Regulatory process for organ scaling discovered

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A new study has shed light on the process by which fruit flies develop with their body proportions remaining constant. The study, conducted by the research group of Professor Markus Affolter at the Biozentrum of the University of Basel and Sven Bergmann's group at the Department of Medical Genetics, University of Lausanne, has demonstrated that the morphogen Dpp and the feedback regulator Pentagone are key factors responsible for proportional tissue growth in wings of a fruit fly. This process keeps the body plan of the fruit fly *Drosophila* constant. Their research results, published October 25 in the online, open-access journal *PLoS Biology*, might also be important for organ growth in other organisms.

One of the most interesting and perhaps mysterious questions in developmental biology is to understand how organisms develop from an embryo to an adult with their body proportions remaining constant over generations. External factors such as nutrition and temperature generally impact the overall size of an organism, but leave body proportions unaffected. Fish kept in too small aquaria, for example, just grow proportionally smaller and flies kept under starving conditions have proportionally smaller heads, abdomens, legs and wings. The phenomenon of keeping proportions during growth is called 'scaling' and has been subject of study for decades. Indeed, how scaling is achieved has, until recently, not been very well understood.

In an attempt to solve open questions regarding scaling, Affolter's and Bergmann's research groups have made a large step forward. In the new

study they analyze the scaling process of the *Drosophila* wing; more specifically the insect's wing imaginal disc, the precursor tissue of the adult wing. Using a combination of experimental and mathematical approaches, they could demonstrate that the morphogen called Decapentaplegic (Dpp) plays a central role in regulating and scaling wing growth and patterning via the regulation of Pentagone. A morphogen produces different cellular responses depending on its concentration, and the two groups found that, as the disc grows, the Dpp response expands and scales with the tissue size. Naturally, the morphogen itself needs to be regulated and controlled. In this study, they identify Pentagone, one of Dpp's recently discovered transcriptional targets, as the first negative feedback controller responsible for scaling. Hence, scaling is achieved in the wing due to the feedback loop between the signaling activity of Dpp and its regulator Pentagone. Besides this, Affolter's and Bergmann's groups could also show that scaling is not perfect at all positions during wing disc growth and that scaling of the target gene domains is best where they have a function.

Affolter's and Bergmann's groups used the wing of the fruit fly *Drosophila* as a model to study scaling quantitatively during growth. Similar to the micro-macro link – a term used in social sciences – scaling is defined as the preservation of proportions of gene expression domains with tissue size during growth. In other words, proportions found on the micro-level of gene expression are found on the macro-level of wing formation. "Better insight into the molecular control of scaling will have large consequences for the understanding of how nature has developed such robust body plans", explains Affolter.

More information: Hamaratoglu F, de Lachapelle AM, Pyrowolakis G, Bergmann S, Affolter M (2011) Dpp Signaling Activity Requires Pentagone to Scale with Tissue Size in the Growing Drosophila Wing Imaginal Disc. PLoS Biol 9(10): e1001182. doi:10.1371/journal.pbio.1001182