. Nutr.** 131: 841S-845S, 2001.
30. Bixel, M., Shimomura, Y., Hutson, S.M., and Hamprecht, B. Distribution of key enzymes of branched-chain amino acid metabolism in glial and neuronal cells in culture. **J. Histochem. Cytochem.** 49: 407-418, 2001.
31. Shimomura, Y., Obayashi, M., Murakami, T., and Harris, R.A. Regulation of branched-chain amino acid catabolism: nutritional and hormonal regulation of activity and expression of the branched-chain α -keto acid dehydrogenase kinase. **Curr. Opin. Clin. Nutr. Metab. Care** 4: 419-423, 2001.
32. Ishigure, K., Shimomura, Y., Murakami, T., Kaneko, T., Takeda, S., Inoue, S., Nomoto, S., Koshikawa, K., Nonami, T., and Nakao, A. Human liver disease decreases enzyme activities in valine catabolism; methacrylyl-CoA hydratase and β -hydroxyisobutyryl-CoA hydrolase. **Clin. Chim. Acta** 312: 115-121, 2001.
33. Xu, M., Nagasaki, M., Obayashi, M., Sato, Y., Tamura, T. and Shimomura, Y. Mechanism of activation of branched-chain α -keto acid dehydrogenase complex by exercise. **Biochem. Biophys. Res. Commun.** 287: 752-756, 2001.

34. *Li, Z., Murakami, T., Nakai, N., Nagasaki, M., Obayashi, M., Xu, M., Sato, J., Oshida, Y., Sato, Y., and Shimomura, Y. Modification by exercise training of activity and enzyme expression of hepatic branched-chain α -ketoacid dehydrogenase complex in streptozotocin-induced diabetic rats. **J. Nutr. Sci. Vitaminol.** 47: 345-350, 2001.
35. *Shimomura, Y., Murakami, T., Nakai, N., Nagasaki, M., Obayashi, M., Li, Z., Xu, M., Sato, Y., Kato, T., Shimomura, N., Fujitsuka, N., Tanaka, K., and Sato, M. Suppression of glycogen consumption during acute exercise by dietary branched-chain amino acids in rats. **J. Nutr. Sci. Vitaminol.** 46: 71-77, 2000.
36. Kobayashi, R., Shimomura, Y., Otsuka, M., Popov, K.M., and Harris, R.A. Experimental hyperthyroidism causes inactivation of the branched-chain α -ketoacid dehydrogenase complex in rat liver. **Arch. Biochem. Biophys.** 375: 55-61, 2000.
37. Nakai, N., Kobayashi, R., Popov, K.M., Harris, R.A., and Shimomura, Y. Determination of branched-chain α -keto acid dehydrogenase activity state and branched-chain α -keto acid dehydrogenase kinase activity and protein in mammalian tissues. **Methods Enzymol.** 324: 48-62, 2000.
38. Popov, K.M., Shimomura, Y., Hawes, J.W., and Harris, R.A. Branched-chain α -keto acid dehydrogenase kinase. **Methods Enzymol.** 324: 162-178, 2000.
39. Hawes, J.W., Zhao, Y., Popov, K.M., Shimomura, Y., and Harris, R.A. Production of recombinant E1 component of branched-chain α -keto acid dehydrogenase complex. **Methods Enzymol.** 324: 200-207, 2000.
40. Shimomura, Y., Murakami, T., Nakai, N., Huang, B., Hawes, J.W., and Harris, R.A. 3-Hydroxyisobutyryl-CoA hydrolase. **Methods Enzymol.** 324: 229-240, 2000.
41. Xu, M., Nakai, N., Ishigure, K., Nonami, T., Nagasaki, M., Obayashi, M., Li, Z., Sato, Y., Fujitsuka, N., Murakami, T., and Shimomura, Y. The α -ketoisocaproate catabolism in human and rat livers. **Biochem. Biophys. Res. Commun.** 276: 1080-1084, 2000.
42. Kato, T., Goto, H., Niwa, Y., Ohmiya, N., Hayakawa, T., Murakami, T., Nakai, N., Hutson, S.M., and Shimomura, Y. Expression of mRNA for *c-myc* and branched-chain aminotransferases in human gastric cancer cells and tissues. **J. Clin. Biochem. Nutr.** 29: 29-36, 2000.
43. *Kobayashi, R., Shimomura, Y., Murakami, T., Nakai, N., Otsuka, M., Arakawa, N., Shimizu, K., and Harris, R.A. Hepatic branched-chain α -keto acid dehydrogenase complex in female rats: activation by exercise and starvation. **J. Nutr. Sci. Vitaminol.** 45: 303-309, 1999.
44. Suryawan, A., Hawes, J.W., Harris, R.A., Shimomura, Y., Jenkins, A.E., and Hutson, S.M. A molecular model of human branched-chain amino acid metabolism. **Am. J. Clin. Nutr.** 68: 72-81, 1998.
45. Fujii, H., Shimomura, Y., Murakami, T., Nakai, N., Sato, T., Suzuki, M., and Harris, R.A. Branched-chain α -keto acid dehydrogenase kinase content in rat skeletal muscle is decreased by endurance training. **Biochem. Mol. Biol. Int.** 44: 1211-1216, 1998.
46. Tsukamura, M., Goto, H., Arisawa, T., Hayakawa, T., Kobayashi, R., Nakai, N., Murakami, T., Sugiyama, S., and Shimomura, Y. The activity of branched-chain α -keto acid dehydrogenase complex in rat digestive tracts: Effects of dietary protein and exercise. **Biochem. Mol. Biol. Int.** 42: 717-722, 1997.
47. Kobayashi, R., Shimomura, Y., Murakami, T., Nakai, N., Fujitsuka, N., Otsuka, M., Arakawa, N., Popov, K.M., and Harris, R.A. Gender difference in regulation of branched-chain amino acid catabolism. **Biochem. J.** 327: 449-453, 1997.
48. Harris, R.A., Hawes, J.W., Popov, K.M., Zhao, Y., Shimomura, Y., Sato, J., Jaskiewicz, J., and Hurley, T.D. Studies on the regulation of the mitochondrial α -ketoacid dehydrogenase complexes and their kinases. **Advan. Enzyme Regul.** 37: 271-293, 1997.
49. Shimomura, Y. Regulation of branched-chain α -keto acid dehydrogenase complex in rat liver and skeletal muscle by exercise and nutrition. In "Alpha-Keto Acid Dehydrogenase Complexes" (Patel, M.S., Roche, T.E., and Harris, R.A., eds.), pp. 177-186, Birkhäuser Verlag, Basel, 1996.
50. Jaskiewicz, J., Zhao, Y., Hawes, J.W., Shimomura, Y., Crabb, D.W., and Harris, R.A. Catabolism of isobutyrate by colonocytes. **Arch. Biochem. Biophys.** 327: 265-270, 1996.
51. Hawes, J.W., Jaskiewicz, J., Shimomura, Y., Huang, B., Bunting, J., Harper, E.T., and Harris, R.A. Primary structure and tissue-specific expression of human β -hydroxyisobutyryl-coenzyme A hydrolase. **J. Biol. Chem.** 271: 26430-26434, 1996.

52. Taniguchi, K., Nonami, T., Nakao, A., Harada, A., Kurokawa, T., Sugiyama, S., Fujitsuka, N., Shimomura, Y., Hutson, S.M., Harris, R.A., and Takagi, H. The valine catabolic pathway in human liver: Effect of cirrhosis on enzyme activities. **Hepatology** 24: 1395-1398, 1996.
53. Popov, K.M., Zhao, Y., Shimomura, Y., Jaskiewicz, J., Kedishvili, N.Y., Irwin, J., Goodwin, G.W., and Harris, R.A. Dietary control and tissue specific expression of branched-chain α -ketoacid dehydrogenase kinase. **Arch. Biochem. Biophys.** 316: 148-154, 1995.
54. Ooiwa, T., Goto, H., Tsukamoto, Y., Hayakawa, T., Sugiyama, S., Fujitsuka, N., and Shimomura, Y. Regulation of valine catabolism in canine tissues: tissue distributions of branched-chain aminotransferase and 2-oxo acid dehydrogenase complex, methacrylyl-CoA hydratase and 3-hydroxyisobutyryl-CoA hydrolase. **Biochim. Biophys. Acta** 1243: 216-220, 1995.
55. Fujii, H., Tokuyama, K., Suzuki, M., Popov, K.M., Zhao, Y., Harris, R.A., Nakai, N., Murakami, T., and Shimomura, Y. Regulation by physical training of enzyme activity and gene expression of branched-chain 2-oxo acid dehydrogenase complex in rat skeletal muscle. **Biochim. Biophys. Acta** 1243: 277-281, 1995.
56. Shimomura, Y., Fujii, H., Suzuki, M., Murakami, T., Fujitsuka, N., and Nakai, N. Branched-chain α -keto acid dehydrogenase complex in rat skeletal muscle: Regulation of the activity and gene expression by nutrition and physical exercise. **J. Nutr.** 125: 1762S-1765S, 1995.
57. Harris, R.A., Popov, K.M., Zhao, Y., Kedishvili, N.Y., Shimomura, Y., and Crabb, D.W. A new family of protein kinases - The mitochondrial protein kinases. **Advan. Enzyme Regul.** 35: 147-162, 1995.
58. Kanamori, S., Sugiyama, S., Goto, H., Hayakawa, T., Shimomura, Y., and Ozawa, T. Effects of dietary fiber on dimethylhydrazine-induced changes in prostanoid concentrations in rat colonic mucosa. **Clin. Exp. Pharmacol. Physiol.** 22: 739-742, 1995.
59. Nonami, T., Taniguchi, K., Kurokawa, T., Kasai, Y., Takagi, H., Sugiyama, S., Shimomura, Y., and Hutson, S.M. Low activity of branched-chain α -keto acid dehydrogenase complex in human liver. **Am. J. Clin. Nutr.** 62: 1023, 1995.
60. Frey, N., Christen, U., Jenö, P., Yeaman, S.J., Shimomura, Y., Kenna, J.G., Gandolfi, A.J., Ranek, L., and Gut, J. The lipoic acid containing components of the 2-oxoacid dehydrogenase complexes mimic trifluoroacetylated proteins and are autoantigens associated with halothane hepatitis. **Chem. Res. Toxicol.** 8: 736-746, 1995.
61. Hawes, J.W., Schnepf, R.J., Jenkins, A.E., Shimomura, Y., Popov, K.M., and Harris, R.A. Roles of amino acid residues surrounding phosphorylation site 1 of branched-chain α -ketoacid dehydrogenase (BCKDH) in catalysis and phosphorylation site recognition by BCKDH kinase. **J. Biol. Chem.** 270: 31071-31076, 1995.
62. Zhao, Y., Popov, K.M., Shimomura, Y., Kedishvili, N.Y., Jaskiewicz, J., Kuntz, M.J., Kain, J., Zhang, B., and Harris, R.A. Effect of dietary protein on the liver content and subunit composition of the branched-chain α -ketoacid dehydrogenase complex. **Arch. Biochem. Biophys.** 308: 446-453, 1994.
63. Fujii, H., Shimomura, Y., Tokuyama, K., and Suzuki, M. Modulation of branched-chain 2-oxo acid dehydrogenase complex activity in rat skeletal muscle by endurance training. **Biochim. Biophys. Acta** 1199: 130-136, 1994.
64. Shimomura, Y., Murakami, T., Fujitsuka, N., Nakai, N., Sato, Y., Sugiyama, S., Shimomura, N., Irwin, J., Hawes, J.W., and Harris, R.A. Purification and partial characterization of 3-hydroxyisobutyryl-coenzyme A hydrolase of rat liver. **J. Biol. Chem.** 269: 14248-14253, 1994.
65. Zhao, Y., Hawes, J.W., Popov, K.M., Jaskiewicz, J., Shimomura, Y., Crabb, D.W., and Harris, R.A. Site-directed mutagenesis of phosphorylation sites of the branched chain α -ketoacid dehydrogenase complex. **J. Biol. Chem.** 269: 18583-18587, 1994.
66. Murakami, T., Shimomura, Y., Fujitsuka, N., Nakai, N., Sugiyama, S., Ozawa, T., Sokabe, M., Horai, S., Tokuyama, K., and Suzuki, M. Enzymatic and genetic adaptation of soleus muscle mitochondria to physical training in rats. **Am. J. Physiol.** 267: E388-E395, 1994.
67. Harris, R.A., Popov, K.M., Zhao, Y., and Shimomura, Y. Regulation of branched-chain amino acid catabolism. **J. Nutr.** 124: 1499S-1502S, 1994.
68. Harris, R.A., Popov, K.M., Kedishvili, N.Y., Zhao, Y., Shimomura, Y., Robbins, B., and Crabb, D.W. Molecular cloning of the branched-chain α -ketoacid dehydrogenase kinase and the CoA-dependent methylmalonate semialdehyde dehydrogenase. **Advan. Enzyme Regul.** 33:

- 255-265, 1993.
69. Shimomura, Y., Fujii, H., Suzuki, M., Fujitsuka, N., Naoi, M., Sugiyama, S., and Harris, R.A. Branched-chain 2-oxo acid dehydrogenase complex activation by tetanic contractions in rat skeletal muscle. **Biochim. Biophys. Acta** 1157: 290-296, 1993.
 70. Popov, K.M., Kedishvili, N.Y., Zhao, Y., Shimomura, Y., Crabb, D.W., and Harris, R.A. Primary structure of pyruvate dehydrogenase kinase establishes a new family of eukaryotic protein kinases. **J. Biol. Chem.** 268, 26602-26606, 1993.
 71. Harris, R.A., Popov, K.M., Shimomura, Y., Zhao, Y., Jaskiewicz, J., Nanaumi, N., and Suzuki, M. Purification, characterization, regulation and molecular cloning of mitochondrial protein kinases. **Advan. Enzyme Regul.** 32: 267-284, 1992.
 72. Shimomura, Y., Kotsuka, H., Saitoh, S., and Suzuki, M. Effects of exercise and nutrition on branched-chain amino acid metabolism: Activation of branched-chain alpha-ketoacid dehydrogenase complex by exercise and effect of high-fat diet intake on the activation of the enzyme complex. **Medicine and Sport Science** (Karger, Basel) vol. 37 "Integration of Medical and Sports Sciences", pp. 342-348, 1992.
 73. Harris, R.A., Shimomura, Y., Popov, K.M., Zhao, Y., Hu, H., and Crabb, D.W. Regulation of hepatic branched-chain amino acid catabolism. In "Regulation of Hepatic Function" (Grunnet, N., and Quistorff, B., eds.), pp. 374-385, Munksgaard, Copenhagen, 1991.
 74. Shimomura, Y., Nanaumi, N., Suzuki, M., and Harris, R.A. Immunochemical identification of branched-chain 2-oxo acid dehydrogenase kinase. **FEBS Lett.** 288: 95-97, 1991.
 75. Nanaumi, N., Shimomura, Y., and Suzuki, M. Branched-chain 2-oxoacid dehydrogenase kinase activity is regulated by alteration of protein thiol groups. **Biochem. Int.** 25: 137-141, 1991.
 76. Popov, K.M., Shimomura, Y., and Harris, R.A. Purification and comparative study of the kinases specific for branched chain α -ketoacid dehydrogenase and pyruvate dehydrogenase. **Protein Expression and Purification** 2: 278-286, 1991.
 77. Shimomura, Y., Suzuki, T., Saitoh, S., Tasaki, Y., Harris, R.A., and Suzuki, M. Activation of branched-chain α -keto acid dehydrogenase complex by exercise: Effect of high-fat diet intake. **J. Appl. Physiol.** 68: 161-165, 1990.
 78. Harris, R.A., Zhang, B., Goodwin, G.W., Kuntz, M.J., Shimomura, Y., Rougraff, P., Dexter, P., Zhao, Y., Gibson, R., and Crabb, D.W. Regulation of the branched-chain α -ketoacid dehydrogenase and elucidation of a molecular basis for maple syrup urine disease. **Advan. Enzyme Regul.** 30: 245-263, 1990.
 79. Harris, R.A., Goodwin, G.W., Paxton, R., Dexter, P., Powell, S.M., Zhang, B., Shimomura, Y., and Gibson, R. Nutritional and hormonal regulation of the activity state of hepatic branched-chain α -keto acid dehydrogenase complex. **The Annals of the New York Academy of Sciences** 573: 306-313, 1989.
 80. Shimomura, Y., Kuntz, M.J., Suzuki, M., Ozawa, T., and Harris, R.A. Monovalent cations and inorganic phosphate alter branched-chain α -ketoacid dehydrogenase-kinase activity and inhibitor sensitivity. **Arch. Biochem. Biophys.** 266: 210-218, 1988.
 81. Zhang, B., Paxton, R., Goodwin, G.W., Shimomura, Y., and Harris, R.A. Preservation of the activity state of hepatic branched-chain 2-oxo acid dehydrogenase during the isolation of mitochondria. **Biochem. J.** 246: 625-631, 1987.
 82. Shimomura, Y., Paxton, R., Ozawa, T., and Harris, R.A. (1987) Purification of branched chain α -ketoacid dehydrogenase complex from rat liver. **Anal. Biochem.** 163: 74-78.
 83. Harris, R.A., Paxton, R., Goodwin, G.W., Kuntz, M.J., and Shimomura, Y. Regulation of branched-chain amino acid metabolism. **Biochem. Soc. Trans.** 14: 1005-1008, 1986.

(3) 過去5年間の本学会での活動状況

<学会役員等>

- 平成18年度～平成21年度 支部選出理事
- 平成20年度～平成21年度 庶務担当理事
- 平成18年度～平成21年度 参与
- 平成22年度～現在 評議員
- 平成16年度～現在 JNSV誌編集委員
- 平成22年度～現在 日本栄養・食糧学会誌編集委員
- 平成22年度～現在 新公益法人制度対応WG委員
- 平成22年度～現在 第12回アジア栄養会議(2015ACN)組織委員

<学会大会の座長、シンポジスト>

- 平成18、19、22年度 学会大会の座長
- 平成21年度 学会大会シンポジウム-4「アミノ酸の新しい機能とこれからの展開」のシンポジスト

(4) 特記事項

平成13年度

味の素賞 BCAA 基礎研究賞