MICROBIAL SIGNALLING AND COMMUNICATION

Microbial chemical signals have been found to mediate the regulation of diverse metabolic reactions and processes such as antibiotic production, pathogenesis, sexual conjugation, sporulation and differentiation. Their study has the potential to secure advances in our ability to control microbial processes to our benefit. This volume presents information at the forefront of knowledge in this exciting field and includes contributions on a range of organisms (both prokaryote and eukaryote, unicellular and multicellular) and signalling molecules. As such, it will provide an invaluable resource for professional microbiologists and an excellent reference text for advanced students.

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MICROBIAL SIGNALLING AND COMMUNICATION

EDITED BY

R. R. ENGLAND, G. HOBBS, N. J. BAINTON AND D. McL. ROBERTS

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The Society would like to dedicate this volume to
the memory of Professor Gordon S. A. B. Stewart
who died on 27th February 1999, aged 47.

He worked in many areas of microbiology, including rapid methods and the use of bioluminescent reporter genes. Gordon was instrumental in the discovery that bacteria communicate by small signalling molecules, and his group and their many collaborators have made significant contributions to the field of bacterial quorum sening using *N*-acyl homoserine lactones. The main focus of his later work was directed at breaking bacterial communication by blocking the small molecule language to attenuate bacterial pathogenicity, thereby providing a new concept for anti-infectives.

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EDITORS' PREFACE

Inspection of the primary research journals reveals a healthy and increasing interest in microbial signalling and communication. It is therefore timely to bring together, in this volume, current understanding on this topic, in a range of microbial systems.

By way of introduction to the subject, it is appropriate to start with literal definitions. The word signal is defined as 'to send, notify, announce, communicate by means of signals', whereas communication is defined as 'that which is communicated, a letter, a message, information imparted by speech, writing, etc.' Taking these two interrelated dictionary definitions as they stand would suggest that, fundamental to each, there is an absolute requirement for a 'language', based upon a set of symbols, by which the signaller can communicate and be understood by the signalled. As human beings, we are constantly signalling and communicating in the form of words, gestures, symbols, etc., to ourselves and to each other. These communications allow us to carry out many diverse functions in a 'social' environment with relative speed and efficiency, hopefully enabling us to enjoy and survive another day. At a simpler level, it is known that, for successful cell division to occur within a culture of mammalian cells, there is a requirement for extracellular growth factors called cytokines, which act as chemical signals. It is becoming clear that similar chemicals also occur in higher plants, multicellular invertebrates and ciliates. Within the world of micro-organisms, signalling, communication, and hence information flow, also occur.

Language is the common factor among all methods of communication used by biological organisms. Certain chapters within this volume will attempt to decode and translate the different languages and, by definition, the vocabularies (chemical signal molecules) utilized by a wide range of different micro-organisms within various environmental situations. For some micro-organisms we know the chemical structure of the signal molecule(s) utilized; however, in others the structures are far less clear. As you read through the book you will learn how, and under what conditions, micro-organisms communicate with each other and also with other biological cells, and how, in some instances, we can exploit this knowledge.

The opening chapter by Williams demonstrates the diverse nature of signalling and communication throughout the microbial world and sets the agenda for the rest of the book. One feature that is highlighted in the first chapter, and also in the chapter by Kaprelyants *et al.*, is the recent rapid advances that have been made in the field of bacterial cell–cell communication. This has been facilitated by the discovery of the chemical nature of the signal molecules involved. In most cases they have been shown to be small peptides or a modified form of homoserine lactone. These types of signal molecules have often been referred to as 'pheromones' or 'autoinducers'. If we accept the definition of a pheromone, as 'substances which are secreted to the outside by an individual and received by a second individual of the same species, which elicit a behavioural or a developmental process', then their *raison d'être* becomes clearer. In most cases this can be viewed as a density-dependent or quorum sensing process, by which a signal molecule that cannot be detected by an individual bacterium, or even by low numbers of bacteria, is released into the local environment. Only when bacteria are at relatively high numbers, or within a confined environment, will a threshold level of signal molecule be reached that can initiate specific gene expression required for the 'survival' mechanisms peculiar to the genus of bacterium involved. Thus we have the captivating situation of intercellular communication, by signalling, from bacteria that may not be in close physical contact. The chapter by Greenberg provides an introduction to the role of acylhomoserine lactone (AHL) and quorum sensing in Gram-negative bacteria. This is followed by Swift *et al.* who describe the role of AHL and quorum sensing circuits in two genera of pathogenic Gram-negative bacteria: *Aeromonas*, which is an emerging pathogen of fish and man; and *Yersinia*, a genus that includes pathogens known to infect humans and also certain fish, such as trout. The chapter by Pesci and Iglewski continues the theme of signalling and communication in pathogenic Gram-negative bacteria by reviewing the two separate quorum sensing systems (*las* and *rhl*) in *P. aeruginosa*.

It is probably reasonable to say that less is known about signalling and communication involving peptide molecules. The chapter by Dunny *et al.* reviews the work being carried out on the many roles of sex pheromone peptides in *Enterococcus* conjugation. This is followed with a chapter by Kaiser, in which he describes his elegant work on peptide signalling molecules and on their role in multicellular differentiation of the gliding bacterium, *Myxococcus xanthus*.

Exploitation of the knowledge available to us is becoming distinctly possible, for example, understanding the role of acylhomoserine lactones, in terms of influencing production of particular natural products such as antibiotic production (carbapenems) in *Erwinia carotovora* (McGowan and Salmond) and butyrolactones controlling antibiotic production (viginiamycin) in *Streptomyces virginiae* (Yamada).

Pheromones are not only produced by bacteria. Events in pheromone pathways of yeasts are similar to those found in higher eukaryotes. The fission yeast, *Schizosaccharomyces pombe*, has proved to be an excellent organism for studying the communication processes. Davey describes the production and action of peptide hormones on target cells; also how the cell recovers from the effects of stimulation and returns to a resting state. Continuing the eukaryotic theme, chemical communication between fungal hyphae is discussed. Gooday explains how pheromones involved in the crosstalk between hyphae are structurally very diverse, ranging from oxygen to complex peptides. In all cases these molecules interact with specific chemoreceptors, coupled to signal transduction pathways within the hyphae.

The life cycle of the slime mould *Dictyostelium discoideum* incorporates key features of morphogenesis found in higher organisms, e.g. chemotaxis, cellular differentiation and multicellular organization. The chapter by Sherratt *et al.* shows how mathematical modelling of cell streams in *D. discoideum* can provide reassuring evidence that we do now appear to understand the fundamentals of signal mechanisms.

Microbial–plant cell communication is addressed in the book and is discussed both from pathogenic and symbiotic aspects. The signalling molecules involved in bacterial–plant cell communication can be broadly classified as: synthesized metabolites, e.g. syringolides produced by *Pseudomonas syringae* that infects soybean; secreted proteins, e.g. non-specific plant-degrading enzymes that in some bacteria are regulated via quorum sensing; proteins that are delivered into plant cells causing a hypersensitive response, which eventually kills the invasive bacteria; and nodulation signalling proteins produced by the symbiont *Rhizobium* spp.

Gow *et al.* discuss plant pathogenicity and describe the signalling interactions between the eukaryotes *Phytophthora* and *Pythium* and their host-plant cells. The hallmark of these organisms is their ability to form zoospores that are required for the dispersal of the organism through films of water within wet soils. The signalling systems involve chemical and electrical signals generated by the host plant to guide zoospores to the plant which eventually leads to invasion of the plant cells. Much of the work described deals with zoospore–root and zoospore–zoospore interactions.

Understanding the mechanisms by which plant-associated pathogens/symbionts produce/regulate synthesis of signalling molecules or respond to plant-induced signals will be of immense benefit to the agricultural industry. It could lead to the development of blocking or enhancing agents, either *ex planta* or *in planta*, depending on the particular requirement.

Moving on from plant-associated micro-organisms, another extremely important topic that is addressed is bacterial–animal cell communication. It is recognised that infective bacteria are able to alter eukaryotic signal transduction pathways and thus host-cell functions. As a consequence, invasive pathogenic bacteria are able to overcome the defence mechanisms of their animal host and to reproduce in the tissues. Within the last few years there have been considerable advances in the molecular detail of communication and signalling between pathogenic bacteria and animal host cells. In particular, the mammalian cell targets of some of the bacterial effector proteins have been investigated. To help illustrate the advances made in this important area, work is presented on the interaction of enteropathogenic *Escherichia coli* (EPEC) and enterohaemorrhagic *E. coli* (EHEC) with mammalian intestinal enterocytes (Frankel *et al.*) and on the Yop system of

Yersinia spp. that obstructs a cellular immune response (Neyt and Cornelis). Clearly, a better understanding of pathogenic bacteria–host cell communication would allow the rational design/development of drugs that could block bacterial effector protein action and/or synthesis.

Another group of organisms that is discussed, and for many people will be new to them, is the dinoflagellates. These organisms dominate the plankton of the subtropics in the world's oceans and consequently are important ecologically and economically. However, very little is known about signalling mechanisms that have been proposed to mediate cellular processes including encystment, cell division and bioluminescence. Cell-to-cell recognition of endosymbiotic relationships between the coral–dinoflagellate associations is only just beginning to be understood (Burkholder and Springer).

The authors have presented an excellent range of current reviews on microbial signalling and communication, which hopefully will encourage more scientists from widely diverse disciplines (academic, medical and industrial) to embrace the topic. We thank all contributors for the considerable amount of effort and time afforded to produce each chapter.

R. R. England, G. Hobbs, N. J. Bainton and D. McL Roberts
January 1998