RecA Protein

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The RecA protein of *Escherichia coli* is the prototypic DNA strand exchange protein. It assembles on single-stranded DNA to form a helical nucleoprotein filament that is the active species for all RecA protein-dependent functions. This protein–DNA complex is responsible for three mutually exclusive functions: DNA recombination, induction of the SOS response and SOS mutagenesis.

Introduction

The RecA protein of *Escherichia coli* is a multifunctional protein that is essential to three distinct, but related biological processes: (1) general genetic recombination; (2) regulation of the coordinated expression of many unlinked genes in response to DNA damage, known as the SOS response; and (3) the error-prone replicative bypass of DNA lesions, resulting in a highly mutagenic repair of DNA. Not surprisingly, mutations in *recA* are pleiotropic, affecting not only recombination, but also DNA repair, mutagenesis and cell division (Bianco *et al.*, 1998).

To mediate this broad spectrum of biological events, RecA protein possesses three major biochemical activities: (1) the homologous pairing and exchange of DNA; (2) adenosine triphosphate (ATP)- and DNA-dependent coproteolytic processing of effector proteins; and (3) interaction with mutagenic protein factors to facilitate error-prone DNA synthesis past DNA lesions.

The DNA strand exchange activity is characteristic of a class of proteins that are essential to genetic recombination, a biological process in which two homologous DNA molecules pair and exchange regions of their DNA strands. These proteins facilitate the actual exchange of single strands of DNA between the participating DNA partners. The RecA protein of *E. coli* is the prototypic member of this family of functionally and genetically similar proteins.

The coprotease activity is another unique property of RecA protein. This activity is the highly specific catalysis of the self-cleavage of proteins (LexA repressor, UmuD mutagenesis factor and lambdoid phage repressor proteins), which is dependent on both ATP and single-stranded DNA (ssDNA).

The third activity of RecA protein is its direct participation in the replication-dependent bypass of mutagenic lesions in DNA. This function requires binding of the processed mutagenic complex Umu(D′)$_2$C to the RecA protein filament that has assembled at the site of the DNA lesion, thereby enabling DNA synthesis beyond the lesion.

Each of these processes is discussed in more detail below.

The Structure of RecA Protein

For RecA protein to function in these processes, it must assemble on ssDNA to form a nucleoprotein filament known as the presynaptic complex (Story *et al.*, 1992). This filament is an adaptable structure, capable of performing three separate functions (**Figure 1**): homologous recombination (interaction with double-stranded DNA, dsDNA), SOS induction (cleavage of the LexA repressor) and SOS mutagenesis (interaction with the processed Umu(D′)$_2$C complex) (**Table 1**).

The active nucleoprotein filament is a helical complex of RecA protein monomers wrapped around ssDNA at a stoichiometry of 3 nucleotides per monomer and 6.2 monomers per turn (**Figure 2a–d**). Under certain conditions, RecA protein will also form filaments on dsDNA. Filament assembly is highly cooperative and occurs in the 5′→3′ direction relative to the ssDNA to which it is bound. The resulting filament has a regular, right-handed, helical structure, and the prominent feature is a large helical groove (**Figure 2a**). One side of the groove is smooth, while the other is penetrated by the protrusion of the individual monomers (**Figure 2b**). This groove is the binding site for the LexA repressor and is proposed to be involved in the binding of dsDNA. The binding of the LexA repressor and dsDNA to the nucleoprotein filament is competitive, indicating that they bind at the same, or overlapping site, on the filament.

The nucleoprotein filament can exist in two forms: active and inactive. The inactive filament is formed in the absence of a nucleoside triphosphate (NTP) cofactor and exists in a collapsed conformation with a helical pitch of 6.5 nm. The binding of an NTP cofactor (typically ATP), converts RecA protein to a high-affinity ssDNA-binding state, which is the active conformation of RecA protein that is required for all the activities of the protein. This active form of the filament has an extended conformation with a helical pitch of 9.5 nm. It is this extended conformation that is the active species in RecA protein-promoted reactions.
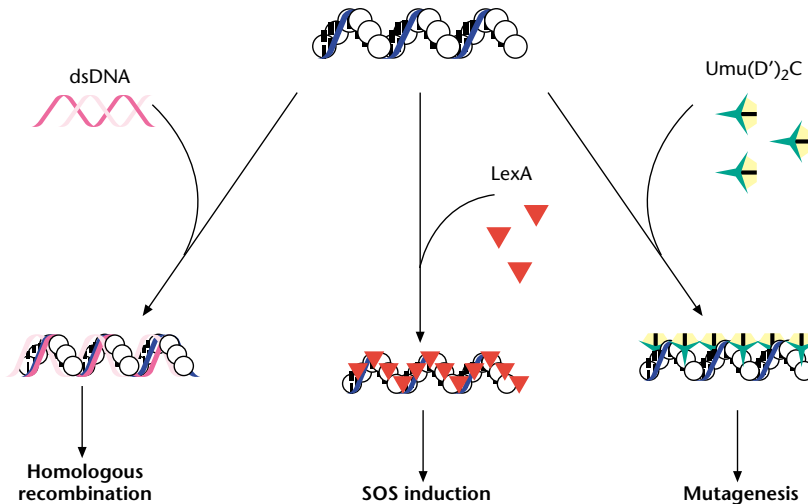
Figure 1 Roles of the RecA nucleoprotein filament in DNA metabolism. A schematic showing the three mutually exclusive functions of the RecA protein filament. Adapted from Rehrauer WM, Bruck I, Woodgate R, Goodman MF and Kowalczykowski SC (1998).

**Table 1** Requirements for RecA protein-dependent processes

Requirement	Homologous recombination	SOS induction	Mutagenesis
[RecA protein]	Basal level	Initially, basal level Later, induced levels	Only induced levels of RecA protein
Stoichiometry in the first site	1:3 (RecA:nt)	1:3 (RecA:nt)	1:3 (RecA:nt)
Stoichiometry in the second site	3:1 (bp:RecA monomer)	1:2 (LexA monomer:RecA monomers)	1:2 (Umu (D′)$_2$C complex:- RecA monomers)
Cofactor requirement	NTP binding and hydrolysis	Only NTP binding	Only NTP binding
Competition (at the second site)	dsDNA binding excludes LexA or Umu (D′)$_2$C binding	LexA binding prevents dsDNA or Umu (D′)$_2$C binding	Umu (D′)$_2$C binding excludes dsDNS or LexA binding

Within the active form of the nucleoprotein filament, the conformation of both ss- and dsDNA differs significantly from that of B-form DNA. The bound DNA is extensively stretched (to approximately 150% the length of B-form) and, in the case of dsDNA, the helix is also unwound. Electron micrographic analysis and neutron scattering reveal that the DNA is located near the axis of the nucleoprotein filament.

DNA strand exchange proteins isolated from a wide variety of organisms including bacteriophage, budding yeast and humans (Ogawa *et al.*, 1993) are very similar (**Figure 3**) and assemble into nearly identical nucleoprotein filament structures, highlighting the importance of the nucleoprotein filament in RecA protein function. Thus, the assembly of RecA protein onto ssDNA promotes formation of the nucleoprotein filament that is the central structure in RecA protein function. This unique structure (the filament) has the capacity to bind dsDNA and catalyse the exchange of single strands of duplex DNA; to bind and cleave repressors and proteins important to mutagenesis; and also, to bind and target the Umu(D′)$_2$C complex to DNA lesions, thereby facilitating SOS mutagenesis.

Figure 2 The nucleoprotein filament formed by RecA protein. (a) A filament formed on dsDNA with ATPγS as cofactor. (From Stasiak A and Egelman EH, 1988.) The striations in the filament indicate the groove discussed in the text. Bar = 0.1 nm. (b) Close-up of the filament (the DNA is not visible) shown in (a). The asterisks indicate the lobes of monomers that protrude into the groove and the white arrow indicates the smooth surface of the groove. (c, d) Cross-sections of the filament showing a single turn. (b) and (c) are three-dimensional re-constructions of electron micrographs of RecA filaments formed on dsDNA with ATPγS. (d) Single turn of the RecA filament as seen in the crystal structure (Story *et al.*, 1992). The individual monomers are coloured alternately in orange and yellow. The numbers in (c) and (d) indicate the six monomers making up the turn in the cross-section; the DNA would be located in the central hole, but is not shown.
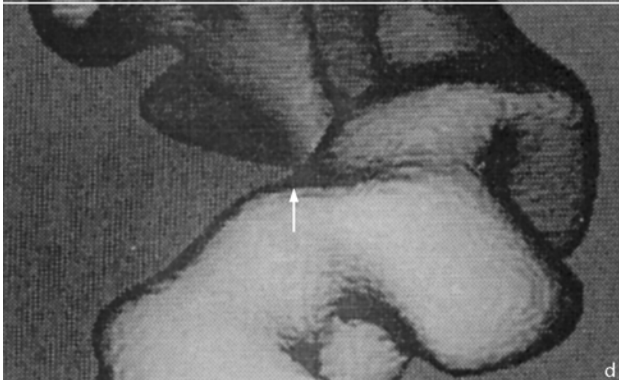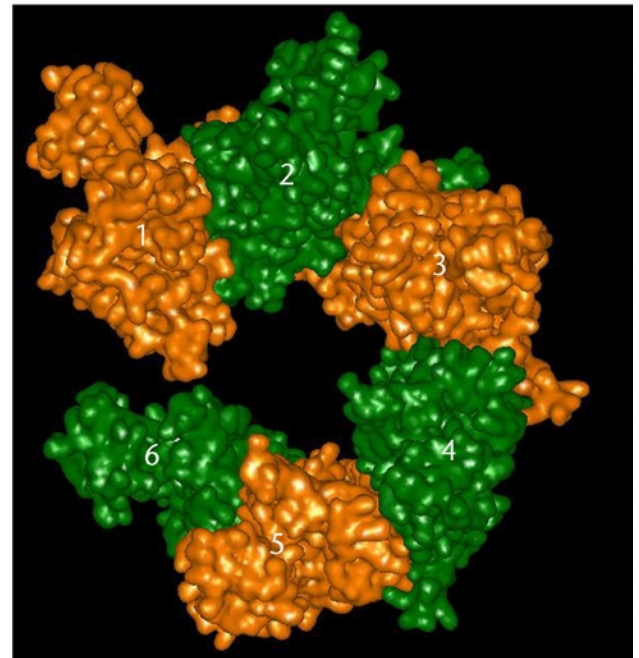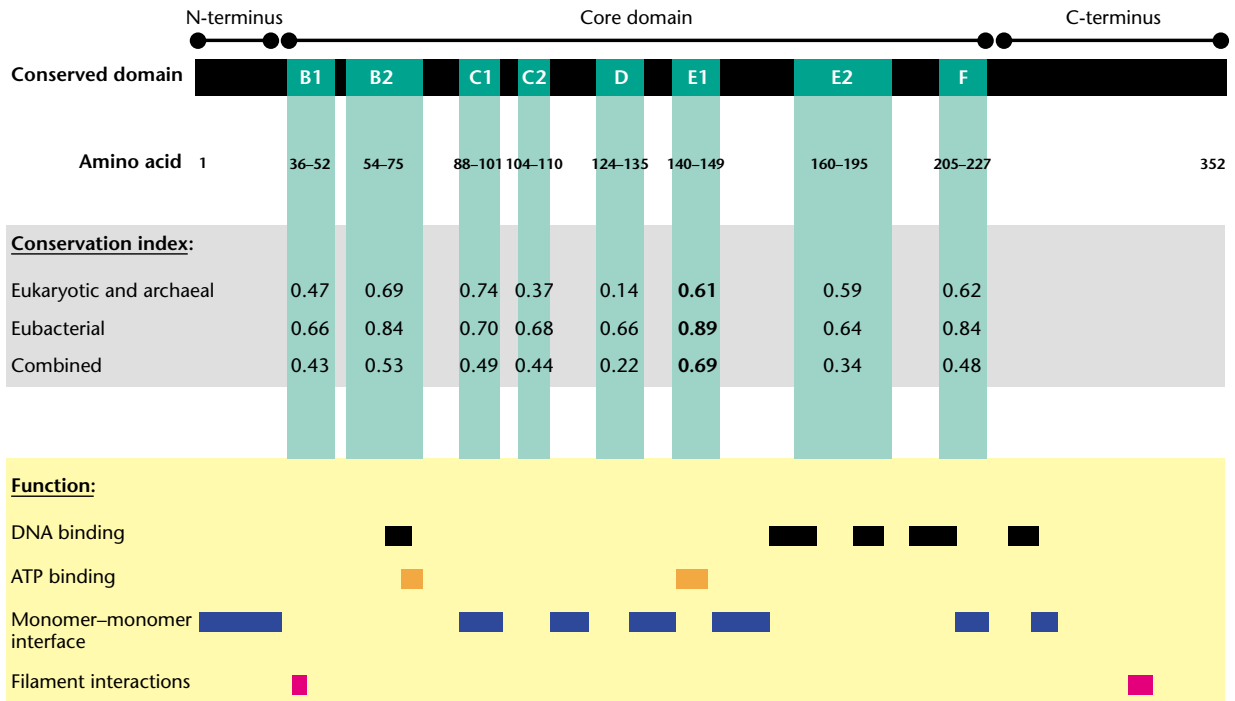
(a)

(b)

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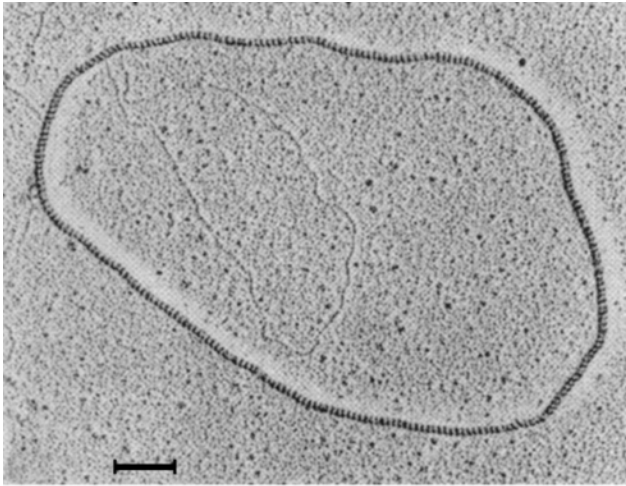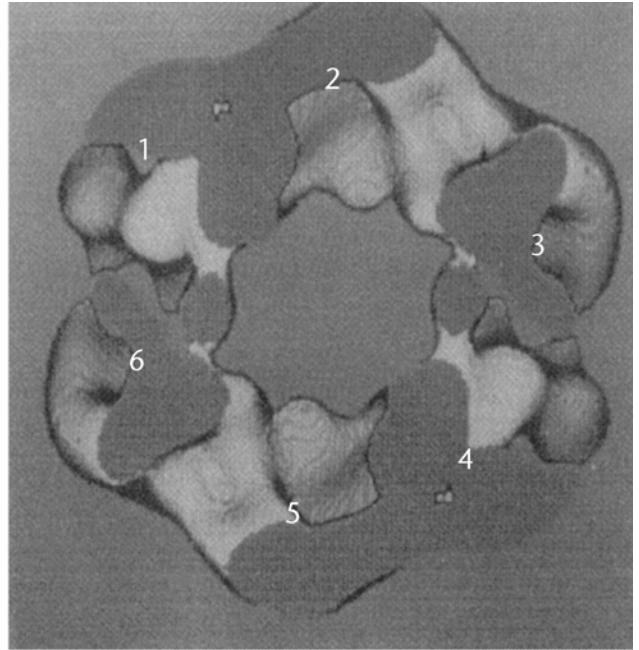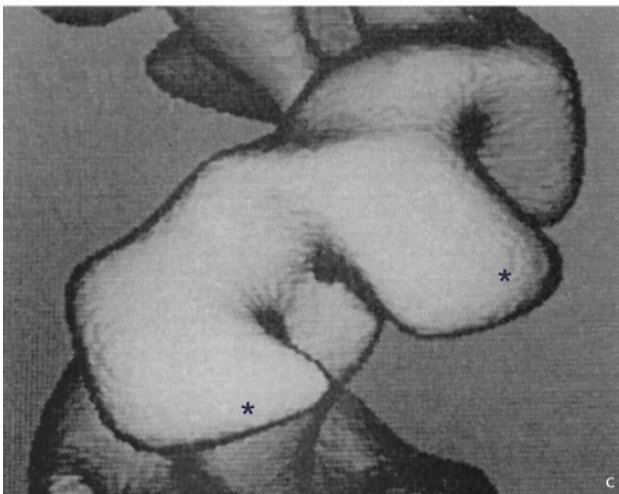
Figure 3 Functional map of the RecA protein. RecA protein is presented as a linear amino acid sequence. There are eight highly conserved subdomains found in all RecA protein homologues. These are highlighted in green, and the amino acids corresponding to each domain are shown at the top of each domain. The conservation index (CI) for each subdomain is shown in the grey box. A CI = 1.00 indicates that this region is invariant in all RecA protein homologues. The combined index is a combined analysis of all RecA protein homologues and the number shown is not an average CI of the eubacterial, eukaryotic and archaeal conservation indices. The functional domains of RecA protein are highlighted in the peach box. The regions involved in DNA binding (black), ATP binding (orange), the monomer–monomer (M-M) interface (blue) and filament–filament interactions (cerise) are displayed.

The Role of RecA Protein in DNA Strand Exchange

RecA protein promotes the exchange of single strands of DNA between two homologous DNA molecules (Shibata *et al*., 1979). The functional form of RecA protein in this reaction is the extended, presynaptic filament assembled on ssDNA. The nucleoprotein filament possesses two DNA-binding sites: the primary site, which is required for assembly and is in contact with the ssDNA, and the secondary site, which is constituted only upon filament formation and is located outside of the central axis of the filament. The secondary site is responsible for binding both the incoming dsDNA and, following DNA strand exchange, the displaced ssDNA product of this reaction.

DNA strand exchange catalysed by RecA protein is the paradigm for homologous pairing processes *in vitro* (**Figure 4**). The most widely studied substrates are circular ssDNA (isolated from φX174 or M13 phage) and linear dsDNA (usually the linearized, replicative forms of these phages). Many pairs of substrates can be used, provided that one of them is at least partially single stranded. The

products of the complete exchange of DNA stands are nicked, circular dsDNA and linear ssDNA.

DNA strand exchange can be divided into three experimentally distinguishable steps: (1) presynapsis, (2) synapsis, and (3) DNA heteroduplex extension (**Figure 4**; Cox and Lehman, 1981). In presynapsis, RecA protein assembles onto ssDNA to form the nucleoprotein species that is active in the homology search. Synapsis is a complex step, conceptually composed of random nonhomologous contacts occurring between the presynaptic complex and naked dsDNA; the search for DNA sequence homology; and base-pair switching, all resulting in the formation of a plectonemic, joint molecule intermediate. DNA heteroduplex extension then completes the reaction by migrating the nascent DNA heteroduplex joint in a polar fashion.

Presynapsis

In this stage of the reaction, RecA protein assembles in an ordered fashion onto ssDNA to produce the active nucleoprotein complex. Due to limitations imposed by DNA secondary structure, RecA protein is unable to form a contiguous nucleoprotein filament. The single-stranded
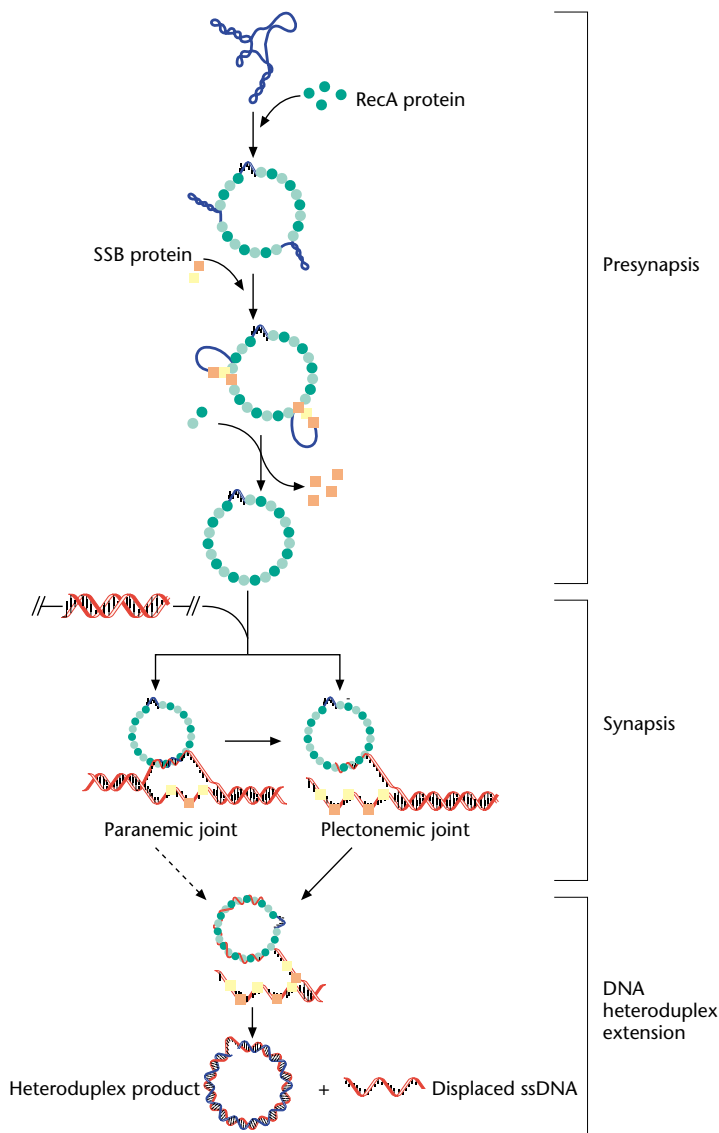
Figure 4 The DNA strand exchange reaction promoted by the RecA protein. RecA protein is represented as round dots and ssDNA-binding (SSB) protein as squares. The three stages shown are: presynapsis, synapsis and DNA heteroduplex extension. Adapted from Bianco PR, Tracy RB and Kowalczykowski SC (1998) DNA strand exchange proteins: A biochemical and physical comparison. *Frontiers in Bioscience* **3**: D570–D603.

DNA-binding protein (SSB protein) of *E. coli* is an accessory factor whose role is to remove the secondary structure; the SSB protein is then displaced by further binding of the RecA protein. This results in the formation of a complete nucleoprotein filament and the concomitant reconstitution of the second DNA-binding site. The second DNA-binding site exists only in the complete nucleoprotein filament, is vacant, and is used to bind a second DNA molecule (either ss- or dsDNA) (Howard-Flanders *et al.*, 1984).

Synapsis

During this stage of the reaction, dsDNA binds to the filament and, upon homologous recognition, a plectonemic joint molecule intermediate is formed (defined below). The second DNA molecule binds to the secondary DNA-binding site of the nucleoprotein filament in a sequence-independent fashion. Once bound, a search for homology takes place. The search is rapid, occurring within minutes, and requires that the binding of dsDNA to the secondary site be both weak and transient. The problem of the homology search is analogous to the problem that

sequence-specific DNA-binding proteins face in locating their target sequence. However, for RecA protein, the scale of the search problem is much larger: the binding protein is the entire nucleoprotein filament (which can consist of thousands of protein monomers, depending on the ssDNA length). Since the binding of RecA protein to ssDNA is largely nonspecific, specificity in the search process is conferred by the sequence of the ssDNA within the filament. Although the entire nucleoprotein filament is involved in the search for homology, the minimum length of homology required for recognition is as low as 15 nucleotides *in vitro*, which is somewhat less than that needed *in vivo*, where homologous recombination requires, minimally, about 23–40 base pairs of homology.

The recognition of homology takes place when the ssDNA within the presynaptic filament hydrogen bonds, presumably via non-Watson–Crick base pairing, to the bound dsDNA, in a mechanism that does not require stable triplex DNA formation (Howard-Flanders *et al.*, 1984). How then does RecA protein 'sense' when homology has been located? During the homology search process, the dsDNA is topologically unwound, and is 'tested' for complementarity with the ssDNA within the filament. It is the recognition of homology between these two DNAs that provides the signal to RecA protein that homology has been located and base switching occurs. This requires a local denaturation of the dsDNA molecule and the coordinate exchange of the identical single strands of DNA. These steps may be simultaneous or separated in time, but the result is production of an intermediate known as a joint molecule. Immediately after base-pair switching, the heteroduplex dsDNA product occupies the primary site, whereas the displaced ssDNA occupies the secondary site (Mazin and Kowalczykowski; 1998).

Two types of joint molecules may form, depending on the topological constraints of the DNA: either paranemic or plectonemic. A paranemic joint is one in which the individual complementary strands do not intertwine, producing a molecule that is base paired, but not topologically linked. A plectonemic joint is one in which the incoming single strand is intertwined around its complement, as in native dsDNA. In the reaction displayed in **Figure 4**, paranemic joints form at interior sites of duplex DNA, and plectonemic joints form at the ends of the duplex substrate. Since there are far more internal sites than end sites, paranemic joints are more likely to form and are thus likely intermediates on the reaction pathway to the formation of the more stable, plectonemic joint molecules.

DNA heteroduplex extension

Once a plectonemic joint has formed, the branch migration phase of DNA strand exchange commences (Cox and Lehman, 1981). During this phase, the DNA heteroduplex in the nascent joint molecule is extended until complete exchange of DNA strands occurs, resulting in a nicked, double-stranded circle. Though kinetically distinct, branch migration may not be a mechanistically separate step, but rather may represent a continuation of plectonemic joint molecule formation. Branch migration proceeds in a $5'\rightarrow3'$ direction relative to the incoming single strand (the same direction as RecA protein polymerization, Register and Griffith, 1985), at a rate of 2–$10\,\text{bp s}^{-1}$, requires ATP hydrolysis, and induces torsional stress in the dsDNA.

Energetics

RecA protein is a DNA-dependent NTPase with a single active site present in each monomer for the binding and hydrolysis of ATP and other NTPs (Ogawa *et al.*, 1978; Roberts *et al.*, 1978). The enzyme can hydrolyse ATP with either ss- or dsDNA as cofactor. The active species in ATP hydrolysis is the nucleoprotein filament, with ATP being hydrolysed uniformly throughout the filament and with no detectable enhancement at filament ends. Hydrolysis of ATP to adenosine diphosphate (ADP) results in conformational changes in RecA protein that serves to modulate RecA between the 'high-affinity' DNA-binding and 'low-affinity' DNA-binding states, respectively.

Since ATP hydrolysis coincides with the pairing and exchange of DNA strands, it was initially thought that ATP hydrolysis was a requirement for DNA strand exchange. It is now known, however, that neither the hydrolysis of ATP nor the presence of a high-energy phosphate bond is necessary for DNA strand exchange (Menetski *et al.*, 1990). DNA strand exchange requires only that RecA protein assumes the high-affinity ssDNA-binding state brought about by ATP binding. The binding of either the nonhydrolysable analogue of ATP, ATPγS, or the noncovalent complex of ADP–AlF$_4^-$, also induces the high-affinity DNA-binding state of RecA protein and supports DNA strand exchange. Although the hydrolysis of ATP is not required for the exchange of DNA strands, it is needed to dissociate RecA protein from the heteroduplex products of DNA strand exchange once the reaction is complete, to facilitate the bypass of structural barriers such as heterologous sequences, and to maintain the polarity of DNA strand exchange.

In addition to ATP, other NTP cofactors also support DNA strand exchange. The key factor in determining whether an NTP can function as a cofactor is its ability to stabilize the high-affinity ssDNA-binding state of RecA protein. This ability is directly related to the $S_{0.5}$ value for that cofactor (where $S_{0.5}$ is the substrate concentration required for half-maximal ATPase activity). Only those NTP cofactors whose $S_{0.5}$ value is 100–$120\,\mu\text{mol L}^{-1}$ or lower are capable of stabilizing the DNA strand exchange-active conformation of RecA protein. Thus, in addition to ATP, either dATP, purine riboside triphosphate, or

uridine triphosphate (UTP) can function as cofactors for DNA strand exchange *in vitro*. Of these, ATP, dATP and UTP are likely cofactors for RecA protein-promoted processes *in vivo*.

The Regulatory Role of RecA Protein

The SOS regulon is a group of approximately 20 unlinked genes (**Table 2**) whose expression is induced to high levels following exposure to DNA-damaging agents. The enzymes encoded by these induced genes function to excise DNA damage and to facilitate the error-prone, recombinational repair of DNA. RecA protein plays a key role as a regulator of the SOS regulon and inducible DNA repair, where it functions as a coprotease, stimulating the autocatalytic cleavage of a number of proteins (Ogawa *et al.*, 1978; Roberts *et al.*, 1978.

The primary controller of the expression of the genes in the SOS regulon is the LexA repressor, which binds to the SOS box of these SOS-inducible genes and limits their transcription. After a DNA-damaging event such as ultraviolet (UV) irradiation, the coprotease activity of RecA protein becomes 'activated'. Activation occurs due to the generation of ssDNA resulting either from the action of nucleases or from stalled replication forks. The ssDNA is bound by RecA protein in the presence of an NTP cofactor, promoting nucleoprotein filament formation that leads to cleavage of the LexA repressor and induction of SOS genes, including *recA*. Genes with operators that bind LexA protein weakly are the first to be expressed fully (e.g., *recA*). If the damage persists, or if sufficiently high quantities of the damaging agent are used, the concentration of activated RecA protein increases, leading to further cleavage of LexA protein, and to derepression of even those genes whose operators bind LexA tightly (e.g. *sulA*).

Under normal cellular conditions, *recA* expression is repressed and the basal level of RecA protein is maintained at ~ 1000 molecules per cell. Following LexA repressor cleavage, the level of RecA protein in the cell increases by as much as 20-fold. The increase in the level of RecA protein is rapid, occurring at a rate of 10 molecules per second, and reaches a maximum within 1 h of a DNA-damaging event. RecA protein levels return to the basal level within 4–6 h following the initial damage event. This reduction is presumably due to removal of the inducing signal via recombinational repair of the DNA damage eliminating the agent that activated RecA protein. As a result, the intracellular concentration of LexA repressor increases, since RecA protein is no longer able to induce its cleavage. This re-establishes repression of the SOS system and returns the cell to its uninduced state.

Table 2 Genes of the SOS regulon

Gene	Position (min)	Gene product function
lexA	91.6	Represses transcription of ~ 20 genes by binding to operators
recA	60.8	DNA strand exchange; induces SOS; activates UmuD; SOS mutagenesis
recN	59.1	Unknown
recQ	86.2	DNA-dependent ATPase and helicase; can both promote homologous recombination and disrupt illegitimate recombination
sulA (sfiA)	22.0	Inhibits cell division
umuD	26.5	Active in SOS mutagenesis as cleaved UmuD′; forms complex with UmuC
umuC	26.5	Forms a complex with UmuD and Umu(D′)$_2$
uvrA	91.9	Excision-repair nuclease subunit A; part of the UvrABC endonuclease that initiates excision repair
uvrB	17.5	Helicase and ATPase; excision-repair nuclease subunit B; part of the UvrABC endonuclease that initiates excision repair
uvrC	43.0	Excision-repair nuclease subunit C; part of the UvrABC endonuclease that initiates excision repair
uvrD	86.1	DNA-dependent ATPase and helicase required for excision repair
ruvA	41.9	Forms a complex with RuvB; recognizes Holliday junctions
ruvB	41.9	Forms a complex with RuvA; branch migration helicase
ssb	92.0	Binds to ssDNA
dnaN	83.6	DNA synthesis as part of DNA polymerase III
dnaQ	5.1	DNA synthesis as part of DNA polymerase III
dinF	91.7	Unknown
dinG	18.0	Unknown

The Role of RecA Protein in Mutagenic Bypass

When an unrepairable DNA lesion is encountered by DNA polymerase III, replication is stalled until an error-prone lesion bypass occurs. For this to occur, a special, or modified error-prone DNA polymerase is required to insert an incorrect nucleotide opposite the lesion (producing a mutation) and then allowing normal DNA synthesis. This process is referred to as SOS mutagenesis or error-prone repair, and is the last recourse to ensure cell survival when all other error-free processes have acted (Tang *et al.*, 1998).

SOS mutagenesis requires high levels of functional *umuC* and *umuD* gene products. In exponentially growing *E. coli*, these proteins are expressed at a low, basal level (due to LexA binding to the SOS box of the *umuDC* operon) with approximately 180 UmuD proteins per cell and an undetectable amount of UmuC protein. Following DNA damage, the levels of RecA protein increase and this results in (a) the cleavage of the LexA repressor causing derepression of expression of the *umuDC* operon leading to an increase in the levels of UmuC protein to 200 molecules per cell and UmuD protein to 2400 copies per cell and (b) the proteolytic processing of UmuD to UmuD′ by the activated RecA protein (Nohmi *et al.*, 1988). This processing yields two fragments of UmuD protein: a small N-terminal fragment and a larger, C-terminal fragment. It is the C-terminal fragment (referred to as UmuD′) that is the active species in UV-induced mutagenesis (Nohmi *et al.*, 1988); two UmuD′ molecules associate with UmuC, forming the Umu(D′)$_2$C complex. These complexes bind to and are targeted by the activated RecA nucleoprotein filament to DNA lesions where they are proposed to function as a specialized elongation factor to interact with a stalled DNA polymerase III, helping it to resume DNA synthesis across the lesion.

Summary

RecA protein is an essential component of homologous recombination and DNA repair in *E. coli*. The key, universally conserved structure in each of these processes is the RecA nucleoprotein filament. It is a ternary complex consisting of RecA protein, ssDNA and an NTP cofactor. This structure has the capacity to bind, in a mutually exclusive manner, dsDNA, the LexA repressor and the Umu(D′)$_2$C complex. Binding of dsDNA to the filament allows RecA protein to function as a DNA strand exchange protein. The binding of the LexA repressor to the filament induces an autocatalytic cleavage which inactivates the repressor which, in turn, results in derepression of the SOS regulon. Finally, the binding of the processed Umu(D′)$_2$C complex to the filament switches the role of RecA protein from a recombination one to a mutagenic one. The *in vitro* capabilities of this specialized nucleoprotein filament are consistent with the roles of RecA protein *in vivo*, and explain the pleiotropic effects of mutations in the *recA* gene.

References

Bianco PR, Tracy RB and Kowalczykowski SC (1998) DNA strand exchange proteins: A biochemical and physical comparison. *Frontiers of Bioscience* **3**: D570–D603.

Cox MM and Lehman IR (1981) RecA protein of *Escherichia coli* promotes branch migration, a kinetically distinct phase of DNA strand exchange. *Proceedings of the National Academy of Sciences of the USA* **78**: 3433–3437.

Howard-Flanders P, West SC and Stasiak A (1984) Role of recA protein spiral filaments in genetic recombination. *Nature (London)* **309**: 215–220.

Mazin AV and Kowalczykowski SC (1998) The function of the secondary DNA-binding site of RecA protein during DNA strand exchange. *EMBO Journal* **17**: 1161–1168.

Menetski JP, Bear DG and Kowalczykowski SC (1990) Stable DNA heteroduplex formation catalysed by the *Escherichia coli* RecA protein in the absence of ATP hydrolysis. *Proceedings of the National Academy of Sciences of the USA* **87**: 21–25.

Nohmi T, Battista JR, Dodson LA and Walker GC (1988) RecA-mediated cleavage activates UmuD for mutagenesis: mechanistic relationship between transcriptional derepression and posttranslational activation. *Proceedings of the National Academy of Sciences of the USA* **85**: 1816–1820.

Ogawa T, Wabiko H, Tsurimoto T, Horii T, Masukata H and Ogawa H (1978) Characteristics of purified recA protein and the regulation of its synthesis *in vivo*. *Cold Spring Harbor Symposia of Quantitative Biology* **43**: 909–916.

Ogawa T, Yu X, Shinohara A and Egelman EH (1993) Similarity of the yeast RAD51 filament to the bacterial RecA filament. *Science* **259**: 1896–1899.

Register JC, 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. *Journal of Biological Chemistry* **260**: 12308–12312.

Rehrauer WM, Bruck I, Woodgate R, Goodman MF and Kowalczykowski SC (1998) Modulation of RecA nucleoprotein function by the multigenic UmuD′C protein complex. *Journal of Biological Chemistry* **273**: 32384–32387.

Roberts JW, Roberts CW, Craig NL and Phizicky EM (1978) Activity of the *Escherichia coli* recA-gene product. *Cold Spring Harbor Symposia on Quantitative Biology* **43**: 917–920.

Shibata T, DasGupta C, Cunningham RP and Radding CM (1979) Purified *Escherichia coli* recA protein catalyzes homologous pairing of superhelical DNA and single-stranded fragments. *Proceedings of the National Academy of Sciences of the USA* **76**: 1638–1642.

Stasiak A and Egelman EH (1988) Visualization of recombination reactions. In: Kucherlapati R and Smith GR (eds) Genetic Recombination, pp 265–308. Washington, DC: American Society for Microbiology.

Story RM, Weber IT and Steitz TA (1992) The structure of the *E. coli* recA protein monomer and polymer. *Nature (London)* **355**: 318–325.

Tang M, Bruck I, Eritja R, Turner J, Frank EG, Woodgate R, O'Donnell M and Goodman MF (1998) Biochemical basis of SOS-induced mutagenesis in *Escherichia coli*: reconstitution of in vitro lesion bypass dependent on the UmuD′$_2$C mutagenic complex and RecA protein. *Proceedings of the National Academy of Sciences of the USA* **95**: 9755–9760.

Further Reading

Anderson DG and Kowalczykowski SC (1998) Reconstitution of an SOS response pathway: derepression of transcription in response to DNA breaks. *Cell* **95**: 975–979.

Camerini-Otero RD and Hsieh P (1995) Homologous recombination proteins in prokaryotes and eukaryotes. *Annual Review of Genetics* **29**: 509–552.

Eggleston AK and West SC (1996) Exchanging partners: recombination in *E. coli*. *Trends in Genetics* **12**: 20–26.

Friedberg EC, Walker GC and Siede W (1995) *DNA Repair and Mutagenesis*. Washington, DC: ASM Press.

Kowalczykowski SC (1991) Biochemistry of genetic recombination: Energetics and mechanism of DNA strand exchange. *Annual Review of Biophysics and Biophysical Chemistry* **20**: 539–575.

Kowalczykowski SC and Eggleston AK (1994) Homologous pairing and DNA strand-exchange proteins. *Annual Review of Biochemistry* **63**: 991–1043.

Kowalczykowski SC, Dixon DA, Eggleston AK, Lauder SD and Rehrauer WM (1994) Biochemistry of homologous recombination in *Escherichia coli*. *Microbiological Reviews* **58**: 401–465.

Roca AI and Cox MM (1997) RecA protein: structure, function, and role in recombinational DNA repair. *Progress in Nucleic Acid Research and Molecular Biology* **56**: 129–223.

Stasiak A and Egelman EH (1988) Visualization of recombination reactions. In: Kucherlapati R and Smith GR (eds) *Genetic Recombination*, pp. 265–308. Washington, DC: ASM Press.

Walker GC (1996) The SOS Response of *Escherichia coli*. In: Neidhardt FC and Curtiss R (ed.) Escherichia coli *and* Salmonella: *Cellular and Molecular Biology*, vol. 1, pp. 1400–1416. Washington, DC: ASM Press.