Critical Reviews in Biochemistry and Molecular Biology, 42:41–63, 2007

ISSN: 1040-9238 print / 1549-7798 online
DOI: 10.1080/10409230701260258

informa
healthcare

Regulation of Bacterial RecA Protein Function

Michael M. Cox
Department of Biochemistry, University of Wisconsin–Madison, Madison, WI

ABSTRACT The RecA protein is a recombinase functioning in recombinational DNA repair in bacteria. RecA is regulated at many levels. The expression of the recA gene is regulated within the SOS response. The activity of the RecA protein itself is autoregulated by its own C-terminus. RecA is also regulated by the action of other proteins. To date, these include the RecF, RecO, RecR, DinI, RecX, RdgC, PsiB, and UvrD proteins. The SSB protein also indirectly affects RecA function by competing for ssDNA binding sites. The RecO and RecR, and possibly the RecF proteins, all facilitate RecA loading onto SSB-coated ssDNA. The RecX protein blocks RecA filament extension, and may have other effects on RecA activity. The DinI protein stabilizes RecA filaments. The RdgC protein binds to dsDNA and blocks RecA access to dsDNA. The PsiB protein, encoded by F plasmids, is uncharacterized, but may inhibit RecA in some manner. The UvrD helicase removes RecA filaments from RecA. All of these proteins function in a network that determines where and how RecA functions. Additional regulatory proteins may remain to be discovered. The elaborate regulatory pattern is likely to be reprised for RecA homologues in archaeans and eukaryotes.

KEYWORDS RecA, recombination, repair, DNA, replication fork, RecF, RecO, RecR, DinI, RecX

INTRODUCTION

Recombination plays a critical role in DNA repair and genome maintenance. However, it is equally critical to regulate where, when, and how recombination takes place. When unregulated, recombination can lead to genome instability and carcinogenesis. Meiotic recombination in eukaryotes is under tight regulation, ensuring the proper spacing and complete chromosomal coverage of the recombination events that are needed for proper chromosome segregation (Cohen *et al.*, 2001; de Massy, 2003; Hillers *et al.*, 2003; Thompson *et al.*, 1999). Defects in many recombination functions result not only in DNA repair defects, but also in more general genomic instability. Much of this is associated with stalled replication forks (Bjergbaek *et al.*, 2002; Chakraverty *et al.*, 1999; Kolodner *et al.*, 2002; Myung *et al.*, 2001; Myung *et al.*, 2002; Osborn *et al.*, 2002; Thompson *et al.*, 2002; van Gent *et al.*, 2001; Venkitaraman, 2001). Regulation determines which pathway is used to correct a double strand break in DNA in eukaryotes (Haber, 2000). Humans with mutations conferring a hyperrec phenotype have an increased risk

Address correspondence to Michael M. Cox, Department of Biochemistry, University of Wisconsin–Madison, 433 Babcock Drive, Madison, WI 53706-1544. E-mail: cox@biochem.wisc.edu

for cancer (Bishop *et al.*, 2003). Mitotic recombination is regulated, at least in part, by the mismatch repair system in eukaryotes (Chen *et al.*, 1998; Datta *et al.*, 1996). In many cases, the operative regulatory mechanisms are not well defined.

The pattern is not limited to eukaryotes. Mutations in some bacterial recombination proteins reduce homologous recombination and associated repair processes, but can produce large increases in illegitimate recombination (Hanada *et al.*, 2000; Hanada *et al.*, 1997; Lovett *et al.*, 2002; Lovett *et al.*, 1995). Much of this genomic instability is again associated with stalled replication forks (Bierne *et al.*, 1994; Cox *et al.*, 2000; Hanada *et al.*, 1997; Hyrien, 2000; Kowalczykowski, 2000; Kuzminov, 1999). The potential deleterious consequences of unregulated recombination are as obvious in bacteria as they are in eukaryotes.

The recombinases of the RecA family represent an obvious target for regulation. The highly conserved bacterial RecA protein is found in virtually all bacteria (Brendel *et al.*, 1997; Roca *et al.*, 1990; Roca *et al.*, 1997). The only bacteria found to date that lack a gene encoding RecA protein are certain endosymbionts that have undergone dramatic genome size reductions (Moran *et al.*, 2000; Tamas *et al.*, 2002). True structural and functional homologues of RecA have been found in bacteriophage (Jiang *et al.*, 1993), in archaea (Sandler *et al.*, 1996; Seitz *et al.*, 1998; Seitz *et al.*, 2001), and in eukaryotic cells (Baumann *et al.*, 1998; Bishop, 1994; Gupta *et al.*, 1997; New *et al.*, 1998; Ogawa *et al.*, 1993; Shinohara *et al.*, 1992; Sung, 1994). These proteins typically promote the central steps of recombination and recombinational DNA repair in the pathways that utilize them. Recombination in general is a complex process now known to involve dozens of individual proteins. This review focuses on those proteins that directly affect or modulate RecA protein function in some manner.

THE RecA PROTEIN

The biochemistry of RecA protein has recently been reviewed in detail (Cox, 2006; Cox, 2007). A short introduction is provided here so that readers can approach the information about regulation without the need to read other articles. The RecA protein of *Escherichia coli* (EcRecA) is the prototype of this class of protein and it has three very different roles in the cell. First, it promotes the central steps of recombination, aligning and pairing two DNA molecules, and then promoting a strand switch followed by branch migration (Cox, 1999;

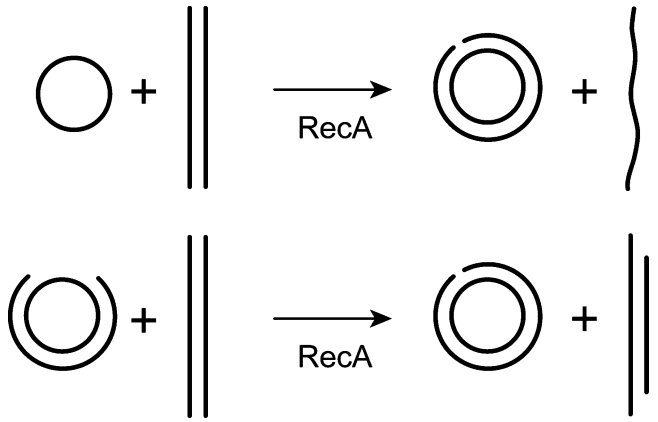

FIGURE 1 **DNA strand exchange reactions. The most common model reactions used in vitro are shown. The three-strand reaction is shown at the top. RecA filaments form on the circular single strand DNA. The duplex is then aligned with the single strand, and the strand exchange is initiated. The reaction requires about 15 min at 37°C when bacteriophage DNAs (ϕX174 or M13) are employed. The four-strand reaction is shown at the bottom. The gap in the circular duplex serves both as a nucleation point for RecA protein filament formation and as a location for the initiation of DNA strand exchange.**

Cox, 2002; Cox, 2003; Lusetti *et al.*, 2002). *In vitro*, the RecA protein catalyzes a DNA strand exchange reaction (Figure 1) that serves as the major experimental model for its recombination activities. Second, RecA itself has a regulatory function. RecA has an activity generally referred to as its coprotease function, facilitating the autocatalytic cleavage of the LexA repressor (Little, 1991) as required for induction of the SOS response (Walker *et al.*, 2000). The RecA coprotease activity also facilitates the autocatalytic cleavage of the UmuD protein to the activated UmuD', a component of DNA polymerase V (Pham *et al.*, 2002; Tang *et al.*, 1999). The affected proteins (LexA, UmuD, and a few others) cleave themselves only when they are bound to an activated RecA filament. Third, RecA functions to directly facilitate replicative bypass of DNA lesions by DNA polymerase V during SOS, utilizing a mechanism that is gradually yielding to investigation (Dutreix *et al.*, 1989; Echols *et al.*, 1991; Pham *et al.*, 2002; Schlacher *et al.*, 2006; Schlacher *et al.*, 2005; Schlacher *et al.*, 2006; Tang *et al.*, 1999).

EcRecA protein is a 352-residue polypeptide chain (Mr 37,842). The structure of RecA protein was elucidated by Story and Steitz in 1992 (Story *et al.*, 1992; Story *et al.*, 1992), and multiple structures of RecA and its homologues have appeared since (Conway *et al.*, 2004; Datta *et al.*, 2003; Datta *et al.*, 2003; Datta *et al.*, 2000; Krishna *et al.*, 2006; Qian *et al.*, 2005; Rajan *et al.*, 2004; Wu *et al.*, 2004; Wu *et al.*, 2005; Xing *et al.*, 2004;

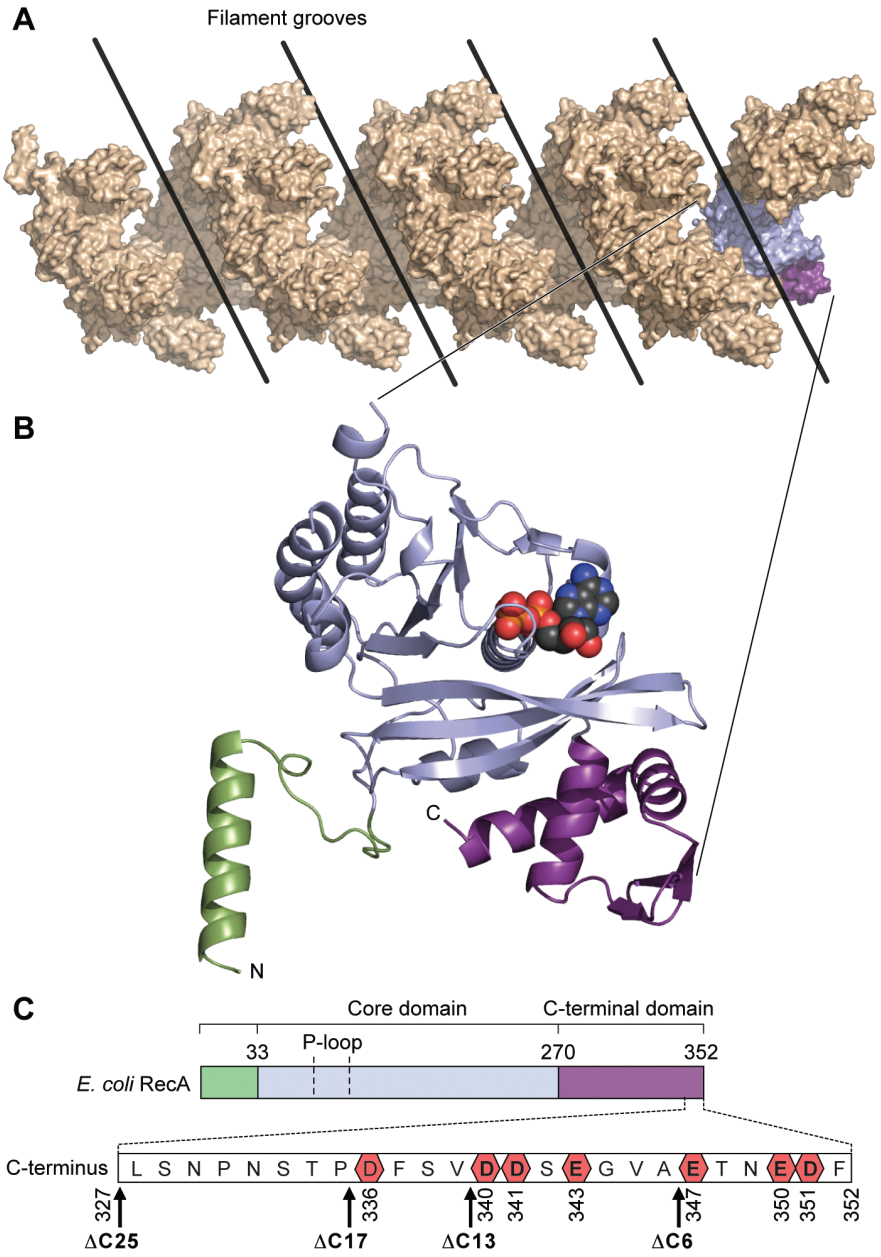

FIGURE 2 **RecA protein structure. The figure is available in color in the online publication. (A) A filament is shown, based on the structure of Story and Steitz (Story *et al.*, 1992; Story *et al.*, 1992), with 24 subunits (four turns of the filament). (B) One monomeric subunit of the larger filament is colored differently in panel a, and enlarged here in a ribbon diagram. The core domain is in blue, with bound ADP shown as a space-filling model. The N- and C-terminal domains are shown in green and purple, respectively. (C) The sequence of the C-terminal 25 amino acid residues (disordered in all of the published crystal structures) is shown. Arrows indicate the locations of C-terminal truncations used in a recent characterization of C-terminus function (Eggler *et al.*, 2003; Lusetti *et al.*, 2003; Lusetti *et al.*, 2003).**

Xing *et al.*, 2004). Unfortunately, none of these structures includes bound DNA, and much remains to be elucidated about the DNA binding sites on this protein. The monomer structure (Figure 2) has a large core domain, and two smaller domains at the N- and C-termini. The core domain is the prototype of a motif called the RecA fold, found to be common to a range of other proteins including motor proteins such as the F1 ATPase, multiple helicases, DNA transport proteins, and certain other transporters (Abrahams *et al.*, 1994; Amano *et al.*, 1994; Bianchet *et al.*, 1997; Bird *et al.*, 1998; Egelman, 2000; Gomis-Ruth *et al.*, 2001; Yu *et al.*, 1997). In the active RecA filament, ATP is bound at the subunit-subunit interface (Cox *et al.*, 2006; VanLoock *et al.*, 2003). A depiction of the RecA filament, based on the Story and Steitz structure, is shown in Figure 2. There are six RecA monomers per helical turn of the filament, corresponding to the 18 bp per turn extended

conformation of the DNA bound within the filament. The helical groove providing access to the filament interior can be seen between the monomers colored gray.

In principle, any activity of EcRecA may be regulated, but most work has focused on the recombinational function of RecA. The DNA strand exchange reaction has three distinct phases (Cox, 1999; Cox, 2002; Cox, 2003; Lusetti *et al.*, 2002). RecA protein first binds to the single-stranded or gapped DNA substrate, producing a right-handed helical filament containing one RecA monomer for every 3 nucleotides or base pairs of DNA. Next, a homologous duplex DNA is aligned with the single strand already within the filament and a nascent hybrid DNA product is formed. Extension of this nascent hybrid DNA occurs in the final reaction phase, in which the capacity of the filament to promote a strand switch is augmented by ATP hydrolysis.

ATP hydrolysis (dATP readily substitutes) renders the DNA strand exchange reaction unidirectional (Jain *et al.*, 1994; Shan *et al.*, 1996), allows it to bypass substantial structural barriers in the DNA substrates (Kim *et al.*, 1992; Rosselli *et al.*, 1991; Shan *et al.*, 1996), and permits strand exchange reactions involving 4 DNA strands (Kim *et al.*, 1992; Shan *et al.*, 1996). Models for how RecA protein couples ATP hydrolysis to these activities have been described (Cox, 2003; Cox, 2007). RecA protein will promote replication fork regression, a reaction that may be relevant to RecA function at an arrested replication fork. This reaction requires ATP hydrolysis.

Much of the regulation characterized to date is directed at the assembly and disassembly of RecA filaments. RecA filaments assemble on DNA in discrete nucleation and extension phases, with the former generally being rate-limiting (Figure 3). Nucleation occurs more rapidly on single-stranded DNA (ssDNA) than on double-stranded DNA (dsDNA). Nucleation on ssDNA is greatly slowed if SSB is bound to the ssDNA. Once nucleation is achieved (often with the aid of regulatory proteins), filament growth occurs primarily on the 3′-proximal end (5′ to 3′ direction) (Register *et al.*, 1985; Shan *et al.*, 1997). RecA binding here is a simple reversible association of ATP-liganded RecA monomers. The reported rates of 5′-to-3′ filament growth range from 120 to 1200 subunits min^{-1} (Galletto *et al.*, 2006; Joo *et al.*, 2006; Shivashankar *et al.*, 1999; van der Heijden *et al.*, 2005). Dissociation occurs primarily on the 5′-proximal end. The release of RecA monomers at this end is not part of a simple reversible binding process, as

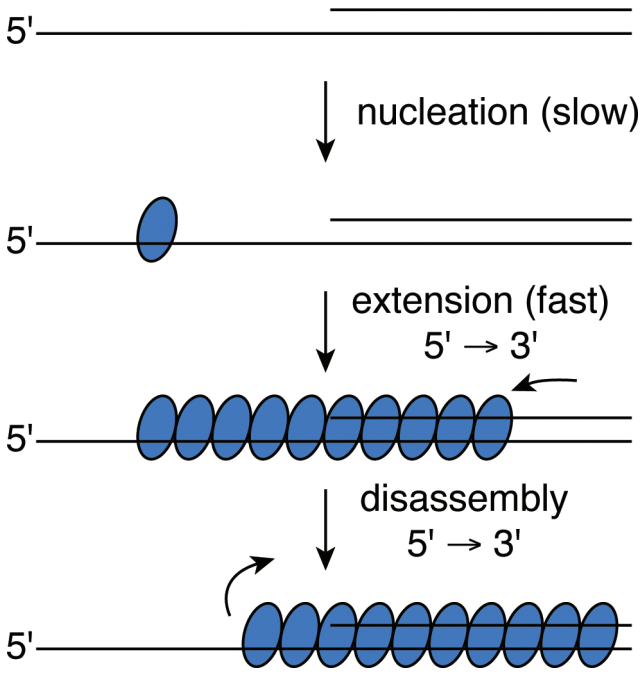

FIGURE 3 **RecA protein filament formation on DNA. The figure is available in color in the online publication. RecA protein filaments are generally formed in two distinct phases, nucleation and extension. Nucleation occurs most readily on single strand DNA. Extension proceeds largely in the 5′ to 3′ direction, and can continue readily into any adjacent duplex DNA. Direct binding to duplex DNA is observed if the slow nucleation step is overcome, and certain RecA mutant proteins are proficient at the rapid nucleation of filament formation on duplex DNA.**

dissociation is coupled to ATP hydrolysis–(a fact that is not entirely accounted for in recent attempts to measure dissociation constants and/or filament growth at the disassembly end in the presence of ATP using single-molecule approaches (Galletto *et al.*, 2006; Joo *et al.*, 2006). Dissociation from ssDNA occurs at a rate of ~70 monomers per minute (Arenson *et al.*, 1999), rising to 120 monomers per minute when the filament is bound to dsDNA (Cox *et al.*, 2005; Shivashankar *et al.*, 1999). The monomer-monomer interface should be identical on both filament ends. When ATP analogues that cannot be hydrolysed are substituted for ATP, the filaments should be able to grow in either direction, as has been observed (Galletto *et al.*, 2006).

The DNA inside a RecA filament is in an unusual conformation (Cox, 2006; Nishinaka *et al.*, 1997). It is extended by 50% to 60%, and underwound to ~18 base pairs per turn. The resulting strain might facilitate both the exchange of DNA strands and the homology search that precedes it (Cox, 2006; Klapstein *et al.*, 2004). Each RecA monomer in the filament covers three nucleotides or DNA base pairs.

Once formed, filaments that hydrolyse ATP are dynamic, continuing to grow and shorten at the appropriate ends. When bound to a DNA circle, they might contain breaks where dissociation at a disassembly end is rapidly compensated for by association to the trailing assembly end. Again, the filaments on ssDNA and dsDNA differ, with the ATP hydrolysis turnover rate per monomer being ~30 ATP molecules per minute on the former and 20 per minute on the latter.

The properties of RecA filaments formed on different DNA substrates are diagnostic of different filament states (Cox, 2006; Haruta *et al.*, 2003). As RecA binds to ssDNA in the presence of ATP, it undergoes a transition between states, designated O and A, respectively. The A state on ssDNA is converted to a state, designated P, on dsDNA. The capacity of RecA protein to pair DNAs and promote DNA-strand exchange improves in the progression O to A to P, and many filament properties change.

REGULATION OF RecA FUNCTION

The activity of RecA protein, and presumably all related recombinases, is regulated on at least three levels. First, *recA* gene expression is controlled within the SOS regulon. This aspect of RecA function will not be considered here. Second, RecA protein is subject to autoregulation. Its activities are suppressed, to degrees that vary with conditions, by the C-terminus (and perhaps other parts) of the protein. Third, the activity of RecA protein is modulated by a growing array of other proteins.

AUTOREGULATION OF RecA PROTEIN FUNCTION

In most of the published RecA crystal structures, the C-terminal 25 amino acids (Figure 2) are disordered. Recent work has shown that this part of the RecA polypeptide, and particularly the C-terminal 17 amino acid residues, acts as a kind of autoregulatory flap (Eggler *et al.*, 2003; Lusetti *et al.*, 2003a, 2003b). The first studies of the RecA C-terminus indicated that DNA binding (particularly dsDNA binding) and some DNA pairing functions were enhanced when all or large segments of the C-terminal 25 amino acid segment were removed (Benedict *et al.*, 1988; Tateishi *et al.*, 1992). An extensive follow-up demonstrated that removal of 17 amino acid residues enhances a wide range of RecA activities. The wild type RecA protein requires the addition of 6 to 8 mM Mg ion for optimal DNA strand exchange function. The deletion mutant no longer requires free Mg^{2+} ion for optimal strand exchange activity (Lusetti *et al.*, 2003a). The same truncated RecA protein binds more quickly to duplex DNA (Lusetti *et al.*, 2003b), rapidly displaces SSB on single-stranded DNA (Eggler *et al.*, 2003), and promotes the cleavage of LexA protein more rapidly when bound to duplex DNA (Lusetti S. L., unpublished data). This C-terminal peptide appears to affect virtually every RecA function, with almost all activities being more robust when it is absent. As such, it is a logical interaction point for other proteins that modulate RecA function.

REGULATION OF RecA PROTEIN BY OTHER PROTEINS

Overview

Classically, the regulation of RecA has focused on loading of the protein onto single-stranded DNA. There are two major pathways for RecA loading, and these in turn define the two major recombination pathways of *E. coli*, laid out over three decades ago by Clark and coworkers (Clark *et al.*, 1994; Horii *et al.*, 1973; Kowalczykowski *et al.*, 1994; Kuzminov, 1999).

During conjugation, the major pathway for recombination utilizes the RecBCD helicase/nuclease, and is called the RecBCD pathway. This pathway is generally required to process DNA ends at the sites of double strand breaks. As detailed later, RecBCD processes a DNA end to create a long single-strand extension on the 3′-ending strand, upon which RecA protein can be loaded. The RecA then aligns this single-stranded DNA with homologous sequences in a duplex, and promotes a DNA strand invasion as a first step in the repair of a double strand break (Figure 4).

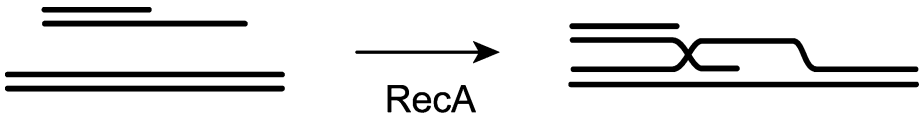

FIGURE 4 **The DNA strand invasion reaction. The single strand extension in the top DNA has a 3′ terminus. The single-stranded region serves as a loading point for RecA protein filament formation. The RecA then pairs this single strand region with a complementary strand in another duplex, leading to the strand invasion reaction shown.**

The RecF, RecO, and RecR proteins (often abbreviated RecFOR) have been highlighted as prototype mediator proteins (Beernik *et al.*, 1999; Sancar *et al.*, 1993), necessary to load RecA protein onto SSB-coated DNA (Sandler, 2001; Umezu *et al.*, 1993; Umezu *et al.*, 1994). The RecFOR recombination pathway appears to complement the RecBCD path. The *recF*, *recO*, and *recR* genes form an epistatic group tailored more for the repair of DNA gaps than double strand breaks (Asai *et al.*, 1994; Courcelle *et al.*, 1997; Horii *et al.*, 1973; Kolodner *et al.*, 1985; Wang *et al.*, 1984). The RecFOR path plays a secondary role during conjugational recombination. When the RecBCD pathway is removed by mutation of one of the genes encoding the RecBCD helicase/nuclease, the recombinational defect is suppressed by mutations in *sbcA*, *sbcB*, or *sbcCD* (Bidnenko *et al.*, 1999). During conjugation, the RecFOR pathway supplants the RecBCD pathway only in a *recBCD*$^{-}$ *sbc(A, B, or CD)* genetic background (Clark *et al.*, 1994; Horii *et al.*, 1973; Kowalczykowski *et al.*, 1994; Kuzminov, 1999). However, the major function of recombination in bacteria is the repair of stalled or collapsed replication forks (Cox *et al.*, 2000; Kowalczykowski, 2000; Kuzminov, 1999). In this context, the RecFOR and RecBCD pathways appear to be equally important (Cox, 1999; Galitski *et al.*, 1997; Steiner *et al.*, 1998).

The RecBCD and RecFOR functions seem sufficient to target RecA filaments to the locations requiring them, yet recent work has shown that RecA regulation is much more complex. The RecF, RecO, and RecR proteins modulate both the assembly and disassembly of RecA filaments (Shan *et al.*, 1997), and RecF protein in particular may have multiple functions (Rangarajan *et al.*, 2002; Sandler, 1996). Several additional proteins play important roles. The DinI protein stabilizes RecA filaments (Lusetti *et al.*, 2004). The RecX protein blocks RecA filament extension, leading to net disassembly in certain contexts (Drees *et al.*, 2004). Certain helicases, such as UvrD, act to disrupt RecA filaments (Lovett *et al.*, 1995; Mendonca *et al.*, 1993; Morel *et al.*, 1993; Petranovic *et al.*, 2001). The PsiB (Bagdasarian *et al.*, 1992; Bailone *et al.*, 1988) and RdgC (Moore *et al.*, 2003; Ryder *et al.*, 1996) proteins have been implicated by genetic studies in the suppression of RecA activity by mechanisms that are still largely undefined. The study of proteins that regulate RecA function is still in its early stages. Recent studies have highlighted the growing complexity of the network of proteins that regulate RecA protein.

Surprisingly, the RecBCD and RecFOR functions that load RecA protein are not as ubiquitous in the eubacteria as is RecA protein itself (Rocha *et al.*, 2005; Sandler, 2001). The RecFOR proteins are more widespread than the RecBCD enzymes (Rocha *et al.*, 2005). In a survey of the genomes of 117 bacterial species, the *recB* and *recC* genes are missing in 77 of them (Rocha *et al.*, 2005). An orphan variant of the recD gene is present in 30 of these species (Rocha *et al.*, 2005). In some species, the homologous *addAB* system replaces *recBC*, but both RecBC and AddAB are absent in at least 33 species, including *Mycoplasma*, *Helicobacter*, *Campylobacter*, *Desulfovibrio*, *Ralstonia*, *Bdelovibrio*, *Nitrosomonas*, *Bacteroides*, *Wolinella*, *Corynebacterium*, and *Streptomyces* species (Rocha *et al.*, 2005). In contrast, RecFOR is entirely lacking in only nine species. However, these three proteins are not always found together. RecR protein is the most widespread, missing in all but the nine that have no RecFOR components (Rocha *et al.*, 2005). RecF is missing 29 times, and RecO 17 times. Many of the *Mycoplasma* have RecO and RecR, but no RecF or RecBCD/AddAB. The ε-proteobacteria group tends to have RecR protein alone. The *Buchnera* endosymbionts (which lack RecA protein) and a few *Mycoplasma* species appear to lack all of the known systems for loading RecA protein onto DNA (Rocha *et al.*, 2005).

SSB

The single-strand DNA binding protein (SSB) of *Escherichia coli* was first reported in 1972 (Sigal *et al.*, 1972). It was the second example of a protein in this class, with the gene 32 protein of bacteriophage T4 being the first (Alberts *et al.*, 1970). Like RecA recombinases, SSB-class proteins are ubiquitous and essential to DNA metabolism in all organisms. The eukaryotic equivalent is the heterotrimeric replication protein A (RPA) protein. In *E. coli*, the *ssb* gene is essential for cell viability (Curth *et al.*, 1996; Lohman *et al.*, 1994; Meyer *et al.*, 1990). Each of these proteins features a DNA binding motif called a oligonucleotide/oligosaccharide binding fold (OB fold). The *E. coli* SSB polypeptide (M_r 18,843) includes one OB fold in a large amino-terminal domain. EcSSB functions as a homotetramer (Molineux *et al.*, 1975; Weiner *et al.*, 1975). Most bacterial SSB proteins are similar. Exceptions are the SSB proteins of *Deinococcus radiodurans* and *Thermus* sp., with polypeptides that encompass two OB folds and function as homodimers (Dabrowski *et al.*, 2002; Eggington *et al.*, 2004).

SSB plays a complicated role in RecA reactions. RecA filament nucleation is inhibited, and under some conditions blocked entirely, if SSB is allowed to coat the DNA prior to RecA addition (Bork *et al.*, 2001; Kowalczykowski *et al.*, 1987; Lavery *et al.*, 1990; Shan *et al.*, 1997; Umezu *et al.*, 1994). This inhibition of binding nucleation is overcome in the bacterial cell by the mediator proteins, RecO and RecR (Bork *et al.*, 2001; Hobbs *et al.*, 2007; Morimatsu *et al.*, 2003; Shan *et al.*, 1997; Umezu *et al.*, 1994). However, WT EcRecA protein does not bind well to secondary structure in ssDNA, and addition of SSB after RecA protein disrupts the secondary structure and allows RecA to form a contiguous filament on the DNA (Kowalczykowski *et al.*, 1987).

SSB is sometimes viewed as a DNA-binding polypeptide that is otherwise inert, but the reality is more complex. SSB interacts directly and specifically with a wide range of proteins involved in DNA metabolism, including PriA (Cadman *et al.*, 2004), uracyl-DNA glycosylase (Acharya *et al.*, 2002, Handa, 2001 #4619), exonuclease I (Genschel *et al.*, 2000), the χ subunit of DNA polymerase III (Gulbis *et al.*, 2004; Witte *et al.*, 2003), RecO protein (Hobbs *et al.*, 2007; Kantake *et al.*, 2002; Umezu *et al.*, 1994), TopB (DNA topoisomerase III) (Butland *et al.*, 2005), the nucleases RecJ and SbcB (Butland *et al.*, 2005), the RecG helicase (Butland *et al.*, 2005), and the RecQ helicase (Butland *et al.*, 2005). SSB has its own conserved acidic C-terminus (Figure 5), and most of the protein-protein interactions occur at the C-terminus (Acharya *et al.*, 2002; Cadman *et al.*, 2004; Curth *et al.*, 1996; Genschel *et al.*, 2000; Gulbis *et al.*, 2004; Handa *et al.*, 2001; Kinebuchi *et al.*, 1997; Ma *et al.*, 2004; Richard *et al.*, 2004; Savvides *et al.*, 2004; Witte *et al.*, 2003; Yuzhakov *et al.*, 1999). Instead of an inert DNA coating that must be displaced for DNA metabolism to proceed, SSB may instead be viewed as an organizational scaffold where DNA metabolic complexes are assembled. Making the issue of SSB function more intriguing, the protein exhibits multiple single-stranded DNA binding modes that depend on salt concentration (Bujalowski *et al.*, 1987; Bujalowski *et al.*, 1988; Lohman *et al.*, 1994). Potential effects of these different SSB binding modes on reactions in which SSB is a participant has not been properly assessed in most cases.

In addition to its effects on RecA filament formation, SSB plays a role in DNA strand exchange, binding to the displaced single-strand product and facilitating its release from the filament (Lavery *et al.*, 1992).

The RecBCD Helicase/Nuclease

The *E. coli recB* and *recC* genes were identified in early screens for mutations that produced defects in standard recombination assays (Clark *et al.*, 1965; Emmerson, 1968). The *recD* gene was discovered only two decades later (Amundsen *et al.*, 1986), after a third integral subunit was recognized as a required component. The RecB (M_r 133,973 (Finch *et al.*, 1986)), RecC (M_r 128,860 (Finch *et al.*, 1986)), and RecD (M_r 66,973 (Finch *et al.*, 1986)) proteins function as a heterotrimeric complex.

RecBCD is part of a broader family of eubacterial enzymes called either RecBCD or AddAB. The RecBCD helicase/nuclease both unwinds and degrades duplex DNA from one end. The recent elucidation of the structure of the RecBCD enzyme bound to DNA has capped several decades of careful investigation and rendered the pathway in three dimensions (Singleton *et al.*, 2004). The RecB subunit possesses a 3′ to 5′ helicase activity, and the RecD subunit has a 5′ to 3′ helicase activity (Dillingham *et al.*, 2003; Taylor *et al.*, 2003; Yu *et al.*, 1998). The nuclease function, sequestered in a separate domain of RecB, generally degrades the 3′-ending strand more efficiently at first. When RecBCD encoun-

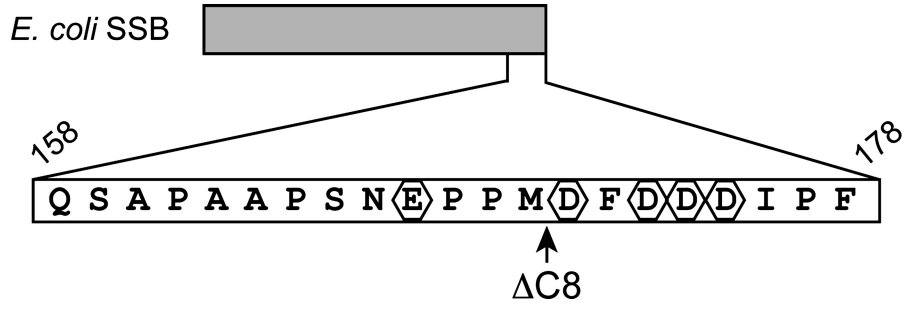

FIGURE 5 **The SSB C-terminus. The single strand DNA binding protein of *E. coli* has an acidic C-terminus, similar to other bacterial SSB proteins. The C-terminus is a site for interaction with many other proteins involved in DNA metabolism. Deletion of the eight C-terminal amino acid residues eliminates many of these interactions.**

ters a copy of an 8 base pair sequence called *chi* (5′-GCTGGTGG-3′), a site in the RecC subunit binds to *chi* on the 3′-ending strand and prevents its further degradation. The 5′-ending strand is then degraded, leading to the creation of a long 3′ single strand extension at the end. Finally, RecBCD actively loads RecA protein onto the single-strand segments it creates (Anderson *et al.*, 1997; Arnold *et al.*, 2000; Churchill *et al.*, 1999), utilizing an interaction site in the RecB subunit (Churchill *et al.*, 2000). RecBCD is not a dedicated RecA regulatory function. However, its dynamic interaction with RecA makes it an important factor in RecA biochemistry *in vivo*, and it provides one of the key pathways that direct assembly of RecA protein filaments. Given the tendency of RecA filaments to disassemble in the 5′ to 3′ direction, it will be interesting to learn if RecBCD not only triggers the loading of RecA onto the 3′ single strand extensions that it creates, but also stabilizes the 5′-proximal ends of the assembled filaments. Alternatively, other proteins such as DinI protein (described below), might serve as the stabilizing factor.

The RecFOR Proteins

Mediator proteins are nearly as ubiquitous as recombinases, ensuring the targeted assembly of recombinase filaments. In *E. coli*, the RecF, RecO, and RecR proteins function in this capacity, and perhaps have other functions as well. Given the non-ubiquitous distribution of the *recFOR* genes in eubacteria (Rocha *et al.*, 2005), it is not clear that this class of mediator is present in all bacterial species. However, RecFOR provides a good prototype for investigation of bacterial mediator function.

The RecF Protein

The *E. coli recF* gene was discovered (Horii *et al.*, 1973) as a UV sensitive, recombination-deficient mutant in a *recBC sbcBC* background. Although it has never been implicated in replication, the gene is contained in an operon that also includes the *dnaA*, *dnaN*, and *gyrB* genes. The sequenced *recF* gene encodes a 357-amino acid polypeptide (Mr 40,519 (Blanar *et al.*, 1984)). The RecF protein has been purified and characterized *in vitro* (Griffin *et al.*, 1990; Madiraju *et al.*, 1992; Madiraju *et al.*, 1991; Morimatsu *et al.*, 2003; Umezu *et al.*, 1993; Umezu *et al.*, 1994; Webb *et al.*, 1995; Webb *et al.*, 1997; Webb *et al.*, 1999). It binds to ssDNA with an apparent stoichiometry of 1 RecF monomer per 15 nucleotides (Madiraju *et al.*, 1991). In the presence of ATP, the RecF protein also binds to dsDNA (Madiraju *et al.*, 1992; Webb *et al.*, 1995). The protein contains a consensus nucleotide-binding fold (Walker A box). The protein binds ATP, and has a weak DNA-dependent ATPase activity (k_{cat} about 1.0 min^{-1}) (Webb *et al.*, 1995; Webb *et al.*, 1999). ATP hydrolysis leads to RecF dissociation from DNA (Webb *et al.*, 1999).

The structure of the RecF protein from *Deinococcus radiodurans* has recently been elucidated by Koroleva and coworkers (2007). The RecF protein exhibits extensive structural similarity with the head domain of the eukaryotic Rad50 protein (Figure 6), but lacks the long coiled-coil domain of Rad50 (Koroleva *et al.*, 2007). RecF belongs to the ATP-binding cassette (ABC) ATPase family of proteins, and it has the Walker A, Walker B, and signature motifs characteristic of that family. ATP binding triggers RecF dimerization (Koroleva *et al.*, 2007). Mutations in the Walker A (K36R) (Webb *et al.*, 1999), Walker B (D300N) (Koroleva *et al.*, 2007), and the signature (S268R) (Koroleva *et al.*, 2007) motifs all disrupt ATP hydrolytic activity.

RecF protein has been proposed to direct RecA loading to the boundaries of single strand gaps in duplex DNA (Hegde *et al.*, 1996; Morimatsu *et al.*, 2003). However, a report that RecF binds specifically to the duplex-ssDNA junction at DNA gaps (Hegde *et al.*, 1996) has not been confirmed (Webb *et al.*, 1999).

The RecO Protein

The *E. coli recO* gene was identified by Kolodner and colleagues (Kolodner *et al.*, 1985). It is situated in an operon with the *rnc* gene, which encodes ribonuclease III, and the *era* gene, which encodes a GTP-binding protein with sequence similarities to the yeast RAS proteins (Ahnn *et al.*, 1986). The sequenced *recO* gene encodes a protein with 242 amino acids (M_r 27,260) and includes a Walker A box (Morrison *et al.*, 1989; Takiff *et al.*, 1989). The purified protein binds to both ssDNA and dsDNA and behaves as a monomer in solution (Luisi-DeLuca, 1995; Luisi-DeLuca *et al.*, 1994; Umezu *et al.*, 1993; Umezu *et al.*, 1994). Binding or hydrolysis of ATP has not been reported. The protein forms a functional complex with the RecR protein, as described below.

RecO protein promotes an ATP-independent renaturation of complementary DNA strands (Luisi-DeLuca *et al.*, 1994). This reaction is enhanced when RecO forms a complex with the SSB protein (Kantake *et al.*, 2002).

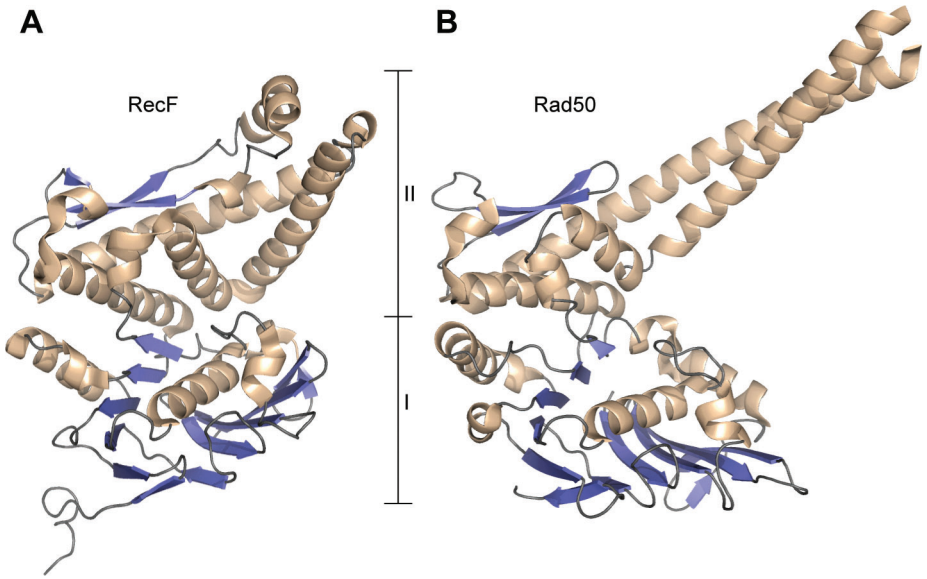

FIGURE 6 **The structure of the RecF protein of *Deinococcus radiodurans*, shown at left (Koroleva *et al.*, 2007). The figure is available in color in the online publication. There are two domains delineated to the right of the structure, and the site for ATP binding and hydrolysis is located at the interface between the domains. For comparison, the closely related structure of the head domain of the Rad50 protein of yeast is shown at right. Rad50 is a component of a system that promotes non-homologous end joining. Coordinates for the RecF protein provided by Dr. Sergey Korolev (St. Louis University) prior to publication.**

The renaturation reaction promoted by RecO-SSB is inhibited by the RecR protein, suggesting the presence of a RecR-SSB competition for RecO complex formation (Kantake *et al.*, 2002). The RecO-SSB DNA renaturation activity is reminiscent of the reaction promoted by the eukaryotic Rad52 protein (Mortenson *et al.*, 1996; Reddy *et al.*, 1997; Sugiyama *et al.*, 1998), and could function in some RecA-independent pathways for recombination and recombinational DNA repair.

The structure of the RecO protein from *Deinococcus radiodurans* has been elucidated (Leiros *et al.*, 2005; Makharashvili *et al.*, 2004). The protein contains three domains that include an OB fold, a helical bundle, and a zinc-finger motif moving from the N- to C-terminus (Figure 7). Sites for interactions with DNA and other proteins have been suggested (Leiros *et al.*, 2005; Makharashvili *et al.*, 2004) and some of these have been tested, but more work is needed to define these complexes.

RecR Protein

The *recR* gene was identified in 1989 by Mahdi and Lloyd (Mahdi *et al.*, 1989; Mahdi *et al.*, 1989). It is co-transcribed with the *dnaX* gene and shares an operon with a small open reading frame of unknown function called orf-12 or *ybaB*. The *recR* gene encodes a 201 amino acid protein (M_r 21,965). The sequence includes two putative DNA-binding motifs (helix-turn-helix and zinc finger) (Alonso *et al.*, 1993). The purified protein has been examined *in vitro*, where it was studied in concert with the RecF and RecO proteins (Shan *et al.*, 1997; Umezu *et al.*, 1993; Umezu *et al.*, 1994; Webb *et al.*, 1995; Webb *et al.*, 1997). There is no indication that the *E. coli* RecR protein alone binds directly to DNA, although the RecR proteins from *D. radiodurans* (Lee *et al.*, 2004) and *B. subtilis* (Alonso *et al.*, 1993) do. The *E. coli* RecR protein is a dimer in solution (Umezu *et al.*, 1994). The structure of the *D. radiodurans* RecR protein (44% identity with EcRecR) has recently been determined (Lee *et al.*, 2004). The protein crystallizes as a tetrameric ring with a central hole large enough to accommodate a molecule of dsDNA (Lee *et al.*, 2004) (Figure 8). Koroleva and colleagues (2007) have suggested that the EcRecR protein may require a not-yet-identified clamp-loading function to effect binding to DNA.

Interaction of RecF, O, and R Proteins

Several lines of evidence indicate that these three proteins function at the same stage of recombination, and tie them to a role in displacing SSB and modulating RecA filament assembly. The phenotypes of mutations in the three genes are very similar, defining them as an epistatic group (Clark *et al.*, 1994; Smith, 1989). Mutations in all three genes are partially suppressed by *recA*441 and *recA*803 mutations (Wang *et al.*, 1993). *In vitro*, the same RecA441 (previously tif) and RecA803 proteins exhibit an enhanced capacity to displace SSB

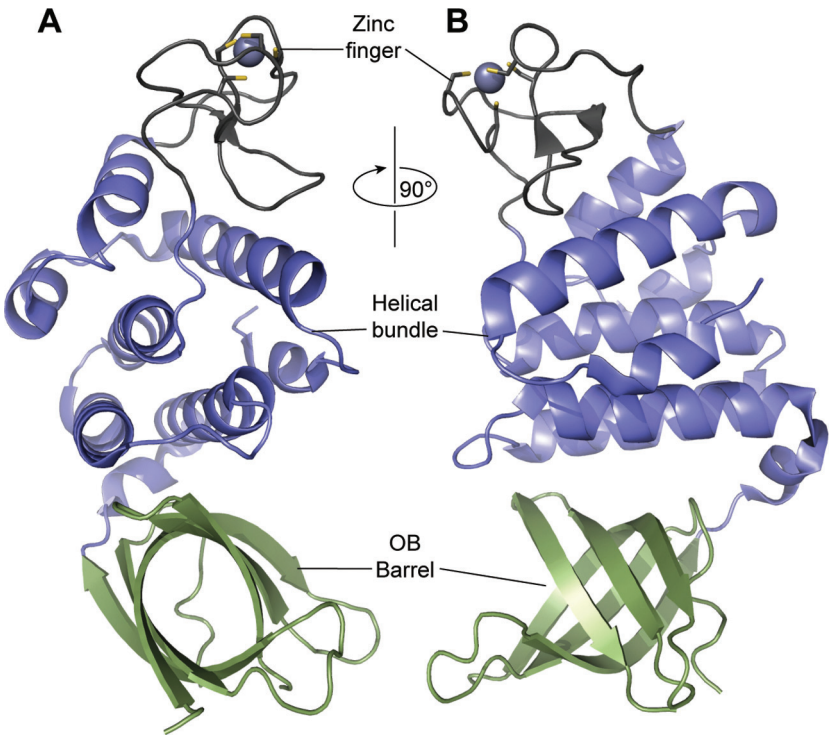

FIGURE 7 **The structure of the RecO protein of *Deinococcus radiodurans* (Leiros *et al.*, 2005; Makharashvili *et al.*, 2004). The figure is available in color in the online publication. The structure is oriented with the amino-terminal OB fold shown at bottom, the helical bundle in the middle, and the C-terminal zinc finger domain at top. A 90° rotation of the structure is shown in panel B.**

and bind ssDNA (Lavery *et al.*, 1988; Madiraju *et al.*, 1992). In addition, a gene in bacteriophage λ called *ninB* or *orf* (described further below) has been identified which can replace *recF*, *recO*, and *recR* functions in lambda recombination (Sawitzke *et al.*, 1992; Sawitzke *et al.*, 1994). *In vivo*, mutant bacteria missing any of the *recFOR* functions exhibit a delayed activation of the SOS response that might reflect slow formation of the RecA filaments required to facilitate LexA cleavage (Madiraju *et al.*, 1988; Whitby *et al.*, 1995). *E. coli* strains in which SSB is overexpressed exhibit a *recFOR*-like phenotype (Moreau, 1988), again suggesting that these proteins function together in overcoming the barrier to RecA filament nucleation represented by SSB.

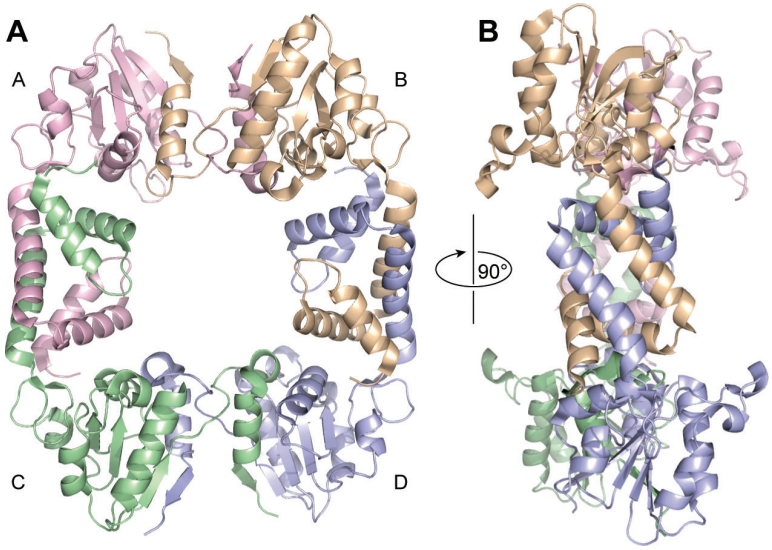

FIGURE 8 **The structure of the RecR protein of *Deinococcus radiodurans* (Lee *et al.*, 2004). The figure is available in color in the online publication. The protein is arranged as a tetrameric ring, with a space in the middle large enough to accommodate a double-stranded DNA molecule. Parts of the A and C, and B and D, subunits overlap extensively.**

A more detailed examination of the literature, however, shows that the roles of these proteins are not always confluent. In particular, RecF protein is an apparent outlier. RecF activity can be toxic to the cell at least in some contexts. In a strain lacking the function of PriA protein, the additional loss of RecO is about 10 times more deleterious than the loss of either RecF or RecR (Grompone *et al.*, 2004). The effect of RecO loss is moderated in *recOrecR* or *recOrecF* strains, suggesting that RecF and RecR are doing something deleterious to the cell in the absence of RecO. An earlier report identified *recF* mutants as the most deleterious in the presence of a *priA* mutation (Sandler *et al.*, 1996). The apparent discrepancy may be explained by some extra steps taken in the former study (Grompone *et al.*, 2004) to avoid the appearance of suppressors in the very sick *recOpriA* strains. Both studies, however, draw a clear distinction between the effects of *recF* and *recO* mutations in the *priA* background. The RecF protein, but not RecO or RecR, is needed for the activation of mutagenic translesion DNA synthesis (TLS) (Rangarajan *et al.*, 2002). This work suggests that RecF may work with RecOR in some processes and independently in others. As already noted, the *recFOR* genes do not always occur together in bacterial genomes (Rocha *et al.*, 2005; Sandler, 2001). In *Bacillus subtilis* (which has all three genes), RecF protein recruitment to repair foci is preceded by the appearance of RecO protein by several minutes (Kidane *et al.*, 2004). Overexpression of RecF protein in *E. coli* reduces SOS induction, UV resistance, and viability at 42°C (Sandler *et al.*, 1993). The overexpression of the RecOR proteins suppresses many of the effects of either RecF overexpression (Sandler, 1994) or a recF null mutation (Sandler *et al.*, 1994). These varied results suggest that the current pictures of RecFOR and RecF function require expansion.

The functional distinction between RecF and RecO proteins is also quite evident *in vitro* (Shan *et al.*, 1997; Umezu *et al.*, 1993; Umezu *et al.*, 1994; Webb *et al.*, 1995; Webb *et al.*, 1997). RecR protein forms alternative complexes with RecF and RecO protein (Bork *et al.*, 2001; Morimatsu *et al.*, 2003; Shan *et al.*, 1997; Webb *et al.*, 1995; Webb *et al.*, 1997). The RecR TOPRIM domain is the interaction site for both RecF and RecO (Honda *et al.*, 2006). RecF protein generally interferes with RecOR function (Bork *et al.*, 2001; Hobbs *et al.*, 2007), and strongly competes with RecO for the formation of complexes with RecR (Bork *et al.*, 2001).

The EcRecOR complex stimulates RecA protein binding to ssDNA coated with SSB, in a process that is not further stimulated by RecF protein under most conditions (Bork *et al.*, 2001; Hobbs *et al.*, 2007; Shan *et al.*, 1997; Umezu *et al.*, 1993; Umezu *et al.*, 1994). Early models indicated that RecOR does not displace SSB, but instead binds to it to form a RecO-RecR-SSB complex that facilitates RecA nucleation (Shan *et al.*, 1997; Umezu *et al.*, 1994). RecO and RecR proteins remain associated with the RecA filament after it is formed (Shan *et al.*, 1997; Umezu *et al.*, 1994). In addition to stimulating nucleation of RecA filament formation on SSB-coated ssDNA, the EcRecOR complex prevents a net end-dependent dissociation from linear ssDNA (Shan *et al.*, 1997). It is not yet clear whether the evident stability of RecA filaments formed when RecOR is present reflects an actual stabilization of the 5′-proximal ends of RecA filaments, a rapid re-nucleation of RecA at RecOR complex sites after the previous RecA filament dissociation commences, or both. The EcRecO and EcRecR proteins are not active independently in these processes. Both must be added to see a stimulation of EcRecA filament loading.

The formation of a RecOR-SSB complex might obviate a direct interaction of RecOR with ssDNA. However, RecOR functions surprisingly slowly in the loading of RecA onto SSB-coated ssDNA. When RecOR concentrations are optimized, the lag in RecA loading can be reduced by more than five-fold. However, a lag of about 10 minutes remains (Hobbs *et al.*, 2007). The slow step in the activation of RecOR is not the binding of SSB, but the displacement of SSB to permit the formation of a direct RecOR-ssDNA complex (Hobbs *et al.*, 2007). The only condition that eliminates the 10 minutes lag is to add RecOR to the ssDNA prior to the SSB. RecOR is functional as a RecA nucleation site only when this complex with ssDNA is formed (Hobbs *et al.*, 2007). When SSB is present on the ssDNA, the pathway leading to the formation of a RecOR-ssDNA complex functional in RecA loading involves an interaction with the SSB C-terminus. When a deletion mutant of SSB lacking the eight C-terminal amino acids replaces the wild type SSB, RecOR function is largely eliminated (Hobbs *et al.*, 2007).

Does RecF protein contribute to RecOR function? RecF inhibits the RecOR-mediated loading of RecA onto SSB-coated ssDNA under most conditions (Bork *et al.*, 2001; Hobbs *et al.*, 2007; Shan *et al.*, 1997; Umezu *et al.*, 1993; Umezu *et al.*, 1994). There is no evidence

yet reported for an interaction between the RecO and RecF proteins. With one exception (Morimatsu *et al.*, 2003) discussed below, there are no reports of a stimulatory effect of RecF on any RecA activity. However, the presence of RecO and RecR appears to nullify a strong inhibitory effect of RecF on RecA-mediated reactions *in vitro* (Umezu *et al.*, 1993). Optimized *in vitro* reconstitution of several steps of one major pathway for recombination-dependent replication restart requires the presence of the RecOR proteins (Xu *et al.*, 2003). RecF protein reduces the stimulation provided by RecOR in this reaction, probably as a result of its negative effects on RecA loading (Xu *et al.*, 2003).

The RecF and RecR proteins form a complex in an ATP and DNA-dependent fashion (Webb *et al.*, 1995). The RecFR complex binds primarily to dsDNA, and the complex is stable enough to halt RecA filament extension (Webb *et al.*, 1997). The RecR protein stimulates the RecF ATPase, but reduces the rate of RecF transfer from one DNA to another (Webb *et al.*, 1995; Webb *et al.*, 1999).

It is always possible that the failure to detect the formation or activity of a RecFOR complex could reflect a failure to find the right reaction conditions. One recent study has provided evidence that RecF, O, and R can act together to facilitate RecA protein filament formation on SSB-coated DNA gaps (Morimatsu *et al.*, 2003). In this study, an enhancement of RecOR-mediated loading of RecA onto SSB-coated ssDNA by RecF protein was observed when DNA substrates contained single strand gaps bordered by short duplex regions (Morimatsu *et al.*, 2003). The positive effects of RecF protein depended on the inclusion of a large excess of SSB protein relative to available SSB binding sites (Morimatsu *et al.*, 2003). The reason for the excess SSB requirement is not clear. The extra SSB may be titrating some factor that affects the formation of the proposed RecFOR complexes. No physical evidence for a RecFOR complex has appeared.

The DinI and RecX Proteins

These two proteins are related in the sense that they have opposing activities, each antagonizing the function of the other.

The RecX Protein

The RecX protein of *Escherichia coli* (M_r 19,293) is encoded by the *E. coli* version of a widespread bacterial gene often found just downstream or even overlapping the *recA* gene (De Mot *et al.*, 1994; Papavinasasundaram *et al.*, 1997; Sano, 1993; Vierling *et al.*, 2000; Yang *et al.*, 2001). In a few cases, the gene is found in another region of the chromosome (Stohl *et al.*, 2001). In *E. coli*, the *recX* gene is just downstream of the recA gene, and expressed from the *recA* promoter via a 5% to 10% transcriptional read-through of a hairpin sequence separating the two genes (Pages *et al.*, 2003). The first indications that recX was involved in RecA regulation appeared in the early 1990s (De Mot *et al.*, 1994; Sano, 1993). In some bacterial species, RecX protein is necessary to overcome deleterious effects of overexpression of RecA protein, implying that RecX is a negative modulator of RecA expression or function (Papavinasasundaram *et al.*, 1998; Sano, 1993; Sukchawalit *et al.*, 2001; Vierling *et al.*, 2000). Deletion of the gene in *E. coli* produces no clear phenotype (Pages *et al.*, 2003), although overexpression of the *recX* gene can reduce the induction of the SOS response (Stohl *et al.*, 2003). When purified, both the *Mycobacterium* RecX (Venkatesh *et al.*, 2002) and the *E. coli* RecX protein (Stohl *et al.*, 2003) inhibit the ATPase and strand exchange activities of RecA protein *in vitro*. The RecX protein binds deep within the major helical groove of an AMPPNP-stabilized RecA filament (VanLoock *et al.*, 2003).

The RecX protein acts as a RecA inhibitor by blocking the extension of RecA filaments during assembly, almost certainly by capping the filament (Drees *et al.*, 2004a). When RecA filaments have been formed on circular ssDNAs, there is generally no net dissociation and ATP hydrolysis proceeds at a constant steady state. There are generally breaks in the filaments where dissociation at a disassembly end can occur, but the resulting ends are quickly filled in by growth of the trailing filament assembly end (Figure 3). When RecX protein is added at relatively low concentrations (about one RecX per 20–100 bound RecA monomers), a net disassembly of the RecA filaments occurs that takes 10–15 min to complete. Detailed characterization of this phenomenon led to the filament capping model (Drees *et al.*, 2004a) (Figure 9). The moderating effect of RecA C-terminal deletions provides evidence that the RecA C-terminus plays a significant role in the RecX-RecA interaction (Drees *et al.*, 2004b).

The DinI Protein

The*E. coli* DinI protein is a small (81 amino acids; M_r 8,818) polypeptide that was identified a decade ago in a search for new LexA-regulated genes (Lewis

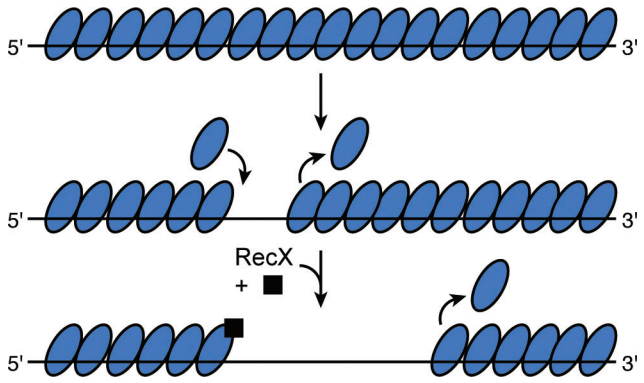

FIGURE 9 **A filament capping mechanism for RecX protein. The figure is available in color in the online publication. At discontinuities in a RecA filament, RecA can dissociate from the disassembly filament end. Rapid growth of the trailing assembly end fills in the gap. RecX protein can bind to the assembly end and block filament assembly, leading to net filament disassembly. Note that RecX protein also binds to RecA filaments along the entire filament length. After (Drees *et al.*, 2004).**

et al., 1994). DinI protein is induced very early in the SOS response (Kenyon *et al.*, 1980; Yasuda *et al.*, 1998; Yasuda *et al.*, 1996). Overexpression of the DinI protein in *E. coli* results in UV sensitivity and inhibits the induction of the SOS response (Yasuda *et al.*, 1998). It was initially proposed that DinI plays a role in bringing the SOS response to an end (Voloshin *et al.*, 2001; Yasuda *et al.*, 1998; Yasuda *et al.*, 2001). DinI has been purified by several different research groups. DinI inhibits the RecA-mediated cleavage of the UmuD protein (Yasuda *et al.*, 2001). The structure of the DinI protein has been elucidated by NMR (Ramirez *et al.*, 2000). The C-terminal 17 amino acid residues of DinI features six negatively charged residues, arranged much like they are in the 17 C-terminal amino acid residues of the RecA protein. A separate NMR study suggested that the DinI protein interacts with the core domain of RecA (Yoshimasu *et al.*, 2003). DinI has only limited effect on the RecA-mediated LexA cleavage *in vitro* (even though UmuD cleavage is strongly inhibited) (Yasuda *et al.*, 1998; Yasuda *et al.*, 2001).

In contrast to RecX, biochemical characterization establishes that the DinI protein has a positive effect on RecA filament stability (Lusetti *et al.*, 2004). DinI strongly stabilizes RecA filaments under conditions in which it is present at somewhat superstoichiometric concentrations relative to RecA (Lusetti *et al.*, 2004). Filament disassembly is almost completely suppressed. The effect can be seen dramatically in an electron microscope (Lusetti *et al.*, 2004). Further, most DNA strand exchange is not blocked by the DinI. A DinI effect on DNA strand exchange is dependent on the structure of the ends of the duplex DNA employed in the assay *in vitro* (Lusetti *et al.*, 2004). Even when the initiation of strand exchange is slowed by DinI, there is no effect of DinI on the strand exchange reaction once it is initiated. Overall, DinI protein appears to greatly enhance RecA filament stability while leaving most RecA functions largely intact.

The interaction between DinI and RecA is modulated by the RecA C-terminus. Removal of the C-terminal 17 amino acid residues of RecA strongly enhances the interaction between the two proteins (Lusetti *et al.*, 2004). This is consistent with the C-terminus of RecA being a target for RecA modulators.

This effects of DinI on RecA filament stability and on the autocatalytic cleavage of UmuD protein has led to a new hypothesis for DinI action in which DinI is a selective modulator. During SOS, DinI is induced with somewhat faster kinetics than RecA (Voloshin *et al.*, 2001), consistent with an activator function; it does not appear late in SOS, as would be expected for a protein involved in shutting down the SOS response. The only RecA function that seems to be reliably suppressed by DinI is the cleavage of UmuD. The SOS response is under temporal regulation such that nonmutagenic DNA repair processes are induced early and the mutagenic TLS DNA polymerases come into play only late in SOS (Nohmi *et al.*, 1988; Sutton *et al.*, 1999; Sutton *et al.*, 2000). Thus, the presence of DinI early in SOS could suppress the activation of DNA polymerase V while leaving most other RecA activities intact (Figure 10). This could be part of a regulatory scheme delaying the onset of the mutagenic phase of the SOS response.

The role of DinI is distinct from that of Rec(F)OR. DinI does not affect the loading of RecA onto SSB-coated ssDNA (Lusetti *et al.*, 2004). Instead, DinI stabilizes RecA filaments after they are formed.

The DinI and RecX Proteins Each Antagonize the Function of the Other

DinI protein stabilizes the RecA filament, and RecX destabilizes it (Lusetti *et al.*, 2004). With sufficient DinI protein present, a challenge with low concentrations of RecX has no effect on RecA filaments (Lusetti *et al.*, 2004). If DinI protein is added after the RecX protein challenge, the filaments recover. High concentrations of RecX (nearly stoichiometric with RecA protein) do displace the DinI protein and destabilize the RecA filament. In addition to its capping function, the RecX

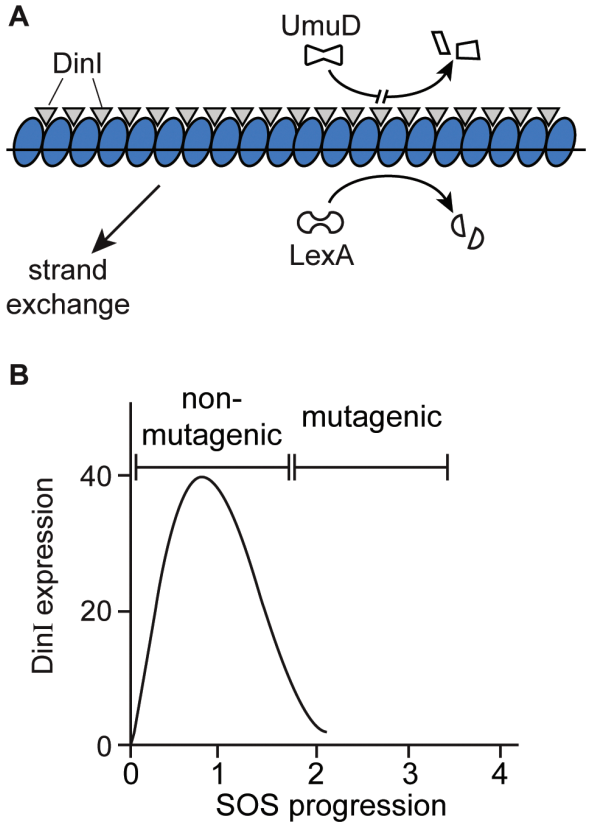

FIGURE 10 **DinI regulation of SOS. The figure is available in color in the online publication. (A) The DinI protein binds all along the length of the RecA filament, stabilizing it and preventing dissociation. The function of the RecA filament is subtly affected by DinI (Lusetti *et al.*, 2004). DNA strand exchange with at least some DNA substrates proceeds normally. The autocatalytic cleavage of LexA protein is reduced somewhat, but the autocalytic cleavage of the UmuD protein is essentially blocked (Yasuda *et al.*, 1998; Yasuda *et al.*, 2001). (B) The DinI protein is induced early in the SOS response (the kinetics shown here are adapted from (Voloshin *et al.*, 2001)). This induction pattern can explain the observed temporal regulation of the SOS response. At early stages in SOS, DinI blocks cleavage of UmuD protein, and thus blocks the activation of the mutagenic DNA polymerase V. The non-mutagenic processes of DNA repair thus predominate early in the SOS response. As DinI levels recede, cleavage and activation of UmuD protein can occur, leading to the formation of active DNA polymerase V. This initiates the mutagenic phase of the SOS response.**

protein appears to compete with DinI for binding sites in the RecA filament groove. This idea meshes well with the binding of RecX within the RecA filament groove as seen in the EM studies of Egelman and colleagues (VanLoock *et al.*, 2003). The replacement of RecX with DinI is a relatively slow process, occurring over 10 minutes or more (Lusetti *et al.*, 2004). In effect, RecA-RecX and RecA-DinI define two RecA filament forms that are functionally distinct.

The RecF Protein Antagonizes RecX Function

The interaction of RecX with other proteins in the RecA regulatory web is not limited to its antagonistic relationship with DinI. RecX protein inhibits the loading of RecA protein to SSB-bound ssDNA under most conditions, even when the RecOR proteins are included in the reaction. However, when RecF is present, the inhibitory effects of RecX protein disappear. RecF blocks RecX function, likely via a direct interaction between the two proteins (Lusetti *et al.*, 2006). To completely neutralize the effects of RecX, RecF is generally required at concentrations equivalent or somewhat greater than that of RecX protein. This provides an alternative mechanism for RecF to affect RecA filament formation in a positive way. By interfering with the function of a protein that blocks RecA filament extension, RecF can facilitate the extension phase of RecA filament formation (Lusetti *et al.*, 2006), complementing its postulated role in facilitating the nucleation phase.

The PsiB and RdgC Proteins

These proteins are implicated in the modulation of RecA filament formation and/or function, but have either not been purified or characterized minimally *in vitro*. Both have the potential for new insights into modes of RecA regulation.

The PsiB Protein

The PsiB protein is encoded by a number of conjugative plasmids (Delver *et al.*, 1997; Sarno *et al.*, 2002). PsiB proteins are generally small, ~140 amino acid residues giving a molecular mass of 15–16 kDa. PsiB inhibits the induction of SOS when conjugation is taking place, presumably by interacting with the RecA protein or blocking RecA filament formation (Bagdasarian *et al.*, 1986). The*psiB* gene is transferred early in conjugation and transcribed transiently (Bagdasarian *et al.*, 1986). None of the known PsiB proteins have been studied *in vitro*.

When bacterial cells are starved, there is a transient induction of the SOS response that leads to genome-wide hypermutation. This is called adaptive mutation, and it requires RecA function both directly and for the SOS induction (McKenzie *et al.*, 2000; McKenzie *et al.*, 2001). In this context, DinI protein has little effect on the SOS response, but PsiB is a potent inhibitor (in cells with an F plasmid) (McKenzie *et al.*, 2000). These results again suggest that PsiB is an inhibitor of RecA function (and reinforce the impression that DinI is not an inhibitor. Also of interest, the IncN plasmid pKM101 (broad host range) encodes both a PsiB protein and a RecX protein (Delver *et al.*, 1997).

The RdgC Protein

RdgC is a fairly abundant DNA binding protein that appears to affect the function of RecA and RecFOR. The *rdgC* gene is located near *sbcC* and *sbcD* on the *E. coli* chromosome, encoding a protein of M_r 33,862 (Ryder *et al.*, 1996). A deletion of the *rdgC* gene by itself has little obvious effect. However, the same deletion in a *recBCsbcBC* background is viable only if the RecA and RecF proteins are functional (hence, recombination-dependent growth or *rdg*) (Ryder *et al.*, 1996). The RdgC protein is also important in a *priA* background. The poor viability of *priA* mutants is suppressed by certain mutations in *dnaC* such as *dnaC*212 These allow the DnaC protein to circumvent PriA in the pathway by which the DnaB helicase is loaded onto a repaired fork structure (Sandler *et al.*, 2000; Sandler *et al.*, 1999). Introducing an *rdgC* deletion into a *priAdnaC212* background confers a slow growth phenotype (Moore *et al.*, 2003). Suppressors of several types arise rapidly in these strains. First, the slow growth is suppressed by mutations that eliminate RecF, RecO or RecR function (Moore *et al.*, 2003). This suggests that an inappropriate loading of RecA protein onto ssDNA causes the slow growth. It also suggests that the RdgC protein has a role in preventing the inappropriate loading or function of RecA protein. The slow growth is also suppressed by certain mutations in the *ssb* gene (Moore *et al.*, 2003). The characterized *ssb* mutants are R97C and Δ115–144. These *ssb* alterations could define interaction points for Rec(F)OR. The RdgC protein is present at about 1000 copies per cell (compared to about 800 tetramers of SSB) (Moore *et al.*, 2003), and *in vitro* the protein binds to both ssDNA and dsDNA (Moore *et al.*, 2003).

In vitro, RdgC protein is a potent inhibitor of RecA protein function. It competes with RecA for DNA binding sites, particularly on dsDNA (Drees *et al.*, 2006). When bound to the duplex substrate of DNA strand exchange, RdgC effectively sequesters the dsDNA and prevents its use by the RecA filaments bound to the homologous duplex (Drees *et al.*, 2006). It is not yet clear how this might affect RecA in the cell, since RdgC does not appear to interact with RecA protein. To affect RecA function *in vivo*, RdgC would need to be targeted to sites of RecA assembly. The RdgC protein is interesting on its own. It is present in the cell at a level comparable to SSB, and it uniformly coats dsDNA (Drees *et al.*, 2006). It might be considered a double-stranded DNA binding protein (DSB?), a kind of duplex DNA counterpart to SSB. Rdg C crystallizes as a dimeric ring, with head to head and tail to tail organization. The 30Å central hole provides a likely DNA binding site (Briggs *et al.*, 2007).

The UvrD Helicase

In every organism, there appear to be helicases that antagonize recombination functions. This is perhaps best characterized in yeast. The yeast Srs2 helicase negatively modulates recombination (Aboussekhra *et al.*, 1989; Aguilera *et al.*, 1988). Additional work suggests that Srs2 actively removes recombination complexes or structures *in vivo* (Chanet *et al.*, 1996; Kaytor *et al.*, 1995; Milne *et al.*, 1995; Schild, 1995). The yeast Sgs1 protein is a helicase from the RecQ family (Gangloff *et al.*, 1994). A combination of *srs2* and *sgs1* null mutants results in a near-lethal slow growth phenotype (Fabre *et al.*, 2002; Klein, 2001; Lee *et al.*, 1999; Mankouri *et al.*, 2002). Mutations in a number of recombination functions, including Rad51, Rad52, Rad55, and Rad57, alleviate the defect in the *sgs1 srs2* double mutant (Fabre *et al.*, 2002; Klein, 2001). The work indicates that Sgs1 and Srs2 are involved in the removal of toxic recombination intermediates, and can partially substitute for each other. *In vitro*, the Srs2 helicase will disrupt Rad51 protein filaments and interfere with their DNA strand exchange activity (Krejci *et al.*, 2003; Veaute *et al.*, 2003).

In bacteria, parallels are evident but less developed. The RuvA and B proteins displace RecA filaments *in vitro* (Adams *et al.*, 1994), but the genetics provides only limited support for this role *in vivo*. There may be better candidates, and null mutants of the *uvrD* gene have a phenotype implicating the UvrD protein in recombinational DNA repair (Mendonca *et al.*, 1995). UvrD is induced as part of the SOS response, and has a putative role in dismantling RecA filaments.

The EcUvrD protein (or *E. coli* DNA helicase II; M_r 81,859) is encoded by a gene located at about 84 minutes on the *E. coli* chromosome. UvrD is homologous to the somewhat smaller *E. coli* Rep helicase, and can even form heterodimers with Rep (Wong *et al.*, 1993). Deletion of both the *rep* and *uvrD* genes in *E. coli* is lethal (Washburn *et al.*, 1991). As Rep has been shown to remove proteins from the DNA (Yancey-Wrona *et al.*, 1992), it has been proposed that Rep might serve to remove proteins in the path of the replication fork (DNA synthesis is slowed 50% in cells lacking Rep function (Lane *et al.*, 1975)). UvrD could in principle play a

similar role in recombination and repair, and genetic studies suggest that it does.

UvrD plays a role in many aspects of DNA metabolism, although its detailed molecular function remains somewhat enigmatic. This helicase is involved in both methyl-directed mismatch repair (Lahue *et al.*, 1989; Modrich, 1989) and the DNA excision repair mediated by the UvrABC excinuclease (Kumura *et al.*, 1985). A role in chromosomal replication is suggested by the constitutive induction of the SOS response that is observed in many *uvrD* mutant cells (George *et al.*, 1994; Ossanna *et al.*, 1989), presumably because replication forks are stalling in these strains. Cells lacking UvrD function have a defect in recombinational DNA repair (Howard-Flanders *et al.*, 1981; Lloyd, 1983; Mendonca *et al.*, 1993). At the same time, *uvrD*$^{-}$ strains have a hyperrecombination phenotype, with large increases in illegitimate recombination (Lovett *et al.*, 1995; Washburn *et al.*, 1991). Certain alterations of UvrD can suppress the phenotypes of *ruvB* and *recJ* (Lovett *et al.*, 1995) mutations, further suggesting a complex involvement in recombination processes. Perhaps most important, UvrD has a demonstrated anti-recombinase function *in vivo* that may involve the destabilization of recombination intermediates, the complexes that form them, or both (Lovett *et al.*, 1995; Morel *et al.*, 1993; Petranovic *et al.*, 2001). In strains lacking the RecBCD pathway, *recQ* and *uvrD* null mutations are synthetically lethal (Mendonca *et al.*, 1995).

The EcUvrD protein is a 3′ to 5′ helicase (Matson, 1986) (as is Rep and the yeast Srs2 helicase) and unwinds duplex DNA best when there is a 3′ single strand extension upon which to bind and initiate. However, UvrD also exhibits significant unwinding activity even when initiating the reaction at a nick (Runyon *et al.*, 1990) or blunt end, and this capability could be important for repair systems designed to address strand breaks. In addition, UvrD will unwind RNA-DNA hybrids in a reaction more robust than the unwinding of DNA (Matson, 1989), perhaps suggesting a role in replication fork repair on the lagging strand. The UvrD helicase functions as a dimer (Ali *et al.*, 1999; Maluf *et al.*, 2003), although the protein binds well to single-stranded DNA as a monomer (Maluf *et al.*, 2003; Mechanic *et al.*, 1999; Velankar *et al.*, 1999).

Finally, and significantly, Petit and collaborators have demonstrated that the UvrD helicase dismantles RecA filaments *in vitro* (Veaute *et al.*, 2005). Filament disassembly was monitored by electron microscopy in this study (Veaute *et al.*, 2005). In the same series of experiments (Veaute *et al.*, 2005), Rep helicase did not promote RecA filament disassembly, indicating that this may be a specialized role of the UvrD protein.

CONCLUDING REMARKS

The known regulatory protein network affecting the bacterial RecA recombinase is in an expansion phase. The proteins already assigned to the network are incompletely understood, and new proteins are being added. Obvious questions for future investigation are highlighted throughout the text above. Prospects for successful biochemical reconstitution of recombinational DNA repair depend upon a better understanding of these regulatory processes. The mechanistic issues are important in part because a very similar situation exists in eukaryotes. The stakes are substantial, especially in human cells where recombination represents a significant cancer-avoidance system.

There is an intriguing possibility that additional regulatory proteins remain to be discovered in bacteria, even in *E. coli*. In every genome, the functions of many genes remain unknown. In *E. coli*, a significant number of uncharacterized open reading frames exist in operons where other genes are dedicated to DNA metabolism. Some recent additions to the list of RecA regulatory proteins (e.g., RecX, DinI) are encoded by genes that generate quite subtle phenotypes when mutated, and were not identified in classic genetic screens for recombination functions. In spite of the limited genetic effects, these proteins have important regulatory functions. Genomics provides some new paths for relevant gene discovery. Interesting new candidates for RecA regulatory functions already exist. For example, mutations in the *E. coli mgsA* (*rarA*) gene produce a phenotype that partially overlaps with that of *recA mutants,* and the gene is orthologous to a eukaryotic gene (yeast MGS1) that plays a role in maintaining genome stability (Shibata *et al.*, 2005). The MgsA protein could be a regulator and/or a function that complements RecA at stalled replication forks. The relatively slow action of RecOR and the sometimes confusing results with RecF protein suggest that one or more additions to the RecFOR protein family may remain to be found. Genetic studies in *Bacillus subtilis* may provide a guide. A mutation designated *recL* is epistatic to the *recFOR* genes in *Bacillus*, producing the RecFLOR complementation group (Carrasco *et al.*, 2001; Fernandez *et al.*, 1999; Petit *et al.*, 2002). The gene

corresponding to *recL* has not been identified. There are actually five separate mutations in *B. subtilis* that affect recombination but have not been assigned to genes: *recH*, *recL*, *recP*, *recV* (formerly *recD*) and *rec3* (J. Alonso, personal communication). Some or all of these might have a regulatory role with respect to RecA. It is not clear even in *Bacillus* that the search for recombination functions has been saturated. It is also not clear how many of the *Bacillus* genes will turn out to have *E. coli* homologues, or how many additional *E. coli* recombination functions may be present.

ACKNOWLEDGMENTS

Work described from the author's laboratory was supported by grant GM52725 from the National Institutes of Health of the United States of America. The author thanks Sergey Korolev for sharing his group's RecF structural results prior to publication and for permitting the use of structural data prior to release for use in the generation of Figure 6. The author also thanks past and present members of the Cox laboratory for numerous discussions and insights that contributed to the work described here.

REFERENCES

Aboussekhra, A., Chanet, R., Zgaga, Z., Cassier-Chauvat, C., Heude, M., and Fabre, F. 1989. RADH, a gene of Saccharomyces cerevisiae encoding a putative DNA helicase involved in DNA repair. Characteristics of radH mutants and sequence of the gene. *Nucleic Acids Research* 17:7211.

Abrahams, J.P., Leslie, A.G., Lutter, R., and Walker, J.E. 1994. Structure at 2.8 A resolution of F1-ATPase from bovine heart mitochondria. *Nature* 370:621.

Acharya, N., and Varshney, U. 2002. Biochemical properties of single-stranded DNA-binding protein from Mycobacterium smegmatis, a fast-growing mycobacterium and its physical and functional interaction with uracil DNA glycosylases. *J Mol Biol* 318:1251.

Adams, D.E., Tsaneva, I.R., and West, S.C. 1994. Dissociation of RecA filaments from duplex DNA by the RuvA and RuvB DNA repair proteins. *Proc Natl Acad Scie USA* 91:9901.

Aguilera, A., and Klein, H.L. 1988. Genetic control of intrachromosomal recombination in Saccharomyces cerevisiae. I. Isolation and genetic characterization of hyper-recombination mutations. *Genetics* 119:779.

Ahnn, J., March, P.E., Takiff, H.E., and Inouye, M. 1986. A GTP-binding protein of Escherichia coli has homology to yeast RAS proteins. *Proc Natl Acad Sci USA* 83:8849.

Alberts, B.M., and Frey, L. 1970. T4 bacteriophage gene 32: a structural protein in the replication and recombination of DNA. *Nature* 227:1313.

Ali, J.A., Maluf, N.K., and Lohman, T.M. 1999. An oligomeric form of E. coli UvrD is required for optimal helicase activity. *J Mol Biol* 293:815.

Alonso, J.C., Stiege, A.C., Dobrinski, B., and Lurz, R. 1993. Purification and properties of the RecR protein from Bacillus subtilis 168. *J Biol Chem* 268:1424.

Amano, T., Yoshida, M., Matsuo, Y., and Nishikawa, K. 1994. Structural model of the ATP-binding domain of the F1-beta subunit based on analogy to the RecA protein. *FEBS Lett* 351:1.

Amundsen, S.K., Taylor, A.F., Chaudhury, A.M., and Smith, G.R. 1986. recD: the gene for an essential third subunit of exonuclease V. *Proc Nat Acad Sci USA* 83:5558.

Anderson, D.G., and Kowalczykowski, S.C. 1997. The translocating RecBCD enzyme stimulates recombination by directing RecA protein onto ssDNA in a chi-regulated manner. *Cell* 90:77.

Arenson, T.A., Tsodikov, O.V., and Cox, M.M. 1999. Quantitative analysis of the kinetics of end-dependent disassembly of RecA filaments from ssDNA. *J Mol Biol* 288:391.

Arnold, D.A., and Kowalczykowski, S.C. 2000. Facilitated loading of RecA protein is essential to recombination by RecBCD enzyme. *J Biol Chem* 275:12261.

Asai, T., and Kogoma, T. 1994. The RecF pathway of homologous recombination can mediate the initiation of DNA damage-inducible replication of the Escherichia coli chromosome. *J Bacteriol* 176: 7113.

Bagdasarian, M., Bailone, A., Angulo, J.F., Scholz, P., and Devoret, R. 1992. PsiB, an anti-SOS protein, is transiently expressed by the F sex factor during its transmission to an Escherichia coli K-12 recipient. *Mol Microbiol* 6:885.

Bagdasarian, M., Bailone, A., Bagdasarian, M.M., Manning, P.A., Lurz, R., Timmis, K.N., and Devoret, R. 1986. An inhibitor of SOS induction, specified by a plasmid locus in Escherichia coli. *Proc Natl Acad Sci USA* 83:5723.

Bailone, A., Backman, A., Sommer, S., Celerier, J., Bagdasarian, M.M., Bagdasarian, M., and Devoret, R. 1988. PsiB polypeptide prevents activation of RecA protein in *Escherichia coli. Mol Gen Genet* 214:389.

Baumann, P., and West, S.C. 1998. Role of the human Rad51 protein in homologous recombination and double-stranded break repair. *Trends Biochem Sci* 23:247.

Beernik, H.T.H., and Morrical, S.W. 1999. RMPs: recombination/replication mediator proteins. *TIBS* 24:385.

Benedict, R.C., and Kowalczykowski, S.C. 1988. Increase of the DNA strand assimilation activity of RecA protein by removal of the C terminus and structure-function studies of the resulting protein fragment. *J Biol Chem* 263:15513.

Bianchet, M.A., Ko, Y.H., Amzel, L.M., and Pedersen, P.L. 1997. Modeling of nucleotide binding domains of ABC transporter proteins based on a F1-ATPase/recA topology: structural model of the nucleotide binding domains of the cystic fibrosis transmembrane conductance regulator (CFTR). *J Bioenergetics Biomembranes* 29: 503.

Bidnenko, V., Seigneur, M., Penel-Colin, M., Bouton, M.F., Ehrlich, S.D., and Michel, B. 1999. sbcS sbcC null mutations allow RecF-mediated repair of arrested replication forks in rep recBC mutants. *Mol Microbiol* 33:846.

Bierne, H., and Michel, B. 1994. When replication forks stop. *Mol Microbiol* 13:17.

Bird, L.E., Subramanya, H.S., and Wigley, D.B. 1998. Helicases: a unifying structural theme? *Curr Opin Struct Biol* 8:14.

Bishop, A.J.R., and Schiestl, R.H. 2003. Role of homologous recombination in carcinogenesis. *Exp Mol Pathol* 74:94.

Bishop, D.K. 1994. RecA homologs Dmc1 and Rad51 interact to form multiple nuclear complexes prior to meiotic chromosome synapsis. *Cell* 79:1081.

Bjergbaek, L., Cobb, J.A., and Gasser, S.M. 2002. RecQ helicases and genome stability: Lessons from model organisms and human disease. *Swiss Med Wkly* 132:433.

Blanar, M.A., Sandler, S.J., Armengod, M.E., Ream, L.W., and Clark, A.J. 1984. Molecular analysis of the recF gene of Escherichia coli. *Proc Natl Acad Scie USA* 81:4622.

Bork, J.M., Cox, M.M., and Inman, R.B. 2001. The RecOR proteins modulate RecA protein function at 5′ ends of single-stranded DNA. *EMBO J* 20:7313.

Brendel, V., Brocchieri, L., Sandler, S.J., Clark, A.J., and Karlin, S. 1997. Evolutionary comparisons of RecA-like proteins across all major kingdoms of living organisms. *J Mole Evol* 44:528.

Briggs, G.S., McEwan, P.A., Yu, J., Moore, T., Emsley, J., and Lloyd, R.G. 2007. Ring structure of the Escherichia coli DNA binding protein RdgC associated with recombination and replication fork repair. *J Biol Chem* In press.

Bujalowski, W., and Lohman, T.M. 1987. Limited co-operativity in protein-nucleic acid interactions. A thermodynamic model for the interactions of Escherichia coli single strand binding protein with single-stranded nucleic acids in the "beaded", (SSB)65 mode. *J Mol Biol* 195:897.

Bujalowski, W., Overman, L.B., and Lohman, T.M. 1988. Binding mode transitions of Escherichia coli single strand binding protein-single-stranded DNA complexes. Cation, anion, pH, and binding density effects. *J Biol Chem* 263:4629.

Butland, G., Peregrin-Alvarez, J.M., Li, J., Yang, W.H., Yang, X.C., Canadien, V., Starostine, A., Richards, D., Beattie, B., Krogan, N., Davey, M., Parkinson, J., Greenblatt, J., and Emili, A. 2005. Interaction network containing conserved and essential protein complexes in Escherichia coli. *Nature* 433:531.

Cadman, C.J., and McGlynn, P. 2004. PriA helicase and SSB interact physically and functionally. *Nucleic Acids Research* 32:6378.

Carrasco, B., Fernandez, S., Petit, M.A., and Alonso, J.C. 2001. Genetic recombination in Bacillus subtilis 168: Effect of Delta helD on DNA repair and homologous recombination. *J Bacteriol* 183:5772.

Chakraverty, R.K., and Hickson, I.D. 1999. Defending genome integrity during DNA replication: a proposed role for RecQ family helicases. *Bioessays* 21:286.

Chanet, R., Heude, M., Adjiri, A., Maloisel, L., and Fabre, F. 1996. Semidominant mutations in the yeast Rad51 protein and their relationships with the Srs2 helicase. *Mol Cell Biol* 16:4782.

Chen, W.L., and Jinks-Robertson, S. 1998. Mismatch repair proteins regulate heteroduplex formation during mitotic recombination in yeast. *Mol Cell Biol* 18:6525.

Churchill, J.J., Anderson, D.G., and Kowalczykowski, S.C. 1999. The RecBC enzyme loads RecA protein onto ssDNA asymmetrically and independently of chi, resulting in constitutive recombination activation. *Genes Develop* 13:901.

Churchill, J.J., and Kowalczykowski, S.C. 2000. Identification of the RecA protein-loading domain of RecBCD enzyme. *J Mol Biol* 297:537.

Clark, A.J., and Margulies, A.D. 1965. Isolation and characterization of recombination-deficient mutants of *Escherichia coli* K12. *Proc Natl Acad Sci USA* 53:451.

Clark, A.J., and Sandler, S.J. 1994. Homologous genetic recombination: the pieces begin to fall into place. *Crit Review Microbiol* 20:125.

Cohen, P.E., and Pollard, J.W. 2001. Regulation of meiotic recombination and prophase I progression in mammals. *Bioessays* 23:996.

Conway, A.B., Lynch, T.W., Zhang, Y., Fortin, G.S., Fung, C.W., Symington, L.S., and Rice, P.A. 2004. Crystal structure of a Rad51 filament. *Nature Struct Mol Biol* 11:791.

Courcelle, J., Carswell-Crumpton, C., and Hanawalt, P. 1997. *recF* and *recR* are required for the resumption of replication at DNA replication forks in *Escherichia coli*. *Proc Natl Acad Sci USA* 94:3714.

Cox, J.M., Abbott, S.N., Chitteni-Pattu, S., Inman, R.B., and Cox, M.M. 2006. Complementation of one RecA protein point mutation by another—Evidence for trans catalysis of ATP hydrolysis. *J Biol Chem* 281:12968.

Cox, J.M., Tsodikov, O.V., and Cox, M.M. 2005. Organized unidirectional waves of ATP hydrolysis within a RecA filament. *PLoS Biol* 3:231.

Cox, M.M. 1999. Recombinational DNA repair in bacteria and the RecA protein. *Prog Nucleic Acids Res Mol Biol* 63:310.

Cox, M.M. 2002. The nonmutagenic repair of broken replication forks via recombination. *Mutation Res Fund Mol Mech Mutagen* 510:107.

Cox, M.M. 2003. The bacterial RecA protein as a motor protein. *Ann Rev of Microbiol*. 57:551.

Cox, M.M., The bacterial RecA protein: structure, function, and regulation, In: *Topics in Current Genetics*, Rothstein, R., and Aguilera, A., Eds., Heidelberg: Springer-Verlag, 2006, in press.

Cox, M.M. 2007. Motoring along with the RecA protein. *Nature Revi Mol Cell Biol* 8:in press.

Cox, M.M., Goodman, M.F., Kreuzer, K.N., Sherratt, D.J., Sandler, S.J., and Marians, K.J. 2000. The importance of repairing stalled replication forks. *Nature* 404:37.

Curth, U., Genschel, J., Urbanke, C., and Greipel, J. 1996. In vitro and in vivo function of the C-terminus of Escherichia coli single-stranded DNA binding protein. *Nucleic Acids Research* 24:2706.

Dabrowski, S., Olszewski, M., Piatek, R., Brillowska-Dabrowska, A., Konopa, G., and Kur, J. 2002. Identification and characterization of single-stranded-DNA-binding proteins from Thermus thermophilus and Thermus aquaticus - new arrangement of binding domains. *Microbiol* 148:3307.

Datta, A., Adjiri, A., New, L., Crouse, G.F., and Jinksrobertson, S. 1996. Mitotic crossovers between diverged sequences are regulated by mismatch repair proteins in saccharomyces cerevisiae. *Mol Cell Biol* 16:1085.

Datta, S., Ganesh, N., Chandra, N.R., Muniyappa, K., and Vijayan, M. 2003. Structural studies on MtRecA-nucleotide complexes: insights into DNA and nucleotide binding and the structural signature of NTP recognition. *Proteins* 50:474.

Datta, S., Krishna, R., Ganesh, N., Chandra, N.R., Muniyappa, K., and Vijayan, M. 2003. Crystal structures of Mycobacterium smegmatis RecA and its nucleotide complexes. *J Bacteriol* 185:4280.

Datta, S., Prabu, M.M., Vaze, M.B., Ganesh, N., Chandra, N.R., Muniyappa, K., and Vijayan, M. 2000. Crystal structures of *Mycobacterium tuberculosis* RecA and its complex with ADP-AlF4: implications for decreased ATPase activity and molecular aggregation. *Nucleic Acids Research* 28:4964.

de Massy, B. 2003. Distribution of meiotic recombination sites. *Trends Genetics* 19:514.

De Mot, R., Schoofs, G., and Vanderleyden, J. 1994. A putative regulatory gene downstream of recA is conserved in gram-negative and gram-positive bacteria. *Nucleic Acids Research* 22:1313.

Delver, E.P., and Belogurov, A.A. 1997. Organization of the leading region of incn plasmid pkm101 (r46)—a regulon controlled by cup sequence elements. *J Mol Biol* 271:13.

Dillingham, M.S., Spies, M., and Kowalczykowski, S.C. 2003. RecBCD enzyme is a bipolar DNA helicase. *Nature* 423:893.

Drees, J.C., Chitteni-Pattu, S., McCaslin, D.R., Inman, R.B., and Cox, M.M. 2006. Inhibition of RecA protein function by the RdgC protein from Escherichia coli. *J Biol Chem* 281:4708.

Drees, J.C., Lusetti, S.L., Chitteni-Pattu, S., Inman, R.B., and Cox, M.M. 2004a. A RecA filament capping mechanism for RecX protein. *Mol Cell* 15:789.

Drees, J.C., Lusetti, S.L., and Cox, M.M. 2004b. Inhibition of RecA protein by the Escherichia coli RecX protein—Modulation by the RecA C terminus and filament functional state. *J Biol Chem* 279:52991.

Dutreix, M., Moreau, P.L., Bailone, A., Galibert, F., Battista, J.R., Walker, G.C., and Devoret, R. 1989. New recA mutations that dissociate the various RecA protein activities in Escherichia coli provide evidence for an additional role for RecA protein in UV mutagenesis. *J Bacteriol* 171:2415.

Echols, H., and Goodman, M.F. 1991. Fidelity mechanisms in DNA replication. *Annu Rev Biochem* 60:477.

Egelman, E. 2000. A common structural core in proteins active in DNA recombination and replication. *Trends Biochem Sci* 25:180.

Eggington, J.M., Haruta, N., Wood, E.A., and Cox, M.M. 2004. The single-stranded DNA-binding protein of *Deinococcus radiodurans. BMC Microbiol* 4:2.

Eggler, A.L., Lusetti, S.L., and Cox, M.M. 2003. The C terminus of the Escherichia coli RecA protein modulates the DNA binding competition with single-stranded DNA-binding protein. *J Biol Chem* 278:16389.

Emmerson, P.T. 1968. Recombination deficient mutants of Escherichia coli K12 that map between thy A and argA. *Genetics* 60:19.

Fabre, F., Chan, A., Heyer, W.D., and Gangloff, S. 2002. Alternate pathways involving Sgs1/Top3, Mus81/ Mms4, and Srs2 prevent formation of toxic recombination intermediates from single-stranded gaps created by DNA replication. [erratum appears in *Proc Natl Acad Sci U S A.* 2003 Feb 4;100(3):1462]. *Proc Natl Acad Sci USA* 99:16887.

Fernandez, S., Kobayashi, Y., Ogasawara, N., and Alonso, J.C. 1999. Analysis of the Bacillus subtilis recO gene: RecO forms part of the RecFLOR function. *Mol Gene Genet* 261:567.

Finch, P.W., Storey, A., Brown, K., Hickson, I.D., and Emmerson, P.T. 1986. Complete nucleotide-sequence of recD, the structural gene for the alpha-subunit of Exonuclease V of Escherichia coli. *Nucleic Acids Research* 14:8583.

Finch, P.W., Storey, A., Chapman, K.E., Brown, K., Hickson, I.D., and Emmerson, P.T. 1986. Complete nucleotide-sequence of the Escherichia coli RecB Gene. *Nucleic Acids Research* 14:8573.

Finch, P.W., Wilson, R.E., Brown, K., Hickson, I.D., Tomkinson, A.E., and Emmerson, P.T. 1986. Complete nucleotide-sequence of the Escherichia coli recC Gene and of the thyA-recC intergenic region. *Nucleic Acids Research* 14:4437.

Galitski, T., and Roth, J.R. 1997. Pathways for homologous recombination between chromosomal direct repeats in Salmonella typhimurium. *Genetics* 146:751.

Galletto, R., Amitani, I., Baskin, R.J., and Kowalczykowski, S.C. 2006. Direct observation of individual RecA filaments assembling on single DNA molecules. *Nature*. advanced online publication.

Gangloff, S., McDonald, J.P., Bendixen, C., Arthur, L., and Rothstein, R. 1994. The yeast type I topoisomerase Top3 interacts with Sgs1, a DNA helicase homolog: a potential eukaryotic reverse gyrase. *Mol Cell Biol* 14:8391.

Genschel, J., Curth, U., and Urbanke, C. 2000. Interaction of E. coli single-stranded DNA binding protein (SSB) with exonuclease I. The carboxy-terminus of SSB is the recognition site for the nuclease. *Biol Chem* 381:183.

George, J.W., Brosh, R.M., Jr., and Matson, S.W. 1994. A dominant negative allele of the Escherichia coli uvrD gene encoding DNA helicase II. A biochemical and genetic characterization. *J Mol Biol* 235: 424.

Gomis-Ruth, F.X., Moncalian, G., Perez-Luque, R., Gonzalez, A., Cabezon, E., de la Cruz, F., and Coll, M. 2001. The bacterial conjugation protein TrwB resembles ring helicases and F1-ATPase. *Nature* 409:637.

Griffin, T.J.t., and Kolodner, R.D. 1990. Purification and preliminary characterization of the Escherichia coli K-12 recF protein. *J Bacteriol* 172:6291.

Grompone, G., Sanchez, N., Ehrlich, S.D., and Michel, B. 2004. Requirement for RecFOR-mediated recombination in priA mutant. *Mol Microbiol* 52:551.

Gulbis, J.M., Kazmirski, S.L., Finkelstein, J., Kelman, Z., O'Donnell, M., and Kuriyan, J. 2004. Crystal structure of the chi:psi sub-assembly of the Escherichia coli DNA polymerase clamp-loader complex. *Eur J Biochem* 271:439.

Gupta, R.C., Bazemore, L.R., Golub, E.I., and Radding, C.M. 1997. Activities of human recombination protein Rad51. *Proc Natl Acad Sci USA* 94:463.

Haber, J.E. 2000. Partners and pathways—repairing a double-strand break. *Trends Genet* 16:259.

Hanada, K., Iwasaki, M., Ihashi, S., and Ikeda, H. 2000. UvrA and UvrB suppress illegitimate recombination: Synergistic action with RecQ helicase. *Proc Natl Acad Sci USA* 97:5989.

Hanada, K., Ukita, T., Kohno, Y., Saito, K., Kato, J., and Ikeda, H. 1997. RecQ DNA helicase is a suppressor of illegitimate recombination in Escherichia coli. *Proc Natl Acad Sci USA* 94:3860.

Handa, P., Acharya, N., and Varshney, U. 2001. Chimeras between single-stranded DNA-binding proteins from Escherichia coli and Mycobacterium tuberculosis reveal that their C-terminal domains interact with uracil DNA glycosylases. *J Biol Chem* 276:16992.

Haruta, N., Yu, X.N., Yang, S.X., Egelman, E.H., and Cox, M.M. 2003. A DNA pairing-enhanced conformation of bacterial RecA proteins. *J Biol Chem* 278:52710.

Hegde, S.P., Rajagopalan, M., and Madiraju, M.V. 1996. Preferential binding of Escherichia coli RecF protein to gapped DNA in the presence of adenosine (gamma-thio) triphosphate. *J Bacteriol* 178:184.

Hillers, K.J., and Villeneuve, A.M. 2003. Chromosome-wide control of meiotic crossing over in C-elegans. *Curr Biol* 13:1641.

Hobbs, M.D., and Cox, M.M. 2007. SSB limits RecOR binding onto single strand DNA. *J Biol Chem.* in press.

Honda, M., Inoue, J., Yoshimasu, M., Ito, Y., Shibata, T., and Mikawa, T. 2006. Identification of the RecR Toprim domain as the binding site for both RecF and RecO. *Biol Chem* 281:18549.

Horii, Z., and Clark, A.J. 1973. Genetic analysis of the RecF pathway to genetic recombination in *Escherichia coli* K12: isolation and characterization of mutants. *J Mol Biol* 80:327.

Howard-Flanders, P., and Bardwell, E. 1981. Effects of recB21, recF143, and uvrD152 on recombination in lambda bacteriophage-prophage and Hfr by F- crosses. *J Bacteriol* 148:739.

Hyrien, O. 2000. Mechanisms and consequences of replication fork arrest. *Biochimie*. 82:5.

Jain, S.K., Cox, M.M., and Inman, R.B. 1994. On the Role of ATP Hydrolysis in RecA Protein-Mediated DNA Strand Exchange III. Unidirectional Branch Migration and Extensive Hybrid DNA Formation. *J Biol Chem*. 269:20653.

Jiang, H., Giedroc, D., and Kodadek, T. 1993. The role of protein-protein interactions in the assembly of the presynaptic filament for T4 homologous recombination. *J Biol Chem* 268:7904.

Joo, C., McKinney, S.A., Nakamura, M., Rasnik, I., Myong, S., and Ha, T. 2006. Real-time observation of RecA filament dynamics with single monomer resolution. *Cell* 126:515.

Kantake, N., Madiraju, M., Sugiyama, T., and Kowalczykowski, S.C. 2002. Escherichia coli RecO protein anneals ssDNA complexed with its cognate ssDNA-binding protein: A common step in genetic recombination. *Proc Natl Acad Sci USA* 99:15327.

Kaytor, M.D., Nguyen, M., and Livingston, D.M. 1995. The complexity of the interaction between RAD52 and SRS2. *Genetics* 140:1441.

Kenyon, C.J., and Walker, G.C. 1980. DNA-damaging agents stimulate gene expression at specific loci in *Escherichia coli*. *Proc Natl Acad Sci USA* 77:2819.

Kidane, D., Sanchez, H., Alonso, J.C., and Graumann, P.L. 2004. Visualization of DNA double-strand break repair in live bacteria reveals dynamic recruitment of Bacillus subtilis RecF, RecO and RecN proteins to distinct sites on the nucleoids. *Mol Microbiol* 52:1627.

Kim, J.I., Cox, M.M., and Inman, R.B. 1992. On the role of ATP hydrolysis in RecA protein-mediated DNA strand exchange. I. Bypassing a short heterologous insert in one DNA substrate. *J Biol Chem* 267: 16438.

Kim, J.I., Cox, M.M., and Inman, R.B. 1992. On the role of ATP hydrolysis in RecA protein-mediated DNA strand exchange. II. Four-strand exchanges. *J Biol Chem* 267:16444.

Kinebuchi, T., Shindo, H., Nagai, H., Shimamoto, N., and Shimizu, M. 1997. Functional domains of Escherichia coli single-stranded DNA binding protein as assessed by analyses of the deletion mutants. *Biochemistry* 36:6732.

Klapstein, K., Chou, T., and Bruinsma, R. 2004. Physics of RecA-mediated homologous recognition. *Biophysical J* 87:1466.

Klein, H.L. 2001. Mutations in recombinational repair and in checkpoint control genes suppress the lethal combination of srs2Delta with other DNA repair genes in Saccharomyces cerevisiae. *Genetics* 157:557.

Kolodner, R., Fishel, R.A., and Howard, M. 1985. Genetic recombination of bacterial plasmid DNA: effect of RecF pathway mutations on plasmid recombination in Escherichia coli. *J Bacteriol* 163:1060.

Kolodner, R.D., Putnam, C.D., and Myung, K. 2002. Maintenance of genome stability in *Saccharomyces cerevisiae*. *Science* 297:552.

Koroleva, O., Makharashvili, N., Courcelle, C.T., Courcelle, J., and Korolev, S. 2007. Structural conservation of RecF and Rad50: implications for DNA recognition and RecF function. *EMBO J*. in press.

Kowalczykowski, S.C. 2000. Initiation of genetic recombination and recombination-dependent replication. *Trends Biochem Scie* 25:156.

Kowalczykowski, S.C., Clow, J., Somani, R., and Varghese, A. 1987. Effects of the Escherichia coli SSB protein on the binding of Escherichia coli RecA protein to single-stranded DNA. Demonstration of competitive binding and the lack of a specific protein-protein interaction. *J Mol Biol* 193:81.

Kowalczykowski, S.C., Dixon, D.A., Eggleston, A.K., Lauder, S.D., and Rehrauer, W.M. 1994. Biochemistry of homologous recombination in Escherichia coli. . *Microbiol Rev* 58:401.

Kowalczykowski, S.C., and Krupp, R.A. 1987. Effects of Escherichia coli SSB protein on the single-stranded DNA-dependent ATPase activity of Escherichia coli RecA protein. Evidence that SSB protein facilitates the binding of RecA protein to regions of secondary structure within single-stranded DNA. *J Mol Biol* 193:97.

Krejci, L., Van Komen, S., Li, Y., Villemain, J., Reddy, M.S., Klein, H., Ellenberger, T., and Sung, P. 2003. DNA helicase Srs2 disrupts the Rad51 presynaptic filament. *Nature* 423:305.

Krishna, R., Manjunath, G.P., Kumar, P., Surolia, A., Chandra, N.R., Muniyappa, K., and Vijayan, M. 2006. Crystallographic identification of an ordered C-terminal domain and a second nucleotide-binding site in RecA: new insights into allostery. *Nucleic Acids Research* 34: 2186.

Kumura, K., Sekiguchi, M., Steinum, A.L., and Seeberg, E. 1985. Stimulation of the UvrABC enzyme-catalyzed repair reactions by the UvrD protein (DNA helicase II). *Nucleic Acids Research* 13:1483.

Kuzminov, A. 1999. Recombinational repair of DNA damage in Escherichia coli and bacteriophage lambda. *Microbiol Mol Biol Rev* 63:751.

Lahue, R.S., Au, K.G., and Modrich, P. 1989. DNA mismatch correction in a defined system. *Science* 245:160.

Lane, H.E., and Denhardt, D.T. 1975. The rep mutation. IV. Slower movement of replication forks in Escherichia coli rep strains. *J Mol Biol* 97:99.

Lavery, P.E., and Kowalczykowski, S.C. 1988. Biochemical basis of the temperature-inducible constitutive protease activity of the RecA441 protein of *Escherichia coli*. *J Mol Biol* 203:861.

Lavery, P.E., and Kowalczykowski, S.C. 1990. Properties of recA441 protein-catalyzed DNA strand exchange can be attributed to an enhanced ability to compete with SSB protein. *J Biol Chem* 265:4004.

Lavery, P.E., and Kowalczykowski, S.C. 1992. A postsynaptic role for single-stranded DNA-binding protein in recA protein-promoted DNA strand exchange. *J Biol Chem* 267:9315.

Lee, B.I., Kim, K.H., Park, S.J., Eom, S.H., Song, H.K., and Suh, S.W. 2004. Ring-shaped architecture of RecR: implications for its role in homologous recombinational DNA repair. *EMBO J* 23:2029.

Lee, S.K., Johnson, R.E., Yu, S.L., Prakash, L., and Prakash, S. 1999. Requirement of yeast SGS1 and SRS2 genes for replication and transcription. *Science* 286:2339.

Leiros, I., Timmins, J., Hall, D.R., and McSweeney, S. 2005. Crystal structure and DNA-binding analysis of RecO from Deinococcus radiodurans. *Embo J* 24:906.

Lewis, L.K., Harlow, G.R., Greggjolly, L.A., and Mount, D.W. 1994. Identification of high affinity binding sites for lexa which define new DNA damage-inducible genes in Escherichia coli. *J Mol Biol* 241:507.

Little, J.W. 1991. Mechanism of specific LexA cleavage - autodigestion and the role of RecA coprotease. *Biochimie* 73:411.

Lloyd, R.G. 1983. lexA dependent recombination in uvrD strains of Escherichia coli. *Mol General Genet* 189:157.

Lohman, T.M., and Ferrari, M.E. 1994. Escherichia coli single-stranded DNA-binding protein: multiple DNA-binding modes and cooperativities. . *Annu Rev Biochem* 63:527.

Lovett, S.T., Hurley, R.L., Sutera, V.A., Aubuchon, R.H., and Lebedeva, M.A. 2002. Crossing over between regions of limited homology in Escherichia coli: RecA-dependent and RecA-independent pathways. *Genetics* 160:851.

Lovett, S.T., and Sutera, V.A. 1995. Suppression of recJ exonuclease mutants of Escherichia coli by alterations in DNA helicases II (UvrD) and IV (HelD). *Genetics* 140:27.

Luisi-DeLuca, C. 1995. Homologous pairing of single-stranded DNA and superhelical double-stranded DNA catalyzed by RecO protein from *Escherichia coli*. *J. Bacteriol.* 177:566.

Luisi-DeLuca, C., and Kolodner, R. 1994. Purification and characterization of the Escherichia coli RecO protein. Renaturation of complementary single-stranded DNA molecules catalyzed by the RecO protein. *J Mol Biol* 236:124.

Lusetti, S.L., and Cox, M.M. 2002. The bacterial RecA protein and the recombinational DNA repair of stalled replication forks. *Annu Rev Biochem* 71:71.

Lusetti, S.L., Hobbs, M.D., Stohl, E.A., Chitteni-Pattu, S., Inman, R.B., Seifert, H.S., and Cox, M.M. 2006. The RecF protein antagonizes RecX function via direct interaction. *Mol Cell* 21:41.

Lusetti, S.L., Shaw, J.J., and Cox, M.M. 2003a. Magnesium ion-dependent activation of the RecA protein involves the C terminus. *J Biol Chem* 278:16381.

Lusetti, S.L., Voloshin, O.N., Inman, R.B., Camerini-Otero, R.D., and Cox, M.M. 2004. The DinI protein stabilizes RecA protein filaments. *J Biol Chem* 279:30037.

Lusetti, S.L., Wood, E.A., Fleming, C.D., Modica, M.J., Korth, J., Abbott, L., Dwyer, D.W., Roca, A.I., Inman, R.B., and Cox, M.M. 2003b. C-terminal deletions of the Escherichia coli RecA protein - Characterization of in vivo and in vitro effects. *J Biol Chem* 278:16372.

Ma, Y., Wang, T., Villemain, J.L., Giedroc, D.P., and Morrical, S.W. 2004. Dual functions of single-stranded DNA-binding protein in helicase loading at the bacteriophage T4 DNA replication fork. *J Biol Chem* 279:19035.

Madiraju, M.V., and Clark, A.J. 1992. Evidence for ATP binding and double-stranded DNA binding by Escherichia coli RecF protein. *J Bacteriol* 174:7705.

Madiraju, M.V., Lavery, P.E., Kowalczykowski, S.C., and Clark, A.J. 1992. Enzymatic properties of the RecA803 protein, a partial suppressor of recF mutations. *Biochemistry* 31:10529.

Madiraju, M.V., Templin, A., and Clark, A.J. 1988. Properties of a mutant *recA*-encoded protein reveal a possible role for *Escherichia coli recF*-encoded protein in genetic recombination. *Proc Natl Acad Sci USA* 85:6592.

Madiraju, M.V.V.S., and Clark, A.J. 1991. Effect of RecF protein on reactions catalyzed by RecA protein. *Nucleic Acids Research* 19:6295.

Mahdi, A.A., and Lloyd, R.G. 1989. Identification of the recR locus of Escherichia coli K-12 and analysis of its role in recombination and DNA repair. *Mol General Genet* 216:503.

Mahdi, A.A., and Lloyd, R.G. 1989. The recR locus of Escherichia coli K-12: molecular cloning, DNA sequencing and identification of the gene product. *Nucleic Acids Research* 17:6781.

Makharashvili, N., Koroleva, O., Bera, S., Grandgenett, D.P., and Korolev, S. 2004. A novel structure of DNA repair protein RecO from Deinococcus radiodurans. *Structure* 12:1881.

Maluf, N.K., Fischer, C.J., and Lohman, T.M. 2003. A dimer of Escherichia coli UvrD is the active form of the helicase in vitro. *J Mol Biol* 325:913.

Mankouri, H.W., Craig, T.J., and Morgan, A. 2002. SGS1 is a multicopy suppressor of srs2: functional overlap between DNA helicases. *Nucleic Acids Research* 30:1103.

Matson, S.W. 1986. Escherichia coli helicase II (urvD gene product) translocates unidirectionally in a 3′ to 5′ direction. *J Biol Chem* 261:10169.

Matson, S.W. 1989. Escherichia coli DNA helicase II (uvrD gene product) catalyzes the unwinding of DNA.RNA hybrids in vitro. *Proc Natal Acad Sci USA* 86:4430.

McKenzie, G.J., Harris, R.S., Lee, P.L., and Rosenberg, S.M. 2000. The SOS response regulates adaptive mutation. *Proc Natal Acad Sci USA* 97:6646.

McKenzie, G.J., Lee, P.L., Lombardo, M.J., Hastings, P.J., and Rosenberg, S.M. 2001. SOS mutator DNA polymerase IV functions in adaptive mutation and not adaptive amplification. *Molecular Cell* 7:571.

Mechanic, L.E., Hall, M.C., and Matson, S.W. 1999. Escherichia coli DNA helicase II is active as a monomer. *J Biol Chem* 274:12488.

Mendonca, V.M., Kaiser-Rogers, K., and Matson, S.W. 1993. Double helicase II (uvrD)-helicase IV (helD) deletion mutants are defective in the recombination pathways of Escherichia coli. *J Bacteriol* 175: 4641.

Mendonca, V.M., Klepin, H.D., and Matson, S.W. 1995. DNA helicases in recombination and repair: construction of a delta uvrD delta helD delta recQ mutant deficient in recombination and repair. *J Bacteriol* 177:1326.

Meyer, R.R., and Laine, P.S. 1990. The single-stranded DNA-binding protein of *Escherichia coli*. *Microbiol Rev*. 54:342.
Milne, G.T., Ho, T., and Weaver, D.T. 1995. Modulation of Saccharomyces cerevisiae DNA double-strand break repair by SRS2 and RAD51. *Genetics* 139:1189.
Modrich, P. 1989. Methyl-directed DNA mismatch correction. *J Biol Chem* 264:6597.
Molineux, I.J., and Gefter, M.L. 1975. Properties of the Escherichia coli DNA-binding (unwinding) protein interaction with nucleolytic enzymes and DNA. *J Mol Biol* 98:811.
Moore, T., McGlynn, P., Ngo, H.P., Sharples, G.J., and Lloyd, R.G. 2003. The RdgC protein of Escherichia coli binds DNA and counters a toxic effect of RecFOR in strains lacking the replication restart protein PriA. *EMBO J* 22:735.
Moran, N.A., and Baumann, P. 2000. Bacterial endosymbionts in animals. *Curr Opin Microbiol* 3:270.
Moreau, P.L. 1988. Overproduction of single-stranded-DNA-binding protein specifically inhibits recombination of UV-irradiated bacteriophage DNA in *Escherichia coli*. *J Bacteriol* 170:2493.
Morel, P., Hejna, J.A., Ehrlich, S.D., and Cassuto, E. 1993. Antipairing and strand transferase activities of E. coli helicase II (UvrD). *Nucleic Acids Research* 21:3205.
Morimatsu, K., and Kowalczykowski, S.C. 2003. RecFOR proteins load RecA protein onto gapped DNA to accelerate DNA strand exchange: A universal step of recombinational repair. *Molecular Cell* 11:1337.
Morrison, P.T., Lovett, S.T., Gilson, L.E., and Kolodner, R. 1989. Molecular analysis of the Escherichia coli recO gene. *J Bacteriol* 171:3641.
Mortenson, U.H., Bendixen, C., Sunjevaric, I., and Rothstein, R. 1996. DNA strand annealing is promoted by the yeast Rad52 protein. *Proc Natl Acad Sci USA* 93:10729.
Myung, K., Datta, A., Chen, C., and Kolodner, R.D. 2001. SGS1, the Saccharomyces cerevisiae homologue of BLM and WRN, suppresses genome instability and homeologous recombination. *Nature Genet* 27:113.
Myung, K., and Kolodner, R.D. 2002. Suppression of genome instability by redundant S-phase checkpoint pathways in Saccharomyces cerevisiae. *Proc Natal Acad Sci USA* 99:4500.
New, J.H., Sugiyama, T., Zaitseva, E., and Kowalczykowski, S.C. 1998. Rad52 protein stimulates DNA strand exchange by Rad51 and replication protein A *Nature* 391:337.
Nishinaka, T., Ito, Y., Yokoyama, S., and Shibata, T. 1997. An extended DNA structure through deoxyribose-base stacking induced by RecA protein. *Proc Natl Acad Sci USA* 94:6623.
Nohmi, T., Battista, J.R., Dodson, L.A., and Walker, G.C. 1988. RecA-mediated cleavage activates UmuD for mutagenesis: mechanistic relationship between transcriptional derepression and posttranslational activation. *Proc Natal Acad Sci USA* 85:1816.
Ogawa, T., Yu, X., Shinohara, A., and Egelman, E.H. 1993. Similarity of the yeast RAD51 filament to the bacterial RecA filament. *Science* 259:1896.
Osborn, A.J., Elledge, S.J., and Zou, L. 2002. Checking on the fork: the DNA-replication stress-response pathway. *Trends Cell Biol*. 12:509.
Ossanna, N., and Mount, D.W. 1989. Mutations in uvrD induce the SOS response in Escherichia coli. *J Bacteriol* 171:303.
Pages, V., Koffel-Schwartz, N., and Fuchs, R.P. 2003. recX, a new SOS gene that is co-transcribed with the recA gene in Escherichia coli. *DNA Repair* 2:273.
Papavinasasundaram, K.G., Colston, M.J., and Davis, E.O. 1998. Construction and complementation of a recA deletion mutant of Mycobacterium smegmatis reveals that the intein in Mycobacterium tuberculosis recA does not affect RecA function. *Mol Microbiol* 30:525.
Papavinasasundaram, K.G., Movahedzadeh, F., Keer, J.T., Stoker, N.G., Colston, M.J., and Davis, E.O. 1997. Mycobacterial recA is cotranscribed with a potential regulatory gene called recX. *Mol Microbiol* 24:141.
Petit, M.A., and Ehrlich, D. 2002. Essential bacterial helicases that counteract the toxicity of recombination proteins. *EMBO J* 21:3137.
Petranovic, M., Zahradka, K., Zahradka, D., Petranovic, D., Nagy, B., and Salaj-Smic, E. 2001. Genetic evidence that the elevated levels of Escherichia coli helicase II antagonize recombinational DNA repair. *Biochimie* 83:1041.
Pham, P., Seitz, E.M., Saveliev, S., Shen, X., Woodgate, R., Cox, M.M., and Goodman, M.F. 2002. Two distinct modes of RecA action are required for DNA polymerase V-catalyzed translesion synthesis. *Proc Natal Acad Sci USA* 99:11061.
Qian, X.G., Wu, Y., He, Y.J., and Luo, Y. 2005. Crystal structure of Methanococcus voltae RadA in complex with ADP: Hydrolysis-induced conformational change. *Biochem*. 44:13753.
Rajan, R., and Bell, C.E. 2004. Crystal structure of RecA from Deinococcus radiodurans: Insights into the structural basis of extreme radioresistance. *J Mol Biol* 344:951.
Ramirez, B.E., Voloshin, O.N., Camerini-Otero, R.D., and Bax, A. 2000. Solution structure of DinI provides insight into its mode of RecA inactivation. *Protein Sci* 9:2161.
Rangarajan, S., Woodgate, R., and Goodman, M.F. 2002. Replication restart in UV-irradiated Escherichia coli involving pols II, III, V, PriA, RecA and RecFOR proteins. *Mol Microbiol* 43:617.
Reddy, G., Golub, E.I., and Radding, C.M. 1997. Human Rad52 protein promotes single-strand DNA annealing followed by branch migration. *Mutation Res*. 377:53.
Register, J.C., III and Griffith, J. 1985. The direction of RecA protein assembly onto single strand DNA is the same as the direction of strand assimilation during strand exchange. *J Biol Chem* 260: 12308.
Richard, D.J., Bell, S.D., and White, M.F. 2004. Physical and functional interaction of the archaeal single-stranded DNA-binding protein SSB with RNA polymerase. *Nucleic Acids Research* 32:1065.
Roca, A.I., and Cox, M.M. 1990. The RecA protein: structure and function. *CRC Critical Reviews in Biochem Mol Biol* 25:415.
Roca, A.I., and Cox, M.M. 1997. RecA protein: structure, function, and role in recombinational DNA repair. . *Prog Nucleic Acid Res Mol Biol*. 56:129.
Rocha, E.P.C., Cornet, E., and Michel, B. 2005. Comparative and evolutionary analysis of the bacterial homologous recombination systems. *PLoS Genetics* 1:e15.
Rosselli, W., and Stasiak, A. 1991. The ATPase activity of RecA is needed to push the DNA strand exchange through heterologous regions. *EMBO J* 10:4391.
Runyon, G.T., Bear, D.G., and Lohman, T.M. 1990. Escherichia coli helicase II (UvrD) protein initiates DNA unwinding at nicks and blunt ends. *Proc Natal Acad Sci USA* 87:6383.
Ryder, L., Sharples, G.J., and Lloyd, R.G. 1996. Recombination-dependent growth in exonuclease-depleted recBC sbcBC strains of Escherichia coli K-12. *Genetics* 143:1101.
Sancar, A., and Hearst, J.E. 1993. Molecular matchmakers. *Science* 259:1415.
Sandler, S.J. 1994. Studies on the mechanism of reduction of UV-inducible sulAp expression by recF overexpression in Escherichia coli K-12. *Mol Gen Genet* 245:741.
Sandler, S.J. 1996. Overlapping functions for *recF* and *priA* in cell viability and UV-inducible SOS expression are distinguished by *dnaC809* in *Escherichia coli* K-12. *Mol Microbiol* 19:871.
Sandler, S.J. 2001. RecFOR protein. *Encyclopedia of Life Sciences*. Nature Publishing Group:online.
Sandler, S.J., and Clark, A.J. 1993. Use of high and low level overexpression plasmids to test mutant alleles of the recF gene of Escherichia coli K-12 for partial activity. *Genetics* 135:643.
Sandler, S.J., and Clark, A.J. 1994. RecOR suppression of recF mutant phenotypes in Escherichia coli K-12. *J Bacteriol*176:3661.
Sandler, S.J., and Marians, K.J. 2000. Role of PriA in replication fork reactivation in Escherichia coli. *J Bacteriol* 182:9.
Sandler, S.J., Marians, K.J., Zavitz, K.H., Coutu, J., Parent, M.A., and Clark, A.J. 1999. dnaC mutations suppress defects in DNA replication- and recombination-associated functions in priB and priC double mutants in Escherichia coli K-12. *Mol Microbiol* 34:91.

Sandler, S.J., Samra, H.S., and Clark, A.J. 1996. Differential suppression of priA2::kan phenotypes in Escherichia coli K-12 by mutations in priA, lexA, and dnaC. *Genetics* 143:5.

Sandler, S.J., Satin, L.H., Samra, H.S., and Clark, A.J. 1996. recA-like genes from three archaean species with putative protein products similar to Rad51 and Dmc1 proteins of the yeast Saccharomyces cerevisiae. *Nucleic Acids Research* 24:2125.

Sano, Y. 1993. Role of the recA-related gene adjacent to the recA gene in Pseudomonas aeruginosa. *J Bacteriol* 175:2451.

Sarno, R., McGillivary, G., Sherratt, D.J., Actis, L.A., and Tolmasky, M.E. 2002. Complete nucleotide sequence of Klebsiella pneumoniae multiresistance plasmid pJHCMW1. *Antimicrob Agents Chemother* 46:3422.

Savvides, S.N., Raghunathan, S., Futterer, K., Kozlov, A.G., Lohman, T.M., and Waksman, G. 2004. The C-terminal domain of full-length E. coli SSB is disordered even when bound to DNA. *Protein Science* 13:1942.

Sawitzke, J.A., and Stahl, F.W. 1992. Phage lambda has an analog of Escherichia coli recO, recR and recF genes. *Genetics* 130:7.

Sawitzke, J.A., and Stahl, F.W. 1994. The phage lambda orf gene encodes a trans-acting factor that suppresses Escherichia coli recO, recR, and recF mutations for recombination of lambda but not of E. coli. *J Bacteriol* 176:6730.

Schild, D. 1995. Suppression of a new allele of the yeast RAD52 gene by overexpression of RAD51, mutations in srs2 and ccr4, or mating-type heterozygosity. *Genetics* 140:115.

Schlacher, K., Cox, M.M., Woodgate, R., and Goodman, M.F. 2006. RecA acts in trans to allow replication of damaged DNA by DNA polymerase V. *Nature* 442:883.

Schlacher, K., Leslie, K., Wyman, C., Woodgate, R., Cox, M.M., and Goodman, M.F. 2005. DNA polymerase V and RecA protein, a minimal mutasome. *Mol Cell* 17:561.

Schlacher, K., Pham, P., Cox, M.M., and Goodman, M.F. 2006. Roles of DNA polymerase V and RecA protein in SOS damage-induced mutation. *Chem Rev* 106:406.

Seitz, E.M., Brockman, J.P., Sandler, S.J., Clark, A.J., and Kowalczykowski, S.C. 1998. RadA protein is an archaeal RecA protein homolog that catalyzes DNA strand exchange. *Gene Develop* 12:1248.

Seitz, E.M., Haseltine, C.A., and Kowalczykowski, S.C. 2001. DNA recombination and repair in the Archaea. *Archaea: Ancient Microbes, Extreme Environoments, And The Origin Of Life* 50:101.

Shan, Q., Bork, J.M., Webb, B.L., Inman, R.B., and Cox, M.M. 1997. RecA protein filaments: end-dependent dissociation from ssDNA and stabilization by RecO and RecR proteins. *J Mol Biol* 265: 519.

Shan, Q., Cox, M.M., and Inman, R.B. 1996. DNA strand exchange promoted by RecA K72R. Two reaction phases with different Mg2+ requirements. *J Biol Chem* 271:5712.

Shibata, T., Hishida, T., Kubota, Y., Han, Y.W., Iwasaki, H., and Shinagawa, H. 2005. Functional overlap between RecA and MgsA (RarA) in the rescue of stalled replication forks in Escherichia coli. *Genes Cells* 10:181.

Shinohara, A., Ogawa, H., and Ogawa, T. 1992. Rad51 protein involved in repair and recombination in S. cerevisiae is a RecA-like protein. *Cell* 69:457.

Shivashankar, G.V., Feingold, M., Krichevsky, O., and Libchaber, A. 1999. RecA polymerization on double-stranded DNA by using single-molecule manipulation: The role of ATP hydrolysis. *Proc Natal Acad Sci USA* 96:7916.

Sigal, N., Delius, H., Kornberg, T., Gefter, M.L., and Alberts, B. 1972. A DNA-unwinding protein isolated from Escherichia coli: its interaction with DNA and with DNA polymerases. *Proc Natl Acad Sci USA*. 69:3537.

Singleton, M.R., Dillingham, M.S., Gaudier, M., Kowalczykowski, S.C., and Wigley, D.B. 2004. Crystal structure of RecBCD enzyme reveals a machine for processing DNA breaks. *Nature* 432:187.

Smith, G.R. 1989. Homologous recombination in prokaryotes: enzymes and controlling sites. *Genome* 31:520.

Steiner, W.W., and Kuempel, P.L. 1998. Sister chromatid exchange frequencies in Escherichia coli analyzed by recombination at the dif resolvase site. *J Bacteriol* 180:6269.

Stohl, E.A., Brockman, J.P., Burkle, K.L., Morimatsu, K., Kowalczykowski, S.C., and Siefert, H.S. 2003. Escherichia coli RecX inhibits RecA recombinase and coprotease activities in vitro and in vivo. *J Biol Chem* 278:2278.

Stohl, E.A., and Seifert, H.S. 2001. The recX gene potentiates homologous recombination in Neisseria gonorrhoeae. *Mol Microbiol* 40:1301.

Story, R.M., and Steitz, T.A. 1992. Structure of the RecA Protein-ADP complex. *Nature* 355:374.

Story, R.M., Weber, I.T., and Steitz, T.A. 1992. The structure of the *E. coli* RecA protein monomer and polymer. *Nature*. 355:318.

Sugiyama, T., New, J.H., and Kowalczykowski, S.C. 1998. DNA annealing by RAD52 protein is stimulated by specific interaction with the complex of replication protein A and single stranded DNA. *Proc Natal Acad Sci USA* 95:6049.

Sukchawalit, R., Vattanaviboon, P., Utamapongchai, S., Vaughn, G., and Mongkolsuk, S. 2001. Characterization of Xanthomonas oryzae pv. oryzae recX, a gene that is required for high-level expression of recA. *FEMS Microbiol Lett* 205:83.

Sung, P. 1994. Catalysis of ATP-dependent homologous DNA pairing and strand exchange by yeast RAD51 protein. *Science* 265:1241.

Sutton, M.D., Opperman, T., and Walker, G.C. 1999. The Escherichia coli SOS mutagenesis proteins UmuD and UmuD′ interact physically with the replicative DNA polymerase. *Proc Natal Acad Sci USA* 96:12373.

Sutton, M.D., Smith, B.T., Godoy, V.G., and Walker, G.C. 2000. The SOS response: recent insights into umuDC-dependent mutagenesis and DNA damage tolerance. *Annu Rev Genet* 34:479.

Takiff, H.E., Chen, S.M., and Court, D.L. 1989. Genetic analysis of the rnc operon of Escherichia coli. *J Bacteriol* 171:2581.

Tamas, I., Klasson, L., Canback, B., Naslund, A.K., Eriksson, A.S., Wernegreen, J.J., Sandstrom, J.P., Moran, N.A., and Andersson, S.G.E. 2002. 50 million years of genomic stasis in endosymbiotic bacteria. *Science* 296:2376.

Tang, M.J., Shen, X., Frank, E.G., O'Donnell, M., Woodgate, R., and Goodman, M.F. 1999. UmuD $'_2$C is an error-prone DNA polymerase, Escherichia coli pol V. *Proc Natal Acad Sci USA* 96:8919.

Tateishi, S., Horii, T., Ogawa, T., and Ogawa, H. 1992. C-terminal truncated Escherichia coli RecA protein RecA5327 has enhanced binding affinities to single- and double-stranded DNAs. *J Mol Biol* 223:115.

Taylor, A.F., and Smith, G.R. 2003. RecBCD enzyme is a DNA helicase with fast and slow motors of opposite polarity. *Nature* 423:889.

Thompson, L.H., and Schild, D. 1999. The contribution of homologous recombination in preserving genome integrity in mammalian cells. *Biochimie* 81:87.

Thompson, L.H., and Schild, D. 2002. Recombinational DNA repair and human disease. *Mutation Res-Fund Mol Mech Mutagen* 509:49.

Umezu, K., Chi, N.W., and Kolodner, R.D. 1993. Biochemical interaction of the Escherichia coli RecF, RecO, and RecR proteins with RecA protein and single-stranded DNA binding protein. *Proc Natl Acad Sci USA* 90:3875.

Umezu, K., and Kolodner, R.D. 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. *J Biol Chem* 269:30005.

van der Heijden, T., van Noort, J., van Leest, H., Kanaar, R., Wyman, C., Dekker, N., and Dekker, C. 2005. Torque-limited RecA polymerization on dsDNA. *Nucleic Acids Research* 33:2099.

van Gent, D.C., Hoeijmakers, J.H.J., and Kanaar, R. 2001. Chromosomal stability and the DNA double-stranded break connection. *Nature Rev Genet* 2:196.

VanLoock, M.S., Yu, X., Yang, S., Galkin, V.E., Huang, H., Rajan, S.S., Anderson, W.F., Stohl, E.A., Seifert, H.S., and Egelman, E.H. 2003. Complexes of RecA with LexA and RecX differentiate between active and Inactive RecA nucleoprotein filaments. *J Mol Biol* 333: 345.

VanLoock, M.S., Yu, X., Yang, S., Lai, A.L., Low, C., Campbell, M.J., and Egelman, E.H. 2003. ATP-mediated conformational changes in the RecA filament. *Structure* 11:1.

Veaute, X., Delmas, P., Selva, M., Jeusset, J., Le Cam, E., Matic, I., Fabre, F., and Petit, M.A. 2005. UvrD helicase, unlike Rep helicase, dismantles RecA nucleoprotein filaments in Escherichia coli. *EMBO J* 24: 180.

Veaute, X., Jeusset, J., Soustelle, C., Kowalczykowski, S.C., Le Cam, E., and Fabre, F. 2003. The Srs2 helicase prevents recombination by disrupting Rad51 nucleoprotein filaments. *Nature* 423: 309.

Velankar, S.S., Soultanas, P., Dillingham, M.S., Subramanya, H.S., and Wigley, D.B. 1999. Crystal structures of complexes of PcrA DNA helicase with a DNA substrate indicate an inchworm mechanism. *Cell* 97:75.

Venkatesh, R., Ganesh, N., Guhan, N., Reddy, M.S., Chandrasekhar, T., and Muniyappa, K. 2002. RecX protein abrogates ATP hydrolysis and strand exchange promoted by RecA: Insights into negative regulation of homolgous recombination. *Proc Natal Acad Sci USA* 99:12091.

Venkitaraman, A.R. 2001. Chromosome stability, DNA recombination and the BRCA2 tumour suppressor. *Curr Opin Cell Biolo* 13:338.

Vierling, S., Weber, T., Wohlleben, W., and Muth, G. 2000. Transcriptional and mutational analyses of the Streptomyces lividans recX gene and its interference with RecA activity. *J Bacteriol* 182:4005.

Voloshin, O.N., Ramirez, B.E., Bax, A., and Camerini-Otero, R.D. 2001. A model for the abrogation of the SOS response by an SOS protein: a negatively charged helix in DinI mimics DNA in its interaction with RecA. *Gene Develop* 15:415.

Walker, G.C., Smith, B.T., and Sutton, M.D., The SOS response to DNA damage, In: *Bacterial Stress Responses*, Storz, G., and HenggeAronis, R., Eds., Washington, D.C., American Society of Microbiology, 2000, 131.

Wang, T.C., Chang, H.Y., and Hung, J.L. 1993. Cosuppression of recF, recR and recO mutations by mutant recA alleles in Escherichia coli cells. *Mutation Research* 294:157.

Wang, T.V., and Smith, K.C. 1984. recF-dependent and recF recB-independent DNA gap-filling repair processes transfer dimer-containing parental strands to daughter strands in Escherichia coli K-12 uvrB. *J Bacteriol* 158:727.

Washburn, B.K., and Kushner, S.R. 1991. Construction and analysis of deletions in the structural gene (uvrD) for DNA helicase II of Escherichia coli. *J Bacteriol* 173:2569.

Webb, B.L., Cox, M.M., and Inman, R.B. 1995. An interaction between the Escherichia coli RecF and RecR proteins dependent on ATP and double-stranded DNA. *J Biol Chem* 270:31397.

Webb, B.L., Cox, M.M., and Inman, R.B. 1997. Recombinational DNA repair - the RecF and RecR proteins limit the extension of RecA filaments beyond single-strand DNA gaps. *Cell* 91:347.

Webb, B.L., Cox, M.M., and Inman, R.B. 1999. ATP hydrolysis and DNA binding by the *Escherichia coli* RecF protein. *J Biol Chem* 274: 15367.

Weiner, J.H., Bertsch, L.L., and Kornberg, A. 1975. The deoxyribonucleic acid unwinding protein of *Escherichia coli*. Properties and functions in replication. *J Biol Chem* 250:1972.

Whitby, M.C., and Lloyd, R.G. 1995. Altered SOS induction associated with mutations in recF, recO and recR. *Mol General Genet* 246:174.

Witte, G., Urbanke, C., and Curth, U. 2003. DNA polymerase III chi subunit ties single-stranded DNA binding protein to the bacterial replication machinery. *Nucleic Acids Research* 31:4434.

Wong, I., Amaratunga, M., and Lohman, T.M. 1993. Heterodimer formation between Escherichia coli Rep and UvrD proteins. *J Biol Chem* 268:20386.

Wu, Y., He, Y., Moya, I.A., Qian, X.G., and Luo, Y. 2004. Crystal structure of archaeal recombinase RadA: A snapshot of its extended conformation. *Mole Cell* 15:423.

Wu, Y., Qian, X.G., He, Y.J., Moya, I.A., and Luo, Y. 2005. Crystal structure of an ATPase-active form of rad51 homolog from Methanococcus voltae—Insights into potassium dependence. *J Biol Chem* 280:722.

Xing, X., and Bell, C.E. 2004. Crystal structures of Escherichia coli RecA in a compressed helical filament. *J Mol Biol* 342:1471.

Xing, X., and Bell, C.E. 2004. Crystal structures of Escherichia coli RecA in complex with MgADP and MnAMP-PNP. *Biochemistry* 43:16142.

Xu, L.W., and Marians, K.J. 2003. PriA mediates DNA replication pathway choice at recombination intermediates. *Mol Cell* 11:817.

Yancey-Wrona, J.E., and Matson, S.W. 1992. Bound Lac repressor protein differentially inhibits the unwinding reactions catalyzed by DNA helicases. *Nucleic Acids Research* 20:6713.

Yang, M.K., Chou, M.E., and Yang, Y.C. 2001. Molecular characterization and expression of the recX gene of Xanthomonas campestris pv. citri. *Curr Microbiol* 42:257.

Yasuda, T., Morimatsu, K., Horii, T., Nagata, T., and Ohmori, H. 1998. Inhibition of Escherichia coli RecA coprotease activities by DinI. *EMBO J* 17:3207.

Yasuda, T., Morimatsu, K., Kato, R., Usukura, J., Takahashi, M., and Ohmori, H. 2001. Physical interactions between DinI and RecA nucleoprotein filament for the regulation of SOS mutagenesis. *EMBO J* 20:1192.

Yasuda, T., Nagata, T., and Ohmori, H. 1996. Multicopy suppressors of the cold-sensitive phenotype of the pcsA68 (dinD68) mutation in Escherichia coli. *J Bacteriol* 178:3854.

Yoshimasu, M., Aihara, H., Ito, Y., Rajesh, S., Ishibe, S., Mikawa, T., Yokoyama, S., and Shibata, T. 2003. An NMR study on the interaction of Escherichia coli DinI with RecA-ssDNA complexes. *Nucleic Acids Research* 31:1735.

Yu, M., Souaya, J., and Julin, D.A. 1998. The 30-kDa C-terminal domain of the RecB protein is critical for the nuclease activity, but not the helicase activity, of the RecBCD enzyme from Escherichia coli. *Proc Natl Acad Sci USA* 95:981.

Yu, X., and Egelman, E.H. 1997. The RecA hexamer is a structural homologue of ring helicases. *Nature Structural Biology*. 4:101.

Yuzhakov, A., Kelman, Z., and O'Donnell, M. 1999. Trading places on DNA—a three-point switch underlies primer handoff from primase to the replicative DNA polymerase. *Cell* 96:153.