

THE HORMONAL CONTROL OF GENE TRANSCRIPTION

Edited by

PHILIP COHEN

and

J. GORDON FOULKES



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Editor's foreword

Over the past few years there have been considerable advances in our understanding of cellular control mechanisms, and current research is now linking areas of biology that were previously thought of as being quite separate. *Molecular Aspects of Cellular Regulation* is a series of occasional books on multidisciplinary topics, which illustrate general principles of cellular regulation. Previous volumes described *Recently Discovered Systems of Enzyme Regulation by Reversible Phosphorylation* (Volumes 1 and 3), *The Molecular Actions of Toxins and Viruses* (Volume 2), *Molecular Mechanisms of Transmembrane Signalling* (Volume 4) and *Calmodulin* (Volume 5). This sixth volume, *The Hormonal Control of Gene Transcription*, has now been published, to highlight recent important advances in our understanding of this topic which is linking two of the most active areas of current biochemical and molecular biological research (hormone action and gene transcription) and leading to the emergence of unifying concepts.

It will be apparent from reading the book that major advances have stemmed from the identification of small oligonucleotide sequences, termed response elements, which are located in the promoter regions of genes and permit transcription in response to extracellular signals. Response elements define regions of the DNA that interact with specific DNA-binding proteins, termed transcription factors, which are themselves the key to the regulation of gene expression. It is becoming clear that extracellular signals control transcription either by binding directly to such proteins, as in the case of steroid and thyroid hormones, or by inducing a post-translational modification (i.e. phosphorylation/dephosphorylation). Such ligand-protein interactions and post-translational modifications allow the transcription factors to enter the nucleus or alter their interaction with DNA, thereby increasing or decreasing the rate of transcription by RNA polymerase II. Nine years ago one of the Editors concluded a review article by predicting that the 'study of phosphorylation of proteins in the cell nucleus will become a major growth area over the next few years'¹. In retrospect,

¹ Cohen, P. (1982) *Nature* **296**, 613-620.

this prediction has proved to be premature, because the explosion of activity in this area is only just about to happen. Although many of the Chapters in this book hint at the involvement of phosphorylation in the control of gene expression, only in the cases of the cyclic AMP response element binding protein (CREB) and the transcription factor NF- κ B have the importance of phosphorylation been established with some certainty. In many cases, mechanistic details will almost certainly require the establishment of *in vitro* transcription systems, the lack of which is still a major barrier to progress. There is increasing evidence that some extracellular signals exert their effects by activating cytosolic proteins which only then enter the nucleus to control gene transcription. The mechanisms involved in transnuclear membrane signalling are likely to become a further key area of research into the hormonal control of gene expression.

The first section (Chapter 1–4) provides introductory overviews to the processes of gene transcription, the regulation of RNA polymerase II and cellular signal transduction for readers who are not experts in these areas. The second section (Chapters 5–7) describes the mechanism of action of steroid and thyroid hormones and retinoic acid, the third section (Chapters 8–12) the control of gene expression by second messenger systems, and the fourth (Chapters 13–17) the regulation of transcription by polypeptide hormones. Regulation of transcription by environmental stress is discussed in the fifth section (Chapters 18–20), while the final section (Chapters 21 and 22) reviews transcriptional controls during embryogenesis. The Editors believe that this book provides a state of the art overview for both specialists and non-specialists to this important and rapidly developing area of biological research.

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