

美国医师执照考试

High-Yield™ *Cell and Molecular Biology*

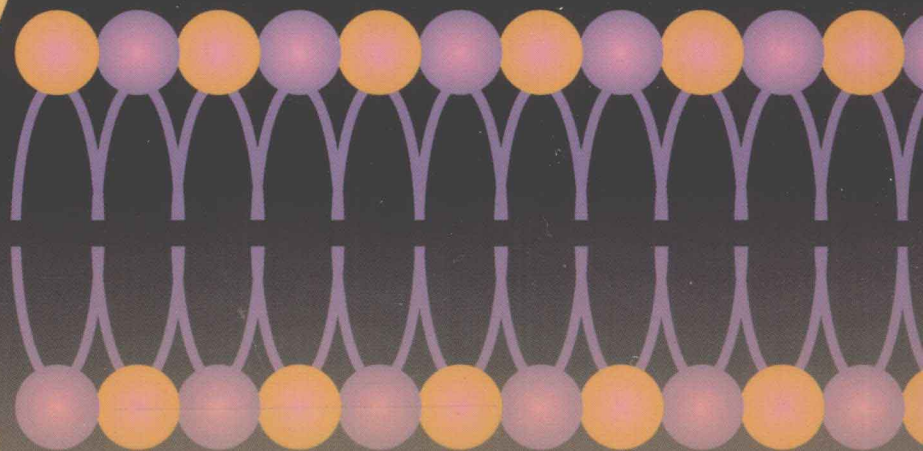
细胞与分子生物学

(第3版)

RONALD W. DUDEK

High-Yield™ Cell and
Molecular Biology is designed to:

- Provide a quick review
- Prepare you for the
USMLE Step 1
- Clarify difficult
concepts



北京大学医学出版社

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High-Yield™ 细胞与分子生物学

Cell and Molecular Biology

(第3版)

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出版说明

High-Yield™ 系列丛书是针对美国医师执照考试 (United States Medical Licensing Examination, USMLE) 的知名品牌图书, 受到世界各地读者的欢迎。该系列丛书具有以下特色:

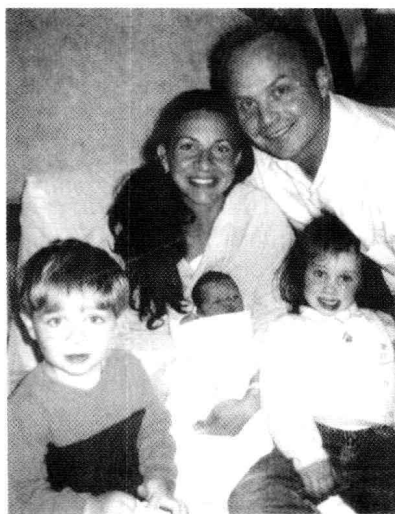
1. 内容高度概括, 重点突出, 有利于读者快速掌握学科的核心知识。
2. 编排新颖, 既有基础知识要点的介绍, 又有以疾病为核心的综合归纳, 并体现了相关学科的横向联系。
3. 语言规范、地道, 既有利于读者快速掌握专业词汇, 又有利于医学英语思维的培养。

本系列丛书是参加美国医师执照考试的必备辅导用书, 也可作为我国医学院校从事双语教学的教材和参考用书, 对教师进行英语授课, 学生学习、参加考试具有重要的参考价值。

北京大学医学出版社

This book is dedicated to my good friend Ronald Cicinelli, who is now a retired vice-president of The Chase Bank. In our 40 years of friendship, I have witnessed his dedication to family and friends. Ron brings a unique combination of strength and kindness to every personal interaction. I have been honored to know him for all these years. His life has been and continues to be, a “high-yield” life.

This book is also dedicated to my godson Alec Ronald Walker, born April 28, 2005. Alec joins a remarkable and loving family of parents Tim and Laura, sister Gabriella, and brother Brandson. Alec will certainly be given all the guidance necessary for a successful life, which will give me great joy to witness. My admonishment to my dear godson is to remember: “To whom much is given, much is expected.”



Preface

The impact of molecular biology today and in the future cannot be underestimated. Gene therapy and cloning of sheep are explained and discussed in the daily newspapers.

The clinical and etiological aspects of diseases are now being explained at the molecular biology level. Drugs are being designed right now by various pharmaceutical companies to impact molecular biological processes in the treatment of disease (cancer, obesity, etc.). Molecular biology will be increasingly represented on the USMLE Step 1. One of my main concerns in writing this book was NOT to write a review of basic molecular biology but to write a book that addressed molecular biology from a clinical perspective that would be useful and necessary for our future physicians. I was greatly assisted in this matter by two medical students who took an unsolicited interest in "High Yield Cell and Molecular Biology" third edition because they appreciated the growing importance of molecular biology for the future physician. In this regard, I would like to acknowledge the significant contribution of Mr. Jonah Cohen, a third-fourth-year student at the Brown Medical School and published cancer researcher in NF- κ B signal transduction, and Mr. Fateh Bazerbachi, a third-year student at Damascus University School of Medicine (Syria). Jonah Cohen was especially helpful in limiting the scope of material to hone in on the most clinically relevant issues and eliminating some far-reaching material that was included in the second edition. Fateh Bazerbachi was especially helpful in identifying new information and clarifying some difficult areas to understand. I found their assistance to be very helpful and it should benefit all my readers.

How will medical schools teach the clinical relevance of molecular biology to our future physicians? Medical school curricula are already filled with needed and relevant "traditional" courses. Where will the time needed to teach a molecular biology course be found? I suspect what will happen is that many of the "traditional" courses will extend their discussion of various topics down to the molecular biology level. This approach will work, but it will in effect make molecular biology somewhat disjointed. The student will learn some molecular biology in a biochemistry course, some in a microbiology course, and some in a histology course, etc. The problem this presents for students reviewing for USMLE Step 1 is that molecular biology information will be scattered among various course notes.

The solution: High Yield Cell and Molecular Biology, third edition. In this third edition, I have consolidated the important clinical issues related to molecular biology that are obvious "grist-for-the-mill" for USMLE Step 1 questions and included many of the insightful suggestions of my readers and reviewers. It is my feeling that "High Yield Cell and Molecular Biology" will be of tremendous benefit to any serious review for USMLE Step 1. Please send your feedback, comments, and suggestions to me at dudekr@ecu.edu for inclusion into the next edition.

Ronald W. Dudek, PhD

Abbreviations

5-HT	5-hydroxytryptamine
ABC	ATP-binding cassette
ABL	Abelson murine leukemia
<i>abl/bcr</i>	Abelson murine leukemia viral gene/breakpoint cluster region oncogene
abl	Abelson mouse leukemia
AC	adenylate cyclase
ACTH	adrenocorticotropin hormone
ADA	adenosine deaminase
ADH	antidiuretic hormone or vasopressin
AMPA	α -amino-3-hydroxy-5-methyl-4-isoxazole propionic acid
ANP	atrial natriuretic peptide
anti-MuSK	anti-muscle specific receptor tyrosine kinase
API	activator protein -1
Apaf-1	apoptotic peptidase activating factor
APC	familial adenomatous polyposis coli
AT ₁	angiotensin
ATM	ataxia telangiectasia mutated
ATR	ataxia telangiectasia and RAD3- related
B ₁ and B ₂	bradykinin _{1,2} receptors
BACs	bacterial artificial chromosomes based on the F-factor plasmids
BASC	BRCA1-associated genome surveillance complex
BAT	biliary acid transporter
Bcl-2	B-cell CLL/lymphoma 2
BCR	breakpoint cluster region
BK _{Ca}	large (big) conductance Ca ²⁺ -activated K ⁺ channel protein
BLM	Bloom
BOR	branchio-oto-renal
BRCA	breast cancer
Btk	Bruton tyrosine kinase
C bands	constitutive heterochromatin bands
C/EBP	CCAAT/enhancer binding protein
CaM-kinase	Ca ⁺⁺ /calmodulin-dependent protein kinase
CAP	catabolite activator protein
CCK	cholecystokinin
CCP	citrulline containing proteins
CD 40	cluster of differentiation 40
CD40LG	cluster of differentiation 40 ligand
CENP	centromeric proteins
CF	cystic fibrosis
CGH	comparative genome hybridization
Chk	checkpoint kinase
COMT	catechol-O-methyltransferase
cosmid	cohesive sticky ends of the bacteriophage λ inserted into a plasmid
COX	cyclooxygenase I and II
CRE	cAMP response element
CREB	cAMP response element binding protein
CTP	citrate transport protein
CURL	compartment for uncoupling of receptor and ligand
CYBB	cytochrome b-245 beta polypeptide; also called gp91
D1, D2	dopamine 1,2
DAG	diacylglycerol
DCC	deleted in colon carcinoma

DDB2	d amage-specific DNA b inding gene 2
DGCR	Di George chromosomal r egion
DPE	d ownstream p romoter e lement
DSCR	D own syndrome c ritical r egion
E2F	e longation f actor 2
EBV	E pstein B arr v irus
EGF	e pidermal g rowth f actor
EGFR	e pidermal g rowth f actor r eceptor
ELN	e lastin
env	e nvelope
erb	e rythro b lastosis
ERCC3	e xcision r epair c ross- c omplementing (rodent gene)
ERG	e rythroblastosis virus E26 oncogene like (avian)
ERV	e ndogenous r etro v iral
EYA1	e yes a bsent gene 1
Fab	f ragment; a ntigen b inding
F-actin	f ilamentous a ctin
Fas	f aint s ausage
FAT	f atty a cid t ransporter
F _C	f ragment; c rystallizable
fes	f eline s arcoma
FGF	f ibroblast g rowth f actor
FISH	f luorescence i n s itu h ybridization
FMR 1	f ragile X m ental r etardation 1
Fos	F inkel-Biskes-Jenkins o steogenic s arcoma
FSH	f ollicle- s timulating h ormone
FUS	f usion gene
G	trimeric G TP-binding proteins
G ₀ , G ₁ , G ₂	g ap z ero, o ne, t wo
GABA _A	g amma- a minobutyric a cid _A
GABRA 1	α 1 subunit of the g amma- a minobutyric acid r eceptor subtype A 1
GAD ₆₅	g lutamic a cid d ecarboxylase 65
gag	g roup specific a ntigens
G-CSF	g ranulocyte c olony s timulating f actor
GLUT1-5	g lucose t ransporters 1-5
GM-CSF	g ranulocyte- m onocyte c olony s timulating f actor
GpIb	p latelet g lycoprotein Ib
GRE	g lucocorticoid r esponse e lement
H ₁ , H ₂	h istamine _{1,2}
H2A, H2B, H3, H4	h istone proteins
Ha-ras	H arvey mouse sarcoma-ras
HDV	h uman d elta v irus
HIV-1	h uman i mmunodeficiency v irus-1
HLA	h uman l eucocyte a ntigen
HLA-DRB1	major histocompatibility complex or h uman l eukocyte a ntigen, class II, DR b eta 1
HLH	h elix-loop- h elix
HMRE	h eavy m etal r esponse e lement
Hsp	h eat s hock p rotein
HSRE	h eat s hock r esponse e lement
IAP	i nhibitor of a poptosis
IGH	i mmunoglobulin H
IKBKG	i nhibitor of k appa light polypeptide gene enhancer in B cells, k inase g amma
IK _{Ca}	i ntermediate conductance Ca ²⁺ -activated K ⁺ channel protein
IKK- gamma	I k appa B k inase g amma chain
IL-2	i nterleukin-2
Inr	i nitiator sequence
IP ₃	i nositol triphosphate
IRE	i nterferon- γ r esponse e lement
ISP42	i mport s ite p rotein 42
ITGB2	i ntegrin b eta 2
K _A	transient outward rectifier voltage-gated K ⁺
K _{AA}	a rachidonic a cid modulated metabolically-gated K ⁺
K _{ACh}	a cetyl ch oline-activated metabolically-gated K ⁺
K _{ATP}	A TP-sensitive metabolically-gated K ⁺
Kb	k ilobase; a thousand (10 ³) bases
K _{IR}	i nward rectifier voltage-gated K ⁺
Ki-ras	K irsten mouse sarcoma-ras
K _V	delayed rectifier voltage-gated K ⁺

<i>lac</i> operon	l actose operon
LDL	low d ensity l ipoprotein
LH	luteinizing h ormone
LIMK1	lin-11 i sl-1 m ec3 k inase 1
lin-4	abnormal cell l ineage- 4
LINE	long i nterspersed n uclear e lement
LTB ₄ , LTC ₄ , LTD ₄	leuko t riene B ₄ , C ₄ , D ₄
LTR	long t erminal r epet transposons
L-type Ca ²⁺	long-lasting C a ²⁺
mACH	m uscarinic a cetyl c holine
MaLR	m ammalian r etrotransposon-like
MAP	m itogen- a ctivated p rotein
Mb	m egabase; a million (10 ⁶) bases
M-CSFR	m acrophage c olony- s timulating f actor r eceptor
Mdc1	m ediator of DNA d amage c heckpoint protein- 1
MDM	m urine d ouble- m inute
MDR	m ulti d rug resistance
Mep-1	m ethionine amino p eptidase- 1
mGlu	m etabotropic g lutamate receptor
MHC	m ajor h istocompatibility c omplex
miRNA	m i c ro r ibon n ucleic a cid
MJD	M achado- J oseph d isease; SCA3
MLH	m utant L h omologue gene
MLL	m yeloid/lymphoid or mixed-lineage l eukemia (trithorax homolog, <i>Drosophila</i>)
MOAT	m ultispecific o rgan a nion t ransporter
MSH	m utant S h omologue gene
MTOC	m icro t ubular o rganizing c enter
myb	m yeloblastosis
myc	m yelocytosis virus gene
MyoD	m yo g enic d ifferentiation 1 protein
nACH	n icotinic a cetyl c holine receptor
NAD	n icotinamide a denine d inucleotide
NADH	n icotinamide a denine d inucleotide reduced form
NBT test	n itro b lue t etrazolium test
NEMO	NF -kappa B e ssential m odifier
NF	n uclear f actor
NF-1	n euro f ibromatosis
NFAT	n uclear f actor of a ctivated T -cells
NGF	n erve g rowth f actor
NMDA	N - m ethyl- D - a spartate
N-myc	n euroblastoma m yelocytosis
N-ras	n euroblastoma r as
Nsd1	n uclear receptor-binding S ET- d omain 1
NTRK	n eurotrophic t yrosine k inase r eceptor
OCT-1	o ctanucleotide binding protein- 1
p arm	p etite or short a rm of a chromosome
P ₁ , P _{2Y}	p ur i nergic _{1,2Y}
P _{2X}	p ur i nergic _{2X}
PACs	P1 artificial chromosomes based on the P1 bacteriophage
Pax3	p aired b ox 3
PBX1	p re- B -cell leukemia transcription factor 1
PDGF	p latelet- d erived g rowth f actor
PHOX	p hagocyte NADPH o xidase
PIP ₂	p hosphatidylinositol b iphosphate
Pit-1	p ituitary specific factor- 1
PKA	p rotein k inase A , which is a cAMP-dependent protein kinase
PKG	p rotein k inase G ; a cGMP-dependent protein kinase
PL _C	p hospholipase C
PML	p romyelocyte
<i>pml/rara</i>	p romyelocyte/ r etinoic a cid r eceptor α
PMS	p ost m eiotic s egregation gene
Pol	p olymerase
PRE	p horbol ester response e lement
pro	p rotease
PTH	p arathyroid h ormone
q arm	q ueue or long a rm of a chromosome
Q bands	fluorochrome q uinacrine positive b ands
R bands	Giemsa negative; light bands; r everse b ands

RAG1	r ecombination a ctivating g ene- 1
RAR α	r etinoic a cid r eceptor α gene
ras gene	r at s arcoma g ene
Rb	r etinoblastoma
RISC	r ibonucleic acid i nduced s ilencing c omplex
S phase	s ynthesis p hase
SCA3/MJD	s pinocerebellar a taxia/ M achado- J oseph d isease gene
SCID	s evere c ombined i mmune d eficiency
SCIDA	s evere c ombined i mmune d eficiency a thabasca
SF-1	s teroidogenic f actor- 1
SH2D1A	S H ₂ d omain protein 1A
SH ₂ -domain	s equences h omology proteins
SINE	s hort i nterspersed n uclear e lement
siRNA	s mall i nterfering r ibonucleic acid
sis	s imian s arcoma
SK _{Ca}	s mall conductance Ca ²⁺ -activated K ⁺
SLAM	s ignaling l ymphocyte a ctivation m olecule
snoRNA	s mall n ucleolar r ibonucleic acid
snRNA	s mall n uclear r ibonucleic acid
snRNP	s mall n uclear r ibonucleoprotein particles
Sos	son-of-sevenless
SRA-1 RNA	s teroid r eceptor a ctivator 1 r ibonucleic acid
Src	s arcoma
SRE	s erum growth factor r esponse e lement
SSB	s ingle strand b inding protein
SSR	s imple s equences r epetition
Stat-1	s ignal t ransduction and a ctivation of t ranscription factor- 1
T3,T4	thyroid hormone
TBP	T A-TA-binding protein
TCOF1	T reacher C ollins F ranceschetti 1
TDP	thymidine 5'- d iphosphate
TFII	general t ranscription f actors for RNA polymerase II
TGF β	t ransforming g rowth f actor β receptor
TI	t ranscription i nitiation
TNF	t umor n ecrosis f actor
TopBP1	t opoisoemerase b inding p rotein 1
TPM3	t ropomyosin 3
trp operon	t ryptophan o peron
TSH	thyroid s timulating h ormone
T-type Ca ²⁺	t ransient Ca ²⁺
TXA ₂	thromboxane A ₂
UTR	u ntranslated r egion
uvrABC	U V radiation A TP-binding c assette
V ₁ ,V ₂	vasopressin _{1,2} receptors
VCFS	velocardiofacial s ndrome
VEGF	v ascular e ndothelial g rowth f actor
VHL	von H ippel-Lindau
VIP	v asoactive i ntestinal p olypeptide
VS	V arkud s atellite
WAGR	W ilms tumor, a niridia, g enitourinary abnormalities, and mental r etardation
WT1	W ilms t umor gene
Xce	X -controlling e lement
Xic	X -inactivation c enter
XIST	X inactive s pecific t ranscripts
XLA	X -linked Infantile a gammaglobulinemia (Bruton)
XLP	X -linked l ymphoproliferative D isease
XPV	x eroderma p igmentosum v ariant gene
YACs	y east a rtificial c hromosomes

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Chromosomal DNA

I The Biochemistry of Nucleic Acids (Figure 1-1). A nucleoside consists of a nitrogenous base and a sugar. A nucleotide consists of a nitrogenous base, a sugar, and a phosphate group. DNA and RNA consist of a chain of nucleotides, which are composed of the following components:

A. NITROGENOUS BASES

1. Purines

- Adenine (A)
- Guanine (G)

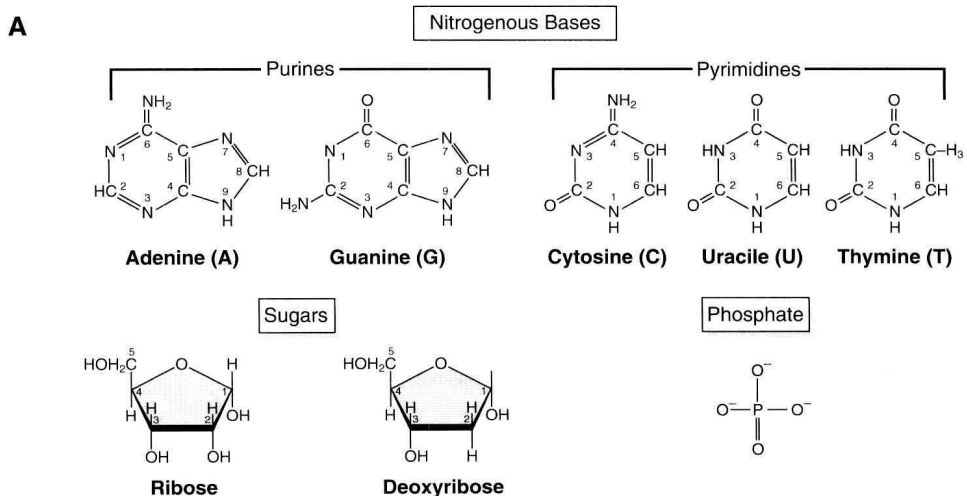
2. Pyrimidines

- Thymine (T)
- Cytosine (C)
- Uracil (U) which is found in RNA

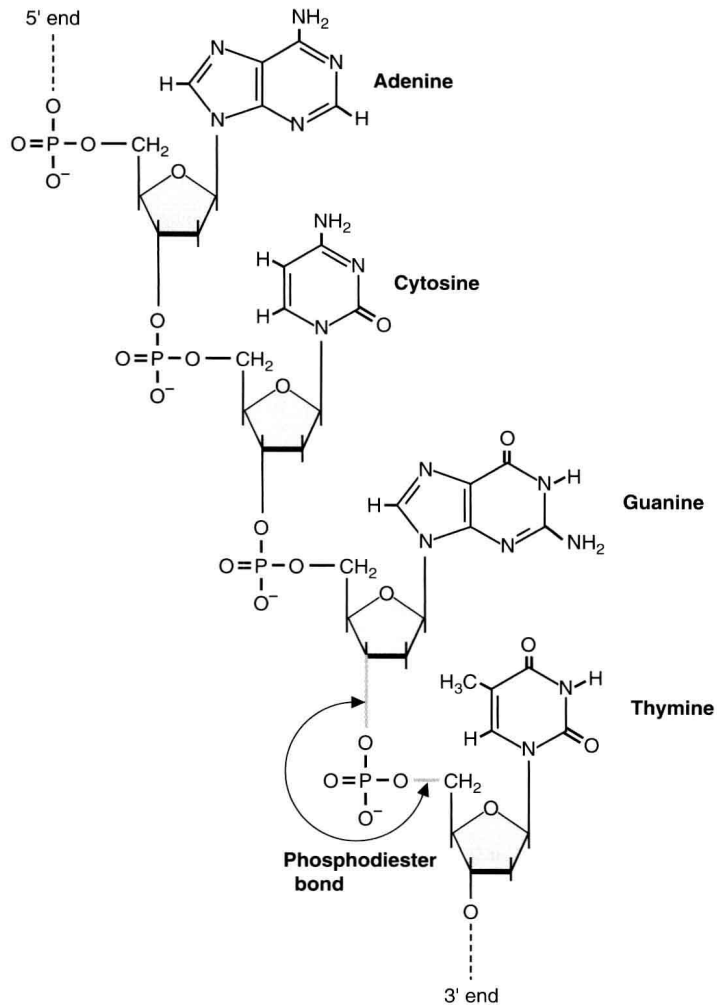
B. SUGARS

- Deoxyribose
- Ribose which is found in RNA

C. PHOSPHATE (PO_4^{3-})



● **Figure 1-1 (A)** Structure of the biochemical components of DNA and RNA (purines, pyrimidines, sugars, and phosphate). (continued)

B

● **Figure 1-1 (Continued) (B)** Diagram of a DNA polynucleotide chain. The biochemical components (purines, pyrimidines, sugar, and phosphate) form a polynucleotide chain through a 3',5'-phosphodiester bond. If a piece of DNA contains 20% thymine, how much guanine does the piece of DNA contain? If the piece of DNA contains 20% thymine, then the piece of DNA will contain 20% adenine which equals 40% (thymine and adenine). The remaining 60% will consist of cytosine and guanine which are paired. Consequently, the piece of DNA will contain 30% guanine. A good mnemonic to remember which nitrogenous bases are purines is **Pure As Gold** (**A**denine and **G**uanine are **Pur**ines).

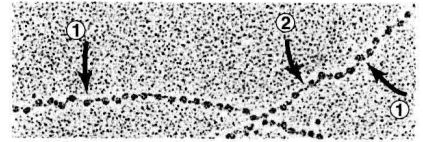
II Levels of DNA Packaging (Figure 1-2)

A. DOUBLE HELIX DNA

1. The DNA molecule is two complementary polynucleotide chains (or DNA strands) arranged as a double helix which are held together by **hydrogen bonding** between laterally opposed base pairs (bps).
2. DNA can adopt different helical structures which include: **A-DNA** and **B-DNA** which are right-handed helices with 11 and 10 bps per turn, respectively, and **Z-DNA** which is a left-handed helix with 12 bps per turn.
3. In humans, most of the DNA is in the B-DNA form under physiological conditions.

B. NUCLEOSOME (Figure 1-2)

1. The most fundamental unit of DNA packaging is the **nucleosome**. A nucleosome consists of a **histone protein octamer** (two each of H2A, H2B, H3, and H4 histone proteins) around which 146 bps of DNA is coiled in 1.75 turns.
2. The nucleosomes are connected by spacer DNA, which results in 10-nm diameter chromatin fiber that resembles a “beads on a string” appearance by electron microscopy. Figure 1-2 shows an electron micrograph of DNA that was isolated and subjected to treatments to unfold DNA into a 10-nm diameter chromatin fiber. The globular structure (“bead”; arrow 1) is the nucleosome. The linear structure (“string”; arrow 2) is spacer DNA.
3. The 10-nm diameter chromatin fiber is the first DNA structure that an endonuclease attacks in an apoptotic cell.
4. Histones are small proteins containing a high proportion of **lysine** and **arginine** that impart a positive charge to the proteins that enhances its binding to negatively charged DNA.
5. **Histone acetylation** reduces the affinity between histones and DNA. An increased acetylation of histone proteins will make a DNA segment more likely to be transcribed into RNA and hence any genes in that DNA segment will be expressed (i.e., \uparrow acetylation of histones = expressed genes).
6. **Histone methylation** of lysine and arginine by **methyltransferases** also occurs.

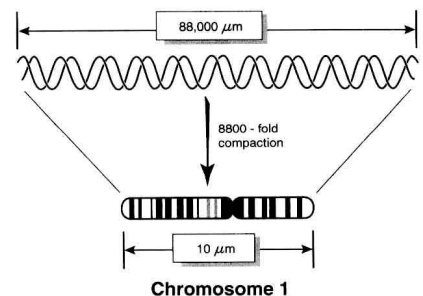


● Figure 1-2 Nucleosome.

C. 30-NM CHROMATIN FIBER

1. The 10-nm nucleosome fiber is joined by H1 histone protein to form a 30-nm chromatin fiber.
2. During interphase of mitosis, chromosomes exist as 30-nm chromatin fibers organized in a **primary loop pattern** called **extended chromatin** (~300-nm diameter). The extended chromatin can also be organized in a **secondary loop pattern** as seen in condensed metaphase chromosomes. (Note: when the general term “chromatin” is used, it refers specifically to the 30-nm chromatin fiber organized as extended chromatin).

- D. COMPACTION (Figure 1-3).** During metaphase of mitosis, chromosomes can become highly compacted. For example, human chromosome 1 contains about 260,000,000 bps. The distance between each base pair is 0.34 nm. So that the physical length of the DNA comprising chromosome 1 is 88,000,000 nm or 88,000 μm ($260,000,000 \times 0.34 \text{ nm} = 88,000,000 \text{ nm}$). During metaphase, all the chromosomes condense such that the physical length of chromosome 1 is about 10 μm . Consequently, the 88,000 μm of DNA comprising chromosome 1 is reduced to 10 μm , resulting in a 8800-fold compaction. Figure 1-3 shows double helix DNA of chromosome 1 that is unraveled and stretched out measuring 88,000 μm in length. When chromosome 1 condenses as occurs during mitosis, the length is reduced to 10 μm . This is a 8800-fold compaction.



● Figure 1-3 Chromosome Compaction.