Biochimica et Biophysica Acta 1808 (2011) 885–891

Contents lists available at ScienceDirect

Biochimica et Biophysica Acta

journal homepage: www.elsevier.com/locate/bbamem

Review

Crossing the membrane in Archaea, the third domain of life ☆

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ARTICLE INFO

Article history:
Received 4 January 2010
Received in revised form 18 March 2010
Accepted 18 March 2010
Available online 27 March 2010

Keywords:
Archaea
Protein translocation
Signal recognition particle
Translocon
Signal peptidase
Twin arginine translocation

ABSTRACT

Many of the recent advancements in the field of protein translocation, particularly from the structural perspective, have relied on Archaea. For instance, the solved structures of the translocon from the methanoarchaeon *Methanocaldococcus jannaschii* of the ribosomal large subunit from the haloarchaeon *Haloarcula marismortui* and of components of the SRP pathway from several archaeal species have provided novel insight into various aspects of the translocation event. Given the major contribution that Archaea have made to our understanding of how proteins enter and traverse membranes, it is surprising that relatively little is known of protein translocation in Archaea in comparison to the well-defined translocation pathways of Eukarya and Bacteria. What is known, however, points to archaeal translocation as comprising a mosaic of eukaryal and bacterial traits together with aspects of the process seemingly unique to this, the third domain of life. Here, current understanding of archaeal protein translocation is considered. This article is part of a Special Issue entitled Protein translocation across or insertion into membranes.

Contents

1. Introduction

Life on Earth is divided into three distinct domains, namely the Eukarya, the Bacteria and the Archaea [1]. Although it is now clear that Archaea are major denizens of so-called 'normal' environments, such as oceans, soil and even our own intestinal flora [2], Archaea remain best known as extremophiles, able to thrive in some of the most physically adverse conditions on the planet. As such, Archaea have been detected at extremes of pH, salinity, pressure and temperature [3].

Able to cope with environmental challenges for the most part not encountered by other life forms, it is not surprising that Archaea have come up with novel biological solutions to cope with their unique surroundings. The archaeal plasma membrane offers an example of one such domain-specific trait. The phospholipids that comprise the archaeal plasma membrane are composed of polyisoprenyl groups ether-linked to the *sn*-2,3 positions of a glycerol backbone and not the fatty acyl groups ester-linked to the *sn*-1,2 positions of glycerol that make up eukaryal and bacterial phospholipids [4,5]. It is believed that

☆ This article is part of a Special Issue entitled Protein translocation across or insertion into membranes.

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doi:10.1016/j.bbamem.2010.03.020

the ether bonds of the archaeal phospholipids would be more stable in the face of extreme environments. In addition, archaeal membranes may rely upon a monolayer structure composed of tetraether bipolar phospholipids, offering additional stability [6]. On the other hand, many aspects of archaeal biology find parallels in Bacteria and Eukarya. In terms of general traits related to protein translocation, Archaea resemble Bacteria morphologically, with both being surrounded by a plasma membrane enclosing a cytoplasm lacking organelles. On the other hand, protein translation in Archaea shows similarities to the eukaryal process, with ribosomes from the two domains showing similar antibiotic sensitivities [7].

While the study of Archaea has provided insight into strategies employed by Nature to cope with extreme environments, the related abilities of archaeal proteins and other cellular components to survive harsh conditions have also been exploited in structure-based studies aimed at enhancing our understanding of biological phenomena common to all organisms, yet not previously accessible for detailed analysis. At the same time, addressing the archaeal version of many biological processes has served to uncover unique solutions to problems encountered across evolution. In other instances, analysis of a given biological system from the archaeal perspective has served to link previously unrelated bacterial and eukaryal players. As described in this review, the study of protein translocation in Archaea has provided examples of each of these scenarios (Table 1).

2. Targeting

Before proteins can be translocated across the archaeal plasma membrane, they must first be correctly targeted. In Eukarya and Bacteria, the signal recognition particle (SRP) is responsible for delivering selected translating ribosomes to the membrane across which a given nascent polypeptide must cross, i.e., the membrane of the endoplasmic reticulum or the plasma membrane, respectively. Likewise, Archaea also contain SRP. However, despite the reported ability of archaeal SRP54 to interact with a signal sequence [8], experimental verification of a role for SRP in archaeal protein targeting and translocation remains lacking.

At first glance, the archaeal SRP is strikingly similar to its eukaryal counterpart, albeit simpler (Fig. 1). As in Eukarya, the archaeal SRP includes a 7S RNA molecule that assumes a secondary structure much like that seen in the eukaryal particle [9]. In addition, SRP19 and SRP54, two of the six protein components of the eukaryal SRP, are also part of the archaeal SRP. Nonetheless, aspects of SRP are unique to Archaea, with many of these domain-specific traits becoming apparent upon reconstitution of archaeal SRP from its purified components [8,10,11] as well as following structural examination of SRP, its sub-complexes or its individual components [12–20].

2.1. SRP RNA

Unlike the range of sizes seen with bacterial SRP RNA, archaeal SRP RNA contains on the order of 300 nucleotides, much like its human equivalent [9,21]. Likewise, eukaryal and archaeal SRP RNA contain seven helices each. Indeed, despite an overall lack of sequence conservation, archaeal SRP RNA can be folded into a secondary structure virtually identical to that of human SRP RNA, albeit with helix 1, formed upon pairing of the 5′ and 3′ ends of the molecule, being restricted to archaeal SRP RNA [9] and helix 7 only being found in the eukaryal molecule [22]. Helix 1 is, however, seen in *Bacillus subtilis* SRP RNA [23]. It is also of note that despite their phylogenetic and phenotypic diversity, archaeal SRP RNA molecules display striking similarities in even the finer details of secondary structure, including the position and sizes of internal loops within helix 5, the major backbone of the molecule.

2.2. SRP19

SRP reconstitution studies have shown that as in Eukarya, SRP19 plays a role in SRP assembly in Archaea, interacting with SRP RNA to facilitate SRP54 binding [8,10]. However, in contrast to the situation in Eukarya, the interaction between SRP RNA and SRP54 is not entirely SRP19-dependent in Archaea, with significant amounts of SRP RNA-SRP54 binding occurring in the absence of SRP19 [8,11,24]. Indeed, in *Haloferax volcanii*, the gene encoding SRP19 can be deleted without any apparent effect on cell growth, membrane protein insertion, protein secretion or ribosome levels [25]. The ability of SRP RNA and SRP54 to interact in the absence of SRP19 could reflect the need of Archaea for a stable SRP, given the environmental challenges that these microorganisms can encounter [10].

Addressing archaeal SRP19 binding to SRP RNA offers the opportunity to assess the contribution of SRP19 to SRP assembly. Accordingly, the results of various studies, including the biochemical description of the binding of *Archaeoglobus fulgidus* SRP19 to a fragment of SRP RNA comprising helices 6 and 8 [26] and structural analysis of *Methanocaldococcus jannaschii* SRP19 in complex with SRP RNA helix 5 and/or

Table 1
Sec pathway-mediated protein translocation across evolution.

	Archaea	Bacteria	Eukarya
Membrane lipids	polyisoprenyl ether-linked *sn*-2,3 to glycerol	fatty acyl groups ester-linked *sn*-1,2 to glycerol	fatty acyl groups ester-linked *sn*-1,2 to glycerol
Targeting			
Co- or post-translational?	post-translational secretion co-translational membrane protein insertion	post-translational secretion co-translational membrane protein insertion	co-translational secretion and membrane protein insertion (post-translational secretion possible in yeast)
SRP	7S RNA, SRP19, SRP54	4.5S RNA, Ffh	7S RNA, SRP9, SRP14, SRP19, SRP54, SRP68, SRP72
SRP receptor	FtsY	FtsY	SRα, SRβ
Targeting chaperones	unknown	SecB	Hsp70 (for post-translational secretion in yeast)
Translocon			
Core components	SecYEβ	SecYEG	Sec61αβγ
Auxiliary components	SecDF, YidC (?)	SecDFyajC, YidC	TRAM, Sec62/Sec63
Driving force of translocation	for secretion, unknown for membrane proteins, nascent polypeptide elongation (?)	SecA ATPase activity proton motive force nascent polypeptide elongation	nascent polypeptide elongation Hsp70 and BiP ATPase activity for post-translational secretion in yeast
Signal peptidase			
Oligomeric state	Monomer	Monomer	Multimer
Catalytic residues	Ser-His or Ser-His-Asp	Ser-Lys	Ser-His or Ser-His-Asp