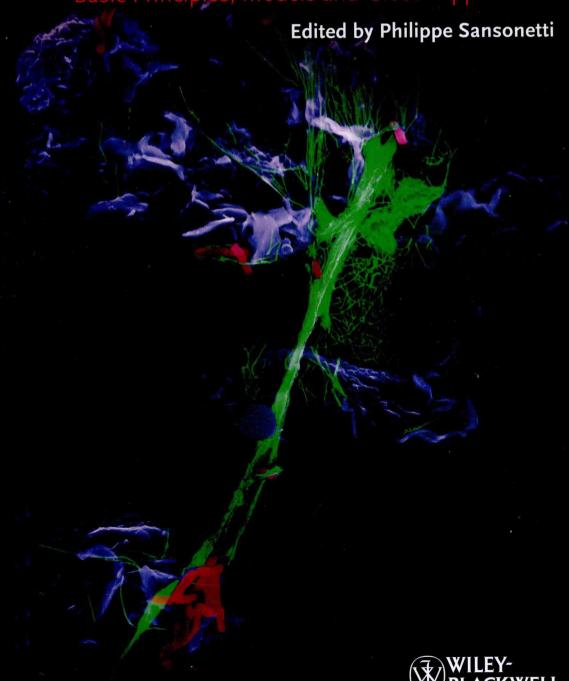


Bacterial Virulence

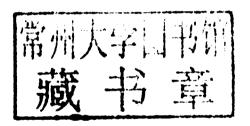
Basic Principles, Models and Global Approaches



Edited by Philippe Sansonetti

Bacterial Virulence

Basic Principles, Models and Global Approaches





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The Editor

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Neutrophil Granulocytes

Cover

(blue) are the first line of defense against invading microorganisms. They fight bacteria (*Shigella flexneri*, red) by phagocytosis or by formation of the recently discovered Neutrophil Extracellular Traps (NETs, green) that capture and kill pathogens like bacteria, fungi and parasites. With kind permission from Volker

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Preface

Microbial virulence is a fast-moving field. From molecular genetics to cell biology and signaling, from genomics to dynamic imaging of infectious processes both in vitro and in vivo, from immunology to inflammation and cancer, few concepts and techniques in life sciences have not been applied, over the last years, to better decipher the detailed mechanisms of infections. A single volume could not account for these amazing progresses that encompass both sub-cellular dissection of the signals elicited by the engagement of cell targets by microbial effectors, and supracellular integration of these microbe-cell cross-talks in a global scheme of tissue or organ infection. This transition from cellular microbiology to tissue microbiology is possibly one of the most striking recent trends in our discipline. It has been made possible by the combination of improved animal models of infection, including transgenic and KO mice and real time imaging methods such as two-photon microscopy. Tissue microbiology, as it currently evolves, is also creating a very fertile ground for collaborations between microbiologist and immunologists. Interactions started with the deciphering of innate mechanisms of host defenses in the presence of pathogens, particularly how the host can discriminate among commensal microorganisms and true pathogens in order to initiate an inflammatory response that is adapted to the level of the threat. Interactions continue with the molecular and cellular analysis of interference mechanisms between pathogens and adaptive immune responses. A scheme emerges according to which, at key anatomic barriers of the host body, sensing mechanisms discriminate pathogens from commensals, elicit an inflammatory response, both humoral and cellular, that is aimed at eradicating the aggressive pathogen, possibly at the cost of significant tissue damage and fatal rupture of this barrier. The pathogen itself modulates this response, thereby achieving better colonization and invasion of this barrier, thus of the host. This Yin and Yang strategy of pathogenic microbes reflects a long co-evolution between the eukaryotic and prokaryotic kingdoms. It can be read in the microbial genomes through recognition of pathogenicity genes and islands reflecting the "construction" of these pathogens under the host selective pressure. Evolution of pathogens from their commensal ancestors is another illustration of Darwin's theory.

This volume gathers among the best experts in the field of bacterial pathogenesis to illustrate the above statements. Following introductory chapters on the genetic

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identity of pathogens and new developments in the understanding of the antimicrobial strategies of a first-line defense cell, the neutrophil, the book goes on describing paradigms of rupture, colonization - invasion and inflammatory injury of major barriers of the body. These paradigms illustrate the integration of cellular microbiology, tissue microbiology, and immunopathology in acute and chronic modes of infection, the latter possibly leading to cancer as is the case of gastric infection by *Helicobacter pylori*. Hopefully, this angle provides a very dynamic view of infectious processes as they develop. The last part should be seen as an opening on two novel developments that will be increasingly be part of the study of infections, i.e. the understanding of the mechanisms of tolerance of our commensal microbiota and how the rupture of tolerogenic signals may participate to diseases, and the molecular bases of species specificity of pathogens, the subversion of which is central to the concept of emergence of new infectious diseases.

Paris, December 2009

Philippe Sansonetti

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