

Tetsuya Hosooka, MD, PhD

Education

1994: M.D. in Tokushima University School of Medicine.

2002: Ph.D. in Kobe University Graduate School of Medicine.

Employment

2021-Present: Associate Professor, Department of Nutrition and Life Sciences, School of Food and Nutritional Sciences, and Graduate School of Integrated Pharmaceutical and Nutritional Sciences, University of Shizuoka.

2021-Present: Visiting Associate Professor, Division of Diabetes and Endocrinology, Kobe University Graduate School of Medicine.

2019-2021: Associate Professor, Division of Development of Advanced Therapy for Metabolic Disease, Kobe University Graduate School of Medicine.

2010-2019: Assistant Professor, Division of Diabetes and Endocrinology, Kobe University Graduate School of Medicine.

2008-2010: Postdoctoral Fellow, Division of Endocrinology, Diabetes, and Metabolism, Department of Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School.

2007: COE Postdoctoral Fellow, Division of Diabetes and Endocrinology, Kobe University Graduate School of Medicine.

2002-2007: Postdoctoral Fellow, Division of Diabetes and Endocrinology, Kobe University Graduate School of Medicine.

1994-1998: Resident, Kobe Medical Center, Kobe Rosai Hospital, and Suma Red Cross Hospital.

Representative publications

1. EMPA-KIDNEY Collaborative Group. Effects of empagliflozin on progression of chronic kidney disease: a prespecified secondary analysis from the empa-kidney trial. *Lancet Diabetes Endocrinol.* 12: 39-50, 2024.
2. EMPA-KIDNEY Collaborative Group. Impact of primary kidney disease on the effects of empagliflozin in patients with chronic kidney disease:

secondary analyses of the EMPA-KIDNEY trial. *Lancet Diabetes Endocrinol.* 12: 51-60, 2024.

3. Kasahara N, Imi Y, Amano R, Shinohara M, Okada K, Hosokawa Y, Imamori M, Tomimoto C, Kunisawa J, Kishino S, Ogawa J, Ogawa W, Hosooka T (corresponding author). A gut microbial metabolite of linoleic acid ameliorates liver fibrosis by inhibiting TGF- β signaling in hepatic stellate cells. *Sci Rep.* 13: 18983, 2023.
4. Hosokawa Y, Hosooka T (corresponding author), Imamori M, Yamaguchi K, Itoh Y, Ogawa W. Adipose tissue insulin resistance exacerbates liver inflammation and fibrosis in a diet-induced NASH model. *Hepatol Commun,* 7: e0161, 2023.
5. Kanagaki S, Tsutsui Y, Kobayashi N, Komine T, Ito M, Akasaka Y, Nagasawa M, Ide T, Omae N, Nakao K, Rembutsu M, Iwago M, Yonezawa A, Hosokawa Y, Hosooka T, Ogawa W, Murakami K. Activation of AMP-activated protein kinase (AMPK) by a small-molecule compound that inhibits AMPK interaction with prohibitins. *iScience,* 26: 106293, 2023.
6. The EMPA-KIDNEY Collaborative Group; Herrington WG, Staplin N, Wanner C, Green JB, Hauske SJ, Emberson JR, Preiss D, Judge P, Mayne KJ, Ng SYA, Sammons E, Zhu D, Hill M, Stevens W, Wallendszus K, Brenner S, Cheung AK, Liu ZH, Li J, Hooi LS, Liu W, Kadowaki T, Nangaku M, Levin A, Cherney D, Maggioni AP, Pontremoli R, Deo R, Goto S, Rossello X, Tuttle KR, Steubl D, Petrini M, Massey D, Eilbracht J, Brueckmann M, Landray MJ, Baigent C, Haynes R. Empagliflozin in Patients with Chronic Kidney Disease. *N Engl J Med.* 388: 117-127, 2023.
7. Hirata Y, Nomura K, Kato D, Tachibana Y, Niikura T, Uchiyama K, Hosooka T, Fukui T, Oe K, Kuroda R, Hara Y, Adachi T, Shibasaki K, Wake H, Ogawa W. A Piezo1–KLF15–IL-6 axis mediates immobilization-induced muscle atrophy. *J Clin Invest.* 132: 1-13, 2022.
8. Yoshida N, Yamashita T, Osone T, Hosooka T, Shinohara M, Kitahama S, Sasaki K, Sasaki D, Yoneshiro T, Suzuki T, Emoto T, Saito Y, Ozawa G, Hirota Y, Kitaura Y, Shimomura Y, Okamatsu-Ogura Y, Saito M, Kondo

- A, Kajimura S, Inagaki T, Ogawa W, Yamada T, Hirata KI. Bacteroides spp. promotes branched-chain amino acid catabolism in brown fat and inhibits obesity. *iScience*, 24: 103342, 2021.
9. Kuramoto N, Nomura K, Kohno D, Kitamura T, Karsenty G, Hosooka T, Ogawa W. Role of PDK1 in skeletal muscle hypertrophy induced by mechanical load. *Sci Rep*. 11: 3447, 2021.
 10. Nabatame Y, Hosooka T (co-first author), Aoki C, Hosokawa Y, Imamori M, Tamori Y, Okamatsu-Ogura Y, Yoneshiro T, Kajimura S, Saito M, Ogawa W. Kruppel-like factor 15 regulates fuel switching between glucose and fatty acids in brown adipocytes. *J Diabetes Investig*. 12: 1144-1151, 2021.
 11. Hosooka T, Hosokawa Y, Matsugi K, Shinohara M, Senga Y, Tamori Y, Aoki C, Matsui S, Sasaki T, Kitamura T, Kuroda M, Sakaue H, Nomura K, Yoshino K, Nabatame Y, Itoh Y, Yamaguchi K, Hayashi Y, Nakae J, Accili D, Yokomizo T, Seino S, Kasuga M, Ogawa W. The PDK1-FoxO1 signaling in adipocytes controls systemic insulin sensitivity through the 5-lipoxygenase-leukotriene B4 axis. *Proc Natl Acad Sci USA*. 117: 11674-11684, 2020.
 12. Hirata Y, Nomura K, Senga Y, Okada Y, Kobayashi K, Okamoto S, Minokoshi Y, Imamura M, Takeda S, Hosooka T, Ogawa W. Hyperglycemia induces skeletal muscle atrophy via a WWP1/KLF15 axis. *JCI Insight*. 4: e124952, 2019.
 13. Hosooka T, Ogawa W. A novel role for the cell cycle regulatory complex cyclin D1-CDK4 in gluconeogenesis. *J Diabetes Invest*. 7: 27-8, 2016.
 14. Ijuin T, Hosooka T, Takenawa T. Phosphatidylinositol 3,4,5-trisphosphate phosphatase SKIP links endoplasmic reticulum stress in skeletal muscle to insulin resistance. *Mol Cell Biol*. 36: 108-18, 2015.
 15. Asahara S, Etoh H, Inoue H, Teruyama K, Shibutani Y, Ihara Y, Kawada Y, Bartolome A, Hashimoto N, Matsuda T, Koyanagi-Kimura M, Kanno A, Hirota Y, Hosooka T, Nagashima K, Nishimura W, Inoue H, Matsumoto M, Higgins MJ, Yasuda K, Inagaki N, Seino S, Kasuga M, Kido Y. Paternal allelic mutation at the *Kcnq1* locus reduces pancreatic β -cell mass by

- epigenetic modification of Cdkn1c. *Proc Natl Acad Sci U S A*. 112: 8332-7, 2015.
16. Hosooka T, Nomura K, Ogawa W. VEGF-B as a therapeutic target to prevent ectopic fat deposition. *J Diabet Invest*. 4:525-527, 2013.
 17. Matsubara T, Mita A, Minami K, Hosooka T, Kitazawa S, Takahashi K, Tamori Y, Yokoi N, Watanabe M, Matsuo E, Nishimura O, Seino S. PGRN is a key adipokine mediating high fat diet-induced insulin resistance and obesity through IL-6 in adipose tissue. *Cell Metab*. 15: 38-50, 2012.
 18. Norseen J, Hosooka T (co-first author), Hammarstedt A, Yore MM, Kant S, Aryal P, Kiernan UA, Phillips DA, Maruyama H, Kraus BJ, Usheva A, Davis RJ, Smith U, Kahn BB. Retinol-binding protein 4 inhibits insulin signaling in adipocytes by inducing proinflammatory cytokines in macrophages through a c-jun N-terminal kinase- and toll-like receptor 4-dependent and retinol-independent mechanism. *Mol Cell Biol*. 32: 2010-9, 2012.
 19. Sakai M, Matsumoto M, Tujimura T, Yongheng C, Noguchi T, Inagaki K, Inoue H, Hosooka T, Takazawa K, Kido Y, Yasuda K, Hiramatsu R, Matsuki Y, Kasuga M. CITED2 links hormonal signaling to PGC-1alpha acetylation in the regulation of gluconeogenesis. *Nat Med*. 18: 612-7, 2012.
 20. Shimizu S, Hosooka T, Matsuda T, Asahara S, Koyanagi-Kimura M, Kanno A, Bartolome A, Etoh H, Fuchita M, Teruyama K, Takahashi H, Inoue H, Mieda Y, Hashimoto N, Seino S, Kido Y. DPP4 inhibitor vildagliptin preserves β -cell mass through amelioration of endoplasmic reticulum stress in C/EBP β transgenic mice. *J Mol Endocrinol*. 49: 125-35, 2012.
 21. Matsuda T, Kido Y, Asahara S, Kaisho T, Tanaka T, Hashimoto N, Shigeyama Y, Takeda A, Inoue T, Shibutani Y, Koyanagi M, Hosooka T, Matsumoto M, Inoue H, Uchida T, Koike M, Uchiyama Y, Akira S, Kasuga M. Ablation of C/EBPbeta alleviates ER stress and pancreatic beta cell failure through the GRP78 chaperone in mice. *J Clin Invest*. 120: 115-26, 2010.
 22. 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, Kasuga M. Muscle-specific overexpression of heparin-binding epidermal growth factor-like growth factor increases peripheral glucose disposal and insulin sensitivity. *Endocrinology* 150: 2683-91, 2009.
23. Hosooka T, Noguchi T, Kotani K, Nakamura T, Sakaue H, Inoue H, Ogawa W, Tobimatsu K, Takazawa K, Sakai M, Matsuki Y, Hiramatsu R, Yasuda T, Lazar MA, Yamanashi Y, Kasuga M. Dok1 mediates high-fat diet-induced adipocyte hypertrophy and obesity through modulation of PPAR-gamma phosphorylation. *Nat Med.* 14: 188-93, 2008.
24. Ogura T, Noguchi T, Murai-Takebe R, Hosooka T, Honma N, Kasuga M. Resistance of B16 melanoma cells to CD47-induced negative regulation of motility as a result of aberrant N-glycosylation of SHPS-1. *J Biol Chem.* 279: 13711-20, 2004.
25. Takada T, Noguchi T, Inagaki K, Hosooka T, Fukunaga K, Yamao T, Ogawa W, Matozaki T, Kasuga M. Induction of apoptosis by stomach cancer-associated protein-tyrosine phosphatase-1. *J Biol Chem.* 277: 34359-66, 2002.
26. Hosooka T, Noguchi T, Nagai H, Horikawa T, Matozaki T, Ichihashi M, Kasuga M. Inhibition of the motility and growth of B16F10 mouse melanoma cells by dominant negative mutants of Dok-1. *Mol Cell Biol.* 2001. 21: 5437-46.
27. Inagaki K, Yamao T, Noguchi T, Matozaki T, Fukunaga K, Takada T, Hosooka T, Akira S, Kasuga M. SHPS-1 regulates integrin-mediated cytoskeletal reorganization and cell motility. *EMBO J.* 19: 6721-31, 2000.