sor and UmuD is facilitated by RecA only when it is in the form of a filament. Schlacher and colleagues[14] demonstrate that UmuD is not cleaved when RecA is bound to the DNA substrate with the six-nucleotide overhang used in their polymerase assays. Thus, stimulation of Pol V by RecA does not require a RecA filament. Importantly, lesion bypass by Pol V is achieved with only Pol V and RecA protein present, which form the minimal mutasome.

So, how might the minimal mutasome be constructed? Once a fork stalls at a lesion, replication of the leading and lagging strands uncouples, resulting in the appearance of single-stranded DNA (**Fig. 1**). RecA protein binds to the single-stranded DNA and most likely initiates filament formation. RecA also binds to a nucleotide cofactor such as dATP, and facilitates the cleavage of LexA protein, leading to derepression of the SOS genes. UmuD and UmuC proteins are synthesized, and UmuD associates with the RecA filament, perhaps at the site of the lesion, where it is cleaved to generate UmuD′. Schlacher and colleagues[14] propose that UmuD′$_2$ is bound to RecA* during TLS, and this complex is associated with the single-stranded DNA on the template strand. They base this proposal on results from their fluorescence anisotropy studies showing that both RecA and RecA1730 stimulate the binding of Pol V and UmuD′ to DNA in the presence of a nucleotide cofactor, with nearly identical kinetics. Perhaps this RecA* is a remnant of a previously existing filament formed on the single-stranded DNA that facilitated cleavage of UmuD. The continued interaction of UmuD′ with RecA* may shift the equilibrium of RecA and single-stranded DNA-binding protein (SSB) for DNA, as proposed for the LexA-RecA interaction, resulting in deformation of the RecA filament and an increase in the number of SSB molecules associated with the DNA[16]. This could lead to an inhibition of strand exchange and pave the road for translesion synthesis. Next, the RecA*–UmuD′2 complex may recruit UmuC, in association with another molecule of RecA. Schlacher and colleagues[14] show that RecA binds to Pol V, but not to UmuD′, in the absence of DNA. This leads them to suggest that RecA associates with the UmuC subunit of Pol V. Once RecA-UmuC associates with RecA*-UmuD′$_2$, the minimal mutasome is poised for TLS.

The next step will be to determine how RecA stimulates DNA synthesis by Pol V. RecA could alter the conformation of Pol V, resulting in optimum placement of the catalytic residues of the protein, the DNA and the incoming dNTP such that the rate of synthesis would increase. RecA may somehow act as a tether that 'pulls' Pol V through the lesion. Determining how RecA1730 may interfere with TLS in the presence of wild-type RecA may help elucidate the direct role of RecA in TLS.

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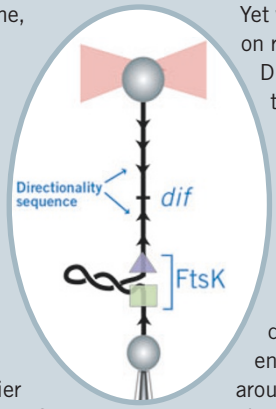
Hanging around at *dif*

During replication of the circular *Escherichia coli* genome, chromosome dimers can form. These dimers must be resolved into monomers before they can be segregated into daughter cells. Resolution occurs at *dif* sites by a site-specific recombinase, XerCD. Another multimeric protein complex, FtsK, assists in dimer resolution by bringing the two *dif* sites together. FtsK also associates with the cell membrane and helps to partition DNA into daughter cells by acting as a pump that drives DNA through the septum.



A recent study (Pease *et al.*, *Science* **307**, 586–590, 2005) has uncovered interesting new facets of the movement of FtsK on the DNA. This single molecule study confirms that FtsK is the premier speedster of the cell. It translocates along DNA at rates of up to 5 kb per second without unwinding the DNA—making FtsK the fastest motor protein yet identified. It also has muscle, able to maintain high speed against significant load.

FtsK was observed to move bidirectionally without losing contact with DNA, suggesting that there is more than one motor in the complex (schematized as purple triangle and green square). While both motors seem to be capable of bidirectional movement, only one is active at a time. This leads to accumulation of supercoiled DNA between the motors. For actual translocation to occur, the supercoiled DNA must be released through the rear motor (green square).

Yet while FtsK has the potential to move bidirectionally on random DNA, net movement was unidirectional on DNA containing a *dif* site. Particularly notable is that the net movement occurred in the same direction on all molecules. To examine what specifies this directionality, regions of chromosomal DNA surrounding the *dif* site were tested. In each case, when FtsK bound to the DNA it traveled toward the *dif* site (movement indicated by arrows). But FtsK did not stop at *dif*. Instead, it was observed to go beyond *dif*, and then seemed to hit a site that caused it to reverse direction and travel back toward *dif* again. Thus, the end result is that FtsK reaches a state where it oscillates around the *dif* site.

It is proposed that there exist short, asymmetric sequences that signal when the active motor is moving toward *dif*; this would direct the FtsK movement to facilitate dimer resolution. An implication of this model is that these sites must be oriented in opposite directions from the origin of replication. This concept parallels the regulation of the activity of *E. coli* RecBCD helicase by an asymmetric octameric sequence (*chi*). Genomic analysis has revealed that *chi* sequences are oriented predominantly in the direction away from the origin of replication, which may be rationalized with the function of RecBCD in repairing broken replication forks.

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