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EVO–DEVO

Plastic flies

A study in *Drosophila melanogaster* shows that variation in how different organs respond to developmental malnutrition is regulated by the expression level of the forkhead transcription factor FOXO. This work suggests that variation in phenotypic plasticity — that is, the ability of a genotype to produce varied phenotypic outcomes, depending on the environment — might have a simple developmental basis.

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Nutritional deficiency during development normally leads to smaller sized adults, and although most body organs shrink in scale to the whole body, some tissues notably do not. In fruitflies in particular, the authors show that male genitalia resist the reduction in size that is caused by dietary restriction: that is, they have low phenotypic plasticity. The basis of variation in nutritional sensitivity between organs is not known, but given the established role of insulin/insulin-like growth factor (IGF) signalling (IIS) in linking nutritional status to growth in all animals, the authors focused on components of this pathway to explain variation in organ plasticity in response to starvation.

The authors' hypothesis was that male genitalia are somehow insensitive to signalling by insulin. But which step in the IIS pathway might be responsible for this effect? First, the authors established that the mechanism was cell-autonomous. One piece of evidence came from observing the consequences of mutations in the gene for the insulin receptor (*Inr*) or its substrate, *chico*, each of which genocopy starvation in well fed larvae. Adult male genitalia of these mutants showed a lower size reduction than other organs did — an effect that, for *Inr*, was caused by a cell-autonomous maintenance in proliferation rate in genitalia compared to other organs.

Second, to identify the position in the IIS pathway that was responsible, the authors genetically perturbed each pathway member downstream of *Inr* and *chico*: only genes that act upstream of the responsible gene would, when mutated, genocopy nutritional starvation and therefore affect the size of genitalia less than they would a control organ (in this case, the wing). This systematic experiment led them to the transcription factor FOXO, a negative growth regulator that is activated when IIS falls. In *foxo* loss-of-function mutants, wings and genitalia are affected to the same degree by nutritional deficiency, hinting that FOXO is required to maintain differences in plasticity between these two organs.

The proposed model is that genitalia are somehow better able to resist activation of FOXO in response to reduced IIS, enabling this organ to grow at a rate that is independent of the amount of IIS and therefore of nutritional status. The authors show that the mechanism by which genitalia resist nutritional stress is by having lower expression levels of *foxo*. Enforcing low *foxo* expression in other imaginal discs was sufficient to confer insulin insensitivity and to lower plasticity to these organs when starved. Conversely, upregulation of *FOXO* in genitalia increased the developmental plasticity of this organ.

Although the generality of the model remains to be explored, this work suggests that variation in plasticity between organs or individuals may be caused by varying the expression of genes that couple nutritional sensing to developmental or behavioural pathways.

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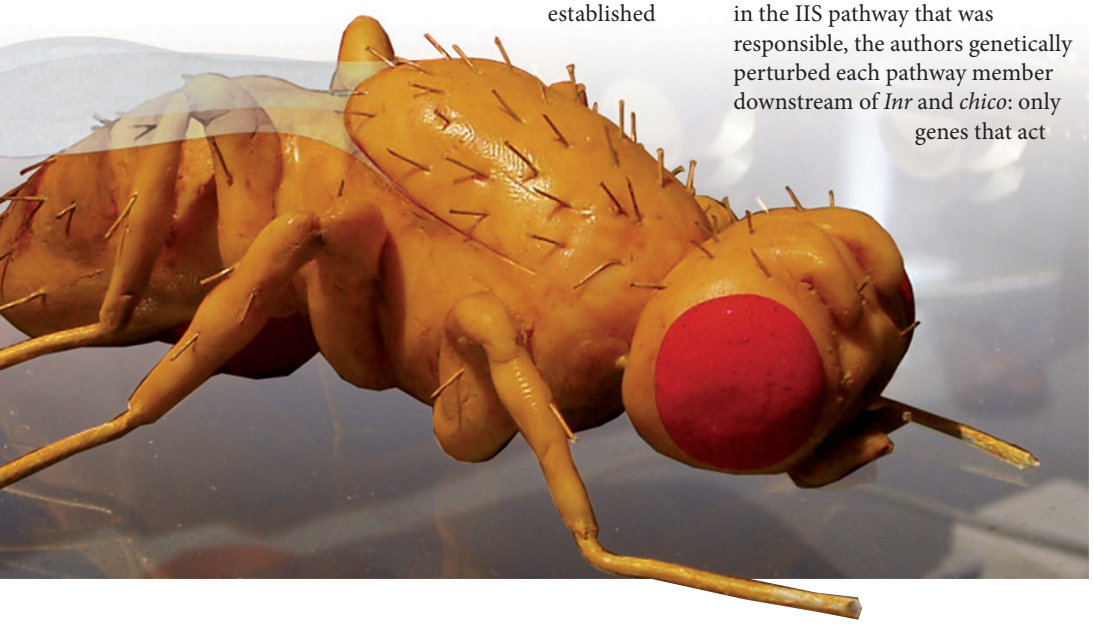

ORIGINAL RESEARCH PAPER Tang, H. Y. *et al.* FOXO regulates organ-specific phenotypic plasticity in *Drosophila*. *PLoS Genet.* **7**, e1002373 (2011)