

The signal recognition particle of Archaea

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It is becoming increasingly clear that similarities exist in the manner in which extracytoplasmic proteins are targeted to complexes responsible for translocating these proteins across membranes in each of the three domains of life. In Eukarya and Bacteria, the signal recognition particle (SRP) directs nascent polypeptides to membrane-embedded translocation sites. In Archaea, the SRP protein targeting pathway apparently represents an intermediate between the bacterial and eukaryal systems. Understanding the archaeal SRP pathway could therefore reveal universal aspects of targeting not detected in current comparisons of the eukaryal and bacterial systems while possibly identifying aspects of the process either not previously reported or unique to Archaea.

Today, it is generally accepted that life on earth can be divided into three distinct domains: the Eukarya, Bacteria and Archaea¹, with each domain possessing a variety of defining biochemical, genetic and physiological traits. Despite their differences, each domain encounters the same set of problems when transferring proteins across the barrier presented by phospholipid-based membranes. The challenge of protein translocation begins with protein targeting, that is, the correct delivery of extracytoplasmic proteins to proteinaceous translocation complexes embedded in the membrane (Box 1). Eukarya, Bacteria and Archaea all contain components of the signal recognition particle (SRP), a ribonucleoprotein complex involved in the targeting of nascent proteins to translocation sites²⁻⁶ (Fig. 1). In Eukarya, the SRP pathway is relatively well characterized, and significant strides have been made in elucidating the role of the bacterial SRP in recent years. By contrast, little is known about the SRP pathway in Archaea, the most recently described and least well understood domain of life.

The SRP pathway of Eukarya and Bacteria

In Eukarya, once approximately 70 amino acids of a nascent polypeptide chain destined to enter the secretory pathway (including the cleavable amino-terminal signal sequence) have emerged from the ribosome, both the nascent chain and the ribosome are recognized by the SRP (Fig. 2). In higher Eukarya, this complex consists of six proteins (SRP54, SRP19 and the SRP68/72 and SRP9/14 heterodimers) and a 7S RNA²⁻⁵. Yeast SRP differs from the mammalian particle owing to the functional replacement of SRP9/14 by an SRP14 homodimer and by the presence of the yeast-specific protein SRP21 (Ref. 7). Upon binding to the signal sequence, SRP arrests further elongation of the nascent chain. The ternary complex consisting of the ribosome, nascent polypeptide and SRP is then targeted to the membrane as a result of the affinity of

the SRP for the membrane-bound SRP receptor and of the ribosome for the Sec61 $\alpha\beta\gamma$ translocation complex^{8,9}. Interaction of the SRP with the SR α subunit initiates a concerted series of GTP-dependent events leading to release of the SRP from the complex, transfer of the signal sequence from SRP54 to the Sec61 complex and the subsequent resumption of protein translation directly into the translocation apparatus^{10,11}.

The first hints that the SRP pathway might be universal came with the discovery of bacterial homologues of the SRP components. Comprising only Ffh (an SRP54 homologue) and a 4.5S RNA, the simpler bacterial SRP acts together with FtsY (an SR α homologue)^{12,13} in the biogenesis of a sub-population of inner-membrane proteins¹⁴⁻¹⁷, and could also play a role in targeting extracytoplasmic proteins^{18,19}. The bacterial SRP has been shown to target ribosomes translating membrane proteins to the integral SecYEG translocation machinery, where membrane insertion occurs^{20,21}. Evidence suggesting that the SRP might act subsequent to FtsY-mediated targeting of ribosomes to the membrane has, however, been presented²².

Archaeal SRP pathway components

The presence of SRP-related components in all Archaea examined to date indicates that the targeting of nascent archaeal extracytoplasmic proteins occurs in a similar manner as in Eukarya and Bacteria, yet the often distinctive biological strategies developed by Archaea raise the possibility that aspects of the SRP pathway might be unique to this domain. Examination of currently identified archaeal SRP components suggests that this could indeed be the case.

SRP RNA

The archaeal SRP includes a 7S RNA composed of four domains, together containing seven helices (Fig. 1). Despite the overall lack of sequence conservation, archaeal SRP RNA can be folded into a secondary structure very similar to that of human 7S RNA, apart from an additional helix (helix 1) formed upon pairing of the 5' and 3' ends of the archaeal molecule, and the absence of helix 7, which is only found in the eukaryal molecule²³. Although not found in Eukarya, helix 1 is found in the SRP RNA of the Gram-positive bacterium *Bacillus subtilis*²⁴. As the secondary structure of the *Alu* domain of archaeal SRP RNA, comprising helices 1-4 and much of helix 5, resembles its eukaryal counterpart, it is conceivable that, like the eukaryal

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Box 1. Archaeal protein translocation

The SRP pathway feeds proteins destined to reside beyond the confines of the cytoplasm to the evolutionarily conserved Sec protein-translocation system. As observed with the SRP pathway, examination of protein translocation in Archaea reveals both universal aspects of the process as well as archaeal-specific features^{a,b}.

Signal sequences

In all three domains, secreted proteins and some classes of membrane proteins are synthesized as preproteins, containing a cleavable amino-terminal extension known as the signal sequence. Signal sequences contain 20–30 amino acid residues organized into three distinct regions: a positively charged N-region, a hydrophobic H-region and a short C-region terminating in the signal sequence cleavage site. Such sequences are recognized by targeting systems, such as the SRP pathway. Although archaeal signal sequences are highly similar to those of Eukarya and Bacteria, modified as well as non-classical signal sequences have been detected in Archaea.

The Sec complex

Protein translocation across the eukaryotic ER and bacterial plasma membrane occurs at Sec61 $\alpha\beta\gamma$ and SecYEG, respectively. The core components of these complexes, Sec61 $\alpha\gamma$ and SecYE, are homologous. Archaea also contain Sec61 α /SecY- and Sec61 γ /SecE-homologue-encoding genes. In both cases, the archaeal proteins are more similar to the eukaryal rather than bacterial versions. The third components of the eukaryotic and bacterial translocation complexes, Sec61 β and SecG, respectively, are not homologous. No archaeal versions of Sec61 β nor SecG have been reported, suggesting that Archaea rely on a simpler dimeric complex or that a third, hitherto undetected, archaeal-specific component exists.

In addition to the core complex, translocation machineries might enlist various auxiliary proteins. In Bacteria, SecDF serves to modulate the membrane association of SecA, the essential ATPase component of the translocation apparatus. Eukarya contain neither SecDF nor SecA. The existence of archaeal SecDF-encoding genes is therefore surprising given that no archaeal version of SecA has been detected. Thus, archaeal SecDF could assume novel roles. Other auxiliary proteins, such as eukaryal translocating-chain-associated membrane protein (TRAM) or Oxa1, or bacterial YidC or YvaL, are absent in Archaea.

Signal peptidase

During, or shortly after, the translocation of a preprotein across the membrane, the signal sequence is cleaved by type I signal peptidase. Although revealing similar substrate specificities, bacterial and eukaryotic signal peptidases differ in molecular composition. The signal peptidases of Archaea appear to consist of a single protein as in bacteria yet are more similar in sequence to a subunit of the eukaryal signal peptidase than to the bacterial version.

Membrane phospholipids

In Bacteria, the presence and character of membrane and non-bilayer lipids affect the translocation process. Unlike bacterial (and eukaryal) phospholipids, composed of fatty acyl groups linked through ester bonds to a glycerol backbone, archaeal phospholipids consist of repeating isoprenyl subunits linked to a glycerol backbone through an ether bond. Whether these uniquely archaeal membrane lipids also modulate the translocation process remains unknown.

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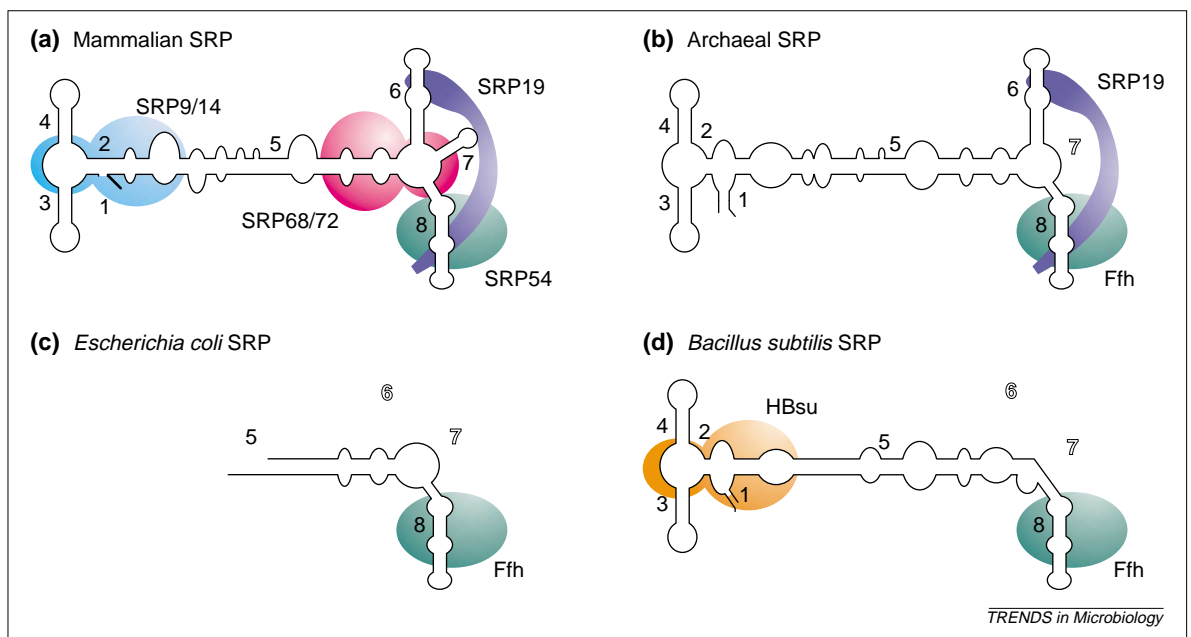
molecule, this region of the archaeal 7S RNA could contain binding sites for SRP9/14-like proteins. In higher Eukarya, SRP9/14 is responsible for the translational pause in the targeting process. To date, SRP9/14 sequences have not been detected in archaeal genomes, although this could be the result of the absence of conserved sequence motifs rather than the absence of structural elements. Although it can be speculated that unique archaeal proteins could substitute for the SRP9/14 dimer in providing an as-yet-undescribed translation-arresting role, it is also conceivable that the putative tRNA-like structure of the archaeal SRP RNA *A/u* domain could directly interact with the ribosome, independent of SRP9/14 (Ref. 25). It has also been proposed that archaeal 7S RNA contains SRP68/72-binding sites²⁶, despite the failure of archaeal

genome searches to detect the presence of these proteins. If these proteins are indeed absent in Archaea this suggests that the appearance of SRP68 and SRP72 occurred subsequent to the proposed divergence of the archaeal and eukaryal branches of the tree of life, an event which occurred after development of a 7S RNA molecule possessing a common conformation. Alternatively, these regions of archaeal 7S RNA might interact with functional homologues of SRP68/72 not identifiable by current genome analysis techniques.

SRP54/Ffh

In addition to SRP RNA, the SRP of all organisms investigated to date²⁷ includes SRP54 or its prokaryotic counterpart, Ffh (fifty-four homologue) (Fig. 3a). Like its eukaryal and bacterial

Fig. 1. The signal recognition particle (SRP) through evolution. Representative schematic drawings of (a) mammalian SRP, (b) archaeal SRP, (c) *Escherichia coli* SRP and (d) *Bacillus subtilis* SRP are shown. SRP RNA is drawn such that parallel lines correspond to Watson-Crick base-paired regions, bulges correspond to unpaired regions, and numbers correspond to SRP RNA helix number. Outlined numbers reflect missing helices. SRP9/14 is shown in blue, SRP68/72 in pink, SRP54/Ffh in green, SRP19 in purple and HBSu in orange.



counterparts^{28,29}, the archaeal Ffh G-domain also encompasses the five signature elements (G1–G5), which have been shown to interact with the GDP/GTP–Mg²⁺ complex (Fig. 3b). Accordingly, full-length archaeal Ffh, as well as its isolated NG-domain, displays intrinsic GTP-hydrolysing activity^{30,31}. The carboxy-terminal domain, responsible for binding both the signal sequence of the nascent polypeptide chain and SRP RNA in Bacteria and Eukarya, is less conserved in Archaea yet contains an RNA-binding element (RBE in Fig. 3),

shown to be essential in Bacteria³². As such, archaeal Ffh proteins interact with heterologous SRP RNA from both closely and distantly related organisms^{26,30}. Although methionine residues in the carboxyl domain of Ffh, involved in signal-sequence binding in eukaryal and bacterial SRP54/Ffh (Refs 32,33), are replaced by other flexible, hydrophobic residues or by isoleucines in hyperthermophilic crenarchaea, it is unlikely that Archaea rely on a novel mode of signal-sequence binding. Indeed, the ability of *Archaeoglobus fulgidus* Ffh to associate with the signal sequence of bovine preprolactin²⁶ hints that SRP54/Ffh binding to signal sequences might follow universal rules, with minor modifications in the archaeal domain³⁴.

Recent crystallographic analysis of the Ffh NG-domain from the archaeon *Acidianus ambivalens* has provided detailed insight into archaeal Ffh function³¹. As reported for the NG-domain of *Thermus aquaticus* Ffh (the other Ffh for which structural information exists³⁵), the *A. ambivalens* structure includes a four-helix-bundle N-domain connected via a 15-amino-acid linker peptide to a Ras-like GTPase G-domain. The archaeal G-domain includes the I-box insertion element, a motif detected exclusively in members of the SRP GTPase superfamily, in which it might act as an intrinsic nucleotide exchange factor responsible for the high dissociation constants of SRP GTPases³⁶. The G-domains of the *A. ambivalens* and *T. aquaticus* proteins superimpose with a root mean squared deviation of 1.5 Å, indicating an evolutionarily conserved structure. Nevertheless, significant differences exist in the intra- and inter-domain organization of the two proteins. These differences are reflected in the organization of the four-helix bundle in the N-domain, the angle between the N- and G-domains and the conformation of the I-box with respect to the G-domain of the protein (Fig. 4).

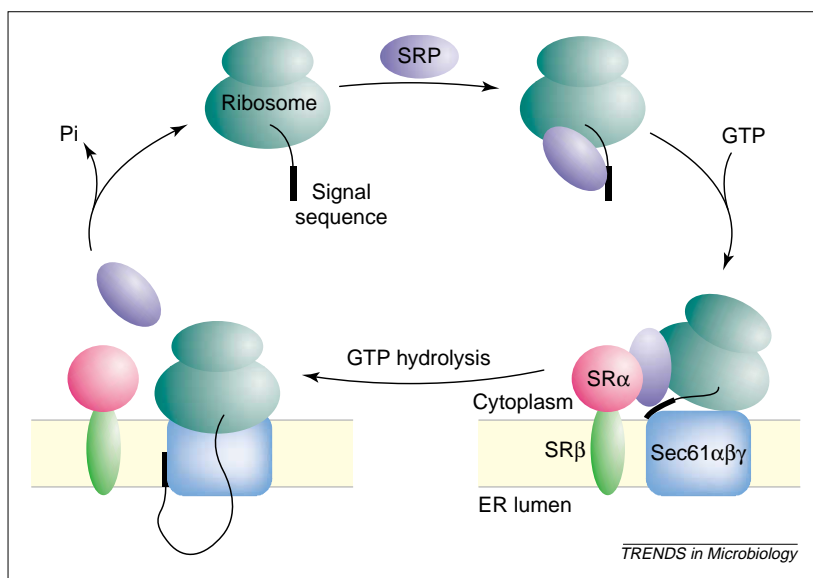


Fig. 2. The signal recognition particle (SRP) pathway of higher Eukarya. SRP (purple) binds to and arrests translation by ribosomes (green) in the process of translating signal sequence-containing nascent polypeptides (black). SRα (pink) binds the translating ribosome–SRP complex and, via the interaction of SRα with SRβ (light green), the nascent chain is delivered to the endoplasmic reticulum (ER) membrane, where Sec61αβγ (light blue), the site of translocation, is found. There, as a result of a cascade of GTP-dependent events, the SR–SRP–ribosome complex disassembles. The ribosome, bound to Sec61αβγ, now continues protein translation; the growing polypeptide chain is fed directly into the protein-translocation apparatus. Liberated SRP and SRα can now participate in the next round of protein targeting.

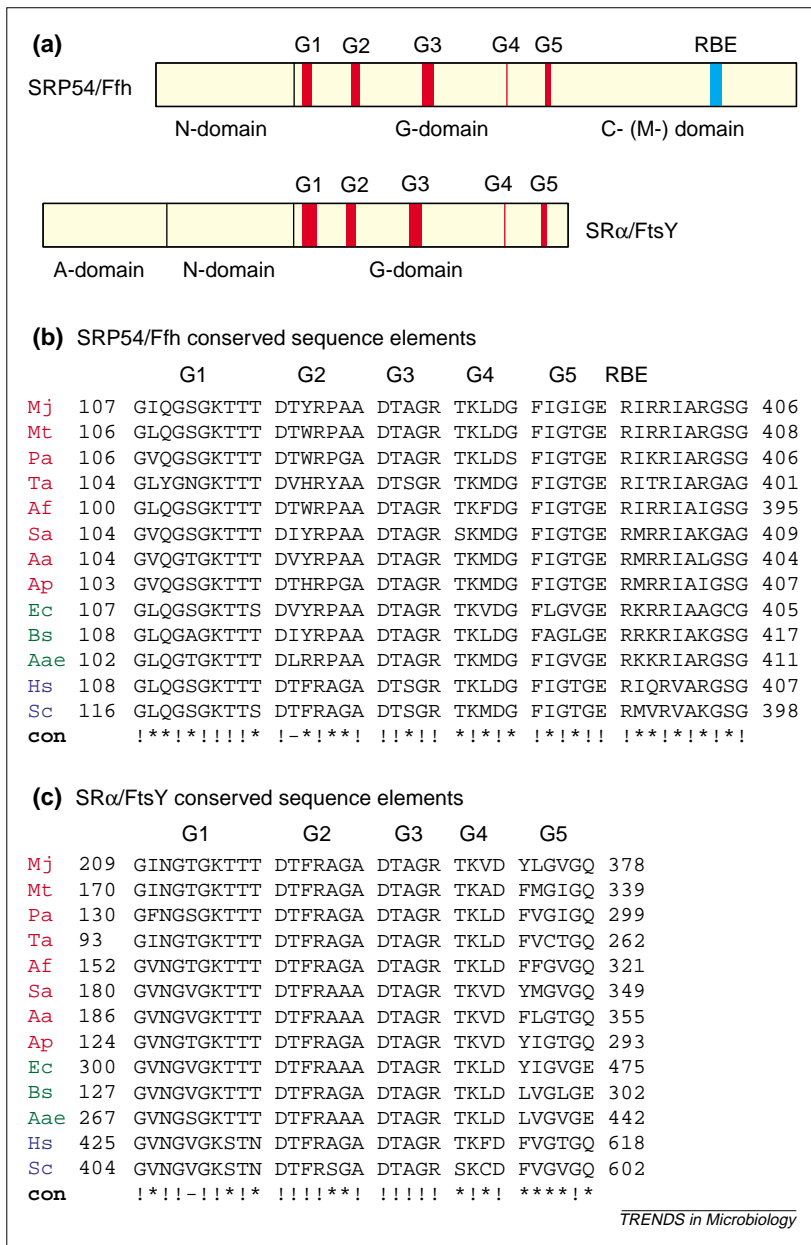


Fig. 3. Sequence comparisons of archaeal SRP54/Ffh and SR α /FtsY proteins. (a) Domain structure of SRP54/Ffh and SR α /FtsY proteins. G1–G5: GDP/GTP binding elements (red); RBE: RNA-binding element (blue). Conserved sequence elements of (b) SRP54/Ffh and (c) SR α /FtsY proteins in Archaea (red), Bacteria (green) and Eukarya (blue) are shown. Conserved residues are indicated by exclamation marks in the line labelled con, whereas homologous residues are indicated by stars. Abbreviations: Mj, *Methanococcus jannaschii*; Mt, *Methanobacterium thermoautotrophicum*; Pa, *Pyrococcus abyssi*; Ta, *Thermoplasma acidophilum*; Af, *Archaeoglobus fulgidus*; Sa, *Sulfolobus acidocaldarius*; Aa, *Acidianus ambivalens*; Ap, *Aeropyrum pernix*; Ec, *Escherichia coli*; Bs, *Bacillus subtilis*; Aae, *Aquifex aeolicus*; Hs, *Homo sapiens*; Sc, *Saccharomyces cerevisiae*.

SRP19

To date, SRP19 sequences have been identified in all completed archaeal genomes, suggesting that the archaeal SRP includes an SRP19 subunit. Although the eukaryal SRP contains SRP19, no bacterial version of this protein has been reported.

Accordingly, SRP RNA helix 6, present in Eukarya and Archaea yet absent in Bacteria, has been shown to bind SRP19 (Ref. 37). Recently, it was shown that *A. fulgidus* SRP19 strongly binds to *in vitro*-transcribed, full-length *A. fulgidus* SRP RNA as well

as shorter versions of *Methanococcus jannaschii* and human SRP RNA containing helices 6, 8 and the distal part of helix 5 (Ref. 26). Efforts directed at reconstitution of an archaeal SRP have also addressed the interaction between Ffh, SRP19 and SRP RNA^{26,34}. As in mammals³⁷, binding of archaeal Ffh to SRP RNA was enhanced in the presence of SRP19. Such observations suggest conservation of this facet of SRP assembly and/or function in Archaea and Eukarya.

SRP72, 68, 14 and 9

In Eukarya, SRP68/72 is involved in docking the nascent polypeptide–ribosome–SRP complex to the endoplasmic reticulum (ER) membrane^{3–5}. Both components (as well as SRP19 and SRP RNA) have been localized to the nucleolus of mammalian cells, where the heterodimer might play a role in SRP assembly or activation^{38,39}. As Archaea do not contain a nucleolus, they might rely on a different mechanism for the interaction of SRP subunits, that is, one not requiring the contribution of SRP68/72. This might explain the failure of genome searches to reveal archaeal homologues of these SRP components. Alternatively, structural homologues of eukaryal SRP68/72 might assume such a role in Archaea.

Archaeal equivalents of SRP9/14, which, in higher Eukarya, plays a role in ribosomal translation arrest, might also exist. This hypothesis is supported by recent studies in Bacteria, which, like Archaea, lack SRP9/14. It was shown that in *B. subtilis*, the 10-kD a histone-like HBSu protein binds to the SRP RNA *Alu* domain as part of an RNA–Ffh–HBSu complex (Fig. 1)⁴⁰. Although the role of HBSu in *B. subtilis* SRP remains unanswered, examination of the crystal structure of DNA-binding protein II (Ref. 41), a protein from the related *Bacillus stearothermophilus* possessing >90% sequence homology to *B. subtilis* HBSu, reveals a tertiary structure similar to that of SRP9/14 (Refs 40,42). Although archaeal versions of HBSu have not been detected, other small nucleic acid-binding proteins could fulfil similar roles in Archaea.

Nascent polypeptide-associated complex

The archaeal SRP pathway could involve additional components, such as the nascent polypeptide-associated complex (NAC). In Eukarya, NAC is thought to prevent the interaction of the SRP with ribosomes translating signal sequence-less nascent polypeptides, that is, those polypeptides not designated for interaction with the protein-translocation machinery, thereby maintaining the fidelity of protein export⁴³. This hypothesis has, however, recently been challenged⁴⁴. Although no archaeal version of NAC has been described, a strictly conserved open-reading frame (ORF) of unknown function containing a domain weakly homologous to the mammalian NAC α -subunit has been detected in several thermophilic Archaea⁴⁵.

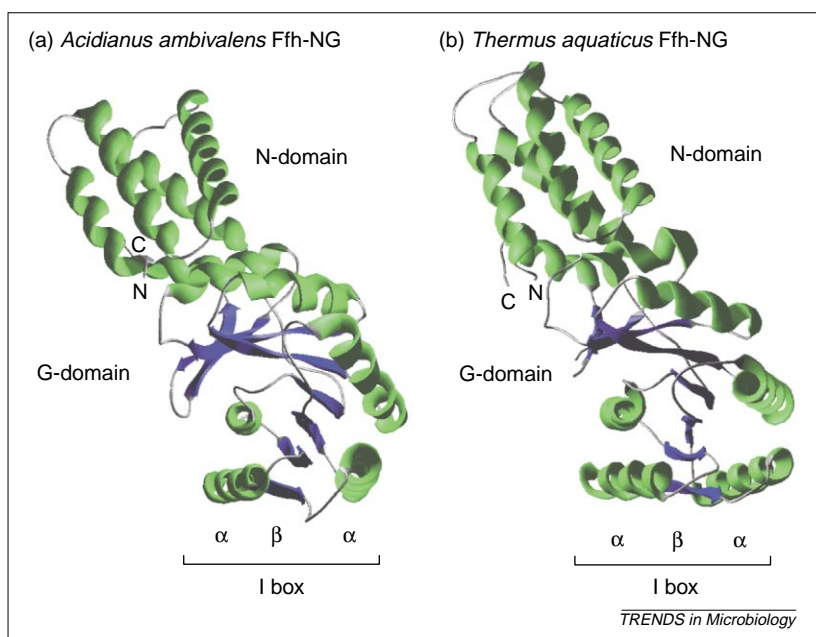


Fig. 4. (a) α ribbon presentation of the NG-domain of Ffh from the crenarchaeon *Acidianus ambivalens* and (b) the bacterium *Thermus aquaticus*. α -helices are coloured in green, β -pleated sheets are displayed in blue. An insertion element (I-box) is designated by the $\alpha\beta\alpha$ structure at the base of each structure. N and C refer to the amino- and carboxyl termini of the proteins, respectively.

Binding of the SRP to the archaeal plasma membrane

Once the SRP has bound a nascent polypeptide chain, the resulting complex must be delivered to the membrane, where the protein-translocation complex is located, in a process mediated by the SRP receptor (SR). All examined organisms²⁷ encode the SR α -subunit or its prokaryotic homologue, FtsY, underlying the prominence of this component of the targeting process. Examination of the currently sequenced archaeal *ftsY* genes reveals a high degree of conservation within the carboxy-terminal N- and G-domains to other SR α /FtsY proteins and to SRP54/Ffh NG-domains, including the five canonical G sequence elements involved in Mg²⁺-GDP/GTP binding in both proteins (Fig. 3c). Thus, like archaeal Ffh (Ref. 30), archaeal FtsY also hydrolyses GTP in a Mg²⁺-dependent manner, with hydrolysis drastically decreasing in G1–G5 sequence element mutants or in the presence of equimolar amounts of GDP (Ref. 46).

In contrast to the conserved NG-domain, only minor conservation exists in the archaeal A-domain, the hydrophilic amino-terminal region of the protein²⁷. The function of the A-domain is less obvious, although in Bacteria it might be responsible for the binding of FtsY to the phospholipids of the plasma membrane⁴⁷. This binding presumably occurs via the cluster of positive charges found at the extreme amino-terminal region of the acidic amino-acid-enriched A-domain⁴⁸, possibly in collaboration with a second region contained within the G-domain of the protein⁴⁹. The A-domains of archaeal FtsY display a low overall charge, owing to a balanced ratio of acidic and basic side chains, yet contain several lysine and arginine residues in non-conserved positions in the amino-terminal region of the domain⁴⁶. Thus, although it can be speculated that archaeal FtsY

interacts with membranes via positively charged residues in the A- and G-domains of the protein as suggested for *E. coli* FtsY (Refs 47–49), the manner of FtsY–phospholipid binding could be unique to Archaea, given the unusual ether-based phospholipids that comprise archaeal membranes⁵⁰.

The archaeal SRP pathway – a hybrid of the eukaryal and bacterial systems?

Assessment of the current level of understanding of the archaeal SRP pathway reveals that the archaeal system includes selected aspects of both the eukaryal and bacterial pathways. In terms of molecular organization, the archaeal SRP is clearly more similar to the eukaryal particle than to its bacterial counterpart (Fig. 1). As discussed above, archaeal SRP contains a 7S RNA molecule which assumes a eukaryal-like secondary structure to which two components (SRP19 and SRP54/Ffh) also found in the eukaryal complex are bound. The archaeal SRP RNA might also contain binding sites for other SRP components currently found only in Eukarya.

Despite the diversity of SRP composition across the three domains of life, the overall structure of SRP GTPases and, accordingly, properties of GTP binding as well as intra- and inter-molecular signal transduction mechanisms between the various domains of Ffh and FtsY, are, however, largely conserved, probably having originated early in evolution (see below).

In the association of SRP with the plasma membrane, Archaea apparently invoke a bacteria-like approach. In terms of molecular size, archaeal FtsY proteins are, in general, more reminiscent of bacterial FtsY proteins than eukaryal SR α . As in *E. coli*¹⁹, archaeal FtsY exists in equilibrium between the membrane-bound and soluble states^{46,51} *in vivo*, with the majority being detected in the cytoplasm. In the apparent absence of prokaryotic SR β -like components, an integral protein responsible for membrane association of peripheral SR α in Eukarya⁵², the intrinsic affinity of FtsY proteins for phospholipids could prove fundamental in directing the archaeal FtsY-bound ribosome–nascent chain–SRP complex to the membrane. Thus, in the primary membrane-binding step, the archaeal version of FtsY could be functionally closer to its bacterial than to its eukaryal counterpart.

Archaeal translation, SRP and translocation

Presently, it is unclear whether the archaeal SRP acts to link protein translation to translocation^{53,54}, as does its eukaryal (and possibly its bacterial⁵⁵) counterpart. Furthermore, it remains unknown whether the translocation of secretory and membrane proteins display similar relations to protein translation in Archaea and what role is assumed by the SRP in these processes. Although the SRP is involved in the translocation of both secreted and membrane proteins in Eukarya^{3–6}, SRP appears necessary for insertion of a subset of inner-membrane proteins in *E. coli*^{13–15,20,55}, and possibly for targeting of some secreted proteins^{18,19}.

Questions for future research

- Does the archaeal SRP act coincidentally with, or following, protein translation?
- Do both secreted and membrane-spanning proteins rely on SRP for their biogenesis in Archaea?
- Does SRP-mediated protein targeting in Archaea require an arrest or delay in protein translation?
- Does archaeal SRP contain novel components such as structural homologues of SRP9/14 or SRP68/72?
- Do the archaeal SRP and its receptor modulate each other's GTPase activity?
- What are the temporal and physical properties of archaeal FtsY binding to the plasma membrane?

To date, research addressing these questions in Archaea has focused on the biogenesis of the membrane protein bacterioopsin in *H. salinarum*. The co-sedimentation of 7S RNA and bacterioopsin mRNA with membrane-bound polysomes, the puromycin-mediated release of 7S RNA from polysomes and the correlation of ribosome-bound 7S RNA with bacterioopsin expression, as well as more recent kinetic labelling studies, all point to a co-translational, SRP-dependent mode of protein translocation in Archaea^{56,57}. By contrast, the necessity of the seventh and ultimate transmembrane helix of bacterioopsin for membrane insertion of the protein upon heterologous expression in *Haloflex volcanii* argues for a post-translational mode of translocation⁵⁸. Use of bacterioopsin as a reporter for archaeal SRP function must, however, be considered with caution, given the unusual signal sequence of this protein⁵⁶.

The evolution of SRP

Examination of the sequences, structures and interactions of SRP components suggests that current versions of the ribonucleoprotein complex evolved from an ancestral SRP, composed of at least a 7S-RNA-like structure to which two proteins, that is, SRP19 and Ffh, were bound. In bacteria, emergence of the SecA/SecE protein targeting pathway⁵⁹ (possibly in parallel with the SRP pathway) resulted in a structural and functional reduction of the ancestral SRP, leading to the modern version of the bacterial SRP. Interestingly, *B. subtilis* SRP RNA could represent a more primitive version of today's bacterial SRP RNA, displaying a secondary structure closer to archaeal than to other bacterial SRP RNAs. Notably,

it has been proposed that Archaea and Gram-positive bacteria comprise a subdomain of the prokaryotic kingdom⁶⁰. In Archaea and Eukarya, the proposed ancestral SRP core structure – SRP54/Ffh, SRP19 and 7S RNA – would have been maintained during evolution. Indeed, phylogenetic analysis of SRP54/Ffh and SRP/FtsY suggests a common origin for these proteins in Archaea and Eukarya⁶¹. Given the relative complexity of the eukaryal cell, novel SRP elements might have been recruited, imparting additional functions to the primitive particle. Although the ancient SRP could have survived unchanged in Archaea, present-day Archaea might have developed a targeting complex as powerful as its eukaryal counterpart, yet relying on a different mechanism owing to the presence of archaeal-specific SRP components. The archaeal 7S RNA *Alu* domain, differing in primary sequence yet sharing a common secondary structure with its eukaryal counterpart, represents an ideal site for interaction with these putative archaeal components. Thus, today's Archaea would not be regarded as primitive creatures, but rather as organisms with highly evolved targeting systems. Perhaps archaeal ribosomes, known to contain structural elements found in neither Eukarya nor Bacteria⁶², interact with the SRP in a novel manner to couple protein translation to targeting.

Conclusions

The archaeal SRP pathway apparently represents an intermediate between the bacterial and eukaryal systems to which archaeal-specific features might have been added. The archaeal SRP relies on a 7S RNA molecule very similar to the eukaryal molecule yet apparently contains only two of the six SRP proteins found in the eukaryal particle. Like Bacteria, the archaeal version of the SRP receptor seemingly contains a single protein subunit, which displays an intrinsic affinity for the plasma membrane. This apparent hybrid-like nature suggests that understanding the archaeal SRP pathway will greatly advance our comprehension of the SRP-mediated protein targeting system. Further analysis of the archaeal SRP system will also help elucidate how Archaea cope with the often extreme conditions of their environments. Furthermore, such study will encourage the use of extremophilic enzymes, genetically engineered for secretion. With the upcoming release of additional genomic sequences from a variety of Archaea, as well as development of improved molecular tools, an understanding of the archaeal SRP protein targeting process is within our sights.

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