Rev. A **38**, 3043 (1988). For a counterexample, see J. H. Bilgram, M. Firmann, W. Känzig, *Phys. Rev. B* **37**, 685 (1988).
13. E. Ben-Jacob, N. Goldenfeld, J. S. Langer, G. Schön, *Phys. Rev. A* **29**, 330 (1984).
14. J. S. Langer, *ibid.* **33**, 435 (1986).
15. P. Pelcé and Y. Pomeau, *Stud. Appl. Math.* **74**, 245 (1986); M. Ben Amar and Y. Pomeau, *Europhys. Lett.* **2**, 307 (1986).
16. D. Kessler, J. Koplik, H. Levine, in *Proceedings of the NATO Advanced Research Workshop on Patterns, Defects, and Microstructures in Non-Equilibrium Systems* (Austin, Texas, March 1986), ASI Series E, 121, D. Walgraef, Ed. (Nijhoff, Dordrecht, 1987).
17. A. Barbieri, D. C. Hong, J. S. Langer, *Phys. Rev. A* **35**, 1802 (1987).
18. D. Meiron, *ibid.* **33**, 2704 (1986).
19. M. Ben-Amar and B. Moussallam, *Physica D* **25**, 7 (1987); *ibid.*, p. 155.
20. D. A. Kessler, J. Koplik, H. Levine, *Phys. Rev. A* **33**, 3352 (1986); D. A. Kessler and H. Levine, *Phys. Rev. B* **33**, 7867 (1986).
21. B. I. Shraiman, *Phys. Rev. Lett.* **56**, 2028 (1986).
22. R. Combescot, T. Dombre, V. Hakim, Y. Pomeau, A. Pumir, *ibid.*, p. 2036; *Phys. Rev. A* **37**, 1270 (1988).
23. D. C. Hong and J. S. Langer, *Phys. Rev. Lett.* **56**, 2032 (1986); *Phys. Rev. A* **36**, 2325 (1987).
24. See the discussion of the work of M. Kruskal and H. Segur, in (*6*).
25. A. Barbieri and J. S. Langer, *Phys. Rev. A*, in press.
26. D. Kessler and H. Levine, *Phys. Rev. A* **36**, 4123 (1987).
27. Y. Couder, N. Gerard, M. Rabaud, *ibid.* **34**, 5175 (1986); Y. Couder, O. Cardoso, D. Dupuy, P. Tavernier, W. Thom, *Europhys. Lett.* **2**, 437 (1986).
28. D. Kessler and H. Levine, *Phys. Rev. A* **33**, 2621 (1986); *ibid.*, p. 2634 (1986); *Europhys. Lett.* **4**, 215 (1987).
29. Ya. B. Zel'dovich, A. G. Istratov, N. I. Kidin, V. B. Librovich, *Combust. Sci. Technol.* **24**, 1 (1980).
30. R. Pieters and J. S. Langer, *Phys. Rev. Lett.* **56**, 1948 (1986); R. Pieters, *Phys. Rev. A.* **37**, 3126 (1988).
31. M. Barber, A. Barbieri, J. S. Langer, *Phys. Rev. A* **36**, 3340 (1987).
32. J. S. Langer, *ibid.*, p. 3350.
33. R. Deissler, *J. Stat. Phys.* **40**, 371 (1985).
34. The relation between noise and sidebranching has been examined experimentally by A. Dougherty, P. D. Kaplan, J. P. Gollub, *Phys. Rev. Lett.* **58**, 1652 (1987); see also A. Dougherty and J. P. Gollub, *Phys. Rev. A* **38**, 3043 (1988).
35. This article is based in large part on the text of the author's Marian Smoluchowski Memorial Lecture presented in Warsaw, Poland, on 17 March 1988. I thank the Polish Academy of Sciences for its hospitality. I also thank Y. Couder, M. Glicksman, and J. Maher for providing photographs and information. The research described here was supported by U.S. Department of Energy grant DE-FG03-84ER45108 and by National Science Foundation grant PHY 82-17853, supplemented by funds from the National Aeronautics and Space Administration.

Unity in Function in the Absence of Consensus in Sequence: Role of Leader Peptides in Export

L. L. RANDALL* AND S. J. S. HARDY

Passage of proteins across membranes during export from their site of synthesis to their final destination is mediated by leader peptides that paradoxically exhibit a unity of function in spite of a diversity of sequence. These leader peptides act in at least two stages of the export process: at entry into the pathway and subsequently during translocation across the membrane. How selectivity is imposed on the system in the absence of a consensus among the sequences of leader peptides is the main issue discussed here.

BIOLOGICAL MEMBRANES NOT ONLY DEFINE THE BOUNDaries between cells and their environments, but also bring about essential separation of functions within cells by establishing internal compartments. Thus, the main role of membranes, for which the hydrophobic center of the lipid bilayer is responsible, is that of a barrier to the passage of water-soluble molecules. However, membranes cannot be inviolate barriers, since besides being selectively permeable to small molecules and ions, they must also allow passage of selected proteins in order to maintain functional organelles and to mediate secretion.

L. L. Randall is a professor in the Biochemistry/Biophysics Program, Washington State University, Pullman, WA 99164. S. J. S. Hardy is a senior lecturer at the Department of Biology, University of York, Heslington, York Y01 5DD, United Kingdom.

*To whom correspondence should be addressed.

Common Themes in Protein Export

The transfer of polypeptides across membranes is thus fundamental to life. Studies of such transfer in a number of different systems have revealed significant similarities, suggesting that there is a single basic mechanism on which secondary system–specific differences are imposed. The passage of polypeptides across the membranes of the endoplasmic reticulum during secretion in eukaryotes and the export of proteins from the cytoplasm to the periplasm and outer membrane in gram-negative bacteria such as *Escherichia coli* are so alike that each of the two systems appears able to recognize and transfer the proteins handled by the other: thus, findings established in investigations of eukaryotic secretion are usually directly applicable to export from *E. coli* and vice versa. Here our discussion is based predominantly on information obtained from studies of the latter.

Models for Export

As has long been known, polypeptides that are exported from bacteria or that are secreted from eukaryotic cells transiently carry at their amino termini stretches of amino acids (designated signal or leader sequences) that play a critical role in these processes (*1, 2*). In spite of intensive investigation over many years, we are not yet in a position to make definitive statements concerning the function of these sequences at the molecular level. Nevertheless, there has been no shortage of informed speculation about their role. Two early models that attributed radically different roles to leader sequences, the signal hypothesis (*3*) and the membrane trigger hypothesis (*4*),

have been particularly influential. The signal hypothesis ascribes a single role to the sequence, that of being the recognition element for the export or secretion apparatus, which then accomplishes the remainder of the process. In contrast, the membrane trigger hypothesis emphasizes the importance of conformation. The leader sequence is seen as an element that by interacting with the remainder of the protein mediates binding to a factor that confers a conformation, competent for export, upon the precursor. For both of these hypotheses, the lack of amino acid sequence similarity in leader peptides raises puzzling questions. For the signal hypothesis, how would a single export apparatus specifically and accurately recognize and interact with the bewildering variety of sequences? For the membrane trigger hypothesis, how could we explain that the different leader sequences are functionally interchangeable (that is, the leader sequence of one protein may replace that of another and mediate its export) when it might be expected that the match of the leader sequence and the remainder of the protein would be important? It is this conundrum of unity in function of leaders in the absence of identity in their sequences that we address here.

Role of the Leader

In our discussion we consider possible roles of the leader sequences in the export process, which we divide into three stages: entry into the pathway, translocation across the membrane, and release on the opposite side. The entry stage comprises all events occurring in the cytosol up to and including the initial association of precursors with the membrane. The translocation stage is defined so as to include not only the actual translocation of the polypeptides through the membranes, but also the passage of the precursor from the site of entry on the membrane to the translocation site should they be physically separated. The release stage encompasses removal of the leader peptide by leader peptidases, folding of the processed polypeptide into the mature conformation, and dissociation from the membrane. We can easily dispense with discussion of the release step. At that time, the leader sequence is proteolytically removed, and clearly with its removal comes termination of its active participation. If the leader sequence is not removed, the precursor polypeptide remains membrane bound (*5*). Release from the membrane requires, in addition to cleavage of the leader, a change in the conformation of the mature portion of the polypeptide (*6*).

In contrast to our summary dismissal of the release stage, we shall present a more substantial consideration of the earlier stages of the export process in which the leader sequences have active roles. Features that are common to leader sequences may provide insight into the nature of these roles. Even though the leaders vary in length and amino acid sequence, they all comprise three regions: a positively charged amino-terminal region, a central hydrophobic core, and a polar carboxyl-terminal region ending with the cleavage site (*7*). Leader peptides containing mutations that decrease the efficiency of export have been characterized for numerous exported proteins(*8*). Comparison of the mutationally altered sequences with those of the corresponding wild-type leaders has established the importance of hydrophobicity to the function of leader peptides (*9*). Further indication of the importance of hydrophobicity is provided by the correlation of the ability of chemically synthesized leader peptides of the outer membrane protein LamB to mediate export in vivo with their ability to interact in vitro with phospholipids (*10*). In addition, a hydrophobic nature is the property common to the randomly cloned sequences that, when placed at the amino terminus of yeast invertase, were shown to mediate its secretion (*11*). Thus, at some stage of export, hydrophobicity of the leader has a crucial role. Investigations of the export of maltose-binding protein to the periplasm of *E. coli* (*12*) indicate that this requirement for a hydrophobic core in the leader is expressed not during the entry stage, but rather during the translocation stage. It was shown that initial association of precursor with the membrane requires the presence of a leader; however, two mutated leaders that have substitutions of charged amino acids for hydrophobic residues and that therefore do not sustain export in vivo were shown to fulfill this function. Thus, these mutational changes do not affect entry, but manifest defects at the translocation stage that follows membrane association. Other investigators have earlier concluded that the leader has at least two separable functions (*11, 13*), one of which is likely to be involved in the translocation stage.

The properties that define a sequence as an active leader are governed by the parameter that is crucial to the particular function under consideration. With this in mind, let us now address the role of the leader during the three stages of export. For the processing and release stage, activity requires that the amino acyl residues at positions -3 and -1 (the first amino acyl residue of the mature protein is defined as position $+1$) are restricted to those with relatively small side chains (*14*). For the translocation stage, the lack of consensus among leader sequences would present no problem if the only crucial parameter were that of hydrophobicity, which could be provided by innumerable combinations of amino acids. However, the role of the leader at the entry stage must impose specificity upon the system. Only proteins destined for export should enter the pathway and become membrane bound. If the same apparatus mediates export of many proteins in any one cell type, as seems to be the case (*2*), one would expect these proteins to contain a consensus sequence that could be recognized by a common receptor. Nevertheless, within one cell, an immense diversity is allowed among the leader sequences that mediate selective entry into the export pathway. What might be the nature of the interactions involved? We shall come back to this question.

Conformation of Precursors

At this point, we depart from discussion of the precise function of the leader and briefly consider the significance of conformation of the precursor to the export process. For all soluble exported proteins studied, the presence of a leader does not confer upon the precursor a stable conformation different from that of the mature species (*15*). Nevertheless, during export in *E. coli* (*16*) as well as during import of protein into mitochondria (*17, 18*), precursors must not be folded into the structure characteristic of the mature species. It seems probable that the passage of the polypeptide through the membrane requires a loose structure. Indeed, a protein in transit to the mitochondrial matrix was isolated as a partially translocated species that was transmembrane and thus not fully folded (*19*). Stimulated by the observation (*17*) that a chimeric precursor composed of a mitochondrial presequence fused to dihydrofolate reductase was imported by mitochondria unless its native structure was stabilized by folate analogs, Rothman and Kornberg (*20*) speculated that there exists a class of enzymes, "unfoldases," that disrupt previously established tertiary structure. However, it seems that in *E. coli* precursors arrive at export sites before they have acquired the conformation characteristic of the mature species. The pertinent evidence is as follows: from the earliest time it can be detected in the cell, newly synthesized precursor maltose-binding protein is devoid of stable structure (*16*); the product of *secB*, a gene known to be involved in export, slows the folding of precursor maltose-binding protein synthesized in vitro (*21*); and a soluble factor, which renders precursor OmpA (an outer membrane protein) competent for translocation into vesicles in vitro, functions only if added to the

denatured precursor (*22*). Presently it is not clear whether bacterial export and biogenesis of mitochondria differ in detail; nevertheless, in the absence of direct evidence for the existence of an enzyme that unfolds proteins in *E. coli*, there is no need to postulate that one exists in bacteria. Rather, we propose that not only translocation but even entry into the pathway is possible only for polypeptides that have not yet attained their native conformation. The imposition upon the system of such a stricture would provide an early editing function and thereby eliminate the binding of polypeptides that could not be translocated because they had already acquired a conformation incompatible with export. Once bound, the precursor would be kept from assuming the thermodynamically favored conformation until it could be translocated, processed, and released from the membrane.

Nature of the Interactions

Let us now return to the question of the nature of interactions that mediate the selective entry into the pathway. We can postulate two extremes: that these interactions involve recognition of specific amino-acyl side chains in the precursor, or that they involve recognition only of secondary or tertiary structural elements. The simple and popular idea that the leader peptide is the sole element directly recognized during the initial phase of export implies recognition of secondary structural features, since as we have already emphasized, there is no consensus among leader peptides. However, if in the initial interactions, the polypeptide chain is to be kept from folding into a state that is not competent for translocation, components of the apparatus must interact with at least some portion of the polypeptide that lies outside of the leader. Support for this notion is provided by investigations that demonstrate an involvement of regions of the mature portion of the precursor in efficient export (*21, 23*). Thus, a plausible hypothesis is that the unit initially recognized includes elements both from the leader peptide and from the remainder of the polypeptide. If the recognized unit is a specific sequence, the necessary consensus might be found, for instance, in the mature portion of the precursor among the clusters of hydrogen-bonding side chains that are characteristic of the boundaries of helices (*24, 25*) and that are thought to act as a stereochemical code for helix formation (*24*). These hydrogen-bonding clusters might be accessible in the precursor and be recognized by the export apparatus before the helix is formed.

If, however, the unit recognized is a structural element, it may be exposed only transiently. Even though the final conformations of precursors are similar to those of the mature species (*15*), it has been shown in two cases that the folding pathways are modulated by the presence of the leader sequences (*26*). These kinetic effects indicate that the leader interacts transiently with portions of the precursor that lie within the mature region. Such interaction could either create or expose an element of structure that would be recognized by a component of the export apparatus, which would bind and maintain the precursor in the competent state (Fig. 1). How might such an element of structure be recognized in a specific way without a contribution from specific side chains? We might consider the role of the leader to be the transient stabilization of an unstructured polypeptide. Might it simply be flexibility or the exposure of hydrophobic portions of the polypeptide that is crucial? If the interactions do involve a distinct element of structure, the leader may be part of that structure. For example, it might associate with another portion of the polypeptide to form a loop of β strand. Alternatively, the leader might not be directly recognized but might interact with the mature portion to expose an amino acid sequence that would otherwise be inaccessible or to stabilize an intermediate in the folding pathway that would otherwise be too short-lived to be recognized. The covalent cross-linking of the leader of preprolactin to a component of the mammalian export apparatus (*27*) does not distinguish among these alternatives, since the leader might bind near the recognition element in order to stabilize it. Recognition of an intermediate in folding would necessitate the existence of the same unit of structure along the folding pathway of the many proteins that use the same export apparatus. Similar structural units may be common among folding intermediates of almost all proteins. Indeed, it has been proposed by Rose and his colleagues (*28*) that there are a limited number of primitive folding units that by hierarchic condensation associate in a stepwise fashion to generate the final conformation of proteins. These primitive units, which are candidates for the recognized elements, include repetitive structures such as helices and sheets and nonrepetitive structures such as reverse turns, omega loops, and other compact units (*28*). If recognition of a structural unit is to be essentially independent of specific side chains, helices are poor candidates, since the repeating elements of the backbone are hydrogen bonded and masked by the projecting side chains. Better suited are β structures that would contain accessible amide and carbonyl groups that could be engaged in periodic patterns of hydrogen bonding.

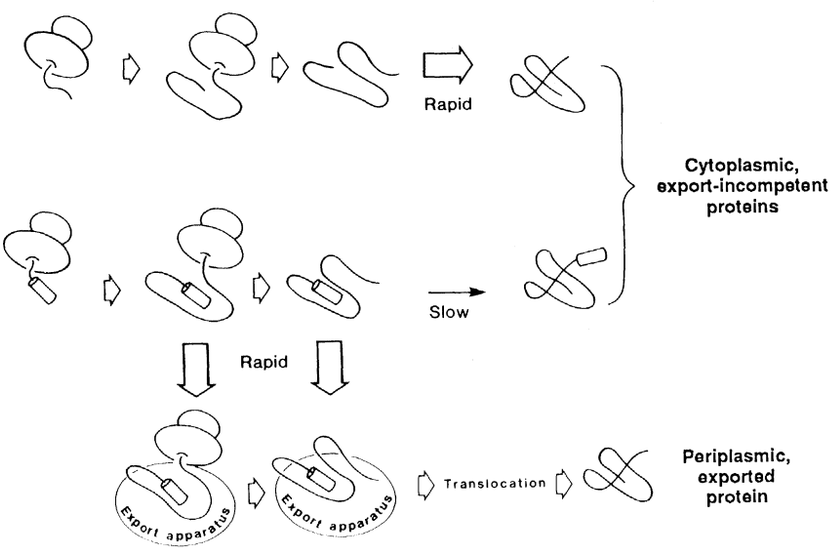

Fig. 1. A model for the role of leader peptides in entry into the export pathway. We propose that there is a kinetic partitioning between the pathway of productive export and the folding of precursors into export-incompetent conformations. The leader peptide interacts transiently with a portion of the mature region of the polypeptide to modulate folding. This interaction creates or exposes an element of structure that is recognized by a component of the export apparatus. Interaction with components of the export apparatus (whether they are cytosolic or membrane associated) blocks further folding and maintains the precursor in an export-competent state. Precursors that escape this interaction, or polypeptides synthesized without a leader rapidly fold into a stable native-like structure within the cytoplasm and cannot be exported. The leader peptide has an additional role, which is not shown here, in the translocation of the polypeptide through the membrane.

Components of the Apparatus

The components of the export apparatus that recognize structural elements may be members of a wider family of proteins present in all organisms examined that function in a variety of ways either to disrupt or to prevent formation of incorrect protein structures. These proteins, variously designated as heat-shock proteins, stress-induced proteins, and molecular chaperones, are highly conserved, and are present even in unstressed cells, and are known to hydrolyze adenosine triphosphate (ATP) (*29*). The assignment of export factors to this family has come with the demonstration that mutations in a subset of the heat-shock proteins (hsp70 proteins) in yeast result in accumulation in vivo of precursors of secretory proteins and of a mitochondrial protein (*30*). The same hsp70 proteins were shown to stimulate translocation of proteins into yeast microsomes in vitro (*31*). It has been suggested (*30*) that in yeast the hsp70 proteins perform the function of the putative unfoldase and couple the hydrolysis of ATP to the unfolding of precursors. Bacterial export requires the hydrolysis of ATP (*2*); however, as we have already discussed, the data available indicate that the export apparatus binds the precursors before they attain a stable tertiary structure; thus it seems unlikely that the energy released during the hydrolysis of ATP is used to unfold precursors in bacteria. Rather, we favor the idea that we described in an earlier model (*2*) that hydrolysis of ATP is coupled to transfer of the precursor between components of the export apparatus. Precedents for the proposal that hydrolysis of nucleoside triphosphates is involved in the binding and release of interacting polypeptides are found in general biological phenomena such as the cycling of eukaryotic G regulatory proteins and of the prokaryotic elongation factor EF-T_u. Examples of proteins that hydrolyze ATP during the handling of nonnative protein structures, a role closely related to that proposed here for export factors, are the mammalian immunoglobulin-binding protein [BiP (*32*)], the binding protein for the large subunit of the chloroplast enzyme ribulose bisphosphate carboxylase-oxygenase (*33*), and the bacterial proteins GroEL (*34*) and protease La (*35*).

Concluding Remarks

Over the years, investigators of the export process have advanced many models of great heuristic value. Nevertheless, the function of leader sequences during the selective passage of proteins across membranes has remained a molecular enigma. We do not pretend to have resolved this issue, but have presented a speculative analysis of the role of leader peptides based on experimental observations. We hope that our discussion will stimulate further investigation, and we anticipate that forthcoming results will modify our views. No hypothesis, not even our own, should become so rigid that data are forced into a Procrustean bed (*36*).

REFERENCES AND NOTES

1. V. A. Bankaitis *et al.*, *Curr. Top. Membr. Transp.* **24**, 105 (1985); R. Zimmermann and D. I. Meyer, *Trends Biochem. Sci.* **11**, 512 (1986).
2. L. L. Randall, S. J. S. Hardy, J. R. Thom, *Annu. Rev. Microbiol.* **41**, 507 (1987).
3. G. Blobel and B. Dobberstein, *J. Cell Biol.* **67**, 835 (1975).
4. W. Wickner, *Annu. Rev. Biochem.* **48**, 23 (1979).
5. D. Koshland, R. T. Sauer, D. Botstein, *Cell* **30**, 903 (1982); R. E. Dalbey and W. Wickner, *J. Biol. Chem.* **260**, 15925 (1985).
6. K. Ito and J. R. Beckwith, *Cell* **25**, 143 (1981); D. Koshland and D. Botstein, *ibid.* **30**, 893 (1982); R. Hengge and W. Boos, *J. Bacteriol.* **162**, 972 (1985); A. Minksy, R. G. Summers, J. R. Knowles, *Proc. Natl. Acad. Sci. U.S.A.* **83**, 4180 (1986); R. Fitts *et al.*, *ibid.* **84**, 8540 (1987).
7. D. Perlman and H. O. Halvorson, *J. Mol. Biol.* **167**, 391 (1983); G. von Heijne, *ibid.* **184**, 99 (1985).
8. S. A. Benson, M. N. Hall, T. J. Silhavy, *Annu. Rev. Biochem.* **54**, 101 (1985); D. B. Oliver, *Annu. Rev. Microbiol.* **39**, 615 (1985).
9. H. Bedouelle and M. Hofnung, in *Membrane Transport and Neuroreceptors*, D. Oxender, A. Blume, I. Diamond, C. F. Fox, Eds. (Liss, New York, 1981), pp. 399–403. For review, see M. S. Briggs and L. M. Gierasch, *Adv. Protein Chem.* **38**, 109 (1986).
10. M. S. Briggs *et al.*, *Science* **228**, 1096 (1985).
11. C. A. Kaiser, D. Preuss, P. Grisafi, D. Botstein, *ibid.* **235**, 312 (1987).
12. J. R. Thom and L. L. Randall, *J. Bacteriol.* **170**, 5654 (1988); C. M. Gates and L. L. Randall, unpublished observations.
13. J. P. Ryan and P. J. Bassford, Jr., *J. Biol. Chem.* **260**, 14832 (1985); J. Stader, S. A. Benson, T. J. Silhavy, *ibid.* **261**, 15075 (1986); M. Wiedmann, T. Kurzchalia, E. Hartmann, T. A. Rapoport, *Nature* **328**, 830 (1987).
14. G. von Heijne, *Eur. J. Biochem.* **133**, 17 (1983).
15. H. Inouye and J. R. Beckwith, *Proc. Natl. Acad. Sci. U.S.A.* **74**, 1440 (1977); T. Ferenci and L. L. Randall, *J. Biol. Chem.* **254**, 9979 (1979); K. Ito, *ibid.* **257**, 9895 (1982); J. T. Kadonaga *et al.*, *ibid.* **260**, 16192 (1985).
16. L. L. Randall and S. J. S. Hardy, *Cell* **46**, 921 (1986).
17. M. Eilers and G. Schatz, *Nature* **322**, 228 (1986).
18. ———, *Cell* **52**, 481 (1988).
19. M. Schleyer and W. Neupert, *ibid.* **43**, 339 (1985).
20. J. E. Rothman and R. D. Kornberg, *Nature* **322**, 209 (1986).
21. D. N. Collier, V. A. Bankaitis, J. B. Weiss, P. J. Bassford, Jr., *Cell* **53**, 273 (1988).
22. E. Crooke and W. Wickner, *Proc. Natl. Acad. Sci. U.S.A.* **84**, 5216 (1987); E. Crooke, L. Brunbage, M. Rice, W. Wickner, *EMBO J.* **7**, 1831 (1988).
23. S. A. Benson, E. Bremer, T. J. Silhavy, *Proc. Natl. Acad. Sci. U.S.A.* **81**, 3830 (1984); W. H. Cover *et al.*, *J. Bacteriol.* **169**, 1794 (1987).
24. L. G. Presta and G. D. Rose, *Science* **240**, 1632 (1988).
25. J. S. Richardson and D. C. Richardson, *ibid.*, p. 1648.
26. S. Park, G. Liu, T. B. Topping, W. H. Cover, L. L. Randall, *ibid.* **239**, 1033 (1988).
27. T. V. Kurzchalia *et al.*, *Nature* **320**, 634 (1986).
28. G. D. Rose, *Biophys. J.* **32**, 419 (1980); J. S. Fetrow, M. H. Zehfus, G. D. Rose, *Biotechnology* **6**, 167 (1988).
29. H. R. B. Pelham, *Cell* **46**, 959 (1986); R. J. Ellis, *Nature* **328**, 378 (1987).
30. R. J. Deshaies, B. D. Koch, M. Werner-Washburne, E. A. Craig, R. Schekman, *Nature* **332**, 800 (1988).
31. W. J. Chirico, M. G. Waters, G. Blobel, *ibid.*, p. 805.
32. S. Munro and H. R. B. Pelham, *Cell* **46**, 291 (1986).
33. J. E. Musgrove, R. A. Johnson, R. J. Ellis, *Eur. J. Biochem.* **163**, 529 (1987).
34. K. Tilly, G. N. Chandrasekhar, M. Zylicz, C. Georgopoulos, in *Microbiology*, L. Leive, Ed. (American Society for Microbiology, Washington, DC, 1985), p. 322.
35. L. Waxman and A. L. Goldberg, *Science* **232**, 500 (1986).
36. Procrustes was a legendary brigand of Attica who, in order to conform his victims to the length of his bed, either stretched them or cut off their legs.

37. We acknowledge many colleagues in the fields of protein export and protein folding for useful discussion. We are particularly grateful to G. Rose for suggesting that the clusters of hydrogen-bonding residues at the ends of α helices might comprise the consensus sequence recognized by the export apparatus. Our own work discussed here was supported by U.S.P.H.S. Grant GM29798 to L.L.R. from the NIH and a NATO collaborative grant.

19 July 1988; accepted 8 November 1988