Review Article
Volume 12:7, 2021

Journal of Veterinary Science & Technology

ISSN: 2157-7579 Open Access

Bacterial Protein Secretion with Particular Emphasis to Toxins

Yitbarek Habtamu[1*], Jaleta Shukab[2], and Fanos Tadessef[3]

[1]*Department of Veterinary Science, National Institute for Control and Eradication of Tsetse Fly and Trypanosomosis, Addis Ababa, Ethiopia*

[2]*Department of Veterinary Science, National Veterinary Institute, Bishoftu, Ethiopia*

[3]*Deapartment of Veterinary Science, Addis Ababa University, Bishoftu, Ethiopia*

Abstract

Bacterial cells must transport proteins across their membranes for the biogenesis of membranes and cell walls, motility and nutrient scavenging and uptake, and is also involved in pathogenesis and symbiosis. The translocase is an impressively dynamic nanomachine that is the central component which catalyses trans-membrane crossing. This complex, multi-stage reaction involves a cascade of inter and intra-molecular interactions that select, sort and target polypeptides to the membrane, and in addition, transport through the outer membrane requires ATP or other sources of energy to promote the movement of these polypeptides across or their lateral escape and integration into the phospholipid bilayer, with high fidelity and efficiency. Here, the review addresses the structure and function of the translocase nanomachine and different mechanisms of protein secretion and their transport. The general secretion Sec and twin arginine translocation pathways are the bacterial secretion systems most commonly used to transport proteins across the cytoplasmic membrane. Often, Sec or Tat systems transport unfolded and folded proteins first to the periplasmic space in Gram negative bacteria, where they are processed to obtain their final three-dimensional structure, before being transported across the outer membrane. There are different path ways in which some are sec dependent and others sec independent. Secretion types II, IV, V and VII are sec-dependent pathways while others like type I, III and VI pathways are sec-independent. Secreted proteins can play many roles in promoting bacterial virulence, from enhancing attachment to eukaryotic cells, to scavenging resources in an environmental niche, to directly intoxicating target cells and disrupting their functions. Therefore, the study of protein secretion systems will be an important focus in the field of bacterial pathogenesis, and virulence for the characterization of various bacterial pathogens.

Keywords: Bacteria • Protein secretion • Toxins • Translocase

Introduction

Bacterial pathogens have numerous strategies to efficiently infect and colonize their eukaryotic hosts. Some pathogenic bacteria have evolved complex nanomachine for protein secretions that mediates diverse processes such as proteolysis, hemolysis, cytotoxicity and phosphorylation or dephosphorylation of host cell proteins. Bacteria appear to be simply organized organisms, but endowed with subcellular complex compartments: the cytoplasm, the cytoplasmic or Inner Membrane (IM), the cell wall common to both gram-positive and gram-negative. The later is even more complex with two additional structural features namely periplasmic space and the Outer Membrane (OM). Proteins synthesis and folding performed in the cytoplasm with some exception that folds outside. To exert their effect, they need to be transported in to the supernatant or the bacterial surface, by a process called secretion. Often, Sec or Tat systems transport unfolded and folded proteins first to the periplasmic space in Gram negative bacteria. At this stage they are processed to obtain final three-dimensional structure, before being transported across the outer membrane. The destiny of the protein may go deep in to the host interfere with cellular processes and suppress host defenses through a process called translocation. In addition, transport through the outer membrane requires ATP or other sources of energy, no indications of which exist that they are present at the outer membrane. Secretion systems must therefore be self-energized or harness energy at the cytoplasmic side of the inner membrane [1].

Until type VII secretion is identified recently, there were six major pathways by which these proteins are transported from the bacterial cytoplasm to the extracellular space, four of which depend on the 'general secretory pathway: Type II and Type IV secretion, auto transporters (Type V secretion) and the chaperone/usher pathway. These Sec-dependent pathways export proteins with a short amino

***Address to correspondence:** Yitbarek Habtamu, Department of Veterinary Science, National Institute for Control and Eradication of Tsetse Fly and Trypanosomosis, Addis Ababa, Ethiopia, Tel: 251996860199; E-mail: yithab@yahoo.com*

Received: 02 August, 2021; **Accepted:** 16 August, 2021; **Published:** 23 August, 2021

terminal signal sequence approximately 30 amino acids through the inner membrane to the periplasmic space, where the largely hydrophobic signal sequence is cleaved off by a peptidase. Alternatively, Type II secretion can also be Tat-dependent: proteins are targeted across the inner membrane in their fully folded conformation, by an amino terminal signal peptide containing two arginine residues. Type I and Type III secretion do not depend on the Sec system to fulfill their function. Although first described in 1996, another protein secretion mechanism was recognized in 2006 as being the Type VI secretion mechanism. Therefore, this review aims to describe type I-VII secretion systems specific to bacterial toxins [2].

General Secretion/Translocons/ Pathways

Secretion across the cytoplasmic membrane

Protein secretion from the bacterial cytoplasmic compartment into other compartments of the cell, particularly into or across the cytoplasmic membrane, also occurs. The general secretion Sec and twin arginine translocation Tat pathways are used for this purpose. The Sec and Tat pathways are the most highly conserved mechanisms of protein secretion, and have been identified in all domains of life. Most proteins transported by the Sec and Tat pathways remain inside of the cell, either in the periplasm or the inner membrane. However, in Gram-negative bacteria, proteins delivered to the cytoplasmic membrane or periplasm of the cell by these mechanisms can either stay in those compartments, or need another secretion system. In fact both Sec and Tat systems have several common elements, the mechanism by which they transport proteins differ.

The sec secretion pathway

The "Sec-pathway" is the major route of protein translocation across the cytoplasmic membrane. Proteins that use this route are synthesized as precursors (preproteins) with an amino terminal extension, the signal peptide. The signal peptide consists of three domains made of 20 amino acids: a positively charged N-terminus (N-domain), a hydrophobic central region (H-domain) and a C-terminal domain containing the signal peptidase cleavage site. The signal peptide directs the preproteins to the translocation machinery and is needed for initiation of the translocation process. It also slows down the folding of the mature domain of secretory preproteins, and thereby increases the time window for molecular chaperones. Sec B is a molecular chaperone that interacts and stabilizes preproteins in a translocation-competent (non-aggregated, loosely folded) state and targets them to the membrane [3].

This pathway primarily translocates proteins in their unfolded state. This system consists of three parts: a protein targeting component, a motor protein, and a membrane integrated conducting channel, called the SecYEG translocase. Additionally, a number of Gram-positive bacteria produce Sec accessory proteins that serve important roles in the secretion of specific proteins. While proteins secreted by the Sec apparatus can serve many roles, a number of proteins that promote virulence of bacterial pathogens are transported through this pathway. Pathogens that use Sec-dependent secretion to transport virulence factors across the cytoplasmic membrane include the Gram-negative Bacteria *Vibrio cholerae*, *Klebsiella pneumoniae*, and *Yersinia enterocolitica*.

Proteins that will be secreted into the periplasm or outside of the cell by the Sec pathway contain Sec B-specific signal sequences, while proteins meant to remain in the inner membrane contain a signal recognition particle (SRP)-specific signal sequence. The differences between these two pathways are outlined below.

Sec A pathway

The secA gene was discovered in a screen for proteins that cause a conditionally pleotropic defect in preproteins secretion. The gene encodes a 102 kDa protein of 901 amino acid residues and found the cytosol and at the membrane. The affinity of Sec A is very low for phospholipids, but recognizes the Sec YEG complex with high affmity. Sec A binds the binary Sec B preproteins complex and interacts directly with the signal sequence of the preproteins. Therefore, it is an essential component in the targeting of preproteins to the Sec YEG-complex. Sec A has low endogenous ATPase involved in preprotein translocation but the concentration increased by its interaction with the Sec YEG complex and preproteins. This ATPase activity is termed "Sec A Translocation ATPase" as it is coupled to preprotein translocation. It binds to almost all components that are involved in the translocation process, exhibits ATPase activity, and regulates its expression by binding to its own mRNA.

The Sec B pathway

In many Gram-negative bacteria, proteins destined for transport to the periplasm or outside of the cell contain a removable signal sequence recognized by the Sec B protein. This protein serves as a chaperone, binding to pre-secretory proteins and preventing them from folding. SecB then delivers its substrates to Sec A, a multi-functional protein that both guides proteins to the SecYEG channel, with the help of ATPase. Prior to transport through the SecYEG channel, a protease protein cleaves off the Sec B signal sequence followed by folding of the protein upon delivery to the periplasm. Most proteins delivered by the Sec B system remain in the periplasm, thre are some that will be secreted in to extracellular space with the help of the Type II and Type V secretion systems.

Sec-dependent pathway

Proteins secreted via the Sec-dependent pathways utilize common machinery, the Sec translocase, for transport across the IM and are mainly differentiated based on their mechanisms of secretion across the OM. Sec-dependent pathways include the type II secretion or two-step secretion (T2S) and the auto transporter, or type V secretion. The type IV secretion (T4S), or adapted-conjugation, pathway can be Sec dependent but is mostly considered Sec independent.

Sec-independent

Sec-independent pathways tend to allow direct export from the cytoplasm to the extracellular environment in one step and do not involve periplasmic intermediates. This pathway includes the Type I Secretion (T1S), or ABC (ATP-binding cassette), exporters and the Type III Secretion (T3S) systems [1].Type III secretion system (T3SS) is a highly coordinated multiprotein system which consists of

structural, regulatory and secreted proteins. The structure of the type III secretion nanomachine (or injectisome) is highly conserved among Gram-negative bacteria, such as Salmonella, Shigella, pathogenic *E. coli*, Pseudomonas and Yersinia. An alternative Sec-independent pathway known as Twin-arginine translocation (Tat) is employed for transport of already-folded proteins across the IM. Generally, Tat substrates are targeted to the periplasm of the cell but can also be transported across the OM via the type II pathway, such as the phospholipases of *Pseudomonas aeruginosa* (Figure 1).

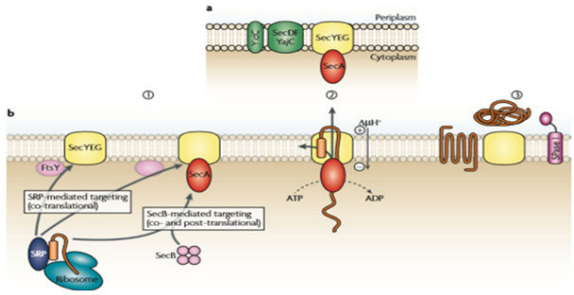

Figure 1. Bacterial protein secretion.

Protein Secretion by Gram Negative Bacteria

The type I secretion system

The type I protein secretion system contains three major components: ATP-binding cassette (ABC) transporters, Outer Membrane Factors (OMF), and Membrane Fusion Proteins (MFP).

ABC transporters: This involves specific ATP-driven protein translocators of the ABC superfamily. They most often consist of two membrane-embedded hydrophobic and two conserved hydrophilic ATP-binding domains. These domains can be either parts of a single polypeptide as for example, the mammalian multidrug resistance transporter (MDR) [37, 38] or the Cystic Fibrosis Chloride Channel (CFTR) or separate polypeptides as in many prokaryotic transport systems. Nevertheless, most of Gram negative ABC protein-mediated transport systems involve accessory proteins. Uptake systems require a soluble periplasmic substrate-binding protein while ATP hydrolysis provides the energy; additional structural components span the whole protein secretion machinery across both inner and outer membranes.

The proteins making up the ABC exporter component of the T1SS can be divided into two major groups: one specific for large proteins from Gram-negative bacteria and another group for exporting small proteins and peptides. The ABC exporters in T1SS contain two cytoplasmic domains for hydrolysis of ATP and two integral transmembrane domains. In general, the phylogeny of ABC transporters reflects their substrate specificity, implying that shuffling rarely occurred among ABC transporters during their history of evolution [4].

Outer membrane factors: Structurally, Outer Membrane Factors provide a transperiplasmic channel penetrating the outer membrane. OMFs have not been evolving in parallel with their primary permeases.

Membrane fusion proteins: The MFP is responsible for connecting the OMF and ABC in the periplasmic space which can be found in Gram-positive bacteria as well as Gram-negative bacteria. The evolution of MFPs is in good agreement with the phylogeny of primary permeases. Some pathogenic strains of *E. coli* that cause urinary tract infections carry plasmids that code for α-hemolysin, a protein toxin that inserts into the membrane of host cells, such as erythrocytes, makes a pore and causes them to lyse. Apart from α-hemolysin, the plasmid codes for the toxin transporter, which is composed of two different parts. One is a translocase proper, HlyB, a member of the 'ATP-Binding Cassette' (ABC) transporter family. The other is a 'membrane fusion' protein, HlyD. A continuous channel forms, apparently by HlyD docking to the outer-membrane protein TolC. The complex spans two membranes and the periplasm (Figure 2).

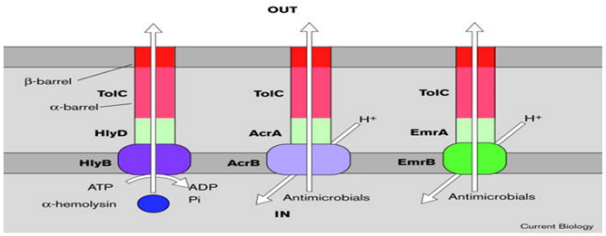

Figure 2. TolC as a universal tunnel: Three different *E. coli* translocases use homologous 'membrane fusion proteins' to dock to TolC.

Genome of T1SS in some bacteria: Similarly, adenylate cyclase toxin (CyaA) of Bordetella pertussis is transported by the T1SS and serves as a primary virulence factor that inhibits innate immune responses and promotes bacterial colonization. The cyaA operon encodes an ABC transporter CyaB, a membrane fusion protein CyaD and a pore-forming protein CyaE. Moreover, the T1SS is also encoded by other pathogenic Gram-negative bacteria such as *Vibrio cholera*, *Pseudomonas aeruginosa* and *Salmonella enterica* for the transport of RTX toxins, proteases and other virulence factors. Legionella pneumophila also expresses a T1SS called Lss system, encoded by the lssXYZABD locus, among which LssB is an ABC transporter and LssD possibly constitutes the outer membrane pore. However, this secretion system appears to be dispensable for bacterial virulence and no substrate has been identified yet.

The type II secretion system

Unlike the T1SS, the Type II Secretion System (T2SS) secretes proteins in two separate steps. First, proteins are translocated across the inner membrane through the general secretion system Sec or Tat and then the proteins are folded in the periplasm and subsequently transported across the outer membrane through the T2SS.The general secretion system Sec functions to translocate many unfolded proteins across the bacterial cytoplasmic membrane. This system is composed of a molecular chaperon Sec B which helps to stabilize unfolded substrates, an ATPase SecA which serves as a motor to drive translocation, a transmembrane channel comprised of the heterotrimeric complex SecYEG, and several accessory proteins. Proteins destined for the Sec secretion system are labeled with an N-terminal signal sequence of about 20~30 amino acids including a positively charged N terminus followed by a stretch of hydrophobic

residues, and redundancy and host specificity commonly exist among the substrates. Since its first discovery in Klebsiella in the late 1980s, the T2SSs has been identified in many pathogenic and environmental strains. These bacteria also utilize T2SS to transport degradation enzymes, such as lipases, phosphatases, cellulases and amylases, to the surrounding milieu for the generation and acquisition of nutrient. Some bacterial toxins are also found secreted by the T2SS, such as the heat-labile enterotoxin from enterotoxigenic E. coli, and the cholera toxin from V. cholerae. The substrate recognition sequence for the T2SS is still unclear, however, it is speculated that the signal is coded in distal regions of the primary sequence which can only be brought together when protein is properly folded.

The type III secretion system

Upon infection, pathogenic bacteria must evade the immune defence of their host in order to multiply that many bacteria secrete toxins as part of their virulence mechanism. In a classical view, toxins are molecules that cause intoxication upon their release by bacteria into the body fluids through the so-called secretion systems. These molecules, currently known as type III effectors, have been shown to act on different host signaling pathways controlling a number of responses and in some cases interfere with cell growth. Type III secretion was discovered and shown to be a distinct export pathway for virulence factors in Gram-negative human, animal and plant pathogens. Various components of the secretory machinery are highly conserved among these bacteria, and many proteins of the Yersinia secretion machinery have homologues in other genera. Type III systems are sec-independent, and are reminiscent of type I secretion in that they transport proteins across both inner and outer membranes in a one-step process. The type III system comprises approximately 20 proteins which assemble at and span the cell envelope, forming a secretion channel which, upon host cell contact, delivers virulence factors directly into the host cell cytoplasm. Type III secretion systems have been discovered in many Gram-negative pathogens, including Yersinia, Pseudomonas, Salmonela, Shigela, Escherichia, Bordetela and chlamydia and in Burkholderia pseudomallei. TTSSs are present not only in bacteria that are pathogenic for animals but also in bacteria pathogenic for plants or even in symbionts for plants and insects [5].

The type IV secretion system

The Type IV Secretion System (T4SS) is evolutionarily related to the bacterial conjugation apparatus. The T4SS spans both membranes and directly transports macromolecules including DNA or protein from the bacterial cytoplasm to other bacteria or the host cell cytosol. Depending on sequence homologies, the T4SS can be further divided into two major classes, IVA such as the VirB/D4 system in Agrobacterium tumefaciens, and IVB, such as the Dot/Icm system in L. pneumophila. The VirB/D4 system is by far the most well characterized T4SS and serves as a prototype for the T4SSs. A. tumefaciens causes tumors in plants by using its T4SS to translocate oncogenic T-DNA and accessory proteins into plant cells. The T4SS of A. tumefaciens is composed of 11 VirB proteins, VirB1-11, and one VirD4 protein. The VirB/D4 translocon is made up of three distinct complexes: core complex, pilus, and coupling protein. The core complex consists of VirB6-10 and constitutes the transfer channel across the inner and outer membranes. The pilus is composed of the major component VirB2 and the minor component VirB5, and it is linked to the core complex protein by interacting with VirB7 which acts to contact the host cell plasma membrane. Coupling protein VirD4 recognizes the substrates by a C-terminal localized signal and delivers them to the transfer channel. Three ATPases, VirB4, VirB11 and the coupling protein VirD4, energize the whole machinery by hydrolyzing ATP.

Type V secretion system (Autotransporter)

Similar to the T2SS, the Type V Secretion System (T5SS) also secrets proteins in a two-step process. Substrates of T5SS possess an N-terminal Sec signal and are translocated across the inner membrane by the Sec system. These substrates either mediate the translocation across the outer membrane by themselves or through a pore formed by their cognate partners. Thus T5SSs can be further divided into two subtypes: the autotransporters and two partner secretion systems. For the autotransporters, the substrate contains an N-terminal Sec signal followed by a passenger domain, and a C-terminal β-barrel domain which is able to form a translocation pore after inserting into the outer membrane, after secreted through the translocation pore from N to C terminus in a hairpin conformation, the passenger domains are cleaved proteolytically at the cell surface. The passenger domain may either remain attached to the outer membrane via non-covalent interaction or be released into the extracellular milieu. Unlike autotransporters, the passenger module and the pore-forming module in the two partner secretion system are expressed as two separate proteins. After both proteins are delivered into the periplasm by the Sec system, the pore-forming protein forms a 16stranded β-barrel in the outer membrane, recognizes the passenger protein by its N-terminal conserved domain and facilitate the translocation of latter across the outer membrane. Similarly, the secreted protein is then either released or still attached to the outer membrane by non-covalent linkage.

The type VI secretion system

Type VI secretion systems (T6SSs) are the most recent bacterial secretion systems to be discovered and, therefore, there is still much to learn about their structure and functions. T6SSs translocate proteins into a variety of recipient cells, including eukaryotic cell targets and, more commonly, other bacteria. T6SSs are very large, with up to 21 proteins encoded within a contiguous gene cluster (100). Thirteen of these proteins appear to be conserved in all T6SSs and are thought to play a structural role in the secretion apparatus. Intriguingly, T6SSs share structural homology to phage tails, and it has been hypothesized that T6SSs may have arisen from inverted phage tails that eject proteins outside of the bacterial cell rather than injecting them inside the cell. It has been proposed that some structural components of the T6SS apparatus may also serve as effector proteins, though other T6SS effector proteins have also been identified. These effectors have many forms and functions, with many directed against the bacterial cell wall and membrane, which supports a role for this secretion apparatus in promoting interspecies bacterial competition. Lending further credence to this hypothesis, many T6SS effectors are encoded alongside a gene that provides immunity to the effector, thereby preventing self-intoxication (Figure 3).

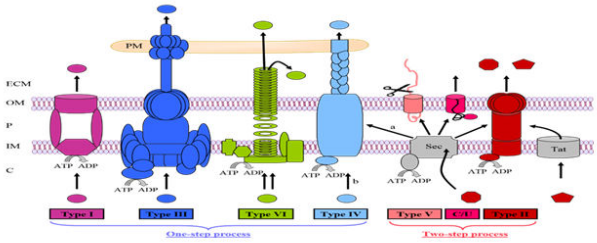

Figure 3. Major protein-secretion systems in Gram-negative bacteria.

Protein Secretion by Gram Positive Bacteria

Gram positive bacteria contain only one lipid bilayer and are surrounded by a very thick cell wall considerably thicker than that of Gram-negative bacteria. Additionally, some species of Gram-positive bacteria, most notably the *Mycobacteria*, contain a cell wall heavily modified by lipids called a mycomembrane. Because of these differences in basic cell structure, it is not surprising that Gram-positive bacteria differ from Gram-negative organisms in their mechanisms of extracellular protein secretion. Like Gram-negative organisms, Gram-positive bacteria employ both the Tat and Sec pathways to transport proteins across the cytoplasmic membrane. However, in many cases, this transport is not sufficient to deliver proteins to their final destinations. Conserved mechanisms of protein secretion in Gram-positive and *Mycobacteria* are used by pathogens to transport important virulence factors out of the cell during mammalian infection.

Sac A2 secretion

Gram-positive organisms, including *L. monocytogenes*, *Bacillus subtilis*, *Clostridium difficile*, *M. tuberculosis*, and *Corynbacteria glutamicum*, actually contain two SecA homologues, called SecA1 and SecA2. In these organisms, SecA1 is essential, and aids in the secretion of proteins via the canonical Sec pathway, as described earlier in this chapter. In contrast, SecA2 is seldom required for growth under standard laboratory conditions, and is used to export a smaller set of proteins. Generally, SecA2 substrates are involved in stress responses and/or cell wall modifications, repair and metabolism. While SecA2 is often not essential for growth under normal laboratory conditions, it is required under specific stress conditions and has also been linked to virulence.

Sortases

Like their Gram-negative counterparts, many Gram-positive pathogens express proteins on their outer surfaces that assist in survival during infection of a mammalian host. Because Gram-positive bacteria lack an outer membrane, these proteins must embed themselves into the Gram-positive cell wall in order to be retained on the outer surface of the bacterium. In order to fulfill this function, Gram-positive bacteria encode a class of enzymes, called sortases, which covalently attach proteins to the cell wall following secretion across the cytoplasmic membrane reviewed.

Exteracellular protein secration by gram positive bacteria

Like the T3SS and T4SS effectors of Gram-negative bacteria, some proteins secreted by Gram-positive pathogens will be delivered to the cytoplasmic compartments of eukaryotic host cells. The mechanisms by which Gram-positive effector proteins reach the cytoplasm of eukaryotic cells are varied, and are in large part exemplified by the self-translocating AB toxin model of delivery. However, recent evidence suggests that some Gram-positive organisms may actually use a protein secretion apparatus to directly deliver certain effector proteins to eukaryotic cells.

Conclusion and Recommendations

Bacterial pathogens utilize a multitude of methods to invade mammalian hosts, damage tissue sites, and thwart the immune system from responding. One essential component of these strategies for many bacterial pathogens is the secretion of proteins across phospholipid membranes. Secreted proteins can play many roles in promoting bacterial virulence, from enhancing attachment to eukaryotic cells, to scavenging resources in an environmental niche, to directly intoxicating target cells and disrupting their functions. As discussed in this review, these proteins may be transferred out of the bacterial cytoplasm through a variety of mechanisms, usually involving the use of dedicated protein secretion systems. For this reason, the studies of protein secretion systems has been an important focus in the field of bacterial pathogenesis, and in recent years have seen significant progress in the characterization of various protein secretion systems in bacterial pathogens. While we keep revealing the fascinating details of the seven secretion systems, there are more novel secretion systems yet to be discovered. Recently, new secretion systems have been described in some Gram-postitive pathogens such as *S. aureus*, *B. anthracis* and *L. monocytogenes*. How ATP is binding and hydrolysis converted to energy required for substrate delivery in T3SSs and T4SSs, how T6SSs activated when the donor bacteria sense the recipients and how a substrate selected for secretion through the T6SS are still questions to be answered. No Sec-dependent signal has been detected on the N-terminal of the substrates suggesting that the T6SS is Sec independent, but the exact nature of the recognition signal remains unknown. Perhaps more attractively, is it possible to develop novel antimicrobial therapeutics based on the antibacterial potential of the T6SS. Therefore, as future prospective further investigation of the secretion systems of bacterial pathogens is recommendable to understand a distinctive mechanism of protein secretion as to tackle the effect of bacteria by developing novel antimicrobial therapeutics or vaccines.

References

1. Thanassi, David G, Stathopoulos Christos, Karkal Aarthi, and Li Huilin. "Protein Secretion in the Absence of ATP: The Autotransporter, Two-Partner Secretion and Chaperone/Usher Pathways of Gram-Negative Bacteria." Mol Membr Biol 22 (2005): 63-72.
2. Natale, Paolo, Bruser Thomas, and Driessen Arnold JM. "Sec-and Tat-Mediated Protein Secretion across the Bacterial Cytoplasmic Membrane-Distinct Translocases and Mechanisms." Biochim Biophys Act 1778 (2008): 1735-1756.

3. Papanikou, Effrosyni, Karamanou Spyridoula, and Economou Anastassios. "Bacterial Protein Secretion through the Translocase Nanomachine." Nat Rev Microbiol 5 (2007): 839-851.
4. Korotkov, Konstantin V, SandkvisMaria t, and Hol Wim GJ. "The Type II Secretion System: Biogenesis, Molecular Architecture and Mechanism." Nat Rev Microbiol 10 (2012): 336-351.
5. Randall, L L, and Hardy S J S. "SecB, One Small Chaperone in the Complex Milieu of the Cell." Cell Mole Life Sci 59 (2002): 1617-1623.

How to cite this article: Habtamu, Yitbarek, Shukab Jaleta, and Tadessef Fanos. "Bacterial Protein Secretion with Particular Emphasis to Toxins." *J Vet Sci Techno*12 (2021) : 104