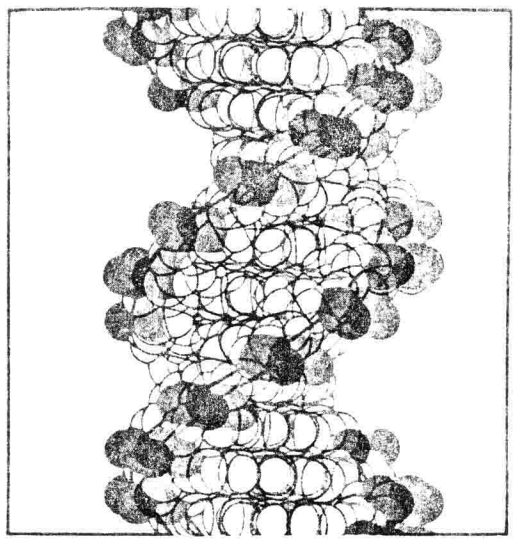
GENES IV

BENJAMIN LEWIN



GENES IV

BENJAMIN LEWIN

1990
Oxford University Press
Oxford New York Tokyo Melbourne
Cell Press, Cambridge

Cell Press, Cambridge, Mass.

Oxford University Press, Walton Street, Oxford OX2 6DP
Oxford New York Toronto
Delhi Bombay Calcutta Madras Karachi
Petaling Jaya Singapore Hong Kong Tokyo
Nairobi Dar es Salaam Cape Town
Melbourne Auckland
and associated companies in
Berlin Ibadan

Oxford is a trade mark of Oxford University Press

Published in the United States
by Oxford University Press, New York
and Cell Press, Cambridge, Mass

British Library Cataloguing in Publication Data
Lewin, Benjamin
Genes—4th edition
1. Genetics
I. Title
575.1
ISBN 0–19–854268–2

Library of Congress Cataloging in Publication Data
Lewin, Benjamin
Genes IV.
Includes bibliographical references
1. Genetics. I. Title. II. Title: Genes four.
QH430.L488 1990 575.1 89-16310
ISBN 0–19–854268–2
ISBN 0–19–854267–4 (pbk.)

Printed in the United States of America

Preface

The main purpose of an organism's existence is (of course) to perpetuate its genetic material, and the properties of the cellular structures by which this is achieved are the crux of heredity. The basic question we wish to answer is: how does a cell give rise to another cell of either identical or different type? What role does the duplication and expression of the genetic material play, and what other factors may be involved? In molecular terms, we want to know how macromolecular structures are assembled *in situ*.

We understand that nucleic acid (DNA or RNA) is perpetuated by a duplicative process in which a parental template is copied to give two identical replicas. By means of the genetic code, the sequence of nucleic acid is expressed in the form of protein; and, by implication, the properties of the various protein products of any cell are responsible for its phenotype, either directly, or indirectly because they catalyze or otherwise participate in the assembly of cellular structures. But to what degree are these structures self-assembling from their components or to what extent do they rely upon pre-existing structures to provide templates?

One might describe the current paradigm of molecular biology in simplistic terms as "DNA makes RNA makes protein, which makes another DNA make RNA make protein"—a cascade in which the expression of one gene leads to expression of another gene. But we must wonder whether this cycle is self-contained or whether it depends upon additional information, for example, the position of particular structures in a particular cell.

Since the original edition, the purpose of *GENES* has been to explain heredity in terms of molecular structures. Of course, by far the major part of any investigation of the basis for inheritance must focus on the genetic material. This edition shares this feature with its predecessors, but makes more explicit a trend that has been implicit in previous editions: we now begin more openly to consider the stages that follow the direct conversion of genetic information into RNA and protein products.

GENES IV rests upon the proposition that the role of molecular biology is to explain in molecular terms the entire series of events by which genotype is converted into phenotype. We may consider the basis of inheritance in terms of three broad questions:

- How is the genetic information carried in sequences of DNA perpetuated and expressed?
- Are cellular structures self-assembled by means of information inherent in the sequences of the proteins or other components?
- What type of information is responsible for the development of differences between cells during embryogenesis?

GENES IV considers the first of these issues in detail, but at present we can touch only partially on the other questions, although they remain in mind while we analyze the regulation of gene expression. The expression of genes in terms of proteins begins with the genetic code, but includes the events responsible for timing of gene expression and for proper location of the protein in the cell. These latter events may take us into ground more distant from the processes involved in gene expression itself, such as the assembly of cellular structures from their components, the nature of positional information, and the establishment of gradients.

If we could read the sequence of DNA of an organism, and express it correctly in the right temporal order, could we construct a living cell? Or is it possible to build certain cellular structures only if we have a pre-existing example? The answer is uncertain, but the perpetuation of cellular

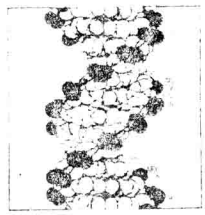
structures is undoubtedly a significant aspect of the relationship between genotype and phenotype.

The starting ground for considering macromolecular assembly is the sorting of proteins into different cellular compartments, a process that depends on their sequences as do their other functions, but which leads into the topic of considering the basis for the construction of compartments. A route toward analyzing the topography of gene expression may be provided by analyzing mutants that assemble defective embryos. Together with the power of present techniques for molecular analysis of gene expression, we may begin to analyze the interactions between gene activation or repression and assembly of the overall cell or multicellular structure.

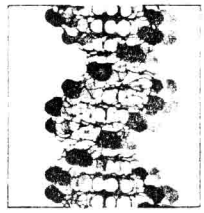
It should scarcely be necessary to say that science is about asking questions, but the common didactic teaching of science makes it worth noting that often in this book it is possible to pose questions that may be in the mind of the researcher, but for which the answers are not (yet) evident. The purpose of this book is to indicate the state of the art in such terms as well as to summarize current knowledge. Within this context, *GENES IV* analyzes gene expression and regulation and considers their consequences for the cell and the organism as a whole.

It is as always a pleasure to thank colleagues who generously have reviewed chapters, and I am especially grateful to Tania Baker, Michael Chamberlin, Ann Ganesan, Alex Gann, Martin Gellert, Michael Green, Joel Huberman, Alexander Johnson, Nancy Kleckner, Arthur Kornberg, Terry Platt, Mark Ptashne, James Rothman, Paul Schimmel, Matthew Scott, Philip Sharp, Allen Smith, Robert Thach, Robert Tjian, Andrew Travers, Harold Varmus, and Harold Weintraub. Michelle Hoffman read the entire manuscript and suggested many editorial improvements. And the production of this book became a family endeavor, in which the efforts of my wife, Ann, were crucial.

Benjamin Lewin
Cambridge, Massachusetts



OUTLINE



CONTENTS

CHAPTER 16
Lytic Cascades and Lysogenic Repression