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Role of Type III secretion system and the CNF_Y toxin for the virulence of enteric Yersiniae

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Enteropathogenic bacteria including EPEC/EHEC, *Salmonella* and *Yersinia* species produce a Type III secretion system (T3SS) to inject a set of effector proteins to manipulate host cells. *Y. pseudotuberculosis* uses this T3SS to apply Yop proteins into professional phagocytes, in particular neutrophils, to prevent phagocytosis and eli¬mination by these immune cells. Several isolates of these enteric pathogens also produce certain toxins, such as the cytotoxic necrotizing factor (CNFY), but the functional consequences of this toxin for host-pathogen interactions during the infection are unknown. We found that CNFY has a strong influence on virulence: a cnfY knockout variant of a naturally toxin-expressing *Y. pseudotuberculosis* isolate is strongly impaired in its ability to disseminate into the mesenteric lymph nodes, liver and spleen, and has fully lost its lethality. The CNFY toxin contributes significantly to the induction of acute inflammatory responses and to the formation of necrotic areas in infected tissues. The analysis of the host immune response demonstrated that presence of CNFY leads to a strong reduction of professional phagocytes and natural killer cells in particular in the spleen, whereas loss of the toxin allows efficient tissue infiltration of these immune cells and rapid killing of the pathogen. Addition of purified CNFY triggers formation of actin-rich membrane ruffles and filopodia, which correlates with the activation of the Rho GTPases RhoA, Rac1 and Cdc42. The analysis of type III effector delivery into epithelial and immune cells *in vitro* and during the course of the infection further demonstrated that CNFY enhances the Yop translocation process and supports suppression of the antibacterial host response. In summary, we highlight the importance of CNFY for pathogenicity by showing that this toxin modulates inflammatory responses, protects the bacteria from attacks of innate immune effectors and enhances the severity of a *Yersinia* infection but reduces the establishment of a persistent infection.

Biography

Petra Dersch graduated in Microbiology at the University of Konstanz and at the Max-Planck-Institute for Terrestrial Microbiology Marburg. She worked as a Postdoc at the Tufts Medical School, Boston/USA, started her own group at the Freie Universität Berlin, and was Junior Research Group Leader at the Robert Koch Institute Berlin. In 2005, she was appointed at the Technische Universität Braunschweig as Associate Professor in Microbiology, and since 2008, she is Head of the Department of Molecular Infection Biology at the Helmholtz Centre for Infection Research in Braunschweig. She is member of various boards, and a current member of the study section, "Microbiology, Virology and Immunology" of the DFG. Since 2016, she is one of the Vice Presidents of the German Society for Hygiene and Microbiology. Her main research field is Molecular Pathogenesis of Enteric Pathogens. She published more than 90 original papers in peer-reviewed international journals, reviews and book chapters.

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