

Lack of TRPV2 impairs thermogenesis in mouse brown adipose tissue

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WT

TRPV2KO



47.4 ± 0.9 g

57.4 ± 1.7 g

Representative pictures of WT and TRPV2KO mice after high fat diet treatment for 8-weeks. The average body weights of WT and TRPV2KO mice were 47.4 ± 0.9 g and 57.4 ± 1.7 g, respectively, after high fat diet treatment for 8-weeks.

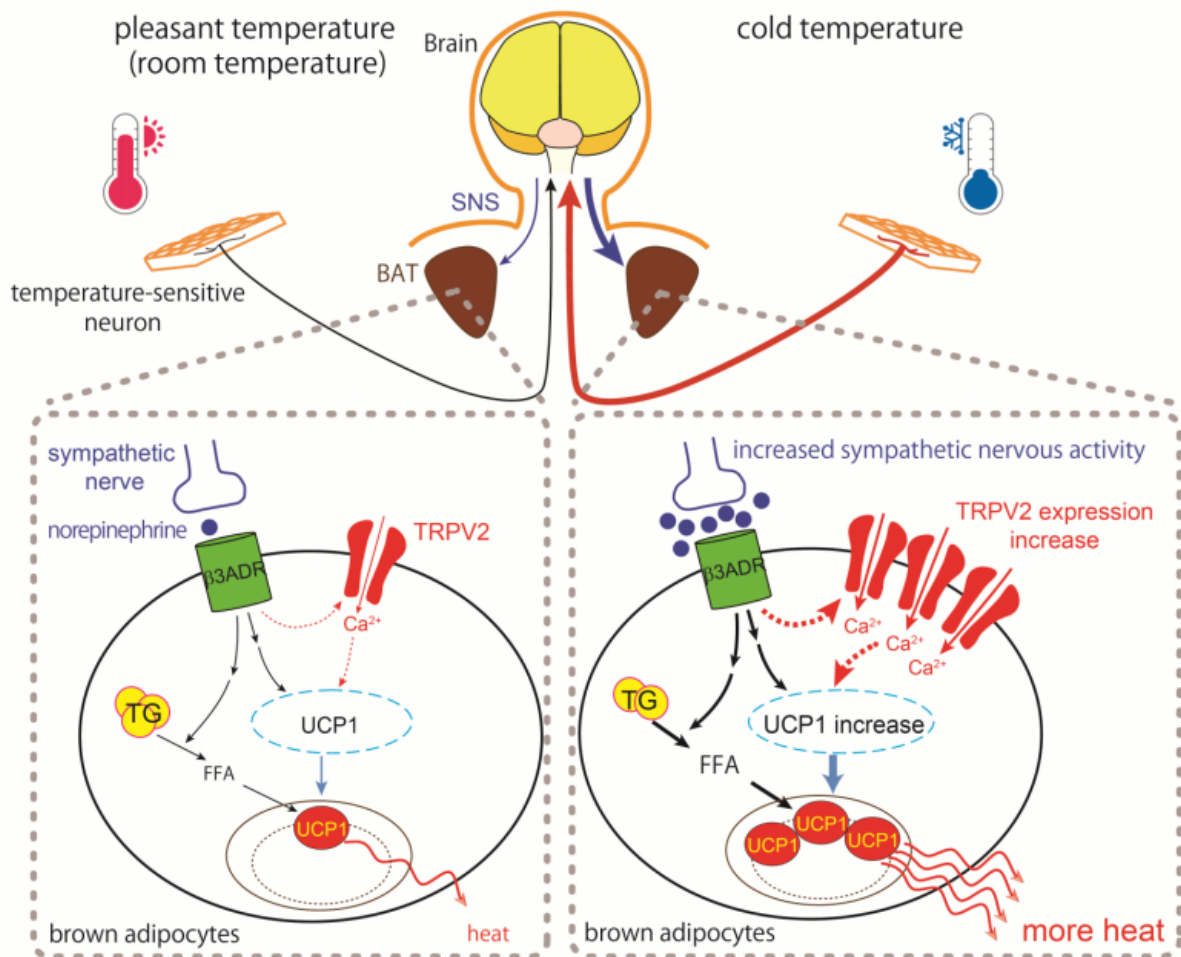
Credit: NIPS/NINS

Brown adipose tissue (BAT), a major site for mammalian non-shivering thermogenesis, could be a target for prevention and treatment of human obesity. Transient receptor potential vanilloid 2 (TRPV2), a Ca²⁺-permeable cation channel, plays vital roles in the regulation of various cellular functions. Professor Makoto Tominaga, Assistant Professor Kunitoshi Uchida and Postdoctoral Research Fellow Wuping Sun from National Institute for Physiological Sciences, Professor Teruo Kawada from Kyoto University, and Professor Yuko Iwata, Professor Shigeo Wakabayashi from National Cerebral and Cardiovascular Center, and their team members have revealed that lack of TRPV2 impairs thermogenesis in mouse brown adipose tissue. This study was supported by grants from the Japanese Ministry of Education, Culture, Sports, Science and Technology and Takeda Science Foundation, and published online in *EMBO reports* on Feb. 12, 2016.

The research team have successfully developed TRPV2 knockout (TRPV2KO) mice, and demonstrated that TRPV2 is expressed in brown adipocytes and that mRNA levels of thermogenic genes are reduced in both cultured brown adipocytes and BAT from TRPV2 KO mice. The induction of thermogenic genes in response to β -adrenergic receptor stimulation (downstream of the sympathetic nerve activation), which usually causes thermogenesis, is also decreased in TRPV2KO brown adipocytes. In addition, TRPV2KO mice have more [white adipose tissue](#) and larger brown adipocytes, and can not keep constant body temperature of around 37 degree C upon cold exposure at 4 degree C. Furthermore, TRPV2KO mice have increased body weight and fat upon [high fat diet](#) treatment (Figure 1), which can be explained by the low thermogenic ability of TRPV2KO mice. Based on these findings, they conclude that TRPV2 has a role in BAT thermogenesis as shown in the model shown in Figure 2 and could be a target for human obesity therapy.

The novelty of this study

1. Mice lacking TRPV2 show cold intolerance and impaired BAT thermogenesis upon sympathetic nerve activation.
2. Mice lacking TRPV2 are prone to be obese upon high fat diet treatment.



BAT thermogenesis is triggered by the release of norepinephrine from the sympathetic nerve terminals which stimulates β 3-adrenergic receptors, turning on a cascade of intracellular events including production of UCP1, a protein involved in thermogenesis. TRPV2-mediated calcium influx could regulate the thermogenic gene expression. At room temperature, the sympathetic nerve

activity is kept in a resting condition and UCP1 expression level is low which causes less heat production. On the other hand, when cold temperature is detected by peripheral temperature-sensitive nerve endings, sympathetic nervous system could be activated, which leads to norepinephrine release from the sympathetic nerves and activation of β 3-adrenergic receptors. Subsequently, TRPV2 expression is up-regulated and more calcium is influxed via TRPV2, facilitating UCP1 expression and heat production. BAT: brown adipose tissue; FFA: free fatty acids; SNS: sympathetic nervous system; β 3ADR: β 3-adrenergic receptor; TG: triglyceride; UCP1: uncoupling protein 1. Credit: NIPS/NINS

The significance of this study

Mice lacking TRPV2 show impaired BAT thermogenesis and are prone to obesity on high fat diet. Activation of TRPV2 in BAT therefore could be an intriguing approach for [human obesity](#) prevention and treatment.

More information: Lack of TRPV2 impairs thermogenesis in mouse brown adipose tissue. Wuping Sun, Kunitoshi Uchida, Yoshiro Suzuki, Yiming Zhou, Minji Kim, Yasunori Takayama, Nobuyuki Takahashi, Tsuyoshi Goto, Shigeo Wakabayashi, Teruo Kawada, Yuko Iwata and Makoto Tominaga. Published online in *EMBO reports* on Feb. 12, 2016.

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