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Review

Oligomeric states of the SecA and SecYEG core components of the bacterial Sec translocon

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Abstract

Many proteins synthesized in the cytoplasm ultimately function in non-cytoplasmic locations. In *Escherichia coli*, the general secretory (Sec) pathway transports the vast majority of these proteins. Two fundamental components of the Sec transport pathway are the SecYEG heterotrimeric complex that forms the channel through the cytoplasmic membrane, and SecA, the ATPase that drives the preprotein to and across the membrane. This review focuses on what is known about the oligomeric states of these core Sec components and how the oligomeric state might change during the course of the translocation of a preprotein.

Keywords: Oligomer; Protein transport; SecA; SecYEG; Translocon

Contents

All cells have mechanisms to export proteins from the cytoplasm to their final destination. Bacteria have several transport pathways including the TAT (twin arginine translocation) that transports folded proteins that often contain co-factors (for a recent review, see [1]), the YidC pathway for membrane proteins (for a recent review, see [2]), and the general secretory (Sec) pathway that translocates unfolded preproteins (for a recent review, see [3]).

The Sec pathway is found in bacteria, archaea and eukaryotic organelles such as chloroplasts and the endoplasmic reticulum. Components of the bacterial Sec translocon include two heterotrimeric membrane spanning complexes, SecYEG and SecDFYajC, and a peripherally associated SecA, although homologues for each component are not universal throughout the three kingdoms of life.

A nascent chain destined for export via the Sec pathway emerges from the ribosome in the *Escherichia coli* cytoplasm. This nascent chain consists of the protein to be secreted linked to a targeting signal called the signal peptide, and together

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known as a preprotein. It may associate directly with SecA or be targeted to SecA in complex with the cytoplasmic chaperone, SecB. SecA directs the preprotein to the membrane where the hydrolysis of ATP by SecA, along with the protonmotive force, promotes translocation across the membrane through the channel comprising three integral membrane proteins, SecY, SecE and SecG. The SecDFYajC complex may promote membrane cycling of SecA to enhance translocation through the SecYE pore [4]. The signal peptide is then cleaved from the preprotein by leader peptidase. An overview of protein export in *E. coli* is shown in Fig. 1. A more complete review of Sec transport components not discussed in detail here can be found in [3].

Components of the Sec translocase were first identified when mutations in the genes encoding SecA (*prlD*) and SecY (*prlA*) suppressed protein export defects caused by signal sequence mutations (for review, see [5]). In 1990, the translocon was reconstituted in liposomes using only purified SecYE(G), SecA and ATP, and found to be sufficient for preprotein translocation [6].

Sixteen years later, much has been learned about the components involved in the translocation of preproteins, how they function and how they interact. However, the biophysical nature of the translocon, and specifically the oligomeric states of its components, remains in question. If we are to fully understand protein export in *E. coli*, a physical description of the proteins involved is needed. While the recent crystal structures of bacterial SecAs [7–9] and the archaeal SecY complex [10] have provided great insight, they are static pictures of a dynamic process. This review focuses specifically on what is currently known of the oligomeric states of SecA and SecYEG.

1. SecA—the translocation motor

The SecA gene was first described in 1982 [11] as coding for a component in secretion. The SecA gene product was identified as a large peripheral membrane protein; biochemical data in a cell free system [12] and in vitro using membrane vesicles [13] confirmed that SecA is involved in protein secretion and furthermore, that it couples ATP to protein translocation [14]. More recent studies suggest that SecA may also act as a cytoplasmic chaperone [15].

SecA may exist in monomer–dimer equilibrium [16,17] with a dissociation constant determined to be 0.25 μM–0.5 μM in an aqueous environment [17]. The cellular concentration of SecA has been estimated at about 5 μM [16] suggesting that SecA is predominantly dimeric in the cytoplasm. In fact, a number of studies indicate that SecA is an antiparallel [7,18] homodimer in the absence of detergent and lipids [18–20]. The ratio of monomer to dimer SecA populations can be altered by temperature and salt concentration [17] and by the presence of translocation ligands [16,21,22]. SecA interacts as a dimer with tetrameric SecB in the cytoplasm [23,24] and while SecB

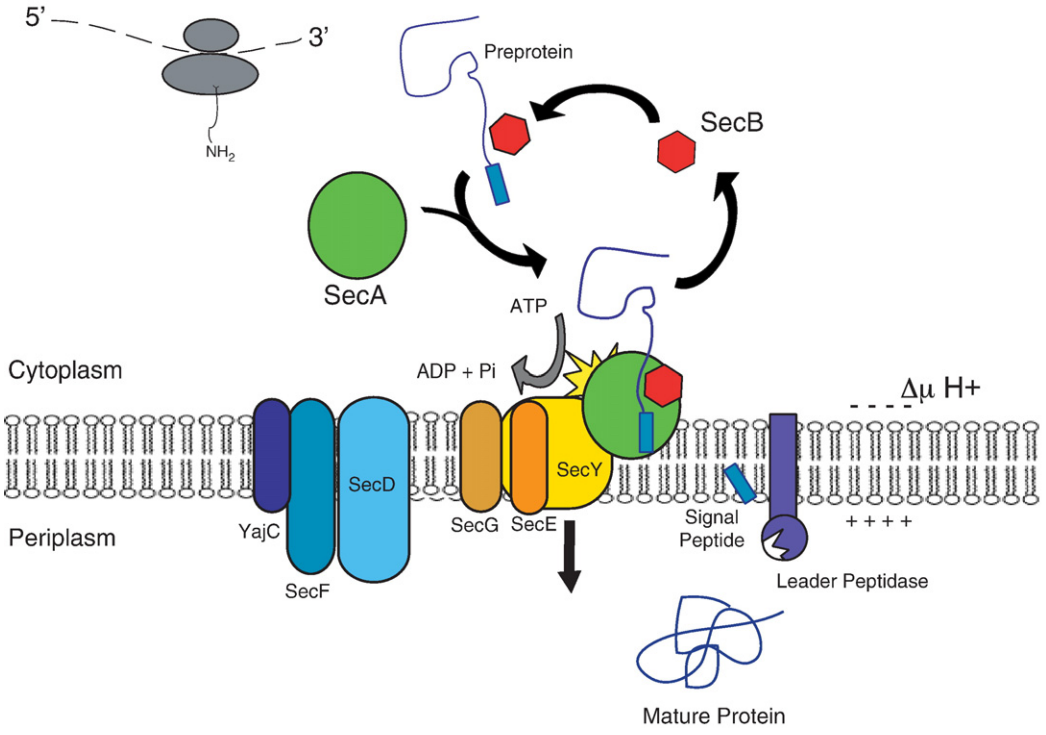

Fig. 1. Schematic representation of the *E. coli* Sec transport system. Most models of Sec-dependent preprotein export share the following features. The nascent chain emerges from the ribosome and may interact with the cytoplasmic chaperone, SecB. The tetrameric SecB associates in the cytoplasm with dimeric SecA. Thus, some preproteins are delivered to SecA via SecB, while others directly interact with SecA without the participation of SecB. Upon interacting with the inner membrane-bound SecYEG, SecA may or may not dissociate to monomer. SecA hydrolyzes ATP and, with the protonmotive force (ΔμH+), drives translocation through the SecYEG pore, composed of one or more subunits. SecDFYajC may enhance translocation by regulating the membrane cycling of SecA. The signal peptide of the preprotein is cleaved on the periplasmic side of the membrane by leader peptidase, releasing the mature protein to its final location.