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Editorial

# The priority program *Signal Pathways to the Cytoskeleton and Bacterial Pathogenesis* (SPP1150)

In 2003 the priority program *Signal Pathways to the Cytoskeleton and Bacterial Pathogenesis* of the Deutsche Forschungsgemeinschaft DFG started with the evaluation of projects by an international board, resulting in the funding of 17 groups from various universities and research centers all over Germany. These groups worked together (with minor changes) over 6 years to address the question of the role of the cytoskeleton in host–pathogen interactions. Most important for the program was the attempt to bring together highly recognized research groups from different scientific fields, covering cell biology, microbiology, pharmacology and toxinology as well as structural biology. One major focus of the program was the field of Cellular Microbiology, which was not a *blank* but an *underdeveloped spot* on the scientific landscape of Germany at the turn of the century.

Major topics of the program were studies on the interactions of pathogens with target cells to manipulate the host cytoskeleton and to hijack its regulators. To this end, bacterial, viral and parasite pathogenetic mechanisms were investigated. One project investigated signal cascades altered by CagA protein, which causes host actin cytoskeleton rearrangement during infection with *Helicobacter pylori* (N. Tegtmeyer and S. Backert). Another project focused on integrin-mediated uptake of bacteria and actin cytoskeletal rearrangements modulated by fibronectin binding of *Staphylococcus aureus* (C. Hoffmann et al.). The dynamic modification of microtubules by effector proteins of intracellular *Salmonella enterica* was studied in a further project (R. Rajashekar and M. Hensel). Also *Legionella* pathogenesis was a topic of the program (C. Lang and A. Flieger). Endogenous regulation of the actin cytoskeleton was a key aspect of the program, including the role of Rho GTPases (even in plants! E. Mucha et al.) and the functions of actin nucleators or elongators like Arp2/3, cordon-bleu, Spir and formins (M.M. Kessels et al., and E. Kerckhoff). Other major topics of the program were toxins acting on the actin cytoskeleton or on its master regulators, the GTP-binding proteins of the Rho family. The family of actin-ADP-ribosylating toxins was studied by comparing the biological activity of binary toxins like *Clostridium botulinum* C2 toxin with *Salmonella enterica* SpvB, which targets host actin at the same site but by different cellular up-take mechanisms (H. Barth and K. Aktories). Many *Yersinia* outer membrane proteins (Yops) affect functions of the cytoskeleton. In the priority program, the role of the actin-activated YopO protein, the RhoGAP YopE and the protease YopT were studied. YopE from *Yersinia enterocolitica* is a bacterial effector, which reaches the host cytosol by type-III secretion and mimics eukaryotic GTPase-activating proteins of the Rho family (M. Aepfelbacher et al.). YopT, which causes proteolytic cleavage just in front of the C-terminal isoprenylated cysteine of Rho GTPases, is an extremely strong inhibitor of Rho actions and causes major redistribution of the cytoskeleton. The structural requirements and functional consequences of its action on Rho GTPases were investigated (G. Schmidt). Rho proteins are also the eukaryotic targets of the family of clostridial glucosylating cytotoxins, including *Clostridium difficile* toxins A (TcdA) and B (TcdB) and *C. sordellii* lethal toxin (H. Genth and I. Just), which inactivate Rho/Ras proteins by glucosylation. These toxins are major virulence factors to cause antibiotic-associated diarrhea and pseudomembranous colitis (*C. difficile* toxins) or gas gangrene and toxic shock syndrome (lethal toxin), respectively. Elucidation of the role of specific Rho/Ras proteins in the action of the toxins was a major aim in the program. Not only bacteria but also viral effector proteins target the cytoskeleton. This was addressed in studies on HIV Nef protein-induced remodeling of the actin cytoskeleton (C. Haller et al.). While many bacterial pathogens hijack host cell actin or its regulators, apicomplexan parasites like *Plasmodium*, the causative agent of malaria, use its own actin cytoskeleton for motility. Recent studies shed light on the regulation of apicomplexan actin as compared to the mammalian actin cytoskeleton (J.M. Sattler et al.). Finally, the power of structural work to understand host–pathogen interaction was excellently documented by studies about host cell membrane receptors (H.H. Niemann).

The collaborations between the research groups and seven international meetings within the program definitely strengthened the field of Cellular Microbiology in Germany. The immense progress of the program would not have been possible without the enthusiastic international reviewer board, which scientifically accompanied the program for more than 6 years and by the permanent support of the DFG. However, of most importance for the initiation, planning and successful realization of the program was the work of Jürgen Wehland, who loved the idea of this priority program and continuously supported the research of the projects. Unfortunately, this brilliant scientist passed away in August 2010 at the early age of 58. This Special Issue of the European Journal of Cell Biology is dedicated to him.

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