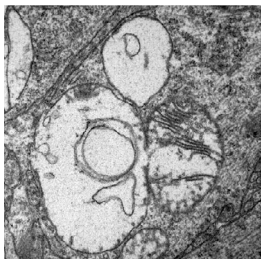
In This Issue

Text by Mitch Leslie
mitchleslie@comcast.net

The long and short of OPA1



Neurons from mice lacking prohibitin 2 and OMA1 carry huge mitochondria that lack cristae.

OMA1 promotes neurodegeneration by tipping the balance between mitochondrial fusion and fission, Korwitz et al. reveal.

OPA1 is one of the key proteins that controls mitochondrial morphology. The protein comes in a long form, which promotes mitochondrial fusion, and a short form, which researchers think spurs fission. Stressed cells often break up their mitochondrial network, activating OMA1, a protease that cleaves OPA1 and helps produce the short version. OMA1-induced mitochondrial breakup is essential for mitophagy and cell death in vitro, but its role in vivo remains unclear.

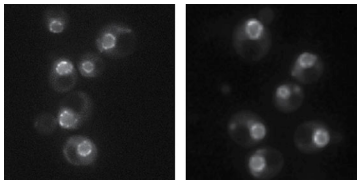
Korwitz et al. probed OMA1's function in mice that lack the mitochondrial protein prohibitin 2 in the forebrain. Levels of the long form of OPA1 decline in these mice, and they therefore develop fatal neurodegeneration. However, when the researchers removed OMA1 from the rodents, their lifespan was significantly extended. Deleting OMA1 allowed the animals to maintain the long form of OPA1 and thwarted formation of the short form.

Mice lacking prohibitin 2 have small brains, but animals that were also missing OMA1 had normal sized brains, suggesting that the loss of OMA1 protects neurons from apoptosis.

Removal of OMA1 also prevented the cells' mitochondrial DNA from deteriorating. However, mitochondria from animals lacking OMA1 and prohibitin 2 weren't normal—they were huge and lacked cristae. The results show that by limiting mitochondrial fusion, OMA1 can trigger cell death and neurodegeneration. However, researchers still need to determine what circumstances lead to activation of the protease in vivo.

Korwitz, A., et al. 2016. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201507022

Ubiquitylation leaves Nup60 a basket case



Nup60 localizes to nuclear pores (left), and it remains there even if it can't be ubiquitylated (right).

Adding ubiquitin to a nuclear pore protein promotes repair of damaged DNA, Niño et al. show.

The functions of nuclear pore complexes extend far beyond transportation into and out of the nucleus. They help organize the genome, manage gene expression, monitor mRNA quality, and stimulate repair of damaged DNA. Posttranslational modifications of nucleoporins (Nups) may help multitasking pores coordinate all of their responsibilities. Niño et al. focused on modifications of one Nup, Nup60, which is part of the basket structure on the pore's nuclear side.

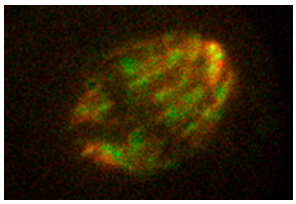
The researchers discovered that Nup60 was ubiquitylated and SUMOylated. Neither modification was necessary for the protein to attach to the pore. However, a version of Nup60 that couldn't be ubiquitylated was more dynamic, rapidly detaching from the pore complex with its partner Nup2. Preventing SUMOylation, in contrast, had no effect on Nup60's dynamics. Niño et al. determined that ubiquitylated Nup60 attaches to the Y complex, a building block of the nuclear pore, likely by binding to a component of the Y complex named Nup84.

How does ubiquitylation of Nup60 alter its function? The researchers found that the modification had no effect on the movement of cargoes through the pore. Instead, their results revealed a role in DNA repair. They found that Nup60 ubiquitylation increased in cells exposed to a DNA-damaging chemical. Cells carrying Nup60 that can't be ubiquitylated displayed a less efficient DNA damage response.

How Nup60 fosters DNA repair remains to be determined. The researchers suggest that Nup60's ubiquitylation might alter the dynamics of the nuclear pore basket and create a protected environment that favors DNA repair.

Niño, C.A., et al. 2016. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201506130

Using speckles to spot protein dynamics



The pattern produced by inducible speckle imaging on the mitotic spindle of a human cell.

Pereira et al. describe a new microscopy technique that allows researchers to more precisely mark molecules whose movements they want to track.

Researchers can follow the movements of proteins with several techniques, including fluorescent speckle microscopy (FSM), which relies on the natural variations in signal intensity that occur when levels of fluorescent molecules in a sample are low. These variations result in a speckled pattern on structures such as microtubules, allowing scientists to monitor changes. However, either the contrast or the available signal is low with FSM, making it difficult to distinguish the speckles.

The method Pereira et al. devised, inducible speckle imaging, directs laser light through a diffuser before it reaches the target cell. Constructive and destructive interference create a 3D pattern of speckles that serve as reference points for tracking changes. Unlike FSM, the technique provides a strong signal and high contrast. Another advantage, the researchers note, is that inducible speckle imaging isn't affected by imperfections in the optical system, which can reduce the resolution of FRAP and other methods of following protein dynamics.

Pereira et al. measured spindle microtubule dynamics in *Drosophila* cells, which have been difficult to pin down with FSM. Their results support the hypothesis that metaphase duration correlates with the speed of microtubule movement toward the spindle pole. The researchers say that the technique could be applied to other long, fairly homogeneous structures in cells, such as membranes and other types of cytoskeletal filaments.

Pereira, A.J., et al. 2016. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201506128