Sulfhydryl Groups of Sodium-Potassium Transport Adenosine Triphosphatase

PROTECTION BY PHYSIOLOGICAL LIGANDS AND EXPOSURE BY PHOSPHORYLATION

(Received for publication, January 11, 1973)

WILLIAM M. HART, JR.,* AND ELWOOD O. TITUS
From the Laboratory of Chemical Pharmacology, National Heart and Lung Institute, National Institutes of Health, Bethesda, Maryland 20014

SUMMARY

Sodium-potassium transport adenosine triphosphatase was partially purified from the outer medulla of rabbit kidney. Paired, identical aliquots of the enzyme were alkylated with N-ethyl[3H]maleimide and N-ethyl[14C]maleimide in the absence and presence of physiological ligands (Na+, Mg2+, ATP, and K+) and inhibitory drugs (ouabain and oligomycin). The pairs were then combined and submitted to preparative acrylamide gel electrophoresis in sodium dodecyl sulfate. In the absence of physiological ligands (E1 conformation), a peptide of 98,000 daltons was found to contain sulfhydryl groups protected by Na+ plus ATP. In the presence of Mg2+ (E2 conformation), sulfhydryl groups on the same peptide were protected by K+ or ouabain. In the presence of Na+, Mg2+, and ATP (phosphorylated state), additional sulfhydryl groups on the 98,000-dalton peptide were exposed to alkylation by N-ethylmaleimide. Both ouabain and oligomycin produced further increases in sulfhydryl group exposure when present during the formation of the phosphopeptide intermediate. All effects of experimental ligands on sulfhydryl group reactivity were confined to the 98,000-dalton peptide, and attempts to further separate peptides within this band by repeated electrophoresis or by hydroxylapatite chromatography were unsuccessful.

Several authors have proposed a hypothetical reaction mechanism for the cation transport adenosine triphosphatase (EC 3.6.1.3) (1–3), involving four sequential partial reactions.

\[
\begin{align*}
E_1 + ATP \rightarrow &\quad Na^+ Mg^{2+} \rightarrow E_1 - P + ADP \\
E_1 - P \rightarrow &\quad Mg^{2+} \rightarrow E_1 - P \\
E_1 - P + H_2O \rightarrow &\quad K^+ \rightarrow E_1 + P_1 \\
E_1 \rightarrow &\quad E_1
\end{align*}
\]

(1) (2) (3) (4)

The first reaction is a sodium- and magnesium-dependent phosphorylation of the enzyme by ATP. The second reaction is a magnesium-dependent change in the conformational state of the phosphorylated form. The third reaction is a potassium-dependent hydrolysis of the second form of the phosphorylated intermediate, and the fourth reaction is a spontaneous relaxation to the original conformation, accompanied by a loss of magnesium ion. Sen et al. (2) have presented a diagrammatic representation of the cycle for ion transport by the enzyme and for binding of its specific inhibitor, the cardiac glycoside ouabain (Scheme I).

\[
E_2 \xrightarrow{\text{ouabain}} E_2 - Ou \xrightarrow{P} E_2 - P - Ou
\]

The enzyme has been partially purified from a variety of mammalian tissues (4–7). These preparations consist of lipoprotein particles that contain two or more peptides, as seen by polyacrylamide gel electrophoresis in sodium dodecyl sulfate. Only one of these peptide components appears to be common to the various preparations, and this has a molecular weight estimated at 98,000 to 98,000 (6–9). Collins and Albers (8) have shown that for a wide variety of sources of the enzyme this peptide is the only constant component and is the peptide labeled by the sodium-dependent incorporation of phosphate from ATP (7, 8). In addition, our laboratory has shown that this peptide contains at least one sulfhydryl group that is protected from alkylation by N-ethylmaleimide in the presence of Na+ and ATP (9).

The present study was undertaken to determine what effects other physiological ligands might have on the reactivity of the protein sulfhydryl groups of the enzyme. In this way it was thought that the probable binding sites for each of the ligands might be localized to one or more of the peptide components of the partially purified preparation.
Preparation of Enzyme—Microsomes were prepared from the outer medulla of rabbit kidney, as described by Jorgensen and Skou (10). The microsomes were then immediately incubated for 30 min at 20°C in 25 mM imidazole, pH 7.0, 0.6 mg per ml of sodium deoxycholate, 1 mg per ml of protein, followed by centrifugation for 1 hour at 35,000 X g (average). The pellet was immediately adjusted to a final concentration of 0.8 M sucrose, 12.5 mM imidazole, pH 7.0, and 2.0 mM potassium iodide. The suspension was immediately adjusted to a final concentration of 0.5 M sucrose and 12.5 mM imidazole, pH 7.0, and then centrifuged for 30 min at 35,000 X g. The pellet was washed once in the same sucrose-imidazole buffer and then suspended by homogenization in a Teflon pestle homogenizer at 4°C in a buffer containing 5.0 mM MgCl₂, 5.0 mM EDTA, 0.1 M 2-mercaptoethanol, 12.5 mM imidazole, pH 7.0, and 2.0 mM potassium iodide. The microsomes were then immediately incubated for 30 min at 20°C in 25 mM imidazole, pH 7.0, and stored at -20°C. Ouabain-sensitive adenosine triphosphatase activity in the final preparation was 400 to 440 pmoles of Pi liberated per hour per mg of protein. Ouabain-insensitive (magnesium-dependent) adenosine triphosphatase activity in the same preparation was 25 to 40 pmoles of Pi liberated per hour per mg of protein.

Disc Gel Electrophoresis—Analytical and preparative disc gel electrophoresis in sodium dodecyl sulfate were carried out as previously described (9). In the preparative column the resolving gel contained 7% acrylamide, N,N-methylenebisacrylamide, and 1% (v/v) 2-mercaptoethanol. The sample was then submitted to preparative acrylamide gel electrophoresis in sodium dodecyl sulfate as outlined above. Note that the technique of parallel labeling provides each experiment with its own control, such that the molar ratio plots (as in Fig. 2) are a measure of the relative extent of alkylation by N-ethylmaleimide.

RESULTS AND DISCUSSION

The analytical gel pattern of the enzyme preparation used in this study is shown in Fig. 1. The most prominent band has a mobility in 7% gels of about 0.5 and is the 98,000-dalton peptide. EDTA was used to prevent trace contamination by divalent cations. Fractions from the three regions, designated I, II, and III in Fig. 2, were pooled and resubmitted to analytical gels, as shown in Fig. 3. Region I was a heterogeneous mixture of many lower molecular weight peptides, all having

![Fig. 1. Analytical gel electrophoresis in sodium dodecyl sulfate (7% gels) of A, crude microsomal particles, and B, final iodide-treated preparation.](http://www.jbc.org/)

* NEM, N-ethylmaleimide.
FIG. 2. Experiment 1, double labeling of enzyme peptides with N-ethyl[3H]maleimide and N-ethyl[14C]maleimide, followed by preparative gel electrophoresis in sodium dodecyl sulfate. Labeling conditions are outlined in Table I. One milliliter of each fraction of column effluent was mixed with 10 ml of Aquasol (New England Nuclear) and counted in a Packard Tri-Carb. Where molar ratios are expressed, each vial was counted until there was 1% S.D. or less in both channels. O—O, N-ethyl[14C]maleimide; O—O, N-ethyl[3H]maleimide; (scatter plot), log(N-ethyl[3H]maleimide to N-ethyl[14C]maleimide); NEM, N-ethylmaleimide. Results in all subsequent experiments are displayed in identical fashion. Note that the molar ratio plot is arranged so that deviations above the base-line occur in areas where sulfhydryl groups have been protected, while deviations below the line occur in areas where sulfhydryl groups have been exposed.

molecular weights of less than 55,000. Region II contained several bands, the two most prominent of which have molecular weights of 56,000 and 70,000, while Region III contained a single peptide (with minor contaminants at the leading and trailing edges), having a molecular weight of 98,000. The molar ratio plot in Fig. 2 shows the typical degree of point scatter for these experiments.

Fahn et al. and Albers et al. (12-14) were the first to report that preparations of the cation transport adenosine triphosphatase possess associated sodium-dependent transphosphorylation and potassium-dependent neutral phosphatase activities. These have since been accepted as phenomena of the partial Reactions 1 and 3 listed above. Although N-ethylmaleimide was shown to increase the activity of the sodium-dependent transphosphorylation reaction (13), it also causes an inhibition of the potassium-dependent dephosphorylation of the enzyme (partial Reaction 3) (14). Banerjee et al. (15, 16) have shown that in the presence of sodium plus ATP (ligands that bind preferentially to the E1 conformation), the enzyme is protected from this inhibition. Other work in our laboratory established that this same combination of ligands prevented the inhibition of the potassium-dependent umbelliferone phosphatase activity of the enzyme prepared from rabbit brain caused by 1 mM N-ethylmaleimide (9). The sulfhydryl groups protected by these ligands were localized by electrophoresis in sodium dodecyl sulfate and identified as a peptide of 98,000 daltons.

In Experiment 2 (Table I, Fig. 4), the molar ratio plot shows only a slight if any protection of sulfhydryl groups on the 98,000-dalton peptide. Banerjee et al. (15), using an enzyme prepared from mammalian kidney, reported that the potassium-dependent dephosphorylation activity was inhibited more effectively at 5 mM N-ethylmaleimide and that this inhibition was prevented by sodium plus ATP. These results were confirmed by Experiment 3 (Fig. 5) at the higher concentration of alkylating agent, the degree of protection is much stronger.

In Experiment 3 the 98,000-dalton peptide was bound to 23.6 nmoles of N-ethyl[3H]maleimide and 21.7 nmoles of N-ethyl[14C]maleimide. Using the data reported by Hansen et al. (17) for the ATP-binding capacity of sodium-potassium transport adenosine triphosphatase from ox brain, we calculated that approximately 9.9 nmoles of ATP binding sites (and therefore active centers) were associated with each form of label. This yields an approximation of two sulfhydryl groups alkylated per active center of enzyme, with 10% of the total available sulfhydryl groups being protected from alkylation under the conditions used in Experiment 3.

Fig. 3. Sodium dodecyl sulfate electrophoresis in 7% gels of fractions from regions labeled I, II, and III in Fig. 2.
The affinity of the enzyme system for ouabain is conformationally dependent (2, 3, 18, 19), binding taking place preferentially with the \( E_0 \) or \( E_P \) conformations. Experiment 4 (Fig. 6) shows the effect of 1 mM ouabain on sulfhydryl reactivity in the presence of 2 mM EDTA and no other ligands (\( E_0 \) conformation). At this relatively high concentration of inhibitor, there was very little demonstrable effect. Experiment 5 (Fig. 7) shows the effect of the same concentration of ouabain on sulfhydryl group reactivity in the presence of 3 mM Mg\(^{2+}\) plus 3 mM Pi. Under these conditions the affinity of the enzyme for ouabain is known to be markedly higher (2, 19), and an ouabain-dependent incorporation of Pi is known to take place (18). In this instance, ouabain is seen to have produced protection of sulfhydryl groups, again confined to the 98,000-dalton peptide.

Like ouabain, potassium is also known to have a greater affinity for the \( E_0 \) than for the \( E_1 \) conformation (2). Experiment 6 (Fig. 8) shows the effect of 20 mM K\(^+\) on sulfhydryl reactivity in the presence of 3 mM Mg\(^{2+}\). Again the protected sulfhydryl...
groups were restricted to the region containing the 98,000-dalton peptide.

Banerjee et al. (15) have shown that in the presence of sodium plus ATP magnesium ion markedly increases the ability of N-ethylmaleimide to inhibit sodium-dependent phosphorylation activity. Partial Reactions 1 and 2 involve the sodium- and magnesium-dependent phosphorylation of the enzyme by ATP (2, 20, 21). At lower concentrations of Mg$^{2+}$ (0.3 mM), there is little incorporation of phosphate from ATP, but there is maximal turnover of partial Reaction 1 (12), while maximal incorporation of phosphate from ATP occurs at levels of Mg$^{2+}$ that are equimolar with ATP (21). Experiment 7 (Fig. 9) shows the effect of added Mg$^{2+}$ on sulfhydryl group reactivity in the presence of 100 mM Na$^+$ plus 6 mM ATP. A marked increase in the number of alkylated sulfhydryl groups was shown under the conditions producing the E&P form of phosphorylated intermediate. In this experiment there were 35.0 nmoles of sulfhydryl groups alkylated by N-ethyl[3H]maleimide on the 98,000-dalton peptide in the presence of 0.1 mM Na$^+$ plus 3 mM Mg$^{2+}$. Again using the data of Hansen et al. (17), we calculated that approximately 11.8 nmoles of active center were associated with each form of label (15 mg of enzyme protein in each labeled form). This yields approximately two sulfhydryl groups alkylated per active center in the nonphosphorylated state, and four sulfhydryl groups alkylated per active center in the phosphorylated state.

Since there are at least two major conformations of the phosphorylated state (E1-P and E2-P), the question arose as to whether the state of phosphorylation per se or the conformation of the enzyme was responsible for the marked exposure of reactive sulfhydryl groups. Accordingly, attempts were made to differentiate between the two known conformations of the phosphorylated intermediate, using the marker of sulfhydryl group reactivity. Two drugs known to be specific inhibitors of the cation transport enzyme are ouabain and oligomycin. Ouabain is known to combine selectively with the E2-P conformation of the enzyme (2), thereby producing a stabilization of the phosphorylated state that resists potassium-dependent dephosphorylation. Experiment 8 (Fig. 10) shows the effect of 1 mM ouabain on sulfhydryl reactivity in the presence of 100 mM Na$^+$, 3 mM ATP, and 3 mM Mg$^{2+}$. The effect appears to have been an increase in sulfhydryl group reactivity. Since ouabain is known to stabilize the phosphorylated intermediate in the E2-P conformation, the exposure of sulfhydryl groups seen with phosphorylation is thus shown to be at least partly accounted for by the E2 conformation. Whereas in the presence of Mg$^{2+}$ plus P$_i$, ouabain protected sulfhydryl groups on the 98,000-dalton peptide, in the presence of Na$^+$, Mg$^{2+}$ plus ATP the effect was one of increased exposure. Since the enzyme is known to incorporate P$_i$ in both instances, this result indicates that the two forms of ouabain-bound enzyme (phosphorylated by P$_i$ or ATP) probably have different conformations. This agrees with the findings of Akera and Brody (22) that dissociation of ouabain from its complex with the enzyme occurs at markedly different rates according to whether the complex was formed in the presence of ATP, Na$^+$ plus Mg$^{2+}$, or Mg$^{2+}$ plus P$_i$.

Oligomycin inhibits turnover of the enzyme. Although it does not inhibit the sodium-dependent phosphorylation, the ADP-ATP transphosphorylation, or the potassium-dependent neutral phosphatase activities (12, 20, 23, 24), it does inhibit the potassium-dependent dephosphorylation of the phosphorylated intermediate formed in the presence of the inhibitor (20). It has been
concluded (1, 25) that oligomycin acts by blocking partial reaction (2), the magnesium-dependent transition from \( E_1 \)-P to \( E_2 \)-P. If this is the case, oligomycin should stabilize the \( E_1 \)-P conformation in the presence of \( Na^+ \), \( Mg^{2+} \), and ATP. Experiment 9 (Fig. 11) shows the effect of 20 \( \mu \)g per ml of oligomycin on sulphydryl group reactivity in the presence of sodium-dependent phos-

Fig. 10. Experiment 8, the effect of ouabain on sulphydryl reactivity in the presence of 3 mM \( Mg^{2+} \), 100 mM \( Na^+ \) plus 3 mM ATP. Reaction conditions as in Table I, results plotted as in Fig. 2. The displacement of the base-line of the molar ratio plot from zero was caused by accidental loss of part of the control (\( ^3H \)-labeled) sample. \( NEM \), \( N \)-ethylmaleimide.

Fig. 11. Experiment 9, the effect of oligomycin on sulphydryl reactivity in the presence of 6 mM \( Mg^{2+} \), 100 mM \( Na^+ \) plus 6 mM ATP. Reaction conditions as in Table I, results plotted as in Fig. 2. \( NEM \), \( N \)-ethylmaleimide.

phorylation from ATP. Here the most marked exposure of sulphydryl groups was seen. Within the region of the 98,000-
dalton peptide, there were 38.9 nmoles of \( N \)-ethyl\( ^3H \)maleimide and 62.5 nmoles of \( N \)-ethyl\( ^{14}C \)maleimide, associated with 9.9 nmoles each of active center (again estimated using the data of Hansen et al. (17)). This yields an approximation of four sulphydryl groups alkylated per active center in the presence of \( Na^+ \), \( Mg^{2+} \), and ATP and six sulphydryl groups alkylated per active center in the presence of \( Na^+ \), \( Mg^{2+} \), ATP, and oligomycin. This implies that the greatest extent of conformational change in the enzyme (as reflected by exposure of sulphydryl groups alkylated by \( N \)-ethylmaleimide) is produced by phosphorylation to the \( E_1 \)-P state. Thus, the degree of exposure of sulphydryl groups, or the extent to which their reactivity toward \( N \)-ethylmaleimide is increased, appears to provide an indirect measure of the degree to which the enzyme's native conformation has been altered in attaining the higher potential energy states that accompany incorporation of the terminal ("high energy") phosphate group from ATP.

The localization of effects on sulphydryl group reactivity produced by multiple physiological ligands of the cation transport system to a single peptide, as seen by acrylamide gel electrophoresis in sodium dodecyl sulfate, raises the possibility that what appears to be a single peptide may in fact represent an incompletely dissociated oligomer of multiple subunits. Therefore, attempts were made to further separate the peptide components of the 98,000-dalton band. Figs. 12 and 13 show the results of submitting the 98,000-dalton peptide from Experiments 9 and 14 to hydroxylapatite chromatography in sodium dodecyl sulfate, according to the method of Moss and Rosenblum (26). In both instances a single peak was obtained with a minor shoulder on the trailing side. Fig. 14 shows the results of resubmitting consecutive fractions from within the 98,000-dalton band (taken from the preparative electrophoresis fractions of Experiment 7) to 7% analytical gels. The leading and trailing fractions showed the presence of multiple minor contaminants, but within the central fractions of the peak, there was only one discernible band.

Fig. 12. Hydroxylapatite chromatography of the fractions containing the 98,000-dalton peptide from Experiment 9 (Fig. 11). ---\( -\), \( N \)-ethyl\( ^3H \)maleimide; ---\( -\), \( N \)-ethyl\( ^{14}C \)maleimide. The solid line is an idealized profile of the phosphate gradient. \( NEM \), \( N \)-ethylmaleimide.
The solid line is an idealized profile of the phosphate gradient. Containing the 98,000-dalton peptide from Experiment 4 (Fig. 6). NEM, N-ethyl[3H]maleimide; O- - - O, N-ethyl[14C]maleimide.

FIG. 13. Hydroxylapatite chromatography of the fractions containing the 98,000-dalton peptide from Experiment 4 (Fig. 6). Samples 1 to 6 represent peptides from the fractions collected at 7.0, 7.4, 7.8, 8.2, 8.6, and 9.0 hours, respectively.

If one accepts for the moment that the 98,000-dalton peptide does represent a single, homogeneous peptide, it must have multiple properties of the cation transport system. On the basis of the sulfhydryl protection phenomena, the molecule appears to possess binding sites for sodium, ATP, potassium, and ouabain, while the data for sulfhydryl exposure accompanying phosphorylation appear to reflect conformational changes in the peptide that parallel the potential energy states of the phosphorylated intermediates. Since the binding sites for potassium and ouabain are situated on the exterior surface of the plasma membrane, while the binding sites for sodium and ATP are situated on the interior surface (27), the results of the current study imply that the 98,000-dalton peptide may in fact completely traverse the membrane. Precedents for such proteins already exist. Bretscher (28, 29) has reported a peptide of 105,000 daltons that spans the human erythrocyte membrane, and Marchesi et al. (30) have demonstrated the presence of a glycoprotein of 56,000 daltons that also appears to be represented on both sides of the erythrocyte membrane. Kyte (31) has recently reported that, of the two peptides associated with the most highly purified preparation of cation transport adenosine triphosphatase from canine renal medulla, the smaller peptide is a sialoglycoprotein having a molecular weight of 35,000 to 57,000, depending on the method of estimation. No functional significance has yet been ascribed to this component. The larger peptide has a molecular weight of 84,000 to 98,000, as estimated by gel electrophoresis in sodium dodecyl sulfate (6-9), and a molecular weight of 139,000, as estimated by gel filtration in guanidinium chloride. This larger peptide has a high proportion (47%) of hydrophobic residues, and Kyte suggests that this may result in a greater proportion of bound detergent (as compared to globular hydrophilic proteins), producing falsely low estimates of molecular weight by electrophoresis in sodium dodecyl sulfate. Accepting the higher estimate of molecular weight, he points out that even as a spherical molecule this peptide could easily span a lipid bilayer of 35 to 40 Å.

Fahn et al. (12) originally proposed that the properties of the cation-activated adenosine triphosphatase are consistent with a transport mechanism that derives energy from a phosphate transfer to a macromolecular acceptor in the membrane (the phosphorylated intermediate) and that further transformations would result in carrier-mediated transport by one of three mechanisms: (a) migration of bound phosphate to successive positions within the membrane, the phosphate group itself acting as cation carrier; (b) energy transfer from the phosphorylated group to a non-phosphorylated carrier; or (c) degradation of the energy acquired by phosphorylation through conformational changes of the phosphorylated intermediate that serve to drive the cations through the membrane. From the point of view of sulfhydryl group exposure, it would appear that the largest conformational changes in the phosphate acceptor peptide are a reflection of the phosphorylation itself and that the degree of conformational change is directly related to the potential energy level of the intermediate. This would tend to support the third proposed mechanism of cation transport, whereby the transported ions are forced through the membrane against their electrochemical potential gradients through conformational changes of the phosphorylated intermediate.

REFERENCES
1. Post, R. L., Kiem, S., Torin, T., Orcutt, B., and Sen, A. K. (1969) J. Gen. Physiol. 54, 306s
2. Sen, A. K., Torin, T., and Post, R. L. (1969) J. Biol. Chem. 244, 6506
3. Albers, R. W., Koval, G. J., and Siegal, G. J. (1968) Mol. Pharmacol. 4, 324
4. Jorgensen, P. L., and Skou, J. C. (1971) Biochim. Biophys. Acta 233, 366
5. Jorgensen, P. L., Skou, J. C., and Solomonson, L. P. (1971) Biochim. Biophys. Acta 233, 381
6. Kyte, J. (1971) J. Biol. Chem. 246, 4157
7. Vesugi, S., Dulak, N. C., Dixon, J. F., Hexum, T. D., Dail, J. L., Perdue, J. F., and Hokin, L. E. (1971) J. Biol. Chem. 246, 551
8. Collins, R. C., and Albers, R. W. (1972) J. Neurochem. 19, 1209
9. Hart, W. M., Jr., and Titus, E. O. (1973) J. Biol. Chem. 248, 1385
10. Jorgensen, P. L., and Skou, J. C. (1969) Biochim. Biophys. Acta 233, 39
11. Chignell, C. F., and Titus, E. (1966) J. Biol. Chem. 241, 5083
12. Fahn, S., Koval, G. J., and Albers, R. W. (1966) J. Biol. Chem. 241, 1882
13. Fahn, S., Hurley, M. R., Koval, G. J., and Albers, R. W. (1966) J. Biol. Chem. 241, 1890
14. Albers, R. W., and Koval, G. J. (1966) J. Biol. Chem. 241, 1896
15. Banerjee, S. P., Wong, S. M. E., Khanna, V. K., and Sen, A. K. (1972) Mol. Pharmacol. 8, 8
16. Banerjee, S. P., Wong, S. M. E., and Sen, A. K. (1972) Mol. Pharmacol. 8, 18
17. Hansen, O., Jensen, J., and Norby, J. G. (1971) Nature New Biol. 234, 122
18. Siegal, G. J., Koval, G. J., and Albers, R. W. (1969) J. Biol. Chem. 244, 3264
19. Hansen, O. (1971) Biochim. Biophys. Acta 233, 122
20. Fahn, S., Koval, G. J., and Albers, R. W. (1968) J. Biol. Chem. 243, 1993
21. Post, R. L., Sen, A. K., and Rosenthal, A. S. (1965) J. Biol. Chem. 240, 1437
22. Akera, T., and Brody, T. M. (1971) J. Pharmacol. Exp. Ther. 176, 545
23. Israel, Y., and Titus, E. O. (1967) Biochim. Biophys. Acta 139, 450
24. Inturrisi, C. E., and Titus, E. (1968) Mol. Pharmacol. 4, 591
25. Stahl, W. L. (1968) J. Neurochem. 15, 511
26. Moss, B., and Rosenblum, E. N. (1972) J. Biol. Chem. 247, 5194
27. Whittam, R., and Wheeler, K. P. (1970) Annu. Rev. Physiol. 32, 21
28. Bretscher, M. S. (1971) Nature New Biol. 231, 229
29. Bretscher, M. S. (1971) J. Mol. Biol. 59, 351
30. Marchesi, V. T., Tillack, T. W., Jackson, R. L., Segrest, J. P., and Scott, R. F. (1972) Proc. Nat. Acad. Sci. U. S. A. 69, 1445
31. Kyte, J. (1971) J. Biol. Chem. 247, 7642
Sulphydryl Groups of Sodium-Potassium Transport Adenosine Triphosphatase: PROTECTION BY PHYSIOLOGICAL LIGANDS AND EXPOSURE BY PHOSPHORYLATION
William M. Hart, Jr. and Elwood O. Titus

J. Biol. Chem. 1973, 248:4674-4681.

Access the most updated version of this article at http://www.jbc.org/content/248/13/4674

Alerts:
• When this article is cited
• When a correction for this article is posted

Click here to choose from all of JBC’s e-mail alerts

This article cites 0 references, 0 of which can be accessed free at http://www.jbc.org/content/248/13/4674.full.html#ref-list-1