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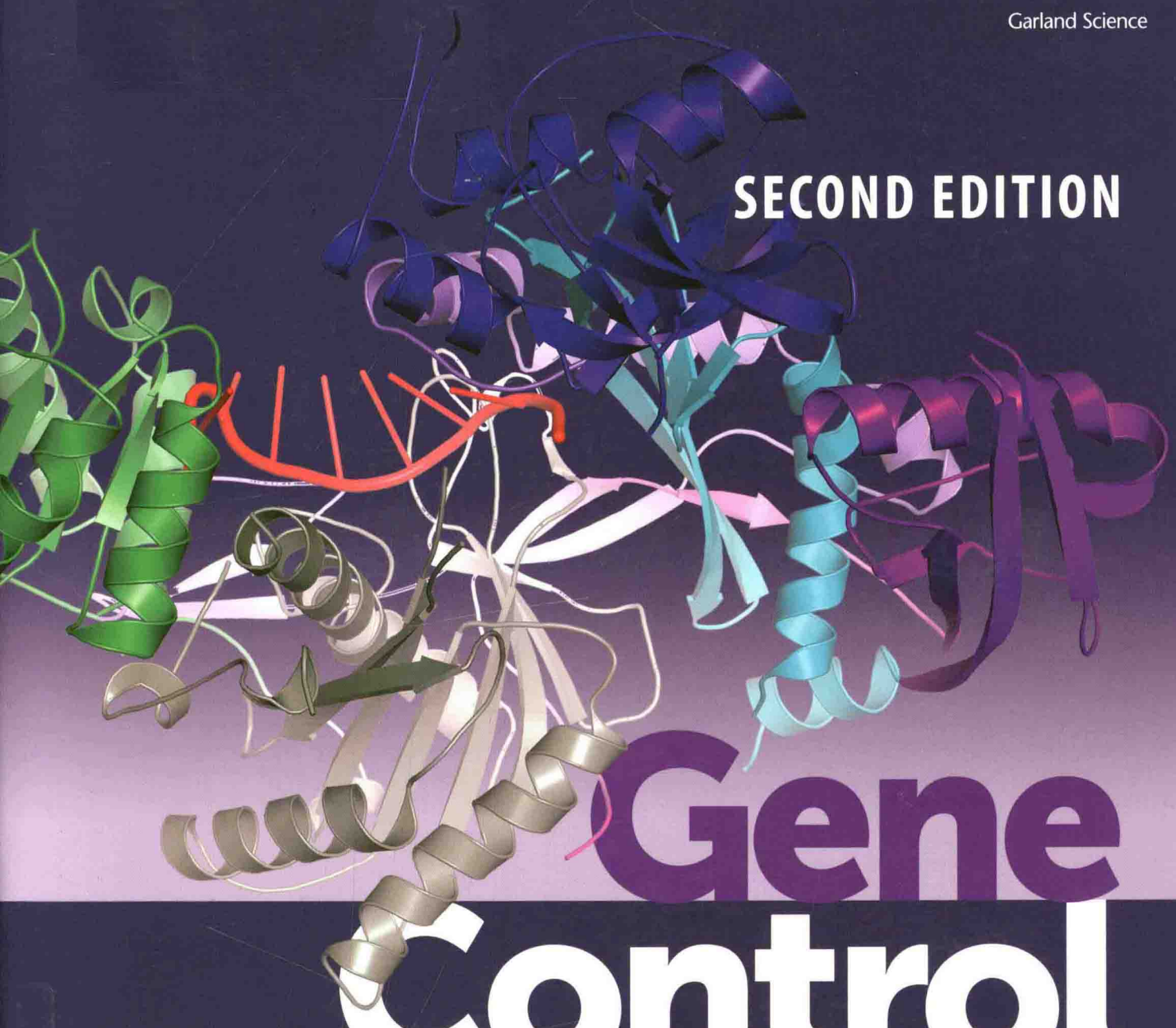

Gene Control

David S. Latchman

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SECOND EDITION

David S. Latchman

Master of Birkbeck, University of London
and Professor of Genetics, Birkbeck and
Institute of Child Health
University College London

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Front cover shows the structure of the human Ago2 protein component of the RNA-induced silencing complex (RISC). Courtesy of Ian J MacRae, The Scripps Research Institute.

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To my mother and in memory of my father

Preface

It is now 25 years since the first edition of my book *Gene Regulation: A Eukaryotic Perspective* was published. Subsequently, four further editions appeared reflecting the enormous advances in the field over the ensuing years. By 2010, these advances allowed both a mechanistic understanding of the processes involved in gene regulation and a detailed analysis of the manner in which they operate in specific biological systems.

The work was therefore significantly expanded and revised to reflect these changes and given a new title, *Gene Control*. In the last few years, the field has developed further, necessitating this second and revised edition of *Gene Control*.

In particular, our understanding of two major themes in gene regulation has advanced considerably in the last few years and this is reflected in this new edition. The first of these is the regulation of chromatin structure and its role in gene regulation. Although a chapter was devoted to this topic in the first edition of *Gene Regulation*, its role was much less well understood at that time than, for example, that of DNA-binding transcription factors. However, over the last 25 years this topic has assumed a central position in our understanding of gene regulation. It is now clear, for example, that as well as the genomic DNA sequence, there exists an epigenome ('epi' is Greek for 'on') involving modifications of the DNA and of the proteins, such as histones, associated with it. Moreover, this epigenome varies between different tissues and cell types in contrast to the relative invariance of the genomic DNA sequence. This allows the epigenome to play a key role in the regulation of gene expression. To reflect this, all the sections dealing with this topic have been extensively revised and updated, while the title of Chapter 3 has been changed to 'The Epigenome: Role of Chromatin Structure in Gene Control.' Moreover, additional sections have been added on these modifications as a target of cellular signaling pathways (Section 8.5) and on the role of the epigenome in cancer (Section 11.4) and other human diseases (Section 12.2).

The second major area to have advanced hugely in recent years is that of regulatory RNAs. At the time the first edition of *Gene Regulation* was published, it was believed that the regulation of gene expression was produced exclusively by regulatory proteins and the possibility of regulatory RNAs had not been put forward. It is now clear, however, that such regulatory RNAs are as important in the regulation of gene expression as regulatory proteins. Moreover, although small regulatory RNAs (20–30 bases in length) were discussed in the first edition of *Gene Control*, further studies have now indicated that longer regulatory RNAs (200 bases or more in length) are also of critical importance in the regulation of gene expression. Accordingly, the sections of this book dealing with this area have been updated and expanded to reflect the key role of all types of regulatory RNAs and to give equal emphasis to the different classes of such RNAs. Moreover, additional sections have been added on the role of regulatory RNAs in cancer (Section 11.6) and other human diseases (Section 12.4).

As with the first edition, the second edition of *Gene Control* is organized into two parts. The first part provides a detailed mechanistic analysis of the processes involved in controlling gene expression. After an introductory chapter, three pairs of chapters deal with the fundamental processes involved in gene regulation. In each pair of chapters, the first chapter deals with the basic process itself and the second deals with the manner in which it is involved in regulating gene expression. Thus, Chapters 2 and 3 deal with chromatin structure and its role in gene regulation, Chapters 4 and 5 deal with the process of transcription itself and the manner in which it is

regulated, while Chapters 6 and 7 deal with post-transcriptional processes and their role in the regulation of gene expression.

In contrast, the second part of the book deals with specific biological processes and the role played by gene control in their regulation. Thus, Chapter 8 deals with cellular signaling processes, Chapter 9 deals with the regulation of gene expression in development and Chapter 10 discusses the key role played by gene regulatory processes in the specification of individual differentiated cell types. Finally, Chapters 11 and 12 deal with the alterations in gene expression that can cause specific human diseases. Thus, Chapter 11 discusses the role of gene regulation in cancer while Chapter 12 deals with gene regulation in inherited and infectious diseases of humans, as well as discussing the manner in which advances in our understanding of gene regulatory processes may lead to improved therapies for human diseases.

Overall therefore it is hoped that the significant revision and updating of this book will allow it to continue to be of value to students, scientists, and clinicians interested in the topic of gene control, which is of such vital importance in both normal development and the proper functioning of the adult organism as well as playing a critical role in the development of different human diseases.

Finally, I should like to thank the staff of Garland Science who have produced this book so efficiently, particularly Elizabeth Owen who originally suggested the restructuring/expansion of this book, as well as being a valuable source of advice throughout the preparation of both editions. As always, I am indebted to Maruschka Malacos who has coped most efficiently with the need to introduce considerable new material as well as to rearrange and modify existing material in the preparation of the new edition.

David S. Latchman CBE

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I would also like to thank all those colleagues who have given permission for material from their papers to be reproduced in this book and have provided images suitable for reproduction.

Online Resources

Accessible from www.garlandscience.com, the Student and Instructor Resource Websites provide learning and teaching tools created for Gene Control. The Student Resource Site is open to everyone, and users have the option to register in order to use book-marking and note-taking tools. The Instructor Resource Site requires registration and is available only to qualified instructors. To access the Instructor Resource Site, please contact your local sales representative or email science@garland.com. Below is an overview of the resources available for this book. On the Website, the resources may be browsed by individual chapters and there is a search engine. You can also access the resources available for other Garland Science titles.

For instructors

Figures

The images in this book are available in two convenient formats: PowerPoint® and JPEG. They have been optimized for display on a computer.

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