Mismatch-, MutS-, MutL-, and Helicase II-dependent Unwinding from the Single-strand Break of an Incised Heteroduplex

Vivian Dao‡ and Paul Modrich§

From the Department of Biochemistry and §Howard Hughes Medical Institute, Duke University Medical Center, Durham, North Carolina 27710

Escherichia coli MutS, MutL, and DNA helicase II are sufficient to initiate mismatch-dependent unwinding of an incised heteroduplex (Yamaguchi, M., Dao, V., and Modrich, P. (1998) J. Biol. Chem., 273, 9197–9201). We have studied unwinding of 6.4-kilobase circular G-T heteroduplexes that contain a single-strand incision, 808 base pairs 5’ to the mismatch or 1023 base pairs 3’ to the mispair as viewed along the shorter path between the two DNA sites. Unwinding of both substrates in the presence of MutS, MutL, DNA helicase II, and single-stranded DNA binding protein was mismatch-dependent and initiated at the single-strand break. Although unwinding occurred in both directions from the strand break, it was biased toward the shorter path linking the strand break and the mispair. MutS and MutL are thus sufficient to coordinate mismatch recognition to the orientation-dependent activation of helicase II unwinding at a single-strand break located a kilobase from the mispair.

The strand specificity necessary for correction of DNA biosynthetic errors by the Escherichia coli mismatch repair system is provided by the transient absence of adenine modification of d(GATC) sequences within newly synthesized DNA (1). Repair is initiated by binding of a MutS homodimer to a mismatch followed by addition of MutL to this complex (2–4). Assembly of this ternary complex activates a MutH-associated endonuclease that cleaves the unmethylated strand at a hemimethylated d(GATC) sequence within newly replicated DNA (5). The single-strand break introduced by MutH, which may occur either 3’ or 5’ to the mismatch on the unmethylated strand, directs the excision of that portion of the unmethylated strand spanning the d(GATC) sequence and the mispair (6, 7). Excision requires MutS, MutL, DNA helicase II (also called MutU), and depending on the strand break to mismatch orientation, a 3’→5’ or 5’→3’ single-strand exonuclease (6, 8).

The accompanying manuscript (9) demonstrates that MutS and MutL greatly enhance the activity of DNA helicase II on incised heteroduplex DNA. In this paper we have used KMnO₄ to determine the site of initiation of mismatch-dependent helix unwinding in DNA substrates containing a site- and strand-specific, single-strand break. Permanganate preferentially attacks single-stranded DNA where it oxidizes the 5,6 double bond of thymine and methylcytosine and reacts to a lesser degree with other bases (10, 11). This single-strand selective reagent has been used previously to detect helix opening associated with promoter melting by bacterial and eukaryotic RNA polymerases (12, 13). Using this approach we show that MutS-, MutL-, and helicase II-dependent unwinding of an incised heteroduplex initiates at the strand break, with the direction of unwinding being biased toward the shorter path between the strand break and the mismatch in a circular heteroduplex.

EXPERIMENTAL PROCEDURES

Proteins and DNA—E. coli MutS (14), MutL (3), and MutH (15) were purified as described previously. DNA helicase II was isolated from an overproducing strain according to Runyon et al. (16). Single-strand DNA-binding protein (SSB)² and T4 polynucleotide kinase were purchased from Amersham Pharmacia Biotech, and restriction endonucleases were purchased from New England Biolabs.

Circular 6440-base pair (bp) G-T heteroduplex and G-C homoduplex DNAs containing a strand- and site-specific, single-strand break were prepared using f1MR phage DNAs (6, 17). The structure of these molecules is illustrated in Fig. 1. DNAs with a single-strand break in the complementary strand at the HinClI site are referred to as 5’-heteroduplexes since the nick is 5’ to the mismatch as viewed along the shorter path (808 base pairs) in the circular DNA. A second configuration, referred to as a 3’-substrate, was prepared by MutH incision of the viral strand at the single GATC site (1023 bp from the mismatch, shorter path) in hemimethylated DNA (6, 15). Corresponding control homoduplexes containing a G-C base pair instead of a mismatch at position 5632 were constructed in a similar manner. DNA size markers were prepared by cleavage of f1MR3 (2) replicative form DNA with appropriate restriction endonucleases.

Oligonucleotides (Table I), which were purchased from Oligos Etc., were 5’-³²P-end-labeled using γ-³²P-ATP (3000 Ci/mmol, New England Nuclear) and T4 polynucleotide kinase according to the recommendations of the manufacturer. Labeling was terminated by addition of EDTA to 10 mM and heating at 65 °C for 10 min. Uncorporated label was removed by passing the solution through Sephadex G-25 (Amer- sham Pharmacia Biotech) equilibrated with 10 mM Tris/HCl (pH 7.6), 1 mM EDTA, and 100 mM NaCl. Labeled oligonucleotide was ethanol precipitated and resuspended in 10 mM Tris/HCl (pH 7.6), 1 mM EDTA.

Chemical Quench Analysis—Chemical quench experiments utilized a KinTek apparatus (KinTek Instruments). Unless specified otherwise, a solution (40 μl) containing 0.5 μg (0.19 pmol) heteroduplex DNA, 1.4 μg MutL (10 pmol as dimer), 2.8 μg MutS (15 pmol as dimer), 0.8 μg of DNA helicase II (10 pmol as monomer) in 50 mM Hepes/KOH (pH 8.0), 0.8 mM dithiothreitol was mixed with 40 μl of 2 mM ATP containing 4 μl of 2 μM ATP containing 4 μM of SSB in the same buffer. Mixing syringes were maintained at 37 °C and reaction times varied between 50 ms and 5 s. Reactions were quenched by injection of 40 μl of freshly prepared 30 mM KMnO₄ in H₂O, and samples were collected in tubes on ice. Approximately 2 s after collection, permanganate oxidation was terminated by addition of 10 μl of 1 M dithiothreitol. Samples were supplemented with 2 μl of 0.5 μM EDTA and 10 μl of 10 mM Tris/HCl (pH 7.6), 1 mM EDTA, and passed through a spin-column containing 5-300 (Amersham Pharmacia Biotech) equilibrated with 10 mM Tris/HCl (pH 7.6), 1 mM EDTA, 0.3 mM NaCl. The column flow-through was extracted with phenol, precipitated with eth-

* This work was supported in part by Grant GM23719 from the National Institute of General Medical Sciences. The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked “advertisement” in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

‡ Present address: Access Pharmaceuticals, 2800 Stemmons Freeway, Dallas, TX 75207.

¶ To whom correspondence should be addressed. Tel.: 919-684-2775; Fax: 919-681-7874; E-mail: modrich@biochem.duke.edu.

² The abbreviations used are: SSB, single-strand DNA-binding protein; bp, base pair(s).
The excision step of methyl-directed mismatch repair requires MutS, MutL, DNA helicase II, an appropriate exonuclease, and a heteroduplex containing a single-strand break (6–8). The accompanying article demonstrates that MutL greatly stimulates helicase II on conventional helicase substrates and that MutS and MutL activate the unwinding activity of helicase II on an incised DNA containing a mismatch (9). We show here that MutS, MutL, and helicase II-dependent unwinding of heteroduplex DNA initiates at the strand break.

**RESULTS**

The excision step of methyl-directed mismatch repair requires MutS, MutL, DNA helicase II, an appropriate exonuclease, and a heteroduplex containing a single-strand break (6–8). The accompanying article demonstrates that MutL greatly stimulates helicase II on conventional helicase substrates and that MutS and MutL activate the unwinding activity of helicase II on an incised DNA containing a mismatch (9). We show here that MutS, MutL, and helicase II-dependent unwinding of heteroduplex DNA initiates at the strand break.

**MutS, MutL, Helicase II, and Mismatch-dependent Unwinding Initiates at the Strand Break**—To determine the site of initiation of heteroduplex unwinding, we have used permanganate, which preferentially oxidizes thymidylate residues in single-stranded DNA (10, 11). Since thymidylate oxidation renders the phosphodiester bond subject to hydrolysis by strong base, the location of oxidized residues can be determined. The circular 6.4-kilobase DNAs used in this work contained a G-T mismatch at position 5632 and a single-strand break either at position 0/6440 on the complementary strand (C) or at position 215 on the viral strand (V). DNAs with a nick on the V strand are dubbed 3’-heteroduplexes for a similar reason. Sites of cleavage by restriction endonucleases used in the experiments are also indicated with coordinates shown corresponding to the nucleotide 5’ to the phosphodiester attacked. Shaded regions correspond to oligonucleotides (Table I) used for indirect end-labeling.

![Image](https://example.com/image.png)

**Fig. 1.** **Structure of f1MR heteroduplexes.** Circular heteroduplex DNAs used in this study contained a G-T mismatch at position 5632 and a single-strand break either at position 0/6440 on the complementary strand (C) or at position 215 on the viral strand (V). DNAs with a nick in the C strand are designated as 5’-heteroduplexes, since the incision lies 5’ to the mismatch along the shorter path that joins the two sites in the circular molecule. DNAs with a nick on the V strand are dubbed 3’-heteroduplexes for a similar reason. Sites of cleavage by restriction endonucleases used in the experiments are also indicated with coordinates shown corresponding to the nucleotide 5’ to the phosphodiester attacked. Shaded regions correspond to oligonucleotides (Table I) used for indirect end-labeling.

| Oligonucleotides | Sequences |
|------------------|-----------|
| C5470            | 5’-GTACTATGGTTGCTTTGAGC-3’ |
| V5470            | 5’-CTTCAACGCAAACATGTAAC-3’ |
| V6287            | 5’-AAATTTTTATCTGGTGGTGA-3’ |
| C6289            | 5’-TTCACGCGAAGGATTTAAAAT-3’ |
| V005             | 5’-TACACTATTAGTGAATGTTG-3’ |
| C005             | 5’-CAAACTCTACTAAGTACAGTA-3’ |

<Table I>

**Helicase II Loading in an Incised Heteroduplex**

**Fig. 2.** **Helix unwinding initiates at the nick with 5’-heteroduplex DNA.** 5’-G-T heteroduplex or 5’-G-C homoduplex DNA containing a nick in the C strand at the HindIII site (Fig. 1) was incubated as indicated with MutS, MutL, DNA helicase II, SSB, and ATP followed by a 2 s quench with 10 mM KMnO₄ (see “Experimental Procedures”). After cleavage with DraI and piperidine treatment to cleave strands at the sites of permanganate oxidation, DNA samples were subjected to electrophoresis through denaturing polyacrylamide gels and electrotransferred to a nylon membrane. Fragments of interest were visualized by indirect end-labeling (7) using 32P-oligonucleotides V6287 and C6289 as probes. As summarized in Table I, these probes hybridize to individual strands of the heteroduplex near the DraI site. Upper panel, permanganate reactive sites on the incised C strand; lower panel, permanganate reactive sites on the continuous V strand. Lanes: 1, complete system, 50 msec reaction; 2, complete, 1 s reaction; 3, complete, 5 s reaction; 4, helicase II omitted, 1 s reaction; 5, MutS omitted, 1 s reaction; 6, complete system, 1 s reaction but no KMnO₄ quench; 7, all proteins omitted, 1 s reaction; 8, complete system, 1 s reaction but G-C homoduplex substituted for heteroduplex; 9, marker for location of the strand break. The strong band that runs with the marker for the strand break in the lower panel is the result of permanganate oxidation of the closed circular V strand near the nick. It was not produced in the absence of the oxidizing agent (lane 6).
Helicase II Loading in an Incised Heteroduplex

Fig. 3. Helix unwinding initiates at the nick with 3'-heteroduplex DNA. Substrates were 3'-G-T heteroduplex or 3'-G-C homoduplex DNA containing a nick in the V strand at the MboI site (Fig. 1). Reactions were performed as described under “Experimental Procedures” and in the legend to Fig. 2. DNAs were cleaved with HinII prior to electrophoresis, and oligonucleotides C005 and V005 were used for indirect end-labeling. Upper panel, permanganate reactive sites on the V strand; lower panel, permanganate reactive sites on the C strand. Lanes: 1, complete system, 50 msec reaction; 2, complete system, 1 s reaction; 3, complete system, 5 s reaction; 4, helicase II omitted, 1 s reaction; 5, MutS omitted, 1 s reaction; 6, complete system, 1 s reaction but no KMnO₄ quench; 7, all proteins omitted, 1 s reaction; 8, complete system, 1 s reaction but GC homoduplex substituted for heteroduplex; 9, marker for location of nick. As noted in the legend to Fig. 2, the strong band in the lower panel results from permanganate oxidation of the covalently continuous strand near the site of the strand break in the open strand.

at the single-strand break was evident as judged by conversion of either the incised (upper panel) or the continuous (lower panel) strand of the molecule to a permanganate-sensitive form. Conversion of that region of the molecule to permanganate-sensitivity in the vicinity of the nick was rapid with a maximal unwinding rate achieved in 5 s or less. An otherwise identical G-C homoduplex did not support the reaction (lane 8), and increased permanganate reactivity was not observed in the absence of helicase II or MutS (lanes 4 and 5) or in the absence of MutL (not shown). Consequently, unwinding observed at the strand break is dependent on MutS, MutL, and helicase II and on the recognition of a mismatch 808-bp distant. Analysis of permanganate sensitivity of the continuous strand of the heteroduplex (Fig. 2, lower panel) revealed that mismatch-provoked unwinding of 5'-heteroduplex occurred to either side of the nick. This observation will be considered further below.

As shown in Fig. 3, virtually identical results were obtained with a 3'-G-T heteroduplex in which the mismatch and strand break were separated by 1023 bp. However, in contrast to results obtained with the 5'-heteroduplex described above, the degree of unwinding of the 3'-substrate increased significantly between 1 and 5 s, perhaps due to the increased distance between the two DNA sites in the latter molecule.

Although presence of a G-T mismatch is known to enhance helix dynamics in the vicinity of the mispair (19, 20), the mismatched thymidylate in the G-T heteroduplex did not detectably react with permanganate under the mild oxidation conditions used. Furthermore, under conditions where single-strand character was rapidly generated at the strand break in the G-T heteroduplex in the presence of MutS, MutL, helicase II, and SSB, permanganate oxidation products were not detected in the vicinity of the mismatch after 5 s incubation. This is illustrated in Fig. 4 for the 5'-G-T heteroduplex, and identical results were obtained with the 3'-substrate (not shown). These results imply that the single-strand character that develops at the strand break in an incised heteroduplex is not the consequence of an unwinding event that initiates at the mispair and propagates to the mismatch. Consequently, we have concluded that unwinding by activated helicase II initiates at the strand break. The extent of unwinding observed with 5'- and 3'-heteroduplexes was about 50–100 nucleotides.

Bias in the Direction of the DNA Helicase II Unwinding—As mentioned above and shown in the lower panels of Figs. 2 and 3, analysis of permanganate sensitivity of the continuous heteroduplex strand demonstrated that unwinding occurs in both directions from the strand break. However, analysis of mismatch-provoked methyl-directed excision tracts produced in extracts and in a purified system has demonstrated that excision is largely restricted to the shorter path between the strand signal and the mismatch in circular heteroduplexes similar to those used here (7). The unwinding reactions described above utilized only a subset of the proteins required for methyl-directed mismatch repair, and helicase II is known to load

2 The mismatched thymidylate residue does react with permanganate under more vigorous conditions (6 mM KMnO₄ for 3 min at 37 °C, L. Blackwell and P. Modrich, unpublished observations).
preferentially onto single-strand regions within otherwise duplex DNA (21). Consequently, it was possible that a directional unwinding preference was masked to some degree by secondary events in which the helicase loaded onto single-stranded DNA produced by orientation-dependent unwinding from the strand break. This possibility was assessed in several ways with potential unwinding preference estimated by summing integrated band intensities of oxidation products produced on the continuous heteroduplex strand to either side of the nick.

As shown in Figs. 5 and 6 (upper panels), directional unwinding from the strand break toward the mismatch via the shorter path in the circular heteroduplex could be demonstrated with both 3'- and 5'-heteroduplexes, but the magnitude of preference for the shorter path decreased monotonically with increasing helicase II concentration. A decrease in preferential unwinding along the shorter path with both substrates also occurred as reaction time increased (Figs. 5 and 6, lower panels), and whereas heteroduplex unwinding from the strand break did not require SSB, presence of the protein conferred a modest increase in directional unwinding (not shown). MutS and MutL are therefore not only sufficient to activate helicase II unwinding from the strand break of an incised heteroduplex, but they also confer directionality on this process.

DISCUSSION

A single hemimodified d(GATC) sequence, which may reside to either side of the mismatch, is sufficient to provide strand specificity to heteroduplex repair by the *E. coli* methyl-directed pathway (8, 22), with mismatch-provoked incision of the unmethylated strand of the d(GATC) site providing a strand break that directs removal of that portion of the new strand spanning the nick and the mispair (5–7). Analysis of reaction intermediates has suggested that excision initiates at the strand break by a mechanism in which helicase II displacement renders the incised strand sensitive to an appropriate 3'- or 5'-single-strand exonuclease, depending on location of the nick 3'- or 5' to the mispair (7). The experiments described here are compatible with this mechanism and demonstrate that MutS and MutL are sufficient to coordinate mismatch recognition to activation of helicase II unwinding at a single-strand break that can be located 800–1,000 bp from the mismatch.

As noted previously (7, 8), the bidirectional nature of the methyl-directed system requires loading of the appropriate hydrolytic activity at the incised d(GATC) sequence to ensure that excision proceeds toward the mispair. The finding that helicase II activation by MutS and MutL results in a significant degree of orientation-dependent unwinding on a nicked heteroduplex suggests that the latter proteins are sufficient to evaluate placement of the strand break 3' or 5' to the mismatch. Despite their separation distance, interaction of the mismatch and the strand break during the course of this reaction is fast...
with maximal initiation of unwinding achieved after 1–5 s under conditions of MutS, MutL, and helicase II excess. Although the molecular events responsible for interaction of the two DNA sites are not fully understood, recent electron microscopy experiments (4) have suggested that MutS translocation along the heteroduplex contour may play a role in this process. Whereas the MutS dimer initially binds to heteroduplex DNA at the mismatch, this complex is converted in the presence of ATP to an α-shaped DNA structure that is stabilized by MutS at the base. The mismatch in such complexes is usually found in the DNA loop. This rearrangement has been attributed to a mechanism in which the two subunits of the MutS dimer act as ATP-driven divergent motors that translocate from the mispair in a bidirectional fashion along the helix contour. MutL stimulates this reaction and when present migrates along the helix with MutS. Under the buffer conditions used for the experiments described here, the rate of MutS-catalyzed formation of α-shaped DNA loops approaches 10,000 bp per min in the absence of MutL (4), sufficiently fast to account for the interaction of the two sites observed in the experiments described here.

Fig. 7 illustrates a mechanism for MutS- and MutL-dependent activation of helicase II unwinding that incorporates these electron microscopy results, as well as the findings presented here and in the accompanying paper (9). Helicase II activation initiates by binding of a MutS dimer to the mismatch (4). MutL adds to the MutS-DNA complex in a reaction that requires ATP but apparently not ATP hydrolysis (3). Although MutL exists as a dimer in solution (3), the stoichiometry of MutL addition has not been established. In a reaction that depends on ATP hydrolysis, the subunits of the MutS dimer leave the mismatch, usually in a bidirectional manner, with MutL moving along the helix with MutS. At a stage in the reaction that remains to be determined, helicase II adds to MutS-MutL-DNA complex, and when a strand break is encountered the activity enters the helix in such a way that unwinding tends to proceed toward the mismatch, irrespective of placement of the nick 3′ or 5′ to the mispair on the incised strand. Since MutL greatly stimulates the activity of helicase II and since the two proteins interact physically (9, 23), it is likely that MutL directly promotes initiation of unwinding by helicase, perhaps by physically facilitating helix entry of the activity at the strand break.

DNA helicas show a preferred polarity during initiation of unwinding (24). The orientation-dependent unwinding from the nick toward the mismatch as described here can be understood in terms of this polarity preference, which for helicase II is 3′ to 5′ (25). Thus, one need only invoke loading of the unwinding activity onto the incised strand when the nick is 3′ to the mismatch or onto the continuous strand when nick is 5′ to the mispair. The suggestion that MutL may have an important role in activating the excision step of bacterial mismatch repair may have implications for the eukaryotic reaction. The mammalian pathway has a mispair specificity similar to that of the bacterial reaction and occurs by a similar bidirectional mechanism. Defects in this system have been implicated in both inherited and sporadic cancers, as well as in cellular resistance to certain DNA damaging agents (26–29). However, in contrast to the MutS and MutL homodimers that are active in the bacterial pathway, human mismatch repair is dependent on MutSa, a heterodimer of the MutS homologs MSH2 and MSH6, and MutLo, a heterodimer of the MutL homologs MLH1 and PMS2 (30–32). Certain MLH1 and PMS2 mutations confer selective directional defects in mismatch repair. Thus, some MLH1 mutations are selectively defective in repair directed by a strand break located 3′ to the mismatch but are proficient in mismatch correction directed by a 5′-strand signal (33). Conversely, a PMS2 mutation has been identified that blocks repair from the 5′-side of the mismatch but not from the 3′-side (34). One interpretation of these findings is that like bacterial MutL, human MutLo functions to activate the mismatch repair excision system, but in the case of the human pathway the two subunits of MutLo differentially function to load a 3′ to 5′ or 5′ to 3′ excision system, depending on the location of the strand break that directs the reaction.

Acknowledgments—We thank Dwayne Allen and Keith Bjornson for comments on the manuscript, and Sam Wilson (National Institute of Environmental Health Sciences) for suggesting the use of permanganate as a probe for single-stranded DNA.

REFERENCES
1. Meselson, M. (1988) in Recombination of the Genetic Material (Low, K. B., ed.), pp. 91–113, Academic Press, San Diego.
2. Su, S.-S., Lahue, R. S., Au, K. G., and Modrich, P. (1988) J. Biol. Chem. 263, 6829–6835.
3. Grilley, M., Welsh, K. M., Su, S.-S., and Modrich, P. (1989) J. Biol. Chem. 264, 1000–1004.
4. Allen, D. J., Makhov, A., Grilley, M., Taylor, J., Thresher, R., Modrich, P., and Griffith, J. D. (1997) EMBO J. 16, 4467–4476.
5. Au, K. G., Welsh, K., and Modrich, P. (1992) J. Biol. Chem. 267, 12142–12148.
6. Lahue, R. S., Au, K. G., and Modrich, P. (1989) Science 245, 160–164.
7. Grilley, M., Griffith, J., and Modrich, P. (1993) J. Biol. Chem. 268, 11830–11837.
8. Cooper, D. L., Lahue, R. S., and Modrich, P. (1993) J. Biol. Chem. 268, 11823–11829.
9. Yamaguchi, M., Xiao, D., and Modrich, P. (1997) J. Biol. Chem. 272, 9197–9201.
10. Hayatsu, H., and Ukita, T. (1967) Proc. Natl. Acad. Sci. U. S. A. 5057–5061.
11. Fritzsche, E., Hayatsu, H., Igloi, G. L., Iida, S., and Ko’sell, H. (1987) Proc. Natl. Acad. Sci. U. S. A. 84, 8924–8938.
12. Sasse-Dwight, S., and Gralla, J. D. (1988) Proc. Natl. Acad. Sci. U. S. A. 83, 8924–8938.
13. Kassavetis, G. A., Braun, R. E., Nguyen, L. L., and Geduldus, E. P. (1990) Cell 60, 235–245.
14. Su, S.-S., and Modrich, P. (1986) Proc. Natl. Acad. Sci. U. S. A. 83, 5657–5661.

---

3 G.-M. Li and P. Modrich, unpublished observations.
Helicase II Loading in an Incised Heteroduplex

15. Welsh, K. M., Lu, A.-L., Clark, S., and Modrich, P. (1987) J. Biol. Chem. 262, 15624–15629
16. Runyon, G. T., Wong, I., and Lohman, T. M. (1993) Biochemistry 32, 602–612
17. Holmes, J., Clark, S., and Modrich, P. (1990) Proc. Natl. Acad. Sci. U. S. A. 87, 5837–5841
18. Fang, W.-H., and Modrich, P. (1993) J. Biol. Chem. 268, 11838–11844
19. Patel, D. J., Pardi, A., and Itakura, K. (1982) Science 216, 581–590
20. Pardi, A., Morden, K. M., Patel, D. J., and Tinoco, I., Jr. (1982) Biochemistry 21, 6567–6574
21. Runyon, G. T., and Lohman, T. M. (1989) J. Biol. Chem. 264, 17592–17512
22. Lahue, R. S., Su, S. S., and Modrich, P. (1987) Proc. Natl. Acad. Sci. U. S. A. 84, 1482–1486
23. Yamaguchi, M. (1997) MutS, MutL, and DNA Helicase II Are Required for Mismatch-provoked Unwinding at a Stroud Scission, Ph.D. thesis, Duke University
24. Lohman, T. M., and Bjornson, K. P. (1996) Annu. Rev. Biochem. 65, 169–214
25. Matson, S. W. (1986) J. Biol. Chem. 261, 10169–10175
26. Eshleman, J. R., and Markowitz, S. D. (1995) Curr. Opin. Oncol. 7, 83–89
27. Kolodner, R. (1996) Genes Dev. 10, 1433–1442
28. Modrich, P., and Lahue, R. (1996) Annu. Rev. Biochem. 65, 101–133
29. Modrich, P. (1997) J. Biol. Chem. 272, 24727–24730
30. Li, G. M., and Modrich, P. (1995) Proc. Natl. Acad. Sci. U. S. A. 92, 1950–1954
31. Drummond, J. T., Li, G.-M., Longley, M. J., and Modrich, P. (1995) Science 268, 1909–1912
32. Palemo, F., Gallinari, P., Iaccarino, I., Lettieri, T., Hughes, M., D'Arrigo, A., Truong, O., Hsu, J. J., and Jiricny, J. (1995) Science 268, 1912–1914
33. Drummond, J. T., Anthoney, A., Brown, R., and Modrich, P. (1996) J. Biol. Chem. 271, 19645–19648
34. Nicolaides, N. C., Littman, S., Modrich, P., Kinzler, K. W., and Vogelstein, B. (1998) Mol. Cell. Biol., 18, 1635–1641