# In This Issue

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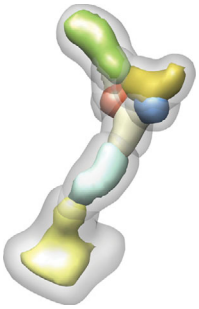
## No crystal structure? No problem



The structure of the Nup84 complex, as deduced from EM and domain deletion mapping results.

It's hard for crystallographers to determine the structures of all the macromolecular assemblies that cell biologists want to get a close look at. But researchers can piece together precise molecular structures by considering other readily available data, Fernandez-Martinez et al. suggest.

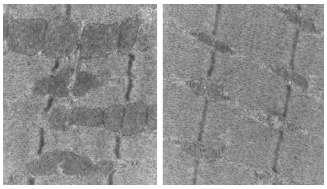
Their new work builds on their previous findings that highlighted the value of low-resolution data, which most labs can obtain fairly easily but rarely use to infer molecular structures. For example, with a technique called domain deletion mapping, which involves pruning particular proteins and then determining which interactions remain and which are disrupted, researchers can deduce the connections between proteins and their orientations within a complex.

Fernandez-Martinez et al. applied the method to the Nup84 complex, which contains seven proteins. Sixteen copies of the complex form the outer rings of the yeast nuclear pore complex (NPC). Electron microscopy and domain deletion mapping allowed the team to obtain spatial restraints, or structural limitations on the complex's architecture. Using a computer algorithm, they could then build possible structures for the Nup84 complex that satisfied these restraints.

Although the analysis confirmed some previous findings, such as the complex's overall arrangement and "Y" shape, it also revealed new features and linked particular functions to specific structures. For example, the findings suggest that three proteins at the top of the "Y," Nup85, Nup120, and Seh1, are particularly important for linking the complex to the rest of the NPC, whereas Nup120 and a related protein, Nup133, are crucial for stabilizing the NPC's interactions with the nuclear envelope.

Fernandez-Martinez, J., et al. 2012. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201109008.

## Slow but steady for NF-κB



Muscle tissue in which the alternative NF-κB pathway is switched on (left) harbors more, longer mitochondria than does control muscle (right).

Marathon runners should give NF-κB a hand. Bakkar et al. show that the transcription factor pushes muscles to make more mitochondria and to produce the type of fiber that tires slowly.

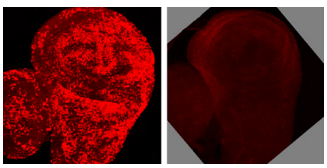
NF-κB has a split personality during muscle development and regeneration. On the one hand, it can be activated by the so-called classical pathway that prevents young muscle cells from differentiating. But NF-κB can also be regulated by an alternative pathway, which involves a distinct set of proteins, including IKKα and RelB. Researchers are just starting to investigate the alternative pathway's role in muscle. In a previous study, Bakkar et al. found that it spurs cultured muscle cells to generate mitochondria.

Now, the researchers gauged the alternative pathway's powers in vivo by analyzing mice that lacked IKKα or RelB. Muscles from the animals had fewer mitochondria than normal and showed signs of an energy shortage. What mitochondria they did contain were less efficient. Overexpressing IKKα had the opposite effect, boosting mitochondrial numbers and power output and inducing muscles to fashion more slow twitch fibers. Although weaker than fast twitch fibers, slow twitch fibers have more stamina and are critical for long-distance runners.

Bakkar et al. found that the alternative NF-κB pathway exerts its effects by activating PGC-1β, a master regulator of mitochondrial biogenesis and function. The researchers also discovered that mTOR, which responds to hormones, growth factors, and nutrient levels, activates the pathway. What triggers mTOR to flip on NF-κB and the alternative pathway remains unclear.

Bakkar, N., et al. 2012. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201108118.

## Caspase conspiracy sets up cells for death



After a dose of radiation, the number of apoptotic cells (red) is much higher in a control imaginal disc (left) than in a disc with mutated Drice (right).

Two caspases work together to determine a cell's propensity for apoptosis, Florentin and Arama show.

Whether an injured cell commits suicide depends on factors such as what tissue it inhabits. A cell's tendency to undergo apoptosis can even change during its lifetime. These differences have intrigued cancer and developmental biologists for years, but researchers have yet to agree on an explanation for cells' variable sensitivities. Florentin and Arama investigated two effector caspases that spur *Drosophila* cells to commit suicide. The two killer proteins, Drice and Dcp-1, are the equivalents of caspase-3 and caspase-7 in mammals.

Although Drice and Dcp-1 cleave similar proteins, they play different roles during apoptosis, the researchers concluded after studying cell death in the larval imaginal disc that becomes the adult fly's wing. Control cells and cells lacking Dcp-1 killed themselves after a dose of radiation. However, cells that were missing Drice remained alive. That doesn't mean Dcp-1 is a pacifist. It is able to trigger apoptosis, Florentin and Arama confirmed when they inserted extra copies of the Dcp-1 gene into cells lacking Drice.

However, Drice appears to be the better of the two caspases at inducing cells to kill themselves. Dcp-1, meanwhile, helps control the rate at which cells die, partly by switching on more Drice. The researchers hypothesize that, by adjusting the ratio of the two caspases, cells can set their sensitivity to apoptosis-inducing stimuli.

Florentin, A., and E. Arama. 2012. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201107133.