

- Introduction
- What Leads to Recombinational DNA Repair?
- Proteins Involved in Recombinational DNA Repair
- Pathways
- Replication Restart Associated with the SOS Response
- Summary

Recombinational DNA Repair in Bacteria: Postreplication

Kevin P Rice, *University of Wisconsin-Madison, Madison, Wisconsin, USA*

Michael M Cox, *University of Wisconsin-Madison, Madison, Wisconsin, USA*

Recombinational DNA repair represents the primary function for homologous DNA recombination in bacteria. Most of this repair occurs at replication forks that are stalled at sites of DNA damage.

Introduction

Deoxyribonucleic acid (DNA) damage is a common occurrence in all cells. A bacterial cell growing in an aerobic environment will suffer 3000–5000 DNA lesions per cell per generation (most of them oxidative in origin). Most of this damage is faithfully repaired by specialized DNA repair systems; however, replication forks will occasionally encounter unrepaired DNA lesions. Because DNA polymerase is usually unable to bypass DNA damage, the complex breaks down in what is best described as an enzymatic train wreck. Under normal cellular growth conditions, nearly every bacterial replication fork will suffer this fate. A stalled replication fork triggers an elaborate enzymatic response, ultimately restoring an active replication fork without introducing a genetic mutation.

While traditionally thought of as an important avenue for the generation of genetic diversity, primarily during conjugation, homologous DNA recombination in bacteria is now understood to be of paramount importance to the general maintenance of the genome. The response to a stalled replication fork involves homologous genetic recombination, followed by a specialized process for the origin-independent reinitiation of replication. The reactivation of stalled replication forks is a housekeeping activity, and represents the primary function of the recombination enzymes and the additional proteins and enzymes needed for replication restart (Cox, 1998).

This article focuses on recombinational DNA repair in *Escherichia coli*.

What Leads to Recombinational DNA Repair?

Normal DNA replication in *E. coli* is initiated by recruiting several proteins to the origin of replication, *oriC*, on the 4.7 million-bp circular chromosome. An active replication

fork (including DNA polymerase III and the DnaG and DnaB proteins) processes in each direction from that origin. The forks eventually meet, yielding two identical copies of the bacterium's genetic material.

Recombinational DNA repair ensues whenever a replication fork is halted by DNA damage prior to normal replication termination. There are at least two major types of damage and corresponding pathways for their repair (Figure 1). If the fork encounters a DNA strand break, a double-strand break that separates one branch of the fork from the rest results. Alternatively, the fork might encounter an unrepaired DNA lesion, leaving the lesion in a single-strand gap at the stalled fork. In at least some cases, such stalled forks are cleaved to generate double-strand breaks. The pathways for reactivation of the replication forks vary to some degree, depending on the DNA structures presented to the cell. The cellular recombinational DNA repair system is an adaptable set of enzymes that can process whatever DNA structures might exist at a collapsed replication fork.

The link between DNA damage, stalled replication forks and homologous recombination is especially easy to see in cells that suffer extensive DNA damage, as may happen upon exposure to ultraviolet light, chemical mutagens or ionizing radiation. In such circumstances, cell growth is halted as DNA replication becomes blocked, and the SOS response is induced. After some period of time, DNA synthesis resumes and the bacteria continue to divide. Resumption of replication is a phenomenon that is completely dependent upon several genes, including most of those associated with homologous recombination. The induction of the SOS response requires the single-strand gaps that appear at stalled replication forks, and no SOS induction is observed unless active replication is occurring in the cell. In cells not undergoing conjugation or transduction, little recombination is observed in the absence of both DNA damage and active replication.

The frequency with which replication fork reactivation is required under normal aerobic growth conditions has

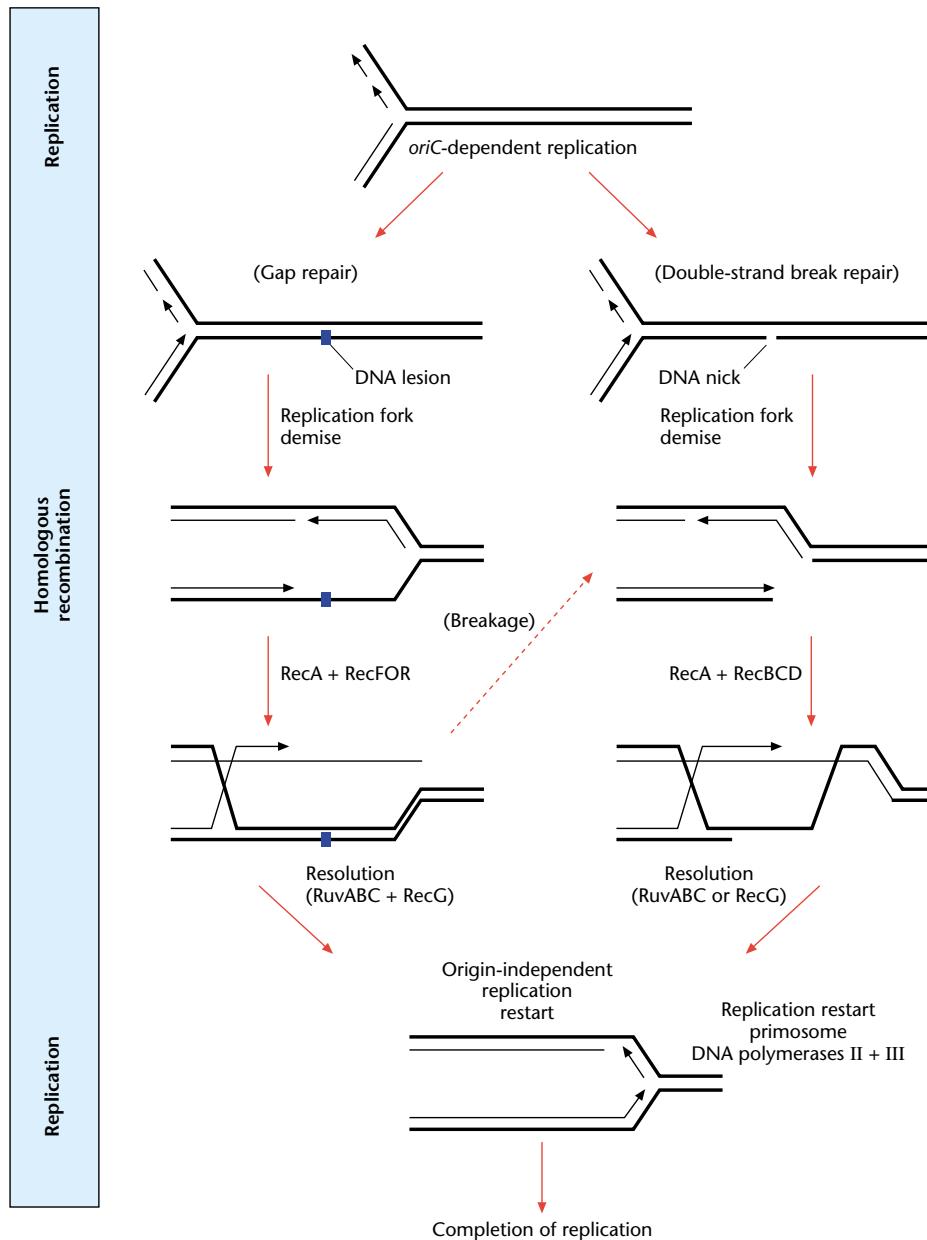


Figure 1 Pathways for the reactivation of stalled replication forks in bacteria. The pathways diverge depending on what type of damage is encountered. If an unrepaired lesion is encountered (left path), the lesion is left in a DNA gap. A complementary strand is recruited from the other side of the replication fork, with the aid of the RecA, RecFOR, and probably other proteins. Once recombination intermediates are processed (using the RuvABC and/or RecG activities), replication is reinitiated by a specialized set of replication restart enzymes. If the fork instead encounters a DNA strand break, a double-strand break results (right path). The major repair pathway in this case utilizes the RecBCD enzyme. Processing of recombination intermediates and replication restart ensues, as described above. Some of the recombination intermediates generated in the gap (left) repair path may be cleaved and thus funnelled into the double-strand break repair path, as indicated by the broken red arrow.

been difficult to quantify. A variety of studies, mostly indirect, have yielded estimates ranging from 15 to 100% of the replication forks that initiate at *oriC*. Bacterial mutants defective in double-strand break repair exhibit unrepaired double-strand breaks in 15–20% of cells. Null mutations in

certain recombination genes, detailed below, produce up to a 50% decrease in viability. Mutations that block replication restart are nearly inviable, suggesting a high percentage of replication forks stalling at DNA damage. The recombination required for replication fork reactiva-

tion often results in DNA crossovers, which can lead to the formation of contiguous chromosome dimers rather than two monomeric chromosomes once replication is completed. If the site-specific recombination system that resolves chromosomal dimers to monomers (the XerCD system) is not functioning, about 15% of the cells have unresolved chromosomal dimers that almost certainly result from recombinational DNA repair of replication forks (Steiner and Kuempel, 1998). Although more quantitation is needed, all of the data reinforce the general idea of recombinational DNA repair as an important housekeeping function in bacterial cells, providing non-mutagenic pathways for the reactivation of replication forks stalled by DNA damage.

Proteins Involved in Recombinational DNA Repair

The reactivation of stalled replication forks requires a wide range of enzymatic activities. The RecA protein is the central factor in recombinational DNA repair. However, several other proteins are required for recombination, including the single-stranded DNA-binding protein (SSB), the RecBCD proteins, the RecFOR proteins, the RecG protein and the RuvABC proteins. Also required is the set of proteins needed for replication restart. The functions of these proteins are integrated, and sometimes redundant. The XerCD site-specific recombination system is also required to undo some of the potentially deleterious effects inherent to recombinational DNA repair.

RecA protein

RecA protein promotes the central steps of any recombinational process, including the alignment of two homologous DNA molecules and the subsequent exchange of DNA strands. The *recA* gene has been identified in every bacterial genome in which it has been sought, and RecA protein has been isolated from perhaps a dozen bacterial species. In addition, structural and functional homologues have been found in archaeans and all eukaryotes, demonstrating the critical and ubiquitous nature of homologous DNA recombination. Null mutants of *recA* in *E. coli* have reduced viability when grown under normal aerobic conditions, with at least 50% of cells in culture being dead and about 10% containing no DNA. When *recA*⁻ genotypes are combined with mutations in any gene that tends to increase the frequency of unrepaired DNA strand breaks, the resulting strain is inviable unless grown anaerobically.

In vitro, RecA protein (37.8 kDa) is a DNA-binding protein with a DNA-dependent adenosine triphosphatase (ATPase) activity. RecA binds readily to single-stranded DNA (ssDNA), nucleating and then assembling unidirectionally

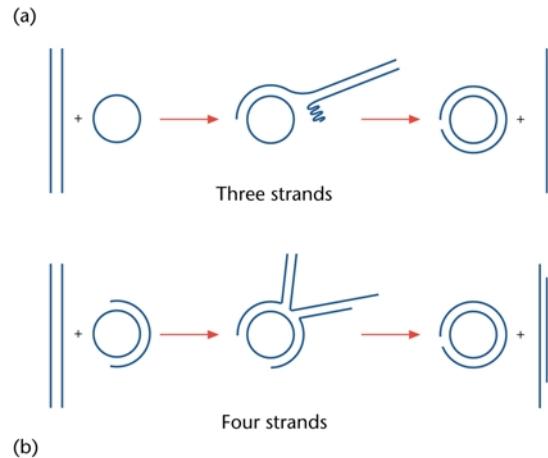
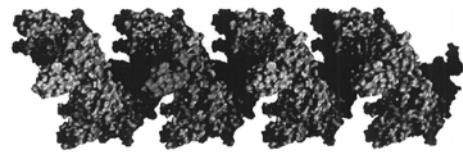


Figure 2 The bacterial RecA protein and DNA strand exchange. (a) A portion of a RecA filament is shown, containing 24 RecA monomers. There are approximately six monomers per turn in the helical filament, and a single monomer is highlighted in red. The DNA is bound in the filament groove. The image is based on the structural work of Randy Story and Thomas Steitz, using PDB file 1REB. (b) Typical DNA strand exchange reactions utilized to study RecA protein function *in vitro*. RecA filaments will form on the single-stranded or gapped DNA circles. DNA pairing and strand exchange will then ensue with the double-stranded linear DNA molecule. The four-strand exchange exhibits an absolute requirement for ATP hydrolysis. The DNA substrates are usually derived from bacteriophage or plasmid DNAs, and the reactions shown were originally chosen for ease of assay.

tionally (5'→3') into a nucleoprotein filament (**Figure 2a**). This filament represents the active species of RecA protein and has several activities that mimic its presumed *in vivo* role. RecA monomers within a DNA-bound filament on ssDNA hydrolyse ATP relatively slowly ($k_{\text{cat}} 30 \text{ min}^{-1}$). RecA protein filaments also undergo end-dependent dissociation from DNA coupled to the hydrolysis of ATP. Monomers dissociate from the filament end opposite to that at which monomers are added during filament assembly. An intact nucleoprotein filament can recruit a duplex DNA molecule and sample for homology (Bazemore *et al.*, 1997). Once homology is aligned and complementary strands are paired, the hybrid DNA is extended via branch migration. DNA strand exchange encompassing thousands of base pairs is facilitated by ATP hydrolysis. RecA can also promote DNA strand exchange between two duplex DNA molecules, although the initial interaction must involve only three strands. This process involves the formation of the four-stranded Holliday

intermediate and is completely dependent upon the hydrolysis of ATP. Some of the common DNA strand exchange reactions employed in laboratory studies of RecA protein are illustrated in **Figure 2b**.

In addition to these biochemical activities, RecA protein also serves a regulatory role in the SOS response to extensive DNA damage. The RecA protein in its active form (bound to DNA and ATP) can interact with the LexA repressor and facilitate its autocatalytic cleavage. This is generally referred to as the RecA coprotease activity. Inactivation of the LexA repressor promotes the expression of several other genes as part of the SOS response, including RecA protein. Finally, RecA is required for the mutagenic replicational bypass of DNA lesions observed during the SOS response, collaborating in this function with DNA polymerase V (the product of the *umuC* and *umuD* genes). The mechanism by which the RecA protein facilitates the action of DNA polymerase V is not known.

Single-stranded DNA-binding protein

In *E. coli*, SSB (18.8 kDa) was first identified as a protein involved in DNA replication. As its name suggests, this protein has the primary function of binding to regions of single-stranded DNA. SSB always binds to ssDNA as a homotetramer (75.4 kDa). The protein displays a range of DNA-binding modes, with solution conditions determining which mode predominates. During replication, the helicase activity of the polymerase complex results in ssDNA that is then used as a template for replication. In the short interval between DNA unwinding and active replication, SSB binds to this DNA and prevents both reannealing and formation of internal secondary structure such as stem-loops. SSB also plays a variety of roles in recombination. At the DNA gap created by an encounter between DNA polymerase and a DNA lesion, SSB coats the exposed ssDNA. SSB inhibits the nucleation of RecA filament formation on single-stranded DNA *in vitro*, although the RecO and RecR proteins (described below) overcome this effect. Once a RecA filament has nucleated, SSB facilitates RecA filament extension by destabilizing regions of secondary structure. It also binds to the displaced DNA strand during the course of RecA protein-promoted DNA strand exchange.

The RecBCD enzyme

The RecB (134 kDa), RecC (129 kDa), and RecD (67 kDa) proteins form a complex that is required for efficient repair of double-strand breaks. The RecBCD enzyme (also called exonuclease V) binds to and processes these ends into recombinogenic substrates that can utilize RecA protein. The enzyme is a DNA-dependent ATPase, and has both helicase and exonuclease activities (Anderson and Kowalczykowski, 1997). Beginning at the DNA end created

by a double-stranded break, the DNA is unwound and degraded, with the 3'-ending strand degraded preferentially under most conditions. When the RecBCD enzyme encounters an 8-bp sequence called χ (chi; 5'-GCTGGTGG), the activity of the protein changes such that the 5'-ending strand is degraded almost exclusively. The result is the creation of a 3' single-strand extension, on to which RecA protein is subsequently loaded. The RecBCD enzyme directly facilitates the loading of RecA protein on to these prepared DNA substrates (Churchill *et al.*, 1999). In *E. coli*, there are 761 χ sequences distributed throughout the chromosome.

The RecFOR proteins

The RecF (40.5 kDa), RecO (26 kDa), and RecR (22 kDa) proteins appear to be important primarily for the repair of DNA gaps presented when DNA polymerase III is stalled at a DNA lesion. *In vitro*, these proteins form several different complexes that modulate the assembly and disassembly of RecA filaments, perhaps defining one of their *in vivo* roles. A complex containing the RecO and RecR proteins facilitates the nucleation of RecA filaments on ssDNA that is coated with SSB (Umeza and Kolodner, 1994). The RecOR complex also prevents the end-dependent disassembly of RecA protein from ssDNA (Shan *et al.*, 1997). The RecR protein makes an alternative complex with the RecF protein. The RecFR complex binds to double-stranded (dsDNA), constraining the extension of RecA filaments much beyond the ssDNA gaps where they are nucleated (Webb *et al.*, 1997). The overall effect of the RecOR and RecFR complexes may be to constrain the RecA filament within the ssDNA gap and stabilize it. The RecF protein has a weak DNA-dependent ATPase activity ($k_{\text{cat}} = 1 \text{ min}^{-1}$, maximum). ATP hydrolysis is stimulated by the presence of the RecR protein. Hydrolysis appears to be coupled to dissociation of RecF from dsDNA. Dissociation is slowed by RecR protein.

RecF protein is involved with replication as well as recombination, and may play a key role at the interface of these processes. Resumption of replication following ultraviolet light exposure is dependent upon RecF protein. There is also evidence for functional overlap between RecF and the replication restart protein PriA (described below). In addition, RecF protein is cotranscribed with certain replication proteins. A role has also been postulated for the RecFR complex in the restart of DNA replication, but no molecular mechanisms have been proposed or demonstrated. In this capacity, the RecFR complex might interact directly with some component of DNA polymerase III.

The RuvABC proteins

The RuvA (22 kDa) and RuvB (37 kDa), and RuvC (18.7 kDa) proteins are involved in the processing of

branched DNA recombination intermediates, especially Holliday junctions (Zerbib *et al.*, 1998).

The RuvA and RuvB proteins make up a complex that promotes branch migration of Holliday junctions and other branched DNA structures. An octamer of RuvA protein forms a complex with a Holliday junction (Figure 3). The RuvB protein functions as a hexamer arranged in a doughnut-like shape. RuvA protein recruits two of these RuvB hexamers to a Holliday junction, arranged such that each hexamer has one DNA arm of the Holliday junction projecting through its central cavity. RuvB protein is a potent DNA-dependent ATPase, with a k_{cat} ranging up to 200 min^{-1} depending on the DNA cofactor and solution conditions. The RuvB protein acts as a DNA pump, moving DNA through the cavity and outward, away from the Holliday junction (Parsons *et al.*, 1995). The overall effect is to promote a rapid migration of the DNA branch (Figure 3).

The RuvC protein is a Holliday junction resolvase, a nuclease activity specialized for the cleavage of Holliday junctions. A RuvC homodimer will bind to and cleave the Holliday junction at two points so as to generate viable recombinants. The RuvAB complex facilitates the activity of RuvC under some conditions, suggesting a direct interaction between the proteins. There appear to be at least two additional Holliday junction resolvases in *E. coli*, one called RusA and another that is yet unidentified.

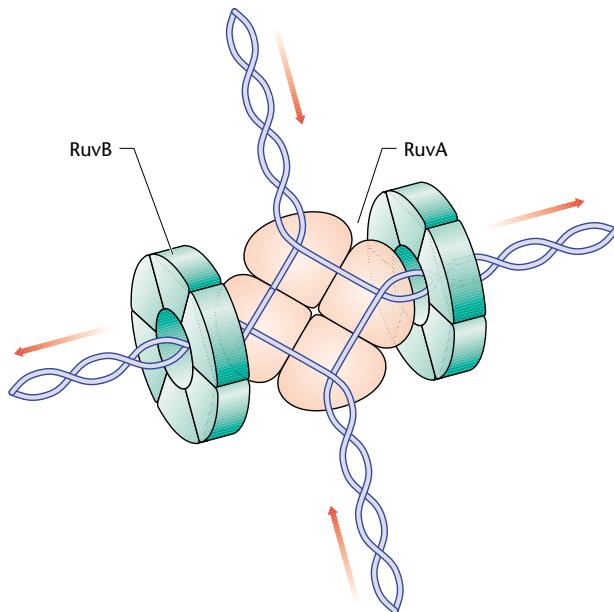


Figure 3 The activity of the RuvAB complex at a Holliday junction. A tetramer of octamer of RuvA protein binds at the junction, and two RuvB hexamers then bind to it as shown. The RuvB hexamers act as DNA pumps, forcing the DNA outward and promoting migration of the branch. The drawing is based on the work of Stephen West and colleagues.

RecG, RecQ and RecJ proteins

There are several other proteins that are involved in recombinational DNA repair in bacteria. The activities of these proteins are only partially understood.

RecG protein (76 kDa) has a function similar to that of the RuvAB complex, promoting the migration of branched DNA structures (Al Deib *et al.*, 1996). RecG appears to bind Holliday junctions or other branched DNA structures as a monomer. Once bound, RecG hydrolyses ATP ($k_{\text{cat}} > 3000 \text{ min}^{-1}$) and migrates the junction (McGlynn and Lloyd, 1999). Although the activity is similar to that of the RuvAB complex, RecG migrates the four-stranded junctions generated by RecA protein in the direction opposite to that of RuvAB. RecG seems to be involved in all recombination pathways, but its precise role is unclear. Mutations that eliminate either RecG function or RuvAB function in the cell have only modest effects on recombinational processes; however, mutations that eliminate both RecG and RuvAB function have severe effects on recombination function, providing evidence for functional overlap. The results also illustrate the importance of these branch migration activities, initially obscured by the modest effects seen in the single mutants.

RecQ protein (67 kDa) is an ATP-dependent DNA helicase. The helicase activity is stimulated by the presence of SSB. A suggested role for RecQ is similar to that of RecBCD enzyme in that it could prepare dsDNA molecules for recombination by creating a region of ssDNA on to which RecA could form a filament. RecQ is a sequence homologue of several eukaryotic helicases, including the Sgs 1 helicase of yeast and the human Wrn and Blm helicases.

The RecJ protein (63 kDa) is a $5' \rightarrow 3'$ single-stranded exonuclease. In the presence of ATP, RecJ can cleave up to 1000 nucleotides of single-stranded DNA per minute. *In vivo*, strains that lack RecJ function exhibit modest defects in recombination, in a pattern that implicates the enzyme in the same pathway as the RecFOR proteins.

Replication-restart proteins

After the recombination steps are complete, DNA polymerization must be reactivated in an origin-independent manner. The proteins responsible for replication restart are largely distinct from those involved in replication initiation that occurs at *oriC*.

The PriA, PriB, PriC, DnaB, DnaC, DnaG and DnaT proteins form a complex known as the replication-restart primosome. Discovered as proteins needed for replication of ϕX174 DNA (and previously called the ϕX174 -type primosome), all of these proteins were previously assumed to be involved in origin-dependent initiation of replication and to prime Okazaki fragment synthesis on the lagging DNA strand. Both genetic and *in vitro* evidence have shown that only DnaB and DnaG are needed at *oriC* and in

the replication forks originating there. However, loss of PriA function almost completely eliminates the origin-independent replication restart needed at stalled replication forks. Strains lacking PriA function are also nearly inviable, providing some of the evidence that the inactivation of replication forks is a common occurrence. The PriA protein binds directly and preferentially to branched DNA molecules, and facilitates the assembly of the complex with the remaining proteins (Liu *et al.*, 1999; Zavitz and Marians, 1991). The complete pathway of replication restart remains to be elucidated in detail.

Bacterial DNA polymerase II, long an enigma, also appears to be involved in origin-independent restart of replication in the nonmutagenic pathways (Rangarajan *et al.*, 1999). This enzyme apparently participates early in the process, before giving way to DNA polymerase III. The precise nature of this process is not understood.

Pathways

An encounter with DNA damage might affect a replication fork in many ways, and there is little information about the fate of the replication enzymes. There are probably many different pathways for fork reactivation that reflect the variety of DNA structures that might occur at a stalled fork. However, most discussions focus on the two likely major paths outlined in **Figure 1**. The pathways are often referred to as the RecF and RecBCD paths; however, many enzymatic functions may overlap, and several other, as yet unappreciated, pathways perhaps exist as variations of the paths described here.

Gap repair (RecF path)

The unrepaired lesion that halts replication can be oxidative damage, a pyrimidine dimer, an abasic site or some other unusual modification. The stalled replication fork probably yields a single-stranded gap that spans the site of damage. In order to provide a template for accurate repair, a complementary strand from the sister chromatid is paired across from the damage. The assembly of an active RecA nucleoprotein filament is modulated by the actions of RecFR and RecOR protein complexes as described above. Strand exchange is initiated either by introducing a nick in the sister chromatid or by a replication fork regression that might be facilitated by either RecA protein or a complex such as RuvAB (the fork regression path is shown in **Figure 1**). RecA promotes alignment of homology between the two DNA branches, followed by a facilitated DNA branch migration. Additional branch migration may involve the RuvAB or RecG proteins. These mechanisms are not mutually exclusive. Once sufficient branch migration has occurred, the strand containing the DNA lesion acquires a complement and

DNA polymerase fills in the gaps. Before recombination is complete, crossovers and branched intermediates are resolved. This could occur simply by migrating a crossover in the opposite direction (toward the original fork) until the crossover is resolved. Alternatively, a protein such as RuvC could resolve the crossovers by cleaving them. Upon converting the recombination substrate back into a viable replication substrate, DNA synthesis is restarted with the aid of DNA polymerase II and the replication restart primosome. The lesion itself is left behind in now duplex DNA, and may be repaired by excision repair or other pathways.

The enzymatic resolution of crossovers associated with homologous recombination can have deleterious consequences for the bacterial chromosome. **Figure 4** illustrates that there are two possible modes of cleavage for a Holliday junction. Cleavage of the strands at site 'B' yields the correct resolution and, upon completion of replication, two functional chromosomes. Resolution via path 'A', in contrast, can result in the generation of a dimeric chromosome that cannot be separated upon cell division. *E. coli* possesses a specialized site-specific recombination system, encoded by the *xerC* and *xerD* genes, to convert dimeric chromosomes to monomers and allow for continuation of the life cycle. The XerC and XerD proteins, in a cell cycle-associated pathway, promote the dimer to monomer conversion acting at specific DNA sequences called *dif*. The site-specific recombination reaction is analogous to that promoted by the integrase of bacteriophage λ , and the enzymes are in the same mechanistic family (Grainge and Sherratt, 1999).

Double-strand break repair (RecBCD path)

If a replication fork encounters an unrepaired single-strand break, or nick, a double-strand break results. As described above, the RecBCD protein is required to process the broken branch, unwinding and degrading the DNA from one end. Once the break has a 3' single-stranded overhang, RecA protein binds to the ssDNA in a process facilitated by the RecBCD complex. This complex orchestrates the invasion of the intact duplex at the location of homology reestablishing branched DNA. Several kinds of DNA-processing steps may then lead to the formation of a structure upon which origin-independent replication restart may occur. While often referred to as the RecBCD pathway, these events probably involve many of the protein functions described in the RecFOR gap repair pathway. Even the RecOR and RecFR proteins might play a role in RecA filament modulation during double-strand break repair.

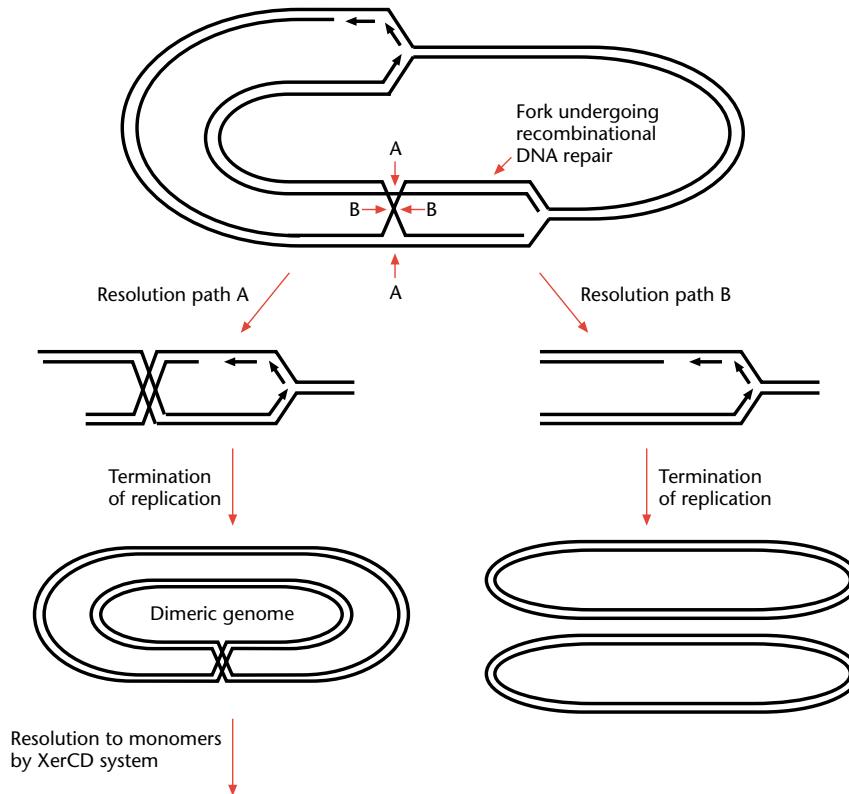


Figure 4 If a Holliday intermediate is formed behind the replication fork via recombinational repair reactions, resolution of the crossover by RuvC or related enzymes can have two different consequences. Resolution via path A will result ultimately in a dimeric chromosome, and will later require conversion to monomers by the site-specific recombination system XerCD.

Replication Restart Associated with the SOS Response

When subjected to high doses of radiation, ultraviolet light or chemical mutagens the numerous DNA lesions bring replication uniformly to a halt in all cells. This triggers induction of the SOS response. This is a coordinated induction of more than a dozen genes, many of which are involved in DNA repair. The RecA protein is involved in the induction of the SOS response (stimulation of the autocatalytic cleavage of the LexA repressor via the RecA coprotease activity) and the *recA* gene is one of those induced.

Replication restart seen in the first 50–60 min after the DNA damage is introduced involves DNA polymerase II and requires PriA and many of the enzymatic functions described above. The nonmutagenic paths for replication restart thus play a role even under SOS-inducing conditions.

Somewhat later, induction of the *umuC* and *umuD* genes produces a new path for replication restart—mutagenic bypass of the lesions. The UmuD protein undergoes a RecA-facilitated cleavage to UmuD' via a mechanism

analogous to LexA repressor cleavage. A UmuD'₂C complex is formed, creating a lesion bypass polymerase known as DNA polymerase V (Tang *et al.*, 1999). Lesion bypass mediated by DNA polymerase V requires SSB, the RecA protein and several protein subunits derived from DNA polymerase III (the β -clamp processivity subunit and the $\gamma\delta$ clamp-loading complex). This polymerase preferentially incorporates deoxyadenosine monophosphate (dAMP) opposite the bypassed lesion, often creating a mutation at the site. A second lesion bypass polymerase, DNA polymerase IV, also contributes to replication during the SOS response.

Summary

Many bacterial replication forks are halted at sites of DNA damage, even under normal growth conditions. The reactivation of these stalled forks is the primary function of the bacterial homologous recombination enzymes, as well as a variety of additional enzymes involved in origin-independent replication restart. This complex set of repair pathways represents an important housekeeping function in bacterial DNA metabolism. Dozens of separate proteins

are involved in the pathways for fork reactivation, many with well-defined activities.

References

- Al Deib A, Mahdi AA and Lloyd RG (1996) Modulation of recombination and DNA repair by the RecG and PriA helicases of *Escherichia coli* K-12. *Journal of Bacteriology* **178**: 6782–6789.
- Anderson DG and Kowalczykowski SC (1997) The recombination hot spot chi is a regulatory element that switches the polarity of DNA degradation by the RecBCD enzyme. *Genes and Development* **11**: 571–581.
- Bazemore LR, Foltastogniev E, Takahashi M and Radding CM (1997) RecA tests homology at both pairing and strand exchange. *Proceedings of the National Academy of Sciences of the USA* **94**: 11863–11868.
- Churchill JJ, Anderson DG and Kowalczykowski SC (1999) The RecBC enzyme loads RecA protein onto ssDNA asymmetrically and independently of chi, resulting in constitutive recombination activation. *Genes and Development* **13**: 901–911.
- Cox MM (1998) A broadening view of recombinational DNA repair in bacteria. *Genes to Cells* **3**: 65–78.
- Grainge I and Sherratt DJ (1999) Xer site-specific recombination. *Journal of Biological Chemistry* **274**: 6763–6769.
- Liu JJ, Xu LW, Sandler SJ and Marians KJ (1999) Replication fork assembly at recombination intermediates is required for bacterial growth. *Proceedings of the National Academy of Sciences of the USA* **96**: 3552–3555.
- McGlynn P and Lloyd RG (1999) RecG helicase activity at three- and four-strand DNA structures. *Nucleic Acids Research* **27**: 3049–3056.
- Parsons CA, Stasiak A, Bennett RJ and West SC (1995) Structure of a multisubunit complex that promotes DNA branch migration. *Nature* **374**: 375–378.
- Rangarajan S, Woodgate R and Goodman MF (1999) A phenotype for enigmatic DNA polymerase II: A pivotal role for pol II in replication restart in UV-irradiated *Escherichia coli*. *Proceedings of the National Academy of Sciences of the USA* **96**: 9224–9229.
- Shan Q, Bork JM, Webb BL, Inman RB and Cox MM (1997) RecA protein filaments: end-dependent dissociation from ssDNA and stabilization by RecO and RecR proteins. *Journal of Molecular Biology* **265**: 519–540.
- Steiner WW and Kuempel PL (1998) Sister chromatid exchange frequencies in *Escherichia coli* analyzed by recombination at the dif resolvase site. *Journal of Bacteriology* **180**: 6269–6275.
- Tang MJ, Shen X, Frank EG *et al.* (1999) UmuD₂C is an error-prone DNA polymerase, *Escherichia coli* pol V. *Proceedings of the National Academy of Sciences of the USA* **96**: 8919–8924.
- Umezumi K and Kolodner RD (1994) Protein interactions in genetic recombination in *Escherichia coli*. Interactions involving RecO and RecR overcome the inhibition of RecA by single-stranded DNA-binding protein. *Journal of Biological Chemistry* **269**: 30005–30013.
- Webb BL, Cox MM and Inman RB (1997) Recombinational DNA repair: the RecF and RecR proteins limit the extension of RecA filaments beyond single-strand DNA gaps. *Cell* **91**: 347–356.
- Zavitz KH and Marians KJ (1991) Dissecting the functional role of PriA protein-catalyzed primosome assembly in *Escherichia coli* DNA replication. *Molecular Microbiology* **5**: 2869–2873.
- Zerbib D, Mezard C, George H and West SC (1998) Coordinated actions of RuvABC in Holliday junction processing. *Journal of Molecular Biology* **281**: 621–630.

Further Reading

- Cox MM (1998) A broadening view of recombinational DNA repair in bacteria. *Genes to Cells* **3**: 65–78.
- Cox MM, Goodman MF, Kreuzer KN *et al.* (2000) The importance of repairing stalled replication forks. *Nature* **404**: 37–41.
- Haber JE (1999) DNA recombination: the replication connection. *Trends in Biochemical Sciences* **24**: 271–275.
- Kogoma T (1996) Recombination by replication. *Cell* **85**: 625–627.
- Kogoma T (1997) Stable DNA replication: interplay between DNA replication, homologous recombination, and transcription. *Microbiology and Molecular Biology Reviews* **61**: 212–238.
- Kuzminov A (1996) *Recombinational Repair of DNA Damage*. Georgetown, TX: Landes.
- Kuzminov A (1999) Recombinational repair of DNA damage in *Escherichia coli* and bacteriophage λ . *Microbiology and Molecular Biology Reviews* **63**: 751–813.
- Marians KJ (1999) PriA: at the crossroads of DNA replication and recombination. *Progress in Nucleic Acid Research and Molecular Biology* **63**: 39–67.
- Mosig G (1998) Recombination and recombination-dependent DNA replication in bacteriophage T4. *Annual Review of Genetics* **32**: 379–413.
- Roca AI and Cox MM (1997) RecA protein: structure, function, and role in recombinational DNA repair. *Progress in Nucleic Acid Research and Molecular Biology* **56**: 129–223.
- Sandler SJ and Marians KJ (2000) Role of PriA in replication fork reactivation in *Escherichia coli*. *Journal of Bacteriology* **182**: 9–13.
- Seigneur M, Bidnenko V, Ehrlich SD and Michel B (1998) RuvAB acts at arrested replication forks. *Cell* **95**: 419–430.
- Shinagawa H (1996) SOS response as an adaptive response to DNA damage in prokaryotes. *EXS* **77**: 221–235.