Exhibit 2

MOLECULAR BIOLOGY OF
THE CELL
THIRD EDITION

Bruce Alberts • Dennis Bray
Julian Lewis • Martin Raff • Keith Roberts
James D. Watson

Garland Publishing, Inc.
New York & London

Text Editor: Miranda Robertson
Managing Editor: Ruth Adams
Illustrator: Nigel Orme
Molecular Model Drawings: Kate Hesketh-Moore
Director of Electronic Publishing: John M-Roblin
Computer Specialist: Chuck Bartelt
Disk Preparation: Carol Winter
Copy Editor: Shirley M. Cobert
Production Editor: Douglas Goertzen
Production Coordinator: Perry Bessas
Indexer: Maija Hinkle

Bruce Alberts received his Ph.D. from Harvard University and is currently President of the National Academy of Sciences and Professor of Biochemistry and Biophysics at the University of California, San Francisco. *Dennis Bray* received his Ph.D. from the Massachusetts Institute of Technology and is currently a Medical Research Council Fellow in the Department of Zoology, University of Cambridge. *Julian Lewis* received his D.Phil. from the University of Oxford and is currently a Senior Scientist in the Imperial Cancer Research Fund Developmental Biology Unit, University of Oxford. *Martin Raff* received his M.D. from McGill University and is currently a Professor in the MRC Laboratory for Molecular Cell Biology and the Biology Department, University College London. *Keith Roberts* received his Ph.D. from the University of Cambridge and is currently Head of the Department of Cell Biology, the John Innes Institute, Norwich. *James D. Watson* received his Ph.D. from Indiana University and is currently Director of the Cold Spring Harbor Laboratory. He is the author of *Molecular Biology of the Gene* and, with Francis Crick and Maurice Wilkins, won the Nobel Prize in Medicine and Physiology in 1962.

Library of Congress Cataloging-in-Publication Data
Molecular biology of the cell / Bruce Alberts . . . [et al.].—3rd ed.
p. cm.
Includes bibliographical references and index.
ISBN 0-8153-1619-4 (hard cover).—ISBN 0-8153-1620-8 (pbk.)
1. Cytology. 2. Molecular biology. I. Alberts, Bruce.
[DNLM: 1. Cells. 2. Molecular Biology. QH 581.2 M718 1994]
QH581.2.M64 1994
574.87—dc20
DNLM/DLC
for Library of Congress 93-45907
CIP

Published by Garland Publishing, Inc.
717 Fifth Avenue, New York, NY 10022

Printed in the United States of America

15 14 13 12 10 9 8 7 6 5 4 3

Front cover: The photograph shows a rat nerve c in culture. It is labeled (*yellow*) with a fluorescer antibody that stains its cell body and dendritic processes. Nerve terminals (*green*) from other neurons (not visible), which have made synapses the cell, are labeled with a different antibody. (Courtesy of Olaf Mundigl and Pietro de Camilli.)

Dedication page: Gavin Borden, late president of Garland Publishing, weathered in during his mid-1980s climb near Mount McKinley with MBoC author Bruce Alberts and famous mountai guide Mugs Stump (1940–1992).

Back cover: The authors, in alphabetical order, crossing Abbey Road in London on their way to lu Much of this third edition was written in a house around the corner. (Photograph by Richard Olivi

carrier protein
Membrane transport protein that binds to a solute and transports it across the membrane by undergoing a series of conformational changes.

cartilage
Form of connective tissue composed of cells (chondrocytes) embedded in a matrix rich in type II collagen and chondroitin sulfate.

catabolism
General term for the enzyme-catalyzed reactions in a cell by which complex molecules are degraded to simpler ones with release of energy. Intermediates in these reactions are sometimes called catabolites.

catalyst
Substance that accelerates a chemical reaction without itself undergoing a change. Enzymes are protein catalysts.

***cdc* gene (cell-division-cycle gene)**
Gene that controls a specific step or set of steps in the cell cycle. Originally identified in yeasts.

Cdk protein—*see* cyclin-dependent protein kinase

cDNA—*see* complementary DNA

cell-adhesion molecule (CAM)
Protein on the surface of an animal cell that mediates cell-cell binding.

cell body
Main part of a nerve cell that contains the nucleus. The other parts are axons and dendrites.

cell cortex
Specialized layer of cytoplasm on the inner face of the plasma membrane. In animal cells it is an actin-rich layer responsible for cell-surface movements.

cell cycle
Reproductive cycle of the cell: the orderly sequence of events by which the cell duplicates its contents and divides into two.

cell division
Separation of a cell into two daughter cells. In eucaryotic cells it entails division of the nucleus (mitosis) closely followed by division of the cytoplasm (cytokinesis).

cell fusion
Process in which the plasma membranes of two cells break down at the point of contact between them, allowing the two cytoplasms to mingle.

cell junction
Specialized region of connection between two cells or between a cell and the extracellular matrix.

cell line
Population of cells of plant or animal origin capable of dividing indefinitely in culture.

cell locomotion (cell migration)
Active movement of a cell from one location to another, particularly the migration of a cell over a surface.

cell-mediated immunity
Immune responses mediated by T lymphocytes.

cell plate
Flattened membrane-bounded structure that forms from fusing vesicles in the cytoplasm of a dividing plant cell and is the precursor of the new cell wall.

cell wall
Mechanically strong extracellular matrix deposited by a cell outside its plasma membrane. It is prominent in most plants, bacteria, algae, and fungi. Not present in most animal cells.

cellulose
Structural polysaccharide consisting of long chains of covalently linked glucose units. It provides tensile strength in plant cell walls.

central nervous system (CNS)
Main information-processing organ of the nervous system. In vertebrates it consists of the brain and spinal cord.

centriole
Short cylindrical array of microtubules, closely similar in structure to a basal body. A pair of centrioles is usually found at the center of a centrosome in animal cells.

centromere
Constricted region of a mitotic chromosome that holds sister chromatids together; also the site on the DNA where the kinetochore forms and then captures microtubules from the mitotic spindle.

centrosome (cell center)
Centrally located organelle of animal cells that is the primary microtubule organizing center and acts as the spindle pole during mitosis. In most animal cells it contains a pair of centrioles.

chaperone (molecular chaperone)
Protein that helps other proteins avoid misfolding pathways that produce inactive or aggregated states.

checkpoint
Point in the eucaryotic cell-division cycle where progress through the cycle can be halted until conditions are suitable for the cell to proceed to the next stage.

chelate
Combine reversibly, usually with high affinity, with a metal ion such as iron, calcium, or magnesium.

chemiosmotic coupling
Mechanism in which a gradient of hydrogen ions (a pH gradient) across a membrane is used to drive an energy-requiring process, such as ATP production or the rotation of bacterial flagella.

chemotaxis
Motile response of a cell or an organism that carries it toward or away from a diffusible chemical.

Chlamydomonas
Unicellular green alga with two flagella.

chlorophyll
Light-absorbing pigment that plays a central part in photosynthesis.

chloroplast
Specialized organelle in green algae and plants that contains chlorophyll and performs photosynthesis. It is a specialized form of plastid.

cholesterol
Lipid molecule with a characteristic four-ringed steroid structure that is an important component of the plasma membranes of animal cells. (*See* Figure 10–8.)

chromaffin cell
Cell that stores adrenaline in secretory vesicles and secretes it in times of stress when stimulated by the nervous system.

chromatid
One copy of a chromosome formed by DNA replication that is still joined at the centromere to the other copy.

chromatin
Complex of DNA, histones, and nonhistone proteins found in the nucleus of a eucaryotic cell. The material of which chromosomes are made.

chromatography
Biochemical technique in which a mixture of substances is separated by charge, size, or some other property by allowing it to partition between a moving phase and a stationary phase.

chromosome
Structure composed of a very long DNA molecule and associated proteins that carries part (or all) of the hereditary information of an organism. Especially evident in plant and animal cells undergoing mitosis or meiosis, where each chromosome becomes condensed into a compact, readily visible thread.

cilium (plural **cilia**)
Hairlike extension of a cell containing a core bundle of microtubules and capable of performing repeated beating movements. Cilia are found in large numbers on the surface of many eucaryotic cells, and they are responsible for the swimming of many single-celled organisms.

cisterna (plural **cisternae**)
Flattened membrane-bounded compartment, as found in the endoplasmic reticulum or Golgi apparatus.

citric acid cycle (TCA, or tricarboxylic acid cycle; Krebs cycle)
Central metabolic pathway found in all aerobic organisms. Oxidizes acetyl groups derived from food molecules to CO_2 and H_2O. Occurs in mitochondria in eucaryotic cells.

clathrin
Protein that assembles into a polyhedral cage on the cytoplasmic side of a membrane so as to form a clathrin-coated pit, which buds off to form a clathrin-coated vesicle.

cleavage
(1) Physical splitting of a cell into two. (2) Specialized type of cell division seen in many early embryos whereby a large cell becomes subdivided into many smaller cells without growth.

clone
Population of cells or organisms formed by repeated (asexual) division from a common cell or organism. Also used as a verb: "to clone a gene" means to produce many copies of a gene by repeated cycles of replication.

cloning vector
Genetic element, usually a bacteriophage or plasmid, that is used to carry a fragment of DNA into a recipient cell for the purpose of gene cloning.

coated pit
Invagination of the plasma membrane associated with a bristlelike layer of protein on its cytoplasmic surface. Pinches off to form a coated vesicle in the process of endocytosis.

coated vesicle
Small membrane-bounded organelle formed by the pinching off of a coated region of membrane. Some coats are made of clathrin, whereas others are made from other proteins.

codon
Sequence of three nucleotides in a DNA or messenger RNA molecule that represents the instruction for incorporation of a specific amino acid into a growing polypeptide chain.

coenzyme
Small molecule tightly associated with an enzyme that participates in the reaction that the enzyme catalyzes, often by forming a transient covalent bond to the substrate. Examples include biotin, NAD^+, and coenzyme A.

coenzyme A
Small molecule used in the enzymatic transfer of acyl groups in the cell. (*See also* **acetyl CoA** and Figure 2–20.)

cofactor
Inorganic ion or coenzyme that is required for an enzyme's activity.

coiled-coil
Especially stable rodlike protein structure formed by two α helices coiled around each other.

collagen
Fibrous protein rich in glycine and proline that is a major component of the extracellular matrix and connective tissues. Exists in many forms: type I, the most common, is found in skin, tendon, and bone; type II is found in cartilage; type IV is present in basal laminae.

combinatorial
Describes any process that is governed by a specific combination of factors (rather than by any single factor), with different combinations having different effects.

complement
System of serum proteins activated by antibody-antigen complexes or by microorganisms. Helps eliminate pathogenic microorganisms by directly causing their lysis or by promoting their phagocytosis.

complementary DNA (cDNA)
DNA molecule made as a copy of mRNA and therefore lacking the introns that are present in genomic DNA. Used to determine the amino acid sequence of a protein by DNA sequencing or to make the protein in large quantities by cloning followed by expression.

complementary nucleotide sequence
Two nucleic acid sequences are said to be complementary if they can form a perfect base-paired double helix with each other.

complex
Assembly of molecules that are held together by noncovalent bonds. Protein complexes perform most cell functions.

conformation
Spatial location of the atoms of a molecule—for example, the precise shape of a protein or other macromolecule in three dimensions.

connective tissue
Any supporting tissue that lies between other tissues and consists of cells embedded in a relatively large amount of extracellular matrix. Includes bone, cartilage, and loose connective tissue.

connexon
Water-filled pore in the plasma membrane formed by a ring of six protein subunits. Part of a gap junction: connexons from two adjoining cells join to form a continuous channel between the two cells.

free-energy change (ΔG)
Change in the free energy during a reaction: the free energy of the product molecules minus the free energy of the starting molecules. A large negative value of ΔG indicates that the reaction has a strong tendency to occur. (*See* Panel 14–1, pp. 668–669.)

G_0 phase
(G-"zero" phase) State of withdrawal from the eucaroytic cell-division cycle by entry into a quiescent G_1 phase; often seen in differentiated cells.

G_1 phase
Gap 1 phase of the eucaryotic cell-division cycle, between the end of cytokinesis and the start of DNA synthesis.

G_2 phase
Gap 2 phase of the eucaryotic cell-division cycle, between the end of DNA synthesis and the beginning of mitosis.

G protein
One of a large family of heterotrimeric GTP-binding proteins that are important intermediaries in cell-signaling pathways. Usually activated by the binding of a hormone or other signaling ligand to a seven-pass transmembrane receptor protein.

GAG (glycosaminoglycan)
Long, linear, highly charged polysaccharide composed of a repeating pair of sugars, one of which is always an amino sugar. Mainly found covalently linked to a protein core in extracellular matrix proteoglycans. Examples include chondroitin sulfate, hyaluronic acid, and heparin.

gamete
Specialized haploid cell, either a sperm or an egg, serving for sexual reproduction.

ganglion (plural **ganglia**)
Cluster of nerve cells and associated glial cells located outside the central nervous system.

ganglioside
Any glycolipid having one or more sialic acid residues in its structure. Found in the plasma membrane of eucaryotic cells and especially abundant in nerve cells.

gap junction
Communicating cell-cell junction that allows ions and small molecules to pass from the cytoplasm of one cell to the cytoplasm of the next.

gastrula
Animal embryo at an early stage of development where cells are invaginating to form the rudiment of a gut cavity. (From Greek *gaster*, belly.)

gene
Region of DNA that controls a discrete hereditary characteristic, usually corresponding to a single protein or RNA. This definition includes the entire functional unit, encompassing coding DNA sequences, noncoding regulatory DNA sequences, and introns.

gene regulatory protein
General name for any protein that binds to a specific DNA sequence to alter the expression of a gene.

general transcription factor
Any of the proteins whose assembly around the TATA box is required for the initiation of transcription of most eucaryotic genes.

genetic code
Set of rules specifying the correspondence between nucleotide triplets (codons) in DNA or RNA and amino acids in proteins.

genome
Total genetic information carried by a cell or an organism.

genomic DNA
DNA constituting the genome of a cell or an organism. Often used in contrast with cDNA (DNA prepared by reverse transcription from messenger RNA).

genotype
Genetic constitution of an individual cell or organism.

germ cells
Precursor cells that give rise to gametes.

germ line
The lineage of germ cells (which contribute to the formation of a new generation of organisms), as distinct from somatic cells (which form the body and leave no descendants).

giga-
Prefix denoting 10^9. (From Greek *gigas*, giant.)

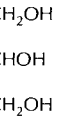
glial cells
Supporting cells of the nervous system, including oligodendrocytes and astrocytes in the vertebrate central nervous system and Schwann cells in the peripheral nervous system.

globular protein
Any protein with an approximately rounded shape; contrasts with highly elongated, fibrous proteins such as collagen.

glucose
Six-carbon sugar that plays a major role in the metabolism of living cells. Stored in polymeric form as glycogen in animal cells and as starch in plant cells. (*See* Panel 2–3, pp. 52–53.)

glutaraldehyde
Small reactive molecule with two aldehyde groups that is often used as a cross-linking fixative.

glycerol
Small organic molecule that is the parent compound of many small molecules in the cell, including phospholipids.



glycocalyx (cell coat)
Carbohydrate-rich layer that forms the outer coat of a eucaryotic cell. Composed of the oligosaccharides linked to intrinsic plasma membrane glycoproteins and glycolipids, as well as glycoproteins and proteoglycans that have been secreted and reabsorbed onto the cell surface.

glycogen
Polysaccharide composed exclusively of glucose units used to store energy in animal cells. Large granules of glycogen are especially abundant in liver and muscle cells.

glycolipid
Membrane lipid molecule with a short carbohydrate chain attached to a hydrophobic tail.

glycolysis
Ubiquitous metabolic pathway in the cytosol in which sugars are incompletely degraded with production of ATP. (Literally, "sugar splitting.")