

Molecular Biology

Principles of Genome Function

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NEW NEW NEW

- A focus on the underlying principles equips students with a robust conceptual framework on which to add further detail from the vast amount of scientific information available to us today.
- An emphasis on commonalities reflects the conserved molecular processes and components that we now know to exist between bacteria, archaea and eukaryotes.
- An integration of key themes and concepts throughout the book reflects how molecular phenomena like chromatin modification and RNA silencing have diverse impacts on genome function, and helps students to appreciate molecular biology as a unified discipline, with many components and phenomena acting in concert, rather than as a series of isolated topics.
- Clear demonstrations of the experimental basis of molecular biology reflect the central importance of experimental evidence to furthering our understanding of molecular biology. Experimental Approach panels describe pieces of research that have been undertaken, and which have been particularly valuable in elucidating difference aspects of molecular biology.

Molecular Biology: Principles of Genome Function offers a fresh, distinctive approach to the teaching of molecular biology. It is an approach which reflects the challenge of teaching a subject that is in many ways unrecognizable from the molecular biology of the 20th century - a discipline in which our understanding has advanced immeasurably, but about which many intriguing questions remain to be answered.

At heart, molecular biology is an experimental science, and a central element to the understanding of molecular biology is an appreciation of the approaches taken to yield the information from which concepts and principles are deduced. However, a mass of experimental evidence can make the grasping of the central ideas and paradigms that the experimental evidence has allowed us to elucidate more difficult. *Molecular Biology* responds to this challenge by complementing its coverage of key concepts in the main body of the text with separate *Experimental Approach* panels, which branch off from the text in a clearly-signposted way. These *Experimental Approach* panels describe pieces of research that have been undertaken, and which have been particularly valuable in elucidating difference aspects of molecular biology.

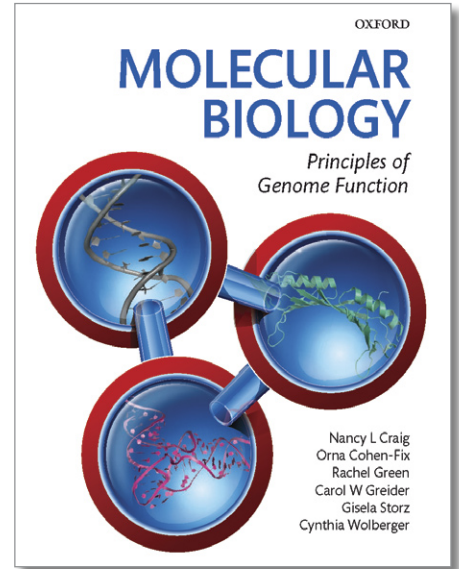
Among the students being taught today are the molecular biologists of tomorrow; these individuals will be in a position to ask fascinating questions about fields whose complexity and sophistication become more apparent with each year that passes. *Molecular Biology: Principles of Genome Function* is the perfect introduction to this challenging, dynamic, but ultimately fascinating discipline.

Readership: Undergraduates and beginning graduates studying molecular biology as part of any bioscience degree programme.

864 pages 2010 978-0-19-956206-0 Paperback £41.99

An engaging textbook that is both thorough and interesting; a rare thing today with textbooks that read like encyclopedias and dictionaries.

Doug Burks, Wilmington University



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1.5 EXPRESSION OF THE GENOME 019

fruit fly had red eyes, but a defect in a gene produced a mutant with white eyes, one could deduce that the function of gene was to determine eye color in some way (Figure 1.18).

This general approach is typically referred to as "forward genetics". For example, Figure 1.20 shows a single mutant Arabidopsis thaliana plant seedling surrounded by a group of wild-type plants. In the example shown, the phenotype of the mutant plant is an elongated stem while the genotype turns out to be a mutation in a gene encoding a blue light photoreceptor. A specific change in the gene for the blue photoreceptor is manifested as this obvious change in the growth properties of the plant. We will sometimes refer to these two different versions of the gene as the wild type and mutant alleles of the gene. An allele is thus a version of a gene.

With a more complete understanding of genomes and their complete composition, and with sophisticated tools of gene manipulation, it is now possible to specifically disrupt a gene of interest in some organisms and to study the phenotypic consequences. This powerful approach is typically referred to as reverse genetics and has been used with wide success to decipher gene functions.

Genotypic changes have phenotypic consequences

In forward genetic studies, the phenotype of the mutant organism is typically reached by the scientist with the ultimate goal being to identify the specific changes in the DNA (mutation) that resulted in the phenotype in question. This type of analysis in principle establishes causality in that a certain change in the DNA results in the physical properties being followed.

Mutations that cause differences from the wild type organism are typically categorized as recessive or dominant. These terms are somewhat misleading here since recessivity that organisms do not always have just a single copy of a given gene. If, in a diploid, the phenotype of the mutant gene product is masked by the presence of the wild-type version, then the mutation is said to be recessive. A common example of a recessive mutation is a change in an enzyme that reduces its activity, but which is compensated for by the wild-type version that provides sufficient activity. By contrast, if a mutant gene product has obvious phenotypic consequences when the wild-type product is present, then the mutation is said to be dominant. A common example of a dominant mutation might be a change in a structural protein that disrupts higher-order protein structure, such that filament formation is globally disrupted by the presence of the mutant protein. Figure 1.21 shows schematically how recessive and dominant mutations impact mouse coat color.

What is the physical nature of the mutations that can cause such phenotypic changes? The mutations can be the result of very small changes in the gene (i.e. the alteration of a nucleotide), the rearrangement of large regions of the chromosome, the insertion of new segments of DNA or the deletion or excision of small or large sections of the genome (Figure 1.22). These changes can result in direct changes to the gene product encoded by a gene, such as the genetic make-up of a protein gene expression (where the actual identity of the gene product is not changed). Mutations that eliminate the function of a gene are termed null or loss-of-function mutations. These types of mutations typically are associated either with a change in the product that completely eliminates function or a large disruption in the DNA sequence that eliminates gene expression.

Figure 1.18 Drosophila mutant with a defective separation gene (Sti) has red eyes in eye (left), white mutant flies (right) in Jerry Bergelson/Science Photo Library

Figure 1.20 Arabidopsis mutant unable to sense blue light. The stem (frons) is elongated in the mutant (right) compared to the wild type (left) in the presence of blue light. Photo by Dr. David B. Clark, University of California, Berkeley

020 CHAPTER 1 GENOMES AND THE FLOW OF BIOLOGICAL INFORMATION

Single nucleotide changes in the DNA sequence can directly result in changes in the identity of the encoded gene product (either RNA or protein). In protein coding genes a change of one nucleotide can be sufficient to change a codon from one which encodes a particular amino acid to one encoding a different one. Such changes in amino acid identity are referred to as missense mutations (Figure 1.23). If the amino acid substitution results in a gene function being completely lost the missense mutation can be thought of as a null mutation. By contrast, other substitutions may result in the production of partially functional gene products.

In some cases, there can be a change in the DNA sequence that introduces a premature stop signal such that only unneeded species of the protein product are made. Such changes are typically referred to as nonsense mutations (Figure 1.23). Sometimes there are changes in the DNA sequence that do not result in obvious phenotypic changes. Such changes are typically referred to as silent mutations (Figure 1.23).

The origin of disease can often be traced to mutations in the organism

In multicellular organisms, there are two general types of cell:

- somatic cells - these constitute the building blocks of the body of an organism and usually transmit their genetic information to daughter cells in the same organism
- germline cells - these are involved in the production of the gametes and transmit the genetic information to the next generation of the organism.

Consequently, mutations found in the germline cells typically affect the progeny of the organism whereas those found in somatic cells affect the organism itself. Our common knowledge of the genetic make-up of an organism and its environmental influences, such as diet and exposure to different environmental conditions, determine the relative extent to which the genotype (nature) and the environment (nurture) influence the phenotype associated with a specific mutation has long been debated and undoubtedly will continue to be a subject of controversy. In the example of the BRCA1 and BRCA2 mutations, other genetic factors clearly influence whether individuals are more or less susceptible to developing cancer, but environmental

Figure 1.21 Effects of dominant and recessive coat color mutations in mice. In the cross between two parent (P) individuals the wild type (left) and mutant (right) alleles contribute a gene with a dominant mutation, all offspring will have the phenotype of the parent carrying the dominant mutation. In the cross between two parent (P) individuals the wild type gene and another parent that contributing a gene with a recessive mutation, all offspring will have the phenotype of the parent carrying the wild type gene.

Figure 1.22 Types of mutation. The insertion of DNA is indicated by a large red arrow. The deletion of DNA is indicated by a large red arrow. The rearrangement, excision of DNA (insertion or resection of DNA) is indicated by a large red arrow.

Cell Signalling

Third Edition

John Hancock

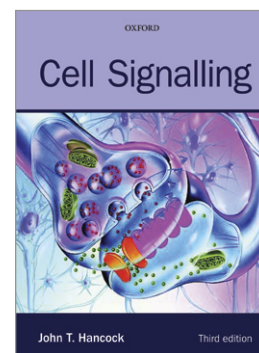
Signalling within and between cells is an essential part of many biological processes, from the development of the body, to the activity of our immune system. *Cell Signalling* presents a carefully structured introduction to this intricate subject, introducing those conserved features that underlie many different extra- and intracellular signalling systems.

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Readership: Advanced undergraduate and beginning graduate students of cell and molecular biology, and biochemistry. Also of interest to students of other biological disciplines who need to have an understanding of cell signalling (for example, immunology and developmental biology).

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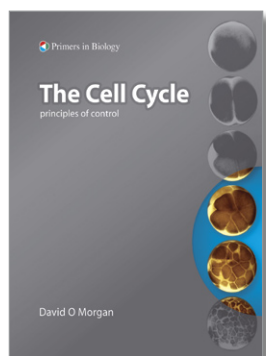
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Primers in Biology

328 pages 2006 978-0-19-920610-0 Paperback £32.99



I have enjoyed reading this textbook cover to cover. I have learned new things from chapters that lie outside of my own specialisation of chromosome duplication, and have made interesting new connections. As a university teacher and researcher, I can strongly recommend David Morgan's textbook to students with a background in molecular biology who are interested in the regulation of the eukaryotic cell cycle.

Torsten Krude in BioEssays

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