

# What is left in the 'post-genome' era?

## Regulation of Gene Expression

edited by K. E. Chapman and S. J. Higgins

Portland Press · May 2001

Paperback £19/\$30

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Since the recent completion of several eukaryotic and prokaryotic genome-sequencing projects, today's molecular geneticists and cell biologists are faced with studies that seek to explain how the expression of their gene(s) of interest is regulated in a specific and timely fashion. *Regulation of Gene Expression* can be recommended for all those who intend to study the subject in more detail. By choosing leading experts in different areas of transcriptional regulation, the editors have provided the reader with a stimulating summary of the current state of research. In addition to explaining most basic mechanisms of transcriptional regulation, the book illustrates how this regulation is involved in central biological processes such as cell division, death and differentiation. Furthermore, consequences of transcriptional deregulation (for example cancer) are used as examples to show the relevance of transcriptional regulation for the understanding and the potential treatment of common diseases. The book provides an excellent link between textbooks and the current status of original publications. At the end of most chapters the main open questions in the respective areas are provided.

Using the regulation of transcription in simple organisms as an example, Marc Ptashne and Alexander Gann elegantly provide evidence of why evolution led to a restricted set of transcriptional regulators, which is used combinatorially to generate flexible transcriptional responses to a constantly changing environment. With the example of the *lac* operon and the phage lambda switch, the authors show how regulated localization can lead to specificity. They then turn to higher eukaryotes, where often several signals and therefore several activating factors are necessary to turn on one gene, such as the interferon- $\beta$  gene after viral infection. The parallels between cytoplasmic signalling pathways and transcriptional regulation systems are highlighted to show how simple binding interactions can provide specificity and combi-

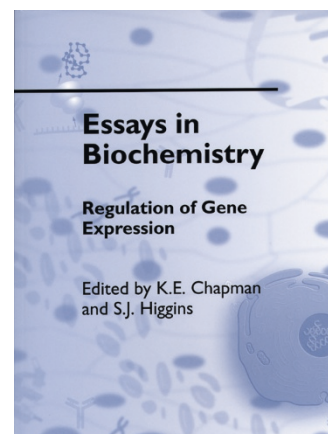
natorial potential to different biological processes. Georgina Lloyd, Paolo Landini and Steve Busby discuss the details of prokaryotic gene regulation and explain the various combinations of activators and repressors that have been observed to regulate promoters in *Escherichia coli*. Gracy Gill's contribution illustrates how the more complex eukaryotes, with genomes that encode two to ten times more genes, use additional factors and promoter elements to regulate gene expression. Alan Wolffe's chapter discusses the active, regulatory role of chromatin remodelling during the regulation of gene expression. He focuses on nucleosome structure, subunit replacement, core histone modification by acetylation and the SWI/SNF superfamily of ATPases. As in all other chapters the complex issues are supported by numerous excellent illustrations.

Richard R. Meehan and Irina Stancheva provide a critical overview of the impact of DNA methylation on the regulation of gene expression during development. Although CpG methylation is essential for vertebrate development it seems unclear whether DNA methylation is simply a consequence of gene inactivation or whether methylation *de novo* is directed by the active targeting of methylation to specific genes. The fact that repressive, chromatin-modifying enzymes are recruited by proteins that bind to methylated CpG sequences is especially emphasized. In the next three chapters the topic of transcriptional regulation is integrated into extracellular signalling, cell cycle, cell death and post-transcriptional regulation. Melanie Lee and Stephen Goodbourn review several examples that illustrate the conversion of extracellular signals to specific promoter activation. They summarize six different signalling pathways and show how regulated localization is used to generate specificity. Ho Man Chan, Noriko Shikama and Nicholas B. La Thangue describe how the product of the retinoblastoma tumour suppressor gene (pRB) regulates the cell cycle by directly

affecting the transcriptional program of a proliferating cell. This example underscores the central role of transcriptional regulation for the proper control of cell cycle progression, which is lost through the inactivation of pRB in about 20% of human tumours. Although transcriptional initiation is the main mode of regulation during gene expression, certain situations favour the regulation of translation (for example, when a rapid increase in the amount of protein is required or localized translation during early development). Christopher G. Proud discusses these examples and the molecular requirements for regulated translation. Martyn Link and David J. Harrison describe the involvement of transcription factors and gene expression in the regulation of programmed cell death. This chapter covers many of the regulatory circuits involved in the regulation of apoptosis, although some have no direct connection to transcriptional regulation.

In his summarizing final chapter, Nick Hastie points out that transcriptional regulators have a central role in developmental decisions and disease, although he admits that other levels of regulation are of increasing significance (for example, alternative splicing and protein modifications). Hastie predicts that with the help of bioinformatics we shall ultimately see four-dimensional expression maps of whole organisms. This will certainly be a valuable 'future perspective'. □

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