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BACTERIAL PHYSIOLOGY

FtsZ and FtsA find the right place

> both studies provide novel mechanistic insights into bacterial cytokinesis

Bacterial cytokinesis is initiated by the assembly of a ring-like structure (the Z ring) at mid-cell that drives cell division through constriction. Two studies now provide new insights into the positioning and membrane association of two components of the *Streptococcus pneumoniae* Z ring, the tubulin-related GTPase FtsZ and the actin-related protein FtsA.

Self-polymerization of FtsZ, the main component of the Z ring, marks the first step in bacterial cytokinesis as it provides an anchor for the accumulation of several other proteins that together form the division septum. Until now, a couple of systems have been identified to position the Z ring in bacteria. The Min and nucleoid occlusion systems are the best characterized to date; they prevent FtsZ ring formation near the cell poles and the nucleoid, respectively. However several bacteria, including the human pathogen *S. pneumoniae*, lack these systems, and how correct Z ring positioning is achieved in these bacteria remained unclear.



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Fleurie *et al.* now identify the *S. pneumoniae* protein mid-cell-anchored protein Z (MapZ) as a key factor that controls positioning of the Z ring. Using fluorescence microscopy of live cells, they showed that MapZ forms a ring-like structure that colocalizes with the Z ring at mid-cell, whereas mutant cells lacking MapZ had mislocalized Z rings and exhibited morphological and growth defects. Interestingly, time-lapse and three-dimensional structured illumination microscopy experiments revealed that at the onset of cell elongation (which precedes cell division), the MapZ ring splits into two rings that migrate from mid-cell to the future division sites of the daughter cells, whereas the position of the FtsZ ring remains unchanged. Subsequently, a third MapZ ring forms at mid-cell, followed by splitting of the FtsZ ring, which moves to the outer MapZ rings at the newly established division sites. The remaining MapZ–FtsZ ring at mid-cell constricts and eventually closes to complete cytokinesis. These findings suggest that MapZ functions as a permanent marker of future cell division sites and positions the Z ring to ensure accurate cell division.

Next, the authors showed that MapZ binds directly to the cell wall component peptidoglycan and that MapZ rings were mislocalized in cells in which peptidoglycan synthesis was inhibited. This, together with the finding that migration of the MapZ rings was coordinated with cell wall synthesis, suggests that MapZ rings are permanently associated with pepitdoglycan and that they are pushed apart during cell elongation. Thus, the migration of MapZ to the future division sites is coupled to cell wall synthesis. Finally, the authors demonstrated that MapZ and FtsZ directly interact, and disruption of this association resulted in FtsZ mislocalization and asymmetric cell division, supporting the notion that MapZ positions the Z ring during cytokinesis.

In a second study, Krupka *et al.* showed that the carboxyl terminus of *S. pneumoniae* FtsA, which anchors the Z ring to the cell membrane during division, functions as an intramolecular switch that controls FtsA polymerization and membrane attachment. In the absence of ATP, FtsA exists as monomers in the cytoplasm. Nucleotide binding to FtsA triggers a conformational shift in the FtsA C-terminal domain that promotes the interaction between FtsA monomers and thus polymerization. In addition, in the ATP-bound state, a C-terminal-located amphipathic helix that contains the membrane-targeting sequence shifts its position towards the membrane, which enables FtsA membrane attachment. The authors propose that local enrichment of FtsA polymers might cause membrane alterations that initiate cell division.

In summary, both studies provide novel mechanistic insights into bacterial cytokinesis. The MapZ protein identified by Fleurie *et al.*, and thus possibly the MapZ-dependent pathway, is conserved in most other Lactobacillales that lack known FtsZ regulatory systems, which highlights the diversity of cell division mechanisms that have evolved in bacteria.

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ORIGINAL RESEARCH PAPERS Fleurie, A. *et al.* MapZ marks the division sites and positions FtsZ rings in *Streptococcus pneumoniae*. *Nature* doi:10.1038/nature13966 (2014) | Krupka, M. *et al.* Role of the FtsA C terminus as a switch for polymerization and membrane association. *mBio* **5**, e02221-14 (2014)

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