Chapter 7→DNA Structure (9-30-05) **(Problems 1, 3, 4, 5, 16, 17, 26)**

Transforming Principle

Frederick Griffith-1928 (Figure 7-2)

Streptococcus pneumonia

Causes pneumonia in humans, lethal in mice.

Strain 1→(S)→normal, virulent, smooth colony from polysaccharide coat

Strain 2→(R)→mutant, avirulent, rough colony without polysaccharide coat

1) Boil S (dead)
2) Mix boiled S with live R→inject mice
3) Mice die
4) Live S cells recovered from dead mice.

Interpretation→cell debris from S strain converted live R strain to live S strain.

This process is called transformation.

Avery, MacLeod and McCarty-1944 (Figure 7-3)

What is the transforming principle?

Experiment

Separated various classes of compounds found in boiled S and tested each class for the ability to transform the R strain to the S strain.

Only DNA caused transformation.

DNA encoded the smooth phenotype.

First demonstration that genes are composed of DNA.

Many scientists still thought protein was the hereditary material.

Hershey & Chase-1952 (Figure 7-4)

Blender Experiment

Phosphorous (P) in DNA; Sulfur (S) in protein.

Incorporate ^{32}P into bacteriophage T2 DNA or ^{35}S into bacteriophage T2 protein.

Infect *E. coli*.

^{32}P found inside the cell but not ^{35}S.

Conclusion→DNA is the hereditary material.

Structure of DNA

DNA is composed of 4 nucleotides (nt) each containing a different nitrogenous base linked to an identical deoxyribose sugar and a phosphate. (Figure 7-5)

Adenine (A); Guanine (G)→purines

Cytosine (C); Thymine (T→pyrimidines

1) Chargaff's rules

   A) T + C = G + A

   B) T = A; G = C

   C) A + T ≠ G + C

2) X-ray crystal data indicating that DNA is long, skinny and helical with two similar parts that are parallel to each other. (Rosalind Franklin & Maurice Wilkens)

3) Jim Watson & Francis Crick solved the DNA structure in 1953. (Nobel prize)

Double helix

Each helix is composed of two antiparallel strands.

(i.e., 5'→' and 3'→5') (Figure 7-8)

Each strand is composed of nucleotides held together by phosphodiester bonds that form between the phosphate from one nt and the deoxyribose sugar from the neighboring nt.

A pairs with T (2 hydrogen bonds).

G pairs with C (3 hydrogen bonds).

Purines pair with pyrimidines.

One strand is complementary to the other.

B-form DNA, right hand helix.

Major and minor grooves. (Figure 7-9)

Implications of DNA structure

1) Suggested a way for DNA replication.
2) Suggested that a genetic code in DNA would specify the amino acid sequence in proteins.

DNA Replication

DNA replication is semiconservative (Meselson & Stahl)-1958. (Figure 7-11)
(i.e., each daughter duplex contains one parental and one newly synthesized daughter strand).

Parental strands of duplex must be unwound which requires breaking hydrogen bonds.

Each parental strand serves as a template or mold for synthesis of its complementary strand.

Replication Fork

Region of unwound DNA where active replication is taking place.

Complementary base pairing provides the basis for fidelity of DNA replication.
(i.e., each template base dictates the complementary base in the new strand).

Replication is a complex process that requires DNA template, dNTPs, DNA polymerase,
and several other enzymes and protein factors.

Chapter 7→DNA Replication (10-1-05)

Mechanism Of DNA Replication

Refer to Figure 7-18 and think 3-D.

DNA Polymerase

Catalyzes the reaction that incorporates each dNTP into the growing DNA strand one nt at a time. (Figure 7-15)

Arthur Kornberg-1959

Isolated DNA polymerase I from *E. coli*. (Nobel prize)

Template + dATP, dCTP---->Replicated DNA
DNA dGTP, dTTP

dNTP → dNMP incorporation + pyrophosphate (P-P)

E. coli

1) **DNA Polymerase I**→3 enzyme activities
   - A) 5'→3' polymerase activity
   - B) 3'→5' exonuclease activity that removes mismatched base pairs (bp)
   - C) 5'→3' exonuclease activity that degrades dsDNA.

2) **DNA Polymerase II and IV**→DNA repair.

3) **DNA Polymerase III**→Major polymerase for chromosomal replication.
   Contains **>** 20 different polypeptide subunits.

Initiation

DNA pol requires a short DNA or RNA primer for initiation.

Primer creates a short DNA:RNA duplex.

Origin of Replication

Fixed point where DNA replication begins.

dnaA protein

Binds to origin and locally unwinds DNA.

(i.e., disrupts H-bonds at the origin).

ssDNA binding protein (ssb)

Stabilizes ssDNA.

DNA Helicase

Disrupts H-bonds holding the two strands together at the replication fork.

Topoisomerase

Creates or relaxes supercoils in DNA.

Primase

Synthesizes an RNA primer ($\approx$ 30 nt) complementary to the DNA resulting in a duplex.

RNA primer extended by DNA polymerase III.

Can't initiate without the primer.

Bidirectional Replication

Replication proceeds in both directions, thereby synthesizing both strands ending at the terminus.

Leading Strand

Synthesized continuously.

Lagging Strand

Synthesized in short, discontinuous fragments (Okazaki fragments). Lagging strand grows in opposite direction of the replication fork.

DNA polymerase I

Removes RNA primer with its 5’→3’ exonuclease and fills in ssDNA gaps with 5’→3’ pol activity.

DNA Ligase

Seals the nicks (phosphodiester bonds) after primers are removed.

Exonuclease Editing

pol I and pol III possess 3’→5’ exonuclease activity that serves as a proofreading and editing function by removing mismatched bases that were incorporated by mistake.

Proofreading greatly enhances the fidelity of DNA replication.

DNA replication takes ≈ 40 min in *E. coli* (about 1000 nt/sec).

Eukaryotic DNA Replication

Similar but more complex.

Telomerase→adds simple DNA repeats to the end of the lagging strand because priming cannot occur.
Uses an RNA template. (Figure 7-25)
Gradual telomere shortening is linked to cell death.

Replication takes ≈ 1.4 hr (yeast) to ≈ 200 hr in some cells.

Must coordinate replication of several chromosomes.

Replication occurs in S phase of the cell cycle.

Multiple points of origin in each chromosome
(≈ 400 for 17 yeast chromosomes).

Chapter 8→Transcription and RNA Processing (10-5-05) **(Problems 2, 4, 12, 13)**

RNA Structure

Ribose (2' OH) replaces deoxyribose. (p. 257)

A, C, G, U (Uracil)→U replaces T (p. 258)

RNA is considered single-stranded but it does base pair.

- G-C (3 H-bonds)
- A-U (2 H-bonds)
- G-U (2 H-bonds)

Hydrogen bonding strength→G:C > A:U > G:U

2 Classes of RNA

I. mRNA (messenger RNA)

Intermediate that transfers the genetic information from DNA to proteins.

Directs protein synthesis.

II. Functional RNA

The RNA molecule is the final gene product (i.e., not translated).

IIa. rRNA (ribosomal RNA)

Component of ribosomes (16S, 23S, 5S).

IIb. tRNA (transfer RNA)

Brings AAs to ribosome during translation.

IIc. snRNA (small nuclear RNA)

Component of the spliceosome for pre-mRNA splicing.

IId. ncRNA (non-codong RNA)

RNA molecules that have regulatory functions.

<u>RNA polymerase (RNAP) and Transcription</u>

RNAP catalyzes RNA synthesis (5’→3’) from one strand of the DNA double helix (template strand) by complementary base pairing.

This process is called <u>transcription</u>. (Figure 8-5)

RNA is the same sequence as the non-template strand except U replaces T.
In prokaryotes a single RNA polymerase synthesizes all RNA.

RNA can be <u>monocistronic</u> (one gene) or <u>polycistronic</u> (more than one gene).

Holoenzyme→$\alpha_2\beta\beta'\omega\sigma$ (6 subunits)
Core enzyme→ $\alpha_2\beta\beta'\omega$ (5 subunits)

$\beta\beta'$ (beta and beta')→polymerization activity.

α_2 (alpha)→interacts with transcription factors.

ω (omega)→facilitates RNAP assembly and has regulatory functions.

σ (sigma)→binds to <u>promoter</u> sequences.

Different σ factors allow recognition of different promoter sequences.

Transcription (3 stages)→Initiation, Elongation, Termination

Initiation

Promoter (-35 and -10 sequences)

Nucleotide sequence that σ binds to.

TTGACA------------------TATAAT------ +1 (start of transcript)

-35 ≈ 17 nt -10 5-8 nt

RNA polymerase holoenzyme binds to the promoter, unwinds the DNA
and catalyzes the incorporation of incoming NTPs via DNA complementarity.

DNA 3' G-C-A-T 5'

RNA 5' C-G-U-A 3'

Energy provided by cleavage of high-energy triphosphate as in DNA replication.

Elongation

Shortly after initiation, σ is released (usually?).

Transcription continues with the core enzyme.

Elongation is also subject to regulation.

(Figures 8-9 and 8-10a)

Termination

RNAP recognizes signals to terminate transcription. Eukaryotes different???

Intrinsic Termination

G-C rich RNA stem-loop followed by several U residues.

RNA polymerase dissociates from DNA template and releases the transcript when it encounters this signal.

(Figure 8-11)

Rho-dependent termination

Rho binds to a rut (Rho utilization) sequence in the nascent transcript (C rich sequence).

Rho translocates along the RNA until it catches RNA polymerase and causes transcription to terminate.

ATP hydrolysis for translocation.

Eukaryotic Transcription

Transcription in nucleus; translation in cytoplasm.
(i.e., RNA is transported from nucleus to cytoplasm).

RNA pol I→rRNA
RNA pol II→mRNA (the vast majority are monocistronic)
RNA pol III→tRNA, snRNA

Transcription is similar to prokaryotes except different promoter sequences and more RNA polymerase subunits.

Transcription Animation

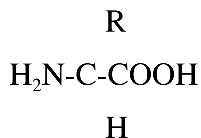
Chapter 9→Proteins and Translation (10-7-05) **(1, 2, 5, 15, 23)**

Biochemical reactions are catalyzed by enzymes that have
3-dimensional (3-D) structures that are crucial for their function.

Genes specify the structure of proteins, therefore genes determine phenotypes of the organism.

Protein Structure (Figure 9-2a)

Proteins are macromolecules composed of amino acids (AAs).



20 different AAs each with a different R group (side chain).
AAs are linked by peptide bonds (condensation reaction).

Polypeptide

Several linked AAs.

Primary (I°) Structure (Figure 9-3a)

Linear array of AAs in a polypeptide.

Secondary (II°) Structure (Figure 9-3b)

Polypeptides fold into repeating structures by forming hydrogen bonds (H-bonds) between the backbone carbonyl (C=O) and amino (N-H) groups of different residues.
α-helix, β-sheet

Tertiary (III°) Structure (Figure 9-3c)

3D structure of a polypeptide generated by H-bonds, ionic interactions, VanDerWalls forces and disulfide bridges (S-S covalent bond) between AA R-groups.

Quaternary (IV°) Structure (Figure 9-3d)

Two or more folded polypeptides bound together forming a complex.

Since genes determine the specific primary AA sequence of proteins, they determine II°, III°, IV° as well.

Genetics and Biochemistry

A change in 1 AA can alter or destroy protein function, while some changes don't affect protein function.

(e.g.) Hb^A→wild type; Hb^S→sickle cell anemia

Many human diseases are caused by blocks in biochemical pathways.

(e.g., PKU)

Temperature Sensitive Alleles

Substitution of an AA

1) **Permissive Temperature**→Produces a functional protein.

2) **Non-permissive Temperature**→Non-functional protein.
   Active site of enzyme unravels at high temp.

Colinearity of Genes and Proteins→Charles Yanofsky (1960s)

Linear sequence of nts in a gene (5'→3') determines the linear sequence of AAs in a polypeptide (N-terminus→C-terminus).

Translation

Conversion of genetic information encoded in mRNA into proteins (polypeptides).

Genetic Code→Nucleotides are "letters" in the code.

(Figure 9-8)

3 nts form the words (codons) representing different AAs.

(i.e., 3 nt triplet codon; non-overlapping).

20 AAs and only 4 different nts.

$4^3 = 64$ words (codons)

64 triplet codons but only 20 amino acids.

Genetic code is redundant (degenerate).

(i.e., most AAs represented by more than one codon).

Reading Frame

The frame in which the triplet codons specify the AAs in a protein.

(e.g.) 5' GCCAUACGCCUACUUGG 3'

Frame 1 ___ ___ ___ ___ ___

Frame 2 ___ ___ ___ ___ ___

Frame 3 ___ ___ ___ ___ ___

The genetic code is universal **EXCEPT** for a few differences in mitochondrial DNA and in the nuclear DNA of some protozoans.

Thus, the genetic code is **NOT** universal.

tRNA Recognition of Codons

Anticodons in tRNA recognize the codons in mRNA by base pairing.   (Figure 9-10)

Wobble

Different tRNAs do not exist for each codon.

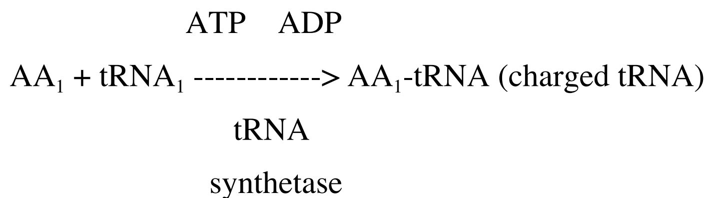
In some cases the 3rd position in the anticodon (5') can pair with more bases than its normal complementary base.   (e.g., G:U)
(Figure 9-12)

Stop Codons

UAA, UAG, UGA   (Figure 9-8)

No corresponding tRNA.
Signals the termination of protein synthesis.

tRNA Charging



charged tRNA = aminoacylated tRNA
tRNA synthetase is an enzyme that charges (aminoacylates) tRNA.

Chapter 9→ Translation (10-10-05)

Ribosomes

Huge complexes consisting of protein and rRNA.

Sites of protein synthesis (translation).

(Figure 9-13)

Prokaryotes

50S subunit + 30S subunit→70S ribosome (3 rRNAs + ~ 50 polypeptides).

50S subunit contains 23S and 5S rRNA

30S subunit contains 16S rRNA

Eukaryotes

60S subunit + 40S subunit→80S ribosome (4 rRNAs + ~ 80 proteins)

60S subunit contains 28S and 5S AND 5.8S rRNA

40S subunit contains 18S rRNA

Translation

initiation, elongation, termination

Initiation (Figure 9-17)

Requires mRNA, ribosomes, charged tRNAs, initiation factors (IF).

In prokaryotes the first AA is N-formylmethionine and is inserted by initiator tRNA ($tRNA^{fMet}$).

Uses normal met codon and anticodon.

N-formyl group is removed later.

Ribosome binding site (rbs) (Figure 9-16)

Shine-Dalgarno (S-D) sequence on mRNA is complementary to the 3' end of 16S rRNA.

(Figure 9-17)

1. mRNA binds to the 30S ribosomal subunit by base pairing with the 3' end of the 16S rRNA.
2. fMet-tRNA binds to the P (peptidyl) site on 30S.
3. 50S ribosomal subunit binds→70S ribosome.

Elongation

Requires elongation factors (EF). (Figure 9-19)

1. Aminoacyl-tRNA binds to the A site.

2. Peptide bond is formed by peptidyltransferase.
   This transfers the growing peptide chain to the AA at the A site.
   Peptidyltransferase activity is part of 23S rRNA.

3. Ribosome translocates by moving one codon along mRNA.
   tRNA at P site is removed and newly formed peptidyl-tRNA moves to P site.

4. Process is repeated.............

**GTP hydrolysis drives ribosome assembly, AA-tRNA binding, and ribosome translocation.

Termination (Figure 9-21)

1. Release factors (RF) bind to the stop codons (proteins, not tRNA).

2. Polypeptide is released from ribosome by cleavage from tRNA.

3. Ribosome dissociates into 2 subunits, mRNA is released.
   Ribosome release factor (RRF) participates in subunit dissociation.

Translation Animation

Nonsense Suppressor Mutations

Mutations in the anticodon loop of tRNA that allow codon-anticodon pairing with stop codons.
Thus, translation continues past the stop codon.
(Figure 9-23)

Chapter 10→Gene Regulation (Prokaryotes) 10-12-05

Regulation of gene expression involves protein-nucleic acid and protein-protein interactions. Regulation occurs at several levels.

1. Initiation of transcription (Repression, Activation)

2. Transcript elongation

3. Regulated Termination (Attenuation, Antitermination)

4. mRNA stability (Steady-state level of mRNA)

5. Efficiency of translation (rbs, Codon usage)

Chapter 10→Regulation of Gene Transcription **Problems 1, 2, 4, 10. 14**

Operon→Genetic unit of coordinate expression.

(e.g., *lacPOZYA*) (Figure 10-4)

Promoter (P)→Specific nucleotide sequence recognized by the sigma subunit (σ) of RNA polymerase.
(e.g.) -10 & -35 sequences

Operator (O)→Specific nucleotide sequence recognized by the repressor.
Often overlaps the promoter sequence.
Note: operators by definition are repressor binding sites. The book is WRONG in stating that activator proteins bind to operators.

Structural Genes (ZYA)→Encode mRNAs (proteins).

***lac* operon (*lacPOZYA*)** (>1000 fold regulation) (Figure 10-6)
Utilization of lactose as a carbon and energy source.

Induction (Relief of Repression)→requires inducer to inactivate the repressor.

The *lac* operon is negatively regulated by LacI (repressor).
In the absence of the inducer (lactose), LacI binds to the operator and blocks RNAP.

Inducer binds to repressor→repressor can't bind to operator→ RNAP binds to the promoter→ transcription→translation
Animation (wild type *lacI*)

***lacI*$^{-}$** →mutations in the *lacI* gene that result in constitutive expression (always on).
Caused by amino acid changes in the DNA binding domain of the protein.

lacI^{+} is *trans*-dominant with respect to *lacI*$^{-}$.

i.e., Wild type LacI can be supplied *in trans* (diffusible product) on a plasmid,
which complements the defect. (Figure 10-9)
Animation (*lacI*-)

***lacI*^{S}**→mutated inducer binding domain of the repressor.

(S=super repressor)

No induction by lactose or IPTG (always off).

lacI^{+} is *trans*-recessive with respect to *lacI*^{S} .

i.e., Wild type LacI is not able to bind to the operator if LacI^{S} is already bound to operator DNA.

(Figure 10-10)

Animation (*lacI*^{S})

***lacO*^{C}**→operator <u>constitutive</u> mutations→mutation in the operator DNA sequence prevents repressor binding (always on).

lacO^{C} mutations are *cis*-dominant.

i.e., Wild type *lacO* supplied in *trans* has no effect on the operon containing the *lacO*^{C} mutation.

(Figure 10-8)

Animation (*lacO*^{C})

Chapter 10→Gene Regulation (Prokaryotes) 10-17-05

Activation

Positive transcription initiation regulatory mechanisms (activation) require protein factor (activator) binding to allow maximum expression of the operon.

(e.g., cAMP-CAP control of *lac* operon.)

Superimposed on the repression/induction system.

Catabolite Repression→glucose is used for carbon and energy source before other sugars are used.

Regulation is mediated by the catabolite activator protein (CAP) and
cyclic adenosine monophosphate (cAMP).

High [glucose]→low [cAMP]
Low [glucose]→high [cAMP]

cAMP binds to and activates CAP.

cAMP-CAP complex activates expression of *lac* operon by binding just upstream of the promoter.
Bound CAP assists RNAP binding by protein-protein interactions with the α subunits of RNAP.

(Figures 10-15 and 10-17)

Dual Positive and Negative Control

(e.g.) arabinose operon (*CaraBAD*) (Figure 10-20)

Negative control mechanism (repression)

In the absence of arabinose, AraC binds to the initiator (*aria*) and to the operator, resulting in the formation of a DNA loop.

The DNA loop prevents transcription by blocking cAMP-CAP binding and RNAP binding.

Positive control mechanism

1. Arabinose binds to *araC* protein (AraC).
2. Arabinose-AraC complex binds to the initiator but not the operator.
3. cAMP-CAP complex binding occurs.
4. Binding of both complexes assists RNAP binding to the promoter.
5. Transcription of *araBAD*→synthesis of enzymes→ utilization of arabinose as a carbon and energy source.

Regulation of Translation

A. Codon usage→rare codons slow up translation resulting in lower expression levels.

B. Protein binding to the ribosome binding site (rbs) blocks initiation of translation by blocking ribosome binding.

C. Sequestration of the RBS in an RNA secondary structure (stem-loop, hairpin). mRNA is unable to base pair with the 3' end of 16S rRNA. Prevents translation initiation.

Chapter 8 (10-19-05)

<u>Eukaryotic RNA Processing</u> (In the nucleus) (Figure 8-13)

1. 5' cap added (7-methyl G) (mRNA protection and translation).
2. Poly (A) tail added to 3' end of transcript (mRNA protection and translation).
   Poly(A) tails are also added to prokaryotic mRNAs.
3. Splicing removes <u>introns</u>. (Figure 8-16)
   (exon-intron-exon→exon-exon + intron)

<u>Splicing</u>

Small nuclear ribonucleoprotein complexes (snRNPs) catalyze removal of introns via splicing.

Some introns are self-splicing.
RNA "enzyme" called a <u>ribozyme</u>.
(Tom Cech→Nobel Prize-1989)

Introns allow rapid generation of new genes by exon shuffling, thus new proteins.

<u>Alternative Splicing</u>

Alternative splicing pathways can result in many proteins from a single gene.
(i.e., the proteome is bigger than the genome)
(Figure 8-14)

Chapter 10→Gene Regulation (Eukaryotes)

Gene Regulation in Eukaryotes

All mRNAs are transcribed by RNAP II.

Eukaryotic Promoters

Required for basal (low level) transcription initiation.

(Figure 10-22)

TATA box

TATA binding protein (TBP) binds to the TATA box (similar to prokaryotic -10 sequence).

Directs RNAP to initiate transcription downstream.

Promoter Proximal Elements

e.g., CAT box and GC box

Typically ~ 100-300 bases upstream of the promoter.

Positions can vary from promoter to promoter.

All 3 elements (TATA, CAT, GC) are recognized by protein factors to assist RNAP binding.

Distance-independent cis-acting Elements

A. Enhancers

Greatly increase transcription initiation at promoters.

Regulatory proteins bind to enhancer elements and assist RNAP binding.

1. Can be several kb away from promoter.
2. Can be in either orientation.
3. Can be 5' or 3' of promoter.
4. Can be tissue specific.

(e.g., DNA binding protein may only be present in some cell types).

Leads to differential gene expression. (i.e., Different genes expressed in different tissues).

B. Silencers

Similar to enhancers but they have an opposite effect (i.e., Repression).

Regulatory proteins (repressors) bind to the silencer and prevent RNAP binding.

Formation of the active transcription complex

TBP and TBP associated factors (TAFs) constitute TFIID.

TFIID and other TFII complexes constitute the general (basal) transcription factors.
(Figure 10-24a).

These factors interact with RNAP and form a pre-initiation complex
via protein-DNA and protein-protein interactions.

Many TAFs and *trans*-acting factors (activators) have 2 domains.

1. DNA-binding domain
2. Transcription activation domain.
   (i.e., interact with other protein factors.)

Initiation complex

(Figure 10-24a)
Ordered assembly of an enormous complex consisting of several factors,
including the basal factors, activators and RNAP II.

Forms a DNA loop via protein-protein interactions bringing together the active complex.

DNA-Binding Motifs

A. Helix-Turn-Helix

One of the two α-helices interacts with the major groove of the double helix. (Figure 10-25)

B. Zinc Finger

Zinc atom complexed by histidine and cysteine residues.

C. Leucine Zipper

Protein dimers form by hydrophobic interactions between leucine residues that are spaced 7 amino acids apart.

Leucines are present in each subunit.

Leucine zippers can be homodimers or heterodimers

Heterodimers increase the number of usable DNA sequences and the variety of protein combinations that can be used to activate or repress genes.

Chapter 10→Gene Regulation (Eukaryotes) 10-21-05

Role of Chromatin in Regulating Eukaryotic Gene Expression

Prokaryotic DNA is relatively "naked" (free of protein).

Eukaryotic DNA is organized in chromatin (packaged in nucleosomes [histones]).
(Figure 10-29a)

Histones H2a, H2b, H3 and H4 (2 each) form an octamer that winds up about 150 bp of DNA.

Nucleosomes can serve as barriers to RNAP binding.

Because the nucleosome organization is dynamic, gene expression can be regulated
without changing the DNA sequence of the gene.

Silent chromatin
Condensed state of the dynamic regions of euchromatin that lead to gene silencing.

Traqnscription is repressed when the TATA box and flanking sequences are wound up in a nucleosome.

Chromatin Remodeling
Changing of nucleosome positions leading to activation or repression of transcription.

SWI-SNF (Switch-Sniff) Chromatin Remodeling Complex
SWI-SNF protein is part of a multisubunit complex that can reposition nucleosomes (ATP hydrolysis),
which frees the TATA box so that RNAP can bind.
(Figure 10-35)

Histone Code
The N-terminal ends of histones protrude from the nucleosome (histone tails).

Specific lysine residues in the histone tails are subject to post-translational modification through the addition of acetyl groups.

Modification can also alter nucleosome formation.

Acetyl modifications are reversible.

(Figure 10-37)

Histone Acetylation and Gene Expression

Histones associated with the nucleosomes of active genes are hyperacetylated (rich in acetyl groups).

Histones associated with the nucleosomes of inactive genes are hypoacetylated (low acetylation).

Histone Acetyltransferase (HAT)→Enzymes responsible for adding acetyl groups to histones.

Histone Deacetylase (HDAC)→ Enzymes responsible for removing acetyl groups from histones.

Some HATs and HDACs were previously identified as transcription factors that can activate or repress gene expression, respectively. Thus, some transcription factors can alter the histone code.

Transcription factors that bind to DNA also appear to recognize a specific histone code (specific acetylation state).

β-interferon Gene
Codes for the antiviral protein interferon.

Normally switched off but is activated upon viral infection.

The assembly of the activated transcription complex is referred to as an enhancesome.

(Figure 10-26)

The enhancesome is nucleosome-free but is surrounded by two positioned nucleosomes, one of which is strategically placed over the TATA box and transcription start site.

A HAT binds to and acetylates the histones of this nucleosome.

Acetylation leads to recruitment of a specific activator protein, RNAP and the SWI-SNF chromatin remodeling complex.

SWI-SNF repositions the nucleosome such that the TATA box is accessible to TBP, thereby allowing transcription.

(Figure 10-38)