Nucleosome Structure and Repair of N-Methylpurines in the GAL1-10 Genes of Saccharomyces cerevisiae*

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Nucleosome structure and repair of N-methylpurines were analyzed at nucleotide resolution in the divergent GAL1-10 genes of intact yeast cells, encompassing their common upstream-activating sequence. In glucose cultures where genes are repressed, nucleosomes with fixed positions exist in regions adjacent to the upstream-activating sequence, and the variability of nucleosome positioning sharply increases with increasing distance from this sequence. Galactose induction causes nucleosome disruption throughout the region analyzed, Galactose induction causes nucleosome disruption throughout the region analyzed, with those nucleosomes close to the upstream-activating sequence being most striking. In glucose cultures, a strong correlation between N-methylpurine repair and nucleosome positioning was seen in nucleosomes with fixed positions, where slow and fast repair occurred in nucleosome core and linker DNA, respectively. Galactose induction enhanced N-methylpurine repair in both strands of nucleosome core DNA, being most dramatic in the clearly disrupted, fixed nucleosomes. Furthermore, N-methylpurines are repaired primarily by the Mag1-initiated base excision repair pathway, and nucleotide excision repair contributes little to repair of these lesions. Finally, N-methylpurine repair is significantly affected by nearest-neighbor nucleotides, where fast and slow repair occurred in sites between pyrimidines and purines, respectively. These results indicate that nucleosome positioning and DNA sequence significantly modulate Mag1-initiated base excision repair in intact yeast cells.

Simple methylating agents, such as methyl methanesulfonate (MMS) and dimethyl sulfate (DMS), produce a variety of damaged bases in DNA of which N7-methylguanine (7MeG) and N2'-methyladenine (3MeA) constitute ~80 and 10%, respectively (1, 2). These N-methylpurines (NMPs), can be enzymatically removed or they can spontaneously depurinate to repair (NER) or certain base excision repair (BER) pathways.

In the nucleus of eukaryotic cells, DNA is packaged into a nucleoprotein complex known as chromatin (9). This complex provides the compaction and structural organization of DNA for processes such as replication, transcription, recombination, and repair. The fundamental subunits of chromatin are nucleosome cores, where ~147 bp of DNA is wrapped around a histone octamer (10). DNA between two adjacent nucleosome cores is called linker DNA, which varies in length from about 20 to 90 bp in different organisms and tissues, or between individual nucleosomes in the same cell (11). The effect of nucleosome structure on NMP repair is not understood. In rat liver cells, it was shown that the overall removal of NMPs occurred at a relatively uniform rate in different chromatin fractions (i.e. active chromatin, bulk genome and nuclear matrix) (12). On the other hand, within the yeast minichromosome YRpS01, there was a mild correlation between repair rates and nucleosome positioning in regions of the inducible GAL1:URA3 fusion gene, but not in the constitutively expressed HIS3 gene on the same plasmid (8).

To further address questions on the effect of nucleosome structure on repair of NMPs in intact cells, we examined repair in the divergent yeast GAL1-10 genes, which share a common upstream-activating sequence (UAS). These genes are induced to very high levels of expression in galactose, but are completely repressed in glucose (13). Extensive studies have been done on isolated nuclei or chromatin to map the nucleosome structure in the GAL1-10 region and the effects of galactose induction (14–17). However, it is possible that subtle changes in nucleosome structure of this region differ in whole cells, and were missed because of the procedure of nuclei and/or chromatin isolation. Thus, to examine the influence of nucleosome structure on repair of NMPs in intact cells, we developed a nucleosome mapping procedure using bleomycin (BLM), which avoids isolation of nuclei or chromatin. This basic glycopeptide-derived antibiotic has been shown to preferentially cleave nucleosome linker DNA in isolated Chinese hamster nuclei (18), lysophosphatidylcholine-permeabilized human cells (19), and whole yeast cells (20). However, BLM has not been used to map nucleosome positions in specific sequences in whole cells, since...
highly specific cleavage in linker DNA has not been achieved. By using the mild nonionic detergent digitonin to efficiently permeabilize yeast cells, and rich medium to effectively stop BLM cleavage during DNA isolation, we were able to map nucleosome structure at nucleotide resolution in the GAL1-10 region in whole yeast cells and directly correlate repair of NMPs with nucleosome structure.

EXPERIMENTAL PROCEDURES

**Yeast Strains**—DBY747 (MAT a ura3-52 his3–Δ1 leu2–3 leu2–112 trpl–128) and its isogenic mutant strains JC8901 (mag1Δ::hisG–URA3–hisG), WXY9379 (rad1Δ::LEU2), and WXY9380 (mag1Δ::hisG rad1Δ::LEU2) were generously provided by Dr. Wei Xiao (University of Saskatchewan, Canada). Strain Y452 (MAT α ura3-52 his3–1 leu2–3 leu2–112 trp1–289 mag1Δ::hisG–URA3–hisG) was provided by Dr. Louise Prakash (University of Texas Medical Branch, Galveston, TX).

**BLM Cleavage of Chromatin and Naked DNA**—Yeast cells were grown at 30 °C in minimal medium containing 2% glucose or 2% galactose to late-log phase (OD600 "1.0). After washing twice with ice-cold 2% glucose for glucose cultures) or 2% galactose (for galactose cultures), the cells were resuspended in 50 mM NaCl, 2 mM MgCl2, 0.02% glucose or galactose, to give a final concentration of 0.05% and 50 °C/DMS treatment, pellets of 2 × 10^9 cells were mixed with 2 ml of ice-cold nuclei isolation buffer (NIB: 50 mM Tris-HCl, 2 mM
with 8M LiCl and left on ice overnight. The samples were then treated with RNase A, and extracted with phenol/chloroform/isoamyl alcohol (25:24:1). After re-precipitation, the DNA was precipitated, and then cooled to an annealing temperature. The attached fragments were labeled using [α-32P]dATP (PerkinElmer Life Sciences) and non-radioactive dCTP, rather than [α-32P]dATP alone (23, 24). The labeled fragments were resolved on sequencing gels and exposed to PhosphorImager screens (Molecular Dynamics). Sequence ladders were generated from PCR products of the GAL1-10 fragments, using the rapid Maxam-Gilbert method (25). The ladders were labeled using the same procedure as that for the BLM or DMS treated DNA samples.

Quantitation of BLM Cleavage and NMPs—The BLM cleavage at individual sites is reflected by the band intensity on a gel. The doses of BLM used were relatively low, to ensure that cleavage by BLM followed single-hit kinetics for the majority of fragments analyzed. However, even under these conditions, a small portion of the fragments still have more than one cleavage, and a small portion of the signal at a site will not show up on a gel if the cleavage occurs upstream (relative to the labeled end) of the site. The effect of this "hidden signal" increases as a cleave site is more distant from the labeled 3’-end, which runs at the bottom of a gel. For a fragment of ~400 nucleotides (i.e. the maximum length quantified on the sequencing gels), the hidden signal at a site close to the top of a gel can be as much as 30% of the total signal in a band. To correct for this, the following algorithm was used: Let A denote the total signal intensity in a gel lane, X the actual signal intensity (i.e. not reduced by upstream cleavages) at position N in a gel lane, and C the total signal intensity upstream of position N (the upstream sites run below position N in a gel lane). The proportion of signal intensity at position N is X/A and the proportion of signal intensity upstream of position N is C/A. If B is the total number of cleavages at position N and those upstream of position N on the same fragment is (X/A) × (C/A), or (X × C/A). If B denotes the observed signal intensity at position N on the gel, then the total number of cleavages at position N and those upstream of position N on the same fragments is (X × C/A). Therefore, the number of cleavages at position N and those upstream of position N on the same fragment is A × [(X/A) × (C/A)], or (X × C/A). If B denotes the observed signal intensity at position N on the gel, then the actual signal intensity (X) at position N is (A × B)/(A – C).

The signal intensity at all pixels in a gel lane was measured by ImageQuaNT software (Molecular Dynamics) and the data transferred to Microsoft Excel. After the gel background signal was subtracted, the
total signal intensities in different lanes of a gel were normalized to the same amount. The signal intensity at all pixels along a gel lane (including the control lanes not cleaved with BLM) was then corrected using the above described equation $X = (A \times B)/(A - C)$. The signal intensities in a lane containing the uncleaved sample were used as a baseline for other lanes that contain BLM cleaved samples. As the signal intensities along a gel lane of uncleaved sample fluctuate, the baseline was smoothed by local averaging of signal intensities (at continuous intervals of 100–200 pixels) in the lane. The corrected signal intensities in a lane containing BLM cleaved sample were then corrected by subtraction of the smoothed baseline. The data was then imported to PeakFit (SPSS, Inc.) to fit and deconvolute peaks corresponding to the individual bands on the gels (24). Quantitation for NMPs followed the same procedure as that for BLM cleavage.

RESULTS

Nucleosome Structure in the GAL1-10 Genes—Wild type (Y452) yeast cells were grown in glucose or galactose medium, permeabilized with digitonin and treated with BLM. The time used for digitonin permeabilization and BLM treatment was 12 min, which is just long enough to see noticeable BLM cleavage in chromatin DNA. Under these conditions, different concentrations of BLM showed a linear response of band intensity (Figs. 1 and 2 and data not shown). Therefore, the cleavage by BLM followed single-hit kinetics for the majority of the chromatin DNA fragments.

Genomic DNA was isolated from the BLM-treated cells and cut with restriction enzyme to release the fragments of interest. A total of 5 overlapping restriction fragments were analyzed for each strand of the GAL1-10 region. The restricted fragments were strand-specifically end-labeled, resolved on DNA sequencing gels, and exposed to phosphorimager screens. For comparison, naked DNA of the same GAL1-10 region was also treated in parallel with the chromatin DNA. As can be seen from the gels in Figs. 1 and 2, naked DNA was cleaved at very low concentrations of BLM (5 milliunits/ml) and Fe$_2$O$_4$ (1 μM), and no cleavage was observed in the presence of BLM or Fe$_2$O$_4$ alone (lanes 1 and 2 in Figs. 1 and 2; data not shown). Almost all pyrimidines' 3' to guanines are cleaved by BLM (compare lanes 2 in each gel with the sequencing lanes C+T and G) consistent with previous reports (26). Most adenines' 3' to guanines are also cleaved, but generally to a lesser extent (Figs. 1 and 2, arrowsheads to the right of gels). Furthermore, some sites of weak cleavage are also observed at pyrimidines' 3' to adenines (Figs. 1 and 2, small horizontal bars on the right side of gels).

Much higher concentrations of BLM and Fe$_2$O$_4$ are needed for cleavage of chromatin DNA in permeabilized cells to reach the same level as that for naked DNA (Figs. 1 and 2). Furthermore, there was consistently more cleavage of chromatin DNA in glucose cultures than in galactose cultures, when the same level of BLM was applied (Figs. 1 and 2; data not shown). Most likely, BLM is hydrolyzed more rapidly in galactose cultures due to the induction of BLM hydrolase, which is encoded by the GAL6 gene (27).

To determine the protection level of a nucleosome to its DNA, the ratios of band intensities for BLM cleavage sites on naked DNA and chromatin DNA (see Figs. 1 and 2) from glucose (open triangles) and galactose (solid triangles) cultures are needed for nucleosome-free DNA in both glucose and galactose cultures. When the same concentration of BLM was applied (Figs. 1 and 2; data not shown). Most likely, BLM is hydrolyzed more rapidly in galactose cultures due to the induction of BLM hydrolase, which is encoded by the GAL6 gene (27).

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The BLM cleavage pattern at most sites in the UAS region is similar between chromatin (both glucose and galactose cultures) and naked DNA (Figs. 1C and 2C), suggesting the UAS region is nucleosome-free in both glucose and galactose cultures. This is in agreement with DNase I (28) and (methionpropyl–EDTA)iron(II) (16) mapping in isolated nucleoli. However, a few sites in the UAS region show inhibition or enhancement of BLM cleavage (Figs. 1C and 2C, UAS region), indicating the binding of nonhistone protein(s), most notably Gal4, to this region may modulate BLM cleavage.

In glucose cultures, where the genes are repressed, a region of about 150 bp on each side of the UAS is strongly protected from BLM cleavage (Figs. 1, B and C, 2, B and C; and 3, see regions marked by ovals e and f), indicating that each of these...
regions contains a nucleosome with a fixed position on DNA. The protection of flanking −150 bp regions (Figs. 1–3, ovals d and g) is less apparent, and the protection diminishes with increasing distance from the UAS (qualitatively represented by the shading of ovals in Figs. 1–3). Indeed, the protection levels can be 10-fold greater in the core regions of nucleosomes (Figs. 1–3), indicating that the variability of nucleosome positions sharply increases with increasing distance from the UAS. These results indicate that the variability of nucleosome positions markedly increases with distance from the UAS in intact cells.

In galactose cultures, where GAL1-10 genes are induced, all the nucleosome core sequences in the GAL1-10 region analyzed are less protected from BLM cleavage (Figs. 1–3), indicating nucleosomes are disrupted upon galactose induction. This disruption is most striking in nucleosomes e and f (Figs. 1–3), which are adjacent to the UAS, than those of nucleosomes a, b, c, h, and i, which are farther away from the UAS. These results indicate that the variability of nucleosome positions sharply increases with increasing distance from the UAS in intact cells.

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**Induction of NMPs in the GAL1-10 Genes**—The same wild type (Y452) yeast cells as those used for nucleosome mapping were used for analyzing NMP induction and repair in the GAL1-10 region. The cells were treated with 0.03% DMS for 2 min to induce NMPs (see “Experimental Procedures”). After different times of repair incubation, genomic DNA was isolated, digested with restriction enzymes, and cleaved at NMPs by hot alkaline treatment. The cleaved fragments were strand-specifically end-labeled, resolved on DNA sequencing gels and exposed to phosphorimager screens. As can be seen from the gels in Figs. 4 and 5, the main type of NMPs induced is 7MeG (e.g., compare 0-h lanes with G lanes), while 3MeA is induced to a much lower extent (e.g., compare 0 h lanes with G and GA lanes). This pattern of NMP induction is similar to that seen with the yeast minichromosome YRpS01 (8) and to that of other past reports (2).

In galactose cultures, a strong protection from DMS methylation is seen at Gs in the triplet sequences of CGG, AGG, or CGC located at both ends of the palindromic Gal4 binding sites (brackets in Figs. 4C and 5C; Gs marked with arrowheads on the right side of gels), consistent with a previous report (29). Meanwhile, an enhancement of methylation can also be seen in some sites of the UAS region, especially in the top strand (Figs. 4 and 5). Moreover, there is a difference between glucose and galactose cultures in NMP yield at several sites in the promoter regions of the two genes (Figs. 4B and 5B, stars on the right side of gels). On the other hand, NMP yields at most sites throughout the region are similar between the two cultures (Figs. 4 and 5), indicating that the presence of nucleosomes does not markedly affect NMP induction. This agrees with a previous in vitro study showing that formation of nucleosomes does not significantly modulate NMP induction by DMS (30).

**Modulation of NMP Repair by Nearest-Neighbor Nucleotides**—The repair rates of NMPs at different sites were dramatically different (>30-fold at sites) (Figs. 4–6). As can be seen from the gels in Figs. 4 and 5, most NMP sites located between pyrimidines (C or T) were repaired much faster than NMPs between purines (A or G), and those located between a purine and a pyrimidine were repaired at intermediate rates.
In order to assess the generality of these observations, the percentages of 7MeGs remaining following different times of repair incubation in the same contexts of nearest-neighbor nucleotides (i.e. between purines, pyrimidines, and between a purine and a pyrimidine) were averaged. As can be seen from Fig. 7, the statistical data confirm these observations. As limited 3MeA sites were available for analysis, the effect of the nearest-neighbor nucleotides on 3MeA repair cannot be analyzed by this method.

Modulation of NMP Repair by Nucleosome Structure in the GAL1-10 Genes—In glucose cultures, the strongest correlation between nucleosome positioning and NMP repair can be seen in the two nucleosomes (e and f) with the most fixed positions (Figs. 4–6). In these regions, slow repair occurs in the nucleosome core DNA and faster repair takes place in nucleosome linker or nucleosome-free DNA (i.e. the UAS region). This correlation sharply fades off in the nucleosomes that are more distant from the UAS, in agreement with the observations that the variability of nucleosome positioning sharply increases with distance from the UAS. This profile of correlation can be seen more clearly after the individual times required for repairing 50% of the NMPs (T1/2) are smoothed (by locally averaging the values in continuous 40-nucleotide intervals) (Fig. 6B). However, with the marked effects of nearest-neighbor nucleotides on NMP repair (see above) superimposed on the effects of nucleosome structure, the nucleosome effect is masked and more difficult to discern in the regions distant from the UAS.

Galactose induction causes enhancement of repair in both strands of the nucleosome core DNA (Figs. 4–6). Indeed, increases of as much as 8-fold occur in the core regions of nucleosomes e and f, which are disrupted most dramatically (Fig. 6C). Interestingly, this galactose-enhancement of NMP repair also fades off with distance from the UAS (Fig. 6C), correlating well with the nucleosome positioning and disruption trends (compare Figs. 3B and 6C).

The Role of NER in NMP Repair—It has been shown that mag1 mutants that are defective in NER (rad1 or rad2 mutants) are extremely sensitive to MMS-induced killing, and the effects of these mutations are synergistic (31). This suggests that NER may provide an alternative pathway for repair of NMPs. To assess the contribution of NER, repair of NMPs was analyzed in different genomic regions of isogenic wild type, mag1, rad1, and mag1 rad1 cells. As examples, NMP repair in regions of the GAL1 gene and the constitutively expressed RPB2 gene, which encodes the second largest subunit of RNA polymerase II, is shown in Fig. 8. As can be seen, essentially normal repair occurred in rad1 cells. In contrast, deletion of the MAG1 gene almost completely abolishes repair of NMPs, although residual repair can be seen if the RAD1 gene is present in the mag1 cells (Fig. 8). Repair analysis in other genomic regions shows the same trends (data not shown), indicating NER plays little, if any, role in the repair of NMPs in S. cerevisiae.

**DISCUSSION**

We have mapped nucleosome structure and repair of N-methylpurines in whole yeast cells. The major nucleosome positions observed in this report agree well with past reports on isolated nuclei or chromatin (15–17). However, in the present study, nucleosomes that occupy fixed positions in the GAL1-10 promoter region were only observed in the regions adjacent to the UAS in glucose cultures, and the variability of positions sharply increases with increasing distance from the UAS (Figs.
This observation fits well with the finding that the binding of Y factor to a short sequence that overlaps the Gal4 binding site II of the UAS serves as a nucleosome positioning boundary (15). In contrast, mapping with isolated nuclei or chromatin showed longer arrays of precisely positioned nucleosomes in the entire GAL1-10 region (15–17). This difference may reflect a selection for lowest energy nucleosome positions in chromatin during nuclei isolation, compared with more dynamic features of nucleosomes that are distant from the UAS in intact cells. This notion agrees well with the NMP repair data (Figs. 4–6), as well as results of nucleotide excision repair of ultraviolet light induced cyclobutane pyrimidine dimers.

Our data strongly suggest that nucleosomes in intact cells inhibit NMP repair. First of all, in nucleosomes with fixed positions (especially e and f), repair is much slower in the core DNA sequences than in linker DNA (Figs. 4–6). Secondly, induction of transcription enhanced NMP repair, with the regions close to the UAS (where nucleosome disruption is most dramatic) being most striking (Fig. 6C). We note that this enhancement is unlikely to be caused by a direct coupling between transcription and repair, as no strand bias for repair is observed in these regions (Figs. 4–6). This enhancement, however, correlates well with nucleosome positioning and disruption profiles (compare Figs. 3B and 6C). As multiple factors seem to influence repair of NMPs, nucleosome affected NMP

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repair may be obscured, especially in the more dynamic nucleosomes in the cell. In addition to the influence of nearest neighbor nucleotides (discussed below), the binding of nonhistone proteins may also affect NMP repair. Indeed, repair of NMPs in the UAS region was faster in glucose cultures than in galactose cultures, where the nonhistone protein Gal4 is bound to the UAS region (Figs. 4C, 5C, and 6). These considerations may explain why little or no correlation between NMP repair and nucleosome positioning is seen in regions distant from the UAS. In a previous report on NMP repair in the yeast minichromosome YRpSo1 (8), we observed a mild correlation between repair rates and nucleosome positioning in some regions of the GAL1:URA3 fusion gene, but not in the HIS3 gene (8). Presumably, these observations reflect differences in dynamics of nucleosome positions in these genes on the minichromosome.

NER and Mag1-initiated BER are synergistic in response to MMS-induced DNA lesions (31), indicating a subset of these lesions may be repaired by both pathways. Furthermore, in vitro experiments with purified human 3-methyladenine-DNA glycosylase (MPG protein), which is the counterpart of yeast Mag1, show that MPG interacts with the human homologue of Rad23 (hHR23) (32). Importantly, this interaction elevates the rate of MPG-catalyzed excision from hypoxanthine-containing substrates (32). Our results with mag1 and rad1 mutant cells suggest that, in S. cerevisiae, repair of NMPs is accomplished primarily by the Mag1-initiated BER pathway, and that NER contributes very little to the repair of these lesions. We also analyzed NMP repair in mutants lacking Rad7, Rad16 and Rad23 proteins, each of which is a component of the NER pathway (33). None of these mutants showed a detectable deficiency in repair of NMPs (data not shown). Thus, it is possible that the substrate shared by NER and Mag1 initiated BER is not NMPs, but a rare DNA lesion that cannot be detected by our technique. We note, however, that a very small amount of repair of NMPs does occur in mag1 cells if Rad1 is present (Fig. 8). This residual repair may be sufficient to cause the observed synergy between NER and the Mag1 initiated BER for MMS-induced lesions.

A number of organisms have a strong backup pathway for repairing NMPs. In E. coli, the AlkA and Tag proteins can initiate repair of these lesions, even though the substrate specificity differs for the two enzymes (34, 35). In Schizosaccharomyces pombe, NMPs may be repaired primarily through the NER pathway, rather than a BER pathway (36). In mammalian cells, a pathway may exist that repairs 7MeG in the absence of the ordinarily used Aag DNA glycosylase (37). However, deletion of the MAG1 gene in S. cerevisiae cells almost completely abolishes NMP repair (Fig. 8 and data not shown), and no NMP repair can be seen in mag1 rad1 double deletion.
cells. This indicates that S. cerevisiae may lack a strong back up pathway for repairing NMPs.

Finally, as observed with the yeast minichromosome YRpS01 (8), there was a significant correlation between the nearest neighbor nucleotides of NMP sites and the repair of NMPs in the yeast genomic GAL1-10 region. These data suggest that the same repair machinery is used for repairing NMPs in genomic and minichromosome DNA. This finding is similar to that of Sweder and Hanawalt (38), who studied repair of ultraviolet light-induced cyclobutane pyrimidine dimers in genomic and minichromosome DNA of yeast.

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REFERENCES
1. Singer, B., and Grunberger, D. (1983) Molecular Biology of Mutagens and Carcinogens, pp. 55–78, Plenum Press, NY
2. Pieper, R. O. (1998) in DNA Damage and Repair, Vol. 2: DNA Repair in higher eukaryotes (Nickoloff, J. A., and Hoekstra, M. F., eds) pp. 199–222, Humana Press Inc., Totowa, NJ
3. Posnick, L. M., and Samson, L. D. (1999) Mutat. Res. 257, 127–143
4. Xiao, W., Chow, B. L., Hanna, M., and Doetsch, P. W. (2001) Mutat. Res. 487, 137–147
5. Hanawalt, P. C. (2001) Mutat. Res. 485, 3–13
6. Scicchitano, D. A., and Hanawalt, P. C. (1998) Proc. Natl. Acad. Sci. U. S. A. 95, 3050–3054
7. Ye, N., Holmqvist, G. P., and O’Connor, T. R. (1998) J. Mol. Biol. 284, 269–285
8. Li, S., and Smerdon, M. J. (1999) J. Biol. Chem. 274, 12201–12204
9. Wolfe, A. P. (1999) Chromatin: Structure and Function, 3rd Ed., pp. 7–172, Academic Press, London and New York
10. Lager, K., Mader, A. W., Richmond, R. K., Sargent, D. F., and Richmond, T. J. (1997) Nature 389, 251–260
11. van Holde, K. E. (1989) Chromatin, pp. 289–354, Springer-Verlag KG, Berlin.
12. Ryan, A. J., Billett, M. A., and O’Connor, P. J. (1996) Carcinogenesis 7, 1497–1503
13. Bash, R., and Lohr, D. (2001) Prog. Nucleic Acids Res. Mol. Biol. 65, 197–259
14. Lohr, D., Torchia, T., and Hopper, J. (1987) J. Biol. Chem. 262, 15589–15597
15. Feder, M. J., Lue, N. F., and Kornberg, R. D. (1988) J. Mol. Biol. 204, 109–127
16. Feder, M. J., and Kornberg, R. D. (1989) Mol. Cell. Biol. 9, 1721–1732
17. Cavalli, G., and Thomas, F. (1989) EMBO J. 8, 4603–4613
18. Koe, M. T., and Heo, T. C. (1978) Nature 271, 83–84
19. Sidik, K., and Smerdon, M. J. (1990) Cancer Res. 50, 1613–1619
20. Moore, C. W. (1998) Cancer Res. 58, 6537–6543
21. Solomon, L. R., Beerelli, R. D., and Moseley, P. L. (1989) Biochemistry 28, 9932–9937
22. Slater, M. L. (1972) J. Bacteriol. 113, 263–270
23. Li, S., and Waters, R. (1996) Carcinogenesis 17, 1549–1552
24. Li, S., Waters, R., and Smerdon, M. J. (2000) Methods: Companion Methods Enzymol. 22, 170–179
25. Sambrook, J., Fritsch, E. F., and Maniatis, T. (1989) Molecular Cloning: A Laboratory Manual, 2nd Ed., pp. 13.95–13.97, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY.
26. D’Andrea, A. D., and Haseultine, W. A. (1978) Proc. Natl. Acad. Sci. U. S. A. 75, 3608–3612
27. Zheng, W., Xu, H. E., and Johnston, S. A. (1997) J. Biol. Chem. 272, 30350–30355
28. Lohr, D. (1984) Nucleic Acids Res. 12, 8457–8474
29. Giniger, E., Varnum, S. M., and Ptashne, M. (1985) Cell 40, 767–774
30. McGhee, J. D., and Felsenfeld, G. (1979) Proc. Natl. Acad. Sci. U. S. A. 76, 2133–2137
31. Xiao, W., and Chow, B. L. (1998)Curr. Genet. 33, 92–99
32. Mass, F., Bouziane, M., Dammann, R., Masutani, C., Hanaoka, F., Pfeifer, G., and O’Connor, T. R. (2000) J. Biol. Chem. 275, 28433–28438
33. Prakash, S., and Prakash, L. (2000) Mutat. Res. 451, 13–24
34. Thomas, L., Yang, C. H., and Goldthwait, D. A. (1962) Biochemistry 21, 1162–1169
35. Seeberg, E., Eide, I., and Bjeras, M. (1995) Trends Biochem. Sci. 20, 391–397
36. Memisoglu, A., and Samson, L. (2000) J. Bacteriol. 182, 2104–2112
37. Smith, S. A., and Engelward, B. F. (2000) Nucleic Acids Res. 28, 3284–3300
38. Sweder, K. S., and Hanawalt, P. C. (1992) Proc. Natl. Acad. Sci. U. S. A. 89, 10696–10700
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