Sometimes beneficial, sometimes damaging: The double role of the enzyme chameau

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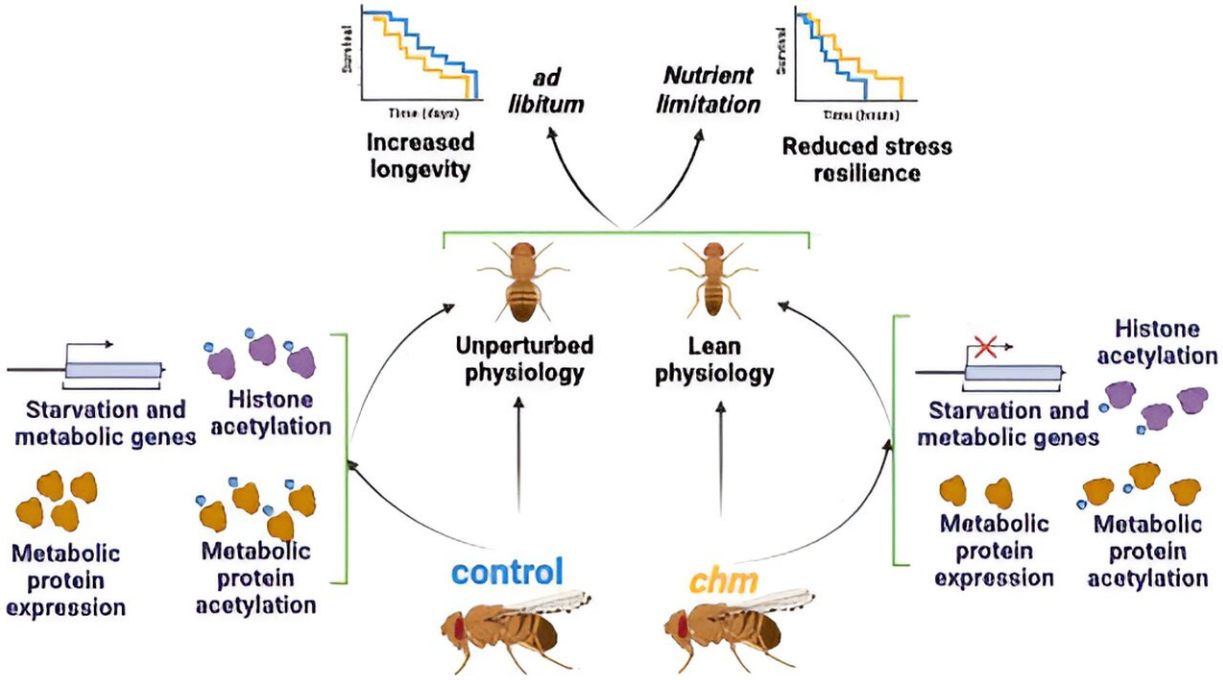

Credit: *EMBO reports* (2023). DOI: 10.15252/embr.202357023

Biologists have discovered why an enzyme is important for the survival of fruit flies, even though it can shorten their lives under certain conditions.

Nothing comes for free—this saying applies very well to the work of

chameau. As researchers led by Axel Imhof from LMU's Biomedical Center Munich (BMC) have demonstrated, the enzyme plays an important role in helping fruit flies to survive periods when food is in short supply. However, this comes at a cost: when there is plenty of food available, chameau has a life-shortening effect. The study is published in the journal *EMBO reports*.

Chameau is an enzyme that chemically modifies proteins, by which it also plays a part in gene regulation. In earlier studies, Imhof and his team had discovered that well-nourished fruit flies live longer if their chameau levels are lowered through mutations. Other researchers had reported a similar effect in mice, when the production of a protein analogous to chameau was reduced.

From an evolutionary perspective, a longer fertile life should lead to more offspring and therefore be favored by evolution. So why does chameau occur in potentially life-shortening quantities? To answer this question, the scientists investigated which mechanisms are influenced by the enzyme.

"The complete absence of chameau results in fatal development defects," says Imhof. "However, we managed to lower the enzyme levels to around a fifth of its normal levels without affecting viability under normal conditions to study it's role in stress response."

Low chameau levels make flies thinner

Their results show that flies with low chameau levels are less well able to deal with hunger. "When flies are starving, their bodies break down storage molecules such as glycogen and fats. With a defect of the enzyme chameau, this process no longer works as effectively," says Imhof. "Flies with normal enzyme levels survived without food up to 40% longer. In the wild, this gives them an advantage, because they can

fly around and search for food during this extra time period."

Furthermore, the scientists observed that flies with very low chameau levels were much thinner than wild types even when fed well. "This means that these flies not only have a problem with the expenditure, but also with the storage of energy," explains Imhof.

Comprehensive molecular analyses revealed that chameau mutations result in a failure to properly regulate the genes and proteins required for energy storage and expenditure. "Based on research with the mouse chameau gene, we believe that similar mechanisms may also exists in vertebrates such as mice and humans" says Imhof. However, this would require further studies.

Adapting to changing environmental conditions

That thin flies live longer under normal conditions but are more sensitive to hunger are essentially two sides of the same coin. As long as there are enough nutrients available, the effects of chameau deficits resemble that of caloric restrictions. "Studies on various organisms have shown that reducing caloric intake can lead to a longer lifespan," says Imhof. When conditions become unfavorable, however, the flies are unable to respond appropriately.

From their findings, the researchers conclude that chameau is important for coping with changing environmental conditions. "As this ability is likely a stronger evolutionary driver than the ability to live a long life, the enzyme has been preserved despite its disadvantages," says Imhof.

More information: Anuroop Venkateswaran Venkatasubramani et al, The fruit fly acetyltransferase chameau promotes starvation resilience at the expense of longevity, *EMBO reports* (2023). DOI: 10.15252/embr.202357023