Chromatin Structure and Gene Expression

Edited by Sarah C. R. Elgin

FRONTIERS IN MOLECULAR BIOLOGY®

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IRL PRESS
at
OXFORD UNIVERSITY PRESS
Oxford New York Tokyo

Oxford University Press, Walton Street, Oxford OX2 6DP

Oxford New York
Athens Auckland Bangkok Bombay
Calcutta Cape Town Dar es Salaam Delhi
Florence Hong Kong Istanbul Karachi
Kuala Lumpur Madras Madrid Melbourne
Mexico City Nairobi Paris Singapore
Taipei Tokyo Toronto
and associated companies in
Berlin Ibadan

Oxford is a trade mark of Oxford University Press

Published in the United States
by Oxford University Press Inc., New York

A catalogue record for this book is available from the British Library

Library of Congress Cataloging-in-Publication Data
Chromatin structure and gene expression / edited by Sarah C.R. Elgin.
(Frontiers in molecular biology)
Includes bibliographical references and index.
1. Chromatin. 2. Gene expression. I. Elgin, Sarah C. R.
II. Series.
QH599.C46 1995 574.87'322—dc20 94–42634

ISBN 0 19 963576 5 (Hbk)
ISBN 0 19 963575 7 (Pbk)

Typeset by
Footnote Graphics, Warminster, Wilts.
Printed in Great Britain by
The Bath Press, Avon

Chromatin Structure and Gene Expression

Frontiers in Molecular Biology

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Preface

In the twenty-plus years since the nucleosome model of chromatin structure emerged, there has been considerable progress in elucidating how that structure contributes to the regulatory process. Much of this advance is due, of course, to the new tools of molecular biology, which have allowed us to analyse the packaging and monitor the expression of individual genes, whether *in vitro* or *in vivo*. During the last few years we have gained a much more detailed understanding of the components of the nucleosome, both the histone octamer and the DNA itself, and we are beginning to see that knowledge reflected in studies of replication and assembly. These topics are discussed in the first three chapters. Our initial efforts to understand the mechanisms of gene expression from the chromatin template have focused on active and activatable genes. Some eukaryotic genes, like the heat shock genes, appear poised for expression in an accessible chromatin structure, while others appear to require a chromatin-remodelling event in the promoter region as part of activation. Once initiated, the transcribing polymerase must continue through a nucleosome array—a difficult task. These topics are discussed in Chapters 4–6. As our understanding of the functional consequences of the nucleosome array has increased, we have been emboldened to explore structure at higher levels, trying to establish molecular mechanisms to explain genetic results that have been well known for many years. The last four chapters deal with evidence for domains, boundaries, and packaging differences in the context of known epigenetic regulation in yeast, fruit flies, and mice. A complete understanding of these higher order effects will be essential to a complete understanding of gene regulation during eukaryotic differentiation and development.

In writing our chapters, we have taken as our starting reference *Chromatin* by Kensal van Holde (1989, Springer-Verlag, New York). This book provides a thorough analysis of work prior to 1988, and should be used by the graduate student as a guide to the earlier literature. Younger students desiring a broad introduction should start with the appropriate chapters in a general text (such as *Molecular biology of the cell* by B. Alberts, D. Bray, J. Lewis, M. Raff, K. Roberts, and J. D. Watson (1994, third edition, Garland Publishing Inc., New York)) or a recent monograph (such as *Chromatin structure and function* by A. Wolffe (1992, Academic Press, London)). Many excellent books are available that provide a more detailed examination of some of the topics considered here: *Understanding DNA* by C. R. Calladine and H. Drew (1992, Academic Press, London), *Structural studies of protein–nucleic acid interactions* by T. A. Steitz (1993, Cambridge University Press, Cambridge), *DNA–protein interactions* by A. A. Travers (1993, Chapman and Hall, London), and *Replication and transcription of chromatin* by R. Tsanev, G. Russev, I. Pashev, and J. Zlatanova (1992, CRC Press, Boca Raton, Florida) may be particularly useful.

It is our hope that this book will find use in discussion courses organized for and by graduate students in the area of chromatin structure/gene expression. We have tried to point out not only recent progress in the field, but also the problems and clues that indicate where the work may lead. Thus in addition to writing a chapter in their own area of experimental work, each author read and commented on one or two other related chapters. These comments were used to formulate the 'Discussion' that appears at the end of each chapter.

Using the tools of molecular biology, genetics, and biochemistry, much progress has been made in defining chromatin structure and identifying potential mechanisms for regulation. Thus, in some areas, the problems before us are well defined. However, other areas remain enigmatic: what do we really mean by 'higher order structure'? Here the situation is most intriguing, if somewhat daunting; much remains to be done. We hope that our younger colleagues will be challenged by the problems posed here, and that some will be motivated to join us in our efforts to understand the regulation of gene expression established by nucleosomal and higher order chromatin structure.

St Louis, Missouri
March 1995

S.C.R.E.

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Abbreviations

aa	amino acid
ANT-C	*Antennapedia* gene complex in *Drosophila*
ARS	autonomously replicating sequence
AS	Angelman syndrome
bHLH	basic helix–loop–helix (protein)
bp	base pairs
BWS	Beckwith–Wiedemann syndrome
BX-C	*bithorax* gene complex in *Drosophila*
CAP	catabolite-gene-activating protein
CD	circular dichroism
CHO	Chinese hamster ovary (cells)
CTD	C-terminal domain, generally of RNA polymerase II
DHFR	dihydrofolate reductase
DMS	dimethyl sulfate
DREV	developmental regulator effect variegation
EBV	Epstein–Barr virus
EDTA	ethylene diaminetetraacetic acid
EM	electron microscope
5-FOA	5-fluoroorotic acid
GH1	globular domain of histone H1
H	histone (used to designate H1, H2A, H2B, H3, H4)
HM loci	the loci containing the silent copies of *HMLα* and *HMRa* (*Saccharomyces cerevisiae*)
HMG	high mobility group proteins
HOS	higher order structure
HP1	heterochromatin protein 1
HS	hypersensitive site
HSE	heat shock element
HSP 70	the 70 000 u heat shock protein
HSF	heat shock transcription factor
HSH	helix–strand–helix (protein structural motif)
hsp	heat shock protein-encoding gene
ICR	internal control region (often applied to 5S RNA gene)
kb	kilobases
LCR	locus control region
LIS	lithium diiodosalicylate
LMPCR	ligation-mediated PCR
LOH	loss of heterozygosity

LTR	long terminal DNA sequence repeat, found at the ends of a retrovirus
MAR	matrix attachment region
min	minute
MMTV	mouse mammary tumour virus
MNase	micrococcal nuclease
NHCP	non-histone chromosomal proteins
NMR	nuclear magnetic resonance
nt	nucleotides
NTP	nucleotide triphosphates
OBR	origin of bidirectional replication
ORC	origin recognition complex, or origin replication complex
Pc-G	*Polycomb* group of genes (*Drosophila*)
PCNA	proliferating-cell nuclear antigen
PCR	polymerase chain reaction
PEH	paired ends of helices (protein structural motif)
PEV	position effect variegation
PIKA	polymorphic interphase karyosomal association
PRE	*Pc*-G response elements
PS	parasegment
PWS	Prader–Willi syndrome
R	ratio of apparent size, determined by gel electrophoresis, to known size of a DNA fragment in bp (Chapter 2)
Rif1	Rap1 interacting factor
RP-A	replication protein A
SAR	scaffold attachment region
scs	special chromatin structures; apparent boundaries of enhancer function
s	second
SFM	scanning force microscope
SIR	silent information regulator
ss-DNA	single stranded DNA
SV40	Simian Virus 40
TAF	TBP-associated factor
TBP	TATA-box-binding protein
TEA	Tris-EDTA-acetate, a neutral buffer used to run DNA gels
TF	transcription factor
trx-G	*trithorax* group of genes (*Drosophila*)
uH2A	ubiquitinated histone H2A
XIC, Xic	X inactivation centre
YAC	yeast artificial chromosomes

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