Current Topics

P1 Plasmids in Dynamic Flux before and after Moving into Daughter Cells

P1 plasmids segregate into daughter *Escherichia coli* cells via “a highly dynamic process involving no fixed cellular location,” according to Stuart Austin and his colleagues at the National Cancer Institute (NCI) in Frederick, Md. Further, it depends on a self-correcting mechanism to assure that each daughter cell receives a full plasmid copy. The research findings are published in the March Journal of Bacteriology (192:1175–1183).

Plasmids were once thought to follow mitosis-like mechanisms as they replicate and move from dividing bacteria into daughter cells. But no one can find evidence for such mechanisms, despite years of searching. Meanwhile, other unusual mechanisms are being reported. For instance, PB171 plasmids produce fibers that push two sister plasmids apart, which Austin calls an “entirely different mechanism” from mitosis. Even so, some researchers cling to the notion that P1 plasmids segregate via a mitotic mechanism, relying on what he considers “very thin evidence.”

To get a fresh look at P1, Austin and his collaborators adapted time-lapse microscopy to follow these plasmids as they replicate and then segregate into daughter bacterial cells. Once replicated, P1 plasmids separate substantially within a host cell, unless they encounter an obstacle, such as the sides or ends of nucleoid space or another plasmid, he says. *E. coli* cells often contain other plasmids—typically about three, although numbers vary. If two daughter P1 plasmids move far apart, they tend to come back together as a pair. Or, if one member of a daughter pair encounters another plasmid, those two may form a new pair but then quickly diverge. Such events typically occur several times per cell per generation.

“Secondary pairing seems counterintuitive, as accurate segregation should require the plasmids to come apart and stay far enough apart to ensure that each daughter cell receives its complement when cell division occurs,” Austin says. “We wondered if this unruly behavior might nevertheless be beneficial to the survival of the plasmid in the growing population.”

To address that question, Austin and his collaborators developed an electronic model to mimic plasmid behavior. “The model resembles actual observations very well,” he says. “Every cell in the population receives at least one plasmid at cell division,” with failures to meet that fidelity about 1 per 10,000 cases. “Moreover, by manipulating the model, we show that re-pairing of sisters and pairing after an encounter with an unrelated copy are both important factors in ensuring fidelity of inheritance.” Indeed, plasmids are spaced more or less evenly within mother cells.

These observations about plasmid behaviors are “contrary to our present understanding,” note Syam P. Anand and Saleem A. Khan of the University of Pittsburgh School of Medicine in Pittsburgh, Pa., whose commentary on the NCI research also appears in the March 2010 Journal of Bacteriology (192:1171–1174). One surprise is that P1 is found in “multiple copies,” whereas it was thought to be found only in low copy numbers, they point out. The NCI findings also cast doubt on “the notion that sister plasmids are always paired and located at fixed positions within a cell and that segregation simply ensures the movement of sister plasmids to different daughter cells.”

Another intriguing suggestion is that plasmids encode “a self-correcting mechanism that places the copies of plasmids apart from each other and at more or less equal distances from each other when they exist within the same cell,” Anand and Khan point out. Meanwhile, they also raise the question of whether what appear to be plasmid pairings are distorted views that come from observing a three-dimensional phenomenon via two-dimensional imaging.

The P1 research findings could contribute to a variety of applications. For example, some plasmids carry genes encoding antibiotic resistance and enzymes for making toxins, others confer the ability on some kinds of soil bacteria to fix nitrogen, and still other plasmids carry genes encoding proteins that degrade complex hydrocarbons, says Aresa Toukdarian of the University of California, San Diego. “Understanding factors that contribute to the stable maintenance of plasmids in the host is important,” especially in the case of low-copy-number plasmids, such as P1. Toukdarian praises the NCI researchers for their “use of more sensitive optical techniques, which allows for localization analysis under conditions that better approximate nature.”

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