Hsp105α Suppresses Hsc70 Chaperone Activity by Inhibiting Hsc70 ATPase Activity*

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Hsp105α is a mammalian member of the HSP105/110 family, a diverged subgroup of the HSP70 family. Hsp105α associates with Hsp70/Hsc70 as complexes in vivo and regulates the chaperone activity of Hsp70/Hsc70 negatively in vitro and in vivo. In this study, we examined the mechanisms by which Hsp105α regulates Hsc70 chaperone activity. Using a series of deletion mutants of Hsp105α and Hsc70, we found that the interaction between Hsp105α and Hsc70 was necessary for the suppression of Hsc70 chaperone activity by Hsp105α. Furthermore, Hsp105α and deletion mutants of Hsp105α that interacted with Hsc70 suppressed the ATPase activity of Hsc70, which by the concomitant appearance of ATPase activity of Hsp105α. As the ATPase activity of Hsp70/Hsc70 is essential for the efficient folding of non-native proteins, Hsp105α is suggested to regulate the substrate binding cycle of Hsp70/Hsc70 by inhibiting the ATPase activity of Hsp70/Hsc70, thereby functioning as a negative regulator of the Hsp70/Hsc70 chaperone system.

Hsp105α and Hsp105β are mammalian stress proteins that belong to the HSP105/110 family. Hsp105α is constitutively expressed and induced by various forms of stress, whereas Hsp105β is an alternatively spliced form of Hsp105α that is specifically produced following heat shock at 42°C (1–3). Hsp105α and Hsp105β suppress the aggregation of denatured proteins caused by heat shock in vitro, as does Hsp70, but refolding activity of these proteins is yet to be revealed (4). These proteins exist as complexes associated with Hsp70 and Hsc70 (a constitutive form of Hsp105) in mammalian cells (5, 6) and suppress the chaperone activity of Hsp70 in vitro and in vivo (4, 7). Furthermore, Hsp105α and Hsp105β are phosphorylated at Ser509 by protein kinase CK2 (CK2) in vitro and in vivo, and the CK2-mediated phosphorylation modulates the inhibitory effect of Hsp105α on Hsp70/Hsc70 chaperone activity (7). Recently, Hsp105α and Hsp105β were suggested to function as a substitute for Hsp70 family proteins to suppress the aggregation of denatured proteins in cells under severe stress, in which the cellular ATP level decreases markedly (8).

The HSP70 family is a major and well-characterized group of heat shock proteins. Several different species of HSP70 family proteins are present in different compartments of eukaryotic cells and play important roles as molecular chaperones that prevent the irreversible aggregation of denatured proteins and assist folding, assembly, and translocation across the membrane of cellular proteins (9, 10). The chaperone activity of Hsp70/Hsc70 relies on its ability to bind to short exposed hydrophobic stretches of polypeptide substrates in an ATP-regulated fashion. The ATP-bound Hsp70/Hsc70 exhibits low affinity and fast exchange rates for substrate, whereas the ADP-bound form has high affinity and slow exchange rates for substrate (11–14). Conversion of ATP-bound Hsp70/Hsc70 to the ADP-bound form is induced by its intrinsic ATPase activity, which is facilitated by co-chaperones of the HSP40 family (15). Many proteins have been identified as regulators of Hsp70/Hsc70-mediated refolding of denatured proteins (16–20). Hip stabilizes the ADP-bound form of Hsp70/Hsc70 and prevents the ATP-ADP cycle of Hsp70/Hsc70 (16). BAG-1 inhibits the chaperone activity of Hsp70/Hsc70 through the promotion of the dissociation of ADP from Hsp70/Hsc70 (17, 18). CHIP suppresses the reaction cycle of Hsp70/Hsc70 by preventing the binding of ATP or inhibiting the hydrolysis of ATP (19, 20).

The predicted secondary structure of Hsp105α and Hsp105β is composed of an N-terminal ATP-binding, a β-sheet, a loop, and a C-terminal α-helical domain, similar to those of HSP70 family proteins (2–3). The β-sheet domain of Hsp105α and Hsp105β binds denatured proteins such as Hsp70/Hsc70 (8). However, although the ATP-binding domain of Hsp105α and Hsp105β is conserved among HSP70 family proteins, the ATP binding of the domain in HSP70 family proteins has not been elucidated. Furthermore, although Hsp105α suppresses the chaperone activity of Hsp70/Hsc70 (4, 7), the precise mechanism of the suppression has not been clarified yet. In the present study, we examined the mechanisms by which Hsp105α regulates Hsc70 chaperone activity and revealed that Hsp105α suppresses the chaperone activity of Hsc70 by inhibiting the ATPase activity of Hsc70 with the concomitant appearance of Hsp105 ATPase activity.

EXPERIMENTAL PROCEDURES

Plasmids—Expression plasmids for His-tagged mouse Hsp105α and deletion mutants of Hsp105α in Escherichia coli have been described previously (4, 7). To construct an expression plasmid (pTrcHis70) for His-tagged human Hsc70 in E. coli, human Hsc70 cDNA derived from the plasmid pHSC7 (21) was subcloned into Xhol-KpnI sites of the expression vector pTrcHisA (RIKEN Gene Bank, Ibaraki, Japan). For the construction of deletion mutants of Hsc70, a PCR was performed with pTrcHis70 as the template and specific primer sets of the expression vector pTrcHisA (RIKEN Gene Bank, Ibaraki, Japan). The deletion mutants were generated by the PCR and cloned into the expression vector pTrcHis70. The deletion mutants were expressed and purified as His-tagged proteins from E. coli cultures and used in the ATPase activity assay.

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total protein separated by SDS-PAGE and detected by Coomassie Brilliant Blue staining.

Among a series of deletion mutants of Hsp105 anion-exchange column chromatography (Amersham Biosciences) (4, lating agarose column chromatography (Invitrogen) followed by Mono Q/H9262 with 100 °C for 1 ha that contains Hsc70/K71A was collected.

His-tagged proteins were purified by Ni2+—chelating agarose and hardly eluted from the Mono Q column. To purify the GST-tagged mouse Hsp105, the unbound fraction that contains Hsc70K71A was collected.

Luciferase (164 nM) was incubated with Hsp105N, mouse Hsp105, Hsp105C3, and then a pull-down assay using Ni2+-chelating agarose was performed. Proteins bound to the beads were eluted, separated by SDS-PAGE, and detected by Western blotting using anti-Hsp70 and anti-PentaHis antibodies (right panel). BSA, bovine serum albumin. N, His-Hsp105N. BL21.

Luciferase activity was assayed, and the relative activity of luciferase is expressed as a percentage of that of the control with Hsc70/Hsp40. Each value represents the means ± S.D. from four independent experiments.

The middle panel shows total protein separated by SDS-PAGE and detected by Coomassie Brilliant Blue staining.

Protein Purification—His-tagged proteins were purified by Ni2+-chelating agarose column chromatography (Invitrogen) followed by Mono Q anion-exchange column chromatography (Amersham Biosciences) (4, 7). Among a series of deletion mutants of Hsp105a, only His-Hsp105C3 (see Fig. 1A) was purified by the Ni2+-chelating agarose column chromatography as the protein was tightly bound to and hardly eluted from the Mono Q column. To purify the GST-tagged mouse Hsp105a, the transformant containing pGEX-105 was grown at 37 °C in LB medium with 100 μg/ml ampicillin until the A600 reached 0.5. After a 3-h treatment with 0.3 mM isopropl-β-D-thiogalactopyranoside at 37 °C, the cells were ruptured by sonication, and the lysate was loaded onto a glutathione-Sepharose 4B column (Amersham Biosciences) equili briated with phosphate-buffered saline (PBS). The column was washed with PBS, and bound protein was eluted with an elution buffer containing 50 mM Tris-HCl, pH 8.0, and 10 mM glutathione (reduced form). To remove the GST tag from GST-Hsc70K71A, 50 μg of GST-Hsc70K71A was incubated with 10 units of ProScission protease (Amersham Biosciences) in 50 μl of cleavage buffer containing 50 mM Tris-HCl, pH 7.5, 150 mM NaCl, 1 mM EDTA, and 1 mM dithiothreitol (DTT) at 5 °C for 24 h. Then, the reaction mixture was incubated with 20 μl of glutathione-Sepharose 4B beads (50% in cleavage buffer) at 4 °C for 1 h, and the unbound fraction that contains Hsc70K71A was collected.

Fig. 1. Determination of domains of Hsp105a and Hsc70 required for their interaction. A, schematic diagram of the domain structure of Hsp105a and deletion mutants (left panel). His-tagged Hsp105a or its mutant (20 μM each) was incubated with Hsc70 (20 μM) in 50 μl of binding buffer for 1 h at 4 °C, and then a pull-down assay using Ni2+-chelating agarose was performed. Proteins bound to the beads were eluted, separated by SDS-PAGE, and detected by Western blotting using anti-Hsp70 and anti-PentaHis antibodies (right panel). BSA, bovine serum albumin. N, His-Hsp105N. Among a series of deletion mutants of Hsp105 anion-exchange column chromatography (Amersham Biosciences) (4, lating agarose column chromatography (Invitrogen) followed by Mono Q/H9262 with 100 °C for 1 h, and then a pull-down assay using Ni2+-chelating agarose was performed. Proteins bound to the beads were eluted, separated by SDS-PAGE, and detected by Western blotting using anti-Hsp70 and anti-PentaHis antibodies (right panel). The middle panel shows total protein separated by SDS-PAGE and detected by Coomassie Brilliant Blue staining.

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Fig. 2. Hsp105a mutants interacting with Hsc70 suppress the Hsc70 chaperone activity. Luciferase (164 nM) was incubated with Hsc70, Hsp40, and Hsp105a or a deletion mutant (2 μM each) at 42 °C for 30 min. Then, to 10-μl aliquots, rabbit reticulocyte lysate was added at 40%, and the mixture was incubated further at 25 °C for 30 min. Luciferase activity was assayed, and the relative activity of luciferase is expressed as a percentage of that of the control with Hsc70/Hsp40. Each value represents the means ± S.D. from four independent experiments. Statistical significance was determined with the unpaired Student’s t test. *, p < 0.05. BSA, bovine serum albumin. N, His-Hsp105N.
Hsc70 was purified from bovine brain by DEAE-CL6B-Sepharose column chromatography (Amersham Biosciences) and ATP-agarose column chromatography due to its tight adsorption to the column, the ATP-binding domain (Hsp105C3) could not be purified by MonoQ column chromatography (Amersham Biosciences) and ATP-agarose column (Promega).

**Analysis of ATP Hydrolysis and ATPase Activity**—ATP hydrolysis was determined as described previously (4). His-tagged Hsp105α or the deletion mutant (2 μM each) was incubated with Hsc70 and Hsp40 (2 μM each) in 20 μl of a buffer containing 30 mM Hepes-KOH, pH 7.5, 40 mM KC1, 5 mM MgCl2, 2 mM DTT, 500 μM ATP, and 1 μCi of [γ-32P]ATP (Amersham Biosciences, 3000 Ci/mmol) at 37 °C for 1 h. Aliquots of reaction mixtures were mixed with 500 μl of stop solution containing 4% (v/v) Norit A charcoal, 0.9 M HCl, 90 mM sodium pyrophosphate, and 2 mM NaH2PO4, and then centrifuged. The radioactivity in the supernatant was measured using a liquid scintillation counter.

For the single turnover ATPase assay, His-tagged Hsp105α or Hsc70 (10 μM) was incubated in a buffer containing 25 mM Hepes-KOH, pH 7.5, 11 mM Mg(OAc)2, 100 μM ATP, and 5 μCi of [γ-32P]ATP (Amersham Biosciences, 3000 Ci/mmol) at 25 °C for 10 min. Aliquots of reaction mixtures were immediately applied onto Polygram CEL 300 polyethyleneimine cellulose plates (Macherey-Nagel) and separated by thin-layer chromatography using a buffer system consisting of 0.5 M formic acid and 0.5 M LiCl. [32P]ATP and [32P]ADP were separated from free [32P]ATP by spinning through a Sephadex G-50 column. Hsp105α-[32P]ATP or Hsp105α-[32P]ADP on the plates were detected by autoradiography, and the percentage of ATP hydrolyzed to ADP in each reaction was calculated after densitometry.

**RESULTS**

Domains Necessary for the Interaction between Hsp105α and Hsc70—To elucidate how Hsp105α regulates the Hsc70 chaperone system, we first examined the interaction between Hsc70 and Hsp105α deletion mutants (Fig. 1A). A series of His-tagged Hsp105α deletion mutants was incubated with Hsc70, and pull-down assays were performed using Ni2+-chelating beads. Hsp105ΔL and Hsp105C5 interacted with Hsc70 the same as wild-type Hsp105α, whereas Hsp105Δβ and Hsp105ΔβL lacking the β-sheet domain failed to interact with Hsc70. Furthermore, Hsc70 did not interact with Hsp105N2 or Hsp105C3, which lacked an α-helix and ATP-binding domain, respectively. These results indicated that all domains of Hsp105α except the loop are essential for the interaction between Hsp105α and Hsc70.

Next, we examined the interaction between Hsp105α and Hsc70 deletion mutants (Fig. 1B). A series of His-tagged Hsc70 deletion mutants was incubated with Hsp105α, and pull-down assays were performed using Ni2+-chelating beads. Hsc70 deletion mutants lacking the N-terminal ATP-binding, β-sheet, or C-terminal α-helix domain did not interact with Hsp105α, suggesting that all domains of Hsc70 are necessary for the binding to Hsp105α.

**Interaction of Hsp105α with Hsc70 Is Required for the Suppression of Hsp70 Chaperone Activity**—We next examined the suppressive effect of Hsp105α and its mutants on Hsc70 chaperone activity.
**FIG. 4. Hsp105 inhibits the hydrolysis of ATP bound to Hsc70.**

A, $\text{[a-32P]}$ATP-bound Hsc70 (1 µM) was incubated with or without Hsp105 (1–4 µM) in the presence or absence of Hsp40 (0.5 µM) at 25 °C for 10 min. B, $\text{[a-32P]}$ATP-bound Hsc70 (1 µM) was incubated with or without Hsp105 or its deletion mutant (1 µM each) in the presence or absence of Hsp40 (0.5 µM) at 25 °C for 10 min. Then, aliquots of samples were immediately applied onto polyethyleneimine cellulose plates, and ATP and ADP were separated by thin-layer chromatography. Spots of ATP and ADP in each lane were quantified by densitometry. Each value represents the ratio of ADP to ATP plus ADP in each lane from two independent experiments.

**FIG. 5. Hsc70 stimulates the hydrolysis of ATP bound to Hsp105.**

A, $\text{[a-32P]}$ATP-bound Hsp105 (1 µM) was incubated with or without Hsc70 (0.5 µM) in the presence or absence of Hsp40 (0.5 µM) at 25 °C for 10 min. B, $\text{[a-32P]}$ATP-bound Hsp105 (1 µM) was incubated with or without Hsp105 or its deletion mutant (1 µM each) in the presence or absence of Hsp40 (0.5–2.0 µM). Conversion of Hsp105-bound ATP to ADP was determined. The amounts of ATP and ADP in each lane were quantified by densitometry. Each value represents the ratio of ADP to ATP plus ADP in each lane from two independent experiments.
ATP binding. The Lys residue at position 71 of human Hsc70, which is essential for hydrolysis of ATP, was substituted with Ala to yield Hsc70K71A (23). Hsc70K71A did not bind ATP (Fig. 6A) but interacted with Hsp105α (Fig. 6B). When ATP-bound Hsp105α was incubated with Hsc70WT or Hsc70K71A, hydrolysis of Hsp105α-bound ATP was observed in the presence or absence of K⁺, and the hydrolysis was not significantly affected by Hsp40 (Fig. 6C). Furthermore, although Hsc70 did not show any ATPase activity in the absence of K⁺, Hsc70WT also enhanced the hydrolysis of Hsp105α-bound ATP in the absence of K⁺. These findings suggest that the ATPase activity of Hsc70 is not necessary for the hydrolysis of ATP bound to Hsp105α, whereas the ATPase activity of Hsp105α is induced by interaction with Hsc70.

**DISCUSSION**

Hsp105α associates with Hsp70/Hsc70 (5, 6) and suppresses its chaperone activity in mammalian cells (4, 7). The mechanism by which Hsp105α regulates the chaperone activity of Hsp70/Hsc70, however, had not been elucidated. Here, we demonstrated that Hsp105α suppresses the ATPase activity of the Hsc70 chaperone, with the concomitant appearance of Hsp105α ATPase activity.
Hsp70/Hsc70 exists in either an ATP- or an ADP-bound form, and nucleotides regulate the substrate binding affinity of Hsp70/Hsc70 (Fig. 7). ATP-bound Hsp70/Hsc70 rapidly associates with and dissociates from unfolded polypeptide substrates or folding intermediates. The substrate binding of Hsp70/Hsc70 is stabilized by conversion of bound ATP to ADP, and this conversion is catalyzed by the intrinsic ATPase activity of Hsp70/Hsc70, which is facilitated by co-chaperones of the HSP40 family (15). Hsp70/Hsc70 substrate complexes dissociate upon the regeneration of Hsp70/Hsc70-ATP. Upon its release from Hsp70/Hsc70, an unfolded polypeptide can fold, aggregate, or be rebound by Hsp40 and Hsp70/Hsc70. Many proteins have been identified as regulators of the Hsp70/Hsc70-mediated refolding of proteins (16–20). Hip, initially identified as a protein that interacts with the ATPase domain of Hsp70/Hsc70, stabilizes the ADP-bound form of Hsp70/Hsc70 and prevents the ATP-ADP cycle of Hsp70/Hsc70, resulting in the inhibition of the Hsp70/Hsc70 chaperone cycle (16). The anti-apoptotic protein BAG-1 inhibits the chaperone activity of Hsp70/Hsc70 through the promotion of the dissociation of ADP from Hsp70/Hsc70 (17, 18). In contrast, CHIP suppresses the ATP reaction cycle of Hsp70/Hsc70 by preventing the binding of ATP or inhibiting the hydrolysis of ATP (19, 20). In addition to these co-chaperones of Hsp70, we showed here that Hsp105α suppresses the substrate binding cycle of Hsc70 by inhibiting the ATPase activity of Hsc70, thereby acting as a negative regulator of the Hsp70/Hsc70 chaperone as does CHIP (Fig. 7). Furthermore, it is worth noting that the inhibitory effect of Hsp105α on Hsp70/Hsc70 chaperone activity is suppressed by the phosphorylation of Hsp105α by CK2, suggesting a finely and rapidly controlled regulation of the Hsp70/Hsc70 chaperone system by the co-chaperone Hsp105α (7).

Hsp105α is composed of an N-terminal ATP-binding domain, a β-sheet domain in the central region, and a C-terminal α-helical domain similar to HSP70 family proteins (2, 3). As all domain structures of Hsp105α except the loop were necessary for the interaction with Hsc70 and all domains of Hsc70 were required for binding to Hsp105α, an almost intact three-dimensional structure of these proteins might be essential for their interaction. Furthermore, although both Hsp105α and Hsc70 bind to non-native proteins via their central β-sheet domain (8, 24–26), Hsp105α did not prevent the interaction of Hsc70 with denatured proteins. Thus, the suppression of Hsp70/Hsc70 chaperone activity by Hsp105α seems not to be due to the prevention of substrate binding of Hsc70.

Despite the conserved ATP-binding domain of HSP105/110 family proteins, no ATP binding or ATPase activity of these proteins had been observed. In this study, we first demonstrated that Hsp105α binds ATP and hydrolyzes ATP to ADP in the presence of Hsc70 with or without its ATPase activity. When Hsp105α suppressed the chaperone activity of Hsc70 by inhibiting its ATPase activity, the hydrolysis of Hsp105α-bound ATP was concomitantly observed (Fig. 5). Furthermore, an Hsp105α mutant defective in ATP binding (Hsp105K69A) did not suppress either the hydrolysis of Hsc70-bound ATP or the chaperone activity of Hsc70. However, since Hsp105K69A did not bind to Hsc70, further study is needed to conclude whether ATPase activity of Hsp105α is necessary for suppression of the ATPase and chaperone activity of Hsc70.

Hsp105α exists with Hsc70 at a molar ratio of 1:10 and associates with Hsp70/Hsc70 in mammalian cells (5, 6). Hsp105α suppresses the aggregation of denatured proteins caused by heat shock in vitro as does Hsp70/Hsc70, but refolding activity of Hsp105α is yet to be revealed (4). However, Hsp70/Hsc70/Hsp105α binds denatured substrates efficiently in the presence of ATP but not ADP, whereas Hsp105α suppresses the aggregation of denatured proteins in the presence of ADP as well as ATP (8). Therefore, Hsp105α is suggested to function as a substitute for Hsp70/Hsc70 to suppress the aggregation of denatured proteins in cells under severe stress, in which the cellular ATP level decreases markedly. Since Hsp70/Hsc70 chaperones participate in many important cellular processes, the present finding that Hsp105α suppresses the chaperone activity of Hsp70/Hsc70 by inhibiting their ATPase activity may provide clues as to the role of Hsp105α in chaperone networks in mammalian cells.

REFERENCES

1. Hatayama, T., Honda, K., and Yukioka, M. (1986) Biochem. Biophys. Res. Commun. 137, 957–963

2. N. Yamagishi, K. Ishihara, and T. Hatayama, unpublished data.
1. Yasuda, K., Nakai, A., Hatayama, T., and Nagata, K. (1995) J. Biol. Chem. 270, 29718–29723
2. Ishihara, K., Yasuda, K., and Hatayama, T. (1999) J. Biol. Chem. 274, 138–142
3. Yamagishi, N., Ishihara, K., Hatayama, T., and Nagata, K. (2000) Biochem. Biophys. Res. Commun. 272, 850–855
4. Ishihara, K., Yasuda, K., and Hatayama, T. (1999) Biochim. Biophys. Acta 1444, 138–142
5. Yamagishi, N., Nishihori, H., Ishihara, K., Ohtsuka, K., and Hatayama, T. (2000) Biochem. Biophys. Res. Commun. 272, 850–855
6. Hatayama, T., Yasuda, K., and Yasuda, K. (1998) Biochem. Biophys. Commun. 248, 395–401
7. Ishihara, K., Yamagishi, N., and Hatayama, T. (2003) Biochim. Biophys. Acta 1444, 138–142
8. Yamagishi, N., Ishihara, K., Saito, Y., and Hatayama, T. (2003) FEBS Lett. 533, 390–396
9. Hendrick, J. P., and Hartl, F.-U. (1993) Annu. Rev. Biochem. 62, 349–384
10. Bukau, B., and Horwich, A. L. (1998) Cell 92, 351–366
11. Palleros, D. R., Welch, W. J., and Fink, A. L. (1991) Proc. Natl. Acad. Sci. U. S. A. 88, 5719–5723
12. Palleros, D. R., Reid, K. L., Shi, L., Welch, W. J., and Fink, A. L. (1993) Nature 365, 664–666
13. Greene, L. E., Zinner, R., Naficy, S., and Eisenberg, E. (1995) J. Biol. Chem. 270, 20676–20677
14. McCarty, J. S., Buchberger, A., Reinstein, J., and Bukau, B. (1995) J. Mol. Biol. 249, 126–137
15. Minami, Y., Hohfeld, J., Ohtsuka, K., and Hartl, F.-U. (1996) J. Biol. Chem. 271, 18617–18624
16. Hohfeld, J., Minami, Y., and Hartl, F.-U. (1995) Cell 83, 589–598
17. Takayama, S., Bimston, D. N., Matsuzawa, S., Freeman, B. C., Aime-Sempe, C., Xie, Z., Morimoto, R. I., and Reed, J. C. (1997) EMBO J. 16, 4887–4896
18. Bimston, D., Song, J., Winchester, D., Takayama, S., Reed, J. C., and Morimoto, R. I. (1998) EMBO J. 17, 6871–6878
19. Ballinger, C. A., Connell, P., Wu, Y., Hu, Z., Thompson, L. J., Yin, L.-Y., and Patterson, C. (1999) Mol. Cell. Biol. 19, 4535–4545
20. Meacham, G. C., Patterson, C., Zhang, W., Younger, J. M., and Cyr, D. M. (2001) Nat. Cell Biol. 3, 100–105
21. Imamoto, N., Matsuzuka, Y., Kurikura, T., Kohno, K., Miyagi, M., Sakiyama, F., Okada, Y., Tsunasawa, S., and Yoneda, Y. (1992) J. Cell Biol. 119, 1047–1061
22. Schlossman, D. M., Schmid, S. L., Braell, W. A., and Rothman, J. E. (1984) J. Cell Biol. 99, 723–733
23. Melanie, C., O'Brien, Flaherty, K. M., and McKay, D. B. (1996) J. Biol. Chem. 271, 15874–15878
24. Flaherty, K. M., DeLuca-Flaherty, C., and McKay, D. B. (1990) Nature 346, 623–628
25. Wang, T. F., Chang, J. H., and Wang, C. (1993) J. Biol. Chem. 268, 26049–26051
26. Morschauser, R. C., Wang, H., Flynn, G. C., and Zuerderweg, E. R. (1995) Biochemistry 34, 6261–6266
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