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Hamada, Daizo

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"OVERVIEW"

Cytoskeleton-modulating Effectors of Enteropathogenic and Enterohaemorrhagic *Escherichia coli*

Daizo Hamada

Laboratory of Structural Transformation, Division of Structural Biology (G-COE), Graduate School of Medicine, Kobe University, 7-5-1 Kusunoki-cho, Chuo-ku, Kobe 650-0017, JAPAN.

Tel. +81-78-382-5817, Fax. +81-78-382-5816, E.mail. daizo@med.kobe-u.ac.jp

Cellular morphology is essential in the maintenance of the shape and stability of cells and tissues. It is also extremely important in preventing infectious viruses or bacteria from penetrating into organs by forming tight networks of intracellular cytoskeletal proteins and cell-cell junctions. Many pathogenic bacteria attack the cytoskeletal proteins of target host cells in order to modulate host cell morphology as a means of facilitating the further penetration of these bacteria into various organs and preventing their clearance by normal immune systems in the host organism. Owing to the complexity of the various systems that regulate the host cell cytoskeleton, numerous types of virulence factors have been evolved by these bacteria in order to interfere with the host cell morphology. It is critical to analyse the roles of these virulence factors in order to understand the mechanisms of defense against bacterial pathogens.

Pathogenic Gram-negative bacteria, including enteropathogenic and enterohaemorrhagic *Escherichia coli* (EPEC and EHEC, respectively), possess type III secretion systems (T3SS) or “injectisomes” that efficiently deliver the virulence factors – often called “*effectors*” or “*effector proteins*” - directly from the

bacterial cell into a host cell. These effectors usually interact with host cell proteins that are involved in modulation of the cytoskeleton and they control or "*hijack*" the system in order to facilitate various subsequent events in bacterial infection. Some of the effectors from EPEC or EHEC, including Tir, intimin, $EspF_U$, EspB and EspL2, affect the morphologies of actin networks in infected host cells and change the shapes of the cells. Recent advancements have clarified the complex mechanisms that uderlie infection by these pathogens.

This minireview series summarizes some of the studies focused on particular effector(s) from EHEC and EPEC that affect the actin cytoskeletal networks in host cells. It provides an overview of the morphological alterations engendered by by Tir, EspFU and intimin, which are probably the major effectors or virulence factors for EHEC and EPEC. In the first article, Campellone introduces an established concept of actin reorganisation and pedestal formation regulated by Tir and $EspF_U$. In the second, Tobe introduces another pathway of actin reorganisation caused by EspL2, which is a novel class of actin-modulating effectors. The third summarizes recent achievements in

understanding the change in actin morphology caused by EspB and various T3SS effectors, which are classified as natively unfolded proteins.

These reviews provide an insight into the complex mechanisms of cytoskeletal morphology changes induced by EPEC and EHEC, and throw light on the underlying problems regarding EPEC and EHEC infections.

Biography

Daizo Hamada is an Assistant Professor at the Graduate School of Medicine, Kobe University. Previously, he was a staff scientist at Osaka Medical Center for Maternal and Child Health (2003-2007) and a research fellow in the laboratories of Y. Goto at Osaka University (2000-2003) and of C. M. Dobson at the University of Oxford (1997-2000). As a student, he read Biochemistry at Osaka University and carried out his PhD work on mechanisms of protein folding. He has received fellowships (DC1 and PD) for young

scientists and, to work abroad, from the Japan Society for Promotion of Science. His research group studies the mechanisms of protein misfolding diseases and bacterial infection.