FtsZ forms the cytoskeletal framework of the cytokinetic ring in bacteria, and appears to play the major role in constriction of the furrow at septation. Until recently, FtsZ had been found in every eu- bacterium and archaeabacterium, and was thought to be the major and essential component of the division machine (Erickson, 1997). FtsZ has also been found in chloroplasts (Osteryoung et al., 1998), which was expected since these plastids originated from bacterial ancestors. An apparent missing link was that FtsZ was absent from mitochondria, which are also of prokaryotic origin. There is no FtsZ in the completed genomes of Saccharomyces cerevisiae and Caenorhabditis elegans, and none in the extensive EST databases from human and animals. Now the mystery of mitochondrial cell division seems well on its way to resolution: most mitochondria have replaced FtsZ with dynamin for division. An important missing link is the recent discovery by Beech et al. (2000), of a mitochondrion that still uses FtsZ. But even as the division of mitochondria is being resolved, a new paradox has appeared, as several prokaryotes have now been discovered to have no FtsZ.

**Chloroplasts Use FtsZ for Division**

Chloroplasts appear to have conserved the bacterial division machine, with an interesting new twist (described below). Two ftsZ genes have been discovered in Arabidopsis, both encoded at genomic loci. One of these, ftsZ1, has a signal peptide that transports it into the chloroplast. The other, ftsZ2, does not, remaining on the cytoplasmic side of the chloroplast (Osteryoung et al., 1998). A ntsense experiments showed that both ftsZ genes are essential for chloroplast division in Arabidopsis (Osteryoung et al., 1998). A homologue of ftsZ was discovered in the moss Physcomitrella, and chloroplast division was completely blocked when the gene was knocked out (Strepp et al., 1998). There are now several chloroplast ftsZ genes, which all show closest similarity to those of cyanobacteria, from which chloroplasts were derived (Osteryoung et al., 1998; Beech et al., 2000). Chloroplasts have also retained other bacterial division genes, including ftsH, ftsW, minC, and minD (Turmel et al., 1999).

**Most Mitochondria Use Dynamin for Division**

The apparent absence of FtsZ in mitochondria raises two questions: where in the evolution of eukaryotes did mitochondria lose their FtsZ, and how do they now divide? The second question has seen great progress in the past year. Two laboratories, working from different directions, have found that S. cerevisiae Dnm1, a dynamin-related protein, is responsible for division of mitochondria (Bleazard et al., 1999; Sesaki and Jensen, 1999). In dnm1 mutant cells, the mitochondria coalesce to form a net of interconnected tubules. The Dnm1 protein has no mitochondrial import sequence, and was localized to the outside surface of the mitochondria, primarily at sites of constriction or at the tips of mitochondria that may have recently divided. A comprehensive study in C. elegans showed similar mitochondrial disruptions for mutations in DRP-1 (Labrousse et al., 1999). A gene knockout of dynA in Dictyostelium blocked division of mitochondria, and also had pleiotropic effects on cytokinesis and nuclear and endosomal morphology (Wienke et al., 1999). The human dynamin-related protein, Drp1/DLP1, seems to be essential for mitochondrial division, and may affect other membrane processes (Smirnova et al., 1998; Pitts et al., 1999). There are multiple dynamins in most species. The dynamins identified above may be orthologs, but they have some important differences in phenotype. Some of them appear to operate primarily on mitochondria, while others affect additional membrane systems. In addition, other dynamin-like proteins are known that affect mitochondrial morphology. Regardless of this complexity, the function of dynamin in mitochondrial division appears to be widespread in eukaryotes.

The two laboratories working on yeast both made the fascinating discovery that another gene, fzo1 (not a dynamin homologue), works antagonistically to dnm1, by causing the fusion of mitochondria (Bleazard et al., 1999; Sesaki and Jensen, 1999). Thus, in the absence of dnm1, fusion dominates and mitochondria coalesce into a network. In the absence of fzo1, there is no fusion and mitochondria divide into small fragments. Remarkably, a double mutant of both dnm1 and fzo1 has largely normal mitochondrial morphology. These two genes operating together generate a balance of division and fusion, creating a dynamic mitochondrial network (Bleazard et al., 1999; Sesaki and Jensen, 1999; Yaffe, 1999).

**Pulling from the Inside, Squeezing from the Outside**

In bacteria, the ring of FtsZ on the inner membrane is thought to constrict and pull the membrane inward. In
chloroplasts, FtsZ1 seems to play the same role, constric-
ting the chloroplast membrane from within. However, there is a new twist, as FtsZ2 is on the outside of the mito-
chondrion. In this position it would appear to be squeezing or pinching the division furrow from the outside. Dnm1
appears to function like the FtsZ2, squeezing or pinching from the outside. This is similar to how dynamin works in
endocytosis, where it forms rings or helices around mem-
brane protrusions and pinches off vesicles. A remarkable
observation in C. elegans was that division of the inner mi-
tochondrial compartment continued when D R P-1 mutants
blocked division of the outer membrane (Labrousse et al.,
1999). This suggests that a dual division mechanism,
squeezing from the outside and constricting from the in-
side, may operate in both mitochondria and chloroplasts.

The Missing Link: A Mitochondrion that
Uses FtsZ

The bacterial ancestor of mitochondria must have used
FtsZ for division, but animal cells and yeast appear to have
replaced FtsZ with dynamin. Are there any eukaryotes
that still use FtsZ for mitochondrial division? The answer
is yes, and Beech and colleagues (2000) have now discov-
ered this missing link. The golden-brown alga M allomonas
splendens has a genomic ftsZ most closely related to ftsZ
of α-proteobacteria, the ancestors of the mitochondrion.
The FtsZ protein is located in patches on the mitochon-
drial membrane, near the center or at the ends of mito-
chondria, similar to the location of Dnm1. This FtsZ is
translocated into the mitochondria, and therefore appears
to operate by constriction from within. It was even able to
modulate the structure of yeast mitochondria when ex-
pressed transgenically in S. cerevisiae, a remarkable obser-
vation since yeast doesn’t use or express FtsZ.

This discovery should spur a search for FtsZ in other mi-
tochondria. A spectrum of eukaryotes may be found, some
using FtsZ, some using dynamin, and perhaps some using
both, for mitochondrial division. Beyond the question of
mitochondrial division, the spectrum of FtsZ- and dyna-
nin-based mechanisms should provide a new tool for
looking at the evolution of eukaryotes (Martin, 2000).

The mechanism by which FtsZ and dynamin operate in
division is not known, but an intriguing observation is that
both form rings or spirals (Fig. 1). Dynamic spirals form at
the neck of endocytic vesicles, and the vesicles may be
pinched off by constriction (Sweitzer and Hinshaw, 1998)
or by a change in the helical pitch (Stowell et al., 1999). An
alternative proposal is that dynamin may be a signaling
molecule, recruiting another, force-generating molecule to
the complex (Sever et al., 1999). FtsZ may power constric-
tion by switching from a mostly straight protofilament to a
curved conformation (Lu et al., 2000).

The New Paradox: Prokaryotes with No FtsZ

Just as the missing link of mitochondrial FtsZ is falling
into place, a new paradox has appeared. Until recently it
seemed a simple story that all eubacteria and archaea used
FtsZ for cell division. Last year the genomic sequences of
two Chlamydia species showed a surprising absence of
ftsZ (Stephens et al., 1998; Kalman et al., 1999). However,
these bacteria are obligate parasites that live in mem-
brane-bound inclusions in their host cells. One possibility
is that they may use the host cell’s machinery for vesicle
trafficking for their own division. Consistent with this pos-
sibility, Boleti et al. (1999) found that a dominant nega-
tive dynamin transfection inhibited the proliferation of
Chlamydia. But an intriguing study by Brown and Rockey
(2000) demonstrated sharp localization of an antigen, per-
haps a peptidoglycan, at the cleavage furrows of Chlamydia.
This implies that the bacteria play some active role in the di-
vision process, and may divide independently of the host.

Even more puzzling is the recent discovery of two free-
living prokaryotes with no FtsZ. Aeropyrum pernix is an
archeon that lives at 90°C in ocean thermal vents. The cells
from laboratory culture are irregular cocci with some
sharp edges, ~1 μm in diameter (Sako et al., 1996).
Clearly, they must have some efficient system for division
to maintain this size and shape. Yet the genomic sequence
shows no ftsZ, nor any other known cell division protein
(Kawarabayasi et al., 1999). Just as surprising, the genome
of Ureaplasma urealyticum has no ftsZ (Glass and Lefko-
witz, http://genome.microbio.uab.edu). This is a myco-
plasma that lives primarily in its host, but can be cultured
in defined medium, so it must have a mechanism for cell
division. These two examples, and perhaps Chlamydia,
suggest the possibility of a completely novel mechanism
for bacterial cell division, still to be discovered.
References

Beech, P.L., T. Nheu, T. Schultz, S. Herbert, T. Lithgow, P.R. Gilson, and G.I. McFadden. 2000. Mitochondrial FtsZ in a chlamyphore alga. Science. 287: 1276–1279.

Bleazard, W., J.M. McCallery, E.J. King, S. Bale, A. Mozdzy, Q. Tieu, J. Nunari, and J.M. Shaw. 1999. The dynamin-related GTPase Dnm1 regulates mitochondrial fission in yeast. Nat. Cell Biol. 2:298–304.

Boleti, H., A. Benmerah, D.M. Ojcius, N. Cerf-Bensussan, and A. Dautry-Brown. 2000. Identification of an antigen localized to an apparent septum within dividing chlamydiae. Infect. Immun. 68:708–715.

Brown, W.J., and D.D. Rockey. 2000. Identification of an antigen localized to an apparent septum within dividing chlamydiae. Infect. Immun. 68:708–715.

Erickson, H.P. 1997. FtsZ, a tubulin homolog, in prokaryote cell division. Proc. Natl. Acad. Sci. U.S.A. 94:519–523.

Glass, J., and E. Lefkowitz. Ureaplasma urealyticum: The Complete Genomic Sequence. http://genome.microbio.uab.edu/uu/uuugen.htm

Kawarabayasi, Y., Y. Hino, H. Orikawa, S. Amazaki, Y. Haikawa, K. Jin-no, M. Takahashi, M. Sekine, S. Baba, A. Anikai, et al. 1999. Complete genome sequence of an aerobic hyper-thermophilic crenarchaeon, Aeropyrum pernix K1. DNA Res. 6:83–101, 145–52.

Labrousse, A.M., M.D. Zappaterra, D.A. Rube, and A.M. van der Bliek. 1999. Chlamydia infection of epithelial cells expressing dynamin and an apparent septum within dividing chlamydiae. J. Cell Sci. 112:1487–1496.

Labrousse, A.M., M.D. Zappaterra, D.A. Rube, and A.M. van der Bliek. 1999. Chlamydia infection of epithelial cells expressing dynamin and an apparent septum within dividing chlamydiae. J. Cell Sci. 112:1487–1496.

Osteryoung, K.W., K.D. Stokes, S.M. Rutherford, A.L. Percival, and W.Y. Lee. 1998. Chloroplast division in higher plants requires members of two functionally divergent gene families with homology to bacterialftsZ. Plant Cell. 10:1991–2004.

Pitts, K.R., Y. Yoon, E.W. Krueger, and M.A. McNiven. 1999. The dynamin-like protein DLP1 is essential for normal distribution and morphology of the endoplasmic reticulum and mitochondria in mammalian cells. Molec. Biol. Cell. 10:4403–4417.

Sako, Y., N. Nomura, A. Uchida, Y. Ishida, H. Morii, Y. Koga, T. Hoaki, and T. Maruyama. 1996. A eukaryotic GTPase gen. nov., sp. nov., a novel aerobic hyperthermophilic archean growing at temperatures up to 100 degrees C. Int. J. Syst. Bacteriol. 46:1070–1077.

Sasaki, H., and R.E. Jensen. 1999. Division versus fusion: Dnm1p and Fzo1p antagonistically regulate mitochondrial shape. J. Cell Biol. 147:699–706.

Sever, S., A.B. Muhlbreg, and S.L. Schmid. 1999. Impairment of dynamin’s GAP domain stimulates receptor-mediated endocytosis. Nature 398:481–486.

Smirnova, E., D.L. Shurland, S.N. Yazantsv, and A.M. van der Bliek. 1998. A human dynamin-related protein controls the distribution of mitochondria. J. Cell Biol. 143:351–358.

Stephens, R.S., S. Kalman, C. Lammel, J. Fan, R. Marathe, L. A ravinid, W. Mitchell, L. Olinger, R.L. Tatusov, Q. Zhao. et al. 1998. Genome sequence of an obligate intracellular pathogen of humans: Chlamydia trachomatis. Science. 282:754–759.

Stowell, M.H., B. Marks, P. Wigge, and H.T. McMahon. 1999. Nucleotide-dependent conformational changes in dynamin: evidence for a mecha-nochemical molecular spring. Nat. Cell Biol. 1:27–32.

Streep, R., S. Scholz, S. Kurse, V. Speth, and R. Reski. 1998. Plant nuclear gene knockout reveals a role in plastid division for the homolog of the bacterial cell division protein FtsZ, an ancestral tubulin. Proc. Natl. Acad. Sci. USA. 95:4368–4373.

Swietler, S.M., and J.E. Hinshaw. 1998. Dynamin undergoes a GTP-dependent conformational change causing vesiculation. Cell. 93:1021–1029.

Turmel, M., C. Otis, and C. Lemieux. 1999. The complete chloroplast DNA sequence of the green alga Nephroselmis olivacea: insights into the architecture of ancestral plastid genomes. Proc. Natl. Acad. Sci. USA. 96:10248–10253.

Wienke, D.C., M.L. Knetsch, E.M. Neuhaus, M.C. Reedy, and D.J. Manstein. 1999. Disruption of a dynamin homologue affects endocytosis, organelle morphology, and cytokinesis in Dictyostelium discoideum. Mol. Biol. Cell. 10:225–243.

Yaffe, M.P. 1999. Dynamic mitochondria. Nat. Cell Biol. 1:149–150.