In This Issue

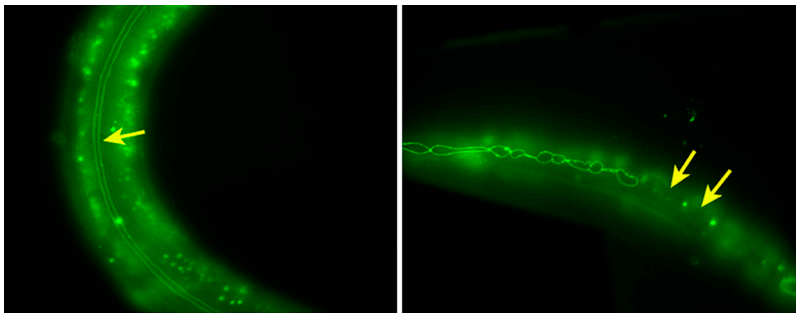
Multifunctional BAF-1

Nuclear assembly happens every cell division. So it's no surprise that nuclear assembly factors are overworked during embryogenesis, when proliferation is maximal. But there's no rest for one weary factor, called BAF-1, who has many jobs left to do even when embryogenesis is over, report Margalit et al. on page 661.

BAF-1 is enriched at the nuclear periphery and is required for the capture of chromosomes in reforming nuclei. It binds to histones, DNA, and nuclear envelope proteins including lamin and emerin.

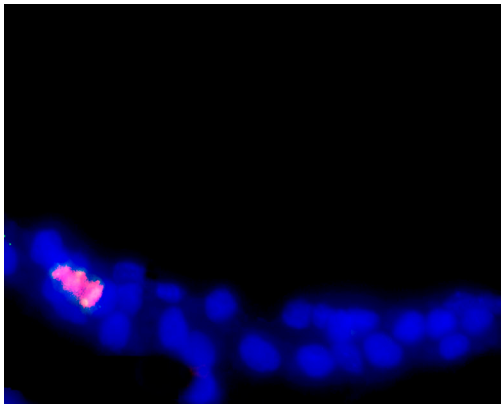
Mutations to lamin and emerin, which are also crucial for nuclear assembly, somehow cause human diseases that manifest later in life, when cell division has lagged. In previous studies, the group found that knocking down the activity of BAF-1 in worms leads to embryonic death. They wondered, however, whether BAF-1, like lamin and emerin, might have functions later in life.

To investigate this question, they used BAF-1–null worms that survived embryogenesis thanks to maternal BAF-1 supplies. These survivors displayed a diverse but reproducible array of tissue-specific defects. The defects suggested that BAF-1 promotes distal tip cell migration, muscle cell integrity, gonad and germline development, and the correct timing of epidermal seam cell fusion—a process that literally seals the worm's skin.



Failure to form a nice neat seam (arrow, left) is just one of the many late-in-life defects of worms that lack BAF (right).

BAF-1 delayed seam cell fusion by binding to the promoter and repressing the expression of the gene for a fusion factor called EFF-1. This newly described transcriptional regulatory activity might also explain BAF-1's other tissue-specific functions. JCB



A MyoD positive embryonic cell (red) keeps its identity even in the foreign environment of the heart.

Cellular career decisions start early

There's always one or two kids in every class who are already certain what they want to be when they grow up. Gerhart and colleagues now report on page 649 that certain cells of the early embryo are no different.

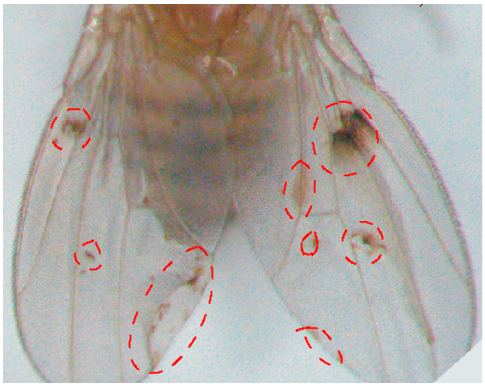
The team is interested in how cells commit to becoming skeletal muscle, which requires the expression of a transcription factor called MyoD. This expression was thought to start in the somites. But George-Weinstein's group discovered that they could detect MyoD mRNA in the blastocyst—a whole day before somites form, when cells are thought to be still pluripotent.

MyoD-expressing cells isolated from the blastocyst were capable of differentiating into skeletal muscle in culture. This ability did not mean, however, that the cells were already committed to muscle differentiation. It was possible that the MyoD mRNA was nonfunctional. Indeed, no MyoD protein was detectable at this stage.

To investigate whether MyoD-positive blastocyst cells were stably committed, the team introduced them into early cardiac muscle and nervous tissue of the embryo. MyoD-negative cells adopted the same fate as their surrounding cells, whereas MyoD-positive cells did not. A small number of MyoD-positive cells also ended up in these foreign environments as part of normal development. Such immigrants continued to express MyoD, although they remained undifferentiated, as the necessary inductive signals for skeletal muscle development were presumably missing.

When MyoD cells were removed from the foreign tissues and cultured, they promptly started turning into skeletal muscle. Seems you can take the MyoD cell out of the muscle, but you can't take the muscle out of the embryonic MyoD cell. JCB

Text by Ruth Williams
ruth.williams@rockefeller.edu



When communal cell death fails in mutant chimeric flies, epithelial tissue remains in patches (circled) across the wing.

Cellular suicide pact

Mass suicides are not the reserve of cults, it appears. On page 567, Link and colleagues report that cells do it too.

Cellular suicide—known as apoptosis—is necessary during development for sculpting the shape of organs and limbs. Most of the time, individual cell suicides are dotted throughout the tissue, and cell corpses are then cleared away by phagocytosis.

Link et al., however, have now captured by live imaging a mass cellular suicide in flies. Epithelial wing cells died in a wave that swept across the developing wing in a matter of minutes. The dead cells were not phagocytosed but were instead swept into the wing veins, which drain into the body.

The authors hypothesize that a released signaling factor or mechanosensory response propagates the swift en masse suicides. A mutant screen for defects in this collective cell death has not yet identified any such instigators but has revealed novel cell death genes, including homeodomain-interacting protein kinase. This gene's product functions in collective cell death and in more conventional examples of programmed cell death.

The authors speculate that communal cell death might be a more widespread phenomenom. Massive cellular suicides might occur, for example, in mammals during development or after rapid hormonal changes, such as mammary gland involution after nursing and the shedding of the uterine lining at menstruation. JCB

Dendritic spines cut loose to mature

Developing dendritic spines need to hold on tight to the extracellular matrix as they seek out partnering neurons. Once they find partners, however, the spine tips must sever their matrix ties to reshape into post-synaptic receiving stations, according to Tian et al. (page 687).

Dendritic spine growth and maturation coincides with the expression of a neuron-specific transmembrane adhesion molecule called ICAM-5. Spines in mice lacking ICAM-5 grow more slowly but mature more quickly, suggesting that the adhesion molecule is needed for spines to find partners but inhibits their subsequent maturation.

Tian et al. now show that spine maturation is possible in neurons because much of ICAM-5 is cleaved into a nonadhesive form during synaptogenesis. This cleavage was promoted by neuron stimulation through receptors for the NMDA and AMPA neurotransmitters.

Receptor activation caused ICAM-5 to be released from the actin cytoskeleton, which in turn promoted its cleavage. Release from the actin network might make it susceptible to destructive enzymes such as the MMP2 and MMP9 matrix metalloproteases, which were needed for ICAM-5 cleavage. JCB

SCAPER speeds and slows the cell cycle

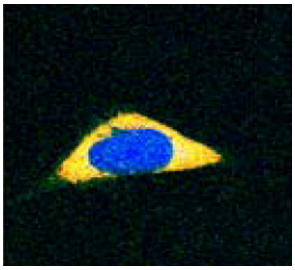
Cyclin A promotes the progression of both S phase and mitosis. A new cyclin A binding protein, identified by Tsang et al. (page 621), helps the S phase push but hinders mitotic progression. The new partner seems to favor S phase by holding cyclin A in the cytoplasm.

To determine how cyclin A pushes forward different stages of the cell cycle, Dynlacht's team looked for new binding partners. They fished out one especially strong candidate, which was associated with the ER, and named it SCAPER (S phase cyclin A–associated protein of the endoplasmic reticulum).

Overexpression of SCAPER delayed progression of cells through M phase, suggesting that the protein blocks this cyclin A activity. But SCAPER deletion prevented cells from entering S phase in a timely manner, conversely indicating that it normally helps cyclin A in this case.

This S phase delay, the authors propose, might be due to cyclin A's entering the nucleus too soon. Recent findings indicate that, although cyclin A is predominantly nuclear, it phosphorylates certain cytoplasmic proteins. Perhaps tethering cyclin A at the ER keeps it in the cytoplasm long enough for necessary S phase–promoting interactions.

The nuclear allotment of cyclin A might be more important for G2 and M phase progression. Too much SCAPER would thus block mitosis by preventing its nuclear entry. Under normal conditions, cyclin A levels would be sufficiently high by G2 that SCAPER can no longer restrain all of it. JCB



SCAPER (red) keeps cyclin A (green) in the cytoplasm to promote S phase progression.