In This Issue

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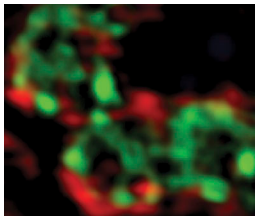
Asterless amplifies Plk4



Superresolution microscopy shows the structure of stable aggregates formed by overexpressed Plk4 (green) and Asl (red).

Klebba and Galletta et al. reveal that the scaffold protein Asterless (Asl) regulates centriole duplication by controlling turnover of the kinase Plk4.

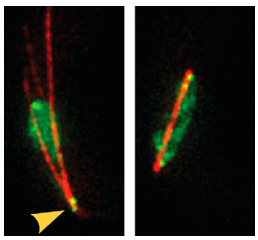
Cells must duplicate their centrioles once, and only once, per cell cycle. In interphase, the master regulator of centriole duplication, Plk4, triggers its own destruction by homodimerizing and phosphorylating itself. In mitosis, however, the phosphatase PP2A reverses this phosphorylation and stabilizes Plk4, allowing the kinase to accumulate on the surface of the mother centriole and license the assembly of a daughter centriole in the following S phase. Plk4 localizes to centrioles by binding to the N terminus of Asl. Surprisingly, given that low Plk4 levels are usually the limiting factor for centriole assembly, overexpressing Asl induces centriole overduplication, suggesting that the scaffold protein may have an additional function besides Plk4 recruitment.

Klebba and Galletta et al. found that overexpressing Asl's C-terminal domain inhibited Plk4 turnover and induced centriole amplification in *Drosophila* S2 cells. This region of the protein contained a second binding site for Plk4, and mutating this site eliminated Asl's ability to promote centriole duplication. Both the N- and C-terminal binding sites helped Asl form an oligomeric complex with Plk4 that stabilized the kinase during mitosis. In interphase cells, however, Asl's N-terminal domain facilitated Plk4's turnover by promoting the kinase's dimerization and autophosphorylation.

The authors now want to investigate how Asl is regulated throughout the cell cycle and how the stable Asl–Plk4 complexes are organized on the surface of centrioles.

Klebba, J.E., B.J. Galletta, et al. 2015. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201410105.

When centromeres fill in for telomeres



During prophase (left), a centromere (green) contacts the SPB (red, arrowhead), enabling this bouquet-deficient cell to form a bipolar meiotic spindle (red, right).

Fennell et al. reveal that centromeres can stand in for telomeres and promote assembly of the fission yeast meiotic spindle.

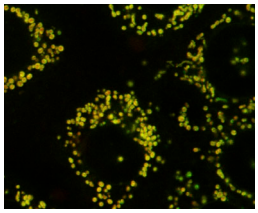
During meiotic prophase, the telomeres of fission yeast chromosomes cluster at the nuclear envelope. This "telomere bouquet" connects, via the inner nuclear membrane SUN protein Sad1, to the spindle pole body (SPB), the yeast equivalent of the centrosome. Mutant yeast unable to form a telomere bouquet have problems inserting their SPBs into the nuclear envelope so that they can form a bipolar meiotic spindle. Around half of these bouquet-deficient yeast still manage to form a spindle, however, so Fennell et al. examined how these cells cope in the absence of telomere–SPB contacts.

The researchers discovered that bouquet-deficient cells could successfully assemble bipolar spindles if their centromeres contacted the SPB during meiotic prophase. Boosting centromere–SPB contacts completely restored meiotic spindle assembly in all bouquet-deficient cells. In contrast, forcing noncentromeric chromatin regions to contact SPBs failed to rescue spindle formation.

Fennell et al. found that telomeres or, in the absence of bouquets, centromeres, promoted the accumulation of Sad1 at SPBs. Reducing Sad1 levels inhibited meiotic segregation, suggesting that the SUN protein plays a key role in SPB insertion and spindle assembly. Senior author Julia Cooper now wants to investigate this pathway in more detail. Because telomeres cluster near the centrosomes of other meiotic cell types and centromeres gather next to interphase SPBs, the pathway may represent a conserved way for chromatin to regulate the spindle apparatus.

Fennell, A., et al. 2015. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201409058.

Mitofusin 2 keeps the respiratory chain on Q



Many mitochondria (green) show reduced membrane potential (indicated by the potentiometric reporter TMRM, red) in fibroblasts lacking MFN2.

Mourier et al. reveal that the mitochondrial fusion protein Mitofusin 2 (MFN2) is required to maintain production of the respiratory chain cofactor coenzyme Q.

The closely related GTPases MFN1 and MFN2 are both required for mitochondrial outer membrane fusion. *Mfn1*-deficient mice nevertheless seem perfectly healthy, but mice lacking *Mfn2* die soon after birth. Moreover, only *Mfn2* has been linked to human diseases, including the peripheral neuropathy Charcot-Marie-Tooth type 2A. Mourier et al. therefore investigated whether loss of *Mfn2* affects mitochondrial function in other ways besides membrane fusion.

The researchers found that mitochondrial respiration and ATP production was impaired in *Mfn2*-deficient cardiomyocytes compared with wild-type and *Mfn1*-deficient cells. The levels and activities of individual respiratory chain protein complexes were unaltered in mitochondria lacking *Mfn2*, but the levels of coenzyme Q, an electron carrier that transfers electrons to respiratory chain complex III, were strongly reduced. Supplementing *Mfn2*-null cells with coenzyme Q partially restored respiratory chain function.

Coenzyme Q is synthesized from organic intermediates generated by the terpenoid biosynthetic pathway. Mourier et al. found that many of the enzymes and metabolites involved in this pathway were down-regulated in the absence of MFN2. Senior author Nils-Göran Larsson now wants to investigate how MFN2 regulates terpenoid synthesis. Because this pathway takes place across multiple subcellular compartments, one possibility is that MFN2 mediates mitochondrial contacts with other organelles. Larsson also hopes that coenzyme Q supplements could help treat patients with diseases caused by mutations in *Mfn2*.

Mourier, A., et al. 2015. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201411100.