Nature Reviews Genetics | AOP, published online 10 November 2009; doi:10.1038/nrg2709

DEVELOPMENT

Size control by divide and rule

Size can be controlled at many levels, including the size a cell attains before it divides and the number of cells that form a complete organ. Therefore, as shown by two recent papers, lessons about growth regulation can be learnt both from studies of intrinsic cellular mechanisms and from studies of groups of cells growing together.

The wing imaginal disc of *Drosophila melanogaster* is a useful system for studying growth control, as its growth parameters have been characterized and the expansion of progeny from particular cells (clones) can be observed. In the wing disc, *Minute* (*M*) mutations are dominant mutations that slow the rate of cell division. Clones that are heterozygous for *M* (*M*/+) are outgrown by faster dividing $M^{+/+}$ cells, but the final size of the disc is normal. How is the correct size achieved irrespective of whether cells grow at the same or at different rates? It has been suggested that cell competition is involved, whereby interaction between *M*/+ and $M^{+/+}$ cells triggers apoptosis in the slow-dividing cells.

To test this proposal, Martín and colleagues inhibited apoptosis by forced expression of anti-apoptotic factors in the posterior compartment of the wing disc. They found that the size of $M^{+/+}$ clones in the posterior compartment was the same as in the anterior compartment, in which apoptosis was normal, and that the final size of the disc was normal. They also used a computer simulation that assumed that *M*/+ and $M^{+/+}$ cells proliferate independently and that the final size of the wing disc compartment is fixed. Predictions from the simulation fitted the experimental data well, and the authors concluded that growth control is dependent on a set limit on the final size of the tissue, not competition between populations of cells.

Di Talia and colleagues investigated intrinsic size regulation in budding yeast. Asymmetric cell division in budding yeast yields a small daughter cell that has a longer delay before division than the larger mother cell, even when cell size differences are taken into account. The daughter cell also has a different gene-expression programme that is controlled by daughter-specific localization of the transcription factors Ace2 and Ash1. Di Talia *et al.* found that forced symmetrical inheritance of Ace2 and Ash1 by mutation of protein or mRNA localization elements caused size control to be the same in mother and daughter cells. They also showed, by microarray analysis and chromatin immunoprecipitation in synchronized cell populations, that Ace2 and Ash1 normally repress expression of the G1 cyclin gene *CLN3* in daughters. These observations suggest that *CLN3* modulates the daughter cell's 'perception' of its size so that a longer delay before cell division is enforced.

Both of these studies highlight the autonomy of cells in determining their rate of cell division. Therefore, in multicellular organisms a key challenge is to identify the non-autonomous mechanisms that fix organ size.

Mary Muers

ORIGINAL RESEARCH PAPERS Martín, F. A., Herrera, S. C. & Morata, G. Cell competition, growth and size control in the *Drosophila* wing imaginal disc. *Development* **136**, 3747–3756 (2009) | Di Talia, S. *et al.* Daughter-specific transcription factors regulate cell size control in budding yeast. *PLoS Biol.* **7**, e1000221 (2009)