to follow developments as the answers to some of these questions emerge. In the meantime, given that macadamia nuts are the richest known source of dietary palmitoleate, perhaps we should indulge while we wait.

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Grasping at Origins

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Chromosome segregation in the bacterium *Caulobacter crescentus* involves propulsion of the replication origin and its capture at one pole of the cell. Bowman et al. (2008) and Ebersbach et al. (2008) now report the discovery of a protein called PopZ that mediates this chromosome capture.

The faithful segregation and inheritance of genetic material is a hallmark of living cells. In eukaryotic cells, chromosome segregation is accomplished by the largely conserved mechanism of mitosis whereby specific DNA sequences (centromeres) are recognized by a protein complex called the kinetochore and are driven toward opposite ends of the cell by a spindle apparatus. Bacteria, in contrast, seem to use a variety of strategies to achieve chromosome segregation. As a consequence, the challenge of elucidating the multiple mechanisms used by bacteria to ensure that each daughter cell faithfully inherits a copy of the genetic material has been daunting. In the aquatic bacterium *Caulobacter crescentus*, chromosome segregation occurs by a harpoon-like mechanism in which the newly duplicated origins of replication of the chromosome become anchored at the extreme opposite poles of the cell. How this anchoring is accomplished has been a mystery. In this issue, Bowman et al. and Ebersbach et al. report the discovery of a protein (PopZ) that forms a Velcro-like surface at the cell poles. PopZ enables chromosome anchoring by grasping onto ParB proteins, which are clustered on the chromosome near the site at which DNA replication is initiated.

The mechanisms of chromosome segregation differ among bacterial species, but two features of the segregation process seem to be common to all bacteria yet distinct from chromosome segregation in eukaryotes. First, chromosome segregation commences during replication rather than after its completion. Second, chromosome segregation is mediated from sites (often ill-defined) located near the origin of replication. As a consequence, chromosome segregation can, and often does, commence shortly after the initiation of replication. What happens next, however, differs markedly from species to species.

In growing cells of *Bacillus subtilis* and *Escherichia coli*, replication commences with the origin located in the central region of the cell. In *B. subtilis*, the newly duplicated origin regions move apart toward opposite ends of the cell and are found at the outer edges of the two masses of daughter DNA molecules known as nucleoids (Figure 1A; Lewis and Errington, 1997; Lin et al., 1997; Webb et al., 1997). In *E. coli*, the origins also move apart but become located in the center of the daughter nucleoids as replication proceeds (Figure 1A; Reyes-Lamothe et al., 2008). A strikingly different situation is found in *Caulobacter* and *Vibrio cholerae* (*V. cholerae* actually contains two chromosomes but for simplicity we only consider the larger one). In both bacteria, replication begins with the origin located near one pole of the cell. Next, one of the two newly duplicated origin regions is propelled like a harpoon all the way across the cell where it becomes anchored at the extreme opposite pole (Figure 1B; Fogel and Waldor, 2006; Viollier et al., 2004).

The two new studies by Bowman et al. (2008) and Ebersbach et al. (2008) now demonstrate how this anchoring

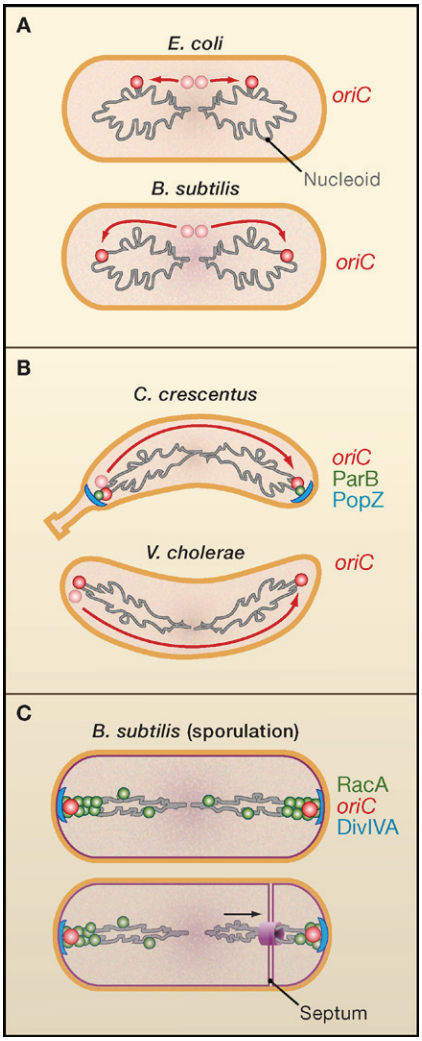

Figure 1. Diverse Mechanisms of Bacterial Chromosome Segregation

(A) Replication origins (*oriC*) in growing cells of *Bacillus subtilis* and *Escherichia coli* have relatively limited movement from their initial positions (faded red spheres) at the beginning of replication. *oriC* migrates to the outer edges of daughter DNA masses (nucleoids) in *B. subtilis* but remains in the center of nucleoids in *E. coli*.

(B) In *Caulobacter crescentus* and *Vibrio cholerae*, *oriC* undergoes a harpoon-like movement from one cell pole to the extreme opposite pole (red arrow). In *C. crescentus*, ParB molecules bound near the origin (but at a distinct site) are captured by PopZ molecules on the inside surface of the pole.

(C) The nucleoid in *B. subtilis* at the start of sporulation (upper cell) is stretched across the cell with the origin-proximal portion anchored at the pole. After asymmetric division (lower cell), the origin-distal portion of the chromosome must be pumped into the smaller cell through a channel (purple) in the septum. RacA molecules, bound to the chromosome at particularly high density near the origin, anchor the chromosome to the poles by interacting with DivIVA molecules on the inside surface of the poles. Purple line indicates the membrane inside the wall of the *B. subtilis* cells before and after division.

takes place. A previously uncharacterized protein in *Caulobacter*, PopZ, accumulates at the cell poles and captures the origin of replication by binding directly to a protein called ParB that was previously known to bind to sites located near the origin of replication (Bowman et al., 2008; Ebersbach et al., 2008). Initially, PopZ localizes to the old cell pole where the unreplicated origin of replication resides. As replication commences, the cell propels one origin of replication (bound by ParB) to the opposite end of the cell. Meanwhile, PopZ accumulates at the new pole to capture the newly arriving origin. This happens in the nick of time, with the majority of cells accumulating PopZ at the new pole just before or as the harpooned ParB/origin complex arrives. Bowman et al. (2008) further show that purified PopZ spontaneously oligomerizes into a filamentous network, readily viewed by electron microscopy, which they suggest may coat the cell pole to form a wide sticky (Velcro-like) target for the incoming origin of replication. In addition, Ebersbach et al. (2008) propose that PopZ is not simply dedicated to the capture of chromosome origins but rather may form a multifunctional platform that recruits several cell-cycle regulatory proteins to the poles.

The PopZ-ParB story is strikingly analogous to an anchoring mechanism involved in a specialized and unrelated mode of chromosome segregation that takes place during spore formation in *B. subtilis*. When sporulation is initiated in *B. subtilis*, two newly duplicated chromosomes are remodeled into a continuous elongated DNA mass that stretches from pole to pole and that eventually segregates to dissimilarly sized daughter cells created by asymmetric cell division. As in growing cells of *B. subtilis*, the two origins of replication in the sporulating cells are at the outer edges of the DNA mass. Unlike growing cells, however, the origins are anchored at the extreme poles of the cell. Anchoring is mediated by the proteins RacA and DivIVA, which are analogous but not homologous to ParB and PopZ, respectively. RacA (the ParB analog) binds to many sites on the chromosome and in particular to a high density of sites clustered in the origin-proximal region of the chromosome and straddling the origin (Figure 1C, top; Ben-Yehuda et al., 2005). RacA molecules both remodel the chromosomes into a filament and also attach the origin-proximal regions to the pole by direct or indirect interaction with DivIVA (the PopZ analog) that decorates the inside surface of the cell poles. Interestingly, because asymmetric cell division takes place before chromosome segregation, one chromosome becomes trapped between the two progeny cells and must be pumped into the smaller cell through a channel in the septum in an ATP-driven process (Figure 1C, bottom; Burton et al., 2007).

The discovery of PopZ resolves the mechanism of *Caulobacter* chromosome capture, but the question remains as to the nature of the motor that drives origin movement. Recently, Toro et al. (personal communication) have shown that force is exerted (uniquely and independently of chromosome position) on the ParB-bound site that is captured and retained at the cell pole (Bowman et al., 2008; Ebersbach et al., 2008). In *V. cholerae*, the origins are separated by ParA, an actin-like protein that mediates the segregation of small bacterial chromosomes known as plasmids (Fogel and Waldor, 2006). ParA interacts with ParB molecules located on the chromosome near the replication origin of *V. cholerae*. Intriguingly, the work of Toro et al. (personal communication) implicates ParA in the harpoon-like movement of the origin in *Caulobacter*. Together with the findings of Bowman et al. (2008) and Ebersbach et al. (2008), these data suggest a cohesive model for chromosome movement in which ParB serves as a hub for both ParA-driven chromosome movement and eventual anchoring of the origin region to the cell pole. Thus, the studies of Bowman et al. (2008) and Ebersbach et al. (2008) not only clarify the mechanism of *Caulobacter* chromosome capture but also provide exciting new avenues for future study.

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Kinesin Motors: No Strain, No Gain

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The processive movement of the dimeric motor protein kinesin 1 along microtubules requires communication between the two motor domains. Yildiz et al. (2008) now show that tension between the motor domains not only is necessary for normal processivity but also may be sufficient for motor motility under some conditions.

Members of the kinesin superfamily of motor proteins are remarkable nanomachines. Most kinesins use the chemical energy stored in ATP to produce directed force along microtubule protofilaments, powering critical cellular processes such as vesicle transport and chromosome segregation (Vale, 2003). Other kinesin family members do not act directly as motors but rather regulate microtubule dynamics. Remarkably, some members of the kinesin family, such as dimeric "conventional" kinesin 1, move processively along their protein tracks by coordinating their two motor domains in a hand-over-hand manner. Kinesin 1 is able to take hundreds of 8 nm steps without falling off, even while pulling a substantial load, thus ensuring that diffusion does not remove the motor and its crucial cargo from the track. This processivity is dependent upon one kinesin motor domain being attached to the microtubule at all times. It remains unknown how exactly processive kinesins coordinate the activities of their two motor domains such that one domain always remains attached to the microtubule. In this issue of *Cell*, Yildiz and colleagues present an elegant study that clarifies this question and uncovers some remarkable features of the kinesin motor.

The molecular architecture of dimeric kinesin 1 partially explains how it might achieve the feat of processivity. Each monomer of kinesin 1 is composed of a core motor domain of some 350 amino acids containing the ATPase catalytic site as well as microtubule-binding sites. Adjacent to the motor domain is the neck linker, a flexible region that has been shown to undergo a nucleotide-dependent transition from a disordered to an ordered structure. The linker is followed by a coiled-coil dimerization domain. Thus, kinesin 1 has two "feet" (the motor domains) connected to each other by a flexible linker that can change conformation and that is long enough to allow the two motor domains to bind to adjacent sites on the microtubule, 8 nm apart. The structure of kinesin 1 allows it to "walk" along the microtubule filaments. Intermotor domain (interhead) communication is known to be necessary for processive movement, but how this communication occurs is unclear. Most theories posit that communication occurs through a "gating" mechanism where a mechanistic step in one head is blocked until a certain step is taken in the other head (reviewed in Block, 2007). Such gating could be chemical in nature, e.g., ATP binding is blocked until a head dissociates from the microtubule (Klumpp et al., 2004; Rosenfeld et al., 2003), or mechanical in nature, e.g., a conformational change in one head pulls, or pushes, the other head off the microtubule (Hancock and Howard, 1999; Spudich, 2006). Of course, it is more than likely that the actual mechanism of interhead communication utilizes both types of gating, as they are not mutually exclusive.

In their new work, Yildiz et al. (2008) used mutant kinesin 1 molecules and optical trapping microscopy to observe how altering the length of the neck linker, and thereby the tension between the heads, affects gating and hence kinesin motility. Several interesting and unexpected results emerged from this study. In the first set of experiments, the authors inserted progressively larger polyproline helices between the linker region and the dimerization domain. When two heads of wild-type kinesin 1 are bound to the microtubule, the native linkers are more or less fully extended.