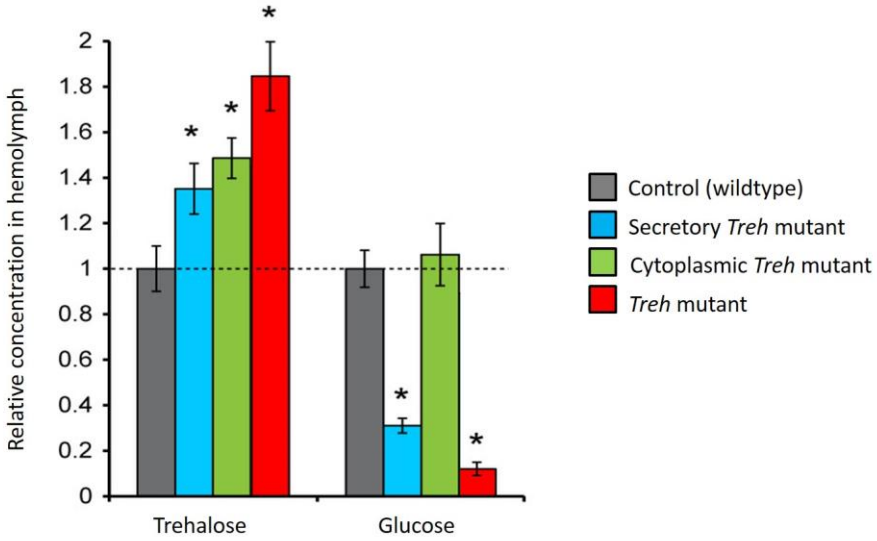
RIKEN Center for Developmental Biology (CDB)
2-2-3 Minatojima minamimachi, Chuo-ku, Kobe 650-0047, Japan

Trehalose important for maintaining body water homeostasis

Sep. 15, 2016–Trehalose is a disaccharide sugar synthesized and used as a source of energy in many plants and insects. In insects, trehalose is the primary sugar compound circulating in the hemolymph (insect circulatory system), and in addition to being an energy source, is thought to play an important role in preventing desiccation due to its stability and chemical inertness. There have been some reports of insects in dry environments having higher levels of trehalose in the hemolymph than their counterparts in other environments. However, many aspects of the physiological role of trehalose and its metabolism remain largely unknown.

Now a new study by CDB student trainee Miki Yoshida of the Laboratory for Growth Control Signaling (Takashi Nishimura, Team Leader) and others reveals the physiological functions of two enzymes involved in trehalose metabolism in *Drosophila*–the trehalose-synthesizing enzyme, trehalose-6-phosphate synthase (Tps1), and the trehalose-hydrolyzing enzyme, trehalase (Treh). They also show the importance of trehalose metabolism for normal growth and development, maintaining systemic water homeostasis, and tolerating desiccation. Their work was published in the online journal, *Scientific Reports*.



Different *Treh* mutants (secretory, cytoplasmic, null) all exhibit higher trehalose levels than wildtype. However, levels of glucose, which is the product of trehalose metabolism, is markedly reduced.

In insects, trehalose is synthesized in the fat body, the insect-equivalent of the mammalian liver, by Tps1, and then released into the hemolymph. Using a *Drosophila Tps1* mutant strain, the lab previously demonstrated that lack of trehalose under starvation or nutrient-deficient conditions has significant effects on growth and viability of the fly (see Science News: February 9, 2015). The Treh enzyme, in contrast to Tps1, functions to breakdown trehalose into two glucose molecules through hydrolysis. Treh is found in two different forms in the body, a secreted form and a cytoplasmic form, due to alternative splicing, but their respective physiological roles remained unclear.

The group began by taking a close look at *Drosophila* carrying mutations in the gene encoding Treh. Using the CRISPER/Cas9 system, they generated different *Treh* mutant strains—for the secreted form, for the cytoplasmic form, and for both forms of Treh. *Treh* mutants for both forms did not survive past pupal stages. Cytoplasmic *Treh* mutants also displayed lethality during pupal stages, whereas secreted *Treh* mutants produced viable adults, indicating that cytoplasmic Treh plays a more critical role in development, especially beyond the pupal stages.

Contact: sciencenews@cdb.riken.jp Fax: +81-78-306-3090
RIKEN CDB, Office for Research Communications

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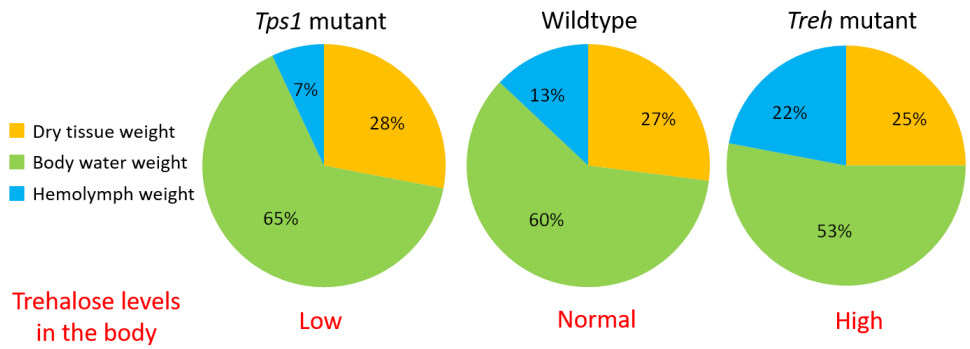

Water content distribution in wildtype, *Tps1* mutant and *Treh* mutant. Relative water content in hemolymph and tissues changes in correlation with fluctuations in trehalose levels.

The team next examined the *Tps1* mutant strain and *Treh* mutant strain to determine the function of trehalose in *Drosophila*. *Tps1* mutants are unable to synthesize trehalose, and consequently have lower levels of trehalose in the body than found in wildtype. *Treh* mutants on the other hand are unable to breakdown trehalose, and thus have higher levels of trehalose than wildtype. They found that both mutants showed markedly reduced levels of glucose, and had lower tolerance for starvation and nutrient-deficient conditions. The group also analyzed the relative water content distribution within the body, and found that when trehalose levels were high, water content increased in the hemolymph but decreased in tissues. Thus, the hemolymph of *Tps1* mutants appeared more viscous than seen in *Treh* mutants. Interestingly, when fly mutants were analyzed for tolerance to desiccation conditions, *Tps1* and *Treh* mutants both showed higher lethality than wildtype, indicating that normal trehalose metabolism as well as high levels of trehalose is essential for protecting the fly from desiccation.

“The hemolymph does not function solely as the circulatory system to transport factors within the body. It also serves as the medium where catabolic reactions take place to produce physiologically important molecules,“ says Nishimura. “Here, we revealed conditions when impairment of Tps1 and Treh, two enzymes that have opposing functions, produce similar phenotypes. Our next step will be carry out a closer analysis of *Treh* mutants, focusing on features specific to this mutant. Mutants with high trehalose levels may be useful as a disease model for diabetes, which is characterized by high sugar levels in the body.”

Science News:
February 9, 2015 (http://www.cdb.riken.jp/en/news/2015/researches/0209_6022.html)

Contact: sciencenews@cdb.riken.jp Fax: +81-78-306-3090
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