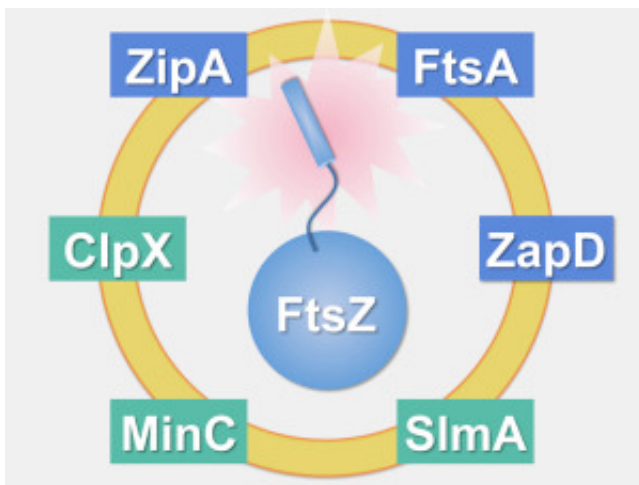


The Keepers of the Ring

Just imagine that you are driving and have a flat tire. Would you find it logical that the design of your car does not allow you to place the jack inside the car trunk? This is exactly how bacteria have evolved their FtsZ protein, the crucial part of the machinery needed every twenty minutes for dividing them into two equal daughters. FtsZ is found swimming freely in the bacterial cytoplasm, where it serves no major known purpose, but it is needed to act at the cytoplasmic membrane, where it is not present for a large part of the cell life. Despite this designers flaw, bacteria are extremely efficient regarding their life cycle. Not only do they proliferate exceedingly well, since their appearance 350 million years ago they populate even the harshest environments on Earth.



The Ring. FtsZ, the main component of the machinery responsible for bacterial division, is assisted by a set of proteins (framed in blue: activators; framed in green: inhibitors) that contribute to anchor it to the membrane, localise it at midcell, stabilise its structure and dispose of spent molecules when constriction is over.

At division bacteria need to split their rigid envelope exactly at midcell, a process initiated by the constriction of their membrane exerted by a division ring containing FtsZ. How does it go to the spot where it is needed at the exact time when it is required, is the topic that we have discussed in our recent review “The Keepers of the Ring”. We have compiled the available data, including some obtained at our laboratory in the Spanish National Biotechnology Centre, regarding how FtsZ is guided and tethered by FtsA and ZipA to the central position of the membrane, and how it is prevented by the Min proteins from causing aberrant divisions if occupying other inconvenient sites as the cell poles. Equally important for the cell is that the envelope does not split while the pair of replicated chromosomes are not separated at each of the two halves. This would be lethal, as the genetic information contained in the bacterial chromosome would not be inherited in its entirety by each daughter. Moreover, were one chromosome be trapped by the constricting machinery, its

physical integrity would be jeopardized. Bacteria, as the model *Escherichia coli*, avoid this catastrophe by using another protein, SlmA, in combination with short patches dispersed in the DNA sequence of their chromosome. Together, they avoid that the division ring exerts a guillotine effect on the chromosome.

An amazing finding regarding the interaction of FtsZ with its keepers, as ZipA and MinC, is that it is established through the same portion of the protein, a central hub in which signals having different origins and even disparate instructions are integrated. The central hub also marks the final fate of FtsZ. Once division is completed, FtsZ is no longer useful and the ClpX protein recognises the central hub and directs FtsZ to be destroyed by the ClpP protease. One attractive, although unproven possibility, would be that these events occur periodically, giving rise to the different stages in the bacterial cycle or even marking the transition from one division to the next.

There is no scarcity of molecules to usher FtsZ through division. Some, as the recently discovered Zap proteins, may modulate the stability of the FtsZ polymers in the division ring. We cannot say if other proteins, even some whose role has not yet been associated to division, may join the ranks of the Keepers of the Ring. Studying the relevance of this selected club of proteins resides not only in finding their beneficial effects for bacteria, but on the wily possibility to discover compounds to neutralise the ring. These would be the much needed new antibiotics essential to fight against the Dark Powers of the Ring, the antibiotic resistant pathogens.

Publication

[The keepers of the ring: regulators of FtsZ assembly.](#)

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