Many bacterial, archaeal, and eukaryotic cells divide by binary fission and do so with precision. Yet until fairly recently it was not clear how even a simple cell such as *Escherichia coli* knows where its middle is so it can divide by septation into two equal daughters. There were many theories, including those that implicated solely physical properties instead of genetic components as the main driver of midpoint recognition. But as with many insights into how cells work, mutants with abnormal phenotypes were crucial to demonstrate that the action of genes was largely responsible. The first hint came from a mutant of *E. coli* that in addition to forming rod-shaped cells containing chromosomal DNA also generated minicells that lacked chromosomes (1). These round minicells, approximately 1 by 1 μm, arise from aberrant septation at cell poles past the edge of the nucleoid, such that they retain a typical Gram-negative envelope and cytoplasm but are devoid of chromosomal DNA. This formation of chromosome-less minicells was also found in mutants of other species, such as *Bacillus subtilis* (2), and opened the way for innovative applications. Because *E. coli* minicells can actively metabolize for hours, they were soon exploited for production and identification of specific peptides encoded by multicopy plasmids—which could easily partition into minicells and persist—as well as for other studies including phage infection. Many of these important advances were published in the *Journal of Bacteriology* (JB) (3).

The ability of mutations, called *min*, to disrupt the normal midcell location of the division septum in several species indicated that this positioning is genetically controlled. Two important papers in JB from Larry Rothfield’s laboratory took the next crucial step of identifying the genes necessary and sufficient for this positioning (4, 5). The first paper elegantly used classical genetics to show that a mutation in only one locus, called *minB*, was needed to make *E. coli* generate many minicells (another locus, *minA*, was originally thought to be involved but was not). The second paper, spearheaded by Piet de Boer, one of JB’s current editors, demonstrated that the *minB* locus encoded several polypeptides. Ironically, perhaps, the authors used maxicells—another method to make chromosome-less *E. coli* cells through UV irradiation—to identify the sizes of these Min proteins. They showed that expressing the *minB* locus either too much or too little could induce minicell formation, suggesting that Min proteins need to be in the correct stoichiometry with themselves and/or their cellular targets.

The important genetic experiments in these two papers eventually gave rise to discoveries that have forever transformed our view of bacterial cell organization. We now know that there are three Min proteins in *E. coli*, and together they self-organize into a protein gradient that oscillates from cell pole to cell pole *en masse* every minute or so, forming a bipolar gradient (6, 7). MinC, a specific inhibitor of the cell division protein FtsZ, as well as the oscillation drivers MinD and MinE, guards the polar regions of the cell from the often overexuberant assembly of FtsZ rings that drive cell division, thus helping to restrict the rings to midcell. Other bacterial Min systems perform fascinating variations on this theme, sometimes not oscillating (e.g., in *B. subtilis*) but still guarding against unwanted FtsZ rings. Many other species lack Min homologs but use alternative septum positioning mechanisms that are only now coming to light. All the mechanistic understanding of these self-organizing gradients in bacteria, including mathematical modeling and exciting recent experiments that reconstitute Min-mediated FtsZ positioning *in vitro* (8), stems from the genetic inferences in the two Rothfield lab papers from JB.

REFERENCES