# Bacterial Protein Toxins

Bacterial toxins that act inside cells interact very specifically with key components of the cell, and some even manipulate the cell in subtle ways for their own purposes. These potent toxins, described in this book, will be of interest to both microbiologists and cell biologists. Some of these toxins are conventional multidomain toxins that are self-programmed to enter cells. Others are delivered by type III mechanisms, often as a package of potent molecules. The molecular targets for all these toxins mediate signal transduction and the cell cycle to regulate the crucial processes of cell growth, cell division, and differentiation. Thus, these potent toxins are not only responsible for disease but also provide a powerful set of tools with which to interrogate the biology of the cell. In addition, such toxins may act directly to promote carcinogenesis and, hence, their study is also of interest in a wider context.

ALISTAIR J LAX is Professor of Cellular Microbiology at King's College London, where he is Head of the Department of Microbiology within the Dental Institute. His research focuses on the novel mitogenic toxin of *Pasteurella multocida*, which activates several signalling pathways in the cell. He coauthored *Cellular Microbiology*, the first textbook on the subject, in 1999.

Over the past decade, the rapid development of an array of techniques in the fields of cellular and molecular biology has transformed whole areas of research across the biological sciences. Microbiology has perhaps been influenced most of all. Our understanding of microbial diversity and evolutionary biology, and of how pathogenic bacteria and viruses interact with their animal and plant hosts at the molecular level, for example, has been revolutionized. Perhaps the most exciting recent advance in microbiology has been the development of the interface discipline of cellular microbiology, a fusion of classic microbiology, microbial molecular biology, and eukaryotic cellular and molecular biology. Cellular microbiology is revealing how pathogenic bacteria interact with host cells in what is turning out to be a complex evolutionary battle of competing gene products. Molecular and cellular biology are no longer discrete subject areas but vital tools and an integrated part of current microbiological research. As part of this revolution in molecular biology, the genomes of a growing number of pathogenic and model bacteria have been fully sequenced, with immense implications for our future understanding of microorganisms at the molecular level.

*Advances in Molecular and Cellular Microbiology* is a series edited by researchers active in these exciting and rapidly expanding fields. Each volume will focus on a particular aspect of cellular or molecular microbiology, and will provide an overview of the area, as well as examining current research. This series will enable graduate students and researchers to keep up with the rapidly diversifying literature in current microbiological research.

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## Role in the Interference with Cell Growth Regulation

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# Preface



Many bacteria and higher eukaryotes live in harmony in a symbiotic relationship that benefits one or both of the partners. Indeed, we are colonised by bacterial cells which outnumber our own cells ten to one. This amicable bacterial lifestyle contrasts with a pathogenic one, in which the bacterium causes damage to its host. This is a potentially dangerous strategy for a bacterium, because the provoked host is capable of fighting back. A pathogenic lifestyle offers short-term gain. By outcompeting other bacteria within its host, the bacterium can achieve local dominance and, by more widespread colonisation, expand its territory more globally. However, evolution has to balance these advantages against the possibility that the bacterium is eliminated. The latter could occur if the bacterium is too weak to prevent its destruction by the strong host defences it has incited or if its potent virulence wipes out the host and, thus, its source of food.

As pathogenicity appears to be such a risky business, it may be an abnormal condition. Evidence to support this view comes from several lines. First, many of the genes involved in virulence appear to be relatively new – that is, new to the organism made pathogenic by their presence. These genes are frequently found on mobile genetic elements such as plasmids, phage, and pathogenicity islands that have recently been acquired by the organism. Secondly, it is thought that many severe diseases begin with ferocious virulence which later abates – mainly as a result of reduced pathogenicity – thereby suggesting that pathogenicity is not such a good strategy after all.

Several types of genes lead to pathogenicity. Bacterial adhesion, the topic of the first book in this series, is the first step a pathogen has to take. However, by itself adhesion does not promote disease: commensal bacteria adhere without causing tissue damage. The main route to bacterial disease is driven by bacterial toxins that specifically attack host cell function. Those toxins

that act inside cells fall into two groups: the classical multidomain toxins and toxins that bacteria inject directly into cells. The latter are also called effector proteins. In each case, these toxins modify important cell functions. Because signalling mechanisms and the regulation of the cell cycle are key to a cell's continued existence, it is not surprising that these components have been targeted by toxins. Equally, it is not surprising that perturbation of these cellular systems frequently leads to aberrant regulation of cell growth.

This book describes toxins that interfere with the regulation of cell growth. Our perspective concerns not just the toxin, but also the cell and the whole organism. Several of the chapters describe the molecular interactions of toxins with their host target, whereas for other toxins these mechanisms are not yet clear. We have also included bacteria for which the precise effects on cell growth have not yet been ascribed to toxin action, on the premise that toxins are likely to be responsible. The relationship between the bacterial perturbation of cell growth and cancer is examined specifically for *Helicobacter pylori*, where various molecular mechanisms have been suggested and, generally, where the evidence is still at the epidemiological stage.

We hope that the reader will gain an understanding of these potent molecules and appreciate how their study not only illuminates infectious disease but also opens doors into exciting aspects of cell biology.