The YidC protein fulfills a dual and essential role in the assembly of inner membrane proteins in *Escherichia coli*. Besides interacting with transmembrane segments of newly synthesized membrane proteins that insert into the membrane via the SecYEG complex, YidC also functions as an independent membrane protein insertase and assists in membrane protein folding. Here, we discuss the mechanisms of YidC substrate recognition and membrane insertion with emphasis on its role in the assembly of multimeric membrane protein complexes such as the $F_1F_0$-ATP synthase.

All living cells contain one or more membranes that separate the cytoplasm from the extracellular environment. In addition, the cytoplasm of eukaryotic cells contains many organelles, each surrounded by one or more membranes. Embedded within these membranes is a wide variety of membrane proteins that function in processes such as energy generation, signal transduction, and the transport of (macro)molecules like proteins and DNA.

In bacteria, the major route of protein export and membrane protein insertion is the Sec pathway. The translocase is a multimeric protein complex that consists of a highly conserved, membrane-embedded protein-conducting channel (the translocon) that can associate with an ATPase (SecA) to mediate protein translocation across the inner membrane or with the ribosome to catalyze the co-translational insertion of membrane proteins into the inner membrane. In yeast, nuclear or mitochondrially encoded proteins embedded in the inner membrane of mitochondria are first transported into or synthesized inside the matrix. Because mitochondria do not contain a Sec translocase, subsequent membrane insertion is catalyzed by Oxa1p, a process originally described for the cytochrome oxidase subunit Cox2p (1). Based on sequence homology to Oxa1p, YidC was identified in bacteria (2). YidC belongs to the Oxa membrane protein family, including Alb3 in chloroplast thylakoids and Oxa1p in mitochondria (1). YidC was found as a protein that can be specifically cross-linked to transmembrane segments (TMSs) of newly synthesized membrane proteins during their membrane insertion via the translocon (3). In addition, the *yidC* gene was found to be essential for cell viability and required for the membrane integration of the phage protein M13 procoat that for long was believed to insert in a spontaneous fashion (4). Collectively, these findings led to the proposal that YidC functions as a membrane protein insertase that can act independently or in concert with the translocon.

The currently identified range of substrates of the YidC-only pathway is relatively limited, as will be discussed below. However, it is striking that they are all part of large oligomeric assemblies, fueling speculations that YidC is involved in the assembly of multimeric (membrane) protein complexes. Here, we will discuss the recent advances in the understanding of the mechanism of YidC function with a special focus on the biogenesis and assembly of membrane protein complexes.

**Role of YidC in Sec-dependent Membrane Protein Insertion**

Cross-linking studies using ribosome-bound nascent chains of the monotopic membrane protein FtsQ identified YidC as a protein that is in the vicinity of the inserting TMS, whereas the flanking hydrophilic regions cross-link to SecY and SecA (3). This interaction has been confirmed for a variety of nascent inner membrane proteins (IMPs) and suggested a role of YidC early in the biogenesis of Sec-dependent IMPs. However, the *in vivo* depletion of YidC shows only a minor effect on the Sec-dependent insertion of CyoA (4), FtsQ (5), and MlaA (6). The *in vitro* reconstitution of the membrane insertion pathway of FtsQ demonstrated that YidC is not required for insertion (7). YidC might, however, fulfill a kinetic role in the lateral release of TMSs from the translocon and/or have a general post-insertion chaperone function as demonstrated for the polytopic IMPs LacY (8) and MlaF (9) (see below).

A screen of the physiological consequences of YidC depletion indicated that YidC plays a role in the insertion of CyoA (10). This led several groups to investigate the pathway of insertion (11–13). CyoA (supplemental Fig. 1, *upper*) is a subunit of the cytochrome *bo* quinol oxidase complex. After cleavage of the signal sequence, mature CyoA spans the membrane twice with a large C-terminal periplasmic domain. CyoA requires SecA, SecYEG, and YidC for membrane insertion. In a first step, a helical hairpin of the signal sequence and the first TMS are inserted in a YidC-dependent manner (supplemental Fig. 2a).
MINIREVIEW: F0c Targeting and Membrane Insertion

(14). The translocation of the second TMS and the periplasmic domain requires the concerted action of SecYEG and SecA. Full-length CyoA and a derived truncate (CyoA-N) comprising only the signal sequence and the first TMS (12) depend on the signal recognition particle (SRP) for insertion, suggesting that these proteins first have to be targeted to the Sec translocase to be inserted in a SecYEG/YidC environment.

The cytochrome bo3 oxidase complex is composed of three different membrane proteins. CyoA is the quinol-binding subunit, whereas CyoB is a large heme-binding IMP with 15 predicted TMSs. The 20-kDa CyoC protein contains five TMSs and is of unknown function. YidC depletion also results in a defect in heme incorporation (10). Thus, subunit insertion, cofactor incorporation, and complex assembly are likely coordinated processes, and this might be the reason why this complex requires YidC.

**YidC as an Independent Insertase**

M13 procoat spans the membrane twice and exposes a negatively charged loop region in the periplasm (supplemental Figs. 1 (upper) and 2b). Initially, it was thought that this phage protein spontaneously inserts into the membrane. However, upon in vivo YidC depletion, the processing of the signal peptide is severely disturbed, and the loop that needs to be translocated is inaccessible to an externally added protease (4). The cellular depletion of YidC causes a loss of the proton motive force (PMF) (10). However, as YidC also catalyzes the insertion of PMF-independent mutants of M13 procoat (15), YidC is directly involved in M13 procoat insertion. Similar results were obtained for the single membrane-spanning phage protein PFB coat (supplemental Fig. 1, upper) (16, 17).

The energetics of membrane insertion of these small coat proteins involve the concerted contribution of hydrophobic interactions of the TMSs with membrane phospholipids, helical hairpin formation (in the case of M13 procoat) (18), and PMF-driven translocation of charged residues (19). YidC has been suggested to provide an amphiphilic surface that shields charged residues and TMSs from the hydrophobic acyl chain environment and charged lipid headgroups, respectively. This results in the final membrane topology of M13 procoat (supplemental Fig. 1, upper) and PFB coat. Interestingly, mutations in YidC that specifically influence the insertion of either M13 procoat or PFB coat have been identified (20), indicating different structural requirements for YidC depending on the identity of the substrate.

As YidC is an essential protein, the phage coat proteins have likely hijacked the YidC-only pathway for their membrane insertion. The small, double membrane-spanning, and ring-forming F0 subunit c of the F1–F0-ATP synthase (F0c) (supplemental Fig. 1, lower) and the double membrane-spanning MscL protein that forms the pentameric mechanosensitive channel of large conductance (supplemental Fig. 1, upper) are *Escherichia coli* membrane proteins that depend on the YidC-only pathway (21–23). As these substrates are endogenous to *E. coli*, a detailed analysis of the features that determine their YidC dependence will likely shed light on the mechanism of targeting, recognition, insertion, and release.

**SRP-mediated Membrane Protein Targeting**

The majority of IMPs are targeted as nascent chains to the Sec translocase by the evolutionarily conserved SRP pathway, thereby preventing aggregation of membrane proteins in the cytosol (24). How targeting is achieved in the YidC-only pathway is the subject of controversy, as conflicting results have been obtained.

The existence of an SRP/YidC pathway has been suggested by in vivo studies in *E. coli* using chimeric protein constructs. Membrane insertion was inhibited in the absence of the SRP complex and YidC, but not in the absence of Sec components (25, 26). On the other hand, it is generally accepted that the YidC-dependent M13 and PFB coat proteins do not require the SRP pathway (16, 27), although they can be cross-linked to the SRP Ffh subunit when stabilized as translational arrested chains (16, 28). An in vitro study using YidC proteoliposomes has shown that the membrane insertion of the authentic *E. coli* YidC-only substrate F0c occurs independently of SRP components. Interestingly, translation and insertion of F0c cannot be uncoupled, which has been attributed to the strong hydrophobicity of F0c and its tendency to aggregate (22). Indeed, an in vivo depletion of Ffh has no effect on the cleavage of a translated Myc tag in F0c (29). On the other hand, hemagglutinin-tagged F0c was shown to interact with Ffh using an in vitro cross-linking approach, whereas in vivo depletion of Ffh interfered with F0c membrane insertion (30).

In vivo depletion of Ffh and FtsY abolishes translocation of the periplasmic loop in MscL (23). In contrast, no effect of Ffh depletion was observed in an in vitro MscL insertion assay using YidC proteoliposomes, whereas under the same set of conditions, the membrane insertion of the Sec- and SRP-dependent FtsQ protein was blocked.3 An involvement of SRP has also been shown for a truncate of pre-CyoA (CyoA-N) C-terminally fused to a reporter domain that in vivo inserts into the membrane in a YidC-dependent and Sec-independent manner (12). In vitro cross-linking studies further suggested that the SRP complex interacts with the first TMS and not with the signal sequence (13).

Currently, the results of these studies are difficult to reconcile with each other, especially as differently tagged F0c subunits appear to yield different results. The contradictions between the results concerning substrate targeting to YidC obtained in in vitro and in vivo systems may have arisen from pleiotropic effects due to cellular depletion of essential genes such as *ffh*, *secY*, *secE*, and *yidC*. For instance, Ffh depletion results in the formation of intracellular membrane structures (31) and induces heat shock proteins, specifically proteases (32). Exhaustive depletion of a gene product takes several genetic changes to yield pleiotropic effects and sheds light on the targeting of YidC-dependent membrane proteins.

Another issue relevant for SRP targeting is that the release of nascent chains from SRP involves the SRP receptor FtsY

3 S. Kol, unpublished data.
and GTP binding and hydrolysis. FtsY is known to bind to SecYEG (33), but a physical interaction between YidC and FtsY remains to be demonstrated. One of the main questions that has remained unanswered is how SRP can discriminate between protein substrates to be funneled to SecY or to YidC.

**YidC-mediated Recognition and Insertion**

Another possible mechanism of targeting is the direct recognition and binding of substrates in the cytosol by YidC without the involvement of other targeting factors. Recognition will likely involve the cytoplasmic accessible hydrophilic regions of YidC. A suitable candidate for this interaction would be the conserved first cytoplasmic loop, but a deletion of this loop did not severely impair membrane insertion of M13 procoat (34). In this respect, it will be interesting to investigate the insertion of genuine *E. coli* YidC substrates to address the possible mechanism of recognition and insertion.

The F₁F₀-ATP synthase subunit F₀c consists of two TMSs that form a helical hairpin. The short N and C termini are translocated into the periplasm, whereas the connecting loop region remains cytosolic (supplemental Fig. 1, lower). The PMF-independent membrane insertion of F₀c can be reconstituted using YidC proteoliposomes (22). Membrane-inserted F₀c obtains the correct topology and even assembles into a large oligomeric complex, comparable in size to the rotor ring found in vivo. Initially, it was suggested that YidC merely stabilizes a spontaneously membrane-inserted state of F₀c until it is incorporated into an oligomeric complex. However, mutants of F₀c that are no longer able to oligomerize still insert into the membrane in a YidC-dependent manner. These studies therefore demonstrate the insertion function of YidC (35).

The recognition of substrates by YidC has recently been addressed by analyzing the contribution of charged amino acid residues in the polar regions of F₀c in membrane targeting and insertion (36). The positive charges in the cytosolic loop of F₀c appear to be important determinants for the initial recognition of YidC. Co-sedimentation of F₀c with inner membranes is strongly dependent on the presence of YidC, suggesting little interaction between F₀c and membrane lipids, and thus favors a direct binding to YidC (supplemental Fig. 2c). The inability of F₀c mutants to associate with YidC results in a defect in the subsequent insertion step. Substrate recognition appears to involve direct electrostatic interactions between YidC and F₀c₀, requiring the positively charged amino acid residues in the cytosolic loop region of F₀c (19). This mode of direct substrate recognition will bypass the need for SRP-mediated targeting.

When the above findings are extrapolated to the mechanism of insertion of M13 procoat, it is tempting to speculate that the observed lipid binding *in vitro* might not represent a genuine intermediate in its membrane insertion (1) but may be due to the high curvature of the liposomes used in these studies. Instead, recognition might also be directly mediated by YidC (supplemental Fig. 2b). Positive charges in M13 procoat are situated at the N and C termini, which, following YidC-mediated membrane insertion, remain in the cytosol. The highly negatively charged periplasmic loop is translocated by a PMF-driven step, yielding a topology that is the reverse of that of F₀c. A mutant of M13 procoat that lacks the charges in the loop is processed independently of the PMF but still depends on YidC for insertion (1). This suggests that the negative charges in the loop region are not essential for YidC-mediated translocation and that topogenesis in the YidC-only pathway is dictated mostly by the positively charged residues remaining in the cytosol. In contrast, the charges present in the translocated regions of substrates determine the Oxa1p dependence (37).

The mechanism of recognition and insertion as described above may also apply to MscL and the CyoA-N truncate (supplemental Fig. 2a), which both contain positively charged amino acids at their N and C termini directly flanking their TMSs. Upon YidC-mediated membrane insertion, the N and C termini are retained in the cytoplasm, whereas the polar loop is translocated into the periplasm. Moreover, the PMF is not required for the insertion of MscL and CyoA-N, probably because their translocated loops carry net charges of −1 and 0, respectively. Analogous to M13 procoat, introduction of negative charges into the periplasmic loop of CyoA-N renders translocation dependent on the PMF (14). It would be of interest to examine the contribution of positively charged amino acids in these proteins to YidC targeting and membrane insertion.

The final stage in stable insertion involves the release of substrates from YidC inside the membrane. Could this process be mechanistically linked to oligomerization? Interestingly, a mutant of F₀c₀ no longer able to oligomerize associates more strongly with YidC than does wild-type F₀c (35). In addition, because Oxa1p (38) and YidC⁴ can be purified together with the ATP synthase complex, a possible scenario is that these proteins remain associated with YidC until correct coupling and assembly of the final native complex are achieved. During these assembly steps, the YidC-interacting region may become buried inside the oligomeric structure and thus dissociate YidC for another round of insertion.

**YidC as a Chaperone and Assembly Factor**

The similarity of biogenesis of the F₁F₀-ATP synthase in yeast and *E. coli* suggests that members of the Oxa family not only are involved in insertion but also chaperone the correct formation of the ATP synthase complex. The F₁F₀-ATP synthase of *E. coli* consists of two subcomplexes: the membrane integral F₀ part (a₁b₂c₁₀) and the peripheral F₁ part (α₁β₁γδε). This is the simplest form of this enzyme, making it an ideal model to study its assembly rather than the more complex forms found in mammalians and lower eukaryotes. The close similarity of its basic structure in all types of energy-transducing membranes suggests an analogous assembly mechanism. Assembly is likely a coordinated process that requires the membrane insertion of the separate F₀ subunits; their stabilization prior to assembly into the F₀ subcomplex with a correct stoichiometry of a, b, and c subunits; and finally, the coupling of the F₀ to the F₁ sector. YidC mediates the membrane insertion of F₀c. In addition, the efficient membrane assembly of F₀,α in *E. coli* requires YidC as well as the translocon (21, 29). Moreover, recent findings indicate that YidC co-purifies with the F₁F₀ complex⁴ and with F₁αβ (39).

⁴ M. J. Saller and A. J. M. Driessen, unpublished data.
MINIREVIEW: \( F_0\) Targeting and Membrane Insertion

In yeast, several accessory proteins that play a role in assembly of the \( F_1F_0\)-ATP synthase have been identified. The chaperones Atp11p and Atp12p facilitate the co-assembly of \( F_1\) subunits \( \alpha \) and \( \beta \), respectively (40). The role of Fmc1p in the assembly of \( F_1\) is less clear, but it may be required for stabilization of the chaperone Atp12p under heat stress conditions (41). The biogenesis of Atp6p \((F_0a)\) has been shown to be highly complex, requiring several chaperones (40, 42). Atp10p acts as a specific chaperone to Atp6p \((F_0a)\) and assists its co-assembly with an Atp9p \((F_0c)\)-F1 subcomplex (40). Oxa1p has recently been shown to interact with an Atp9p \((F_0c)\)-F1 subcomplex and was proposed to act as a chaperone that ensures the correct assembly of the Atp9p \((F_0c)\) ring and the co-assembly with Atp10-chaperoned Atp6p \((F_0a)\) (38). The incorporation of Atp6p \((F_0a)\) into the complex therefore represents one of the last steps in the assembly process.

In bacteria, stable \( F_1F_0\) complexes occur without \( F_0a\) present (43), and the activity of \( F_0a\)-deprived complexes of the thermophilic Bacillus PS3 can be restored by the addition of purified \( F_0a\) (44). Fluorescence studies have shown that \( F_0b\) and a fully assembled \( F_0c\) suffice for the binding of the \( F_1\) subcomplex (45). Analogous to yeast, \( F_0a\) might therefore also be the last component that is added to a complex of \( F_0b\) and the \( F_0c\) ring in vivo. Possibly, \textit{in vivo} the \( F_1\) and \( F_0\) sectors are not yet fully assembled before coupling occurs (46).

In bacterial genomes, the \( atpI\) gene typically precedes the genes encoding the structural subunits of the \( F_1F_0\)-ATP synthase. The function of AtpI has long remained elusive, as it is not essential for the formation of the \( F_1F_0\)-ATP synthase complex. Recently, it was speculated that AtpI functions as a pilot protein facilitating assembly of the complex. Herein, a hybrid \( F_1F_0\) \((F_1\) from \textit{Bacillus} PS3 and \( F_0\) from \textit{Propionigenium modestum}) was expressed in \textit{E. coli}. The \( F_0c\) formation and coupled ATPase activity were found to be dependent on \textit{P. modestum} AtpI (47). \( F_0c\) monomers, as well as the assembled \( F_0c\), can be co-purified with AtpI, indicating a direct chaperone-like interaction. As the deletion of \( atpI\) in \textit{E. coli} results merely in a slightly reduced growth yield (48), it was suggested that YidC may have an overlapping function with AtpI in the assembly of \( F_0c\). However, as it is unlikely that \textit{P. modestum} does not contain a member of the Oxa family, the proposed essential role of AtpI in assembly remains to be established.

The formation of \( F_0c\) is one of the most important steps in the biogenesis of the entire complex, and its availability may even determine the total amount of ATP synthase in mammals (49). Insertion and assembly of \( F_0c\) may therefore represent a highly regulated event. In addition, the complexity of biogenesis and assembly of \( F_0a\) in yeast indicates that incorporation of the proton-translocating subunit is also highly regulated, possibly to prevent misfolding and subsequent ion leakage. Chaperones specific to \( F_0a\) have not been identified in \textit{E. coli}, indicating that the biogenesis of this subunit might be considerably less complex.

The role of YidC in the insertion and assembly of complexes involved in aerobic respiration such as the cytochrome \( bo_3\) quinol oxidase and ATP synthase is well established. A previous study has demonstrated that YidC is also needed for anaerobic respiration. Upon depletion of YidC, the levels of both the nitrate and fumarate reductases and the NuoK subunit of NADH dehydrogenase I were diminished (50). This suggests a more generic role of YidC in the assembly of these integral membrane protein complexes.

YidC and Protein Folding Quality Control Mechanisms

In yeast, Oxa1p links to the quality control mechanism that ensures proper folding and assembly of membrane proteins. In the absence of Oxa1p, a defect in the \( F_1F_0\)-ATP synthase assembly and activity is caused by a reduction in the amounts of Atp6p \((F_0a)\), Atp17p \((\text{subunit f})\), and Atp4p \((F_0b)\). This defect can, however, be overcome by the co-deletion of Yme1p, an intermembrane space protease homologous to FtsH (51). Oxa1p may shield a folding membrane protein from proteolysis by Yme1p. Remarkably, in the absence of both, the ATP synthase can assemble normally and displays restored ATPase activity (51). In this respect, it is interesting to note that YidC co-purifies with FtsH, a protease that degrades misassembled IMPs. As \( F_0a\) has been shown to be a substrate of FtsH (52), also in bacteria, there might be a functional link between YidC-mediated membrane insertion and assembly and the quality control mechanism in the cell that serve to monitor and ensure the correct folding of IMPs (39). In bacteria, it is unknown if co-deletion of \textit{ftsH} is able to suppress the functional requirement for YidC in viability and membrane protein assembly.

Conclusions and Outlook

YidC interacts, at least transiently, with the translocase and associates with hydrophobic TMSs during their insertion into the membrane. What could be the functional significance of this translocase interaction? The high abundance of YidC suggests that it is always in the vicinity of the translocase, thereby allowing for a low affinity interaction with the TMSs of nascent IMPs that insert via SecY. As YidC is not required for Sec-dependent protein insertion, it might be involved in the folding and shielding of IMPs from membrane proteases. So far, YidC chaperone activity has been suggested for the polytopic membrane proteins LacY and MalF, and it will be important to determine whether the chaperone activity is a more general activity of YidC.

Because mitochondria do not contain a Sec translocase, Oxa1p fulfils only the Sec-independent function of YidC. Its role in the membrane assembly of Atp6p \((F_0a)\) is therefore of particular interest and may well be conserved in YidC and other bacterial homologs. Subunit a of the \( F_1F_0\)-ATP synthase is therefore an interesting candidate for studies on the cooperative action of SecYEG and YidC as well as the possible chaperone functions of YidC.

Common features of identified substrates of the YidC-only pathway include the small size of the translocated region and the final assembly into oligomeric complexes, although it should be stressed that phage coat proteins assemble only at a late stage of their biogenesis. What are the features of these protein substrates that are recognized by YidC, and why are only short polar regions translocated by YidC?

Through the biochemical analysis of YidC and its homologs, important functional regions have been determined. Evaluation of the physicochemical characteristics of protein sub-
strates may provide further information about the mechanism by which they are inserted by YidC. However, many questions concerning the mechanism remain. How does YidC facilitate membrane partitioning into the membrane? What is the exact nature of the interaction with SecYEG? Is YidC involved in folding and assembly as a chaperone, and how is this achieved? The elucidation of a low resolution structure of YidC and an atomic structure of its periplasmic domain did not provide the much needed answers (53, 54). Further biochemical studies will provide a deeper insight into the mechanisms of membrane protein insertion and folding.

Acknowledgments—We thank D. J. F. du Plessis and M. J. Saller for discussion.

REFERENCES

1. Dalbey, R. E., and Kuhn, A. (2000) Annu. Rev. Cell Dev. Biol. 16, 51–87
2. Blattner, F. R., Plunkett, G., III, Boucher, C. A., Perna, N. T., Riley, M., Collado-Vides, J., Glasner, J. D., Rode, C. K., Mayhew, G. F., Gregor, J., Davis, N. W., Kirkpatrick, H. A., Goeden, M. A., Rose, D. J., Mau, B., and Shao, Y. (1997) Science 277, 1437–1474
3. Scotti, P. A., Urbanus, M., Brunner, J., de Gier, J. W., von Heijne, G., van der Does, C., Driessen, A. J. M., Oudega, B., and Luirink, J. (2000) EMBO J. 19, 542–549
4. Samuelson, J. C., van der Laan, M., Urbanus, M. L., ten Hagen-Jongman, C. M., Nouwen, N., and Driessen, A. J. M. (2004) J. Biol. Chem. 279, 1659–1664
5. Wagner, S., Pop, O., Haan, G. J., Baars, L., Koningstein, G., Klepsch, M. M., Genevaux, P., Luirink, J., and de Gier, J. W. (2003) J. Biol. Chem. 278, 17881–17890
6. van der Laan, M., Bechtluft, P., Kol, S., Nouwen, N., and Driessen, A. J. M. (2001) EMBO Rep. 2, 524–529
7. van der Laan, M., Bechtluft, P., Kol, S., Nouwen, N., and Driessen, A. J. M. (2000) Proc. Natl. Acad. Sci. U. S. A. 100, 5801–5806
8. Samuelson, J. C., van der Laan, M., ten Hagen-Jongman, C. M., Nouwen, N., Oudega, B., Harms, N., Driessen, A. J. M., and Luirink, J. (2001) Proc. Natl. Acad. Sci. U. S. A. 100, 1400–1405
9. Yi, L., Celebi, N., Chen, M., and Dalbey, R. E. (2004) J. Biol. Chem. 279, 182–187
10. Xie, K., Hess, T., Seppala, S., Rapp, M., von Heijne, G., and Dalbey, R. E. (2007) Biochemistry 46, 15153–15161
11. van der Laan, M., Nouwen, N. P., and Driessen, A. J. M. (2005) Curr. Opin. Microbiol. 8, 182–187
12. Chen, M., Xie, K., Nouwen, N., Driessen, A. J. M., and Dalbey, R. E. (2003) J. Biol. Chem. 278, 23295–23300
13. Wagner, S., Pop, O., Haan, G. J., Baars, L., Koningstein, G., Klepsch, M. M., Genevaux, P., Luirink, J., and de Gier, J. W. (2003) J. Biol. Chem. 278, 17881–17890
14. Samuelson, J. C., van der Laan, M., Urbanus, M. L., ten Hagen-Jongman, C. M., Nouwen, N., and Driessen, A. J. M. (2000) J. Biol. Chem. 275, 1659–1664
15. Wagner, S., Pop, O., Haan, G. J., Baars, L., Koningstein, G., Klepsch, M. M., Genevaux, P., Luirink, J., and de Gier, J. W. (2002) J. Biol. Chem. 277, 7670–7675
16. Serek, J., Kiefer, D., Dalbey, R., and Kuhn, A. (2004) EMBO J. 23, 294–301
17. Xie, K., Hess, T., Seppala, S., Rapp, M., von Heijne, G., and Dalbey, R. E. (2007) Biochemistry 46, 15153–15161
18. van der Laan, M., Nouwen, N. P., and Driessen, A. J. M. (2005) Curr. Opin. Microbiol. 8, 182–187
19. Chen, M., Xie, K., Nouwen, N., Driessen, A. J. M., and Dalbey, R. E. (2003) J. Biol. Chem. 278, 23295–23300