Coordinated Participation of Calreticulin and Calnexin in the Biosynthesis of Myeloperoxidase*

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William M. Nauseef, Sally J. McCormick, and Melissa Goedken
From the Inflammation Program and Departments of Medicine, University of Iowa and Veterans Affairs Medical Center, Iowa City, Iowa 52242

Myeloperoxidase (MPO) is a neutrophil lysosomal hemeprotein essential for optimal oxygen-dependent microbicidal activity. We have demonstrated previously that calreticulin, a luminal endoplasmic reticulum protein, functions as a molecular chaperone during myeloperoxidase biosynthesis, associating reversibly with the heme-free precursor apop-MPO. Because the membrane-bound endoplasmic reticulum protein calnexin is structurally and functionally related to calreticulin, we assessed the role of calnexin in myeloperoxidase biosynthesis. Like calreticulin, calnexin coprecipitated exclusively with glycosylated MPO precursors and with apop-MPO but, in contrast to calreticulin, also with the enzymatically active, heme-containing precursor pro-MPO. To determine if calnexin participated in heme insertion into MPO, we compared the kinetics of chaperone association with MPO precursors using stable transfectants expressing cDNA encoding wild type MPO or mutated forms that do not acquire heme. Transfectants expressing mutant cDNA had prolonged association of MPO-related precursors with calreticulin and especially with calnexin. These studies demonstrate that 1) both calreticulin and calnexin associated with glycosylated apop-MPO; 2) only calnexin associated selectively with the enzymatically active, heme-containing precursor pro-MPO; and 3) mutants unable to incorporate heme had prolonged association with calnexin. These findings represent the first evidence of a specialized role in calnexin in facilitating protein maturation in the endoplasmic reticulum of myeloid cells.

Myeloperoxidase (MPO); donor: H₂O₂ oxidoreductase, EC 1.11.1.7 is a heme-containing lysosomal protein present exclusively in cells of neutrophil and monocyte lineage (1). In concert with hydrogen peroxide generated by the NADPH-dependent oxidase, MPO is a critical component of the most efficient microbicidal system in human neutrophils (1).

Biosynthesis of MPO is restricted to the promyelocyte stage in myeloid development and has been studied extensively using human promyelocytic cell lines (for review, see Refs. 2 and 3). We reported previously that calreticulin (CRT), a high capacity, low affinity calcium-binding protein located in the endoplasmic reticulum (ER) (4, 5), interacts transiently with apop-MPO, the heme-free protein precursor of MPO (6). Based on these studies we suggested that CRT functions as a molecular chaperone during MPO biosynthesis. Several studies have confirmed the ability of CRT to function in a similar fashion in the biosynthesis of a variety of unrelated proteins (for review, see Ref. 7).

Calnexin (CLN), a membrane-bound molecular chaperone located in the ER, shares significant structural and functional features with CRT (8, 9). The regions of greatest similarity between CRT and CLN are those that extend into the lumen of the ER (8, 10, 11) and thus most likely to contribute to their shared capacity to interact with nascent glycoproteins. Published studies of the role of CRT and CLN in the biosynthesis of a given protein have not identified any functional differences in their capacity as molecular chaperones (7). We undertook these studies to determine to what extent CLN participated in MPO biosynthesis and if there were significant differences between these interactions and those we had observed previously between apop-MPO and CRT.

EXPERIMENTAL PROCEDURES

Reagents—The human leukemia cell line PLB-985 (12) was acquired from Dr. Timothy Ley (Washington University, St. Louis, MO) and maintained in RPMI 1640 medium supplemented with 2 mmol/liter glutamine, penicillin-streptomycin, and 5% heat-inactivated fetal calf serum with 5% Serum-plus (JRF Biosciences, Lenexa, KS). Cells were free of mycoplasma infection. Tissue culture medium was obtained from the University of Iowa Cancer Center. For biosynthetic labeling, methionine-free RPMI (Life Technologies, Inc.) was supplemented with 1 mmol/liter pyruvate, 1 mmol/liter glutamine, antibiotics, and 10% dialyzed fetal calf serum. [35S]Methionine (1,320 Ci/mmol) and δ-[¹⁴C]aminoethylglycine (48.2 mCi/mmol) were obtained from Amersham Corp. and DuPont, respectively. Monospecific rabbit polyclonal antisera against MPO has been described previously (13). Antiserum against CRT was generated using baculovirus-expressed recombinant CRT (6, 14) and is available commercially (Affinity Bioreagents, Golden, CO), whereas that against CLN was raised against a synthetic peptide derived from the carboxyl terminus of CLN and was kindly provided by Drs. John J. M. Bergeron and David Y. Thomas of McGill University (Montreal, Canada). There is no cross-reactivity of the antisera against CRT and CLN (data not shown). Protein A was purchased from Life Technologies, Inc. and radiolabeled with 125I at a core facility at the Iowa City Veterans Affairs Medical Center. Additional chemicals and reagents were obtained from Sigma.

Biosynthetic Labeling—PLB-985 cells were grown at 37 °C in an atmosphere of 5% CO₂ in the medium described above. For biosynthetic labeling cells were suspended at 5.0 × 10⁶/ml in methionine-free RPMI with 10% dialyzed fetal calf serum for 60 min. After methionine depletion, 25 mCi/ml [³⁵S]methionine was added and the cells cultured for the specified time interval. At the end of the labeling period, cells were collected by centrifugation for subsequent analysis, as described previously (15). In pulse-chase experiments, cells were resuspended in medium made 1 mM with unlabeled methionine and chased for the specified time interval. In experiments in which the heme group was radiolabeled, cells were cultured for 16–20 h in the presence of medium supplemented with 15 mCi/ml δ-[¹⁴C]aminoethylglycine.

Immunoprecipitation—Immunoprecipitations were done under ei-

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‡ To whom correspondence should be addressed: Dept. of Medicine, University of Iowa, 200 Hawkins Dr., Iowa City, Iowa 52242. Tel.: 319-356-1739; Fax: 319-356-4600; E-mail: william-nauseef@uiowa.edu.

The abbreviations used are: MPO, myeloperoxidase; CRT, calreticulin; ER, endoplasmic reticulum; CLN, calnexin.
ther denaturing or non-denaturing conditions, as described previously (6). For both conditions, 100 ml of lysed cells or 700 ml of culture supernatant was used for immunoprecipitations as described previously (15). Samples were incubated with nonimmune serum for 30 min at 4 °C followed by a 10% suspension of washed protein A-containing Staphylococcus aureus to clear the sample of radiolabeled proteins which might nonspecifically be precipitated. The cleared sample was incubated subsequently with primary antiseraum. The antigen-antibody complexes were recovered with protein A-bearing S. aureus and the pellets washed serially with 1 ml each of 0.5% Triton X-100 in Tris-buffered saline (10 mM Tris/1 ml, pH 7.5, with 150 mM/1 ml NaCl), 2 mM/1 ml urea in 0.5% Triton X-100 in Tris-buffered saline, 1 mg/ml bovine serum albumin in 0.5% Triton X-100 in Tris-buffered saline, and Tris-buffered saline. After the final wash the antigen-antibody complex was released from protein A by heating at 100 °C for 5 min in the presence of SDS sample buffer (62 mM/liter Tris, 2 mM/liter EDTA, 5% β-mercaptoethanol, 2.3% SDS, pH 6.9).

When immunoprecipitations were done under denaturing conditions, the cleared lysate was denatured by making the sample 2% SDS and heating to 100 °C for 2 min. Prior to the addition of the primary antibody, the SDS concentration of the sample was reduced to 0.2% by the addition of dilution buffer (50 mM Tris HCl, pH 7.4, 190 mM NaCl, 2 mM/liter urea in 0.5% Triton X-100 in Tris-buffered saline, 1 mg/ml bovine serum albumin in 0.5% Triton X-100 in Tris-buffered saline, and Tris-buffered saline. After the final wash the antigen-antibody complex was released from protein A by heating at 100 °C for 5 min in the presence of SDS sample buffer (62 mM/liter Tris, 2 mM/liter EDTA, 5% β-mercaptoethanol, 2.3% SDS, pH 6.9).

Analysis of Immunoprecipitated Proteins—Immunoprecipitates were separated by SDS-polyacrylamide gel electrophoresis. The resultant gel was fixed, soaked in 1 mmol/liter sodium salicylate (19), dried, and subjected to autoradiography. Quantitation of immunoreactive signals was generally done using PhosphoImager SF (Molecular Dynamics, Sunnyvale, CA). In some cases the relative intensity of the signal seen in autoradiography was quantitated using densitometry on a Shimadzu CS-9000U Dual Wavelength Flying Spot Scanner (Shimadzu Scientific, Sunnyvale, CA). In some cases the relative intensity of the signal seen in autoradiography was quantitated using densitometry on a Shimadzu CS-9000U Dual Wavelength Flying Spot Scanner (Shimadzu Scientific, Sunnyvale, CA). In some cases the relative intensity of the signal seen in autoradiography was quantitated using densitometry on a Shimadzu CS-9000U Dual Wavelength Flying Spot Scanner (Shimadzu Scientific, Sunnyvale, CA).

RESULTS

CLN Associates with Biosynthetic Precursors of MPO—We have demonstrated previously that CRT associates with apop-MPO early in MPO biosynthesis (20). Like CRT, CLN serves as a molecular chaperone in the biosynthesis and folding of glycoproteins (for review, see Ref. 7). To determine if CLN associates with MPO precursors, PLB-985 cells were pulse labeled with [35S]methionine and chased with unlabeled methionine for 0 and 24 h before lysis. Cell lysates were immunoprecipitated under non-denaturing conditions and analyzed as described under “Experimental Procedures.” Under these conditions, CLN associated with the 90-kDa precursor form of MPO after pulse labeling but after the chase period did not coprecipitate with the remaining 90-kDa precursor or the 59-kDa heavy subunit of mature MPO.

Failure of CLN to associate with nonglycosylated apop-MPO—Several studies demonstrate that CRT and CLN share an affinity for GlcMan3GlcNAc2 oligosaccharides (23–25) and that this property is critical to their role as molecular chaperones for glycoproteins in the ER (7, 24–29). The primary translation product of MPO is glycosylated at five asparagine residues cotranslationally (22). In the presence of tunicamycin, an antibiotic inhibiting cotranslational N-linked glycosylation (30), promyelocytic cells synthesize a nonglycosylated 80-kDa MPO precursor that does not associate with CRT (20) and fails to be processed into mature or enzymatically active protein.2 Similar to CRT, CLN failed to associate with the nonglycosylated form of MPO precursor synthesized in the presence of tunicamycin (Fig. 2), indicating that the MPO precursors require either glycosylation per se, glycosylation-dependent folding, or both for firm association with CRT and CLN.

The Association of CLN and MPO Precursors Is Transient—An essential characteristic of molecular chaperones is the transient nature of their association with folding intermediates in the ER (31). To examine the relative association of MPO precursors with CRT and with CLN, PLB-985 cells were pulse labeled for 60 min (Fig. 3A) or for 120 min (Fig. 3B) and immunoprecipitated sequentially with antisera to CRT, CLN, and MPO. At 1 h, most of the 90-kDa MPO precursor was associated with CRT, with lesser amounts associated with CLN or free of CRT or CLN (61, 3.7, and 18.2%, respectively). In contrast, after 120 min of labeling, only 27.2% of the MPO precursor that does not associate with CRT (20) and fails to be processed into mature or enzymatically active protein.2 Similar to CRT, CLN failed to associate with the nonglycosylated form of MPO precursor synthesized in the presence of tunicamycin (Fig. 2), indicating that the MPO precursors require either glycosylation per se, glycosylation-dependent folding, or both for firm association with CRT and CLN.

CLN Interacts with Apopo-MPO and Pro-MPO—Both MPO precursors, apop-MPO and pro-MPO, coexist in the ER (32), and each migrates as a 90-kDa protein after SDS-polyacrylamide gel electrophoresis. Only the presence of heme in pro-MPO, assessed by incorporation of radiolabel from δ-[515]ami-

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2 W. M. Nauseef, unpublished data.
nolevulinic acid, and the presence of enzymatic activity can distinguish the two glycoproteins (21). We demonstrated previously that CRT associates exclusively with apopro-MPO, the heme-free precursor of MPO (20). Consistent with that observation, immunodepletion of CRT-associated MPO precursors did not decrease the amount of $^{14}$C-labeled pro-MPO from PLB-985 cells (Fig. 4A). To determine if CLN also associated with only the apo-form of MPO, PLB-985 cells cultured in the presence of $\delta$-labeled aminolevulinic acid were immunoprecipitated with antisera against MPO or CLN (Fig. 4B). As noted previously, radiolabeled heme was incorporated into the 90-kDa pro-MPO and the 59-kDa heavy subunit of mature MPO. In contrast to the results when CRT-associated MPO precursors were recovered, a fraction of the heme-containing pro-MPO coprecipitated with CLN. Only $\sim$13% of the pro-MPO present was associated with CLN, indicating either that the association was restricted to a subpopulation of the pro-MPO or that the CLN-pro-MPO complex was relatively unstable under the conditions of immunoprecipitation. Association of CRT and CLN with Mutated Forms of MPO— Taken together these data indicate that CRT and CLN each associated with fully glycosylated apopro-MPO transiently during MPO biosynthesis. Furthermore, CLN associated also with pro-MPO, the heme-containing, enzymatically active precursor. It is not clear from these data whether CLN facilitates heme insertion into the peptide backbone of apopro-MPO or if heme insertion triggers dissociation of CLN from the newly formed pro-MPO. To examine this question in more detail, we compared the interactions of CRT and CLN with MPO precursors expressed in a K562 cell line transfected with wild type or specifically mutated cDNA for MPO (33).

We identified previously a missense mutation in exon 10, whereby an arginine at codon 569 is replaced by a tryptophan (R569W), as one genotype responsible for hereditary MPO deficiency (34). When transfected into K562 cells, mutant cDNA with R569W exhibits a maturational arrest in MPO biosynthesis; heme is not inserted into the mutant apopro-MPO, neither pro-MPO nor mature MPO is formed, and the cells expressing this mutation lack any peroxidase activity attributable to MPO (33). To assess the impact of R569W and its defective heme insertion on the association of CRT and CLN with MPO precursors, we examined MPO biosynthesis in K562 cells transfected with cDNA for normal and mutant MPO.

To verify that chaperone association of MPO precursors in PLB-985 cells was mirrored accurately by the transfected K562 cells, PLB-985 cells and K562 cells expressing normal (pREP-MPO) and mutant (pREP-R569W) cDNA for MPO were pulse labeled for 1 h and immunoprecipitated directly with MPO antisera or immunoprecipitated serially with antisera against CRT or CLN followed by MPO antisera (Fig. 5A). In both pREP-MPO and pREP-R569W cell lines, CRT and CLN coprecipitated with a fraction of the pro-MPO synthesized. Figure 3: Reversible association of CRT and CLN with MPO precursors. PLB-985 cells were radiolabeled for 60 (panel A) or 120 (panel B) min before lysis and immunoprecipitation. Panel A, sequential immunoprecipitations demonstrated that the majority of the 90-kDa MPO precursor was associated with CRT after 60 min with only a fraction associated with CLN. In contrast, at 120 min (panel B), there was a redistribution of chaperone-associated 90-kDa MPO precursor with less associated with CRT and more with CLN than seen at 60 min of label. Sequential immunoprecipitations (not shown) demonstrated that the 90-kDa CRT and CLN-associated proteins were MPO precursors.

Roles of Calreticulin and Calnexin in MPO Biosynthesis

Figure 4: Differential association of pro-MPO with CLN but not CRT. PLB-985 cells were biosynthetically radiolabeled with $^{[35]S}$methionine, to label protein, or $\delta$-[labeled aminolevulinic acid, to label the heme group, prior to CRT (panel A) or CLN (panel B) immunoprecipitation. Panel A, under these conditions, heme was incorporated into the 90-kDa pro-MPO and the 59-kDa heavy subunit of mature MPO (not shown) and immunoprecipitated with MPO antisera. However, serial immunoprecipitations of CRT recovered only apopro-MPO; no heme-containing species coprecipitated with CRT. In contrast (panel B), CLN coprecipitated with a fraction of the pro-MPO synthesized.
were labeled for 60 min with [35S]methionine and immunoprecipitated
K562 cells transfected with cDNA encoding the R569W mutated form of Panel A
serum (plexed to CLN in pREP-H502 cells (CLN in the pREP-MPO cells, whereas 31.3% was still com-
prolonged in pREP-H502 cells (Fig. 6 B). In not processed into the subunits of mature MPO (Fig. 6 A)
precursor in pREP-502H lacked peroxidase activity and was
relative to that made by pREP-MPO (Fig. 6 B). After pulse labeling,
the pREP-H502 product appeared to be less stable than normal
distal heme-binding site in MPO (35, 36). After pulse labeling,
Because the replacement of arginine with tryptophan may
significantly alter structure in addition to blocking heme inser-
tion, we created pREP-H502, mutating the histidine that is the
significantly different in substrate specificity for CRT and CLN
have also been noted (27, 37, 43, 44). Despite these similarities
between CRT and CLN, we found evidence of functional dis-
CRN, and CLN have shown striking similarity in the substrates
demonstrated sequential interactions of the folding intermedi-
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Fig. 5. Interactions of CRT and CLN with MPO precursors in transfected K562 cells. Panel A, PLB-985 cells (lanes 1, 4, and 6) or K562 cells transfected with cDNA encoding the R569W mutated form of MPO (lanes 2, 5, and 8) or the cDNA of normal MPO (lanes 3, 6, and 9) were labeled for 60 min with [35S]methionine and immunoprecipitated directly with MPO antiserum (αMPO) or sequentially with CLN antisera (αCLN) or with CRT antiserum (αCRT) followed by MPO antiserum. As seen in PLB-985 cells, which normally express MPO, both K562 transfected cell lines synthesized complexes of CRT and CLN with a 90-kDa biosynthetic precursor of MPO. Panel B, pREP-MPO and pREP-R569W cells were pulse labeled for 30 min and chased for intervals of 0–180 min. At the indicated intervals, samples were immunoprecipitated with CLN antisera and CRT antisera and separated by SDS-polyacrylamide gel electrophoresis. Although the chaperone-MPO precursor complexes decayed during the chase period, the CLN-apopropo-MPO complex persisted significantly longer in the pREP-R569W cells.

complex and the failure of heme insertion may both reflect the misfolded state of the precursor resulting from the R569W missense mutation.

Because the replacement of arginine with tryptophan may
significantly alter structure in addition to blocking heme inser-
tion, we created pREP-H502, mutating the histidine that is the
distal heme-binding site in MPO (35, 36). After pulse labeling,
the pREP-H502 product appeared to be less stable than normal
MPO, as less than 10% of immunoreactive MPO was produced
relative to that made by pREP-MPO (Fig. 6 A). The mutant
precursor in pREP-502H lacked peroxidase activity and was
not processed into the subunits of mature MPO (Fig. 6 A).
In addition, the association of CLN with MPO precursors was
prolonged in pREP-H502 cells (Fig. 6 B). At 5 h of chase, 15.7%
of the MPO precursor associated with CLN was still bound to
CLN in the pREP-MPO cells, whereas 31.3% was still com-
plexed to CLN in pREP-H502 cells (n = 3). Thus, as seen with
cells expressing R569W, alterations in heme insertion were
associated with delayed dissociation of the CLN-MPO precurs-
or complex.

Fig. 6. Dissociation of CRT-apopropo-MPO and CLN-apopropo-
MPO complexes in pREP-H502 cells. Panel A, pREP-H502 cells
were biosynthetically pulse labeled and chased for 20 h before lysis and
immunoprecipitation with MPO antiserum. In contrast to cells expressing
cDNA encoding normal MPO in which the 59-kDa heavy subunit of MPO appeared during the chase period, pREP-H502 cells failed to
generate mature MPO from the 90-kDa apopropo-MPO precursor.
In addition, the 90-kDa MPO precursor was less stable in the pREP-H502 cells.
Panel B, pREP-MPO and pREP-H502 cells were pulse labeled and
chased. Although less MPO was made in pREP-H502, CRT and CLN
associated with the 90-kDa MPO precursor during the chase period in
either cell lines. However the kinetics of the dissociation of the chaperone-apropo-MPO complexes was altered in the pREP-H502 cells.
At 5 h of chase, significantly more mutant apopropo-MPO remained
complexed with CLN than occurred in cells expressing wild type MPO.
to which they bind (23–25), consistent with their structural
homology and similar lectin specificities. Several studies have
demonstrated sequential interactions of the folding intermedi-
ates of the same protein with CRT and CLN during its biosyn-
thetic maturation (37, 38) as well as coincident interaction of a
given substrate with CRT and CLN (7, 39–42), although sig-
ificant differences in substrate specificity for CRT and CLN
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DISCUSSION

MPO is the only heme or lysosomal protein demonstrated to
date to associate with molecular chaperones during its biosyn-
thesis (7). However, as with many other glycoproteins, quality
control during its biosynthesis is mediated by transient asso-
ciation with ER resident proteins. The data presented here
indicate that, like several other glycoproteins, precursors of
MPO associated sequentially with different ER resident pro-
tins, in this case two structurally similar proteins, CRT and

In specific situations in which they have been compared,
CRT and CLN have shown striking similarity in the substrates

The active site in MPO is unusual and has been the subject
of considerable study in the past (36, 45–52). Data derived from
the crystal structure of mature MPO indicate that a protoheme

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IX derivative is associated with the protein backbone via a methylsulfonium bond with methionine 409 and with histidine at positions 261 and 502, the distal and proximal coordination positions, respectively (35). The data presented support the hypothesis, previously proposed by us and others (32, 53, 54), that heme insertion is a prerequisite for proteolytic maturation of MPO precursors into the enzymatically active subunits of mature MPO. On a broader level, the data may suggest that CLN serves a highly specialized function, i.e. to facilitate insertion of the prosthetic group into a hemeprotein, a function previously not attributed to molecular chaperones in the ER and not shared by the structurally related ER protein CRT.

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REFERENCES
1. Klebanoff, S. J. (1991) in Peroxidases in Chemistry and Biology (Everse, J., Everse, K., and Grisham, M. eds) pp. 1–36, CRC Press, Boca Raton, FL.
2. Nauseef, W. M., Olsson, I., and Stromberg-Arnlojts, K. (1988) Eur. J. Haematol. 40, 97–110.
3. Gulberg, U., Andersson, E., Garwicz, D., Lindmark, A., and Olsson, I. (1997) Eur. J. Haematol. 58, 137–153.
4. Michalak, M., Milner, R. E., Burns, K., and Opas, M. (1992) Biochem. J. 285, 681–692.
5. Meldolesi, J., Krause, K. H., and Michalak, M. (1996) Cell Calcium 20, 83–86.
6. Nauseef, W. M., McCormick, S. J., and Clark, R. A. (1995) J. Biol. Chem. 270, 4741–4747.
7. Helenius, A., Trombetta, E. S., Hebert, D. N., and Simons, J. F. (1997) Trends Cell Biol. 7, 193–200.
8. Bergeron, J. M., Brenner, M. B., Thomas, D. Y., and Williams, D. B. (1994) Trends Biochem. Sci. 19, 124–128.
9. Williams, D. B. (1995) Biochem. Cell Biol. 73, 123–132.
10. Wada, I., Indress, D., Cameron, P. H., Ou, W.-J., Doeherty, J. J., III, Louvard, D., Bell, A. W., Dignard, D., Thomas, D. Y., and Bergeron, J. M. (1991) J. Biol. Chem. 266, 16509–16510.
11. Nash, P. D., Opas, M., and Michalak, M. (1994) Mol. Cell. Biochem. 135, 71–78.
12. Tucker, K. A., Lilly, M. B., Heck, L., and Rado, T. A. (1987) Blood 70, 372–378.
13. Nauseef, W. M., Root, R. K., and Malech, H. L. (1983) J. Clin. Invest. 71, 1297–1307.
14. Denning, G. M., Leidal, K. G., Holst, V. A., Iyer, S. S., Pearson, D. W., Clark, J. R., Nauseef, W. M., and Clark, R. A. (1997) Blood 90, 372–381.
15. Nauseef, W. M. (1996) Blood 87, 865–872.
16. Le, A., Stein, J. L., Ferrell, G. A., Shaker, J. C., and Sifers, R. N. (1994) J. Biol. Chem. 269, 7514–7519.
17. Ou, W.-J., Bergeron, J. M., Li, Y., Yang, C. Y., and Thomas, D. Y. (1995) J. Biol. Chem. 270, 18051–18059.
18. Capps, G. G., and Zuniga, M. C. (1994) J. Biol. Chem. 269, 18051–18059.
19. Chamberlain, J. P. (1979) Anal. Biochem. 98, 132–135.
20. Bhaya, M., Ganger, D., and Jensen, D. (1994) Am. J. Med. 97, 169–175.
21. Arnlojts, K., and Olsson, I. (1987) J. Biol. Chem. 262, 10430–10433.
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