The mRNA Transcription/Processing Factor Ssu72 Is a Potential Tyrosine Phosphatase*

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Ssu72 is an essential and highly conserved protein involved in mRNA transcription and 3’-end processing. The biochemical function of Ssu72 was so far unknown. We report here evidence that Ssu72 is a phosphatase that resembles protein tyrosine phosphatases (PTPases). First, recombinant Ssu72 cleaves the phosphotyrosine analogue p-nitrophenylphosphate, and this catalytic activity is impairs by PTPase-inhibiting agents. Second, the Ssu72 sequence contains the CX2R signature motif of PTPases; mutation of the catalytic cysteine in this motif abolishes Ssu72 activity in vitro and has been shown to confer lethality in vivo. Third, secondary structure prediction and site-directed mutagenesis predict that Ssu72 adopts the fold of PTPases of the low molecular weight family. Distinguishing features, such as a short “aspartate loop” at the active site, suggest however that Ssu72 is the founding member of a new phosphatase subfamily. The novel Ssu72 activity may regulate coupling events during mRNA biogenesis.

Over the last few years a wealth of biochemical and genetic data have revealed extended coupling between nuclear events of gene expression (1, 2). In particular, transcription by RNA polymerase II (pol II) is coupled to mRNA processing, including 5’ capping and splicing and 3’-end formation of the transcript. This coupling is achieved by the binding of mRNA processing factors to the phosphorylated C-terminal repeat domain (CTD), a mobile extension of the catalytic core of pol II (3). The CTD becomes phosphorylated during transcription initiation and remains phosphorylated during RNA chain elongation. Several CTD kinases have been described (4), but only one CTD phosphatase, called Fcp1, is known (5, 6). In addition to pol II, several other proteins of the transcription machinery are phosphorylated (7), and RNA processing complexes contain phosphoproteins as well. Phosphorylation and dephosphorylation events are thus crucial for the regulation of transcription-coupled mRNA processing.

Ssu72 was originally identified in a yeast genetic screen. A mutation in the ssu72 gene enhances a defect in the general transcription factor IIB (TFIIB) that confers a shift in the transcription start site (8). Indeed, Ssu72 binds directly to TFIIB (9), and it also interacts with pol II, both genetically and physically (10, 11). Yeast Ssu72 is a subunit of the cleavage and polyadenylation factor (CPF), which together with cleavage factor I and poly(A) polymerase is sufficient for mRNA 3’-end formation (11, 12). Because RNA 3’-end formation and transcription termination are interlinked, and because Ssu72 functions also during transcription initiation, Ssu72 may be involved in a possible coupling between transcription termination and initiation (1). Recent data show that Ssu72 is also involved in transcription elongation (11). The Ssu72 mutation can increase pol II pausing and can counteract the toxicity of 6-azauracil, an inhibitor of pol II elongation (11). Yeast Ssu72 is essential for viability (8) and shares 44% identical amino acid residues with its human homologue. The high degree of conservation suggests that Ssu72 has a similar function in all eukaryotic cells.

Thus Ssu72 is an essential and highly conserved protein involved in eukaryotic mRNA biogenesis. However, the biochemical function of Ssu72 remained unknown. Here we provide evidence that Ssu72 is a phosphatase that resembles protein tyrosine phosphatases (PTPases). PTPases can be divided in four families, including receptor-like, intracellular, dual specificity, and low molecular weight (low M) PTPases (13, 14). We demonstrate that Ssu72 shows similarities to the low M PTPase family but that it also has distinguishing features. Possible functions of this novel enzymatic activity during mRNA biogenesis are discussed.

EXPERIMENTAL PROCEDURES

Cloning and Site-directed Mutagenesis—Gene ssu72 encoding for the 194-amino acid residue human isoform 1 was amplified by PCR from human muscle cDNA using the oligonucleotide primers 5’-CGCATG-CCATGCAATGCGCTCGTCCCCGGCGGG-3’ and 5’-GCTTTTCTCCTGCGCCCCTAGAAAGCCAGGCGTGTC-3’ (mutated positions in bold, restriction sites underlined). Thereby, an NotI restriction site and codons for two additional amino acids, methionine and alanine, were added to the 5’-end of the gene, and at the 3’-end of the gene, the stop codon was removed and a NotI site was added. PCR products were digested and ligated into pET28b (Novagen), resulting in a construct that encodes for the Ssu72 polypeptide chain plus a C-terminal hexahistidine tag. After transformation of ligations products into Escherichia coli XL1 blue cells, plasmid DNA was isolated, and DNA from positive clones was sequenced. The resulting DNA sequence of gene ssu72 agrees with the published sequence (10) but deviates from the data base entry for PNAS-120 (NCBI accession number AAK07538) at two amino acid positions. Apparent mutations encode for residues Lys-182 and Ser-183 instead of Arg-182 and Val-183, respectively. Point mutations were introduced by site-directed mutagenesis with the two step PCR overlap extension method. The mutated gene ssu72 C12S was amplified from the cloned ssu72 plasmid DNA in two steps. In the first step, two independent PCR reactions were carried out. The first reaction was carried out with a T7 promoter forward primer and the primer 5’-GCTCCGGTTCTGGTGGCTCAGG-3’. The second reaction was carried out using the reverse complement counterpart of the latter primer and a T7 terminator reverse primer. In the second step, the entire mutated gene was amplified with both T7 primers from the PCR products of the first step. The resulting PCR product was digested

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The abbreviations used are: pol II, RNA polymerase II; CTD, C-terminal repeat domain; CPF, cleavage and polyadenylation factor; PTPase, protein tyrosine phosphatase; CV, column volume; DTT, dithiothreitol; pNPP, p-nitrophenylphosphate; TF, transcription factor.
with NcoI and NotI and ligated into pET22b (Novagen). For amplification of mutated genes ssu72 R18K, D140A, and D143A, the primers 5'-GGTGGGCGCGCCATGCTTGTCTTGGTTGCGACGAC-3', 5'-CTCTGAGTGGCACAATGACAGTCG-3', and 5'-GGCTCTCTCGTGGTGGTGATGTCGAC-3' were instead used in the first step, respectively, together with their reverse complement counterparts.

**Protein Expression and Purification**—Plasmid DNA harboring the human gene ssu72 was transformed into E. coli BL21 DE3 CodonPlus RIL cells (Stratagene). Cells were grown at 37 °C in LB medium supplemented with chloramphenicol and kanamycin, both at concentrations of 50 μg/ml. Once the cell culture reached an A600 of 0.5, temperature was reduced to 20 °C and cells were induced with 0.5 mM isopropyl-1-thio-D-galactopyranoside and grown over night. Cells were harvested by centrifugation and suspended in buffer A (50 mM Tris-Cl, pH 8.0, 1 mM EDTA, 1 mM DTT) and stored at −80 °C. All protein variants were purified as follows. Cell cultures were grown over night. Cells were induced with 0.5 mM isopropyl-1-thio-D-galactopyranoside and grown over night. Cells were harvested by centrifugation and suspended in buffer A (50 mM Tris-Cl, pH 8.0, 1 mM EDTA, 1 mM DTT) and stored at −80 °C. For purification of recombinant Ssu72, a Potential New Phosphatase

**RESULTS**

**Ssu72 Contains the Signature Motif of Protein Tyrosine Phosphatases**—By visual inspection of the Ssu72 amino acid sequence, we identified the signature motif 11VCX3RS19, which is typical for PTPases. This motif comprises a cysteine and an arginine residue that form part of the active site in all PTPases and are involved in catalysis (15). In PTPases, the cysteine residue is generally responsible for the nucleophilic attack of the substrate phosphorus atom, leading to the formation of a phosphoenzyme intermediate, whereas the arginine residue is involved in stabilization of the transition state (16). Except for the signature motif, there is no apparent sequence homology between Ssu72 and PTPases.

**Ssu72 Cleaves a Phosphotyrosine Analogue**—To test Ssu72 for a potential phosphatase activity, we cloned human Ssu72, over-expressed the protein in E. coli, and purified it to apparent homogeneity (see “Experimental Procedures”). We then subjected the purified recombinant protein to a colorimetric assay based on cleavage of the phosphotyrosine analogue pNPP (see “Experimental Procedures”). Highly purified recombinant Ssu72 could indeed cleave pNPP. Ssu72 activity was strongly dependent on the pH of the buffer and was highest at pH 6.5. At

**Table I**

| Protein | PTPase family | $K_m$ | $V_{max}$ | Specific activity | $k_{cat}$ | $k_{cat}/K_m$ | Reference |
|---------|---------------|-------|-----------|------------------|----------|---------------|-----------|
| ssu72 wild type | 3.6 | 2.24 | 1 | 0.4 | 112 | This work |
| ssu72 D140A | 7.9 | 0.24 | 0.1 | 0.04 | 5 | This work |
| ssu72 D143A | 24 | 0.8 | 0.4 | 0.14 | 6 | This work |
| Bovine PTPase | LMW | 0.31 | ND | 89 | ND | ND | (35) |
| Human HCPTB | LMW | 1.24 | ND | 70 | ND | ND | (18) |
| LPT1 | LMW | 0.017 | ND | 3.2 | ND | ND | (36) |
| VHR | DS | 1.59 | ND | 5.14 | 3240 | (17) |

**Note**

1. LMW, low Mr, PTPase; DS, dual specificity PTPase.
2. Not determined.
pH 6.0, the protein showed 15% of its maximum activity, and below pH 5.5, protein precipitation essentially abolished activity. From pH 6.5 to 9.0, activity progressively decreased to about 10% of the maximum. The temperature optimum for Ssu72 activity was reached at 40 °C, but the protein showed 86% of its maximum activity at 37 °C. To minimize experimental errors and to avoid long incubation times that could lead to enzyme inactivation, further experiments were performed at pH 6.5 and 37 °C under near physiological conditions. Michaelis-Menten kinetics and Lineweaver-Burk analysis revealed a $K_m$ value for pNPP of 3.6 mM (Fig. 1), comparable with values reported for the dual specificity phosphatase VHR (17) and the human low $M_\text{r}$ PTPase HCPTB (18) but 1–2 orders of magnitude higher than that of two other low $M_\text{r}$ PTPases (Table I).

**Ssu72 Activity Is Impaired by Phosphatase Inhibitors**—We next tested whether known phosphatase-inhibiting agents had an effect on Ssu72 activity (Fig. 2A). The anion $\text{BeF}_3^-$, a potent inhibitor of phosphatases that form phosphoaspartate intermediates (19, 20), did not show an effect on Ssu72 activity. Similar results were obtained with the anion $\text{AlF}_4^-$. In contrast, vanadate ions strongly inhibited Ssu72 activity. The addition of 1 mM orthovanadate reduced product formation below 5%. Phosphate ions also inhibited Ssu72 activity but not as strongly as vanadate. Michaelis-Menten analysis revealed that phosphate acts as a competitive inhibitor (Fig. 2B). The $K_i$ value for phosphate, 4.3 mM, is close to the $K_m$ value for pNPP. This shows that phosphate efficiently competes with pNPP for binding to the active site, suggesting that Ssu72 affinity for pNPP is governed by the binding of the phosphoryl group.

The influence of divalent metal ions on Ssu72 activity was also examined (Fig. 2A). The addition of 1 mM Mg$^{2+}$, Mn$^{2+}$, or Ca$^{2+}$ had essentially no effect, but at 10 mM concentrations, product formation was reduced to 60, 45, and 80%, respectively. In contrast, 1 mM Co$^{2+}$, Ni$^{2+}$, or Cu$^{2+}$ were sufficient to abolish activity. Consistently, Ssu72 was inactive after elution from a Ni-NTA-agarose column, but activity was rescued after removal of bound Ni$^{2+}$ ions with a MonoQ column. In keeping with the negative effect of metal ions, EDTA enhanced Ssu72 activity slightly, most likely because of chelation of metal ion traces. Consequently, 10 mM EDTA was included in further experiments. These results showed that Ssu72 activity does not depend on metal ions, but is rather inhibited by them. The oxidizing agent H$_2$O$_2$ also impaired Ssu72 activity (Fig. 2C). Even at very low concentrations, H$_2$O$_2$ abolished catalysis after a 12-min incubation. Activity could however be recovered by adding the reducing agent DTT, demonstrating that Ssu72 oxidation is reversible (Fig 2C).

**The Signature Motif Is Required for Ssu72 Activity**—Inhibition of Ssu72 by metal ions and by oxidation suggested a catalytic role of the cysteine residue in the signature motif. Metal ions would mask the cysteine side chain, with the “soft” ions Co$^{2+}$, Ni$^{2+}$, and Cu$^{2+}$ being more effective because of their strong interaction with the “soft” cysteine sulfur atom or because of an oxidizing effect in the case of Cu$^{2+}$. Consistently, H$_2$O$_2$ would inactivate the cysteine side chain by oxidizing it to sulfenic acid (21). To test directly whether residues in the signature motif are required for Ssu72 activity, we mutated cysteine 12 and arginine 18 to serine and lysine, respectively, purified the resulting Ssu72 variants, C12S and R18K, and subjected them to pNPP cleavage assays. The variant C12S did not cleave pNPP even after incubation for 24 h, showing that cysteine 12 is essential for Ssu72 activity. The variant R18K retained only very low activity, and the catalytic reaction stopped after 10 min, so that kinetic parameters could not be determined. This points to a crucial catalytic role of arginine 18, which does not depend solely on the positive charge of the side chain.

![Figure 2](https://example.com/figure2.png)

**Ssu72 Resembles PTPases of the Low Molecular Weight Family**—The signature motif is found at different locations within the polypeptide sequence of various PTPase families. In receptor-like and intracellular PTPases, the signature motif is found in the second half of the catalytic domain, in dual specificity PTPases it is located near the middle of the sequence, and in low $M_\text{r}$ PTPases it is located in the N-terminal region (22). Because the signature motif of Ssu72 is also found near the N terminus, and because an asparagine residue within the motif is conserved between Ssu72 and low $M_\text{r}$ PTPases (23) but not in
other PTPase families, Ssu72 may be related to low $M_r$ PTPases. A relationship between Ssu72 and low $M_r$ PTPases is strongly supported by secondary structure prediction (program PHD (24)), which revealed that Ssu72 is a mixed $\alpha/\beta$ protein that shows essentially the same succession of secondary structure elements as the low $M_r$ PTPases (22).

An “Aspartate Loop” Contributes to Ssu72 Activity—In addition to the cysteine and arginine residues in the signature motif, the active site of PTPases comprises a crucial aspartate residue (15, 22). In sequences of the low $M_r$ PTPases family, this aspartate is found about 110 residues C-terminal of the signature motif (Fig. 3). In the three-dimensional structure of PTPases, the aspartate is part of a flexible loop, here referred to as the aspartate loop, near the entrance to the active site (23). Based on the assumption that the fold of Ssu72 resembles that of low $M_r$ PTPases, we predicted a region in Ssu72 that corresponds to the aspartate loop (Fig. 3). Indeed this region comprises the two aspartates 140 and 143. Whereas aspartate 143 is invariable, aspartate 140 is highly conserved and is a glutamate in Arabidopsis thaliana Ssu72. To test whether one of the two aspartate residues corresponds to the active site aspartate in PTPases, we individually mutated the two residues to alanine, purified the resulting Ssu72 variants D140A and D143A, and quantified their activities with Michaelis-Menten kinetics. The variant D140A showed a $K_m$ value of 7.9 mM, twice that of wild type Ssu72, and a $V_{\text{max}}$ value 10-fold lower than that of wild type (Table I). The variant D143A showed a 7-fold higher $K_m$ value, but its $V_{\text{max}}$ value was 3-fold lower than that of wild type Ssu72 (Table I). In contrast to the differences in $K_m$ values, Ssu72 wild type and variant D143A had comparable specific activities, but the variant D140A showed a 10-fold lower specific activity than wild type (Table I). Overall, both aspartate mutants of Ssu72 show a decreased catalytic activity, which is reflected in the low $k_{\text{cat}}/K_m$ values (Table I). The kinetic parameters suggest that aspartate 140 is important for transition state stabilization, whereas aspartate 143 is more important for substrate binding. These results establish the region of Ssu72 comprising aspartates 140 and 143 as the counterpart of the catalytically important aspartate loop of PTPases.

**DISCUSSION**

**Ssu72 Is a Potential Tyrosine Phosphatase**—We report here three lines of evidence suggesting that Ssu72 is a phosphatase that resembles PTPases. First, Ssu72 can cleave the phosphotyrosine analogue pNPP and its catalytic activity is impaired by known PTPase-inhibiting agents. Second, Ssu72 contains the signature motif found in all PTPases, and conserved residues in the signature motif are required for activity. Third, secondary structure prediction and site-directed mutagenesis suggest that the overall structure of Ssu72 resembles that of low $M_r$ PTPases, including an aspartate loop that forms part of the active site.

The Phosphatase Signature Motif Is Essential for Cell Viability—Published data demonstrate an essential role of the signature motif in Ssu72 for cell viability. Truncation of an N-terminal protein part that harbors the catalytic cysteine residue is lethal to yeast (8). Most strikingly, a single point mutation of the catalytic cysteine residue to serine suffices to confer lethality (8). The gene encoding for Ssu72 was originally discovered as its ssu72-1 allele, which enhances a genetic defect in TFIIB in yeast (27). The ssu72-1 allele gives rise to a 10-amino acid duplication in the N-terminal region of Ssu72 (8). The duplication corresponds to residues 4–15 in human Ssu72 and comprises the essential cysteine residue.

Implications for the Catalytic Mechanism—The reaction catalyzed by PTPases generally involves two steps and three crucial active site residues. The $\text{CX}_3\text{R}$ signature motif forms the phosphate-binding loop in the active site of all PTPases. The cysteine in the $\text{CX}_3\text{R}$ motif acts as a nucleophile and accepts the PO$_3^-$ moiety from the phosphotyrosine, generating a phosphocysteine intermediate. In a second step, the PO$_3^-$ moiety is transferred to a water molecule, releasing phosphate and regenerating the enzyme. The arginine in the $\text{CX}_3\text{R}$ motif is required for stabilization of the pentacovalent transition state.
In addition, a flexible aspartate loop contributes an aspartate residue to the active site that serves as a general acid/base in both steps of the reaction (13, 25, 26).

Our mutational analysis and inhibitor studies suggest that the reaction mechanism and active site architecture of Ssu72 is similar to that of known PTPases. Similar to PTPases (15), mutation of the cysteine residues in the CXXR motif abolishes Ssu72 activity, and mutation of the arginine residue dramatically reduces activity. Similar to low Mr PTPases, Ssu72 is inhibited by vanadate, which can mimic a pentacovalent transition state. In contrast, Ssu72 activity is not impaired by the 

References

1. Orphanides, G., and Reinberg, D. (2000) Cell 100, 439–451
2. Maniatis, T., and Reed, R. (2002) Nature 416, 499–506
3. Cramer, P., Bushnell, D. A., and Kornberg, R. D. (2001) Science 292, 525–529
4. Prelich, G. (2002) Eukaryot. Cell 1, 153–162
5. Cho, H., Kim, T. K., Mancebo, H., Lane, W. S., Flores, O., and Reinberg, D. (1999) Genes Dev. 13, 1540–1552
6. Keber, M. S., Archambault, J., Lester, W., Holstege, F. C., Gilardi, O., Janusma, D. B., Jennings, E. G., Kouyoudjian, F., Davidson, A. R., Youang, R. A., and Greenblatt, J. (1999) Mol. Cell 4, 55–62
7. Keber, M. S., and Greenblatt, J. (2002) Biochim. Biophys. Acta 1577, 261–275
8. Sun, Z. W., and Hampsey, M. (1996) Mol. Cell. Biol. 16, 1557–1566
9. Wu, W. H., Pinto, I., Chen, B. S., and Hampsey, M. (1999) Genetics 153, 643–652
10. Pappas, D. L., Jr., and Hampsey, M. (2000) Mol. Cell. Biol. 20, 8343–8351
11. Dichtl, B., Blank, D., Ohnacker, M., Friedlein, A., Roeder, D., Langen, H., and Keller, W. (2002) Mol. Cell 10, 1139–1150
12. Cavan, A. C., Boche, M., Krause, R., Grandi, P., Marzioch, M., Bauer, A., Schultz, J., Rick, J. M., Michon, A. M., Cruciat, C. M., Remor, M., Hofert, C., Scheller, M., Brajenovic, M., Ruffner, H., Merino, A., Klein, K., Hidak, M., Dickeon, D., Rud, T., Gnao, V., Bauch, A., Basteke, S., Hohe, B., Leuwe, C., Heutier, M. A., Copley, R. E., Edelmann, A., Querfurth, E., Rybin, V., Drewes, G., Raimb, M., Bouwmeester, T., Bork, P., Seraphin, B., Kuster, B., Neuhaus, B., and Superti-Furga, G. (2002) Nature 415, 411–417
13. Barford, D., Jia, Z., and Tonks, N. K. (1995) Nat. Struct. Biol. 2, 1043–1053
14. Fauman, E. B., and Sapper, M. A. (1996) Trends Biochem. Sci. 21, 413–417
15. Ramponi, G., and Stefani, M. (1997) J. Biochem. Cell Biol. 29, 279–292
16. Burke, T. R., Jr., and Zhang, X. Y. (1998) Biopolymers 47, 225–241
17. Denu, J. M., Zhou, G., Guo, Y., and Dixon, J. E. (1995) Biochemistry 34, 3398–3403
18. Wo, Y.-Y., McCormack, A. L., Shabanowitz, J., Lund, D. F., Davis, J. P., and Zhang, Z.-Y. (1994) J. Biol. Chem. 269, 2730–2737
19. Stuckey, J. A., Schubert, H. L., Fauman, E. B., Dixon, J. E., and Van Etten, R. L. (1995) J. Biol. Chem. 270, 18499–18504
20. Zhan, M., Stweker, A., and Hampsey, M. (1996) Nucleic Acids Res. 24, 2560–2566
21. Kim, J.-H., Cho, H., Ryu, S.-E., and Choi, M.-U. (2000) Arch. Biochem. Biophys. 382, 72–80
22. Stuckey, J. A., Schubert, H. L., Fauman, E. B., Zhan, Z.-Y., Dixon, J. E., and Saper, M. A. (1994) Nature 370, 571–575
23. Zhang, Z., Harms, E., and Van Etten, R. L. (1994) J. Biol. Chem. 269, 25947–25950
24. Davis, J. P., Zhou, M.-M., and Van Etten, R. L. (1994) J. Biol. Chem. 269, 8734–8740
25. Ostein, K., Pohaleski, C. W., and Van Etten, R. L. (1995) J. Biol. Chem. 270, 18491–18499
26. Chambers, R. S., Wang, B. Q., Burton, Z. F., and Dahmus, M. E. (1995) J. Biol. Chem. 270, 14962–14969
27. Barilla, D., Lee, B. A., and Proudfoot, N. J. (2001) Proc. Natl. Acad. Sci. U.S.A. 98, 445–450
28. Chambers, R. S., Wang, B. Q., Burton, Z. F., and Dahmus, M. E. (1995) J. Biol. Chem. 270, 14962–14969
29. Davis, J. P., Zhou, M.-M., and Van Etten, R. L. (1994) J. Biol. Chem. 269, 8734–8740
30. Zhang, Z., Harms, E., and Van Etten, R. L. (1994) J. Biol. Chem. 269, 25947–25950
31. Duyster, J., Baskaran, R., and Wang, Y. J. Y. (1996) Proc. Natl. Acad. Sci. U.S.A. 92, 1555–1559
32. West, L. M., and Corden, J. L. (1995) Genetics 140, 1223–1233
33. Barilla, D., Lee, B. A., and Proudfoot, N. J. (2001) Proc. Natl. Acad. Sci. U.S.A. 98, 445–450
34. Chambers, R. S., Wang, B. Q., Burton, Z. F., and Dahmus, M. E. (1995) J. Biol. Chem. 270, 14962–14969
35. Davis, J. P., Zhou, M.-M., and Van Etten, R. L. (1994) J. Biol. Chem. 269, 8734–8740
36. Ostein, K., Pohaleski, C. W., and Van Etten, R. L. (1995) J. Biol. Chem. 270, 18491–18499
37. Barilla, D., Lee, B. A., and Proudfoot, N. J. (2001) Proc. Natl. Acad. Sci. U.S.A. 98, 445–450
38. Chambers, R. S., Wang, B. Q., Burton, Z. F., and Dahmus, M. E. (1995) J. Biol. Chem. 270, 14962–14969
39. Davis, J. P., Zhou, M.-M., and Van Etten, R. L. (1994) J. Biol. Chem. 269, 8734–8740
40. Ostein, K., Pohaleski, C. W., and Van Etten, R. L. (1995) J. Biol. Chem. 270, 18491–18499
41. Barilla, D., Lee, B. A., and Proudfoot, N. J. (2001) Proc. Natl. Acad. Sci. U.S.A. 98, 445–450
42. Chambers, R. S., Wang, B. Q., Burton, Z. F., and Dahmus, M. E. (1995) J. Biol. Chem. 270, 14962–14969
43. Davis, J. P., Zhou, M.-M., and Van Etten, R. L. (1994) J. Biol. Chem. 269, 8734–8740
44. Ostein, K., Pohaleski, C. W., and Van Etten, R. L. (1995) J. Biol. Chem. 270, 18491–18499
45. Barilla, D., Lee, B. A., and Proudfoot, N. J. (2001) Proc. Natl. Acad. Sci. U.S.A. 98, 445–450
46. Chambers, R. S., Wang, B. Q., Burton, Z. F., and Dahmus, M. E. (1995) J. Biol. Chem. 270, 14962–14969
47. Davis, J. P., Zhou, M.-M., and Van Etten, R. L. (1994) J. Biol. Chem. 269, 8734–8740
48. Ostein, K., Pohaleski, C. W., and Van Etten, R. L. (1995) J. Biol. Chem. 270, 18491–18499
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