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FEMS Microbiology Letters 252 (2005) 1–10

FEMS MICROBIOLOGY Letters

www.fems-microbiology.org

MiniReview

Type III secretion: The bacteria-eukaryotic cell express

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Received 29 March 2005; accepted 17 August 2005

First published online 8 September 2005

Edited by I. Henderson

Abstract

Type III secretion (T3S) is an export pathway used by Gram-negative pathogenic bacteria to inject bacterial proteins into the cytosol of eukaryotic host cells. This pathway is characterized by (i) a secretion nanomachine related to the bacterial flagellum, but usually topped by a stiff needle-like structure; (ii) the assembly in the eukaryotic cell membrane of a translocation pore formed by T3S substrates; (iii) a non-cleavable N-terminal secretion signal; (iv) T3S chaperones, assisting the secretion of some substrates; (v) a control mechanism ensuring protein delivery at the right place and time. Here, we review these different aspects focusing in open questions that promise exciting findings in the near future.

Keywords: Bacterial pathogenesis; EPEC; *Salmonella*; *Shigella*; Type III secretion; *Yersinia*

1. Introduction

Type III secretion (T3S) systems are protein export devices essential for the interaction between Gram-negative bacteria and their eukaryotic hosts. These systems are present in many pathogenic bacteria for animals and plants, but also in endosymbionts. Bacteria use T3S to translocate proteins across lipid membranes and to inject some of them, called "effectors", into the cytoplasm of host cells. Inside the eukaryotic cell cytoplasm, the effectors thwart or hijack host cell signaling to the benefit of the bacteria, in the case of pathogens, or both organisms, in the case of symbionts.

With the sequencing of bacterial genomes, the list of species known to harbour T3S systems has become too long to be listed exhaustively (Table 1). Among the animal pathogens, T3S have been most intensively studied in *Yersinia* spp., *Salmonella* spp., *Shigella* spp., *Pseudomonas aeruginosa*, and enteropathogenic *Escherichia coli* (EPEC) and enterohaemorrhagic *E. coli* (EHEC). The most studied T3S system from a plant pathogen is probably that of *P. syringae*, but this secretion system has also been identified and studied in several other plant pathogens.

The T3S substrates are synthesized in the bacterial cytoplasm and are secreted by a nano-machine, called injectisome, across the bacterial inner membrane, periplasm and the bacterial outer membrane. Some of these secreted proteins, called "translocators" insert in the host cell plasma membrane and mediate the translocation of the effectors across eukaryotic plasma or vacuolar membranes into the host cell cytosol. Secretion of the effectors across the bacterial membranes and translocation through the eukaryotic membrane is thought

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0378-1097/$22.00 © 2005 Published by Elsevier B.V. on behalf of the Federation of European Microbiological Societies.
doi:10.1016/j.femsle.2005.08.036

Table 1
T3S systems of bacterial pathogens for mammals

Bacterium	Diseases	T3S system(s) function(s)[a]
Aeromonas spp.	Opportunistic human pathogen causing gastroenteritis and septicemia (*A. hydrophila*)	Asc
	Furunculosis in salmonids (*A. salmonicida*)	Cytotoxicity on fish cells
Bordetella spp.	Respiratory tract infections, whooping cough (*B.pertussis*, *B. parapertussis*)	Bsc
	Infection of four-legged animals (*B. bronchiseptica*)	Establishment of long term infection Downregulation of inflammation
Burkholderia spp.	Melioidosis: pneumonia and skin abcesses (*B. pseudomallei*)	Bp1 (*B. pseudomallei*) ?
	Glanders (*B. mallei*)	Bp2 (*B. pseudomallei*; *B. mallei*; *B. thailandensis*) ?
	Pulmonar infection of cystic fibrosis patients (*B. cepacia* complex)	Bp3 (*B. pseudomallei*; *B. mallei*; *B. thailandensis*) Survival and escape from macrophage vacuoles; Invasion of non-phagocytic cells Bcsc (*B. cepacia* complex) Important for virulence in the murine model
Chlamydiaceae	Sexual transmitted diseases, trachoma (*C. trachomatis*)	Sct
	Pneumonia, atherosclerosis (*C. pneumoniae*)	Cell internalization
Chromobacterium violaceum	Sporadic infections in humans and mammals resulting in fulminant septicaemia that resembles melidiosis	Civ Similar to Inv (SPI-1) and Mxi-Spa Csa Similar to Ssa (SPI-2)
Citrobacter rodentium	Murine colonic hyperplasia, attaching/effacing lesions 1	Esc Adhesion to the intestinal epithelium Cytoskeleton rearrangements
Desulfovibrio vulgaris	Implicated in ulcerative colitis	Dsc ?
Edwardsiella tarda *Edwradsiella ictaluri*	Hemorrhagic septicemia in fishes, diverse infections in humans	Eds Survival and replication in fish phagocytes
Enteropathogenic *Escherichia coli* (EPEC) and enterohemorrhagic *E. coli* (EHEC)	Diarrhoea, attachment/effacement lesion (EPEC)	Esc
	Diarrhoea, attachment/effacement lesion, haemorrhagic colitis (EHEC)	Colonization Cell attachment Actin remodelling Pedestal formation
Pseudomonas aeruginosa	Pneumonias and chronic bronchopneumonia in patients with cystic fibrosis; ulcerative keratitis	Psc Cytotoxicity Block phagocytosis