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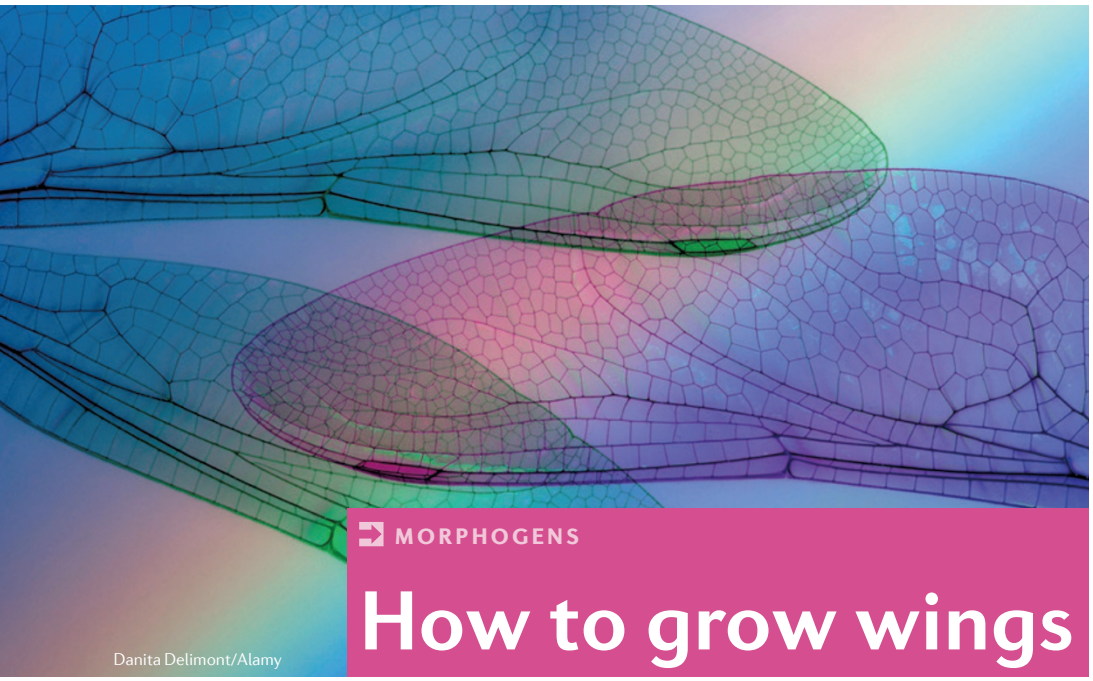

Danita Delimont/Alamy

MORPHOGENS

# How to grow wings

> two independent studies … provide important insights into the mechanism of Dpp-mediated regulation of growth

Decapentaplegic (Dpp), a *Drosophila melanogaster* homologue of the vertebrate bone morphogenetic protein 2/4 (BMP2/4), is known to regulate genes involved in cell proliferation and tissue patterning and is considered a classic morphogen. In the fly wing primordium (the wing disc), Dpp is expressed in a stripe of cells at the anterior–posterior tissue boundary and creates a medially centred gradient, from which the morphogen spreads towards the periphery. For many years, this gradient has served as a model to study how morphogens regulate development of animal tissues. However, although the role of the Dpp gradient in wing patterning is well established, how it affects cell proliferation and tissue growth has been unclear and a subject of debate. Now, two independent studies published in *Nature* provide important insights into the mechanism of Dpp-mediated regulation of growth.

Harmansa *et al.* set out to investigate the requirement of Dpp spreading within the wing disc for proper proliferation and expansion of the tissue. The authors designed a trapping system, whereby morphogen spreading was blocked by its binding to a membrane-targeted nanobody. When expression of the nanobody was induced in cell clones in the wing primordium, Dpp was efficiently trapped on cell surfaces, even when these clones were localized far from the medial morphogen source. This indicated that Dpp efficiently spreads throughout the entire width of the disc. When the expression of the nanobody was induced specifically in the medial source cells, the spreading of Dpp and the expression of Dpp target genes away from the source were blocked. This resulted in both the patterning and the size of the wing blade being greatly affected in the adult fly. Further analysis revealed that upon inhibition of Dpp spreading, growth of the more medial region was strongly affected, whereas the lateral tissue regions could grow at similar rates to the control, suggesting that proliferation of lateral cells is independent of Dpp spreading. Altogether, Harmansa *et al.* provided evidence that spreading of Dpp is necessary to sustain proper proliferation and thus overall growth of the fly wing, but cells in the wing disc have different requirements for Dpp signals, depending on their position within the tissue.

Akiyama and Gibson employed a different strategy to study the role of the Dpp gradient and performed conditional knockout of Dpp expression using the CRISPR–Cas9 strategy. Ubiquitous removal of Dpp largely abolished wing patterning and compromised wing growth, confirming previous data from Dpp mutants. Interestingly, when Dpp expression was abolished specifically in the medial source cells, no major growth defects were observed despite obvious perturbation of Dpp target gene expression throughout the wing disc and defective tissue patterning. These observations suggested that wing disc growth is regulated by an alternative source of Dpp. The authors propose that this source is localized within the anterior wing disc compartment, as the expression of Dpp in this area was necessary and apparently sufficient to sustain normal wing growth. Thus, this study revealed that in the *D. melanogaster* wing disc, the medial Dpp gradient is a crucial regulator of tissue patterning but is not essential for tissue growth.

Collectively, these studies demonstrate that Dpp is indeed an important regulator of *D. melanogaster* wing growth, but they also reveal that the underlying mechanisms are complex and, despite years of research, still poorly understood. It will be important to integrate the results of both studies and formulate a new, revised model of morphogen-dependent tissue growth.

*Paulina Strzyz*

**ORIGINAL ARTICLES** Harmansa, S. *et al.* Dpp spreading is required for medial but not for lateral wing disc growth. *Nature* http://dx.doi.org/10.1038/nature15712 (2015) | Akiyama, T. & Gibson, M. C. Decapentaplegic and growth control in the developing *Drosophila* wing. *Nature* http://dx.doi.org/10.1038/nature15730 (2015)