CELL BIOLOGY

Is MipZ the new MinCD?

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URLs

Online

Bacillus subtilis

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=genomeprj&cmd=Retrieve&dopt=Overview&list_uids=76

Caulobacter crescentus

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=genomeprj&cmd=Retrieve&dopt=Overview&list_uids=298

Escherichia coli

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=genomeprj&cmd=Retrieve&dopt=Overview&list_uids=12319

In *Escherichia coli* and *Bacillus subtilis* the Min system and nucleoid occlusion coordinate chromosome segregation with correct placement of the cell-division site, but surprisingly *Caulobacter crescentus* lacks both of these systems. Reporting in *Cell*, Thanbichler and Shapiro have characterized MipZ, a new player in cell division that coordinates positioning of the cytokinetic FtsZ ring, which contracts resulting in cell fission, with segregation of newly replicated chromosomes.

The freshwater bacterium *C. crescentus* is a paradigm for development owing to its strict and synchronizable progression from a motile swarmer cell to a sessile stalked cell. Caulobacteriologists are armed with not only the complete genome sequence and associated 'omics' technologies, but importantly the full gamut of genetic and cell-biology tools.

Bioinformatic interrogation of the previously characterized cell-cycle-regulated transcriptome of *C. crescentus* led the authors to identify *mipZ*, a cell-cycle regulated gene that is conserved among α -proteobacterial species that lack orthologues of the classic cell-division proteins MinCD. The *mipZ* gene, which initial investigations revealed to be essential, is a member of the ParA superfamily of P-loop ATPases. Par proteins function in DNA partitioning, so sequence homologies provided initial clues to MipZ function.

By modulating expression of the chromosomal *mipZ* gene the authors showed that depletion or overproduction of MipZ resulted in fewer cell-division events and a striking increase in cell length, a classic cell-

division phenotype. The authors took advantage of the utility of *C. crescentus*, with its clear polar markers of either a flagellum or a stalk, for localizing MipZ. Meticulous examination of more than 1000 individual cells progressing through the cell cycle revealed that MipZ moved around the cell in a pattern that matched the chromosomal origin of replication (*Cori*). As ParB docks onto binding sites adjacent to *Cori* to mediate chromosome segregation, and depletion of ParB led to the delocalization of MipZ throughout the cytoplasm, the authors reasoned that MipX might bind to ParB. Indeed *in vivo* and *in vitro* approaches confirmed that a ParB•MipZ complex forms on DNA containing ParB binding sites.

Importantly, the MipZ protein formed a gradient within the cell, peaking at the poles (where ParB is localized) and decreasing towards the mid-cell. The authors argued that ParB might be involved in the dynamic localization of MipZ, and that MipZ might form polymers, in common with other ParA homologues. This hypothesis provided an important link between the localization of daughter chromosome origins at the poles and the position of the FtsZ ring at mid-cell. With this in mind, the authors investigated whether MipZ affected FtsZ ring formation.

Close inspection of labelled FtsZ revealed that at the beginning of the cell cycle, segregation of the newly duplicated origins displaces FtsZ towards the mid-cell, where it coalesces into a ring and initiates cell constriction. FtsZ ring formation was ablated by overexpression of MipZ and mixing MipZ and FtsZ *in vitro* induced bending and shortening

of FtsZ filaments. Therefore, the authors suggest that MipZ alters the structure of FtsZ polymers, evoking comparison with the inhibitory role of MinCD in FtsZ ring formation.

The authors unveiled an elegant model in which MipZ binds to ParB and is colocalized with the newly replicated chromosome origins at the cell poles. Since MipZ actively disrupts FtsZ polymerization, recruitment of MipZ to the poles allows the FtsZ ring to form at the mid-cell and direct cytokinesis. So, it seems that even for a basic cell problem like cell division, bacteria have found more than one solution.

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ORIGINAL RESEARCH PAPER Thanbichler, M. & Shapiro, L. MipZ, a spatial regulator coordinating chromosome segregation with cell division in *Caulobacter*. *Cell* **126**, 147–162 (2006)

Electron micrograph of a *Caulobacter* predivisional cell prepared by negative staining with uranyl acetate. Image kindly supplied by Michael Laub.