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Edited by
Gottfried Unden, Eckhard Thines, and Anja Schüffler

Host – Pathogen Interaction

Microbial Metabolism, Pathogenicity and Antiinfectives

Volume 6

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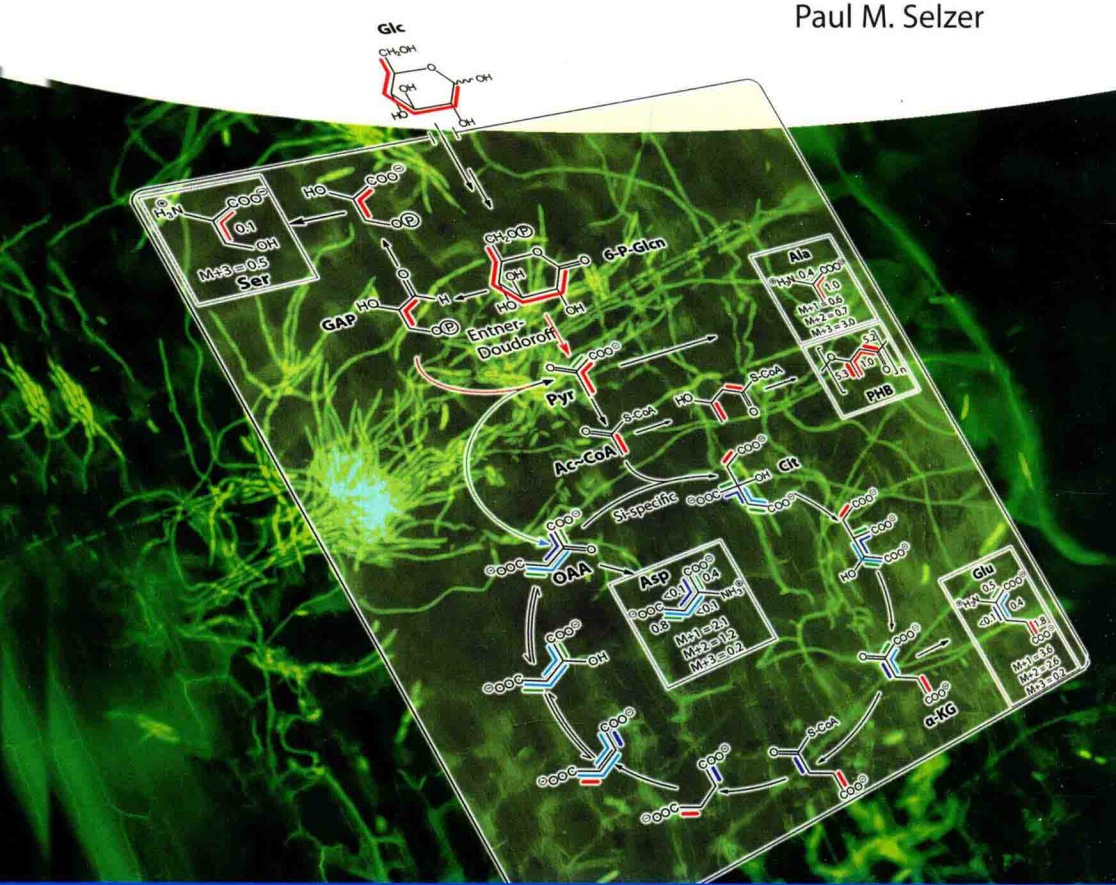

Drug Discovery in Infectious Diseases

Edited by Gottfried Unden, Eckhard Thines, and Anja Schüffler

Host – Pathogen Interaction

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Host – Pathogen Interaction

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Preface

Recent developments in microscopy, genomics, molecular biology, and metabolomic analysis allow a detailed analysis of the intracellular lifestyle of endosymbiotic bacteria. The studies showed changes in the cellular organization of the host cells and the bacteria, as well as new structures and cellular functions of the colonizing bacteria. Pathogenic bacteria not only require specific mechanisms for entering the host cell. Rather development of the intracellular and pathogenic lifestyle requires redirecting and adapting of central metabolic routes for successful survival under the changed metabolic conditions and for overcoming defense reactions of the host. Many central metabolic routes have to be redirected and adapted such as to allow their function under conditions of slow growth, limitation in the supply of oxygen, carbon sources, and metal ions, changes of pH and other adverse conditions. Interestingly, various metabolic traits that were known for a long time become obvious in their significance when considered in the context of bacteria/host metabolic interaction. Therefore, studies on the metabolism of bacteria growing in their host gained significant interest. Central metabolism and its adaptation mechanisms turned out to represent important virulence factors for the survival of the bacteria within their host. Understanding the specific metabolic pathways of the bacteria under conditions of host colonization opened new and unexpected views on bacterial physiology. Part A of the book presents some recent examples of this vast area of bacterial physiology. Part B shed lights on fungi–host interactions in human- and plant-pathogenic systems as well as on signaling processes of fungi involved in environmental changes.

The rapidly increasing number and severity of human and plant diseases caused by pathogenic fungi has recently led to many investigations concerning the pathogenic development and physiology of these organisms as well as interactions with their hosts. Most of our knowledge on pathogenic fungi originates from pathogens in terms of pathogenic development, infection, and spread within the host, the treatment of fungal infections, or the reduction of pathogenic effects. In recent years, the elucidation of host–fungus interaction was largely intensified. Fungi need to control their interaction with their hosts in various ways in penetration processes, survival inside hosts, and acquisition of nutrients. In addition, they have to cope with antifungal metabolites, the plant defense or the host immune system. The host may be confronted with toxic fungal metabolites demanding a response to the infection

itself. In addition, this mutual interaction is affected by several parameters such as environmental changes or abiotic stress. In order to adapt to quickly changing environmental conditions, fungal pathogens have to respond to external signals. Understanding the signaling network and the chemical communication within this interaction could lead to new insights and define new targets to control pathogens. New methodologies contribute to understand essential processes during the life cycle of the pathogens and the initiation of host–pathogen interactions. The "omics" approach consisting of genome data, transcriptome analysis, proteomics, and metabolomics leads to many new possibilities to track pathological processes and elucidate their regulation and signaling.

The editors thank the contributing authors for their excellent work and the series editor Paul M. Selzer for his constructive advice and support.

Mainz and Kaiserslautern
February 2016

Gottfried Unden
Eckhard Thines
Anja Schüffler

Cover Legend

GFP-picture in the background:

Fluorescent microscopic image of a GFP-expressing mutant of the grapevine trunk disease associated fungus *Phaeomoniella chlamydospora* growing in *Vitis vinifera* root tissue.

Picture: courtesy of the IBWF, Kaiserslautern, Germany.

Metabolic scheme part:

Host-adapted metabolism of *Legionella pneumophila* can be determined by ^{13}C-labeling experiments. On the basis of the unique isotopologue patterns, pathways, and fluxes in the formation of metabolic products and their intermediates are reflected. Thereby, information on the core metabolism of the intracellular pathogen and its adaptation to host organisms is gleaned.

Picture: courtesy of Dr Eisenreich, see chapter 2 for details.

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1
Metabolic Adaptation of Human Pathogenic *Yersiniae*

*Ann Kathrin Heroven and Petra Dersch**

Abstract

Colonization, subsequent penetration of epithelial layers as well as persistence and proliferation in subepithelial tissues of the host by bacterial pathogens demand the expression of special sets of virulence factors. In addition, the bacteria need to adapt their metabolism to survive and replicate within the specific host niches. Activated metabolic functions and physiological adaptation processes during their life cycle and the different stages of the infection reflect the complex and dynamic nutritional resources of their environments, interbacterial competition for energy sources and onslaught of bactericidal host responses. The enteric pathogenic *Yersinia* species *Y. pseudotuberculosis* and *Y. enterocolitica* and the causative agent of plague, *Y. pestis*, have adapted to grow in many different environmental reservoirs (e.g., soil, plants, insects) and in warm-blooded animals (e.g., rodents, pigs, humans) with a preference for lymphatic tissues. In the present book chapter, we discuss metabolic adaptations of human pathogenic *yersiniae* to successfully exploit available nutrients and metabolic functions during infection and illustrate the tight link between carbon metabolism and *Yersinia* virulence. Furthermore, current knowledge about the complex regulatory networks used to coordinate and fine-tune the control of metabolic and virulence functions are presented. Deciphering the mechanisms of the function and control of bacterial metabolism within host tissues will not only increase our understanding of host–pathogen interactions, it will also facilitate the identification of potential novel drug targets for future prevention and therapeutic strategies.

Introduction

Infections of human pathogenic *yersiniae* involves a large number of specific pathogenicity factors that mediate efficient resistance against the host defense systems and enable the bacteria to colonize, invade, and multiply successfully within host tissues. The structure, function, and expression of many of these classical

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