

Preface

Three types of cytoplasmic filaments form the cellular cytoskeleton. These filaments often extend from the cell nucleus to the plasma membrane. They stabilise cell shape and provide tensile strength. Different classes of proteins form the different types of filaments: A large number of tissue specific proteins (the intermediate filament proteins) form the intermediate filaments, proteins of the tubulin family build the microtubules, and the actins the microfilaments, which organize the actin cytoskeleton. The cytoskeletal filaments differ in structure and functions. The intermediate filaments have mainly shape stabilising functions. In addition to cell shape stabilising functions the microtubules provide the routes for the intracellular transport of vesicles and form the spindle apparatus during cell division, the actin cytoskeleton participates in a number of motile processes like cell locomotion and more specialized processes as endo- and exocytosis, vesicular transport, and cytokinesis. The supramolecular structure of the cytoskeleton is subjected to constant reorganization according to the cellular activities. In the past the different filament types have been regarded as separate functional entities, recent data, however, strongly indicate structural and functional linkages (as also demonstrated by the contribution by Schwan and Aktories).

Actin is the most abundant protein in many eukaryotic cells. In mammals six tissue-specific isoforms assemble to the actin containing microfilaments, which are often organized into bundles or higher ordered networks. The highly dynamic behaviour of the actin cytoskeleton is regulated by a large number of actin binding proteins (ABP). The ABPs can be grouped into different functional classes, which regulate the assembly or disassembly of actin filaments and are often targets of signalling pathways.

Bacteria have evolved a large arsenal of toxins and effectors, some of which are injected into host cells by type-3 secretion mechanisms to avoid phagocytosis by professional macrophages (see contribution by Aepfelbacher & Wolters). Alternatively, bacterial toxins or virulence factors induce special plasma membrane extensions of non-professional phagocytotic cells, which embrace bacteria leading to their uptake into host cells with the aim to secure their survival by gaining access to nutrients for proliferation, to achieve transport within the cytoplasm or from cell

to cell and finally their release into the environment for further dissemination (see contribution by Stradal & Costa). The actin cytoskeleton is essential for all these processes. Therefore it is not surprising that actin is a preferred target of many bacterial toxins and effector proteins also due to its highly conserved primary and tertiary structure and its intracellular abundance.

With the 11 contributions this volume tries to introduce this fast progressing field of research without pretending completeness. Bacteria have evolved a vast number of tricks to secure their survival and proliferation. Therefore only a few bacteria and their toxins and effectors will be introduced with the intention to indicate common modes of action. The structure, properties and dynamic behaviour of actin cytoskeleton itself and the different classes of actin-binding proteins (ABP) will be introduced with constant reference to bacterial toxins and effectors, which interfere their functions by modifying their normal behaviour (Kühn & Mannherz).

Bacterial toxins or effectors affect either the actin cytoskeleton by modifying actin directly or subverting certain ABPs or signalling pathways leading to the actin cytoskeleton by modifying small GTP-binding proteins terminating at regulatory ABPs (see contributions by Aepfelbacher & Wolters, Lemichez, and Stradal & Costa). Often a bacterium has developed toxins aiming on both mechanisms to influence the actin cytoskeleton like for instance *Photorhabdus luminescens* (contribution by Lang et al.), *Clostridia* (Schwan & Aktories), *Yersinia* (contribution by Aepfelbacher & Wolters).

A number of bacterial toxins modify actin directly by ADP-ribosylation or cross-linking. These modifications subvert the normal functioning of the actin cytoskeleton and thereby secure bacterial survival by inhibiting phagocytosis. This area will be covered by four contributions, which extend from their cellular effects to structural studies illuminating their selectivity. How phagocytosis is normally able to eliminate bacterial invasion is detailed for the uptake of *Borrelia* by macrophages in one contribution (Naj & Linder).

ADP-ribosyltransferases also modify small GTP-binding proteins of the Rho-family resulting in dramatic effects in their signalling capacity to the actin cytoskeleton (one special contribution and part of a number of other contributions). Alternatively, extracellular gastrointestinal pathogens manipulate the signalling pathways leading to the actin cytoskeleton by secreting virulence factors that modify the GTPase cycle of host Rho-GTPases thus securing their survival (This topic will be covered with two contributions (by Lemichez and Stradal & Costa).

Some intracellular bacteria hijack the actin cytoskeleton to their own needs by presenting on one pole bacterial proteins that lead to the assembly of a comet-like F-actin tail able by rapid actin subunit treadmilling to propel the pathogen within the cytoplasm of the host cell and for further dissemination from cell to cell (see contribution by Pillich et al.).

In many instances the analysis of the action of bacterial toxins and virulence factors provided important clues to the function of endogenous ABPs or even helped to identify ABPs, which were binding partners of certain bacterial effector proteins like the Arp2/3 complex as partner of ActA of *Listeria*. Future studies on

bacterial toxins will certainly uncover new insights into their functions and also unravel new aspects of the inherent regulatory mechanism of the actin cytoskeleton, which might also lead to the development of new antibiotic drugs. As a further outlook in this perspective this volume includes a description of the bacterial actins, which are different in primary but similar ternary structure to their eukaryotic counterparts, and their interactors (contribution by Gayathri).

Bochum, Germany

Hans Georg Mannherz



<http://www.springer.com/978-3-319-50046-1>

The Actin Cytoskeleton and Bacterial Infection

Mannherz, H.G. (Ed.)

2017, X, 242 p., Hardcover

ISBN: 978-3-319-50046-1