MUTATIONS

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Dr. Manu Smriti Singh

Department of Biotechnology

Bennett University

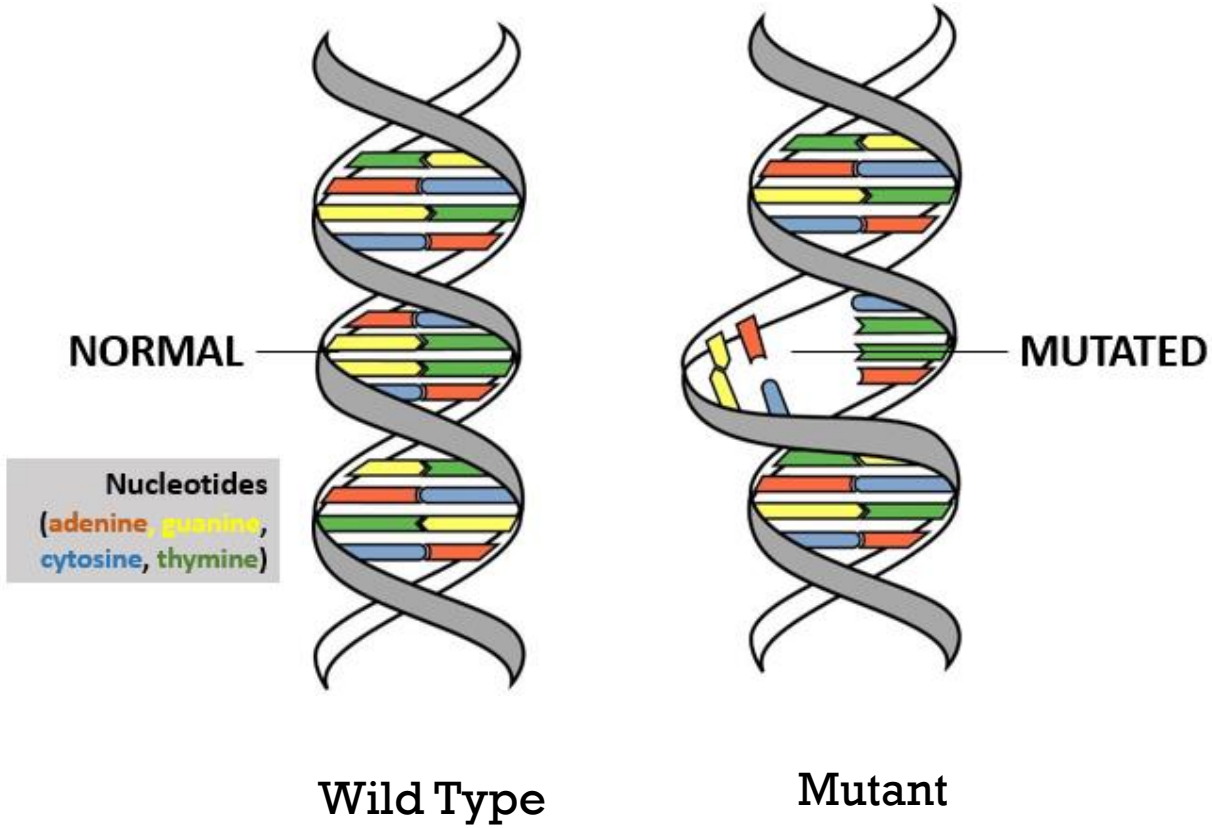
MUTATIONS- FEW AND IMPORTANT

- **Two ways genetic alterations happen:**

-Recombination

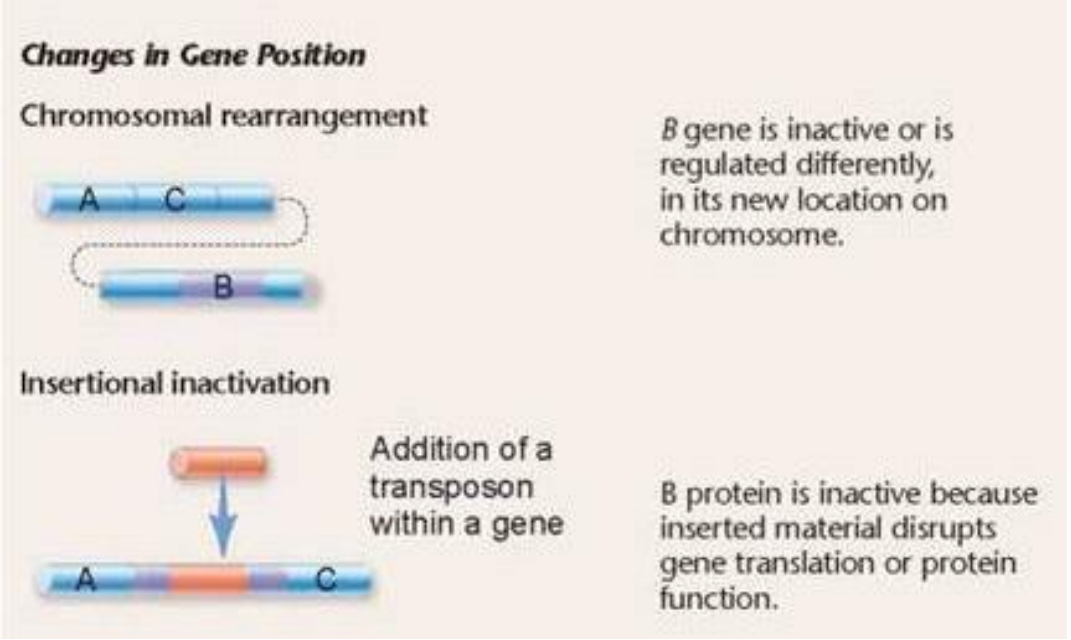
-Mutation

- **Organisms have evolved many different mechanisms to avoid errors during DNA replication and to preserve the DNA from damage.**
- **Some of these mechanisms "proofread" the replicated DNA strands for accuracy and correct any mistakes.**
- **BUT, mistakes happen- Mutation!**
- **Important for evolution**

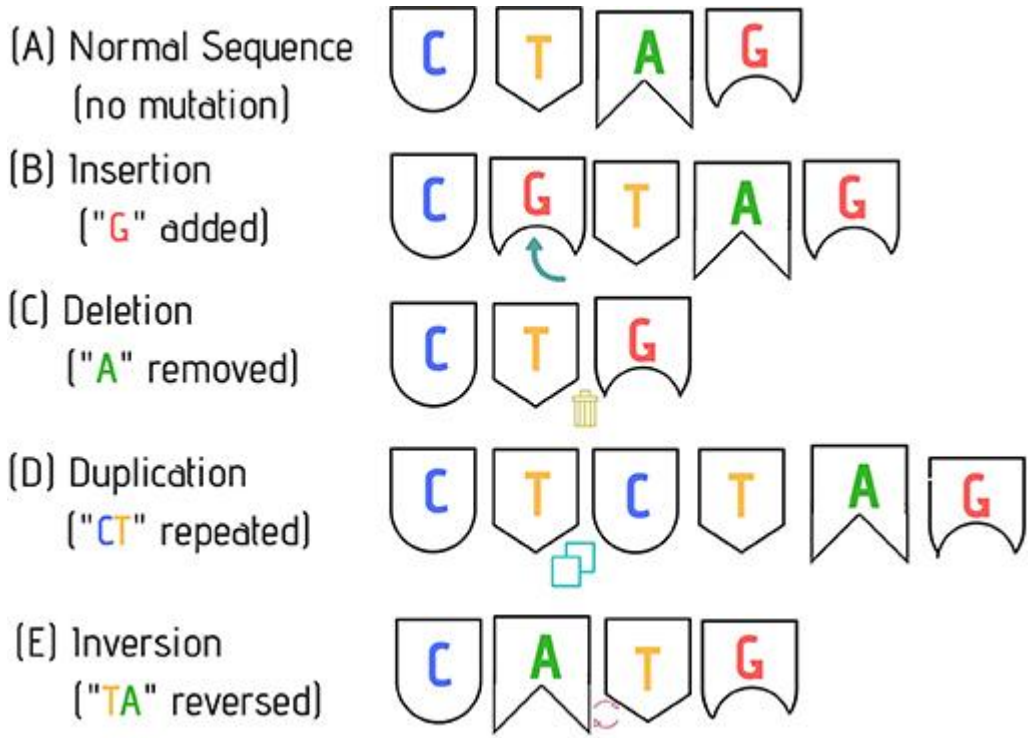


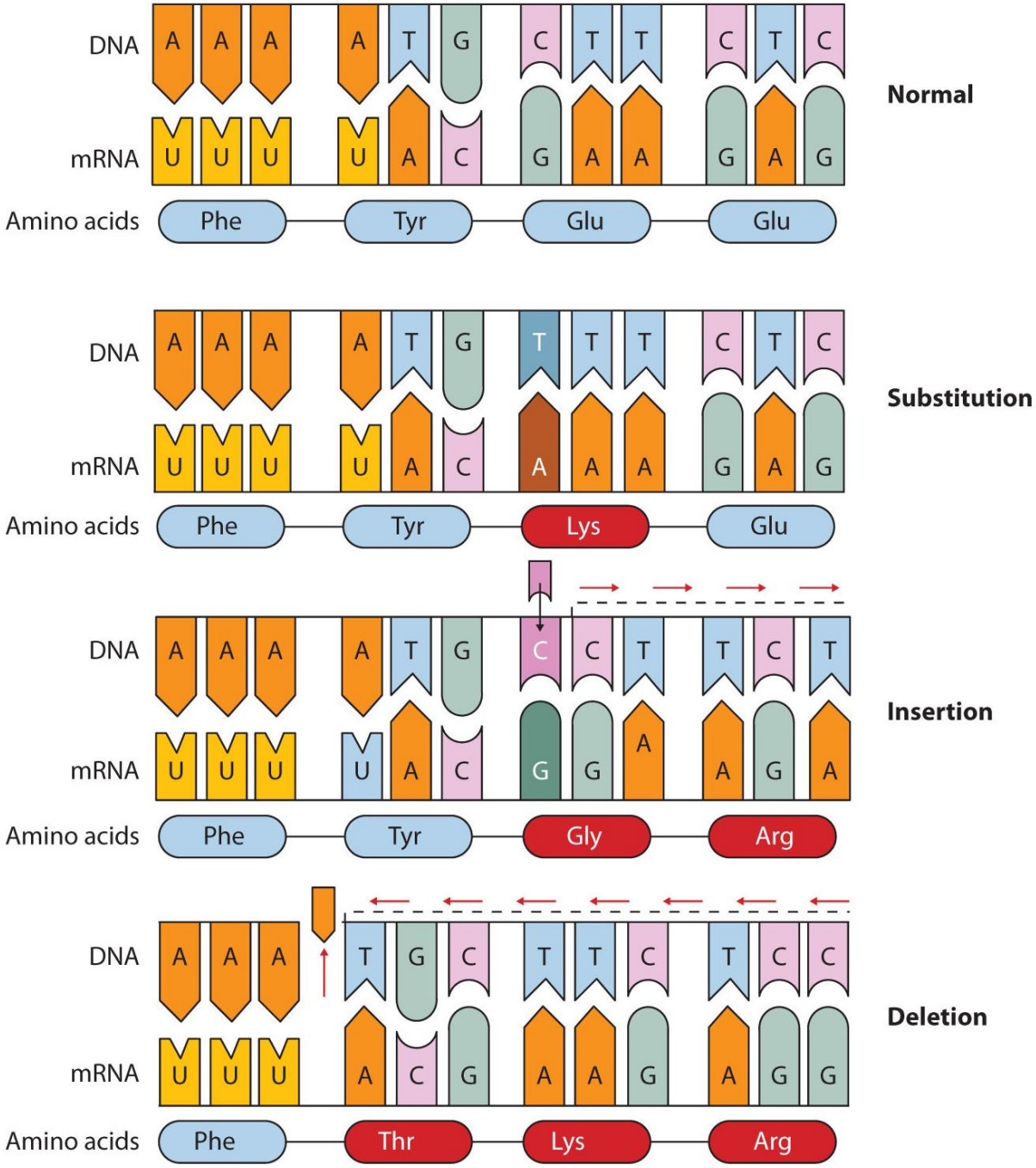
MUTATIONS

- Gene- Number/ Position
- Chromosomal- Number/ Position



POINT MUTATIONS

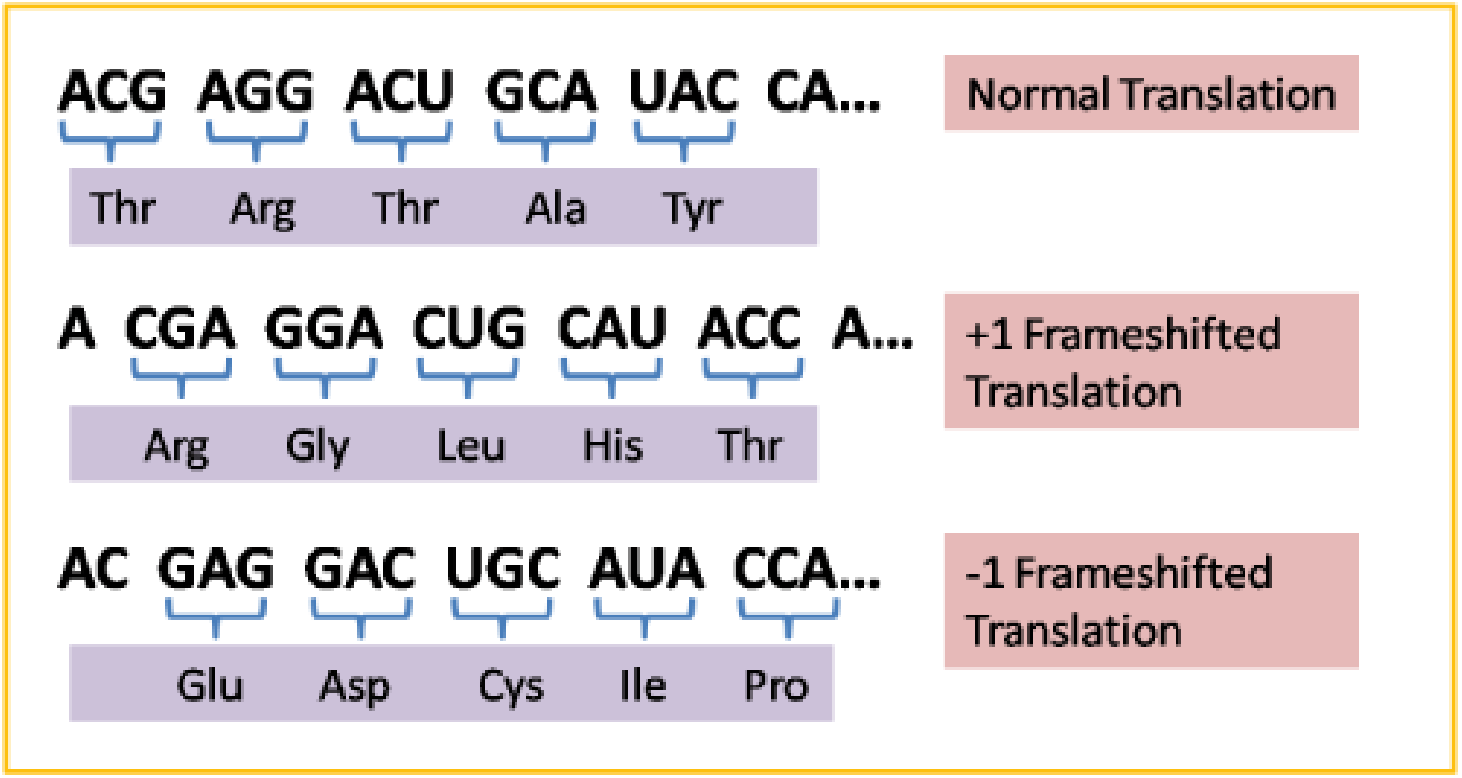




FRAMESHIFT MUTATIONS

THE FAT CAT ATE THE RAT

THE ATC ATA TET HER AT



	No mutation	Point mutations			
		Silent	Nonsense	Missense	
				conservative	non-conservative
DNA level	TTC	TTT	ATC	TCC	TGC
mRNA level	AAG	AAA	UAG	AGG	ACG
protein level	**Lys**	**Lys**	**STOP**	**Arg**	**Thr**

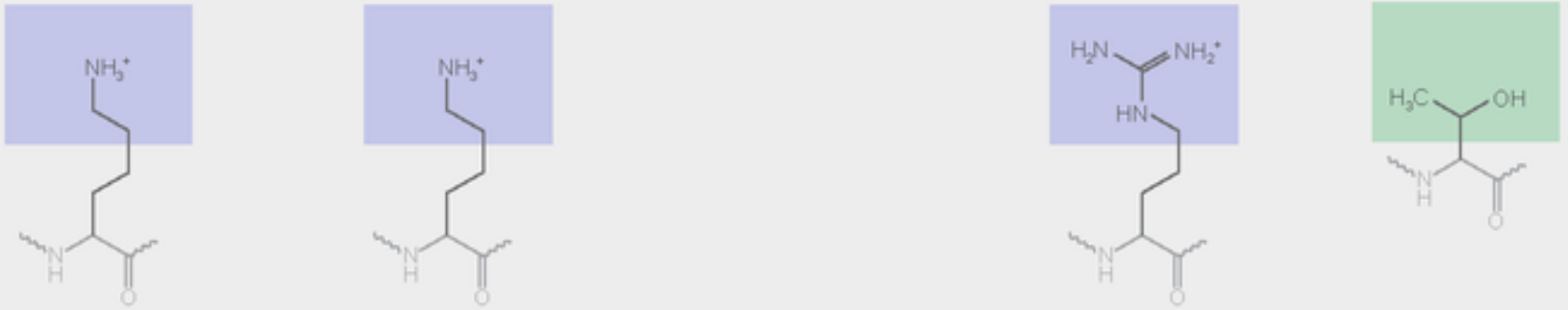
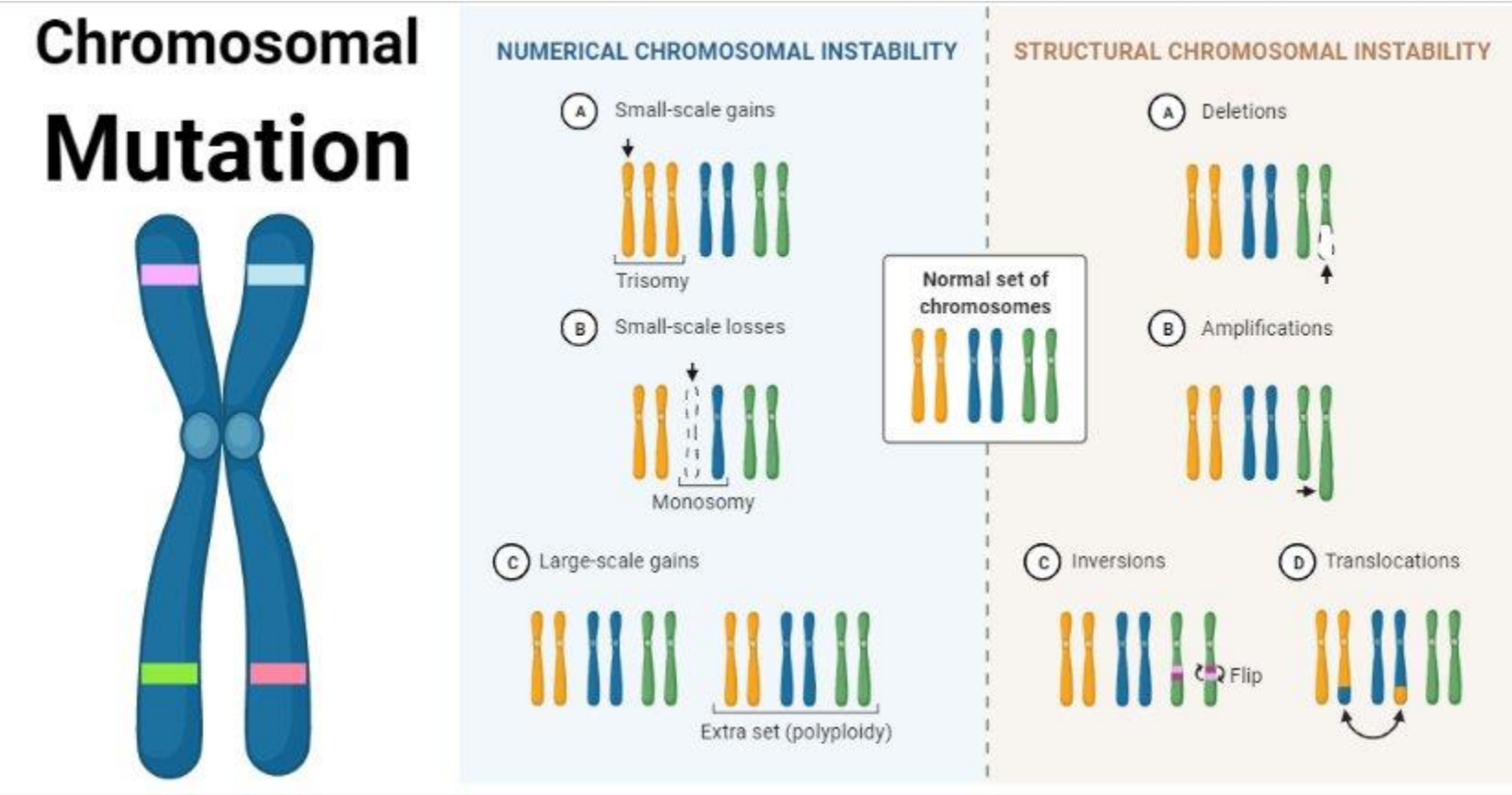


Table 15.1 The Genetic Code

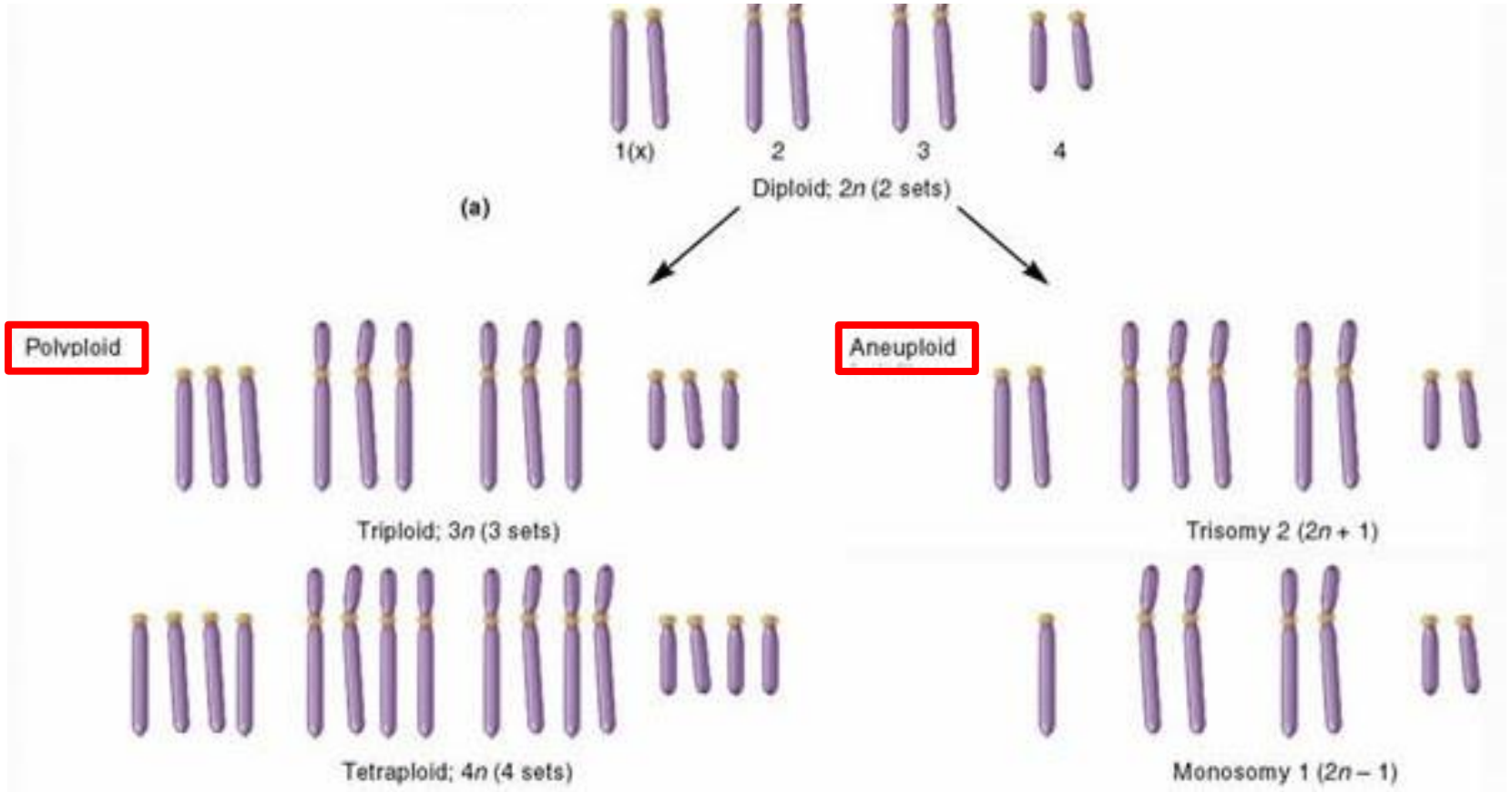
First Letter	Second Letter: U		Second Letter: C		Second Letter: A		Second Letter: G		Third Letter
U	UUU	Phenylalanine	UCU	Serine	UAU	Tyrosine	UGU	Cysteine	U
	UUC		UCC		UAC		UGC		C
	UUA	Leucine	UCA		UAA	Stop	UGA	Stop	A
	UUG		UCG		UAG	Stop	UGG	Tryptophan	G
C	CUU	Leucine	CCU	Proline	CAU	Histidine	CGU	Arginine	U
	CUC		CCC		CAC		CGC		C
	CUA		CCA		CAA	Glutamine	CGA		A
	CUG		CCG		CAG		CGG		G
A	AUU	Isoleucine	ACU	Threonine	AAU	Asparagine	AGU	Serine	U
	AUC		ACC		AAC		AGC		C
	AUA	Methionine; Start	ACA		AAA	Lysine	AGA	Arginine	A
	AUG		ACG		AAG		AGG		G
G	GUU	Valine	GCU	Alanine	GAU	Aspartate	GGU	Glycine	U
	GUC		GCC		GAC		GGC		C
	GUA		GCA		GAA	Glutamate	GGA		A
	GUG		GCG		GAG		GGG		G

A codon consists of three nucleotides read in the sequence shown. For example, ACU codes for threonine. The first letter, A, is in the First Letter column; the second letter, C, is in the Second Letter column; and the third letter, U, is in the Third Letter column. Each of the mRNA codons is recognized by a corresponding anticodon sequence on a tRNA molecule. Some tRNA molecules recognize more than one codon in mRNA, but they always code for the same amino acid. In fact, most amino acids are specified by more than one codon. For example, threonine is specified by four codons, which differ only in the third nucleotide (ACU, ACC, ACA, and ACG).

CHROMOSOMAL MUTATION

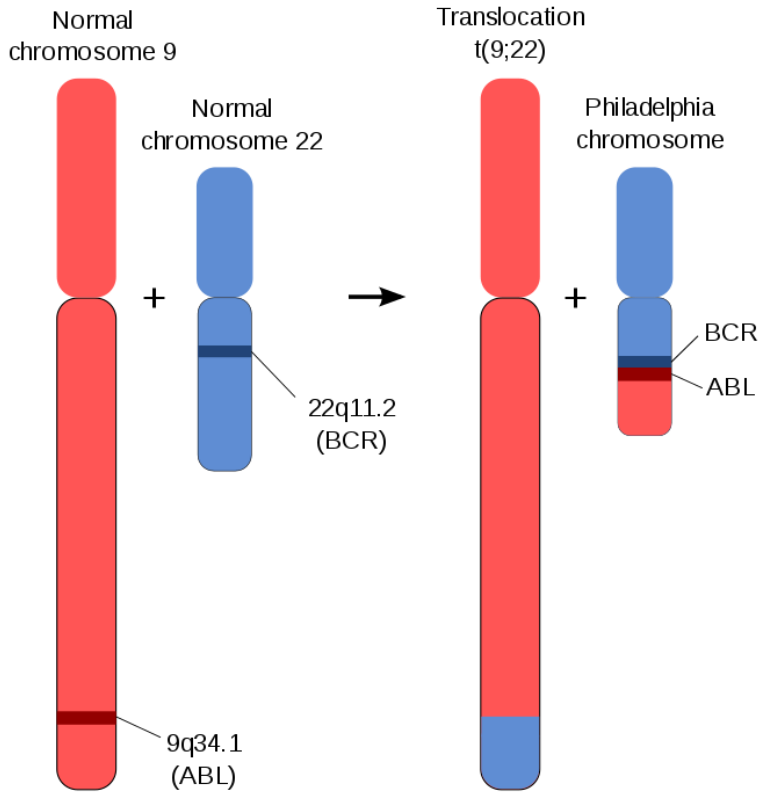


NUMERICAL CHROMOSOMAL MUTATION



GENE MUTATION VERSUS CHROMOSOMAL MUTATION

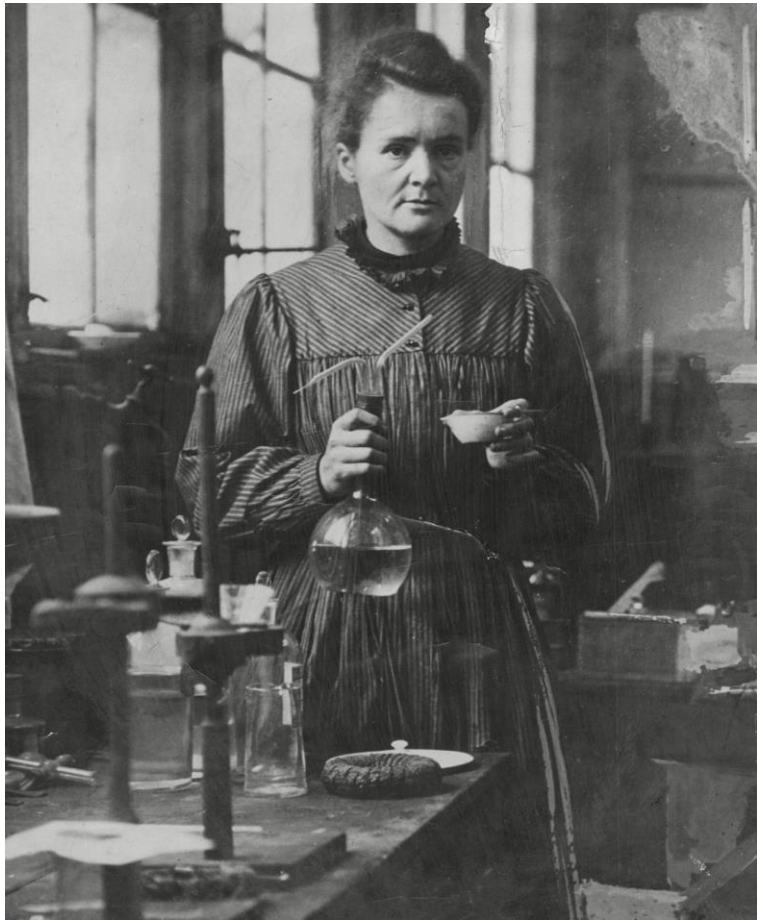
Gene mutation	Chromosomal mutation
Gene mutation is an alteration of the nucleotide sequence of a gene	Chromosomal mutations are alterations in the chromosome structure or chromosome number
Caused by errors in DNA replication and mutagens such as UV and chemicals	Caused by errors in crossing over during meiosis
The alteration occurs in the nucleotide sequence of a gene	The alteration occurs in a segment of a chromosome
A single gene is affected	Several genes are affected
Influence is comparatively low	Can sometimes be lethal
Can cause sickle cell anemia, hemophilia, cystic fibrosis, Huntington syndrome, Tay-Sachs disease, and cancers	Can cause Klinefelter syndrome, Turner syndrome, and Down syndrome



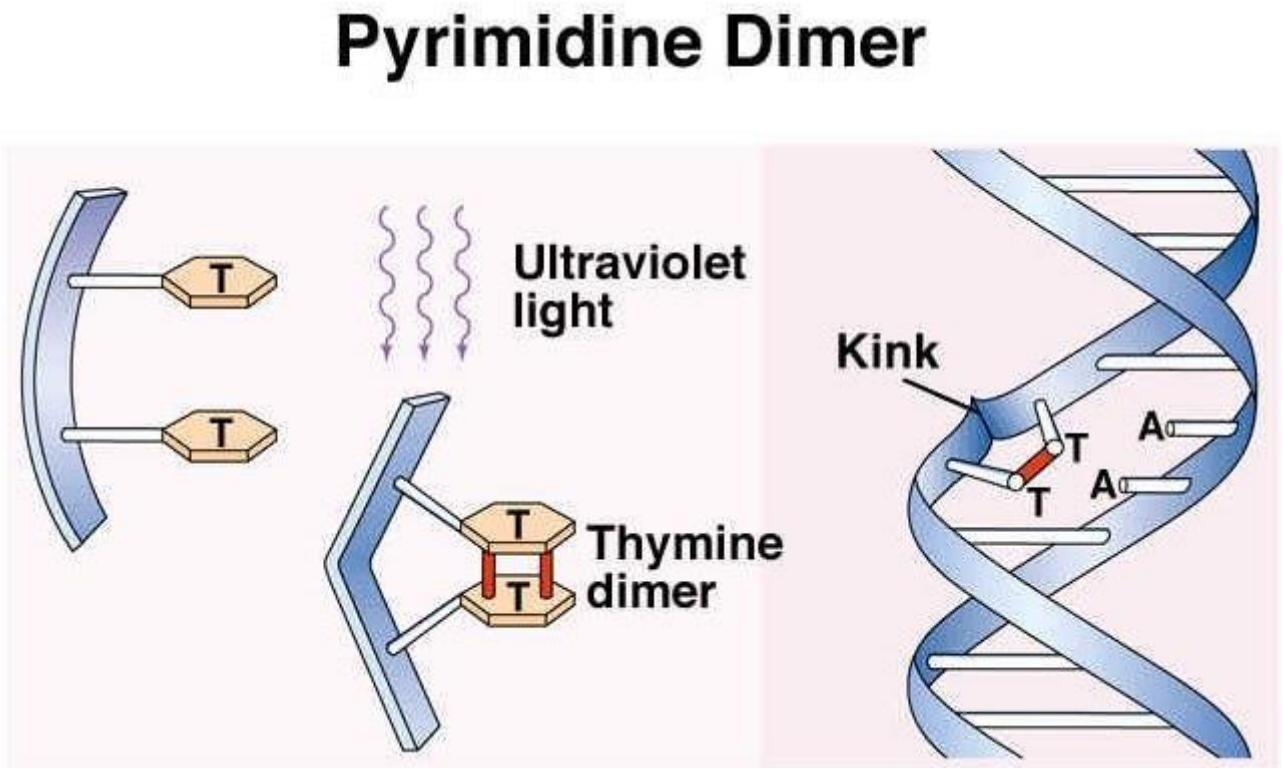
Chronic Myeloid Leukemia (CML)

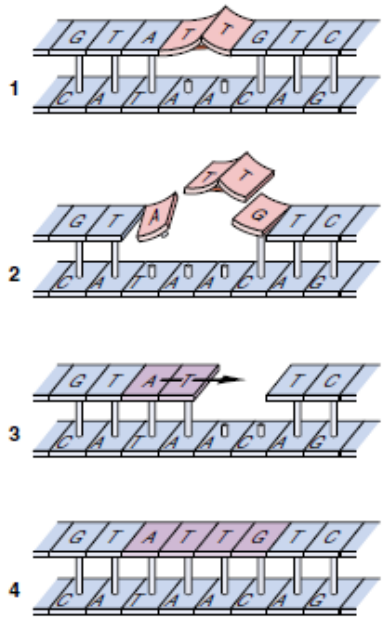
MARIE CURIE

- Polish/ naturalized French
- Discovered Radium and Polonium
- First woman to win Nobel Prize
- Only person to obtain Nobel Prize twice
- First woman to become a professor at the University of Paris in 1906
- Developed mobile radiography for X-ray during World War I to be used in field hospitals
- Died of aplastic anemia (in which bone cannot form red and white cells)
- Because carried radioactive molecules in pocket



MUTATION IN NATURE





- Interfere in replication & transcription
- Cause Xeroderma pigmentosum in absence of repair enzymes
- If not repaired, high risk of skin cancer

MUTATION IN NATURE

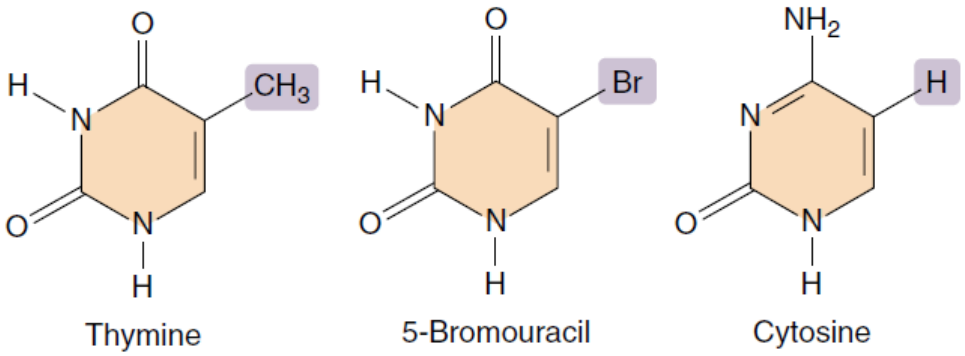


FIGURE 18.5
Chemicals that resemble DNA bases can cause mutations. For example, DNA polymerase cannot distinguish between thymine and 5-bromouracil, which are similar in shape. Once incorporated into a DNA molecule, however, 5-bromouracil tends to rearrange to a form that resembles cytosine and pairs with guanine. When this happens, what was originally an A-T base-pair becomes a G-C base-pair.

MUTATION IN NATURE

Genetic changes in somatic cells do not pass on to off- spring, and so have less evolutionary consequence than germ-line change.

Example of Somatic cell mutation- Colorectal Cancer

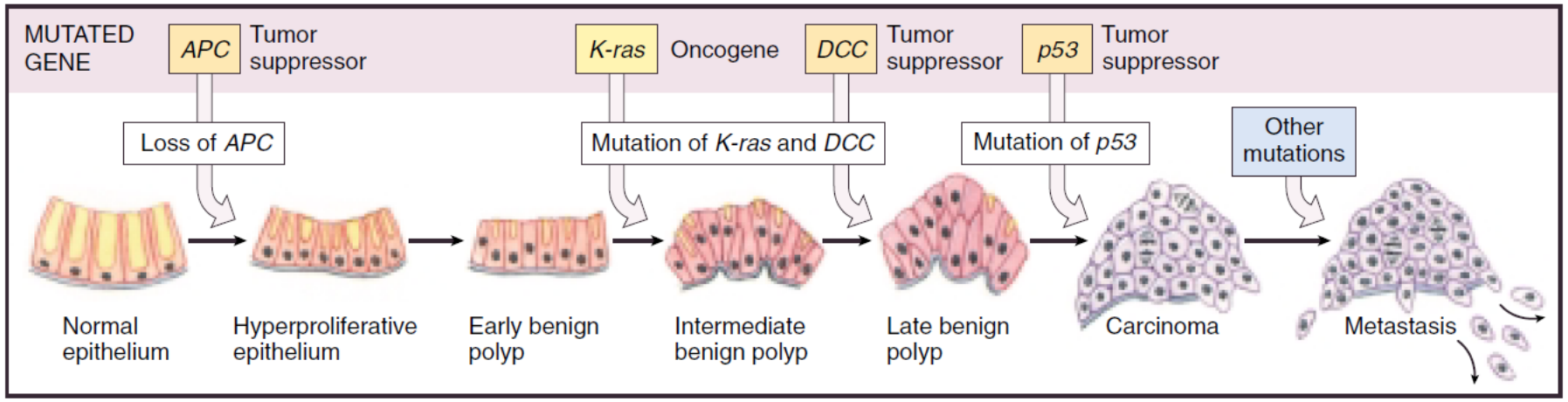


FIGURE 18.16
The progression of mutations that commonly lead to colorectal cancer. The fatal metastasis is the last of six serial changes that the epithelial cells lining the rectum undergo. One of these changes is brought about by mutation of a proto-oncogene, and three of them involve mutations that inactivate tumor-suppressor genes.

A Rough Guide to

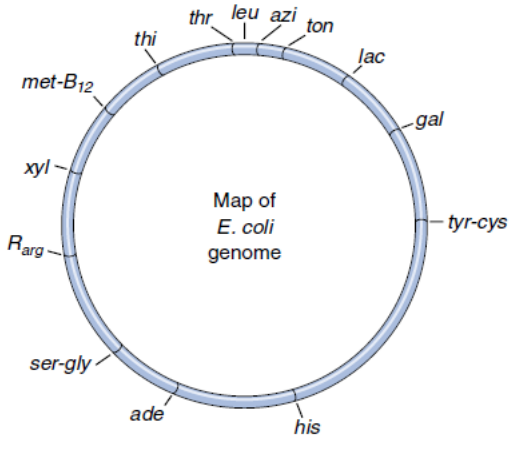
IARC CARCINOGEN CLASSIFICATIONS

The International Agency for Research on Cancer (IARC) classifies substances to show whether they are suspected to cause cancer or not. It places substances into one of five categories depending on the strength of evidence for their carcinogenicity.

GROUP	WHAT DOES IT MEAN?	WHAT DOES IT INCLUDE?
GROUP 1	CARCINOGENIC TO HUMANS	Sufficient evidence in humans. Causal relationship established.	Smoking, exposure to solar radiation, alcoholic beverages and processed meats.
GROUP 2A	PROBABLY CARCINOGENIC TO HUMANS	Limited evidence in humans. Sufficient evidence in animals.	Emissions from high temp. frying, steroids, exposures working in hairdressing, red meat.
GROUP 2B	POSSIBLY CARCINOGENIC TO HUMANS	Limited evidence in humans. Insufficient evidence in animals.	Coffee, gasoline & gasoline engine exhaust, welding fumes, pickled vegetables.
GROUP 3	CARCINOGENICITY NOT CLASSIFIABLE	Inadequate evidence in humans. Inadequate evidence in animals.	Tea, static magnetic fields, fluorescent lighting, polyethene.
GROUP 4	PROBABLY NOT CARCINOGENIC	Evidence suggests no carcinogenicity in humans/animals	1 ONLY 1 CHEMICAL EVER PLACED IN THIS GROUP, OF ALL SUBSTANCES ASSESSED Caprolactam, which is used in the manufacture of synthetic fibres.

THE IARC'S INDEX ONLY TELLS US HOW STRONG THE EVIDENCE IS THAT SOMETHING CAUSES CANCER. SUBSTANCES IN THE SAME CATEGORY CAN DIFFER VASTLY IN HOW MUCH THEY INCREASE CANCER RISK.

BEADLE AND TATUM EXPERIMENT



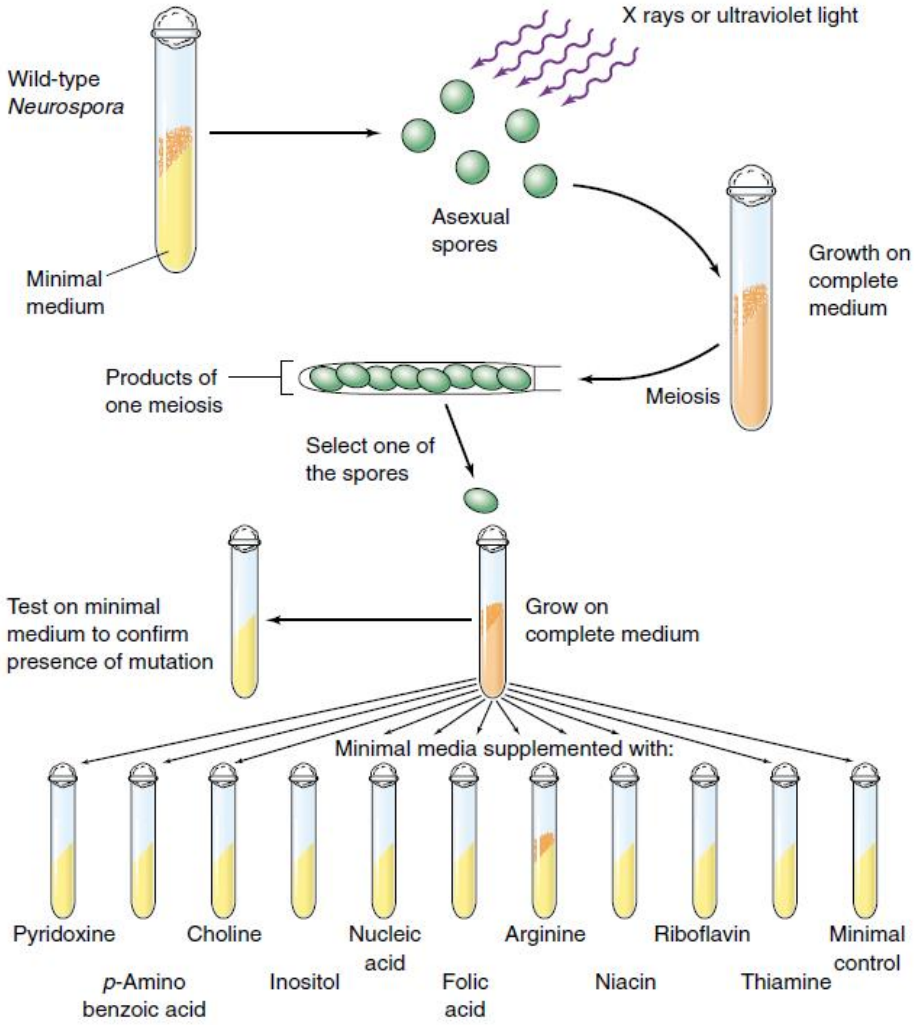
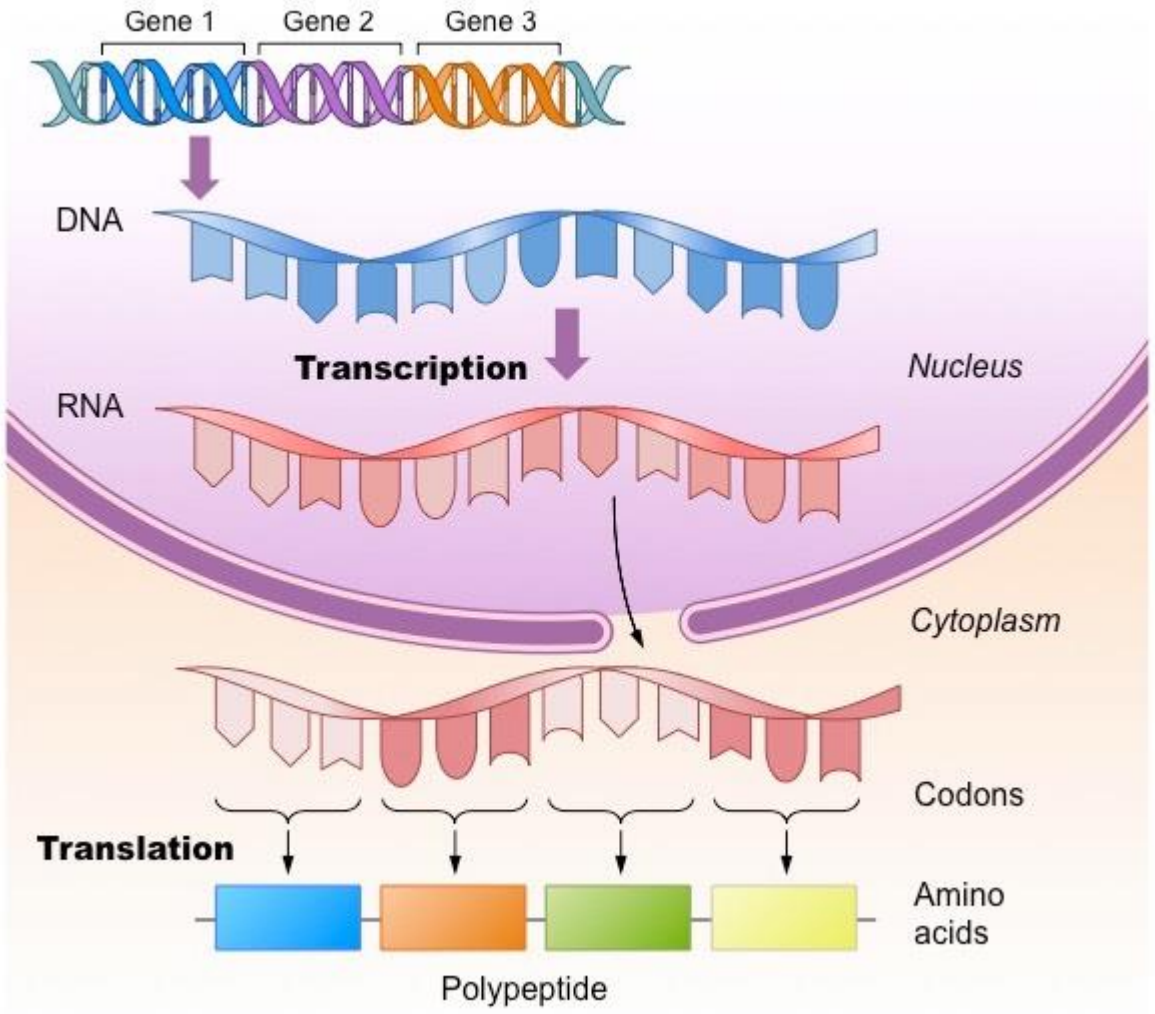


FIGURE 14.20
Beadle and Tatum's procedure for isolating nutritional mutants in *Neurospora*. This fungus grows easily on an artificial medium in test tubes. In this experiment, spores were irradiated to increase the frequency of mutation; they were then placed on a "complete" medium that contained all of the nutrients necessary for growth. Once the fungal colonies were established on the complete medium, individual spores were transferred to a "minimal" medium that lacked various substances the fungus could normally manufacture. Any spore that would not grow on the minimal medium but would grow on the complete medium contained one or more mutations in genes needed to produce the missing nutrients. To determine which gene had mutated, the minimal medium was supplemented with particular substances. The mutation illustrated here produced an arginine mutant, a collection of cells that lost the ability to manufacture arginine. These cells will not grow on minimal medium but will grow on minimal medium with only arginine added.

ONE GENE ONE POLYPEPTIDE HYPOTHESIS



REPLICATION

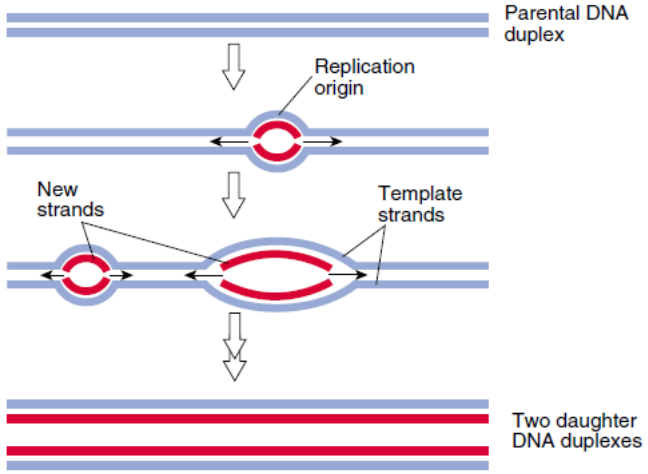
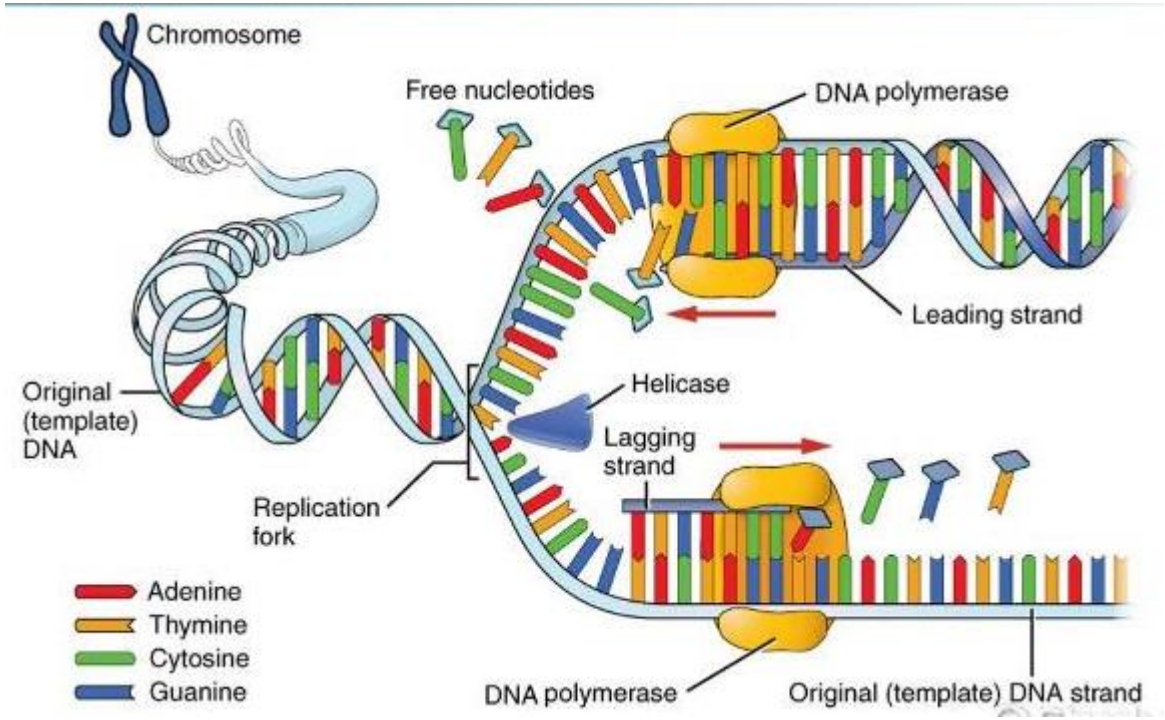


FIGURE 14.13
Origins of replication. At a site called the replication origin, the DNA duplex opens to create two separate strands, each of which can be used as a template for a new strand. Eukaryotic DNA has multiple origins of replication.

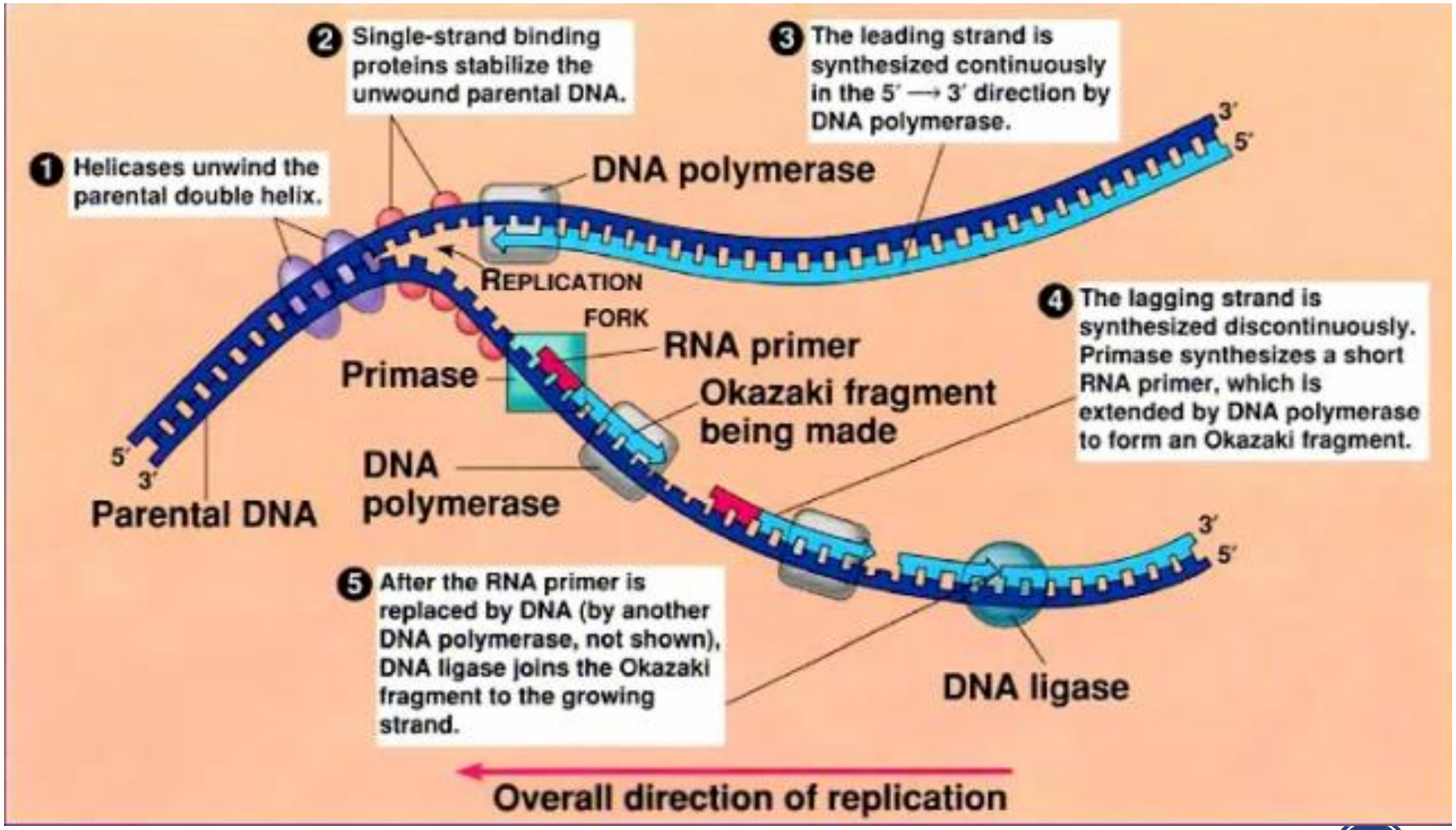


REPLICATION

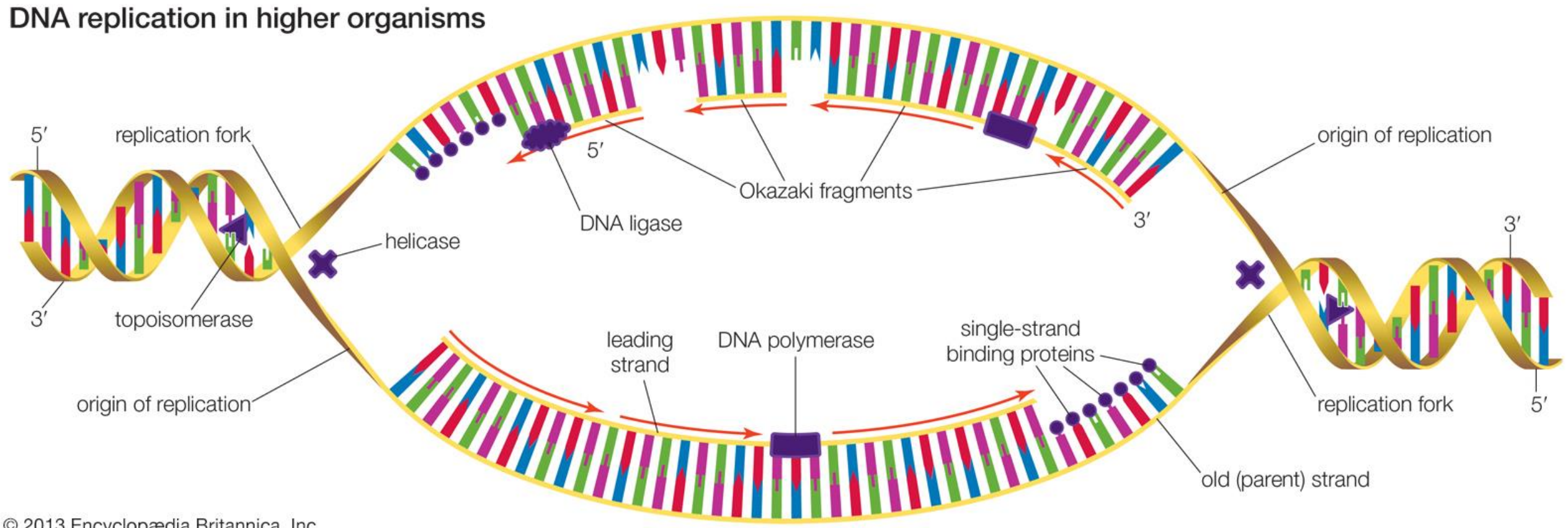
Enzymes:

- **Helicases**
- **Primase**
- **DNA polymerase**
- **Exonuclease**
- **DNA ligase**
- **DNA gyrase/ Topoisomerase**

Protein	Role
Helicase	Unwinds the double helix
Primase	Synthesizes RNA primers
Single-strand binding protein	Stabilizes single-stranded regions
DNA gyrase	Relieves torque
DNA polymerase III	Synthesizes DNA
DNA polymerase I	Erases primer and fills gaps
DNA ligase	Joins the ends of DNA segments



REPLICATION SNAPSHOT



PRIMASE

- Primase is a specilised RNA polymerase
- It synthesis a short strech of RNA in 5’ 3’ direction on a template running in 3’ 5’ direction.
- An RNA primer, about 100-200 nucleotides long, is synthesized by the RNA primase.
- The RNA primer is removed by DANP, using exonuclease activity and is replaced with deoxyribo nucleotides by DNAP

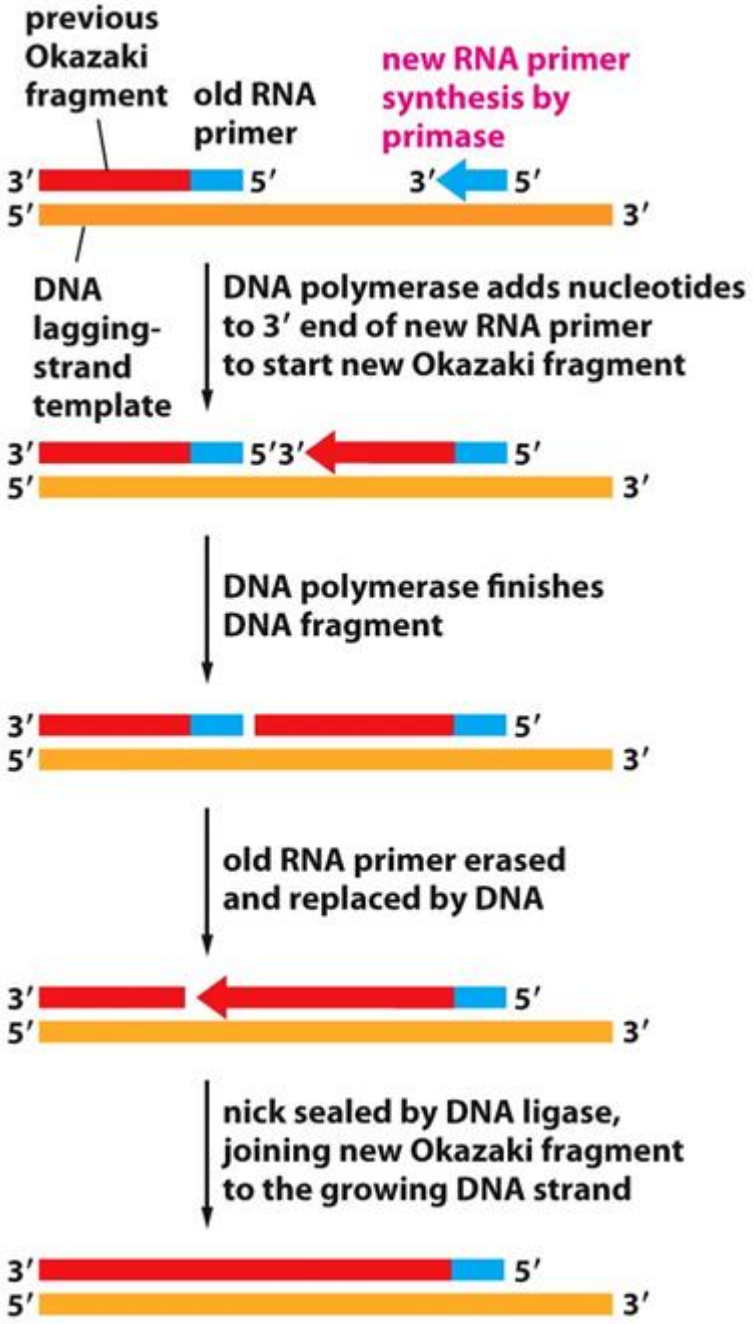
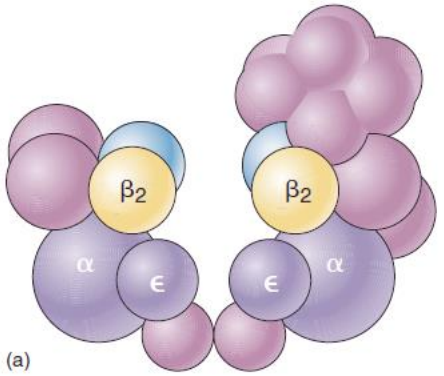
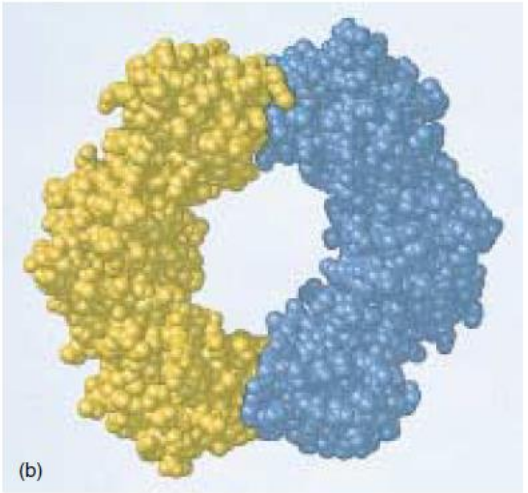


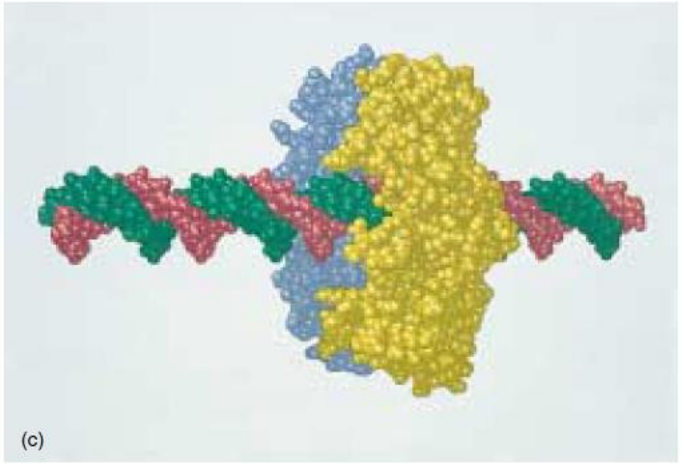
Figure 6-17 Essential Cell Biology, 4th ed. (© Garland Science 2014)

DNA POLYMERASE

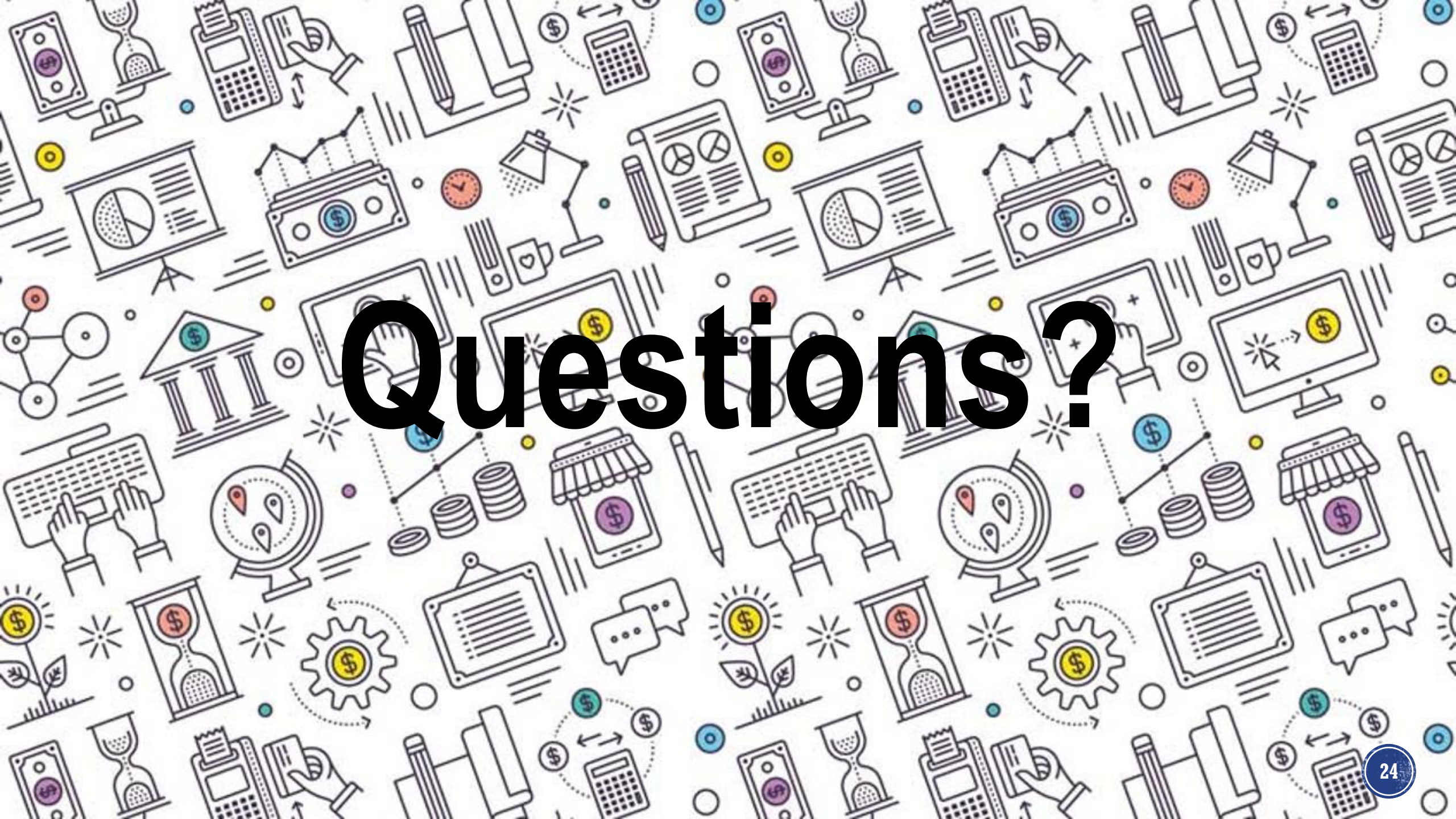
FIGURE 14.15
The DNA polymerase III complex. (*a*) The complex contains 10 kinds of protein chains. The protein is a dimer because both strands of the DNA duplex must be replicated simultaneously. The catalytic (α) subunits, the proofreading (ε) subunits, and the "sliding clamp" (β_2) subunits (*yellow* and *blue*) are labeled. (*b*) The "sliding clamp" units encircle the DNA template and (*c*) move it through the catalytic subunit like a rope drawn through a ring.







Reference: Raven & Johnson Biology
Chapter 14- Replication
Chapter 18- Mutation


Questions?