All the organisms on the earth survive upon detecting and responding to the ambient temperature. The central molecules involved in the temperature detection are so called thermosensitive TRP channels. Thermosensitive TRP channels are composed of 28 channels in 6 subfamilies in mammals and have high calcium permeability. Eleven among them are known to have thermosensitivities. It is believed that cation influx through the ionotropic temperature receptors expressed on the plasma membranes leads to depolarization followed by action potential generation upon activation of voltage-gated sodium channels in the sensory neurons. While thermosensitive TRP channels are involved in a lot of temperature-dependent physiological phenomenon, I would like to focus on the functional interaction between TRP channels and calcium-activated chloride channel, anoctamin 1 (ANO1). TRPV4/ANO1 is involved in the cerebrospinal fluid secretion in mouse choroid plexus epithelial cells. TRPV1, TRPA1/ANO1 interaction is reported to be involved in the enhancement of nociceptive information in mouse sensory neurons. Furthermore, TRPV4/ANO1 interaction is involved in the regulation of saliva and tear secretion in mouse salivary and lacrimal glands. Mice secret saliva to reduce their body temperature, indicating that mice have to produce a lot of saliva when their body temperature is elevated.

Psychological stress-induced sympathetic responses include hyperthermia, tachycardia and hypertension. Wild animals facing with their enemies exhibit these responses to rapidly warm up their body core and facilitate blood circulation for better physical and neural performances, leading to a better chance to survive the "fight or flight" situation. However, humans exposed to intense psychological stressors often suffer from stress symptoms, such as psychogenic fever, recognized as an issue in psychosomatic medicine. We are pursuing the central circuit mechanisms for psychological stress-induced sympathetic responses. Rats given social defeat stress, a sociopsychological stress model, exhibit rapid increases in body temperature, heart rate and blood pressure. In particular, this stress-induced hyperthermia involves sympathetic thermogenesis in brown adipose tissue (BAT). We have revealed that stress activates an excitatory transmission from the dorsomedial hypothalamus (DMH) to the rostral medullary raphe to drive sympathetic outflows to BAT and the heart. Consistently, in vivo optogenetic stimulation of this excitatory pathway elicits sympathetic responses mimicking stress responses. Furthermore, we recently discovered glutamatergic neurons in the prefrontal cortex that transmit stress signals to the DMH. This corticohypothalamic pathway likely mediates the major stress signaling from higher brain regions to the sympathetic nervous system to drive the stress responses.
A common GPCR regulates circadian body temperature in mouse and fly.

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The daily body temperature rhythm (BTR) is basic, essential to maintain homeostasis. BTR is regulated separately from the locomotor activity rhythms, but its molecular basis is largely unknown. While mammals internally produce BTR, the ectotherms, Drosophila exhibit temperature preference rhythm (TPR) behavior, which produces BTR. Here, we demonstrate that Diuretic Hormone 31 receptor (DH31R), mediates TPR during the active phase in Drosophila. DH31R is expressed in the clock cells and its ligand, DH31, acts on the clock cells for mediating TPR. Surprisingly, the mouse homologue of DH31R, calcitonin receptor (CalcR), is expressed in the suprachiasmatic nucleus and mediates body temperature fluctuations during the active phase in mice. Importantly, DH31R and CalcR are not required for coordinating locomotor activity rhythms. Our results provide the first molecular evidences that BTR undergoes regulation distinct from the locomotor activity rhythms and identify DH31R/CalcR as an ancient specific mediator for BTR from ectotherms to endotherms.

Role of the inter-organ neural network from the liver in systemic energy metabolism

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We found that neural signals transmitted from the fatty liver, which enhances the expression of PPAR γ , increase energy consumption in brown adipose tissue (BAT). In addition to the negative feedback mechanism, two other mechanisms are required to maintain fat accumulation at an appropriate level: (1) a mechanism for efficiently storing ingested energy as fat; and; (2) a mechanism to minimize reduction of accumulated fat when energy intake is limited. We have identified the mechanisms described in (1). When liver glucokinase is activated by the excess energy intake, neural signals from the liver are transmitted via the vagus to the brain, which decreases energy expenditure in BAT. In addition, as an example of (2), we found a novel inter-organ neural network from the liver. SGLT2 inhibitors inhibit the reabsorption of urine sugar in the kidneys and produce a state similar to that of low energy intake. When the SGLT2 inhibitors are administered to mice, the level of oxygen consumption is lowered. We found that the reduction of BAT thermogenesis is involved in this mechanism. Selective hepatic vagotomy caused these changes to no longer be observed. These results indicate that neural signals from the liver play an important role in this mechanism. Neural networks from the liver to BAT enable appropriate fat storage and must be advantageous to mammals experiencing frequent starvation, but may cause obesity and make it difficult to recover from it in modern age of plenty.