IN BRIEF

SYSTEMS BIOLOGY

Scaling in flies

How scaling, the process of expanding proportionally, occurs during development is not well understood. Using the *Drosophila melanogaster* wing as a model to study scaling quantitatively, Affolter and colleagues examined whether the activity gradient of the morphogen Decapentaplegic (DPP) scales during imaginal disc growth. First, they established an imaging method to reliably quantify the spatial and temporal changes in the activity gradients of DPP — measured by the expression domains of phosphorylated MAD (P-MAD) and Brinker (BRK), two targets downstream of DPP signalling. They found that both P-MAD and BRK expression domains, and therefore DPP activity gradients, scaled with the tissue size during disc growth and that the scaling was transmitted to target genes (*dad*, *sal* and *omb*). Furthermore, scaling of the DPP activity gradient requires *pentagone* (*pent*), a gene that is repressed by DPP signalling, as *pent* mutants have narrower expression domains of P-MAD and BRK.

ORIGINAL RESEARCH PAPER Hamaratoglu, F. *et al.* Dpp signaling activity requires Pentagone to scale with tissue size in the growing *Drosophila* wing imaginal disc. *PLoS Biol.* **9**, e1001182 (2011)

CELL CYCLE

A new role for RAB5

This study shows that the small GTPase RAB5, which is known to regulate early steps of endocytosis, also plays a part in mitosis. Depletion of RAB5 by RNA interference in human cell lines led to impaired chromosome congression and delayed nuclear envelope disassembly. Chromosome movements are largely mediated by kinetochores, which link centromeric chromatin to microtubules; consistent with this, RAB5-depleted cells showed decreased kinetochore tension and attachment to microtubules. These defects were caused by reduced accumulation of the centromere-associated protein CENPF at kinetochores, indicating that RAB5 regulates this process. Indeed, the authors found that RAB5 and CENPF form a complex around the nuclear envelope. On the basis of their findings, the authors propose that, by interacting with CENPF, RAB5 controls its accumulation at kinetochores after nuclear envelope disassembly has occurred.

ORIGINAL RESEARCH PAPER Serio, G. *et al.* Small GTPase Rab5 participates in chromosome congression and regulates localization of the centromere-associated protein CENP-F to kinetochores. *Proc. Natl Acad. Sci. USA* **108**, 17337–17342 (2011)

DEVELOPMENT

Osteoblasts and osteoclasts keep in touch

Bone homeostasis involves bone resorption (destruction), which is mediated by osteoclasts, followed by bone reformation, mediated by osteoblasts. This study reveals that semaphorin 4D expressed by osteoclasts is integral to the communication between the two cell types. Using *in vitro* assays and genetic mouse models, the authors observed that semaphorin 4D suppresses bone formation. This was mediated through semaphorin 4D binding to its receptor plexin B1 on the surface of osteoblasts, leading to activation of RHOA and its downstream effector, RHO kinase (ROCK). This, in turn, led to increased osteoblast motility (and thereby repulsion of osteoblasts from the bone surface) and inhibition of insulin growth factor 1 (IGF1) signalling (which inhibited osteoblast differentiation). Finally, blocking the interaction of semaphorin 4D and plexin B1 promoted bone formation *in vivo*, indicating that this protein may be a therapeutic target for osteoporosis.

ORIGINAL RESEARCH PAPER Negishi-Koga, T. *et al.* Suppression of bone formation by osteoclastic expression of semaphorin 4D. *Nature Med.* **17**, 1473–1480 (2011)