

Chapter 15 HOW GENES WORK

Genotype to Phenotype

Summary

History

The Genetic Code

Watson and Crick

Characteristics

How the code is used

History

Mendel gave us insight on how traits or characteristics are inherited.

1903 – Sutton and Boveri published the Chromosome Theory of Inheritance:

- Meiosis causes patterns of inheritance observed by Mendel

- Hereditary factors are genes located on DNA.

History

How do genes cause certain traits to appear?

Physicians noted that certain diseases seemed to run in families.

Garrod was interested in one such disease, alcaptonuria.

This disease is characterized by the accumulation of a substance that is excreted in the urine, turning it black.

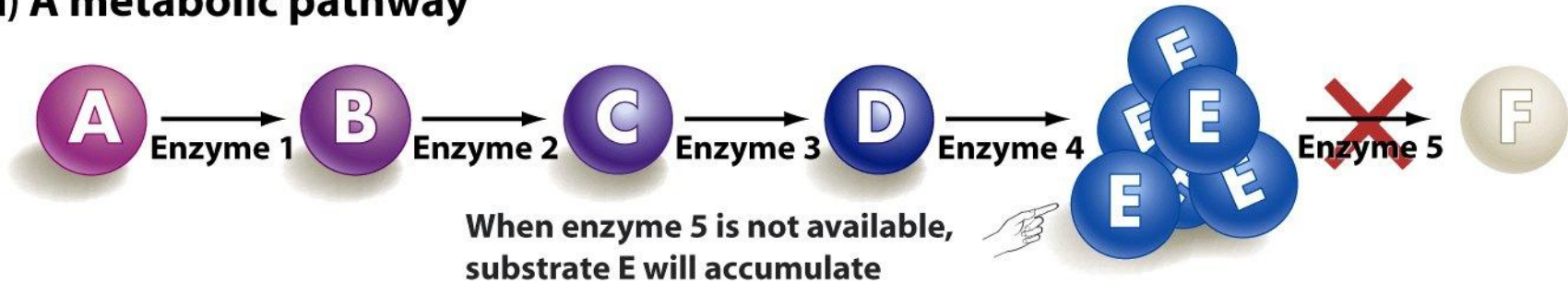
History

Garrod cont'd

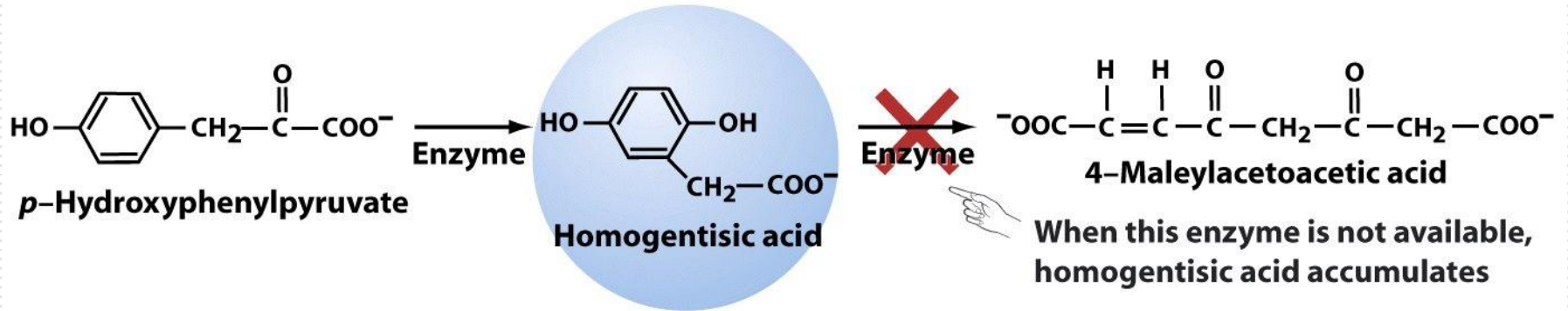
The accumulation of this substance is caused by an error in a metabolic pathway. Metabolic pathways are series of chemical reactions each catalyzed by a certain enzyme (protein – coded for on DNA).

Conclusion: a defect or lack of an enzyme causes accumulation of one of the substrates, fig 15.1.

(a) A metabolic pathway



(b) One metabolic pathway studied by Garrod



History

Garrod cont'd

Certain defects in enzymes are inherited
= Biochemical Basis of Genetic Diseases

Other scientists/physicians studied the effect of altering DNA on biochemical pathways.

Srb and Horowitz proposed the one gene one enzyme hypothesis.

History

Beadle and Tatum – proposed that one could find out what genes do by making them defective.

Today – genes are studied by using organisms with defective or non-functioning genes = “knock out mutants”.

The Genetic Code

How do genes produce certain enzymes/proteins?

Watson and Crick

Because of the structure of DNA, it probably does not catalyze protein synthesis directly.

DNA could act as a “code” used to assemble the 20 different amino acids into different proteins.

The Genetic Code

Watson and Crick cont'd

The code is the particular sequence of bases in a gene (a part of a strand of DNA).

This particular base sequence codes for a particular sequence of amino acids.

When the DNA strands are separated, the code could be "read" and used to join amino acids in the proper sequence, fig 15.3.

DNA sequences can be read when strands in the double helix are separated

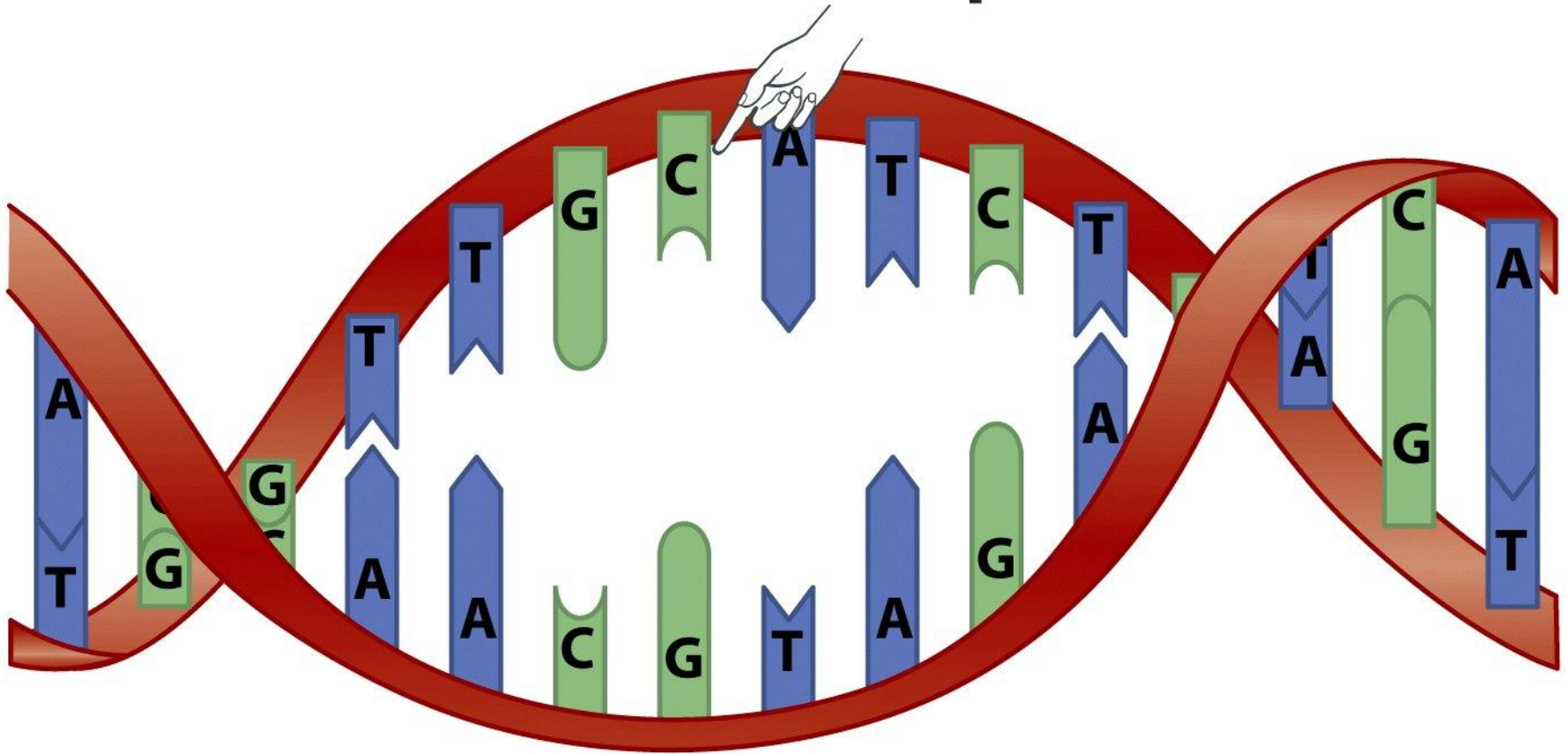


Figure 15-3 Biological Science, 2/e

The Genetic Code

Watson and Crick cont'd

They later decided that the DNA code is not used directly, there must be another step involved. How did they know this?

The Genetic Code

The “other step” is copying the code onto a piece of RNA, specifically messenger RNA (mRNA). mRNA carries the code from the nucleus to the ribosomes, where proteins are made, fig 15.4.

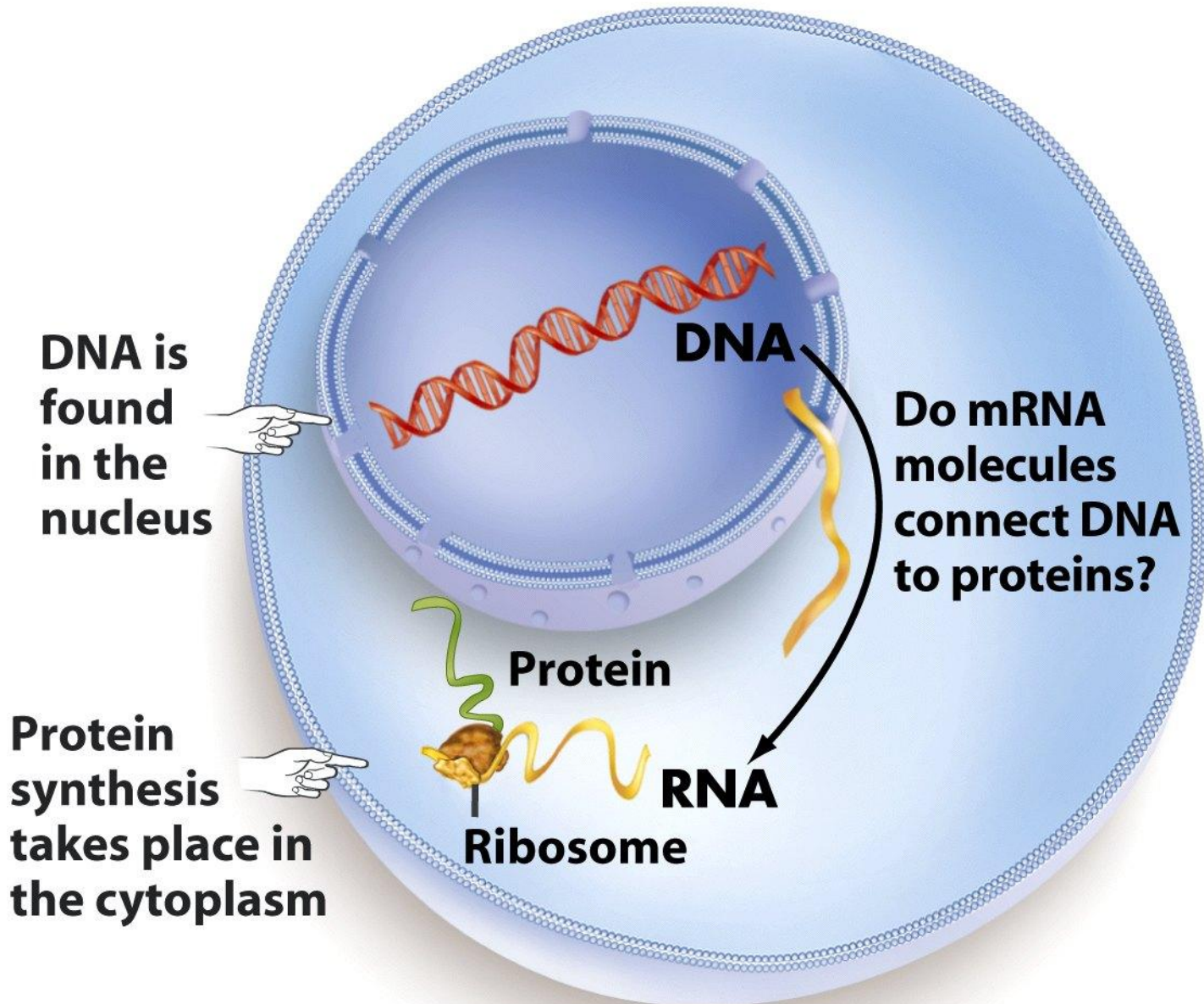


Figure 15-4 Biological Science, 2/e

The Genetic Code

How is mRNA made?

Discovery of RNA polymerase

RNA polymerase "reads" the code on DNA and produces a complementary strand of RNA.

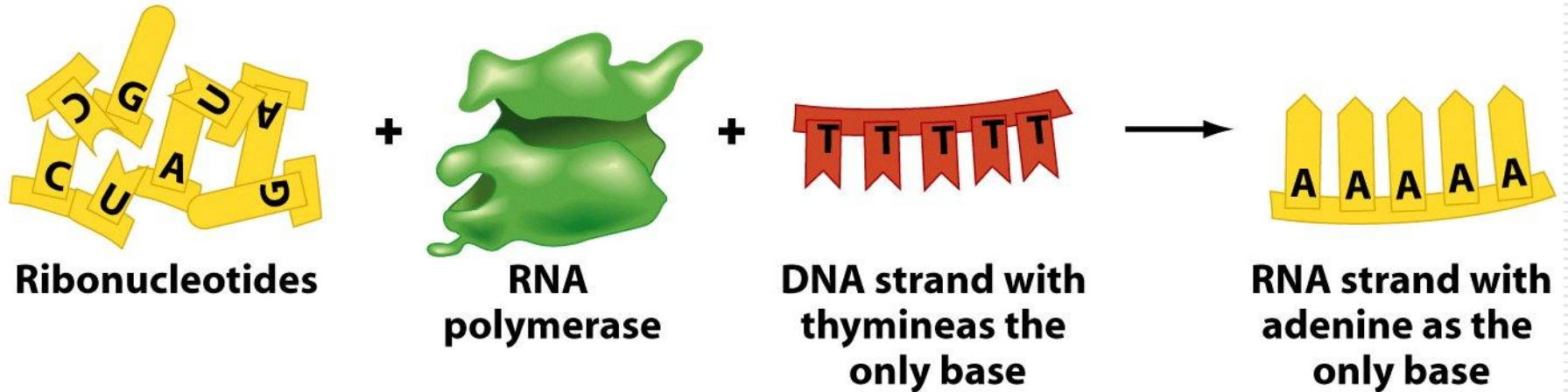
RNA - ribonucleotides

5 carbon sugar – ribose

PO₄ groups

Nitrogenous bases: adenine, cytosine, guanine and **uracil (instead of thymine).

(a) Experimental evidence that RNA is synthesized by complementary base pairing



(b) RNA sequences are complementary to DNA sequences.



Figure 15-5 Biological Science, 2/e

The Genetic Code

The code on DNA

Like letters in a word. The letters are the bases and the word specifies a certain amino acid.

All of the words are 3 bases long = codon. (*Watson and Crick again!*)

Each codon specifies only 1 amino acid. Some amino acids can be specified by more than 1 codon, fig 15.8.

Redundancy & Ambiguity

How will the genetic code work?

Can you code with one base pair?

How many amino acids do you have?

Redundancy & Ambiguity

How many can you code with 2 base pairs?

Ambiguity is.....

Ambiguity

Define Hot

Ambiguity

Define Hot

Temperature

Spicy

Other??

Redundancy & Ambiguity

How many can you code with 2 base pairs?

Ambiguity is.....

3 base pairs?

How many possible combinations with 3 letters?

Redundancy & Ambiguity

What is redundancy?

See/Sea

Two/too

The Genetic Code

There is one codon that signals the beginning of a protein – the start codon.

There are 3 different codons that signal the end of a protein – stop codons.

The collection of codons from the start codon to the stop codon are called the reading frame.

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

Figure 15-8 Biological Science, 2/e

The Genetic Code

What happens if we add or delete a base in the reading frame?

Ex. AUU UGU GGU

The Genetic Code

What happens if we add or delete a base in the reading frame?

Ex. AUU UGU GGU

Frameshift mutation:

The fat cat ate the rat becomes:

TTH efa tca tat eth era t (addition) OR:

Tef atc ata tet her at (deletion)

How severe is this? Total nonsense

Types of mutations

Frameshift (prior slide)

Addition

Deletion

Substitution (More next chapter)

Missense

Nonsense – termination

Silent – (too/two)

Two deletions or additions of bases lead to nonfunctional protein.

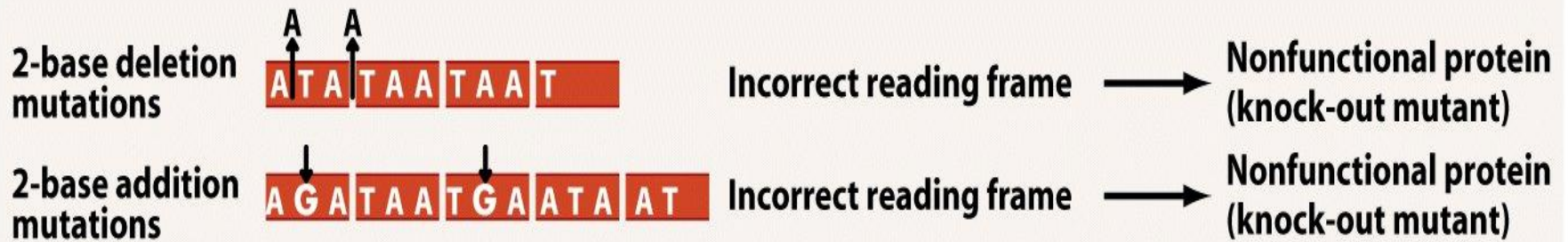


Figure 15-7c Biological Science, 2/e

© 2005 Pearson Prentice Hall, Inc.

General Scheme

DNA (information storage) →
transcription produces...

mRNA (a copy of DNA code) →
translation uses the code to produce a ...

Protein

Changes in the DNA code produce
changes in proteins and this can
change the phenotype, fig 15.10.

One gene One Enzyme hypothesis

Human genome codes 100,000 proteins/enzymes

We have about 30,000 genes

Pieces of some are used multiple times.

How long is a gene?

Insulin 51 amino acids

How many nucleotides?

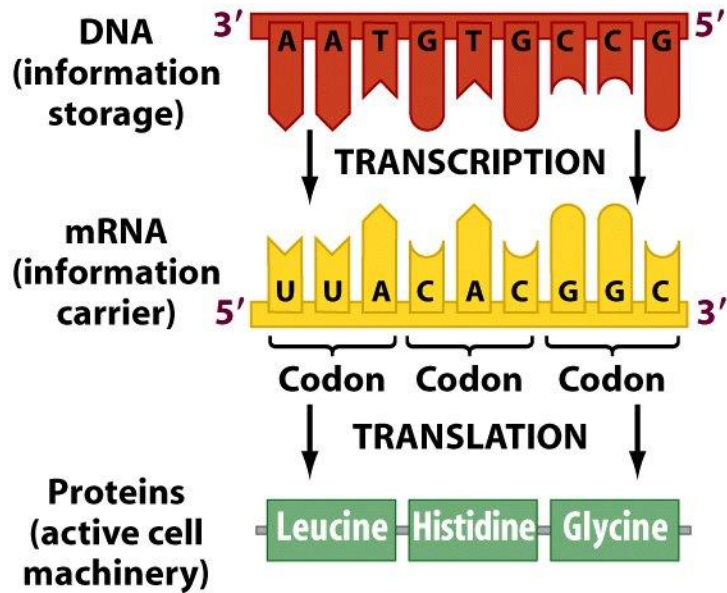
What happens if:

One of a pair of genes is defective for insulin?

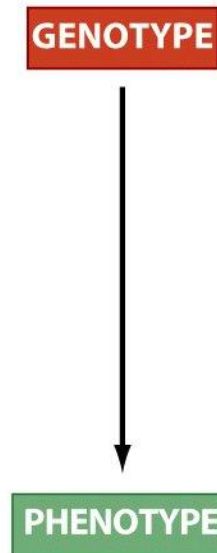
There is a frameshift mutation in insulin?

There is a simple substitution in insulin?

(a) Information flows from DNA to RNA to proteins.



(b) DNA sequences define the genotype; proteins create the phenotype.



(c) Changes in the genotype may lead to changes in the phenotype.

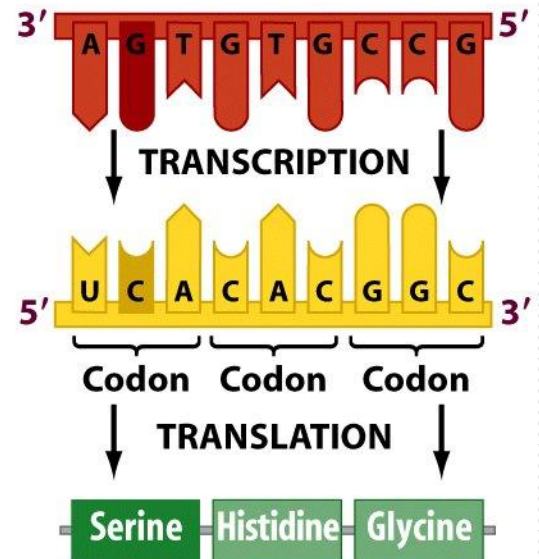


Figure 15-10 Biological Science, 2/e