WILEY-VCH

Encyclopedia of Molecular Cell Biology and Molecular Medicine

Edited by Robert A. Meyers

Volume 16

Second Edition

Index

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Volume 16
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Preface

The *Encyclopedia of Molecular Cell Biology and Molecular Medicine*, which is the successor and second edition of the *Encyclopedia of Molecular Biology and Molecular Medicine* (VCH Publishers, Weinheim), covers the molecular and cellular basis of life at a university and professional researcher level. The first edition, published in 1996–97, was very successful and is being used in libraries around the world. This second edition will almost double the first edition in length and will comprise the most detailed treatment of both molecular cell biology and molecular medicine available today. The Board Members and I believe that there is a serious need for this publication, even in view of the vast amount of information available on the World Wide Web and in text books and monographs. We feel that there is no substitute for our tightly organized and integrated approach to selection of articles and authors and implementation of peer review standards for providing an authoritative single-source reference for undergraduate and graduate students, faculty, librarians, and researchers in industry and government.

Our purpose is to provide a comprehensive foundation for the expanding number of molecular biologists, cell biologists, pharmacologists, biophysicists, biotechnologists, biochemists, and physicians, as well as for those entering molecular cell biology and molecular medicine from majors or careers in physics, chemistry, mathematics, computer science, and engineering. For example, there is an unprecedented demand for physicists, chemists, and computer scientists who will work with biologists to define the genome, proteome, and interactome through experimental and computational biology.

The Board Members and I first divided the entire study of molecular cell biology and molecular medicine into primary topical categories and further defined each of these into subtopics. The following is a summary of the topics and subtopics:

- *Nucleic Acids:* amplification, disease genetics overview, DNA structure, evolution, general genetics, nucleic acid processes, oligonucleotides, RNA structure, RNA replication and transcription.
- *Structure Determination Technologies Applicable to Biomolecules:* chromatography, labeling, large structures, mapping, mass spectrometry, microscopy, magnetic resonance, sequencing, spectroscopy, X-ray diffraction.
- *Biochemistry:* carbohydrates, chirality, energetics, enzymes, biochemical genetics, inorganics, lipids, mechanisms, metabolism, neurology, vitamins.

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- *Proteins, Peptides, and Amino Acids:* analysis, enzymes, folding, mechanisms, modeling, peptides, structural genomics (proteomics), structure, types.
- *Biomolecular Interactions:* cell properties, charge transfer, immunology, recognition, senses.
- *Cell Biology:* developmental cell biology, diseases, dynamics, fertilization, immunology, organelles and structures, senses, structural biology, techniques.
- *Molecular Cell Biology of Specific Organisms:* algae, amoeba, birds, fish, insects, mammals, microbes, nematodes, parasites, plants, viruses, yeasts.
- *Molecular Cell Biology of Specific Organs or Systems:* excretory, lymphatic, muscular, nervous, reproductive, skin.
- *Molecular Cell Biology of Specific Diseases:* cancer, circulatory, endocrinal, environmental stress, immune, infectious, neurological, radiational.
- *Pharmacology:* chemistry, disease therapy, gene therapy, general molecular medicine, synthesis, toxicology.
- *Biotechnology:* applications, diagnostics, gene-altered animals, bacteria and fungi, laboratory techniques, legal, materials, process engineering, nanotechnology, production of classes or specific molecules, sensors, vaccine production.

We then selected some 400 article titles and author or author teams to cover the above topics. Each article is designed as a self-contained treatment which begins with a keyword section including definitions, to assist the scientist or student who is unfamiliar with the specific subject area. The Encyclopedia includes more than 3000 key words, each defined within the context of the particular scientific field covered by the article. In addition to these definitions, the glossary of basic terms found at the back of each volume, defines the most commonly used terms in molecular cell biology. These definitions, along with the reference materials (the genetic code, the common amino acids, and the structures of the deoxyribonucleotides) printed at the back of each volume, should allow most readers to understand articles in the Encyclopedia without referring to a dictionary, textbook, or other reference work. There is, of course, a detailed subject index in Volume 16 as well as a cumulative table of contents and list of authors, as well as a list of scientists who assisted in the development of this Encyclopedia.

Each article begins with a concise definition of the subject and its importance, followed by the body of the article and extensive references for further reading. The references are divided into secondary references (books and review articles) and primary research papers. Each subject is presented on a first-principle basis, including detailed figures, tables and drawings. Because of the self-contained nature of each article, some articles on related topics overlap. Extensive cross-referencing is provided to help the reader expand his or her range of inquiry.

The articles contained in the Encyclopedia include core articles, which summarize broad areas, directing the reader to satellite articles that present additional detail and depth for each subject. The core article Brain Development is a typical example. This 45-page article spans neural induction, early patterning, differentiation, and wiring at a molecular through to cellular and tissue level. It is directly supported, and cross-referenced, by a number of molecular neurobiology satellite articles, for example, Behavior Genes, and further supported by other core presentations, for example, Developmental Cell Biology; Genetics, Molecular Basis of, and their satellite articles. Another example is the core article on Genetic Variation and Molecular Evolution by Werner Arber. It is supported by a number of satellite articles supporting the evolutionary relatedness of genetic information, for example, Genetic Analysis of Populations.

Approximately 250 article titles from the first edition are retained, but rewritten, half by new authors and half by returning authors. Approximately 80 articles on cell biology and 70 molecular biology articles have been added covering areas that have become prominent since preparation of the first edition. Thus, we have compiled a totally updated single source treatment of the molecular and cellular basis of life.

Finally, I wish to thank the following Wiley-VCH staff for their outstanding support of this project: Andreas Sendtko, who provided project and personnel supervision from the earliest phases, and Prisca-Maryla Henheik, who served as the managing editor.

November 2003

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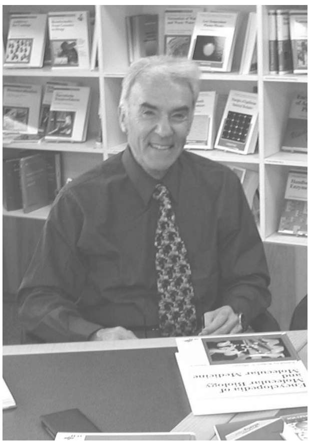
Editor-in-Chief

Editor-in-Chief



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Dr. Meyers earned his Ph.D. in organic chemistry from the University of California Los Angeles, was a post-doctoral fellow at California Institute of Technology and manager of chemical processes for TRW Inc. He has published in *Science*, written or edited 12 scientific books and his research has been reviewed in the *New York Times* and the *Wall Street Journal*. He is one of the most prolific science editors in the world having originated, organized and served as Editor-in-Chief of three editions of the *Encyclopedia of Physical Science and Technology*, the *Encyclopedia of Analytical Chemistry* and two editions of the present *Encyclopedia of Molecular Cell Biology and Molecular Medicine*.

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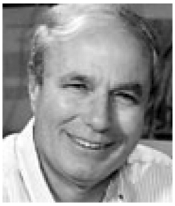

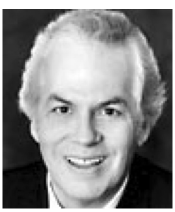

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Cumulative Subject Index Volume 1 to Volume 15

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Glossary of Basic Terms

The most basic terms in molecular cell biology are defined below. These, in combination with the key words listed at the head of each article, provide definitions of all essential terms in this Encyclopedia.

Alleles
Alternative forms of a given gene, inherited separately from each parent, differing in nucleotide base sequence and located in a specific position on each homologous chromosome, affecting the functioning of a single product (RNA and/or protein).

Amino Acid
An organic compound containing at least one amino group and one carboxyl group. In the 20 different amino acids that compose proteins, an amino group and carboxyl group are linked to a central carbon atom, the α-carbon, to which a variable side chain is bound (see pages at the back of each volume).

Amplification
The process of replication of specific DNA sequences in disproportionately greater amounts than are present in the parent genetic material, for example, PCR is an *in vitro* amplification technique.

Apoptosis
Regulated process leading to nonpathological animal cell death via a series of well-defined morphological changes; also called *programmed cell death*.

Bacteriophage (phage)
Any virus (containing DNA or RNA) that infects bacterial cells. Some bacteriophages are widely used as cloning vectors.

Base Pair
Association of two complementary nucleotides in a DNA or RNA molecule stabilized by hydrogen bonding between their base components. Adenine pairs with thymine or uracil (A–T; A–U) and guanine pairs with cytosine (G–C) (see pages at the back of each volume).

Bioinformatics
Computational approaches to answer biological questions and enhance the ability of researchers to manipulate, collect, and analyze data more quickly and in new ways. Experts predict that more biologists will do their work *in silico*, using the computer to synthesize, analyze, and interpret the many terabytes of data now being generated.

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cDNA (complementary DNA)
A DNA copy of an RNA molecule synthesized from an mRNA template *in vitro* using an enzyme called *reverse transcriptase*; often used as a probe.

Cell Cycle
Ordered sequence of events in which a cell duplicates its chromosomes and divides itself into two. Most eukaryotic cell cycles can be commonly divided into four phases: G_1 (G1) period after mitosis but before DNA synthesis occurs; S-phase when most DNA replication occurs; G_2 (G2) phase period of cell cycle when cells contain twice the G1 complement of DNA; and M-phase when cell division occurs, yielding two daughter cells (mitosis) each with one complete genome.

Cell Differentiation
Progressive restriction of the developmental potential and increasing specialization of function that takes place during the development of the embryo and leads to the formation of specialized cells, tissues, and organs.

Cell Division
Separation of a cell into two daughter cells. In higher eukaryotes, it involves division of the nucleus (mitosis) and of the cytoplasm (cytokinesis); mitosis often is used to refer to both nuclear and cytoplasmic division.

Cell Line
A defined unique population of cells obtained by culture from a primary implant through numerous generations.

Chromatin
The complex of nucleic acids (DNA and RNA) and proteins (histones) comprising eukaryotic chromosomes.

Chromosome
In prokaryotes, the usually circular duplex DNA molecule constituting the genome; in eukaryotes, a threadlike structure consisting of chromatin and carrying genomic information on a DNA double helix molecule. A viral chromosome may be composed of DNA or RNA.

Cloning
Asexual reproduction of cells, organisms, genes, or segments of DNA identical to the original.

Cloning Vector *see* Vector

Codon
Sequence of three nucleotides in DNA or mRNA that specifies a particular amino acid during protein synthesis; also called *triplet*. Of the 64 possible codons, three are stop codons, which do not specify amino acids (see pages at the back of each volume).

Complementary Base Pairing
Nucleic acid sequences on paired polymers with opposing hydrogen-bonded bases adenine (designated A) bonded to thymine (T), guanine (G) to cytosine (C) in DNA and adenine to uracil (U) replacing adenine to thymine in RNA (see pages at the back of each volume).

Complementary DNA see cDNA

Dalton
Unit of molecular mass approximately equal to the mass of a hydrogen atom (1.66×10^{-24} g).

Deoxyribonucleic Acid *see* DNA

Diploid
The number of chromosomes in most cells except the gametes. In humans, the diploid number is 46.

DNA (Deoxyribonucleic Acid)
The molecular basis of the genetic code consisting of a poly-sugar phosphate backbone from which thymine, adenine, guanine, and cytosine bases project. Usually found as two complementary chains (duplex) forming a double helix associated by hydrogen bonds between complementary bases.

DNA Cloning (Gene Cloning)
Recombinant DNA technique in which specific cDNAs or fragments of genomic DNA are inserted into a cloning vector, which then is incorporated into cultured host cells (e.g., *E. coli* cells) and maintained during growth of the host cells.

DNA Library
Collection of cloned DNA molecules consisting of fragments of the entire genome (genomic library) or of DNA copies of all the mRNAs produced by a cell type (cDNA library) inserted into a suitable cloning vector.

DNA Polymerase
Enzymes that catalyze the replication of DNA from the deoxyribonucleotide triphosphates using single- or double-stranded DNA as a template.

DNA Transcription *see* Transcription

E. coli (Escherichia coli)
A colon bacillus, which is the most studied of all forms of life.

Embryonic Stem Cells (ES)
Cultured cells derived from the pluripotent inner cell mass of blastocyst-stage embryos.

Epigenetics
Mechanisms of storing and transmitting cellular information additional to those based on DNA sequences.

Escherichia coli see E. coli

Eukaryotes
Organisms whose cells have their genetic material packed in a membrane-surrounded, structurally discrete nucleus and with well-developed cell organelles. Eukaryotes include all organisms except *archaebacteria* and *eubacteria*.

Expression
The process of making the product of a gene, which is either a specific protein giving rise to a specific trait or RNA forms not translated into proteins (e.g. transfer ribosomal RNAs).

Functional Genomics
A discipline that aims to understand how genes are regulated and what they do, largely through massive parallel studies of gene expression over time and in a variety of tissues.

Gamete
Specialized haploid cell (in animals either a sperm or an egg) produced by meiosis of germ cells; in sexual reproduction, the union of a sperm and an egg initiates the development of a new diploid individual.

Gene Cloning *see* DNA Cloning

Gene
A DNA sequence, located in a particular position on a particular chromosome,

which encodes a specific protein or RNA molecule.

Genomics
Comparative analysis of the complete genomic sequences from different organisms; used to assess evolutionary relations between species and to predict the number and general types of proteins produced by an organism.

Genotype
Entire genetic constitution of an individual cell or organism; also, the alleles at one or more specific loci.

Haploid
The number of chromosomes in a sperm or egg cell, half the diploid number.

Heterozygous
Having two different alleles for a given trait in the homologous chromosomes.

Homologies
Similarities in DNA or protein sequences between individuals of the same species or among different species.

Homologous Chromosomes
Chromosome pairs, each derived from one parent, containing the same linear sequence of genes, and as a consequence, each gene is present in duplicate (e.g., humans have 23 homologous chromosome pairs, but the toad has 11 pairs, the mosquito has three pairs, and so on).

Homozygous
Having two identical alleles for a given trait in the homologous chromosomes.

Hybridization
The formation of a double-stranded polynucleotide molecule when two complementary strands are brought together at moderate temperature. The strands can be DNA or RNA or one of each; a technique for assessing the extent of sequence homology between single strands of nucleic acids.

Ligation
The formation of a phosphodiester bond to join adjacent terminal nucleotides (nicks) to form a longer nucleic acid chain (DNA of RNA); catalyzed by ligase.

Marker
A gene or a restriction enzyme cutting site with a known location on a chromosome and a clear-cut phenotype (expression), or pattern of inheritance, used as a point of reference when mapping a new mutant.

Meiosis
In eukaryotes, a special type of cell division that occurs during maturation of germ cells; comprises two successive nuclear and cellular divisions, with only one round of DNA replication resulting in production of four genetically nonequivalent haploid cells (gametes) from an initial diploid cell.

Messenger RNA *see* mRNA

Mitosis
In eukaryotic cells, the process whereby the nucleus is divided, involving condensation of the DNA into visible chromosomes, to produce two genetically equivalent daughter nuclei with the diploid number of chromosomes.

mRNA (messenger RNA)
RNA used to translate information from DNA to ribosome where the information is used to make one or several proteins.

Mutation
The heritable change in the nucleotide sequence of a chromosome.

Nucleotide
The monomer which, when polymerized, forms DNA or RNA. It is composed of a nitrogenous base bonded to a sugar (ribose or deoxyribose), bonded to a phosphate.

Oligonucleotide
A polynucleotide 2 to 20 nucleotide units in length.

Operon
A series of prokaryote genes encoding enzymes of a specific biosynthesis pathway and transcribed into a single RNA molecule.

Organelle
Any membrane-limited structure found in the cytoplasm of eukaryotic cells.

Phage *see* Bacteriophage

Phenotype
The observable characteristics of a cell or organism as distinct from it's genotype.

Plasmid
An extrachromosomal circular DNA molecule found in a variety of bacteria encoding "dispensable functions," such as resistance to antibiotics. Often found in multiple copies per cell and reproduces every time the bacterial cell reproduces. May be used as a cloning vector.

Polymorphism
Difference in DNA sequence among individuals expressed as different forms of a protein in individuals of the same interbreeding population.

Polynucleotide
The polymer formed by condensation of nucleotides.

Probe
A radioactively fluorescent or immunologically labeled oligonucleotide (RNA or DNA) used to detect complementary sequences in a hybridization experiment, for example, identify bacterial colonies that contain cloned genes or detect specific nucleic acids following separation by gel electrophoresis.

Procaryotes (Prokaryotes)
Typically unicellular or filamentous with DNA not located within a nuclear envelope. Prokaryotes include archaebacteria, eubacteria, cyanobacteria, prochlorophytes and mycoplasmas.

Programmed Cell Death *see* Apoptosis

Prokaryotes *see* Procaryotes

Protein
A linear polymer of amino acids linked together in a specific sequence and usually containing more than 50 residues. Proteins form the key structure elements in cells and participate in nearly all cellular activities.

Proteomics
A discipline that promises to determine the identity, function, and structure of each protein in an organelle or cell and to elucidate protein–protein interactions.

Replication
The copying of a DNA molecule duplex yielding two new DNA duplex molecules, each with one strand from the original DNA duplex. Single-stranded DNA

replication results in a single-stranded DNA molecule.

Repressor
A protein that binds to a specific location (operator) on DNA and prevents RNA transcription from a specific gene or operon.

Restriction Fragment Length Polymorphism *see* RFLP

Restriction Mapping
Uses restriction endonuclease enzymes to produce specific cuts (cleavage) in DNA, allowing preparation of a genome map describing the order and distance between cleavage sites.

Reverse Transcription
The synthesis of cDNA from an RNA template as catalyzed by reverse transcriptase.

RFLP (Restriction Fragment Length Polymorphism)
DNA fragment cut by enzymes specific to a base sequence (restriction endonuclease) generating a DNA fragment whose size varies from one individual to another. Used as markers on genome maps and for screening for mutations and genetic diseases.

Ribonucleic Acid *see* RNA

Ribosomes
Small cellular components composed of proteins plus ribosomal RNA that translate the genetic code into synthesis of specific proteins.

RNA (Ribonucleic Acid)
A single-stranded polynucleotide with a phosphate oxyribose backbone and four bases that are identical to those in DNA, with the exception that the base uracil is substituted for thymine.

RNA Interference (RNAi)
Intracellular degradation of RNA that removes foreign RNAs such as those from viruses. These fragments (small, micro, or mini RNA) cleaved from free double-stranded RNA (dsRNA) direct the degradative mechanism to other similar RNA sequences. Used as a technique to silence the expression of targeted genes in a sequence-dependent mode.

RNA Polymerase
The enzyme (peptide) that binds at specific nucleotide sequences, called promoters, in front of genes in DNA, which catalyze transcription of DNA to RNA.

RNA Translation *see* Translation

Stem Cell
A self-renewing cell that divides to give rise to a cell with an identical developmental potential and/or one with a more restricted developmental potential.

Structural Biology
The discovery, analysis and dissemination of three-dimensional structures of protein, DNA, RNA, and other biological macromolecules representing the entire range of structural diversity found in nature.

Transcription (DNA transcription)
Synthesis of an RNA molecule from a DNA template (gene) catalyzed by RNA polymerase.

Transfer RNA *see* tRNA

Translation (RNA translation)
The process on a ribosome by which the sequence of nucleotides in a mRNA

molecule directs the incorporation of amino acids into protein.

tRNA (transfer RNA)
RNA molecules that transport specific amino acids to ribosomes into position in the correct order during protein synthesis.

Vector
A DNA molecule originating from a virus, a plasmid, or a cell of a higher organism into which another DNA fragment can be integrated without loss of the vector's capacity for self-replication. Vectors introduce foreign DNA into host cells where it can be reproduced in large quantities.

Virus
A small parasite consisting of nucleic acid (RNA or DNA) enclosed in a protein coat that can replicate only in a susceptible host cell; widely used in cell biology research.

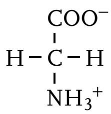
Wild type
Normal, nonmutant form of a macromolecule, cell or organism.

Zygote
A fertilized egg; a diploid cell resulting from fusion of a male and female gamete.

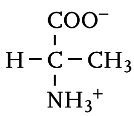
The Twenty Amino Acids that are Combined to Form Proteins in Living Things

Amino acids with nonpolar side chains

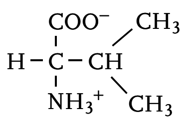
Glycine
Gly
G



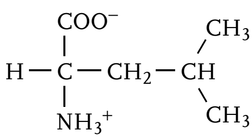
Alanine
Ala
A



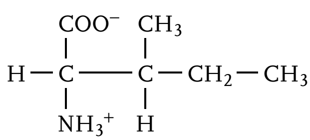
Valine
Val
V



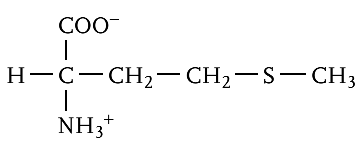
Leucine
Leu
L



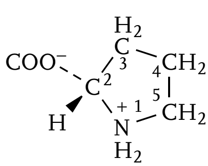
Isoleucine
Ile
I



Methionine
Met
M



Proline
Pro
P



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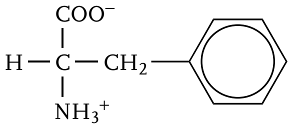
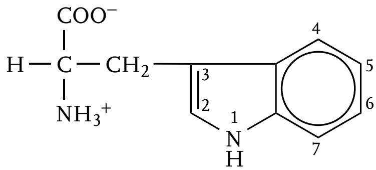
Amino acids with nonpolar side chains (continued)

Phenylalanine
Phe
F

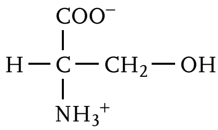


Tryptophan
Trp
W

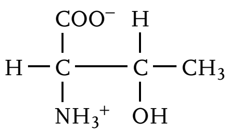


Amino acids with uncharged polar side chains

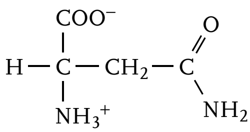
Serine
Ser
S



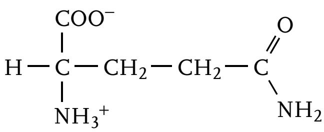
Threonine
Thr
T



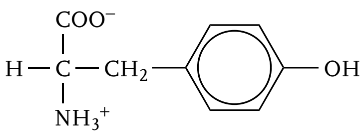
Asparagine
Asn
N



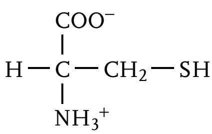
Glutamine
Gln
Q



Tyrosine
Tyr
Y

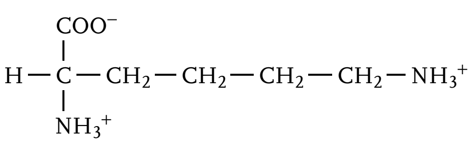


Cysteine
Cys
C



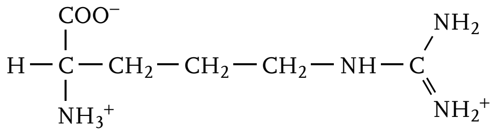
Amino acids with charged polar side chains

Lysine
Lys
K

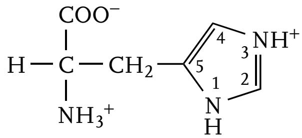


Amino acids with charged polar side chains (continued)

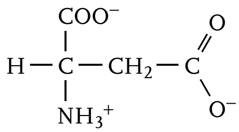
Arginine
Arg
R



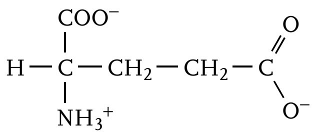
Histidine
His
H



Aspartic acid
Asp
D



Glutamic acid
Glu
E

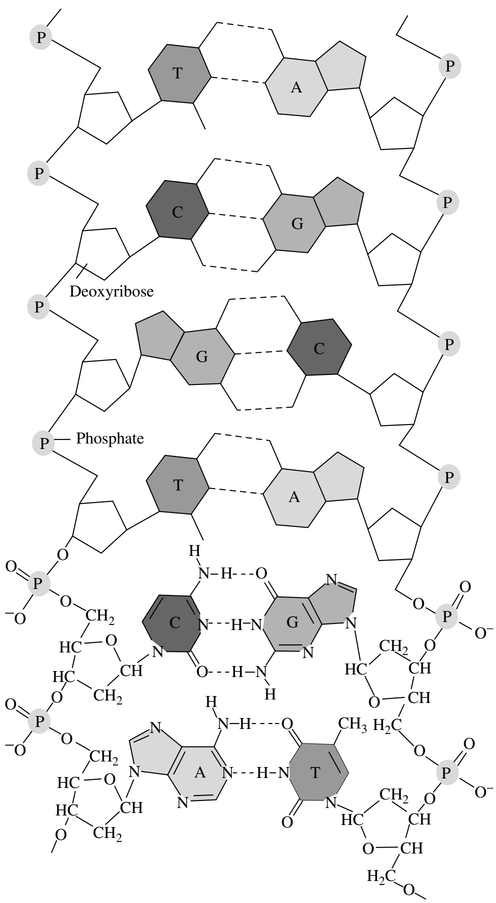


(Figures with kind permission from Voet, D., Voet, J.G., Pratt, C.W. (2001) *Fundamentals of Biochemistry*, Wiley, New York)

The Twenty Amino Acids with Abbreviations and Messenger RNA Code Designations

Amino acid	*One letter symbol*	*Three letter symbol*	*mRNA code designation*
alanine	A	ala	GCU, GCC, GCA, GCG
arginine	R	arg	CGU, CGC, CGA, CGG, AGA, AGG
asparagine	P	asn	AAU, AAC
aspartic acid	D	asp	GAU, GAC
cysteine	C	cys	UGU, UGC
glutamic acid	E	glu	GAA, GAG
glutamine	Q	gln	CAA, CAG
glycine	G	gly	GGU, GGC, GGA, GGG
histidine	H	his	CAU, CAC
isoleucine	I	ile	AUU, AUC, AUA
leucine	L	leu	UUA, UUG, CUU, CUC, CUA, CUG
lysine	K	lys	AAA, AAG
methionine	M	met	AUG
phenylalanine	F	phe	UUU, UUC
proline	P	pro	CCU, CCC, CCA, CCG
serine	S	ser	UCU, UCC, UCA, UCG, AGU, AGC
threonine	T	thr	ACU, ACC, ACA, ACG
tryptophan	W	trp	UGG
tyrosine	Y	tyr	UAU, UAC
valine	V	val	GUU, GUC, GUA, GUG

Complementary Strands of DNA with Base Pairing



Two nucleotide chains associate by base pairing to form double-stranded DNA. A (Adenine) pairs with T (Thymine), and G (Guanine) pairs with C (Cytosine) by forming specific hydrogen bonds. (Figure with kind permission from Voet, D., Voet, J.G., Pratt, C.W. [2001]: Fundamentals of Biochemistry. Wiley: New York.)