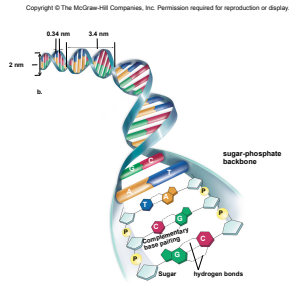


# Molecular Biology of the Gene



## Outline

- Genetic Material
  - Transformation
- DNA Structure
  - Watson and Crick
- DNA Replication
  - Prokaryotic versus Eukaryotic
  - Replication Errors
- Transcription
- Translation
- Structure of Eukaryotic Chromosome

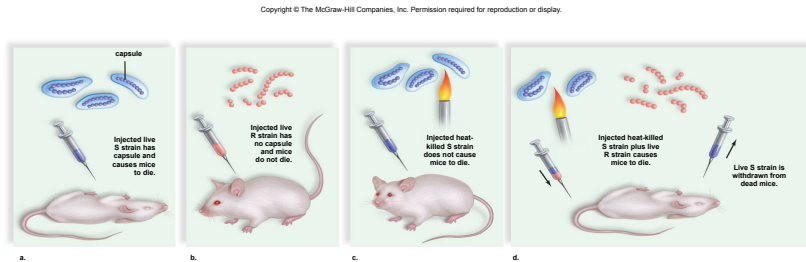
## Genetic Material

- Frederick Griffith investigated virulence of *Streptococcus pneumoniae*
  - Concluded that virulence passed from the dead strain to the living strain
  - Transformation
- Further research by Avery et al.
  - Discovered that DNA is the transforming substance
  - DNA from dead cells was being incorporated into genome of living cells

## Griffith's Transformation Experiment

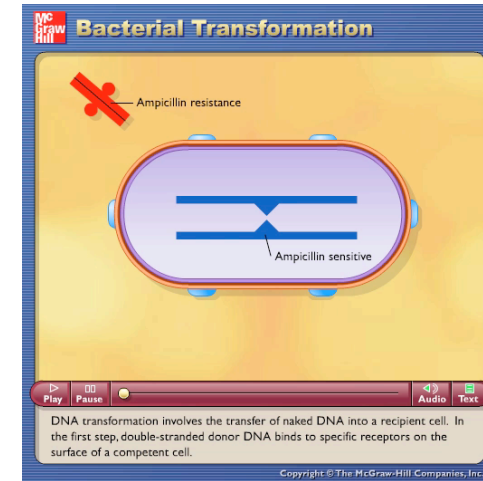
- Mice were injected with two strains of pneumococcus: an encapsulated (S) strain and a non-encapsulated (R) strain.
  - The S strain is virulent (the mice died); it has a mucous capsule and forms "shiny" colonies.
  - The R strain is not virulent (the mice lived); it has no capsule and forms "dull" colonies.

# Griffith's Transformation Experiment



5

# Animation



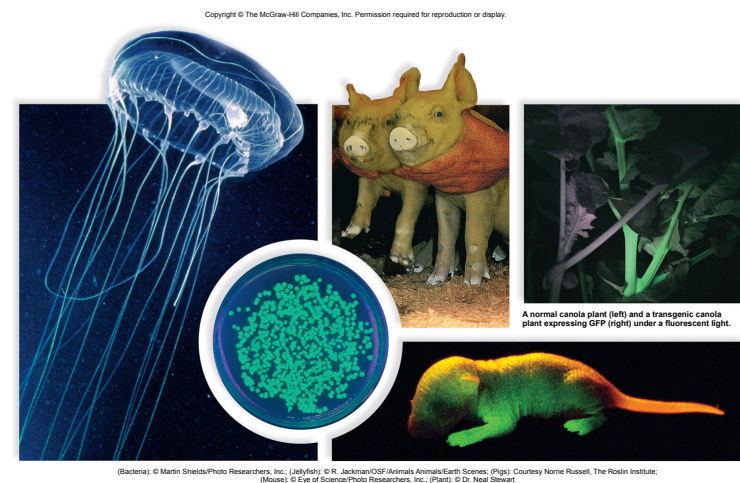
6

# Transformation of Organisms Today

- Result the so-called genetically modified organisms (GMOs)
  - Invaluable tool in modern biotechnology today
  - Commercial products that are currently much used
  - Green fluorescent protein (GFP) used as a marker
    - A jellyfish gene codes for GFP
    - The jellyfish gene is isolated and then transferred to a bacterium, or the embryo of a plant, pig, or mouse.
    - When this gene is transferred to another organism, the organism glows in the dark

7

# Transformation of Organisms



8

## Structure of DNA

- DNA contains:
  - Two Nucleotides with purine bases
    - Adenine (A)
    - Guanine (G)
  - Two Nucleotides with pyrimidine bases
    - Thymine (T)
    - Cytosine (C)

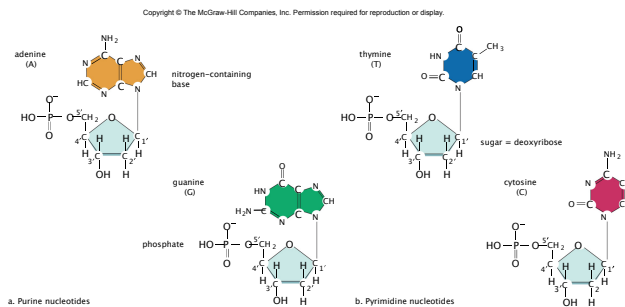
9

## Chargaff's Rules

- The amounts of A, T, G, and C in DNA:
  - Identical in identical twins
  - Varies between individuals of a species
  - Varies more from species to species
- In each species, there are equal amounts of:
  - A & T
  - G & C
- All this suggests DNA uses complementary base pairing to store genetic info
- Human chromosome estimated to contain, on average, 140 million base pairs
- Number of possible nucleotide sequences, 4,140,000,000

11

## Nucleotide Composition of DNA



Species	A	T	G	C
Homo sapiens (human)	31.0	31.5	19.1	18.4
Drosophila melanogaster (fruit fly)	27.3	27.6	22.5	22.5
Zea mays (corn)	25.6	25.3	24.5	24.6
Neurospora crassa (fungus)	23.0	23.3	27.1	26.6
Escherichia coli (bacterium)	24.6	24.3	25.5	25.6
Bacillus subtilis (bacterium)	28.4	29.0	21.0	21.6

c. Chargaff's data

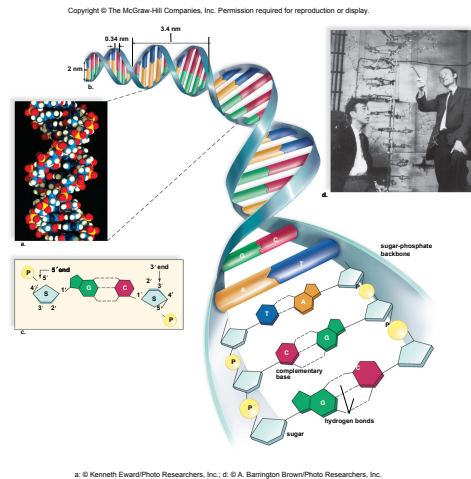
12

## Watson and Crick Model

- Watson and Crick, 1953
  - Constructed a model of DNA
  - Double-helix model is similar to a twisted ladder
    - Sugar-phosphate backbones make up the sides
    - Hydrogen-bonded bases make up the rungs
- Received a Nobel Prize in 1962

15

## Watson/Crick Model of DNA



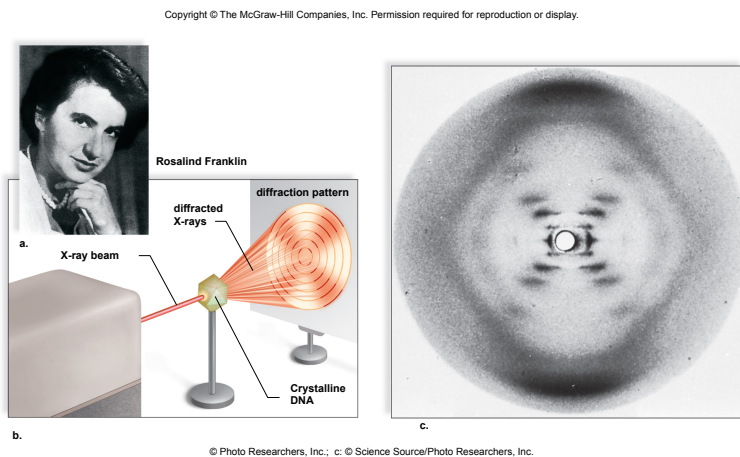
16

## X-Ray Diffraction of DNA

- Rosalind Franklin studied the structure of DNA using X-rays.
- She found that if a concentrated, viscous solution of DNA is made, it can be separated into fibers.
- Under the right conditions, the fibers can produce X-ray diffraction pattern
  - She produced X-ray diffraction photographs.
  - This provided evidence that DNA had the following features:
    - DNA is a helix.
    - Some portion of the helix is repeated.

17

## X-Ray Diffraction of DNA



18

## Dark Lady of DNA



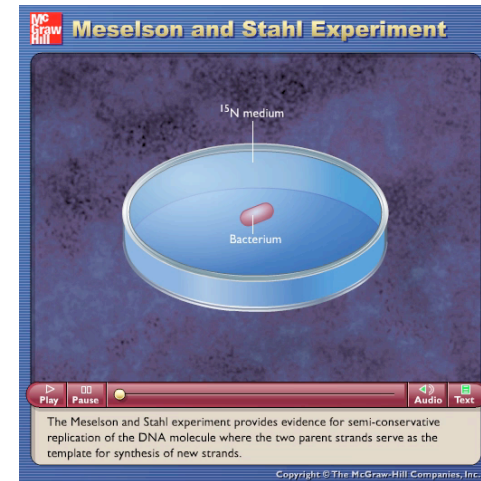
16

## Replication of DNA

- DNA replication is the process of copying a DNA molecule.
- Replication is **semiconservative**, with each strand of the original double helix (*parental* molecule) serving as a **template** (mold or model) for a new strand in a *daughter* molecule.

19

## Animation



18

## Replication: Eukaryotic

- DNA replication begins at numerous points along linear chromosome
- DNA unwinds and unzips into two strands
- Each old strand of DNA serves as a template for a new strand
- Complementary base-pairing forms new strand on each old strand
  - Requires enzyme DNA polymerase

23

## Replication: Eukaryotic

- Replication bubbles spread bi-directionally until they meet
- The complementary nucleotides join to form new strands. Each daughter DNA molecule contains an old strand and a new strand.
- Replication is semiconservative:
  - One original strand is conserved in each daughter molecule i.e. each daughter double helix has *one parental* strand and *one new* strand.

26

# Animation

**DNA Replication**

Play Pause Audio Text

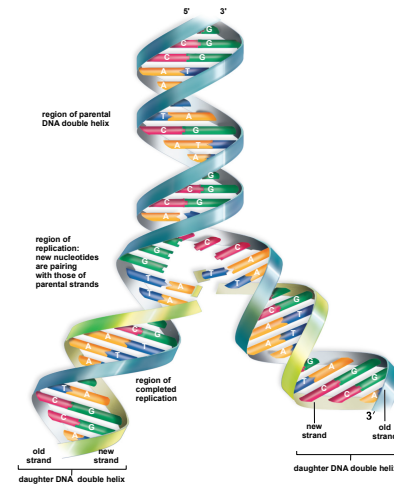
DNA replication begins at a specific point in the DNA molecule called the origin of replication site.

Copyright © The McGraw-Hill Companies, Inc.

21

# Semiconservative Replication of DNA

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.



28

# Animation

**Bidirectional DNA Replication**

Play Pause Audio Text

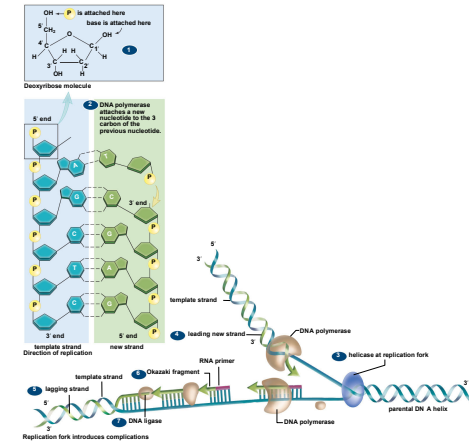
This is referred to as semiconservative replication.

Copyright © The McGraw-Hill Companies, Inc.

23

# Science Focus: Aspects of DNA Replication

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.



31

## Replication: Prokaryotic

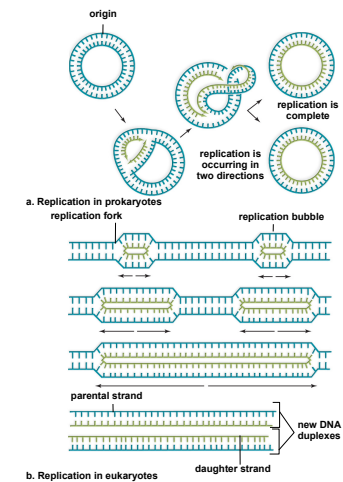
### ● Prokaryotic Replication

- Bacteria have a single circular loop
- Replication moves around the circular DNA molecule in both directions
- Produces two identical circles
- Cell divides between circles, as fast as every 20 minutes

32

## Replication: Prokaryotic vs. Eukaryotic

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.



33

## Replication Errors

- Genetic variations are the raw material for evolutionary change
- Mutation:
  - A permanent (but unplanned) change in base-pair sequence
    - Some due to errors in DNA replication
    - Others are due to DNA damage
  - DNA repair enzymes are usually available to reverse most errors

34

## Animation

The screenshot shows an animation titled "Addition and Deletion Mutations" from McGraw-Hill. It displays a DNA double helix with the following nucleotide sequences:  
5' C G G T A C G T T A A G 3'  
3' G C C A T G C A T T T C 5'  
The sequence is labeled "Wild type". Below the DNA is a control bar with "Play", "Pause", "Audio", and "Text" buttons. A caption reads: "The nucleotide sequence in DNA determines the nucleotide sequence in messenger RNA and, consequently, the sequence of amino acids in a protein." The copyright notice at the bottom is "Copyright © The McGraw-Hill Companies, Inc."

28

## Function of Genes

- Genes Specify Enzymes
  - Beadle and Tatum:
    - Experiments on fungus *Neurospora crassa*
    - Proposed that each gene specifies the synthesis of one enzyme
    - One-gene-one-enzyme hypothesis
- Genes Specify a Polypeptide
  - A gene is a segment of DNA that specifies the sequence of amino acids in a polypeptide
  - Suggests that genetic mutations cause changes in the primary structure of a protein

35

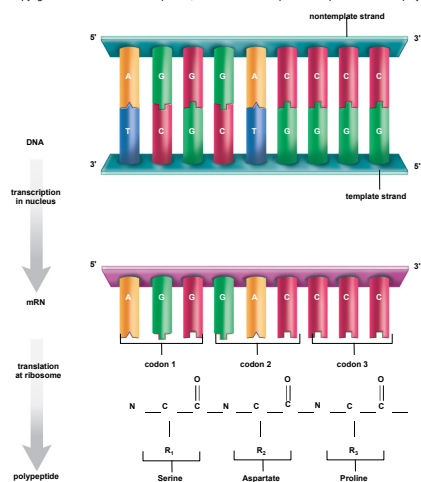
## Protein Synthesis: From DNA to RNA to Protein

- The mechanism of gene expression
  - DNA in genes specify information, but information is not structure and function
  - Genetic info is expressed into structure & function through protein synthesis
- The expression of genetic info into structure & function:
  - DNA in gene controls the sequence of nucleotides in an RNA molecule
  - RNA controls the primary structure of a protein

36

## The Central Dogma of Molecular Biology

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.



38

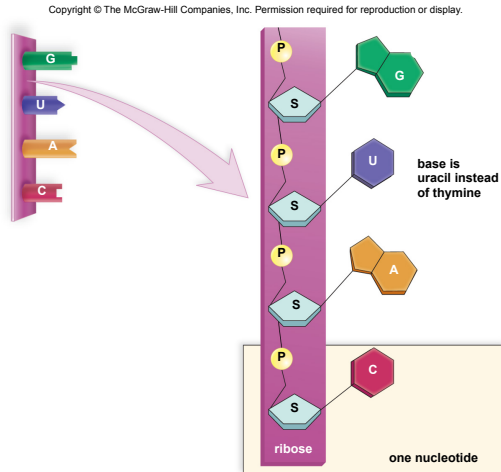
## Types of RNA

- RNA is a polymer of RNA nucleotides
- RNA Nucleotides are of four types: Uracil, Adenine, Cytosine, and Guanine
- Uracil (U) replaces thymine (T) of DNA
- Types of RNA
  - Messenger (mRNA) - Takes genetic message from DNA in nucleus to ribosomes in cytoplasm
  - Ribosomal (rRNA) - Makes up ribosomes which read the message in mRNA
  - Transfer (tRNA) - Transfers appropriate amino acid to ribosome when "instructed"

39



## Structure of RNA



40

## RNA vs. DNA structure

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.

	RNA	DNA
Sugar	Ribose	Deoxyribose
Bases	Adenine, guanine, uracil, cytosine	Adenine, guanine, thymine, cytosine
Strands	Single stranded	Double stranded with base pairing
Helix	No	Yes

41

## The Genetic Code

- Properties of the genetic code:
  - Universal
    - With few exceptions, all organisms use the code the same way
    - Encode the same 20 amino acids with the same 64 triplets
  - Degenerate (redundant)
    - There are 64 codons available for 20 amino acids
    - Most amino acids encoded by two or more codons
  - Unambiguous (codons are exclusive)
    - None of the codons code for two or more amino acids
    - Each codon specifies only one of the 20 amino acids
  - Contains start and stop signals
    - Punctuation codons
    - Like the capital letter we use to signify the beginning of a sentence, and the period to signify the end

42

## The Genetic Code

- The unit of a code consists of codons, each of which is a unique arrangement of symbols
- Each of the 20 amino acids found in proteins is uniquely specified by one or more codons
  - The symbols used by the genetic code are the mRNA bases
    - Function as “letters” of the genetic alphabet
    - Genetic alphabet has only four “letters” (U, A, C, G)
  - Codons in the genetic code are all three bases (symbols) long
    - Function as “words” of genetic information
    - Permutations:
      - There are 64 possible arrangements of four symbols taken three at a time
      - Often referred to as triplets
    - Genetic language only has 64 “words”

43

## Messenger RNA Codons

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.

First Base	Second Base				Third Base
	U	C	A	G	
U	UUU phenylalanine	UCU serine	UAU tyrosine	UGU cysteine	U
	UUC phenylalanine	UCC serine	UAC tyrosine	UGU cysteine	C
	UUA leucine	UCA serine	UAA stop	UGA stop	A
	UUG leucine	UCG serine	UAG stop	UGG tryptophan	G
	CUU leucine	CCU proline	CAU histidine	CGU arginine	U
	CUC leucine	CCC proline	CAC histidine	CGC arginine	C
C	CUA leucine	CCA proline	CAA glutamine	CGA arginine	A
	CUG leucine	CCG proline	CAG glutamine	CGG arginine	G
	AUU isoleucine	ACU threonine	AAU asparagine	AGU serine	U
	AUC isoleucine	ACC threonine	AAC asparagine	AGC serine	C
A	AUA isoleucine	ACA threonine	AAA lysine	AGA arginine	A
	AUG (start) methionine	ACG threonine	AAG lysine	AGG arginine	G
	GUU valine	GCU alanine	GAU aspartate	GGU glycine	U
G	GUC valine	GCC alanine	GAC aspartate	GGC glycine	C
	GUA valine	GCA alanine	GAA glutamate	GGA glycine	A
	GUG valine	GGG alanine	GAG glutamate	GGG glycine	G

44

## Steps in Gene Expression: Transcription

### • Transcription

- Gene unzips and exposes unpaired bases
- Serves as template for mRNA formation
- Loose RNA nucleotides bind to exposed DNA bases using the C=G & A=U rule
- When entire gene is transcribed into mRNA, result is a pre-mRNA transcript of the gene
- The base sequence in the pre-mRNA is complementary to the base sequence in DNA

45

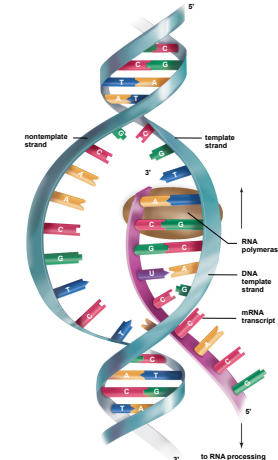
## Transcription of mRNA

- A single chromosome consists of one very long molecule encoding hundreds or thousands of genes
- The genetic information in a gene describes the amino acid sequence of a protein
  - The information is in the base sequence of one side (the "sense" strand) of the DNA molecule
  - The gene is the functional equivalent of a "sentence"
- The segment of DNA corresponding to a gene is unzipped to expose the bases of the sense strand
  - The genetic information in the gene is transcribed (rewritten) into an mRNA molecule
  - The exposed bases in the DNA determine the sequence in which the RNA bases will be connected together
  - RNA polymerase connects the loose RNA nucleotides together
- The completed transcript contains the information from the gene, but in a mirror image, or complementary form

47

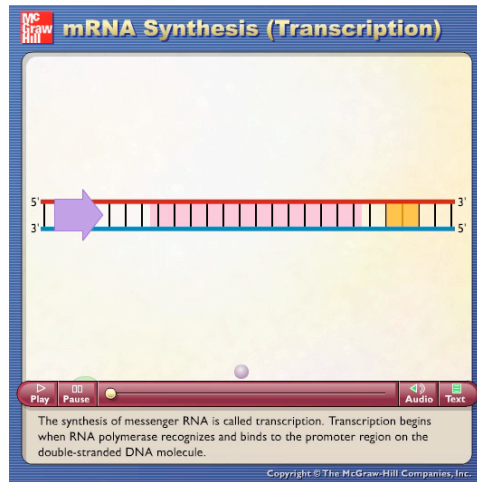
## Transcription

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.



49

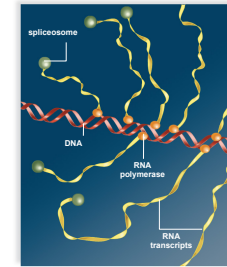
## Animation



41

## RNA Polymerase

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.



© Oscar L. Miller/Photo Researchers, Inc.

52

## Processing Messenger RNA

- Pre-mRNA, is modified before leaving the eukaryotic nucleus.
  - Modifications to ends of primary transcript:
    - Cap of modified guanine on 5' end
      - The *cap* is a modified guanine (G) nucleotide
      - Helps a ribosome where to attach when translation begins
    - Poly-A tail of 150+ adenines on 3' end
    - Facilitates the transport of mRNA out of the nucleus
    - Inhibits degradation of mRNA by hydrolytic enzymes.

53

## Processing Messenger RNA

- Pre-mRNA, is composed of exons and introns.
  - The exons will be expressed,
  - The introns, occur *in* between the exons.
    - Allows a cell to pick and choose which exons will go into a particular mRNA
  - RNA splicing:
    - Primary transcript consists of:
      - Some segments that will not be expressed (introns)
      - Segments that will be expressed (exons)
    - Performed by spliceosome complexes in nucleoplasm
      - Introns are excised
      - Remaining exons are spliced back together
  - Result is mature mRNA transcript

54

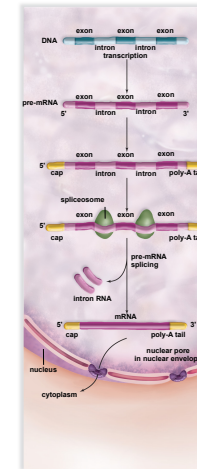
## RNA Splicing

- In prokaryotes, introns are removed by “self-splicing”—that is, the intron itself has the capability of enzymatically splicing itself out of a pre-mRNA

55

## Messenger RNA Processing

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.



57

## Functions of Introns

- As organismal complexity increases;
  - Number of protein-coding genes does not keep pace
  - But the proportion of the genome that is introns increases
  - Humans:
    - Genome has only about 25,000 coding genes
    - Up to 95% of this DNA genes is introns
- Possible functions of introns:
  - More bang for buck
    - Exons might combine in various combinations
    - Would allow different mRNAs to result from one segment of DNA
  - Introns might regulate gene expression
- Exciting new picture of the genome is emerging

59

## Animation

Copyright © The McGraw-Hill Companies, Inc.

48

## Steps in Gene Expression: Translation

- tRNA molecules have two binding sites
  - One associates with the mRNA transcript
  - The other associates with a specific amino acid
  - Each of the 20 amino acids in proteins associates with one or more of 64 species of tRNA
- Translation
  - An mRNA transcript migrates to rough endoplasmic reticulum
  - Associates with the rRNA of a ribosome
  - The ribosome “reads” the information in the transcript
  - Ribosome directs various species of tRNA to bring in their specific amino acid “fares”
  - tRNA specified is determined by the code being translated in the mRNA transcript

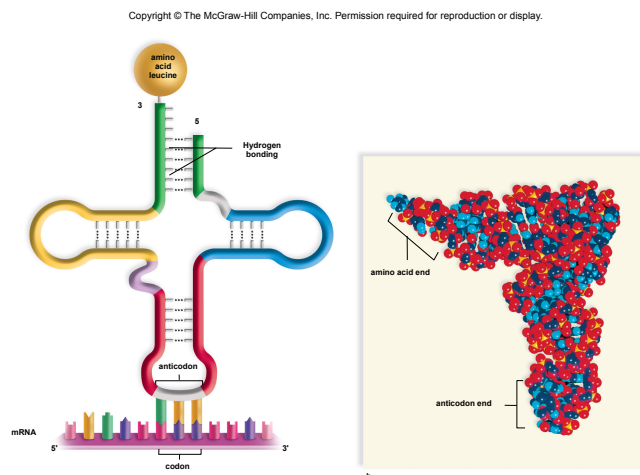
60

## tRNA

- tRNA molecules come in 64 different kinds
- All very similar except that
  - One end bears a specific triplet (of the 64 possible) called the anticodon
  - Other end binds with a specific amino acid type
  - tRNA synthetases attach correct amino acid to the correct tRNA molecule
- All tRNA molecules with a specific anticodon will always bind with the same amino acid

61

## Structure of tRNA



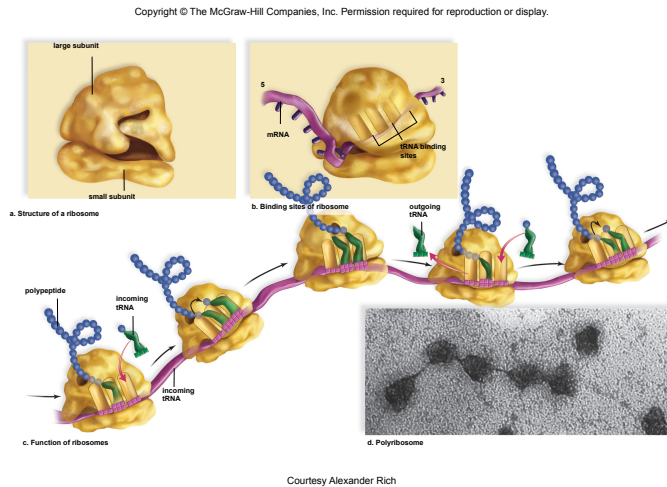
63

## Ribosomes

- Ribosomal RNA (rRNA):
  - Produced from a DNA template in the nucleolus
  - Combined with proteins into large and small ribosomal subunits
- A completed ribosome has three binding sites to facilitate pairing between tRNA and mRNA
  - The E (for exit) site
  - The P (for peptide) site, and
  - The A (for amino acid) site

64

## Ribosomal Structure and Function



65

## Steps in Translation: Initiation

- Components necessary for initiation are:
  - Small ribosomal subunit
  - mRNA transcript
  - Initiator tRNA, and
  - Large ribosomal subunit
  - Initiation factors (special proteins that bring the above together)
- Initiator tRNA:
  - Always has the UAC anticodon
  - Always carries the amino acid methionine
  - Capable of binding to the P site

66

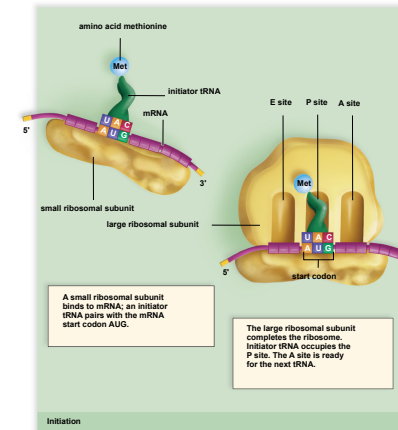
## Steps in Translation: Initiation

- Small ribosomal subunit attaches to mRNA transcript
  - Beginning of transcript always has the START codon (AUG)
- Initiator tRNA (UAC) attaches to P site
- Large ribosomal subunit joins the small subunit

67

## Steps in Translation: Initiation

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.



69

## Steps in Translation: Elongation

- “Elongation” refers to the growth in length of the polypeptide
- RNA molecules bring their amino acid fares to the ribosome
  - Ribosome reads a codon in the mRNA
    - Allows only one type of tRNA to bring its amino acid
    - Must have the anticodon complementary to the mRNA codon being read
    - Joins the ribosome at it's A site
  - Methionine of initiator is connected to amino acid of 2<sup>nd</sup> tRNA by peptide bond

70

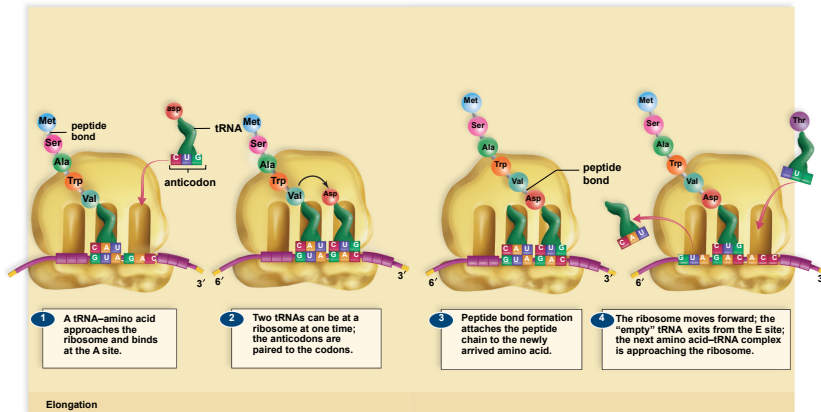
## Steps in Translation: Elongation

- Second tRNA moves to P site (translocation)
- Spent initiator moves to E site and exits
- Ribosome reads the next codon in the mRNA
  - Allows only one type of tRNA to bring its amino acid
    - Must have the anticodon complementary to the mRNA codon being read
    - Joins the ribosome at it's A site
  - Dipeptide on 2<sup>nd</sup> amino acid is connected to amino acid of 3<sup>rd</sup> tRNA by peptide bond

71

## Steps in Translation: Elongation

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.



73

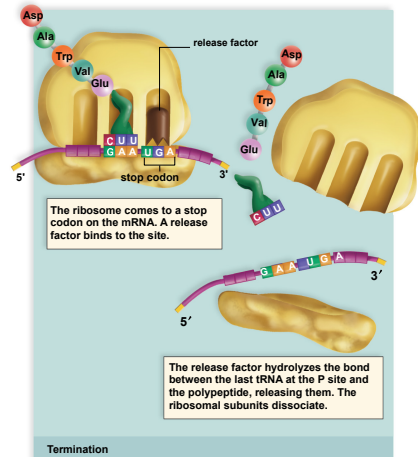
## Steps in Translation: Termination

- Previous tRNA moves to P site
- Spent tRNA moves to E site and exits
- Ribosome reads the STOP codon at the end of the mRNA
  - UAA, UAG, or UGA
  - Does not code for an amino acid
- Polypeptide is released from last tRNA by release factor
- Ribosome releases mRNA and dissociates into subunits
- mRNA read by another ribosome

74

## Steps in Translation: Termination

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.



76

## Animation

How Translation Works

DNA

Play Pause Audio Text

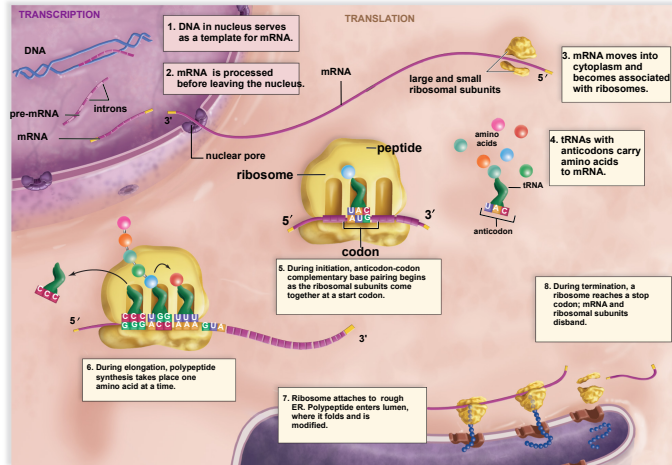
The genetic information stored in DNA is transcribed into messenger RNA and then translated into protein.

Copyright © The McGraw-Hill Companies, Inc.

62

## Summary of Gene Expression (Eukaryotes)

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.



78

## Animation

Protein Synthesis

5' AUGCCGUACGAUCCG 3'

Play Pause Audio Text

Translation is initiated by formation of an initiation complex consisting of the smaller ribosomal subunit, the first amino acid-tRNA and messenger RNA.

Copyright © The McGraw-Hill Companies, Inc.

64

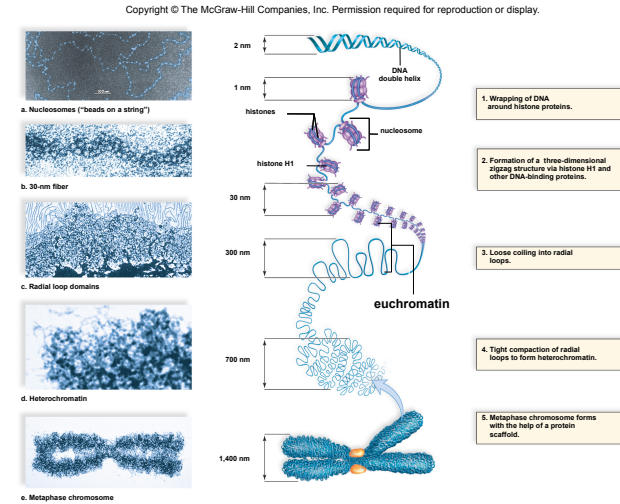


## Structure of Eukaryotic Chromosome

- Contains a single linear DNA molecule, but is composed of more than 50% protein.
- Some of these proteins are concerned with DNA and RNA synthesis,
- Histones, play primarily a structural role
  - Five primary types of histone molecules
  - Responsible for packaging the DNA
    - DNA double helix is wound at intervals around a core of eight histone molecules (called nucleosome)
    - Nucleosomes are joined by “linker” DNA.

80

## Structure of Eukaryotic Chromosome



81

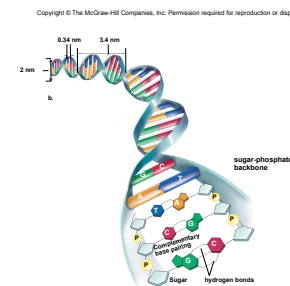
## Review

- Genetic Material
  - Transformation
- DNA Structure
  - Watson and Crick
- DNA Replication
  - Prokaryotic versus Eukaryotic
  - Replication Errors
- Transcription
- Translation
- Structure of Eukaryotic Chromosome

83

Chapter 12: pp. 211 - 232

## Molecular Biology of the Gene



PowerPoint® Lecture Slides are prepared by Dr. Isaac Barjis, Biology Instructor  
Copyright © The McGraw Hill Companies Inc. Permission required for reproduction or display

**BIOLOGY**  
10th Edition

Sylvia S. Mader

1