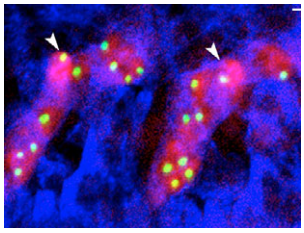
Muscling in on myoblast biology

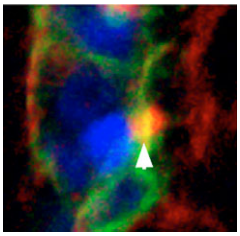
In *Drosophila*, the musculature consists of a stereotypic arrangement of distinct muscles and its development involves two types of myoblast: founder cells (FCs) and fusion-competent myoblasts (FCM). FCs, which are generated from progenitor cells selected from promuscular cell clusters, each fuse with several FCMs to form multinucleated myotubes that migrate under the ectoderm to their target tendons, with which they form strong attachments. This well-defined system is used to investigate many aspects of development, including, as reported in this issue, the control of cell identity, the mechanisms underlying cell fusion, and the control of cell migration and adherence.

On p. 4347, Dubois and colleagues reveal how the *Drosophila* embryonic Dorsal/Acute 3 (DA3) muscle lineage is specified. Sets of transcription factors are thought to endow each FC with the capacity to seed the formation of a distinct muscle type. To investigate this possibility, the researchers used the

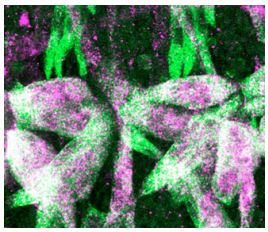


transcription factor Collier (Col), which is expressed in the DA3 muscle and is required for its formation, as a determinant and read-out of DA3 muscle identity. They discover that separate sets of cis-regulatory elements activate *col* in the DA3 promuscular cluster and in the FC progenitor cells and DA3 myofibre. In addition, they show that Col and Nautilus (which is also essential for DA3 muscle formation) act together to ensure that all the nuclei within the DA3 myofibre activate *col* and express the same differentiation program. Overall, these results support the concept of a combinatorial control of muscle identity.

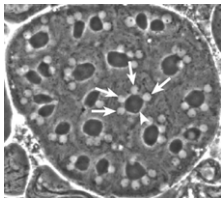
On p. 4357, Richardson and co-workers use live imaging to shed new light on the involvement of cytoskeletal remodelling in myoblast fusion. They show that F-actin accumulates at sites of myoblast fusion and that these actin foci dissolve immediately before fusion occurs. Several mutations have been identified in *Drosophila* that disrupt myoblast fusion, including mutations in *kette*. Kette regulates SCAR/WAVE, an activator of Arp2/3-dependent actin polymerization. The researchers report that in *kette* mutant embryos, enlarged actin foci form that do not dissolve normally. Actin foci dissolution and myoblast fusion also fail in *SCAR* and *Arp2/3* mutants. From their findings, the researchers suggest that Kette-SCAR-Arp2/3-mediated actin polymerization causes a reorganization of actin foci that is required for myoblast fusion and that actin dynamics may also be critical for other cell-cell fusion events.



Finally, on p. 4469, Estrada and colleagues describe how the transmembrane cell adhesion protein Perdido (Perd), which is expressed in FCs and in growing myotubes, interacts with the Glutamate receptor interacting protein (Grip) and also with integrins to mediate myotube projection and

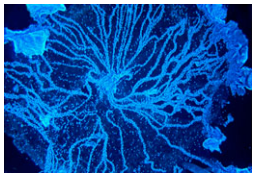


attachment in *Drosophila* embryos. Both of these processes, the researchers report, are defective in *perd* loss-of-function mutants. In vitro, the Perd intracellular domain interacts with a PDZ domain in Grip, another muscle-expressed factor needed for myotube migration. Using a new, whole-embryo RNA interference assay, the researchers also show that *perd* interacts genetically with *Grip* and with *multiple edematous wings*, which encodes one subunit of the αPS1-βPS integrin that is expressed in tendon cells. These results provide novel insights into how Perd regulates myotube migration and attachment and indicate how integrins function during these processes.



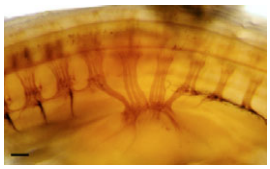
Membrane recycling: not an ARFterthought

During cytokinesis, the central spindle microtubules and the actomysin contractile ring drive dramatic cell shape changes. These shape changes also involve a rapid increase in the plasma membrane surface area, but how is this achieved? Dyer and colleagues propose that the endosomal trafficking component ARF6 promotes rapid membrane addition during spermatocyte cytokinesis in *Drosophila* (see p. 4437). The researchers show that cytokinesis fails in most meiotic divisions in *arf6*-null spermatocytes. They use time-lapse microscopy to show that the rapid addition of membrane to the plasma membrane is defective in these spermatocytes and causes furrow regression. In normal spermatocytes, they report, ARF6 is enriched on recycling endosomes at the central spindle and binds to the centralspindlin component Pavarotti. However, ARF6 is not required for central spindle or actomysin contractile ring assembly or for targeting of recycling endosomes to the spindle. They propose, therefore, that ARF6 promotes the rapid recycling of endosomal membrane stores during cytokinesis, thus coordinating membrane recycling with central spindle formation.



Ang-ling for apoptosis clean up

Macrophages recognize and remove dead cells throughout the body but they also sometimes actively induce apoptosis. Richard Lang and co-workers have been investigating this phenomenon during programmed vascular regression of the hyaloid vessels in the developing mouse eye. They now report that in this system macrophages play an obligatory role in a cell death switch mediated by angiopoietin 2 (Ang2; see p. 4449). Using genetic experiments and the intra-ocular injection of various factors, the researchers show that during hyaloid vessel regression, Ang2 (probably produced by the pericytes that coat small blood vessels) has two effects: it suppresses Akt-mediated cell survival signalling in the vascular endothelial cells (VECs) and it stimulates the production of Wnt7b by macrophages. Wnt7b, the researchers report, stimulates VECs to enter the cell cycle where they die in G1 phase because of the absence of survival signals. This mechanism, the researchers suggest, ensures that macrophages are on hand to sweep up the debris when cell death occurs.



Inside story on Sema3A and axonal pathfinding

During nervous system development, a handful of guidance cues produces a complex neuronal wiring pattern, but exactly how is unclear. Now, on p. 4491, Valérie Castellani and colleagues report that the expression of the repulsive guidance cue semaphorin 3A (Sema3A) by motoneurons sets the sensitivity of their axons to environmental semaphorin sources. Sema3A secreted by peripheral tissues interacts with neuropilin (its receptor) in the growth cones of motoneurons to control motor axon pathfinding, but Sema3A is also expressed by motoneurons themselves during axonal pathfinding. The researchers show that Sema3A overexpression in the neural tube of chick embryos induces the exuberant growth of motor axon projections through normally non-permissive tissues, but that RNAi knockdown of Sema3A in motoneurons inhibits the normal dorsal growth of these neurons. Other experiments indicate that Sema3A expression in motoneurons sets their sensitivity to exogenous Sema3A by regulating neuropilin availability at the growth cone. Thus, the interplay between intrinsic and extrinsic Sema3A may help to organize the axonal pathways of motoneurons.

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