Metabolism and Endocrinology

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Major Scientific Interests of the Group

We have been working to understand the molecular mechanisms of energy metabolism using the newest technologies, such as molecular and cellular biology, gene-engineered animals, genome informatics and trans-omics including lipidomics. We especially focus on lipid metabolism with our original molecular targets: SREBPs, CREBH, Elovl6, CtBP2, and KLF15 (see details in each section) develop new therapeutic approaches for preventing obesity, diabetes, and cardiovascular disease. We reveal that these factors regulate organ lipids in both quantity and quality aspects and energy metabolism, and thus, play pivotal roles in a wide variety of biological and pathological events. Our lab motto is “BREAK the DOGMA”. We always try to open up a new world of science with pieces of novel wisdom to contribute to future therapy for inflammation, cancer, and brain sciences beyond endocrinological and metabolic diseases.

Projects for Regular Students in Doctoral or Master’s Programs

1) Energy metabolism and transcription factors with our main target factors: SREBPs, CREBH, Elovl6, CtBP2, and KLF15 relating to the following projects.
2) Lipid metabolism for various metabolic diseases
3) Pathogenic mechanisms and treatment of diabetes
4) Pathogenic mechanisms and treatment of atherosclerosis

Study Programs for Short Stay Students (one week – one trimester)

1) Transfection and Luciferase assay for analyzing the function of transcription factors
2) Experimental procedures for mouse metabolic disease model. Petting obesity mice and measure blood sugar.

Selected Publications

1) Shimano H, et al. SREBP-regulated lipid metabolism: convergent physiology - divergent pathophysiology. ***Nat Rev Endocrinol.*** **2017** Dec; 13(12):710-730.
2) Oishi Y, et al. SREBP1 Contributes to Resolution of Pro-inflammatory TLR4 Signaling by Reprogramming Fatty Acid Metabolism. ***Cell Metab***. 2017 Feb 7; 25(2): 412-427
3) Zhao H, et al. Elovl6 Deficiency Improves Glycemic Control in Diabetic db/db Mice by Expanding β-Cell Mass and Increasing Insulin Secretory Capacity. ***Diabetes***. 2017 Jul; 66(7): 1833-1846.

4) Takeuchi Y, et al. KLF15 Enables Rapid Switching between Lipogenesis and Gluconeogenesis during Fasting. ***Cell Rep***. **2016** Aug 30; 16(9): 2373-2386.
5) Nakagawa Y, et al. Hepatic CREB3L3 Controls Whole-Body Energy Homeostasis and Improves Obesity and Diabetes. ***Endocrinology***. **2014** Dec; 155(12): 4706-4719.
6) Sunaga H, et al. Deranged fatty acid composition causes pulmonary fibrosis in Elovl6-deficient mice. ***Nat Commun***. **2013**; 4: 2563.
7) Izumida Y, et al. Glycogen shortage during fasting triggers liver-brain-adipose neurocircuitry to facilitate fat utilization. ***Nat Commun***. **2013**; 4: 2316.
8) Matsuzaka T, et al. Elovl6 promotes nonalcoholic steatohepatitis in mice and humans. ***Hepatology***. **2012** Dec; 56(6): 2199-2208.
9) Matsuzaka T, et al. Crucial role of a long-chain fatty acid elongase, Elovl6, in obesity-induced insulin resistance. ***Nat Med*** 2007 Oct; 13(10): 1193-1202.
10) Kato T, et al. Granuphilin is activated by SREBP-1c and involved in impaired insulin secretion in diabetic mice. ***Cell Metab*** 4(2): 143-54, 2006 Aug
11) Nakagawa Y, et al. TFE3 transcriptionally activates hepatic IRS-2, participates in insulin-signaling and , ameliorates diabetes. ***Nat Med*** 12(1): 107-13, 2006 Jan__
12) Ide T, et al. SREBPs suppress IRS-2-mediated insulin signaling in the liver. ***Nature Cell Biology*** 6(4): 351-7, 2004 Apr