Transcription-coupled and Transcription-independent Repair of Cyclobutane Pyrimidine Dimers in the Dihydrofolate Reductase Gene*

Received for publication, June 26, 2002, and in revised form, August 1, 2002
Published, JBC Papers in Press, August 6, 2002, DOI 10.1074/jbc.M206375200

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Using a ligation-mediated polymerase chain reaction technique, we have mapped the repair of ultraviolet light-induced cyclobutane pyrimidine dimers (CPDs) at the nucleotide level in exons 1, 2, and 5 of the dihydrofolate reductase (DHFR) gene in Chinese hamster ovary cells. We found that CPDs are preferentially repaired in the transcribed strand (T strand) and that the order of repair efficiency is exon 1 > exon 2 > exon 5. In the cells with a deletion of the DHFR gene encompassing the promoter region and the first four exons, CPDs are not repaired in the T strand of the residual DHFR gene. These results substantiate the idea that the preferential repair of CPDs in the T strand is transcription depend-

net. However, in the wild type gene we have found that CPDs are efficiently repaired in the nontranscribed strand (NT strand) of exon 1 but not in the NT strand of exons 2 and 5. Probing the chromatin structure of exons 1, 2, and 5 of the DHFR gene with micrococcal nuclease revealed that the exon 1 region is much more sensitive to micrococcal nuclease digestion than the exon 2 and exon 5 regions, suggesting that the chromatin structure in the exon 1 region is much more open. These results suggest that, although preferential repair of the T strand of the DHFR gene is transcription dependent, repair of the NT strand is greatly affected by chromatin structure.

Both prokaryotic and eukaryotic organisms have developed multiple pathways for the repair of major ultraviolet light-induced photoproducts such as cyclobutane pyrimidine dimers (CPDs)¹ of which nucleotide excision repair (NER) is the major pathway (for reviews see Ref. 1–7). NER is also the most versatile DNA repair mechanism, because it can remove not only many types of photoproducts but also bulky DNA lesions induced by environmental carcinogens such as polycyclic aromatic hydrocarbons, aromatic amines, and many therapeutic agents (2–7). Although the recognition and excision of these different kinds of bulky DNA damage may not be identical, in general they follow two distinct subpathways in mammalian cells: 1) transcription-coupled repair (TCR), which can selectively and efficiently repair transcription-blocking DNA damage in the transcribed strand (T strand) of transcriptionally active genes; and 2) global genomic repair (GGR), which is responsible for repairing DNA damage in the noncoding regions, i.e. the nontranscribed strand (NT strand) of transcriptionally active genes and both strands of transcriptionally inactive genes (3–8). It has been found that cells from individuals with Cockayne syndrome have defective TCR, and cells from xeroderma pigmentosum complementation group C patients have defective GGR (9–13).

The majority of our understanding of TCR and GGR is derived from studies on the dihydrofolate reductase gene (DHFR), a transcriptionally active housekeeping gene, and its downstream noncoding region in Chinese hamster ovary (CHO) cells as well as human fibroblasts (8–10, 14, 15). Using a Southern blot-based DNA repair assay to detect the removal of T4 endonuclease V (T4 endo V)-sensitive sites from specific restriction fragments, several laboratories have found that the repair of CPDs is more efficient in the coding region of the DHFR gene than in the downstream noncoding region in mammalian cells (8, 9, 14, 16, 17). Using strand specific probes, several laboratories have found (8, 15–18) that the efficient repair in the coding region of the DHFR gene is the result of preferential repair in the T strand, and the repair in the NT strand of the DHFR gene is similar, if not identical, to that in the downstream noncoding region. The role of transcription in enhancing the repair of CPDs was further substantiated by the reduction in the repair of CPDs in the DHFR gene in cells treated with α-amanitin, which inhibits RNA polymerase II-mediated transcription (19).

Other results from several laboratories (18, 20–23), however, suggest that NER in mammalian cells is much more complex than the current understanding of TCR and GGR would indicate. For example, using a T4 endo V incision method in combination with a ligation-mediated polymerase chain reaction (LMPCR), we found that CPDs are efficiently repaired in both strands of the endogenous adenine phosphoribosyltransferase (APRT) gene in CHO cells and that this repair is independent of transcription (18). In contrast, CPD repair in a translocated APRT gene differs from CPD repair in the endogenous APRT gene (18, 20). In one case CPDs are preferentially repaired in the T strand, and in another case CPDs in both the T and NT strands are not efficiently repaired even though the APRT gene in both cases is transcriptionally active (20). Using the same method, Pfeifer and co-workers (23) have found that, in the human JUN gene, CPDs in the NT strand between nucleotides –40 and +100 relative to the major transcription start site are
repaired as efficiently as in the T strand and that the repair of CPDs along the T strand appears to be faster at the 5’-end and is gradually reduced toward the 3’-end. These discoveries were made possible by the T4 endo V incision method in combination with LMPCR to map CPD distributions at the sequence level (18, 20, 23). Together, these results raise the possibility that CPD repair in transcriptionally active genes may be affected not only by the transcription process but also by genomic context and the “open” chromatin structure at the promoter region of active genes.

Interestingly, the results of experiments measuring CPD repair along the T strand of the DHFR gene have been controversial; both uniform repair and a 5’ to 3’ gradient of repair have been reported (15, 16). To determine whether there is a 5’ to 3’ polarity in CPD repair of the DHFR gene and further test the possibility that factors other than those involved in TCR and GGR affect CPDs repair, we have mapped CPD repair at the sequence level in DHFR genes with or without a promoter region using T4 endo V incision combined with LMPCR. We have found that CPD repair at the 5’-end of the T strand is indeed faster than at the 3’-end, which is consistent with a gradient repair along the T strand, and that CPD repair in the T strand is dependent on the presence of a promoter and active transcription. Although CPDs are not repaired in the NT strand of exons 2 and 5, they are efficiently repaired in the NT strand of exon 1. Probing the chromatin structure with micrococal nuclease (MN) revealed that digestion is significantly faster in exon 1 than in exons 2 and 5, indicating that the chromatin structure in the exon 1 area of the DHFR gene is much more open compared with those in exon 2 and 5. These results suggest that, although preferential repair of the T strand of the DHFR gene is transcription dependent, repair of the NT strand is greatly affected by chromatin structure.

**EXPERIMENTAL PROCEDURES**

**Cell Lines and Culture Conditions**—CHO-AT3-2 cells are DHFR<sup>−</sup>- and contain diploid DHFR<sup>−</sup> loci; both loci are transcriptionally active. CHO-DG22 cells are DHFR<sup>−</sup> mutants; they are hemizygous for the DHFR gene locus, which has a deletion encompassing the whole promoter region and the first four exons (24). CHO-AT3-2 cells were grown in α-minimum Eagle’s medium supplemented with 10% fetal calf serum, and CHO-DG22 cells were grown in F12 medium supplemented with 10% fetal calf serum.

**UV Irradiation and Genomic DNA Isolation**—For UV irradiation, cells were grown to 50–70% confluence in 150-mm dishes and UV-irradiated at a fluence rate of 1 J/m<sup>2</sup>/s for 15 s using GE15118 germicidal lamps (predominant emission, 254 nm) as the UV source. After irradiation, the cells were incubated in fresh medium containing 10 μM 5-bromo-2′-deoxyuridine and 1 μM 5-fluorodeoxyuridine for various periods of time to allow DNA repair for repair kinetic analysis. After incubation, the cells were lysed, and DNA was isolated and purified as described previously (18). Unreplicated DNA was separated from replicated DNA by cesium chloride density gradient centrifugation and used for repair analysis (18).

**Mapping the Repair of CPDs at the Nucleotide Level in Exons 1, 2, and 5 of the DHFR Gene**—A known quantity of purified genomic DNA was treated with T4 endo V followed by photoactivation and then subjected to LMPCR as described previously (18, 20). Oligonucleotide primer sets, which are specific for Chinese hamster DHFR gene sequences, were used to map CPDs in exons 1, 2, and 5 of the DHFR gene (see Table I). Oligonucleotide primers 1-1, 1-4, 1-2, 2-1, 4-1, and 5-4 were the sequence primers used in the first primer extension step of LMPCR; primers 1-2, 1-5, 2-2, 2-5, 5-2, and 5-5 were the PCR primers; and primers 1-3, 1-6, 2-3, 2-6, 5-3, and 5-6 were used to make the hybridization probes. A specific amount of β<sup>3</sup>P-labeled linearized pBR322 phage DNA (~20,000 dpm) was added to each sample at the beginning of the reaction as an internal standard (20). After LMPCR, equivalent counts of β<sup>3</sup>P representing equivalent amounts of template DNA for each time point of the reaction were loaded into each lane of the sequencing gel. After separation by electrophoresis in 8% denaturing polyacrylamide gels, the PCR products were electrotransferred to nylon membranes and hybridized with β<sup>3</sup>P-labeled probes. The membranes were exposed to a phosphorimaging screen and then scanned with the Cyclone (PerkinElmer Life Sciences). The intensity was determined in all CPD-specific bands of the sequencing gel that showed a consistent and measurable signal above background. Background values from T4 endo V-treated, nonirradiated control lanes were subtracted. The intensity at each position was measured from at least three independent experiments, the average value was calculated, and the CPD repair kinetics were established for both T and NT strands in exons 1, 2, and 5 of the DHFR gene.

**RNA Isolation and Strand-specific RT-PCR**—Mesenger RNA was isolated from CHO-AT3-2 cells using a Qiagen Oligotex Direct mRNA Mini kit (Qiagen, Valencia, CA). Extracted mRNA was quantified by UV spectrophotometry, and the quality was examined by electrophoresis in an 1% agarose/formaldehyde gel. The method for strand-specific RT-PCR was the same as described by Nouspikel and Hanawalt (25) with some modifications. Briefly, 1 μg of mRNA was reverse transcribed using a Superscript II kit (Invitrogen). To overcome the nonspecific amplification caused by the secondary structures in the mRNA, which, in turn, would serve as self-primers, reverse transcription was first performed for 20 min at 42 °C in the absence of primer but with 0.6 μl of the dideoxyadenosine triphosphate/deoxynucleoside triphosphate (ddATP/ddTTP) mixture from a sequencing kit (Promega) at a volume of 18 μl (25). Subsequently, dNTP and 50 pmol of strand specific primers for the T or NT strand of the DHFR gene exon 1 were added, and the reaction was continued at 42 °C for an additional 40 min. The sequences of the RT primers specific for the T or NT strand were 5′-CTGAGCAT-TGGCAGGGAAGCTC-3′ (for the T strand) and 5′-GCTGTCACTGGTTCAGCGGTGTA-3′ (for the NT strand). RNA was removed by adding 20 μg/ml RNase A and incubating for 1 h at 37 °C. The purified complementary DNA was then used for amplification with the previously mentioned primers specific for the DHFR gene exon 1.
Nuclei Isolation and Digestion of Chromatin by MN—Methods for nuclei isolation and subsequent MN digestion were the same as described by Kuhnert et al. (26). Briefly, cells (5 × 10^6) were harvested from culture flasks by trypsinization and resuspended in 10 ml of hypotonic buffer (10 mM Tris, pH 8.0, 10 mM NaCl, 5 mM MgCl₂) for 30 min in ice. After centrifugation at 1,400 × g for 2 min, the cells were resuspended in 10 ml of hypotonic buffer and homogenized in a Dounce homogenizer (15 ml, loose pestle, 40 strokes) in the presence of 0.3% IGEPAL CA-630 (Sigma). Nuclei were purified by centrifugation at 1,500 × g for 10 min in hypotonic buffer containing 8.5% sucrose (w/v) and resuspended in digestion buffer (100 mM Tris, pH 8.0, 50 mM NaCl, 3 mM MgCl₂, 1 mM CaCl₂). Ten million nuclei were digested with MN (USB) (1 unit) in 100 μl for 1, 2, 5, and 10 min at 37 °C. Control was an undigested, immediately lysed sample. The digestion was stopped by adding an equal volume of stop solution (200 mM Tris, pH 8.0, 200 mM NaCl, 20 mM EDTA, 2% SDS, 200 μg/ml proteinase K) and incubating for 2 h at 37 °C. DNA was purified and separated by electrophoresis in an 1.5% agarose gel. After staining with ethidium bromide, the separated DNA was transferred to a nylon membrane and hybridized with 32P-labeled probes specific for DHFR exons 1, 2, or 5 (20).

RESULTS

5′ to 3′ Polarity Effect on CPD Preferential Repair in the T Strand of a Transcriptionally Active DHFR Gene—It has been well established that CPDs are preferentially repaired in the T strand of the DHFR gene in CHO cells (8, 14–19). Controversial results, however, have been reported in regard to the repair pattern of CPDs along the T strand of the DHFR gene. Using a Southern blot-based DNA repair assay, both uniform repair and a 5′ to 3′ polarity effect on CPD repair along the T strand of the DHFR gene have been reported (15, 16). To determine the repair pattern of CPDs along the T strand of the DHFR gene, we mapped CPD distribution in exons 1, 2, and 5 of the DHFR gene in UV-irradiated CHO-AT3-2 cells with different post-irradiation incubation times by using the T4 endo V incision method in combination with LMPCR. Results in Fig. 1 and Fig. 2 show that CPDs are efficiently repaired in the T strand of exons 1, 2, and 5, being almost completely repaired after 24 h. However, the initial rate of CPD repair is faster in exon 1 than in exon 2, and it is much faster in exons 1 and 2 than in exon 5. After 4 h of incubation, the percentage of CPDs repaired in exons 1, 2, and 5 of the T strand were 45, 20 and 10%, respectively; after 8 h of incubation, the percentage of CPDs repaired in exons 1, 2, and 5 of the T strand were 80, 75 and 40%, respectively. The times required for 50% of the CPD removal (T_{1/2}) in exons 1, 2, and 5 are 5, 6, and 12 h, respectively.

CPDs Are Efficiently Repaired in the NT Strand of Exon 1 but Not of Exons 2 and 5—Although CPDs are poorly repaired in the NT strand of exons 2 and 5, CPDs are efficiently repaired in the NT strand of exon 1. CPDs in the NT strand of exon 1 are repaired at a rate similar to that of the T strand, being almost completely repaired within 24 h (Fig. 1 and Fig. 2). The efficient CPD repair in the NT of exon 1 raises the possibility that this strand may be part of the transcription unit for the gene located immediately 5′ upstream of the DHFR gene (27). To investigate this possibility, we have tested for the presence of a transcript representing the NT strand sequence of the DHFR exon 1 by strand-specific RT-PCR. Results in Fig. 3 show that no such transcript was detected.

Lack of Preferential Repair in the T Strand of a Truncated DHFR Gene in CHO-DG22 Cells—The efficient CPD repair observed in the T strand of exons 2 and 5 but not in the NT strand of these two exons is in agreement with previous experiments using a Southern blot-based method that quantifies CPDs in a defined DNA fragment (8, 14–19). To further test whether this preferential repair in the T strand is transcription-dependent, we have mapped the repair of CPDs in the exon 5 of CHO-DG22 cells. These cells have a deletion encompassing the entire promoter region and the first four exons of the DHFR gene, and they contain no detectable transcripts corresponding to the remaining exons 5 and 6 (24). The results in Fig. 4 show that CPDs are poorly repaired in both the T and the NT strands of exon 5 in CHO-DG22 cells, with more than 90% of CPDs remaining unrepaired in both strands after 24 h of incubation. These results support the idea that preferential CPD repair in the T strand of the transcriptionally active DHFR gene observed in CHO-AT3-2 cells is transcription dependent.

The Kinetics of MN Digestion in the Exon 1 Region of the DHFR Gene Is Faster than in Exons 2 and 5—The packaging of eukaryotic DNA into chromatin affects many dynamic processes, including DNA repair (28). Using mononucleosome or dinucleosome systems, several laboratories have demonstrated that nucleosomal structure can inhibit the repair of CPDs (29) and other UV light-induced photoproducts (30, 31) in vitro NER assays. These results suggest that the assembly of nucleosomes may restrict the access of DNA repair proteins to the...
damaged bases. It is well established that the kinetics of MN digestion are faster for active genes than for inactive genes and bulk genomic DNA, which indicates that the chromatin structure of actively transcribed genes is relatively "loose" and more accessible to the transcription machinery (32). These results raise the possibility that nucleosome structure and/or nucleosome density in the region around exon 1 of the DHFR gene may be much more open than the chromatin structure in the regions of exons 2 and 5. Consequently, exon 1 is more accessible to the repair machinery, and thus CPDs are efficiently repaired in both strands.

To test this possibility, we have probed the chromatin structure of exons 1, 2, and 5 for their sensitivity to MN digestion. Nuclei isolated from CHO-AT3-2 cells were subjected to digestion with MN for different time periods. The DNA was then purified, separated by electrophoresis, transferred to a nitrocellulose membrane, and hybridized with specific probes for exons 1, 2, or 5, respectively. The results in Fig. 5 show that the chromatin structure in the exon 1 region is much more sensitive to MN digestion than the chromatin in exons 2 and 5 or bulk genomic DNA. Although the distribution of the digested DNA of exons 1, 2, and 5 shows no difference from bulk genomic DNA after 1 min of MN treatment, with longer MN digestion periods the difference in the distribution of digested DNA becomes significant. After 2 min of MN treatment, most of exon 1 is in di-, tri-, tetra-, and pentanucleosome structures with a significant portion in mononucleosome structures. In contrast, most of exons 2 and 5 are in tetranucleosomes and higher nucleosome structures. After 5 min of MN treatment, there are more di- and mononucleosomes in the exon 1 region than those in exons 2 and 5. After 10 min of MN treatment, exon 1 is only in mono- and dinucleosomes, whereas significant amounts of exons 2 and 5 are still in nucleosome structures higher than dinucleosomes. The results in Fig. 5 also demonstrate that bulk genomic DNA is more resistant to MN digestion than the DNA in DHFR exons 1, 2, and 5. We conclude that the chromatin structure in the region of exon 1 is more open than that in the regions of...
Ample evidence has demonstrated that there are two major pathways for CPD repair in mammalian cells, namely TCR and GGR, with the former pathway repairing CPDs in the T strand and the latter pathway repairing CPDs in the NT strand of active genes and noncoding bulk genomic DNA (2–8, 14–19). Many results (33, 34) suggested that cultured rodent cells such as V79 and CHO cells are deficient in GGR of CPDs. However, several lines of evidence indicate that the repair of CPDs in mammalian cells may be much more complicated than our current understanding would indicate. For example, we have recently found that CPDs in both strands of the endogenous APRT gene of CHO cells are efficiently repaired and that this repair is transcription independent (18, 20). Furthermore, we have found that when the APRT gene is integrated at chromosomal positions different from the endogenous position, features of the repair of CPDs are different from those of the endogenous APRT gene even though the transcriptional activity of the integrated gene is the same as that of the endogenous gene. In one case, CPDs are repaired only in the T strand, and in two other cases CPDs are not repaired in either the T or NT strands (20). These results, together with our current findings that CPDs are efficiently repaired in the NT strand of exon 1 of the DHFR gene in CHO cells and that repair of CPDs shows a 5’ to 3’ gradient effect, suggest that CPD repair in mammalian cells is more complicated than via the described TCR and GGR pathways.

We have found that CPDs in the T strand are repaired more efficiently at the 5’-end of the DHFR gene than at the 3’-end of the gene. CPD repair in the T strand of the FMS, JUN, and hypoxanthine phosphoribosyltransferase (HPRT) genes in humans is also more efficient at the 5’-end than at the 3’-end of the gene (23, 35, 36). To further understand the mechanism of this transcription polarity-related repair efficiency in the T strand of the DHFR gene, we probed the chromatin structure at exons 1, 2, and 5 of this gene using MN digestion. The sensitivity to MN digestion reflects chromatin structure, with tight chromatin being more resistant. Our results show that chromatin structure in the exon 1 area is more open than in the exon 2 and 5 areas of the gene. Because transcription opens up chromatin structure, it is possible that the more open chromatin structure observed at the 5’-end as compared with the 3’-end may reflect that, at any given moment, more transcription is taking place at the 5’-end of the gene than at the 3’-end. Indeed, it has been found that the 5’-end of the DHFR gene is transcribed more frequently than the 3’-end, with many of the transcripts being incomplete (27). This suggests that more TCR will occur at the 5’-end of the gene than at the 3’-end of the gene as has been recently suggested by George et al. (36). It may be that additional transcription factors are present not only at the promoter but also throughout the 5’-end of the gene, rendering this region more accessible to the repair machinery than the 3’-end of the gene. The more open chromatin structure observed at exon 1 of DHFR and, consequently, the increased accessibility to NER machinery could explain the efficient repair of the NT strand in the exon 1 region. Efficient repair of CPDs in the NT strand has also been observed in the APRT and JUN genes (18, 20, 23). At the present time we are unable to demonstrate different sensitivities toward MN digestion between these two exon regions, which are too subtle to be detected by MN digestion kinetics, may cause different affinities toward the NER machinery, which may contribute to a polarity-related repair efficiency in the T strand of the DHFR gene.

Based on these results, we propose that the repair efficiency of a region of genomic DNA might be determined by chromatin structure. Most or at least a significant number of active genes may typically have very different chromatin structures than inactive genes or noncoding regions, and these structures may be much more accessible to and/or have a greater affinity for DNA repair proteins. Transcription-induced chromatin changes may enhance accessibility of the active genes to DNA repair or promote TCR in the T strand. If the chromatin structure of an active gene or a region is not already optimal for repair processes, then chromatin remodeling or transcription-induced chromatin changes may enhance the accessibility of this region to repair and promote transcription-coupled repair in the T strand. If the local chromatin structure surrounding a gene has already rendered the region maximally accessible to repair proteins (as may be the case for the exon 1 of the DHFR gene), then transcription would not be necessary to facilitate repair, and both strands might be repaired with equal efficiency.
Repair Heterogeneity of DHFR Gene

Acknowledgments—We thank Dr. Aziz Sancar and Dr. Steven Lloyd for their generous gifts of the plasmid pMS969 containing the photolyase gene and T4 endonuclease V.

REFERENCES

1. Friedberg, E. C. (1985) DNA Repair, pp. 1–78, W. H. Freeman and Company, New York
2. Friedberg, E. C., Walker, G. C., and Siede, W. (1995) DNA Repair and Mutagenesis, pp. 285–310, ASM Press, Washington, D.C.
3. Balajee, A. S., and Bohr, V. A. (2000) Gene (Amst.) 250, 15–30
4. Hanawalt, P. C. (2001) Mutat. Res. 485, 3–13
5. Sancar, A. (1996) Annu. Rev. Biochem. 65, 43–81
6. Wood, R. D. (1997) J. Biol. Chem. 272, 23465–23468
7. de Laat, W. L., Jaspers, N. G. J., and Hoeijmakers, J. H. J. (1999) Genes Dev. 13, 768–785
8. Mellon, I., Spivak, G., and Hanawalt, P. C. (1987) Cell 51, 241–249
9. Venema, J., Mullenders, L. H. F., Natarajan, A. T., van Zeeland, A. A., and Mayne, L. V. (1990) Proc. Natl. Acad. Sci. U. S. A. 87, 4707–4711
10. van Hoffen, A., Natarajan, A. T., Mayne, L. V., van Zeeland, A. A., Mullenders, L. H., and Venema, J. (1993) Nucleic Acids Res. 21, 5890–5895
11. Troelstra, C., Goul, A. V., Wit, J. D., Vermeulen, W., Bootsma, D., and Hoeijmakers, J. H. J. (1992) Cell 71, 839–853
12. van Hoffen, A., Venema, J., Meschini, K., van Zeeland, A. A., and Mullenders, L. H. F. (1995) EMBO J. 14, 360–367
13. Venema, J., van Hoffen, A., Karczag, V., Natarajan, A. T., van Zeeland, A. A., and Mullenders, L. H. (1991) Mol. Cell. Biol. 11, 4128–4134
14. Bohr, V. A., Smith, C. A., Okumoto, D. S., and Hanawalt, P. C. (1985) Cell 40, 359–369
15. Bohr, V. A., Okumoto, D. S., Ho, L., and Hanawalt, P. C. (1986) J. Biol. Chem. 261, 16666–16672
16. Spivak, G., and Hanawalt, P. C. (1996) Mutat. Res. 350, 207–216
17. Tang, M.-s., Pao, A., Zhang, X. S. (1994) J. Biol. Chem. 269, 12749–12754
18. Zheng, Y., Pao, A., Adair, G. M., and Tang, M.-s. (2001) J. Biol. Chem. 276, 16786–16796
19. Christians, F. C., and Hanawalt, P. C. (1992) Mutat. Res. 274, 93–101
20. Feng, Z., Hu, W., Komissarov, E., Pao, A., Hung, M., Adair, G. M., and Tang, M.-s. (2002) J. Biol. Chem. 277, 12777–12783
21. Vreeswijk, M. P., van Hoffen, A., Westland, A., Vrieling, H., van Zeeland, A. A., and Mullenders, L. H. (1994) J. Biol. Chem. 269, 31858–31863
22. Venema, J., Bartosova, Z., Natarajan, A. T., van Zeeland, A. A., and Mullenders, L. H. (1992) J. Biol. Chem. 267, 8852–8856
23. Tu, Y., Tonnaletti, S., and Pfeifer, G. P. (1996) EMBO J. 15, 675–683
24. Urlaub, G., Mitchell, P. J., Kas, E., Chasin, L. A., Funanage, V. L., Myoda, T. T., and Hamlin, J. L. (1986) Somatic Cell Mol. Genet. 12, 555–566
25. Nougak, T., and Hanawalt, P. C. (2000) Mol. Cell. Biol. 20, 1562–1570
26. Kuhnert, P., Peterhans, E., and Pauli, U. (1992) Nucleic Acids Res. 20, 1843–1848
27. Mitchell, P. J., Carothers, A. M., Han, J. H., Harding, J. D., Kas, E., Venolia, L., and Chaisin, L. A. (1986) Mol. Biol. Cell, 425–440
28. Morales, V., Giamarchi, C., Chailieux, C., More, F., Marsaud, V., Le Ricsou, S., and Richard-Poy, H. (2001) Biochimie (Paris) 83, 1029–1039
29. Liu, X., and Smerdon, M. J. (2000) J. Biol. Chem. 275, 23729–23735
30. Hara, R., Mo, J., and Sancar, A. (2000) Mol. Cell. Biol. 20, 9173–9181
31. Ura, K., Araki, M., Sasaki, H., Matsuini, C., Ito, T., Iwai, S., Mizukoshi, T., Kaneda, Y., and Hanaoka, F. (2001) EMBO J. 20, 2004–2014
32. Kornberg, R. D., and Lorch, Y. (1999) Cell 98, 285–294
33. van Zeeland, A. A., Smith, C. A., and Hanawalt, P. C. (1981) Mutat. Res. 82, 173–189
34. Hanawalt, P. C. (2001) Environ. Mol. Mutagen. 38, 89–96
35. Islas, A. L., and Hanawalt, P. C. (1995) Cancer Res. 55, 336–341
36. George, J. W., Salazar, E. P., Vreeswijk, M. P., Lamerdin, J. E., Reardon, J. T., Zdienicka, M. Z., Sancar, A., Kudkhodayan, S., Tebbs, R. S., Mullenders, L. H., and Thompson, L. H. (2001) Mol. Cell. Biol. 21, 7355–7365
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J. Biol. Chem. 2002, 277:38305-38310.
doi: 10.1074/jbc.M206375200 originally published online August 6, 2002

Access the most updated version of this article at doi: 10.1074/jbc.M206375200

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