# DNA Structure and Gene Function

LIU Yang



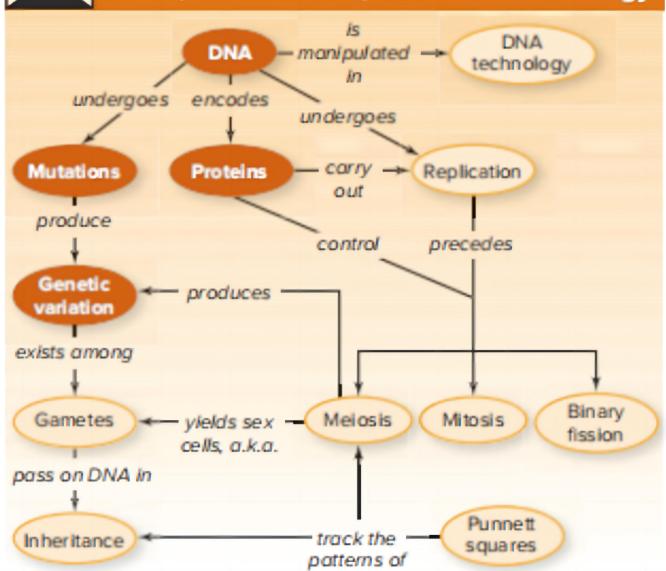
### LEARNING OUTLINE

- 7.1 Experiments Identifed the Genetic Material
- 7.2 DNA Is a Double Helix of Nucleotides
- 7.3 DNA Contains the "Recipes" for a Cell' s Proteins
- 7.4 Transcription Uses a DNA Template to Build RNA
- 7.5 Translation Builds the Protein
- 7.6 Mutations Change DNA Sequences





# SURVEY THE LANDSCAPE DNA, Inheritance, and Biotechnology

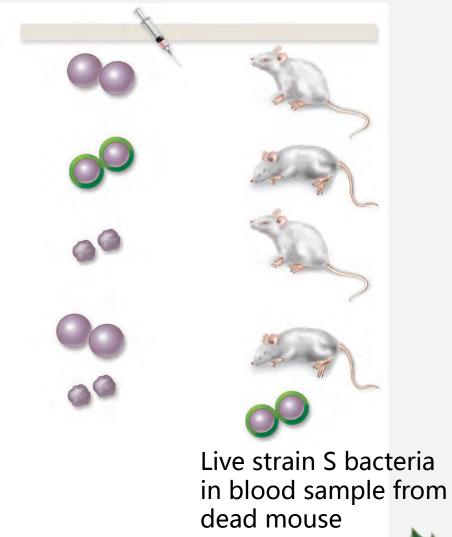




### 7.1 Experiments Identifed the Genetic Material

#### A. Bacteria Can Transfer Genetic Information

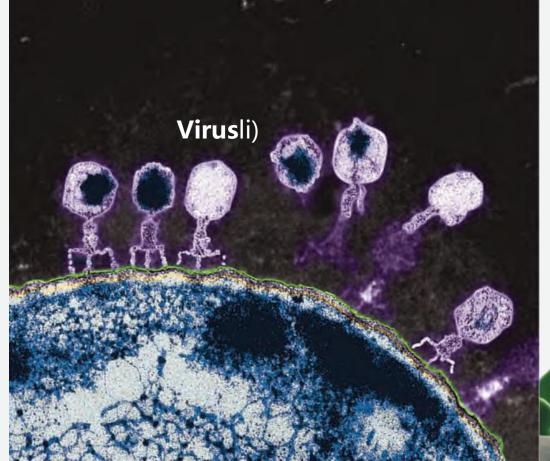
- ➤ In 1928, English microbiologist Frederick Griffith contributed the first step in identifying DNA as the genetic material.
- Something in the heat-killed type S bacteria transformed the normally harmless type R strain into a killer.
- The conclusion: DNA from type S cells altered the type R bacteria, enabling them to manufacture the smooth coat necessary to cause infection. Moreover, their bodies contained live type S bacteria encased in cause infection.



### 7.1 Experiments Identifed the Genetic Material

# B. Hershey and Chase Confrmed the Genetic Role of DNA

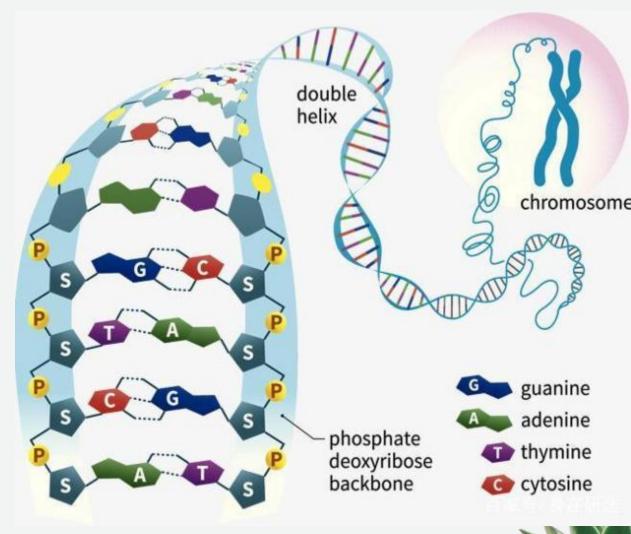
Hershey and Chase used radioactive isotopes to distinguish a bacteriophage's protein coat from its DNA. They showed that the virus transfers DNA (not protein) to the bacterium, and this viral DNA causes bacterial cells to produce viruses.



**Bacterium (E. coli)** 

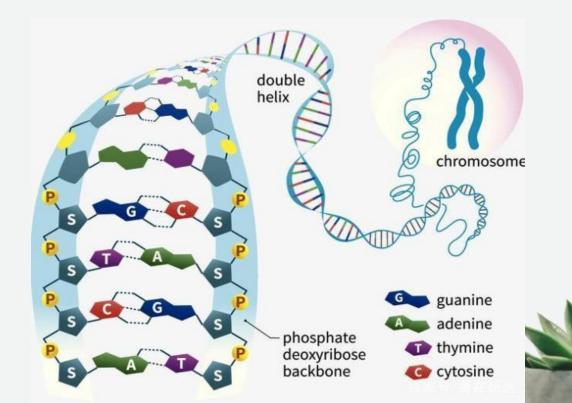
### 7.2 DNA Is a Double Helix of Nucleotides

- The DNA double helix resembles a twisted ladder. The twin rails of the ladder, also called the sugar-phosphate "back-bones," are alternating units of deoxyribose and phosphate joined with covalent bonds.
- The ladder's rungs are A-T and G-C base pairs joined by hydrogen bonds. These base pairs arise from the chemical structures of the nucleotides. Adenine and guanine are purines, bases with a double ring structure. Cytosine and thymine are pyrimidines, which have a single ring. Each A-T pair is the same width as a C-G pair because each includes a purine and a pyrimidine.



### 7.2 DNA Is a Double Helix of Nucleotides

• The two chains of the DNA double helix ar oriented in opposite directions. This head-totail ("antiparallel") arrangement is apparent when the carbon atoms in deoxyribose are numbered. When the nucleotides are joined into a chain, opposite ends of the strand are designated 3 prime (3') and 5 prime (5'). At the same end of the double helix, one chain therefore ends with a free (unbound) 3' carbon, while the other chain ends with a free 5' carbon.



# Figure It Out

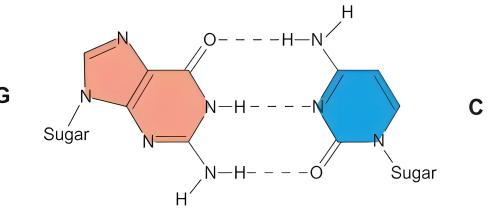
Write the complementary DNA sequence of the following:

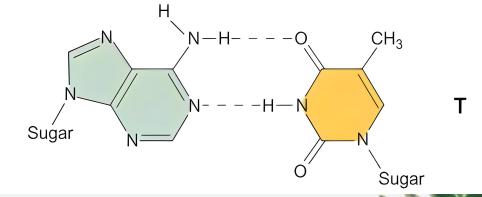
3'-ATCGGATCGCTACTG-5'



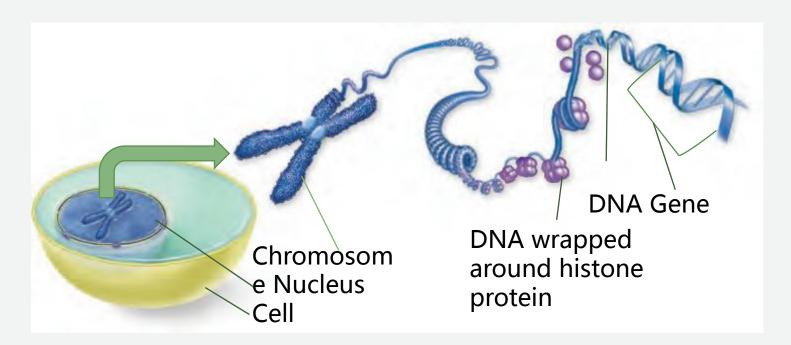
### 7.2 DNA Is a Double Helix of Nucleotides

- Recall that hydrogen bonds form between atoms carrying opposite charges.
- The cytosine and guanine can form three hydrogen bonds. On the other hand, adenine and thymine can form only two. This difference accounts for the G specificity of the A-T and C-G base pairs.
- The hydrogenbonds are weak compared to covalent bonds. While it is true that each hydrogen bond is weak, a DNA molecule consisting of millions of base pairs also has millions of hydrogen bonds. Collectively, these bonds are strong enough to hold the two strands A together yet weak enough to pull apart when the cell needs to use its DNA.





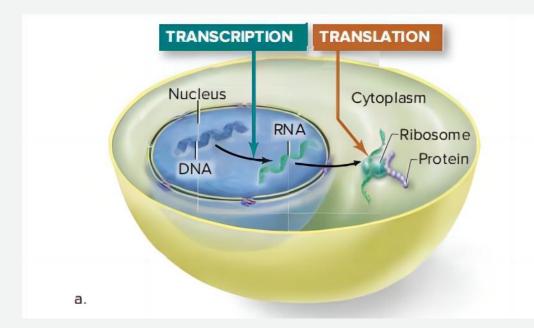
- An organism's genome is all of the genetic material in its cells. Genomes vary greatly in size and packaging.
- The chromosome is tightly coiled; to use its genetic information, the cell must "unpack" the chromosome and expose the double helix. Although much of the DNA has no known function, some of it encodes RNA and proteins.
- Because many proteins are essential to life, each organism has many genes.





# A.Protein Synthesis Requires Transcription and Translation

- The process of protein production.
  - ✓ First, in transcription, a cell "rewrites" a gene's DNA sequence to a complementary RNA molecule.
  - ✓ Then, in translation, the information in RNA is used to assemble a different class of molecule: a protein.





A.Protein Synthesis Requires Transcription and Translation

• According to this model, a gene is therefore somewhat like a recipe in a cookbook. A recipe specifies the ingredients and instructions for assembling one dish, such as spaghetti sauce or brownies. Likewise, a protein-encoding gene contains the instructions for assembling a polypeptide, amino acid by amino acid (the polypeptide subsequently folds to become the finished protein). A cookbook that contains many recipes is analogous to a chromosome, which is an array of genes. A person's entire collection of cookbooks, then, is analogous to a genome.

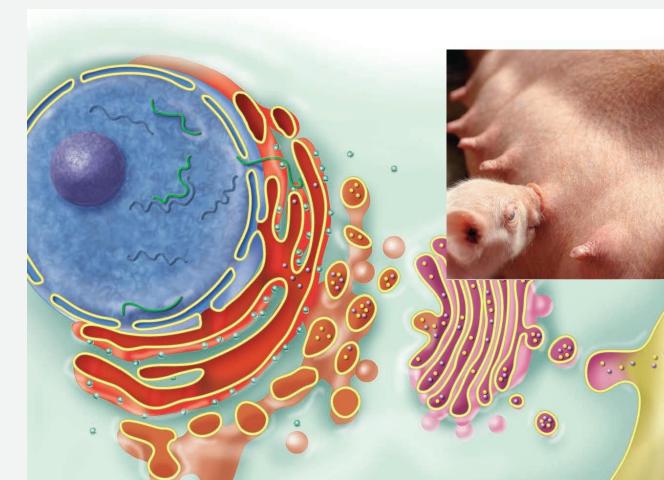


To illustrate DNA's function with a concrete example, sup-pose a cell in a female mammal's breast is producing milk to feed an infant. One of the proteins in milk is albumin. The following steps summarize the production of albumin, starting with its genetic "recipe":

- 1.Inside the nucleus, an enzyme first transcribes the albumin (白蛋白)gene's DNA sequence to a complementary (互补的)sequence of RNA. (A-U; C-G)

  2.After some modification, the RNA emerges from the nucleus and binds to a ribosome (核糖体).
- 3.At the ribosome, amino acids are assembled in a specific order to produce the albumin protein.

The amino acid (氨基酸) sequence in albumin is dictated by the sequence of nucleotides (核苷酸) in the RNA molecule. The RNA, in turn, was transcribed from DNA. In this way, DNA provides the recipe for albumin and every other protein in the cell.



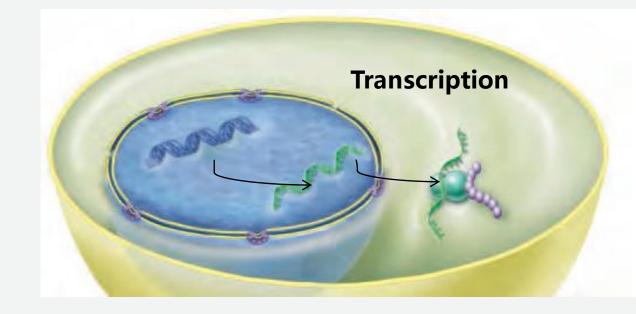
#### B. RNA Is an Intermediary Between DNA and a Protein

- RNA is central to the flow of genetic information. Three types of RNA interact to synthesize proteins:
- Messenger RNA (mRNA) carries the information that specifies a protein. The mRNA is divided into genetic "code words" called codons; a codon is a group of three consecutive mRNA bases that corresponds to one amino acid.
- Ribosomal RNA (rRNA) combines with proteins to form a ribosome, the physical location where translation occurs. Some rRNAs help to correctly align the ribosome and mRNA, and others catalyze formation of the bonds between amino acids in the developing protein.
- Transfer RNA (tRNA) molecules are "connectors" that bind an mRNA codon at one end and a specific amino acid at the other. Their role is to carry each amino acid to the ribosome at the correct spot along the mRNA molecule.

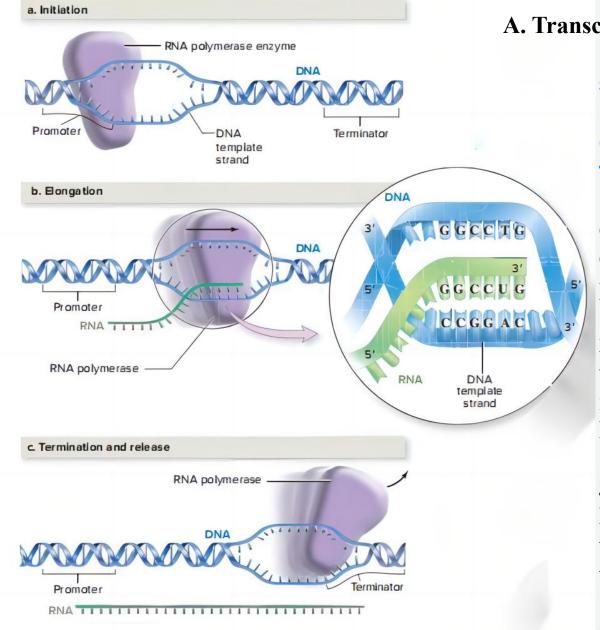
Molecule	Typical Number of Nucleotides	Function
mRNA	500-3000	Encodes amino acid sequence
rRNA	100-3000	Associates with proteins to form ribosomes, which structurally support and catalyze protein synthesis
tRNA	75–80	Physically links the message in mRNA to the amino acid sequence it encodes; binds mRNA codon on one end and an amino acid on the other

# 7.4 Transcription Uses a DNA Template to Build RNA

 Transcription produces an RNA copy of one gene. Recall from our brownie analogy that a gene is a recipe for a protein. According to this analogy, transcription (转录)is like opening a cookbook to a particular page and copying just the recipe for the dish you want to prepare. After the copy is made, the book can return safely to the shelf. Just as you would then use the instructions on the copy to make your meal, the cell uses the information in RNA—and not the DNA directly—to make each protein.



## 7.4 Transcription Uses a DNA Template to Build RNA



A. Transcription Occurs in Three Steps

DNA is a double helix, but only one of the two strands contains the information encoding each protein. This strand, called the template strand, contains the DNA sequence that is actually copied to RNA.

- 1. Initiation: Enzymes unzip the DNA double helix, exposing the template strand. RNA polymerase, the enzyme that builds an RNA chain, may then bind to the promoter (启动子).
- 2. Elongation: RNA polymerase (聚合酶) moves along the DNA template strand in a 3'-to-5' direction, adding nucleotides (核苷酸) only to the 3' end of the growing RNA molecule.
- 3. Termination: A terminator (终止子) sequence in DNA signals the end of the gene. Upon reaching the terminator, the RNA polymerase enzyme separates from the DNA template and releases the newly produced RNA. The DNA molecule then resumes its usual double-helix shape.

# 7.4 Transcription Uses a DNA Template to Build RNA

B. RNA Is an Intermediary Between DNA and a Protein

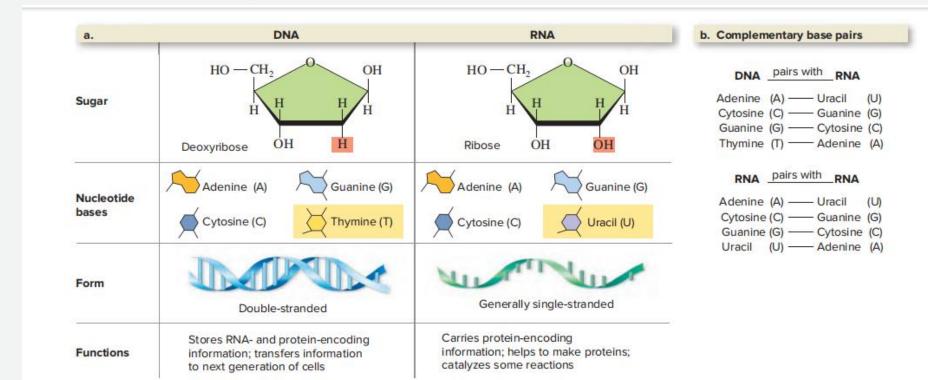
RNA is a multifunctional nucleic acid (核酸) that differs from DNA in several ways.

First, its nucleotides contain the sugar ribose (核糖) instead of deoxyribose.

Second, RNA has the nitrogenous base uracil, which behaves similarly to thymine; that is, uracil binds with adenine in complementary base pairs.

Third, unlike DNA, RNA can be single-stranded (although it often folds into loops).

Finally, RNA can catalyze chemical reactions, a role not known for DNA.



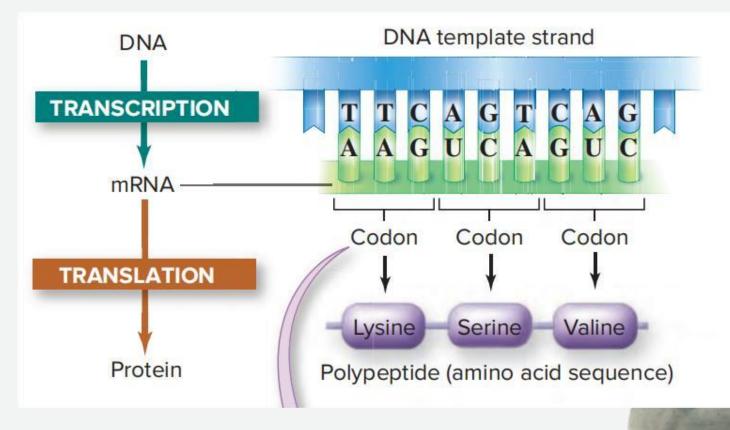
# Figure It Out

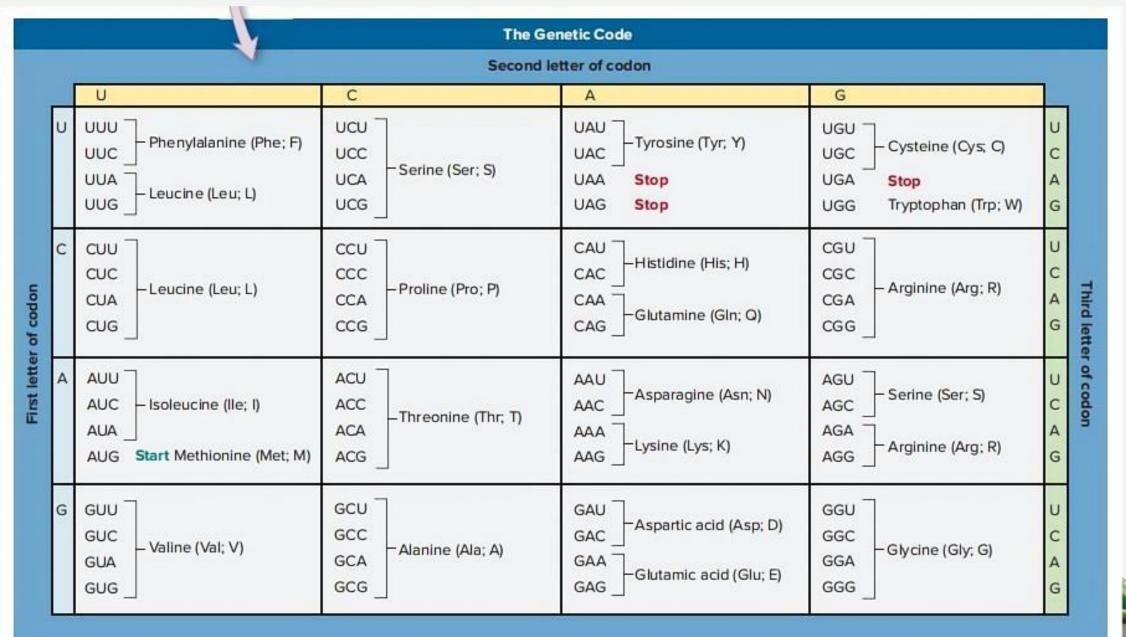
• Write the sequence of the mRNA molecule transcribed from the following DNA template sequence: 3'-TTACACTTGCAA-5'



• A. Transcription (翻译) copies the information encoded in a DNA base sequence into the complementary language of mRNA. Once transcription is complete and mRNA has left the nucleus, the cell is ready to translate the mRNA "message" into a sequence of amino acids. If mRNA is like a copy of a recipe, then translation is

like preparing the dish.

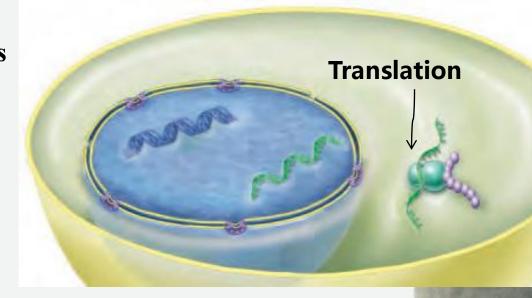


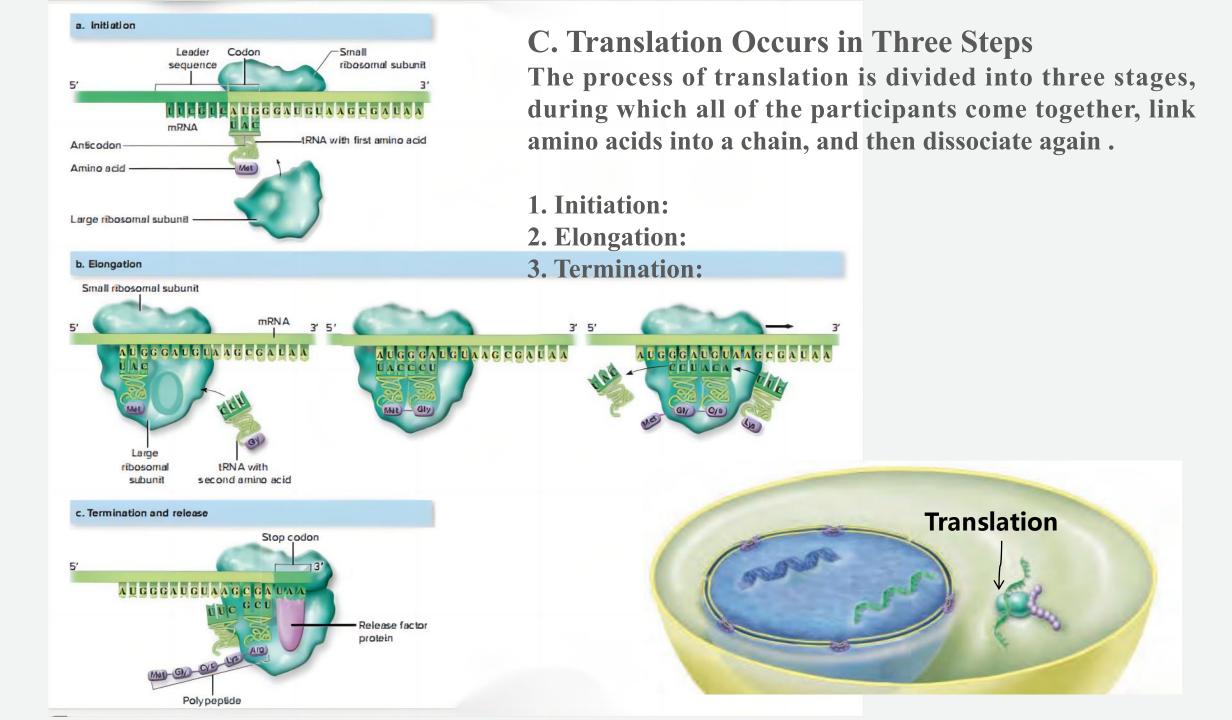




#### B. Translation Requires mRNA, tRNA, and Ribosomes

- Translation—the actual construction of the protein—requires three main types of participants. We have already met the first type: mRNA, the molecule that contains the genetic information encoding a protein. Each three-base codon in mRNA specifies one amino acid.
- The second type of participant is tRNA. These "bilingual" molecules carry amino acids from the cytosol (胞液) to the mRNA being translated. Each tRNA includes an anticodon, a three-base loop that is complementary to one mRNA codon. The other end of the tRNA molecule carries the amino acid corresponding to that codon. For example, a tRNA with the anticodon sequence AAG always picks up the amino acid phenylalanine (苯丙氨酸), which is encoded by the codon UUC.
- The remaining participant in translation is the ribosome. Each ribosome, which has one large and one small subunit, is built of rRNA and proteins. Ribosomes are the sites of translation. That is, in the recipe analogy, a ribosome is the "bowl" where the ingredients come together (and tRNA molecules are helpers that carry those ingredients to the bowl). Each cell has many ribosomes, which may be free in the cytosol or attached to the rough endoplasmic reticulum ( 内质网).





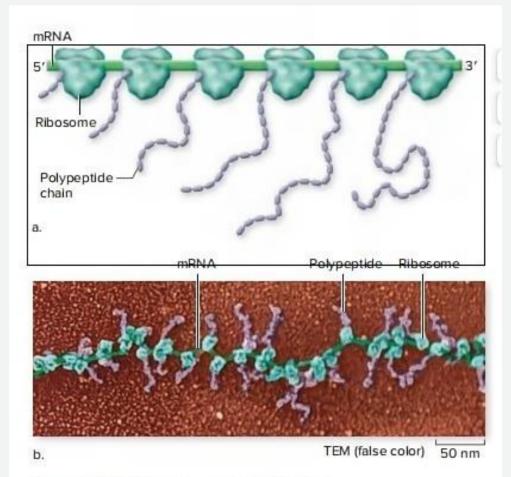


Figure 7.16 Efficient Translation. (a) Multiple ribosomes can simultaneously translate one mRNA. (b) This micrograph shows about 30 ribosomes producing proteins from the same mRNA.

(b): ODr. Elena Kiseleva/SPL/Science Source

- Protein synthesis (蛋白质合成) can be very speedy.
- How can protein synthesis occur fast enough to meet all of a cell' s needs?

The cell maximizes efficiency is by producing multiple copies of each mRNA, giving the cell more than one genetic "recipe" for the ribosomes to read. In addition, dozens of ribosomes may simultaneously translate one mRNA molecule, following each other from the 5' end to the 3' end. These ribosomes zip along the mRNA, incorporating some 15 amino acids per second. Thanks to this fast-moving "assembly line," a cell can make many copies of a protein from the same mRNA.

# Figure It Out

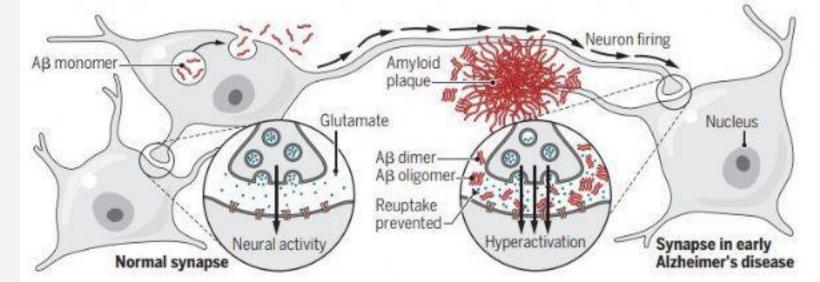
• If a DNA sequence is 3'-AAAGCAGTACTA-5', what is the corresponding amino acid sequence?



- **D. Proteins Must Fold Correctly After Translation**
- Proteins can fold incorrectly if the underlying DNA sequence is altered (see section 7.6), because the encoded protein may have the wrong sequence of amino acids. Serious illness may result.
- Errors in protein folding can occur even if the underlying genetic sequence remains unchanged.
- Alzheimer disease, is associated with a protein called amyloid (淀粉样蛋白), which folds improperly and then forms an abnormal mass in brain cells.
- Likewise, mad cow disease and similar conditions in sheep and humans are caused by abnormal clumps of misfolded proteins called prions (朊病毒) in nerve cells.

#### A vicious cycle of neuronal hyperactivation

Zott et al. show that soluble β-amyloid (Aβ) dimers and oligomers, which are formed during Aβ aggregation, are neurotoxic. They preferentially affect repeatedly activated neurons by blocking glutamate reuptake by neurons and astrocytes. This leads to hyperactivation and eventually neurodegeneration.



预防阿兹海默症(老年痴呆症)的一个好办法:看字说出颜色(就是说出字的颜色, 出颜色(就是论出字的颜色, 而不是说出这个字念什么)。 每天练习,越熟练越好。



A mutation (突变) is any change in a cell's DNA sequence. The change may occur in a gene or in a regulatory region such as an enhancer. Many people think that mutations are always harmful, perhaps because some of them cause such dramatic changes. Although some mutations do cause illness, they also provide the variation that makes life interesting (and makes evolution possible).

To continue the cookbook analogy introduced earlier, a mutation in a gene is similar to an error in a recipe. A small typographical error might be barely noticeable. A minor substitution of one ingredient for another might hurt (or improve) the flavor. But serious errors such as missing ingredients or truncated instructions are likely to ruin the dish.

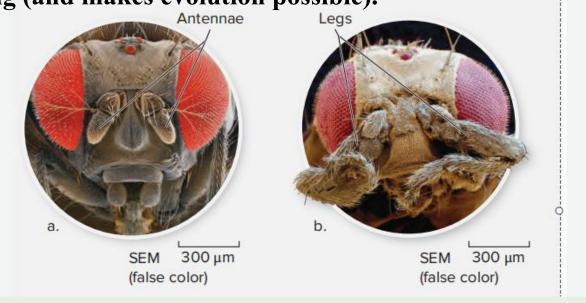


Figure 7.20 Legs on the Head. Mutations in some genes can cause parts to form in the wrong places. (a) Normally, a fruit fly has two small antennae between its eyes. (b) This fly has legs growing where its antennae should be; it has a mutation that affects development.

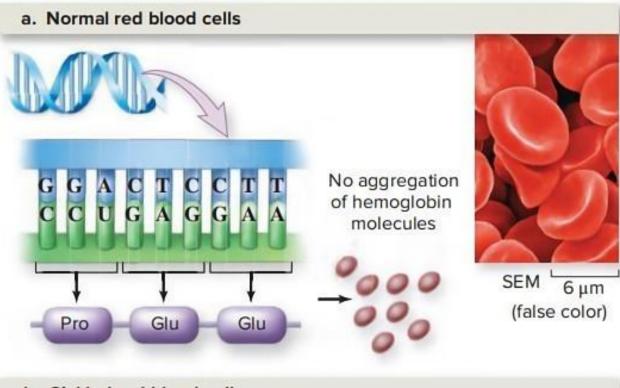
- A. Mutations Range from Silent to Devastating
- A mutation may change one or a few base pairs or affect large portions of a chromosome (染色体). Some are detectable only by using DNA sequencing techniques, while others may be lethal.

#### • Substitution Mutations:

A substitution (取代) mutation is the re placement of one DNA base with another. Such a mutation is "silent" if the mutated gene encodes the same protein as the original gene version. Mutations can be silent because more than one codon encodes most amino acids.

Often, however, a substitution mutation changes a base trip let so that it specifies a different amino acid. This change is called a missense (错义) mutation. The substituted amino acid may drastically alter the protein's shape, changing its function. Sickle (镰刀) cell disease results from this type of mutation in a gene encoding hemoglobin (血红蛋白).

TABLE 7.2 Types of Mutations				
Туре	Illustration			
Original sentence	THE ONE BIG FLY HAD ONE RED EYE			
Substitution (missense)	THO ONE BIG FLY HAD ONE RED EYE			
Nonsense	THE ONE BIG			
Insertion	THE ONE BIG WET FLY HAD ONE RED EYE			
Insertion (frameshift)	THE ONE <b>Q</b> BI GFL YHA DON ERE DEY			
Deletion	THE ONE BIG HAD ONE RED EYE			
Expanding	Generation 1: THE ONE BIG FLY HAD ONE RED EYE			
repeat	Generation 2: THE ONE BIG FLY FLY FLY HAD ONE RED EYE			
	Generation 3: THE ONE BIG FLY FLY FLY FLY FLY HAD ONE RED EYE			



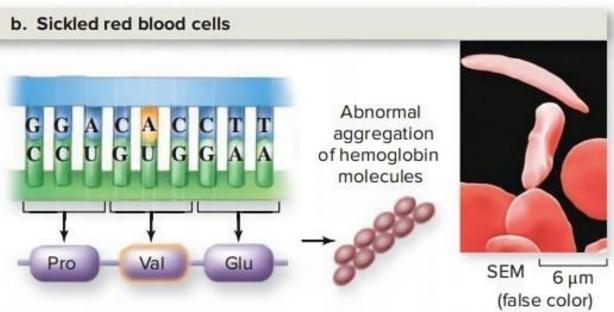


Figure 7.21 Sickle Cell Mutation.

Sickle cell anemia usually results from a mutation in a hemoglobin gene.

- (a) Normal hemoglobin molecules do not aggregate, enabling the red blood cell to assume a rounded shape.
- (b) A substitution mutation causes hemoglobin molecules to clump (aggregate) into rods that deform the red blood cell.

#### A. Mutations Range from Silent to Devastating

- In other cases, called nonsense (无义) mutations, a base triplet specifying an amino acid changes into one that encodes a "stop" codon. This shortens the protein product, which can profoundly influence the organism.
- Base Insertions and Deletions

An insertion (插入) mutation adds one or more nucleotides to a gene; a deletion (删除) mutation removes nucleotides. Either type of mutation may be a frameshift mutation, in which nucleotides are added or deleted by a number other than a multiple of three. Because triplets of DNA bases specify amino acids, such an addition or deletion disrupts the codon reading frame.

#### TABLE 7.2 Types of Mutations

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#### A. Mutations Range from Silent to Devastating

• Expanding Repeats

In an expanding repeat (展开重复) mutation, the number of copies of a three- or four-nucleotide sequence increases over several generations. With each generation, the symptoms begin earlier or become more severe (or both). Expanding genes underlie several inherited disorders, including fragile X syndrome (脆性X综合症) and Huntington disease (亨廷顿舞蹈症).

• Changes in Chromosome Structure Some mutations affect extensive regions of DNA. For example, a large part of a chromosome may be deleted or duplicated during meiosis. One region of a chromosome may also become inverted.

TABLE <b>7.2</b>	Types of Mutations
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Туре	Illustration		
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repeat	Generation 2: THE ONE BIG FLY FLY FLY HAD ONE RED EYE		
	Generation 3: THE ONE BIG FLY FLY FLY FLY FLY HAD ONE RED EYE		

# Figure It Out

- Suppose that a substitution mutation replaces the first A in the following mRNA sequence with a U:
- 5'-AAAGCAGUACUA-3'.
- How many amino acids will be in the polypeptide chain?



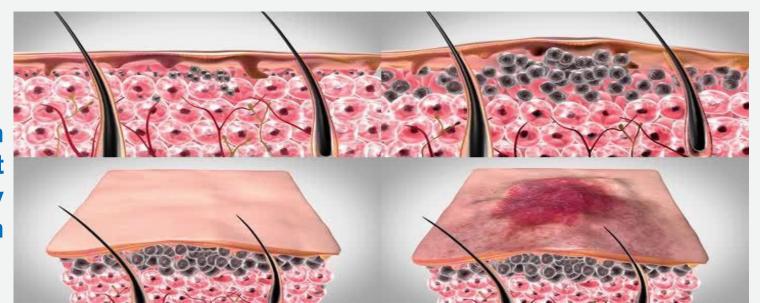
#### Second letter of codon

· ·	112	U	С	А	G	
ter of codon	U	UUU Phenylalanine (Phe; F) UUA UUG Leucine (Leu; L)	UCU UCC UCA UCG	UAU Tyrosine (Tyr; Y) UAC Stop UAG Stop	UGU UGC Cysteine (Cys; C) UGA Stop UGG Tryptophan (Trp; W)	U C A G
	С	CUU CUC CUA CUG	CCU CCC CCA CCG	CAUHistidine (His; H) CACHistidine (His; H) CAAGlutamine (Gln; Q)	CGU CGC Arginine (Arg; R)	U C A G
	A	AUU AUC Isoleucine (IIe; I) AUA Start Methionine (Met; M)	ACU ACC ACA ACG	AAUAsparagine (Asn; N) AAALysine (Lys; K)	AGU Serine (Ser; S)  AGA Arginine (Arg; R)	U C A G
	G	GUU GUC Valine (Val; V) GUA GUG	GCU GCC Alanine (Ala; A)	GAUAspartic acid (Asp; D) GACGAAGIutamic acid (Glu; E)	GGU GGC GGA GGG	U C A G

#### **B. What Causes Mutations?**

- Some mutations occur spontaneously—that is, without outside causes. A spontaneous substitution mutation usually originates as a DNA replication error. Replication errors can also cause insertions and deletions, especially in genes with repeated base sequences, such as GCG CGC....
- The average rate of replication errors for most genes is about 1 in 100,000 bases, but it varies among organisms and among genes. The larger a gene, the more likely it is to mutate. In addition, the more frequently DNA replicates, the more it mutates. Bacteria accumulate mutations faster than cells of complex organisms, simply because their DNA replicates more often. Likewise, rapidly dividing skin cells tend to have more mutations than the nervous system's neurons, which divide slowly if at all.

Melanocytes (黑色素细胞) can undergo mutations at different times, causing them to suddenly gather together and form concentrated moles (痣).

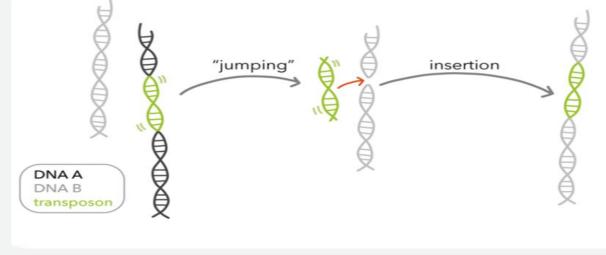


**B. What Causes Mutations?** 

Exposure to harmful chemicals or radiation may also damage DNA. A mutagen is any external agent that induces X-rays, radioactive fallout from atomic bomb tests and nuclear accidents, and chemicals in tobacco and in the environment (such as pollution in soil, air, or water). The more contact a person has with mutagens, the higher the risk for cancer. Coating skin with sunscreen, wearing a lead "bib" during dental X-rays, and avoiding tobacco all lower cancer risk by reducing exposure to mutagenic chemicals and radiation.

Movable DNA sequences are yet another source of mutations. A transposable element, or transposon (转至) for short, is a DNA sequence that can "jump" within the genome. A transposon can insert itself randomly into chromosomes. If it lands within a gene, the transposon can disrupt the gene's function; it

can also leave a gap in the gene when it leaves.



#### **C.Mutations May Pass to Future Generations**

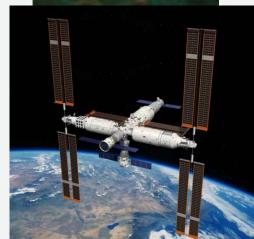
- A germline (种系) mutation is a DNA sequence change that occurs in the cells that give rise to sperm and eggs. Germline mutations are heritable because the mutated DNA will be passed down in at least some of the sex cells that the organism produces. As a result, every cell of the organism's affected offspring will carry the mutation. Such mutations may run in families, or they can appear suddenly. For example, two healthy people of normal height may have a child with a form of dwarfism called achondroplasia (侏儒症).
- Most mutations, however, do not pass from generation to generation. A somatic mutation occurs in nonsex cells, such as those that make up the skin, intestinal tract, or lungs. All cells derived from the altered one will also carry the mutation, but the mutation does not pass to the organism's offspring. The children of a cigarette smoker with mutations that cause lung cancer, for example, do not inherit the parent's damaged genes.

#### **D.Mutations Are Important**

- Mutations are also extremely important because they produce genetic variability. They are the raw material of evolution because they generate new alleles (等位基因), or variants of genes. Except for identical twins, everyone has a different combination of alleles for the 25,000 or so genes in the human genome. The same is true for any genetically variable group of organisms.
- Some of these new alleles are "neutral" and have no effect on an organism's fitness.
- Mutations sometimes enhance an organism's reproductive success.
- Mutations can also be enormously useful in science and agriculture. Geneticists frequently induce mutations to learn how genes normally function. Plant breeders also induce mutations to develop new varieties of many crop species as well as some kinds of grapefruits, rice, cotton, oats.







**China Space Station** 

### **Home Work**

- 1. What are the components of DNA and its three-dimensional structure?
- 2. How do transcription and translation use genetic information?
- 3. What are the three types of RNA, and how does each contribute to protein synthesis?
- 5. What happens during each stage of transcription? Where in the cell does transcription occur?
- 6. What are the roles of the promoter and terminator sequences in transcription?
- 7. What happens in each stage of translation? Where in the cell does translation occur?
- 8. What is a mutation? What causes mutations? What are the types of mutations, and how does each alter the encoded protein?

