The role of *Drosophila* insulin-like peptides in nutrient-dependent lifespan and reproduction

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"...will you still feed me when I'm sixty four" (Beatles, 1967)

Background

Dietary restriction, a reduction of food intake without mal-nutrition, extends lifespan and health in many organisms. We know the **Insulin-IGF Signalling** (IIS) pathway is known to be involved in nutrient sensing and ageing in many organisms. **Drosophila insulin-like peptides** (dilps), the most upstream components of IIS, are known to **respond to food** and a triple knock-out (dilp2-3,5Δ) **extends lifespan**. So dilps may be the components mediating nutrient-dependent ageing...

Objective

We investigated the role of dilps in nutrient-altered ageing by determining **lifespan, fecundity** and **brain-dilp expression** of the long-lived **dilp2-3,5 knockout mutant** and its genetic control (wDah) on a range of food types that differed in sugar and yeast concentration.

Figure 1: *Response surfaces of lifespan, fecundity and dilp expression for wDah (left) and dilp2-3,5Δ (right) for the nine food types (50, 100, 200 gr.l sugar/yeast).*

Results (Figure 1)

Dilp2-3,5Δ flies' lifespan and reproduction was still affected by food, but **the response to food changed**. Dilp2-3,5Δ extended lifespan and decreased reproduction.
In control flies, dilp5 expression increased with yeast level. Dilp2 and -3 expression peaked at high yeast / low sugar.
Unlike controls, **dilp6 expression** increased with yeast in nulls.

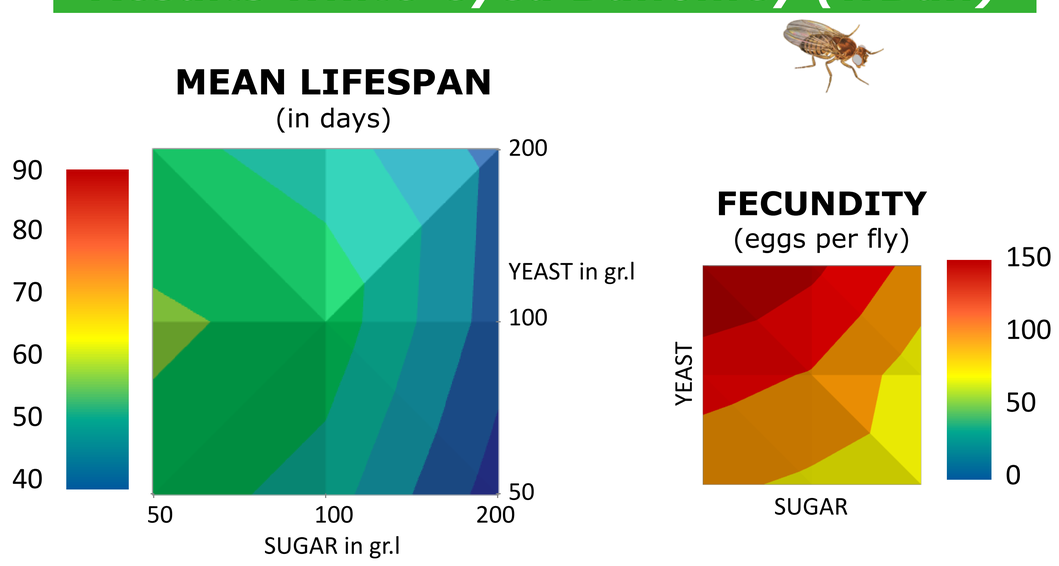
Conclusions

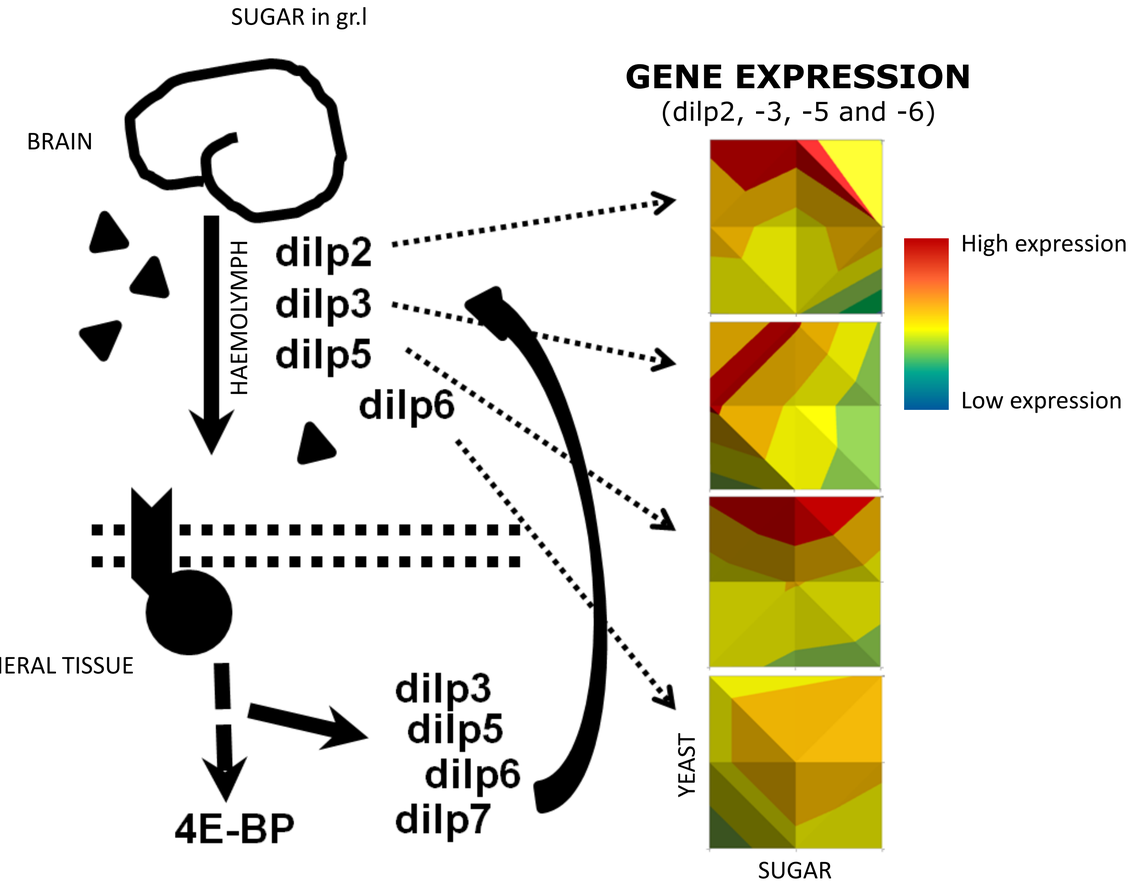
dilp2-3,5 have an important role in ageing as the **knockout increased lifespan on every food type**.
Dilp6 expression may compensate for dilp2-3,5 loss. We can't conclude that dilps solely mediate nutrient-dependent ageing.

Future work

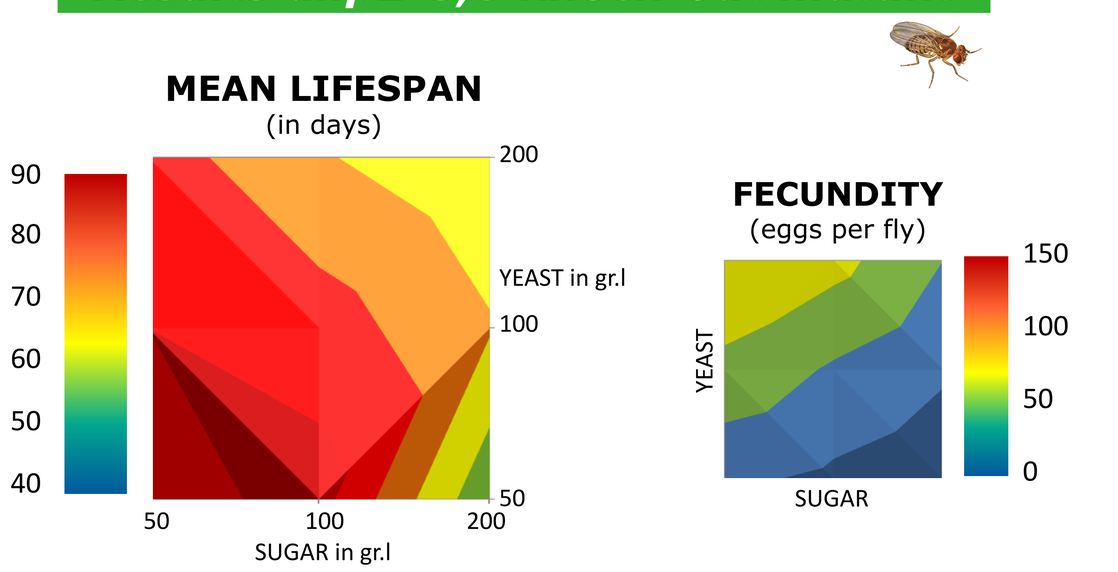
Gene expression of dilps and **4E-BP** (downstream of IIS) in **bodies** to measure the possible effects of 'dilp6 compensation'. If we find a similar response for 4E-BP in dilp2-3,5Δ and wDah, we know dilp6 may compensate for other dilps, or additional pathways are involved in nutrient-dependent ageing.

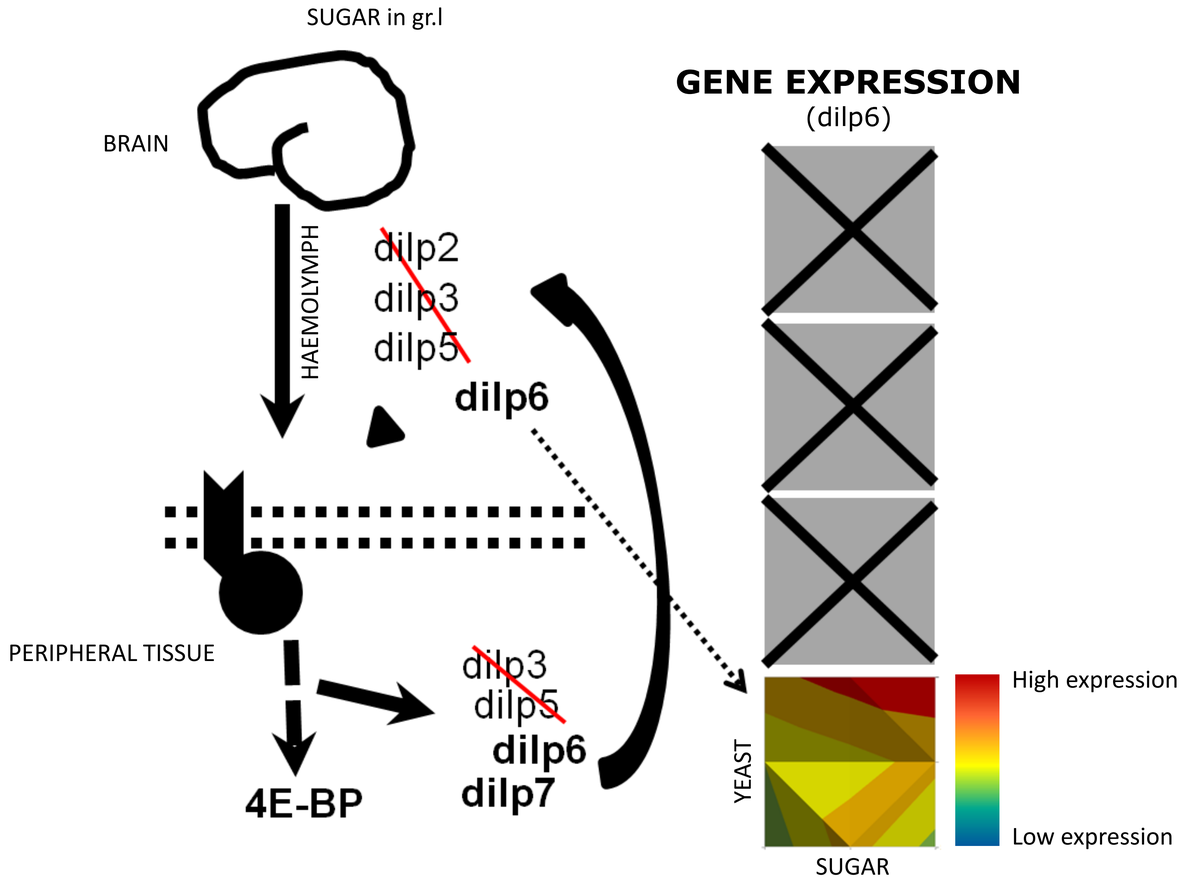
Results white-eyed Dahomey (wDah)





Results dilp2-3,5 knock-out mutant





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