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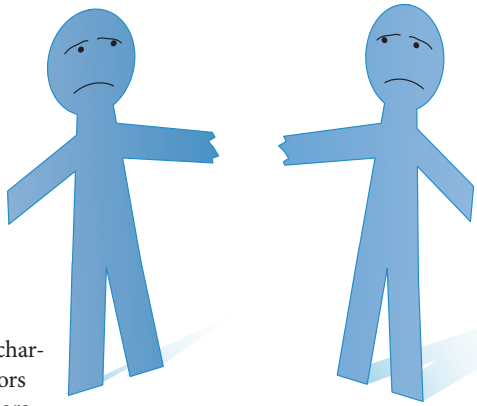

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BACTERIAL GENETICS

Splitting is never easy

> “chromosomal replication is crucial for timing bacterial cell division”

Bacterial cell division by binary fission occurs after the formation of a dividing septum at the midpoint of the cell and requires the concerted action of several bacterial proteins. This process is driven by the tubulin homologue FtsZ, which assembles to form a ring-like structure known as the Z-ring at the site of division and constitutes a scaffold for the cytokinetic machinery. Cell division requires tight spatial and temporal regulation; however, the mechanisms that coordinate cell division with chromosomal replication and segregation are still poorly understood.

Two recent studies shed light on these mechanisms in two distinct bacterial species that have different cell shapes and division mechanisms.

In the first study, van Raaphorst, Kjos and Veening found that in the oval-shaped bacterium *Streptococcus pneumoniae* both chromosomal replication origins localize to the future site of cytokinesis before FtsZ, and that the formation of the Z-ring occurs simultaneously with the initiation of DNA replication. Moreover, chromosomal segregation was shown to drive the positioning of the cell division site. By developing a series of tools for live-cell fluorescence imaging, by specifically cleaving the chromosome using CRISPR–Cas9, and by analysing deletion mutants for specific factors that are known to be involved in division and chromosome segregation, the authors were able to map the cell division process in relation to the cell cycle and characterize the function of the factors involved. In particular, the authors showed that MapZ was not directly involved in the selection of division site as was previously thought, but was crucial for the placement of the division plane at the correct angle, perpendicular to the length axis of the cell. In addition, they found that the condensin-like protein structural maintenance of chromosomes (SMC) was responsible for early segregation of the chromosomal replication origin, and that this was important for the timely localization of the Z-ring.

In the second study, Pang *et al.* showed that in the round-shaped bacterium *Staphylococcus aureus*, the nucleoid occlusion factor Noc controls the initiation of DNA replication and coordinates chromosomal segregation with cell division. Previous studies had shown that Noc binding to the chromosomal replication origins inhibited the assembly of the Z-ring; however, as Noc is not essential in *S. aureus*, other unknown regulators were likely to exist. To find such additional factors, the authors used a transposon mutant screen and found that the deletion of *comEB* and rhomboid (*rbd*) genes, which encode a deaminase involved in dTTP synthesis and a membrane-embedded serine protease, respectively, enhanced the division defect in Noc-deficient cells and were lethal. They then showed that suppressor mutations in the *dnaA* gene, which encodes the initiator of DNA replication, were able to rescue the lethal phenotypes in the double mutants, suggesting a possible link between Noc and chromosomal replication. Indeed, deletion of Noc alone caused over-initiation of DNA replication, and suppressor mutations in *dnaA* ameliorated both this phenotype and the cell division defects displayed by the Noc mutant. Moreover, overexpression of *dnaA* enhanced the phenotypes of the Noc-deficient mutant. Unexpectedly, the authors did not observe any effect on DNA replication for the single *comEB* and *rbd*-deletion mutants, and future studies are required to characterize their possible role in cell division.

Together, these studies have shown, in two distinct bacterial species, that chromosomal replication is crucial for timing bacterial cell division and — in the case of *S. pneumoniae* — for the localization of the cell division site, and have highlighted new functions for bacterial factors that contribute to this tight regulation.

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ORIGINAL ARTICLES van Raaphorst, R., Kjos, M. & Veening, J. W. Chromosome segregation drives division site selection in *Streptococcus pneumoniae*. *Proc. Natl Acad. Sci. USA* **114**, E5959–E5968 (2017) | Pang, T. *et al.* The nucleoid occlusion factor Noc controls DNA replication initiation in *Staphylococcus aureus*. *PLoS Genet.* **13**, e1006908 (2017)