The gene encoding the high output isofrm of nitric oxide synthase represents a large class of alarm and defense genes transcriptionally induced in response to bacterial lipopolysaccharide (LPS). The promoters of most of these genes contain at least two LPS-response elements, one of which commonly binds transcription factor Oct-1. Here we describe a novel LPS-response element identified in the inducible nitric oxide synthase promoter, termed LREAA, which contains critical adenosine residues lying 19-20 base pairs downstream of the proximal NF-κB binding element (NFκBd). Both NFκBd and LREAA are required for LPS-induced promoter activity. A protein partially recognized by antibody against transcription factor Oct-1 binds to the LREAA element constitutively in untreated macrophages while contributing to a DNA-protein complex that includes NF-κB p50 in macophages treated with LPS. NF-κB p50 and the LREAA-binding proteins may together recruit an LPS-triggered transactivator of transcription.

Endotoxic lipopolysaccharide (LPS), the major constituent of the cell walls of Gram-negative bacteria, is one of the most potent agonists in biology. Mammalian, avian, and insect phagocytes (1-4) respond to LPS by altering the expression of numerous genes. This response can help protect the host from infection but can also cause systemic inflammation (1, 2). A recent review catalogued 21 mammalian genes induced by LPS, and in 19 of these LPS-response elements have been characterized (5). Transcription factors binding to these promoter elements have been identified with the following frequency: NF-κB/Rel, 14 genes; NF-IL6, 9 genes; AP-1, 2 genes; and IL1β-UNF1, NF-κBα, NF-κBα, c-Jun/AP2, IRSE-binding protein, NF-M, ATF family members, and c-Jun, 1 gene each. LPS-inducible genes include NOS2 (iNOS), encoding the high output isofrm of nitric oxide synthase (6, 7), which contributes to both antimicrobial defense (8) and LPS-induced hypotension (9). Transcriptional induction of iNOS by LPS (6, 10, 11) requires binding of transcription factor NF-κB/Rel to a promoter element, NFκBd (12), at position -85 to -76 (13-16). Another NFκB binding site NFκBu (12) at position -971 to -962 (13, 14) also plays a role (16).

Although NFκB/Rel is essential for the LPS induction of iNOS, it is not sufficient (12, 17). Additional transcription factors are required (12), which is consistent with the precedent that at least two-thirds of LPS-induced genes studied have more than one LPS-response element (5). In the present work, a second LPS-response element (LREAA) is identified in the iNOS promoter that has not been previously recognized in any gene.

**EXPERIMENTAL PROCEDURES**

**Cell Culture**—The macrophage cell line RAW 264.7 (American Type Culture Collection) was cultured in complete medium (RPMI 1640 supplemented with 10% fetal bovine serum, 2 mM l-glutamine, and 200 μg/ml penicillin and streptomycin) as described (13).

**Reagents**—Poly(dI-dC)poly(dI-dC) was from Pharmacia Biotech Inc. and isotes were from Amersham Corp. Santa Cruz Biotechnology, Inc. (Santa Cruz, CA) supplied affinity-purified goat or rabbit IgGs against synthetic peptides derived from NFκBd proteins p50, p52, p65 (RelA), c-Rel (C), and RelB, and from transcription factors Oct-1, Oct-2, Pit-1, Stat1(γ), c-Jun/AP-1, c-Fos, Ets-1/Ets-2, and C/EBPα. Rabbit IgG against purified recombinant murine IRF-1 was prepared by Tanaka Nomura and Heinz Ruffner and kindly provided by Dr. Luis Reis (University of Zurich, Zurich, Switzerland). LPS from Escherichia coli 0111:B4 was from Sigma.

**Plasmids**—Plasmids p7iNOS-CAT and p8.11iNOS-CAT contain the iNOS promoter and a reporter gene for chloramphenicol acetyltransferase (CAT). p7iNOS-CAT (18) contains a full-length promoter, including a basal promoter and an upstream enhancer; p8.11iNOS-CAT (12) contains only the basal promoter. Polymerase chain reaction-engineered mutations of element NFκBd (from GGG to CTC) and of element LREAA (from AA to CG) were individually introduced into p8.11iNOS-CAT to form p8.11LRE and p8.11LRE, respectively. Similarly, mutant constructs p7LRE and p7LRE were formed from p7iNOS-CAT. DNA sequence analysis confirmed the mutation of these elements without unwanted mutations elsewhere.

**Transient Transfection and CAT Assays**—RAW 264.7 cells were transfected by a modification of the DEAE-dextran procedure (19). The DNA used for transfection was prepared by the EndoFree plasmid kit (QIAGEN Inc., Chatsworth, CA). Media and DNA at the concentrations used contained <50 pg/ml LPS (QCL-1000 kit, BioWhittaker, Inc., Walkersville, MD). Cells were washed twice with serum-free RPMI and suspended at 5-9 x 10^6/ml in RPMI prewarmed to 37 °C containing DEAE-dextran (250 μg/ml) and 50 μM Tris (pH 7.4). 10 μg of DNA was added to 2 ml of cell suspension at 37 °C for 45 min with occasional shaking. Cells were shocked with 10% Me2SO for 1 min at room temperature, washed, and distributed to two 100-mm plates with 10 ml of complete medium. After 24 h at 37 °C, 5% CO2, LPS (100 ng/ml) was added to some of the plates. About 16 h later, the cells were washed with ice-cold phosphate-buffered saline, resuspended in 0.25 M Tris (pH 8.0), and frozen and thawed 3 times. Lysates were centrifuged (11,700 x g, 10 min, 4 °C), and the supernatant was heated at 65 °C for 10 min to inactivate CAT inhibitors and then centrifuged as above. The supernatant (1 or 10 μg) was assayed for CAT by a TLC method (20), and protein content was determined (21).

**Oligonucleotides and Probes**—Single-stranded oligonucleotides (Oligos Etc., Inc., Guilford, CT) were annealed with the complementary strand by polymerase chain reaction to form double-stranded oligomers with 5’ overhang. To prepare probes (see Table I), double-stranded oligomers were filled in by the Klenow fragment of DNA polymerase I with [α-32]dCTP and the three other nonradiolabeled dNTPs. To prepare competitors, all four dNTPs were nonradiolabeled.
**Electrophoretic Mobility Shift Assay**—Binding was tested in 15 μl of solution by incubating 1 μg of nuclear extract with 20 μM HEPES, pH 7.9, 1 mM EDTA, 60 mM KCl, 12% glycerol, 1 mM dithiothreitol, 2 μg of poly(dI-dC)·poly(dI-dC) in the presence or absence of competitor or antibody for 20 min, followed by a 20-min incubation at room temperature with probe (200,000 cpm). Products were electrophoresed at 30 mA for at least 3 h on 4.8% polyacrylamide gels in high ionic strength buffer (50 mM Tris, 380 mM glycine, 2 mM EDTA, pH 8.5) and dried gels were analyzed by autoradiography.

**UV Cross-linking Analysis**—50 μg of nuclear extract and 106 cpm of bromodeoxyuridine-containing probe DLI was reacted in a total volume of 60 μl. The electrophoretic mobility shift assay gel was exposed to x-ray film for 10 min to localize the complex of interest. Excised gel was UV-irradiated (366 nm) 5 cm from an inverted transilluminator at 4 °C for 60 min, boiled with sample buffer for 5 min, and analyzed by 10% SDS-polyacrylamide gel electrophoresis and autoradiography.

**RESULTS**

**An LPS-response Element (LREAA) Distinct from NFkB**

**Confers Inducibility of the iNOS Promoter by LPS**—Construct p8.11iNOS-CAT contains a fragment of the 5′-flanking region of the mouse iNOS gene (−85 to +161) that includes the NFkB element (−85 to −76) and confers LPS-inducible promoter activity on transfected RAW 264.7 mouse macrophages (12). LPS responsiveness was lost in p8.13iNOS-CAT, from which the NFkB element was eliminated (12). In this work, two mutated constructs derived from p8.11iNOS-CAT were prepared by (Fig. 1A) and tested for their promoter activity as induced by LPS (Fig. 1B). In p8.11iNOS-CAT, three nucleotides of the NFkB element were mutated, from GGGACTCTCC to CTCACTCTCC. This reduced LPS-induced promoter activity to 3.2 ± 1.3% of wild type (mean ± S.D., three experiments), consistent with an earlier finding that nuclear protein failed to bind to the NFkB element when it carried the same mutation (12). Surprisingly, mutation of two nucleotides (from AA to CG) located 19–20 base pairs downstream from the 3′ end of the NFkB element, as seen in p8.11iNOS-CAT, also nearly abolished LPS-induced promoter activity leaving only 2.0 ± 0.3% of activity as in wild type (mean ± S.D., three experiments). This new LPS-response element will be called LREAA. When the same mutations of elements NFkB and LREAA were introduced into the full-length promoter construct p7iNOS-CAT (Fig. 1A) to form p7iamond and p7LREEm, LPS-induced transcription was also substantially reduced (Fig. 1C). Therefore, both elements play an important role in the full-length promoter as well as in small fragments.

**Contribution of Both LREAA and NFkB to the Binding of Nuclear Proteins on the iNOS Promoter Correlates with Induction of the Gene by LPS**—Oligonucleotides derived from the iNOS promoter with or without mutation (Table I) were used as probes or competitors in electrophoretic mobility shift assays to analyze the DNA binding activity of nuclear extracts from cells cultured with or without LPS. As described earlier (12), a cycloheximide-sensitive DNA-protein complex termed “X” was formed upon LPS induction when probe B was used (Fig. 2A, lane 2). In Fig. 2B, two other faster migrating complexes, designated “Z” and “Y” in Fig. 2A (not labeled on Fig. 2A in Ref. 12), were present whether or not the cells were exposed to LPS. Without LPS, complex Z was strong and complex Y faint; LPS increased the amount of complex Y without appreciably changing the amount of complex Z (see Fig. 2 in Ref. 12).

Probe D19 nucleotides shorter than probe B at the 3′ end but still contains elements NFkB and LREAA. Probe D had the same binding activity as probe B, forming complexes X, Y, and Z with nuclear extracts from LPS-induced cells (Fig. 2A, lane 4). Thus, the nucleotides between −85 and −50 of the iNOS promoter are sufficient to sustain the formation of all three complexes.

**Comparison assays established that LREAA together with NFkB** contributed to the formation of these complexes. Complexes X and Y but not Z were competed by excess nonlabeled oligomer A containing element NFkB but not LREAA (Fig. 2, compare lanes 2 and 4). Such competition did not occur with oligomer B (labeled with a161), whose NFkB element was mutated (Fig. 2B, compare lanes 2 and 6). On the other hand, oligomer C, which contained the LREAA element, blocked the formation of complex Z (Fig. 2B, compare lanes 1 and 7 with LPS and lanes 2 and 8 with LPS) and most of complex X (compare lanes 2 and 8). No competition was seen using oligomer C (labeled with a mutated LREAA element (lanes 9 and 10)).

**Results of transcription (Fig. 1B)** and competition assays (Fig. 2B) were mirrored by tests of direct binding to mutated probes (Fig. 2, C–E). Taking the formation of complexes X, Y,
and Z upon LPS induction as wild type DNA binding activity (Fig. 2C, lane 2), the incomplete formation of these complexes resulted from mutation of either NFκBd (lane 3) or LREAA (lane 4) in the context of probe D. Probe DkBm containing a point mutation of element NFκBd did not sustain formation of complex X or Y but still formed complex Z (Fig. 2C, lane 3; note its slightly slower migration). On the other hand, complex Z and most of complex X were absent using probe DkBm containing the mutated element LREAA; in the meantime, complex Y became stronger and was accompanied by an complex migrating more slowly than Y (lane 4). Probe DkBmLREm, in which both elements are mutated, formed none of the complexes (lane 5). Probe C, containing LREAA but not NFκBd, formed complex Z alone (Fig. 2F, lanes 1 and 2), whereas no complex formed on the mutated probe CkBmLREm (lanes 7 and 8). Thus, LREAA and NFκBd were the only two elements required for the binding of nuclear factors on the iNOS promoter between nucleotides −85 and −50.

The complex Z that formed with probe C or the mutated probe DkBm shared the same characteristics as the complex Z that formed with wild type probe D. Its formation was independent of exposure to LPS (Fig. 2, D and F, lanes 1 and 2) but dependent on the presence of element LREAA. Formation of complex Z on probe D was competed by excess unlabeled oligomer C containing the element LREAA (Fig. 2, D and F, lanes 3 and 4) but not by the oligomer CkBm in which LREAA is mutated (Fig. 2, D and F, lanes 5 and 6).

On the other hand, the complex Y that formed on probe DkBm was more abundant than that formed on wild type probe D (Fig. 2C, compare lanes 2 and 4). Formation of complex Y required only the element NFκBd, because complex Y that was formed with probe DkBm disappeared in a competition assay with NFκBd containing oligomer A (Fig. 2E, lane 4) but not with oligomer A kBm containing the mutated NFκBd element (not shown).

With probe DkBmLREm, a small amount of complex X was still seen after LPS induction (Fig. 2E, lane 2). This residual complex X was competed by oligomer C (Fig. 2E, lane 6).

p50 and Oct-1-like Proteins Contribute to the DNA-Protein Complexes—Supershift assays gave information about some of the proteins comprising complexes X, Y, and Z. No reaction was detected with antibodies against NF-κB p52, p65, c-Rel, or RelB, or against IRF-1, STAT1 (p91), c-Jun, c-Fos, C/EBP, Ets-1/Ets-2, NF-AT, Oct-2, or Pit 1, except for a partial supershift of complex X with large amounts of anti-c-Rel (not shown). In contrast, anti-NF-κB p50 (a reagent that immunoblotted and supershifted authentic p50 overexpressed upon cell transfection; not shown) completely supershifted complex X (Fig. 3A, lane 2) while leaving complex Z untouched (Fig. 3, A and B, lanes 1 and 2). Moreover, anti-p50 completely supershifted complex Y (marked by an asterisk in lane 2 of Fig. 3A), and such supershift was even clearer when complex Y was formed with probe DkBmLREm (Fig. 3C, lane 3). Thus, p50 is a component of complexes X and Y but is not present (or is not accessible to the antibody) in complex Z.

Anti-Oct-1 (a reagent that supershifted authentic Oct-1 overexpressed upon cell transfection; not shown) partly supershifted complexes X and Z (Fig. 3, A and B, lanes 3 and 4). In contrast, anti-Oct-1 was nonreactive with complex Y as formed with probe DkBmLREm (containing NFκBd but not LREAA) (Fig. 3C, lane 4). As noted above, probe DkBmLREm only supported the formation of complex Z and did so whether or not the cells had been exposed to LPS (Fig. 3B, lanes 5 and 6).

Complex Z was subjected to UV cross-linking followed by SDS-polyacrylamide gel electrophoresis, revealing that the region containing element LREAA bound at least three nuclear proteins with apparent molecular masses of 160, 100, and 60 kDa (Fig. 4).

**Discussion**

The most frequently implicated LPS-response element in mammalian promoters is the 10-base pair κB element (GGGRNNYYCC) that binds transcription factors of the NF-κB/Rel family (5, 24). NFκB frequently associates with other transcription factors to impart specific regulation (25). The present work identifies an LPS-response element termed LRE AA including the dinucleotide AA downstream of NFκBd in the mouse iNOS promoter. An NFκB-like binding site followed closely by an LPS-response element containing an AA dinucleotide was reported in the regulatory region of the major histocompatibility complex class II Aκ gene (26) and later in the mouse granulocyte colony-stimulating factor promoter (27), but...
in neither gene was the AA dinucleotide noted.

The discovery of LRE$_{AA}$ focuses attention on the identity of the transcription factors that bind to it and the nature of their interaction with NF-$\kappa$B. The requisite dinucleotide AA of LRE$_{AA}$ is embedded in an octamer-like sequence, ATGCAAAA. This sequence departs from the canonical octamer (ATGCAAAA) at the eighth position. Conversion of the eighth nucleotide from T to A may reduce or abolish the binding of the ubiquitous transcription factor Oct-1, as evidenced in the human Ig heavy chain gene enhancer, where the Oct-4 element (ATGCAAAA) bound octamer-binding proteins with only very low affinity (28). Similarly, Oct-1 may bind little to the iNOS

![Figure 2](https://example.com/figure2.png)
LREAA. Other transcription factors known to bind the octamer motif include Pit-1 and the B cell-specific Oct-2 (29). However, with oligonucleotide probes derived from iNOS promoter and nuclear extracts from RAW cells, antibodies against Pit-1 and Oct-2 had no effect, while the antibody against Oct-1 caused a partial supershift in the two complexes (Z and X) whose formation depended on LREAA. Thus, an Oct-1 like protein (OLP) is a candidate for one of the transcription factors interacting with LREAA. UV cross-linking analysis indicated that the LREAA-dependent complex Z included at least three nuclear proteins with molecular masses of ~160, ~100, and ~60 kDa. None of these correspond to the molecular mass of Oct-1 (~70 kDa). It is not known which, if any, of these three proteins binds anti-Oct-1 antibody to cause a partial supershift of complex Z. The ~100-kDa species corresponds in size to a component previously detected in complex X (12). The ~100 kDa protein that binds the LREAA may be the same as the ~100 kDa protein that binds NFκB.

Sequence context strongly influences the composition of promoter binding complexes. The practice of using minimal probes to sustain complex formation militates against detecting factors that impart specificity to the induction of genes regulated by widely shared transcription systems such as NF-κB. The present study used relatively long probes. Results with such probes were consistent with findings from reporter constructs including those representing point mutants in the full-length promoter. In earlier work (12) probe A, containing only the NFκB element, supported the LPS-activated binding of p50/p65 and p50/c-Rel. However, this did not fully explain LPS-induced promoter activity of iNOS. First, activation of NF-κB/Rel is not sensitive to cycloheximide (12), but synthesis of iNOS mRNA in the cells under study was cycloheximide-sensitive (30). Second, activation of p50/p65 and p50/c-Rel peaked at 0.5 h after LPS induction and then decreased (12, 16), but synthesis of iNOS mRNA continued for more than 24 h (11, 18). Finally, NF-κB/Rel was activated by LPS in an LPS-hyporesponsive macrophage cell line from C3H/HeJ mice, but iNOS was not induced. Thus, NF-κB/Rel was not sufficient for LPS induction of iNOS (17). In contrast, probes B and D (Ref. 12 and present study) included not only the NFκB element but also downstream sequences that appear to be relatively specific for the iNOS gene. The complexes formed with probes B and D after LPS induction were different from those formed with probe A. In particular, complex X required both NFκB and LREAA, contained additional protein(s) besides those of the NF-κB/Rel family, lacked p65 and c-Rel, and was sensitive to cycloheximide (12).

Sequence analyses suggested that elements for binding of NF-IL6 are present in the iNOS promoter at positions −274 to −266 and −2150 to −2142 (14); the latter was protected by in vivo footprinting during LPS induction (15). However, mice rendered genetically deficient in NF-IL6 produced iNOS normally in response to LPS and interferon-γ (31). Footprinting also showed protection of nucleotide at −258 (within the octamer-like sequence ATGCAAAA) after LPS induction (15). The present report demonstrates that the dinucleotide AA at −256 and −255 is critical to the formation of complex Z, which is inde-
dependent of LPS induction, and that the mutation of AA to CG eliminates both protein binding and promoter activity.

Based on reporter constructs, binding assays, competition experiments, and antibody supershifts, it is hypothesized that both constitutive complex Z and inducible complex X required LREAA and contained OLP, whereas inducible complexes X and Y required NFκBd and contained NF-κB p50. Since no direct interaction between NF-κB and an Oct-1-containing complex has been reported and since p50 lacks a transactivation domain (25), it is postulated that LPS causes a distinct protein to bridge p50 and OLP, contributes to the formation of complex X, and that the mutation of AA to CG eliminates both protein binding and promoter activity.

Together, NF-κB p50 and the activated OLP-containing complex are proposed to recruit a transactivator to complex X, much as Bcl-3 supplies transactivating capacity by binding p50 dimers on DNA (32, 33). Cloning of the proteins in complexes X and Z may provide fresh approaches to the pharmacologic control of iNOS expression and other responses to LPS.

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REFERENCES

1. Morrison, D. C., and Ryan, J. L. (1979) Adv. Immunol. 29, 293–450
2. Raetz, C. R. H., Ulevitch, R. J., Wright, S. D., Sibley, C. H., Ding, A., and Nathan, C. F. (1996) J. Biol. Chem. 271, 11911–11919
3. Lin, A. W., Chang, C. C., and McCormick, C. C. (1996) J. Biol. Chem. 271, 353–361
4. Ip, Y. T., Beach, M., Engstrom, Y., Kadakayil, L., Cai, H., Gonzalez-Crespo, S., Tatei, K., and Levine, M. (1993) Cell 75, 753–763
5. Sweet, M. J., and Hume, D. A. (1996) J. Leukocyte Biol. 60, 8–26
6. Xie, Q.-w., Cho, H. J., Calaycay, J., Mumford, R. A., Swiderek, K. M., Lee, T. D., Ding, A., Troso, T., and Nathan, C. (1992) Science 256, 225–228
7. Chartrain, N. A., Gellar, D. A., Kots, P. P., Sitrin, N. F., Nussler, A. K., Hoffman, E. P., Billiar, T. R., Hutchinson, N. I., and Mudgett, J. S. (1994) J. Biol. Chem. 269, 6765–6772
8. Nathan, C., and Hibbs, J. B., Jr. (1991) Curr. Opin. Immunol. 3, 65–70
9. MacMicking, J. D., Nathan, C., Hom, G., Chartrain, N., Fletcher, D. S., Trumbauer, M., Stevens, K., Xie, Q.-w., Sokol, K., Hutchinson, N., Chen, H., and Mudgett, J. S. (1995) Cell 81, 641–650
10. Nathan, C., and Xie, Q.-w. (1994) J. Biol. Chem. 269, 13725–13728
11. Lorsbach, R. B., Murphy, W. J., Lowenstein, C. J., Snyder, S. H., and Russell, S. W. (1993) J. Biol. Chem. 268, 1908–1913
12. Xie, Q.-w., Kashiwabara, Y., and Nathan, C. (1994) J. Biol. Chem. 269, 4705–4708
13. Xie, Q.-w., Whisnant, R., and Nathan, C. (1995) J. Exp. Med. 177, 1779–1784
14. Lowenstein, C. J., Alley, E. W., Raval, P., Snowman, A. M., Snyder, S. H., Russell, S. W., and Murphy, W. J. (1993) Proc. Natl. Acad. Sci. U. S. A. 90, 9730–9734
15. Goldberg, C. E. P., Revensau, S., Algarte, M., and Leannin, J.-F. (1996) Nucleic Acids Res. 24, 1682–1687
16. Murphy, W. J., Murof, M., Zhang, C. X., Suzuki, T., and Russell, S. W. (1996) J. Exp. Med. 180, 381–393
17. Verrijer, C. P., and Van der Vliet, P. C. (1993) Biochim. Biophys. Acta 1188, 131–139
18. Schreiber, E., Matthias, P., Muller, M. M., and Schaffner, W. (1989) Nucleic Acids Res. 17, 6419
19. Bradford, M. M. (1976) Anal. Biochem. 72, 248–254
20. Baldwin, A. S., Jr. (1996) Annu. Rev. Immunol. 14, 649–681
21. Schreiber, E., Matthias, P., Muller, M. M., and Schaffner, W. (1989) Nucleic Acids Res. 17, 6419
22. Staudt, L. M., Singh, H., Sen, R., Wirth, T., Sharp, P. A., and Baltimore, D. (1986) Nature 320, 640–643
23. Bauele, P. A., and Baltimore, D. (1996) Cell 87, 13–20
24. Bauele, P. A., and Baltimore, D. (1996) Cell 87, 13–20
25. Gravallese, E. M., Boothby, M. R., Smas, C. M., and Glimcher L. H. (1989) Mol. Cell. Biol. 9, 2002–2011
26. Wang, J., Oketani, M., and Watanabe, T. (1991) J. Biol. Chem. 266, 1044–1051
27. Martin, E., Nathan, C., and Xie, Q.-w. (1994) J. Leukocyte Biol. 57, 174–179
28. Golub, E. I., Kim, H., and Volsky, D. J. (1989) Nucleic Acids Res. 17, 4902
29. Gorman, C. M., Moffat, L. F., and Howard, B. H. (1982) Mol. Cell. Biol. 2, 1044–1051
30. Bradford, M. M. (1976) Anal. Biochem. 72, 248–254
31. Schreiber, E., Matthias, P., Muller, M. M., and Schaffner, W. (1989) Nucleic Acids Res. 17, 6419
32. Staudt, L. M., Singh, H., Sen, R., Wirth, T., Sharp, P. A., and Baltimore, D. (1986) Nature 320, 640–643
33. Bauele, P. A., and Baltimore, D. (1996) Cell 87, 13–20
34. Wang, J., Oketani, M., and Watanabe, T. (1991) Mol. Cell. Biol. 11, 75–83
35. Verrijer, C. P., and Van der Vliet, P. C. (1993) Biochim. Biophys. Acta 173, 1–21
36. Xie, Q.-w., and Nathan, C. (1993) in Transaction of the Association of American Physicians, Vol. CVI, pp. 1–12, Williams & Wilkins, Baltimore, MD
37. Tanaka, T., Akira, S., Yashida, K., Umemote, M., Yoneda, Y., Shirafuji, N., Fujiwara, H., Suematsu, S., Yoshia, N., and Kishimoto, T. (1995) Cell 80, 355–361
38. Bours, V., Franzenko, G., Azarenko, V., Park, S., Kanno, T., Brown, K., and Siebenlist, U. (1993) Cell 72, 729–739
39. Fujita, T., Nolan, G. P., Liu, H. C., Scott, M. L., and Baltimore, D. (1993) Genes Dev. 7, 1354–1363
40. Martin, E., Nathan, C., and Xie, Q.-w. (1994) J. Exp. Med. 180, 977–984
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