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Book Reviews

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Biochemistry of signal transduction and regulation

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A Whole is that which has a beginning, a middle and an end Aristotle

The ability to communicate—to send and receive signals—is a fundamental property of living systems. The very existence of multi-cellular organisms depends on cells interacting and talking to one another. And even single-cell organisms need to feel they are not alone sometimes. When the rules of interaction and communication break down it is not surprising that the consequences can be dire, leading, for example, to the anti-social behaviour of cancer cells. Recent years have seen the development of experimental models and tools that have allowed researchers to map the individual components of signalling pathways and glimpse the complexities involved. In short, we are starting to understand how cells respond to extracellular signals from their close neighbours and more distant locations within the body.

Extracellular signals can be peptides and proteins, amino acid derivatives, or lipid-soluble steroids and vitamins. They are classified as growth factors, steroid hormones, cytokines, or neurotransmitters, depending or their chemical structure and/or physiological activity. With the exception of steroid hormones and related ligands for nuclear receptors, the signalling molecule remains extracellular and the message is transduced to the inside of the cell via membrane-bound receptor proteins. These receptors can be grouped into different families depending on their structure and mechanism of action. The main classes of receptor are those that exploit tyrosine phosphorylation, the 7-helix transmembrane receptors, and ligand-gated ion channels. Once the signal has been transduced across the membrane it is further transmitted through combinations of adapter proteins, second messengers, and effector proteins. A common theme running through signalling from different receptors is the phosphorylation or dephosphorylation of serine, threonine, or tyrosine residues in proteins or components of the cell membrane, such as phosphatdyl inositol, leading to altered patterns of gene expression. In *Biochemistry of Signal Transduction and Regulation*, Gerhard Krauss introduces the key molecules and the underlying biochemical mechanisms whereby an extracellular signal is transmitted, often but not exclusively to the nucleus, and an appropriate response elicited.

The book is a little under 500 pages, excluding the index, and divided into 16 chapters. Chapter 1 provides a general introduction to the transcriptional machinery and the control of gene expression. This forms an extensive part of the book, nearly a fifth, and while it is informative, the space might be better utilized by discussing the structure and function of specific transcription factors that have been identified as end points in signalling cascades introduced later in the book, i.e. Elk-1, c-Jun, STATs, NF-AT, and SMAD proteins. The next chapters consider the regulation of enzyme activity (Chapter 2) and a useful overview of the nature of signalling pathways (Chapter 3). Chapter 4 deals with the nuclear receptor superfamily, which includes receptors for steroid hormones, thyroid hormone, and the vitamins A and D. These are intracellular receptors that regulate gene expression directly by binding to DNA and recruiting the cell's transcriptional machinery. Though the chapter on nuclear receptors is self-contained, the following chapters dealing with signalling strategies from the cell membrane involve significant cross-referencing, which reflects our current picture of potential cross-talk between different signals and receptor systems.

The importance of phosphorylation and the kinase enzymes responsible is well known and is amply covered in the chapters dealing with Ser/Thr-specific kinases (Chapter 7), tyrosine-specific kinases (Chapters 8 and 11), and MAPK pathways (Chapter 10) and receptors with intrinsic serine/threonine kinase activity (Chapter 12). Equally important is the removal of specific phosphate groups, and this is illustrated by the fact that a protein tyrosine kinase is found in the bacterium *Yersinia pestis*, the organism that causes plague, and a defect in the protein tyrosine phosphatase IC results in an autoimmune disease in mice resulting in the "mouth eaten" phenotype. Chapter 6 introduces the concept of 'second messengers', which transmit the signal from the receptor to effector proteins, and, in addition to the usual suspects (cAMP, inositol triphosphate, diacyglycerol, calcium ions), we also learn about the lipophilic messenger ceramide and the gas NO. The prominent role played by Ras as a 'central switching station' for different signals and receptors is afforded a chapter on its own (Chapter 9), whereas signalling through trimeric G-proteins, coupled to 7-helix membrane receptors, is covered in Chapter 5. Chapters 13 and 15 attempt to pull the threads of these different pathways together in the regulation of two key cellular processes namely the cell cycle and programmed cell-death (apoptosis). The mechanisms of cell-cycle control and apoptosis are clearly described; however, the reader is left largely to make their own connections with the signals and receptor systems described in previous chapters. It would be nice to see this information much more integrated and the connections outlined where known. Each chapter ends with a list of references, which is of value in following up reviews or original sources of the material covered. The most recent citations are only up to 1998 or 1999, but this is not surprising for a text book covering a very rapidly evolving field of research.

Attempting to provide a comprehensive summary of the field of signal transduction is an ambitious project. *Biochemistry of Signal Transduction and Regulation* should work well as an introductory text for the novice encountering the complexities of signal transduction for the first time. It should also be of more limited use to those working in the field as a reference text. However, unfortunately, the clarity of the text is marred by a number of typographical mistakes and the occurrence of the odd *deutsch ord oder satz*. Errors in the index also detract from what should be a useful reference source.

Signalling pathways clearly have a beginning (receptor), a middle (kinase cascades, second messengers), and an end (changes in gene regulation); however, it is becoming increasingly clear that the 'whole' is not the individual pathway, but how different signals are integrated and participate in 'cross-talk'. The final decision a cell makes as to whether to grow and divide, differentiate, or sacrifice itself for the good of its neighbours will be a balance between mitogenic and non-mitogenic signals received and the cross-talk of different signalling pathways. The mechanisms employed by the cell are many and varied, and the unravelling of these processes represents a major and exciting challenge for researchers. *Biochemistry of Signal Transduction and Regulation* should provide a useful guide to undergraduate students taking Molecular/Cell Biology courses and to new postgraduates entering this field. It should also be of benefit to those of us who have to explain in a clear and concise manner the intricacies of how cells communicate.

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