

## ARL-13 SUMO wrestles receptors into cilia

**S**UMOylation of the small GTPase ARL-13 helps target signaling receptors into primary cilia, [Li et al.](#) reveal.

Primary cilia are microtubule-based membrane protrusions that serve as hubs for multiple signaling pathways. In *C. elegans*, ARL-13 promotes cilia assembly by coordinating intraflagellar transport along ciliary microtubules, and the GTPase is also required for the correct localization of signaling receptors to the ciliary membrane.

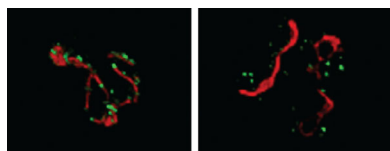
In a yeast two-hybrid screen for ARL-13 binding partners, Li et al. identified UBC-9, an enzyme that conjugates the small, ubiquitin-like modifier SUMO onto target proteins. UBC-9 colocalized with ARL-13 in primary cilia and SUMOylated the GTPase near its C terminus. A non-SUMOylatable ARL-13 mutant localized to cilia and restored ciliogenesis in worms lacking wild-type ARL-13. But the rescued cilia lacked membrane proteins like the mechanosensor polycystin-2, indicating that ARL-13 SUMOylation is

required for the proper ciliary localization of signaling receptors. A constitutively SUMOylated version of ARL-13 successfully restored both ciliogenesis and receptor targeting.

The human homologue of ARL-13, ARL13B, is mutated in the ciliopathy Joubert syndrome. ARL13B was also SUMOylated by UBC9, and this modification was required for the ciliary localization of human polycystin-2. Because polycystin-2 is mutated in polycystic kidney disease, Li et al.'s findings may explain why Joubert syndrome patients have cystic kidneys. Mislocalization of other signaling proteins may underlie additional symptoms associated with the disease. Senior author Jinghua Hu now wants to investigate how SUMOylation regulates ARL-13's function in ciliary targeting. One possibility is that SUMOylation allows ARL-13 to bind an adaptor that links the GTPase to different receptors.

Li, Y., et al. 2012. *J. Cell Biol.* <http://dx.doi.org/10.1083/jcb.201203150>.

## Dnm1's recruitment strategy



**Wild-type Dnm1 (green, left) localizes to mitochondria (red), but a mutant version (green, right) remains cytosolic, resulting in elongated mitochondria that can't undergo fission.**

**B**ui et al. investigate how a dynamin-related GTPase is recruited to the mitochondrial outer membrane to drive mitochondrial fission.

Dynamin binds directly to the plasma membrane to remodel

the lipid bilayer during endocytosis. Dynamin-related proteins, in contrast, remodel other cellular membranes after binding to them via specific adaptor proteins. The mitochondrial fission protein Dnm1, for example, is recruited to yeast mitochondria by Mdv1, though how Dnm1 interacts with this adaptor protein is unclear.

Bui et al. identified several point mutations that prevented

Dnm1 from localizing to mitochondria and supporting mitochondrial fission. The mutations were located in a conserved motif in the "Insert B" domain of Dnm1, a domain found in all dynamin-related proteins but not in dynamin itself, which instead contains a lipid-binding PH domain. Mutations in Dnm1's Insert B domain inhibited the GTPase's interaction with Mdv1. The interaction was rescued by suppressor mutations in Mdv1's  $\beta$ -propeller domain, as was Dnm1's mitochondrial recruitment and organelle fission.

The critical motif in yeast Dnm1 Insert B is well conserved in other fungi but is altered in the mammalian homologue, Drp1. But Mdv1 is also absent in mammals, where it is functionally replaced by several different mitochondrial adaptor proteins. Senior author Janet Shaw therefore thinks that Insert B sequences have co-evolved with their corresponding adaptors. She now wants to confirm the importance of the Insert B domain of mammalian Drp1 and to investigate whether it binds to different adaptors under different conditions.

Bui, H.T., et al. 2012. *J. Cell Biol.* <http://dx.doi.org/10.1083/jcb.201207079>.

## The fellowship of the Z ring



**When coexpressed in fission yeast, FtsZ1 (green) and FtsZ2 (red) coassemble into a complex network of filaments and closed rings (arrow).**

**T**erBush and Osteryoung explore how two cytoskeletal proteins combine to promote chloroplast division.

FtsZ proteins are a family of tubulin-like GTPases that polymerize into "Z rings" at the equator of bacteria and chloroplasts, facilitating cell or organelle division. Bacteria have a single FtsZ gene, whereas plants express two, FtsZ1 and FtsZ2, which have unique functions in chloroplast fission despite coassembling into the organelle's Z ring. The nature of these functions is

unknown, however, so TerBush and Osteryoung investigated the properties of the plant FtsZ proteins by expressing them in fission yeast.

FtsZ1 and FtsZ2 self-assembled into a variety of different structures—including rings—inside yeast cells. FtsZ1 typically

assembled into long cables, whereas FtsZ2 formed more elaborate networks. When the two proteins were coexpressed, they coassembled into structures resembling the FtsZ2 meshworks, suggesting that FtsZ2 is the main determinant of polymer morphology. FtsZ1, on the other hand, appears to control polymer dynamics. Photobleaching experiments revealed that subunit turnover was faster in FtsZ1 filaments than in FtsZ2 structures, but FtsZ2 became more dynamic when copolymerized with FtsZ1. FtsZ1 may therefore help remodel the Z ring as it constricts during chloroplast division.

Turnover is thought to depend on the GTPase activity of FtsZ proteins, and filaments formed by a GTPase-deficient version of FtsZ2 were completely immobile. A GTPase-dead FtsZ1 mutant still formed dynamic filaments, however, suggesting that FtsZ1-containing structures may be less stable because FtsZ1 subunits form weaker interactions with their neighbors. The researchers now want to test this hypothesis by investigating the structure of the interface between FtsZ proteins.

TerBush, A.D., and K.W. Osteryoung. 2012. *J. Cell Biol.* <http://dx.doi.org/10.1083/jcb.201205114>.