Al-Anbar University

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Subject teacher

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Bacterial Secretion Systems

Bacterial secretion systems are important in the pathogenesisof infection and are essential for the interaction of bacteriawith the eukaryotic cells of the host. The gram-negative bacteriahave cell walls with cytoplasmic membranes and outermembranes; a thin layer of peptidoglycan is present. Grampositivebacteria have a cytoplasmic membrane and a verythick layer of peptidoglycan. Some gramnegativebacteria and some grampositive bacteria havecapsules as well. The complexity and rigidity of the cell wallstructures necessitate mechanisms for the translocation ofproteins across the membranes. These secretion systems areinvolved in cellular functions such as the transport of proteinsthat make pili or flagella and in the secretion of enzymes ortoxins into the extracellular environment. The differences incell wall structure between gram-negative and gram-positivebacteria result in some differences in the secretion systems.

Both gram-negative and gram-positive bacteria have ageneral secretion pathway (**Sec**) as the major mechanism for protein secretion. This pathway is involved in the insertionof most of the bacterial membrane proteins and provides themajor pathway for proteins crossing the bacterial cytoplasmicmembrane. Gram-negative organisms have an additional sixmechanisms, secretion systems (SS) 1-6 (sometimes denotedI-VI), for protein secretion. These can be further characterizedas Sec dependent (types 2 and 5) and Sec independent(types 1, 3, 4, 6). Type 2 SS use the general Sec to transport theproteins to the periplasm and then create an outer membranechannel made by a special pore-forming protein complex.This type 2 SS is used to secrete portions of bacterial A B typetoxins,

such as cholera toxin. Similarly, the **type 5 SS**, usesthe general Sec to export an autotransporter to the periplasm;from there it transports itself across the outer membrane. Anexample of this type of SS includes the IgA proteases secretedby ***Haemophilusinfluenzae.***

The **sec**-independent pathwaysinclude the **type 1 secretion system** or **ABC secretion system**(ATP binding cassette) and the **type 3 secretion system**. Thetype 1 and type 3 pathways do not interact with proteins thathave been transported across the cytoplasmic membrane bythe Sec system. Instead, these systems translocate proteinsacross both the cytoplasmic and outer membranes. The type3, which is activated upon contact with a eukaryotic host cell,promotes transport of proteins directly from inside the bacteriumto the inside of the host cell using a needlelike structurecalled an injectosome; when in the host cell cytoplasm, thetransported proteins can manipulate host cell function. The**type 4 secretion pathway** consists of a protein complex thatforms a "tunnel" that is able to directly transport proteins orDNA. The most recent SS to be discovered is the **type 6** SS.This SS plays a role in the secretion of virulence proteins in***V.cholerae***and ***Pseudomonas aeruginosa***among other gramnegativepathogens.Some other examples of the secretion systems and their roles in pathogenesis are shown in Table 4.

Table 4: Examples of Molecules Translocated by Bacterial Secretion Systems and Their Relevance to Pathogenesis

Secretion System	Genus Species	Substrate and Role in Pathogenesis
Type 1 (*Sec*-independent)	*Escherichia coli*	α Hemolysin makes holes in cell membranes
	Proteus vulgaris	Hemolysin
	Morganellamorganii	Hemolysin
	Bordetella pertussis	Adenylatecyclase which catalyzes synthesis of cAMP
	Pseudomonas aeruginosa	Alkaline protease
	Serratiamarcescens	Zn protease yields host cell damage

Type 2 (*Sec* dependent)	*Pseudomonas aeruginosa*	Elastase, exotoxin A, phospholipase C, others
	Legionella pneumophila	Acid phosphatase, lipase, phospholipase, protease, RNAse
	Vibrio cholera	Cholera toxin
	Serratiamarcescens	Hemolysin
Type 3 (*Sec*-independent; contact-dependent)	*Yersinia* species	Ysc-Yop system; toxins that block phagocytosis and induce apoptosis
	Pseudomonas aeruginosa	Cytotoxin
	*Shigella*species	Controls host cell signaling, invasion, and death
	*Salmonella enterica*subspecies *enterica*	Effectors from *Salmonella* pathogenicity islands I and II (SPI1 and SPI2), which promote attachment to and invasion of host cells
	Escherichia coli	Enterohemorrhagic (EHEC) and enteropathogenic (EPEC); disruption of epithelial barriers and tight junctions
	Vibrio parahaemolyticus	Direct cytotoxicity
Type 4 (*Sec*-dependent and Sec-independent) Protein substrates	*Bordetella pertussis*	Pertussis toxin
	Helicobacter pylori	Cytotoxin
	Neisseria gonorrhoeae	DNA export system
DNA substrates	*Helicobacter pylori*	DNA uptake and release system
Type 5 (*Sec* dependent)	*Neisseria gonorrhoeae*	IgA1 protease splits IgA1 in hinge region and destroys antibody activity (*sec*-dependent)
	Haemophilusinfluenzae	IgA1 protease, adhesins
	Escherichia coli	Serine protease, adhesins, type 1 pili, P-pili
	Shigellaflexneri	Serine protease
	Serratiamarcescens	Proteases
	*Bordetella*species	Adhesins
	Bordetella pertussis	Filamentous hemagglutinin
	Yersinia pestis	Capsular antigen
Type 6 (*Sec* Independent)	*Pseudomonas aeruginosa*	Pore-forming toxin Hcp1
	Vibrio cholerae	Virulence proteins
Type 7 (*Sec* dependent)	*Mycobacterium tuberculosis*	CFP-10, ESAT-6 T-cell antigen target

CFP, culture filtrate protein 10 kDa

ESAT-6, early secretory antigenic target-6 kDa

(1) The Requirement for Iron

Iron is an essential nutrient for the growth and metabolismof nearly all microorganisms and is an essential cofactor ofnumerous metabolic and enzymatic processes. The availabilityof iron in humans for microbial assimilation is limited becausethe iron is sequestered by the high-affinity iron-binding proteinstransferrin in serum and lactoferrin

on mucosal surfaces.The ability of a microbial pathogen to efficiently obtainiron from the host environment is critical to its ability to causedisease.

Iron availability affects the virulence of many pathogens.For example, iron is an essential virulence factor in ***Pseudomonasaeruginosa***. The use of animal models in ***Listeria monocytogenes***infection has demonstrated that increased iron resultsin enhanced susceptibility to infection, but iron depletionresults in prolonged survival; iron supplementation therapyyields an increase in lethal infections.

Decreased iron availability can also be important inpathogenesis. For example, the gene for diphtheria toxinresides on a lysogenic bacteriophage, and only strains of***Corynebacteriumdiphtheriae***that carry the lysogenic bacteriophage aretoxigenic. In the presence of low iron availability, there isincreased production of diphtheria toxin and potentiallymore severe disease. The virulence of ***Neisseriameningitidis***for miceis increased 1000-fold or more when the bacteria are grownunder iron-limited conditions.

Human iron deficiency also plays a role in the infectiousprocess. Iron deficiency affects hundreds of millions of peopleworldwide. Iron deficiency can affect multiple organ systems,including the immune system, and can result in impairedcell-mediated immunity and decreased polymorphonuclearcell function. Providing iron therapy during an active infectionprobably should be delayed because many pathogenicmicroorganisms can use the small amounts of supplementaliron, resulting in an increase in virulence.

(2) The Role of Bacterial Biofilms

A biofilm is an aggregate of interactive bacteria attached to asolid surface or to each other and encased in an exopolysaccharidematrix. This is distinct from planktonic or free-livingbacteria, in which interactions of the microorganisms do notoccur in the same way. Biofilms form a slimy coat on solidsurfaces and occur throughout nature. A single species ofbacteria may be involved or more than one species may coaggregateto form a biofilm. Fungi, including yeasts, are occasionallyinvolved. After a biofilm is formed, quorum-sensingmolecules produced by the bacteria in the biofilm accumulate,resulting in a modification of the metabolic activity ofthe bacteria.

The bacteria in the exopolysaccharide matrix may beprotected from the host's immune mechanisms. This matrixalso functions as a diffusion barrier for some antimicrobials,but other antimicrobials may bind to it. Some of the bacteriawithin the biofilm show marked resistance to antimicrobialscompared with the same strain of bacteria grown free livingin broth, which helps to explain why it is so difficult to treatinfections associated with biofilms.

Biofilms are important in human infections that arepersistent and difficult to treat.A few examples include***Staphylococcus epidermidis***and ***S.aureus***infections of centralvenous catheters, eye infections such as that occur withcontact lenses and intraocular lenses, in dental plaque, and inprosthetic joint infections. Perhaps the most profound exampleof a biofilm in human infection is in *P.aeruginosa*airwayinfections in cystic fibrosis patients.

References:

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(2) FAIRBROTHER, R.W. (2013). **A Textbook of Bacteriology, FourthEdition.**