A Role for NF-κB in the Induction of β-R1 by Interferon-β

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Previous experiments have suggested that induction of the β-R1 gene by interferon (IFN) -β required transcription factor ISGF-3 (IFN-stimulated gene factor-3) and an additional component. We now provide evidence that nuclear factor κB (NF-κB) can serve as this component. Site-directed mutagenesis of an NF-κB binding site in the β-R1 promoter or over-expression of an IκBα super-repressor abrogated IFN-β-mediated induction of a β-R1 promoter-reporter. IFN-β treatment did not augment abundance of NF-κB but did lead to phosphorylation of the p65 NF-κB subunit. It is proposed that IFN-β-mediated enhancement of the transactivating competence of NF-κB components is required for inducible transcription of the β-R1 promoter. These results provide a novel insight into the role of NF-κB in the transcriptional response to IFN-β.

Interferons (IFNs) elicit multiple biological responses mediated by the proteins encoded by interferon-stimulated genes (ISGs) (1). IFN-α and β activate transcription of ISGs through the transcription factor interferon-stimulated gene factor-3 (ISGF-3), which interacts with the interferon-stimulated response element (ISRE) present in the promoters of ISGs (2). We previously reported the selective induction of β-R1 by IFN-β but not IFN-α in human fibrosarcoma cells (3, 4). ISGF-3 was essential but not sufficient for IFN-β-dependent induction of β-R1 (3). In the current report we show that the transcription factor nuclear factor-κB (NF-κB) is also involved in the induction of this gene by IFN-β.

NF-κB is a dimer of members of the Rel family of proteins, including p50, p52, c-Rel, RelA/p65, and RelB. NF-κB dimers bind to DNA segments collectively referred to as κB elements (5). In unstimulated cells, NF-κB is sequestered in the cytosol with oligomeric inhibitory components, termed IκB. Stimulation of cells with appropriate inducers results in the rapid degradation of IκB and translocation of NF-κB to the nucleus, where it binds target sequences to initiate transcription. Increasing evidence suggests that a second signaling pathway, independent of IκB degradation (6–10), culminates in phosphorylation of the p65/RelA subunit in its transactivation domain (11).

A role for NF-κB in the induction of ISG in response to IFNs has not been reported. While studying IFN-β activation of β-R1 promoter, we found that modification of pre-existing NF-κB by phosphorylation was essential for IFN-β-induced transcription of β-R1.

EXPERIMENTAL PROCEDURES

Cell Culture—The human fibrosarcoma cell line UI.wt was maintained as described (4). Purified recombinant IFN-β-1b (2 × 10^6 IU/mg) was from Berlex Biosciences (Richmond, CA). Purified IFN-γ (1.9 × 10^6 IU/mg) from Genentech (South San Francisco, CA). TNF-α from Collaborative Biomedical Products (Bedford, MA), was used at a final concentration of 50 ng/ml. IFN-β and γ were used at 1000 and 500 units/ml, respectively, unless mentioned otherwise. Human embryonic kidney 293 cells transfected with interleukin-1R were maintained in Dulbecco’s modified Eagle’s medium with 10% calf serum (12). Z5, a mutant cell line derived from 293- Tk/zea cells (12) exhibits constitutive NF-κB activity as shown by EMSA assays and expression of an NF-κB-dependent promoter.

RNA Isolation and RNase Protection Assay—Total RNA was prepared from IFN-treated cells (13). RNase protection experiments were performed as described (3). The probes used, β-R1 (protects 400 bases), 6-16 (protects 190 bases), and γ-actin (protects 130 bases), were as described (3, 4).

Promoter-Reporter Plasmid Construction and Mutagenesis—Site-directed mutagenesis of the ISRE and κB sequence in pGL3-wt-β-R1 (4) was achieved by multiple rounds of polymerase chain reaction using pGL3-wt-β-R1 as template and appropriate primers (14). Three rounds of polymerase chain reaction were performed using two sets of primers to obtain mISRE-β-R1. The first pair of primers used to make the pGL3-mISRE mutant were 5'-GAAGAGAACAccACAtAAACTCTTGG-3' (forward primer with ISRE sequence underlined) and 3'-ATACGAGCTCTCCGCTGC-5'. The second pair of primers were SacI primer 5'-ATACGAGCTCTCGTGC-3' and 5'-GGCTCAGAGATTgCTG TTCATCTC-3' (backward primer with ISRE sequence underlined and mutagenized nucleotides in lowercase). The first pair of primers used to make pGL3-mκB mutant were 5'-CATGAGCTCAAA GAGTGAATgATCCTGTCGAC-3' (forward primer with κB sequence underlined and mutagenized nucleotides in lowercase) and 3'-ATGGCCACATTTgTgATGTCATGACT-3' (backward primer with κB binding sequence underlined and mutagenized nucleotides in lowercase). Plasmid DNA from two clones for each set of cloning was sequenced to verify the nucleotide sequence.

Transient Transfection Assay—Transient transfections were done as described (4), with 10 μg of β-R1 reporter plasmid, 10 μg of test plasmid DNA and 1 μg of pCH110 β-galactosidase plasmid DNA. The plasmid construct pCMV-1xBo (with Ser70 and Ser72 mutated to Ala) was also reported earlier (15); pCMV-50 was kindly provided by Dr. M. Kieran (16). The pCMV-65 plasmid was generously given by Dr. D. W. Ballard (17). The p561-luciferase construct containing the ISRE from p56 ISG and the 6xIP-10κB-luciferase construct has been reported earlier (4, 7).

Cell Extracts and EMSA—For electrophoretic mobility shift assays (EMSA) the NF-κB binding site (5'-GAGCGAGGGAAATCCGTAAC-3') was used.
Respectfully, I’d be happy to help you with that. Here is the plain text representation of the document:

**RESULTS**

Characterization of IFN-β Signaling to the β-R1 Promoter—We performed a functional analysis of the β-R1 ISRE-like element using wt-β-R1 and mutant mISRE-β-R1 (Fig. 1a). In transient transfection assays, IFN-β responsiveness of mISRE-β-R1 was reduced by more than 80% compared with the wt-β-R1 promoter (Fig. 1a). This result confirmed the requirement of this ISRE-like element for the induction of β-R1 by IFN-β. The induction of mISRE-β-R1 activity by IFN-γ was also significantly reduced by about 70% compared with wt-β-R1 (Fig. 1a). These results are consistent with our earlier observation in U2A cells (which lack the p48/IRF-9 ISRE recognition factor) of loss of induction of β-R1 by IFN-β or IFN-γ (3).

We proposed that a second cis-element might be involved in the induction of the β-R1 gene (3). We had previously observed a synergistic induction of β-R1 by IFN-β and TNF-α, the latter being a well characterized activator of transcription factor NF-κB. Hence, a salient choice for analysis was the κB element on the promoter of β-R1.

Using transient transfection assays, wt-β-R1 or mκB-β-R1 promoter-reporters were analyzed for IFN-β responsiveness. Mutation of the κB element on the promoter of β-R1 markedly reduced IFN-β induction of the promoter, by 70% (Fig. 1b). Induction of the wild-type and mκB-β-R1 constructs by IFN-γ differed only slightly (Fig. 1b). This result indicated that the κB element was specifically required for IFN-β but not IFN-γ-mediated induction.

Requirement of Basal NF-κB Nuclear Activity for Induction of β-R1 Gene by IFN-γ—We used EMSAs to address whether the requirement for the κB binding site was associated with IFN-β induced nuclear translocation and DNA binding by NF-κB. Analysis of extracts of U1.wt cells revealed, as previously reported (20, 21), basal NF-κB DNA binding activity (Fig. 2a). Super-shift experiments showed complexes composed of p65 homodimers, and p65/p50 heterodimers (results not shown). No IFN-β-inducible increase in DNA binding activity was detected.

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FIG. 1. Requirement of ISRE-like and κB cis-element for the induction of β-R1 by IFN-β. a, transient transfection assays were done using wt-β-R1 or the mISRE-β-R1 construct in U1.wt cells as described under “Experimental Procedures.” Data are expressed as percent induction, with the induction of luciferase activity by wt-β-R1 promoter set at 100%. Percent induction of mISRE-β-R1 promoter activity by IFN-β or IFN-γ differed significantly from the wt-β-R1 promoter (p < 0.001, paired t test). b, transient transfection assays were done as described for panel a using wt-β-R1 or the mκB-β-R1. Percent induction of mκB-β-R1 promoter activity by IFN-β but not IFN-γ differed significantly from the wt-β-R1 promoter (p < 0.001, paired t test).

FIG. 2. Requirement of NF-κB nuclear activity for the induction of β-R1 by IFN-γ. a, an EMSA was performed using nuclear extracts from cells treated with IFN-β for varying time periods and analyzed by autoradiography. Results from one of four experiments are shown. ns, nonspecific band. b, densitometric ratio of p65/p55 and p65/p50 to nonspecific band was quantitated by NIH Image, version 1.60. c, EMSA using whole cell extracts from 293 and Z5 cells treated without (C) and with IFN-β (5000 units/ml) for 15 min. Results from one of four experiments is shown. d, cell extracts from untreated Z5 cells (−) were super-shifted with the indicated antibodies. Results from one of two experiments are shown. e, the figure shows an autoradiogram derived from RNase protection analysis of total RNA (10 μg) from 293 and Z5 untreated cells (−), cells treated with IFN-β (5000 units/ml), TNF-α (T, 50 ng/ml), or IFN-β (5000 units/ml) and TNF-α (50 ng/ml) (β+T) for 6 h. Results from one of two experiments is shown. f, transient transfection of U1.wt cells with the wt-β-R1 promoter plasmid together with either an empty vector (1) or a construct expressing super-repressor pCMV-1xIκBα (2). Percent induction of reporter activity in the presence of IκBα by IFN-β differed significantly from the wt-β-R1 promoter (p < 0.001, paired t test). Co-transfection of IκBα without (3) and with the wt-561 promoter plasmid (4) revealed the induction of wt-561 by IFN-β was unaffected by IκBα. g, transient transfection analysis of 6xκB promoter-reporter in U1.wt cells and treated with TNF-α (50 ng/ml) or IFN-β (1000 units/ml) or left untreated. Results shown are an average derived from three experiments.

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3 M. R. S. Rani and R. M. Ransohoff, unpublished data.
by densitometric analysis of the ratios of the specific NF-κB complexes to a nonspecific band (Fig. 2b).

To address the possibility that basal nuclear NF-κB activity might be essential for induction of β-R1 by IFN-β, we analyzed two subcell lines that differed in basal NF-κB. Wild-type 293 cells did not contain basal nuclear NF-κB as detected by EMSA, whereas Z5 cells contained constitutive NF-κB (Fig. 2c).

The major κB binding complex in Z5 cells consisted of p65 and p50 subunits (Fig. 2d). IFN-β treatment did not produce a detectable change in NF-κB in either cell line. RNase protection analysis documented the induction of β-R1 by IFN-β in Z5 cells but not in 293 cells (Fig. 2e), although another type I IFN-inducible gene (6–16) could be induced equally well in both cell lines. TNF-α, in combination with IFN-β, mediated synergistic induction of β-R1 in both Z5 and 293 cells, confirming the existence of an intact NF-κB pathway in both cell lines.

We also observed super-repressor mutant isoform of IκBα in U1.wt cells, resulting in diminished induction of the wt-β-R1 promoter-reporter by IFN-β (Fig. 2f). To exclude non-specific effects of IκBα over-expression, we analyzed IFN-β-mediated induction of a promoter-reporter construct derived from the p561 gene (a type I IFN-induced gene). Induction of the 561 promoter-reporter (which lacks a κB site) was unaffected by IκBα (Fig. 2f). In transient transfection assays, a 6×κB promoter-reporter construct was not activated by IFN-β, but TNF-α gave a 6-fold induction (Fig. 2g).

**Roles of p65 and p50 Proteins in the Induction of β-R1 by IFN-β**—We asked whether homodimers of p50 (which lack a transactivation domain and are transcriptionally inactive) were sufficient to promote β-R1 transcription by virtue of occupancy at the κB site. For these experiments, p50 was over-expressed in U1.wt cells along with the wt-β-R1 promoter-reporter, and reporter gene activation in response to IFN-β was examined. IFN-β responsiveness of the promoter was reduced by 60% to a level similar to that obtained by disruption of the NF-κB binding site (Table I). This result indicated that p50 homodimers were insufficient to support transcription of β-R1 and suggested the requirement of transcriptionally competent NF-κB complexes.

Co-expression of p65 with the wt-β-R1 promoter increased the basal activity of the promoter by 9-fold (Table I). IFN-β treatment further increased promoter activity by 6-fold. Taken together, these results indicated that transcriptionally competent NF-κB complexes were required for maximal transcription of the β-R1 gene in response to IFN-β.

Basal NF-κB activity was essential for IFN-β-mediated transcription of β-R1, although IFN-β treatment did not lead to increased NF-κB (by EMSA). Recent reports (6, 8–11, 27) have shown that phosphorylation of p65 augments NF-κB-dependent gene transcription. To address IFN-β-mediated phosphorylation of NF-κB proteins, cells were metabolically labeled with [32P]orthophosphate, and whole cell extracts were immuno-

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**TABLE I**

**Requirement of p65 but not p50 for the induction of β-R1 by IFN-β**

| Plasmids | Normalized luciferase activity | Relative reporter expression | Fold increase with IFN-β |
|----------|-------------------------------|-----------------------------|-------------------------|
| 1. wt-β-R1 | 0.02 ± 0.005 | 1 | 5.3 |
| 2. wt-β-R1 + pCMV-65’ | 0.15 ± 0.030 | 9.2 | 6.3 |
| 3. wt-β-R1 + pCMV-50’ | 0.02 ± 0.003 | 1 | 2.0 |

a Luciferase activity was normalized for transfection efficiency as described under “Experimental Procedures” and expressed in arbitrary units. All co-transfections were done as reported under “Experimental Procedures.”

b Luciferase activity on transfection of wt-β-R1 in the absence of treatment was set at 1. This value was used to normalize the effects of treatment with IFN-β or over-expression of NF-κB subunits.

c 0.25 μg of pCMV-65 was used along with 10 μg of wt-β-R1 promoter-reporter construct. Basal activity was higher for cells transfected with p65 in the absence of treatment.

d Fold-induction in luciferase activity by IFN-β was significantly less upon co-transfection of wt-β-R1 and pCMV-50 compared to wt-β-R1 with empty vector (p < 0.001, paired t-test).

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**FIG. 3. Phosphorylation of p65 in IFN-β-treated cells.** 

**a.** analysis of phosphorylated NF-κB proteins by in vitro metabolic labeling of U1.wt cells with [32P]orthophosphate (200 μCi/ml). Where indicated the cells were left untreated (C) or treated with IFN-β (β, 5000 units/ml) or TNF-α (T, 50 ng/ml). Cell lysis and immunoprecipitation of the NF-κB complex were performed as described under “Experimental Procedures.” Phosphorylated proteins were separated by SDS-PAGE and autoradiographed. IκBα, nonphosphorylated IκBα; p-IκBα, phosphorylated IκBα. Results from one of two experiments are shown. b, phosphorylation of GST-p65 using nuclear extracts from IFN-β (β)- or TNF-α (T)-treated U1.wt cells. In vitro kinase assays were performed using GST-p65 as a substrate as described under “Experimental Procedures.” The **upper panel** is an autoradiogram and shows phosphorylated p65 (p-p56). The lower panel shows a Western analysis using anti-GST antibody for total p65 (T-p56) protein. c, cells were treated without (C) or with TNF-α (50 ng/ml) or IFN-β (5000 units/ml) for varying time periods and subjected to a Western analysis for IκBα. d, phosphorylation of GST-p56 using nuclear extracts from untreated (C), IFN-β (β)- or TNF-α (T)-treated U1.wt cells. The **upper panel** is an autoradiogram and shows phosphorylated p65. The **lower panel** shows a Western analysis using anti-GST antibody for total p56 protein.

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**DISCUSSION**

Here, we address the role of NF-κB in the induction of β-R1 by IFN-β. We had previously hypothesized that ISGF-3 was

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**FIG. 3. Phosphorylation of p65 in IFN-β-treated cells.** 

**a.** analysis of phosphorylated NF-κB proteins by in vitro metabolic labeling of U1.wt cells with [32P]orthophosphate (200 μCi/ml). Where indicated the cells were left untreated (C) or treated with IFN-β (β, 5000 units/ml) or TNF-α (T, 50 ng/ml). Cell lysis and immunoprecipitation of the NF-κB complex were performed as described under “Experimental Procedures.” Phosphorylated proteins were separated by SDS-PAGE and autoradiographed. IκBα, nonphosphorylated IκBα; p-IκBα, phosphorylated IκBα. Results from one of two experiments are shown. b, phosphorylation of GST-p65 using nuclear extracts from IFN-β (β)- or TNF-α (T)-treated U1.wt cells. In vitro kinase assays were performed using GST-p65 as a substrate as described under “Experimental Procedures.” The **upper panel** is an autoradiogram and shows phosphorylated p65 (p-p56). The lower panel shows a Western analysis using anti-GST antibody for total p56 protein. c, cells were treated without (C) or with TNF-α (50 ng/ml) or IFN-β (5000 units/ml) for varying time periods and subjected to a Western analysis for IκBα. d, phosphorylation of GST-p56 using nuclear extracts from untreated (C), IFN-β (β)- or TNF-α (T)-treated U1.wt cells. The **upper panel** is an autoradiogram and shows phosphorylated p65. The **lower panel** shows a Western analysis using anti-GST antibody for total p56 protein.
Induction of β-R1 by IFN-β Requires NF-κB

essential but not sufficient for the induction of the gene and proposed that an additional component might be required (3). We studied NF-κB because of the striking synergy between TNF-α and IFN-β for induction of β-R1, despite the fact that neither TNF-α nor interleukin-1β alone induced β-R1.

Site-directed mutagenesis of the κB element in the β-R1 promoter or over-expression of a super-repressor mutant of IκBα blocked the induction of the β-R1 gene by IFN-β, indicating that NF-κB components were required. However, IFN-β did not induce increased NF-κB DNA binding activity by EMSA. Further IFN-β treatment did not activate transcription from a NF-κB reporter-construct.

To address the question of whether the physical presence of κB binding activity was sufficient to enhance the transcriptional response of the β-R1 gene to IFN-β, we individually over-expressed transcriptionally inert p50 or transcriptionally active p65. Over-expression of p50 suppressed β-R1 transcription, whereas over-expression of p65 elevated basal β-R1 promoter activity but supported a further 6-fold increase in response to IFN-β. These results confirmed a requirement for active NF-κB complexes to drive maximal transcription of the β-R1 gene.

In Daudi and other cell lines, type I IFN was reported to signal to NF-κB via a pathway involving PI3K and serine-threonine kinase Akt (22). The output of this pathway comprised markedly increased NF-κB. IFN-mediated endogenous NF-κB-dependent gene expression was not documented in these or prior reports (22–24). The signaling pathway described in this report (22), implicated STAT3 as a docking site for PI3K components. Such signaling is not observed in HT1080 cells, where STAT3 activation is dispensable for generating PI3K lipid kinase activity and where physical interaction between STAT3 and PI3K does not occur (25). Given these dissimilar signaling characteristics of type I IFN receptor activation in HT1080 cells as compared with Daudi cells (26), it was expected that increased NF-κB DNA binding activity would not be observed after IFN-β-treatment of HT1080 cells.

Recent reports highlighted the importance of p65 phosphorylation for NF-κB-dependent gene transcription (6, 8–11, 27). Using in vivo metabolic labeling and in vitro phosphorylation of GST-p65, we showed that p65 was phosphorylated in IFN-β-treated cells. A number of kinases have been implicated in the phosphorylation of p65 (8, 9, 11).

This report adds to the multiple roles of NF-κB. Because there is no cytokine-dependent increase in NF-κB DNA binding activity, IFN-β-treated cells represent an excellent system in which to investigate post-translational modification of p65.

REFERENCES

1. Gresser, I. (1990) J. Invest. Dermatol. 95, 66, S.715
2. Darnell, J. E., Kerr, I. M., and Stark, G. R. (1994) Science 264, 1415–1421
3. Rani, M. R., Foster, G. R., Leung, S., Leaman, D., Stark, G. R., and Ranshoff, R. M. (1996) J. Biol. Chem. 271, 22878–22884
4. Rani, M. R., Gauzzi, C., Pellegriini, S., Fear, K. N., Wei, T., and Ranshoff, R. M. (1999) J. Biol. Chem. 274, 1891–1897
5. Chen, F. E., and Ghosh, G. (1999) Oncogene 18, 6845–6852
6. Wang, D., and Baldwin, A. S. (1998) J. Biol. Chem. 273, 29411–29416
7. Sixtmore, N., Leung, S., and Stark, G. R. (1999) Mol. Cell. Biol. 19, 4788–4805
8. Sakurai, H., Chiba, H., Miyoshi, H., Sugita, T., and Toriumi, W. (1999) J. Biol. Chem. 274, 30353–30356
9. Bergmann, M., Hart, L., Lindsay, M., Barnes, P. J., and Newton, R. (1999) J. Biol. Chem. 273, 6607–6610
10. Zhong, H., SuYang, H., Erdjument-Bromage, H., Tempst, P., and Ghosh, S. (1997) Cell 89, 413–422
11. Bird, T. A., Schooley, K., Dower, S. K., Hagen, H., and Virca, G. D. (1997) J. Biol. Chem. 272, 32606–32612
12. Li, X., Commene, M., Burns, C., Vithalani, K., Cao, Z., and Stark, G. R. (1999) Mol. Cell. Biol. 19, 4643–4652
13. Chomczynski, P., and Sacchi, N. (1987) Anal Biochem. 162, 156–159
14. Zhou, Z. H., Chaturvedi, P., Han, Y. L., Aras, S., Li, Y. S., Kolattukudy, P. E., Ping, D., Boss, J. M., and Ranshoff, R. M. (1998) J. Immunol. 160, 3908–3916
15. DiDonato, J. A., Mercurio, F., and Karin, M. (1995) Mol. Cell. Biol. 15, 1302–1311
16. Kieran, M., Blank, V., Logeat, F., Vandekerckhove, J., Lottspeich, F., Le Bail, O., Urban, M. B., Kourilsky, P., Baeuerle, P. A., and Israel, A. (1990) Cell 62, 1007–1018
17. Brockman, J. A., Scherer, D. C., McKinsey, T. A., Hall, S. M., Qi, X., Lee, W. Y., and Ballard, D. W. (1995) Mol. Cell. Biol. 15, 2809–2818
18. Majumder, S., Zhou, L. Z., Chaturvedi, P., Babcock, G., Aras, S., and Ranshoff, R. M. (1998) J. Immunol. 161, 4736–4744
19. Sakurai, H., Miyoshi, H., Toriumi, W., and Sugita, T. (1999) J. Biol. Chem. 274, 10641–10648
20. Piatt, R., Gupta, S., Khosravi-Far, R., Sato, K. Y., Peruchio, M., Der, C. J., and Stanbridge, E. J. (1998) J. Immunol. 161, 1807–1817
21. Wiest, J. S., Burnett, V. L., Anderson, M. W., and Reynolds, S. H. (1994) Oncogene 9, 2449–2454
22. Yang, H. C., Murti, A., Pfeffer, S. R., Kim, J. G., Donner, D. B., and Pfeffer, L. M. (2001) J. Biol. Chem. 276, 13756–13761
23. Yasumoto, K., Okamoto, S., Mukaida, N., Murakami, S., Mai, M., and Matsushima, K. (1992) J. Biol. Chem. 267, 22596–22511
24. Maitreyee, C. K., Sarukaka, A., and Sarker, A. S. (1998) Mol Cell. Biochem. 178, 103–112
25. Rani, M. R., Leaman, D. W., Han, Y., Leung, S., Crane, E., Fisch, E. N., Wollman, A., and Ranshoff, R. M. (1999) J. Biol. Chem. 274, 32507–32511
26. Yang, C. H., Murti, A., Pfeffer, S. R., Basu, L., Kim, J. G., and Pfeffer, L. M. (2001) Proc. Natl. Acad. Sci. U. S. A. 97, 13631–13636
27. Jefferies, C. A., and O’Neill, L. A. (2000) J. Biol. Chem. 275, 3114–3120
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