

# Expression of the Genome

Ch 4: Mechanisms of Transcription

Ch 5: RNA Splicing

Ch 6: Translation

Ch 7: The Genetic Code



# Chapter 7: The Genetic Code

1. The Code Is Degenerate
2. Three Rules Govern the Genetic Code
3. Suppressor Mutations Can Reside in the Same or a Different Gene
4. The Code Is Nearly Universal

### Topic 1:

The code is degenerate

$$4*4*4 = 64$$

20aa

		second position					
		U	C	A	G		
first position (5' end)	U	UUU Phe UUC UUA Leu UUG	UCU UCC Ser UCA UCG	UAU Tyr UAC UAA* stop UAG* stop	UGU Cys UGC UGA* stop UGG Trp	U C A G	third position (3' end)
	C	CUU Leu CUC CUA CUG	CCU CCC Pro CCA CCG	CAU His CAC CAA Gln CAG	CGU CGC Arg CGA CGG	U C A G	
	A	AUU Ile AUC AUA AUG† Met	ACU ACC Thr ACA ACG	AAU Asn AAC AAA Lys AAG	AGU Ser AGC AGA Arg AGG	U C A G	
	G	GUU Val GUC GUA GUG	GCU Ala GCC GCA GCG	GAU Asp GAC GAA Glu GAG	GGU GGC Gly GAA GGG	U C A G	

\* Chain-terminating or "nonsense" codons

† Also used in bacteria to specify the initiator formyl-Met-tRNA<sup>fMet</sup>

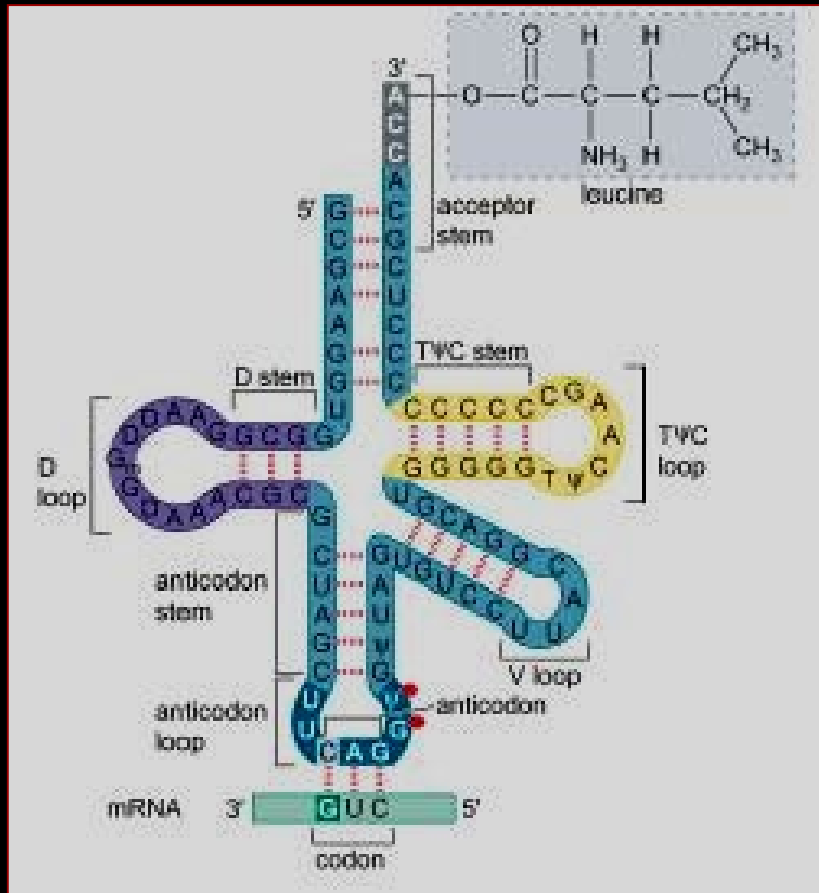
Each amino acid is specified by more than one codon-  
degeneracy (简并性\*).  
Codons specifying the same amino acid are called  
synonyms (同义密码子\*).

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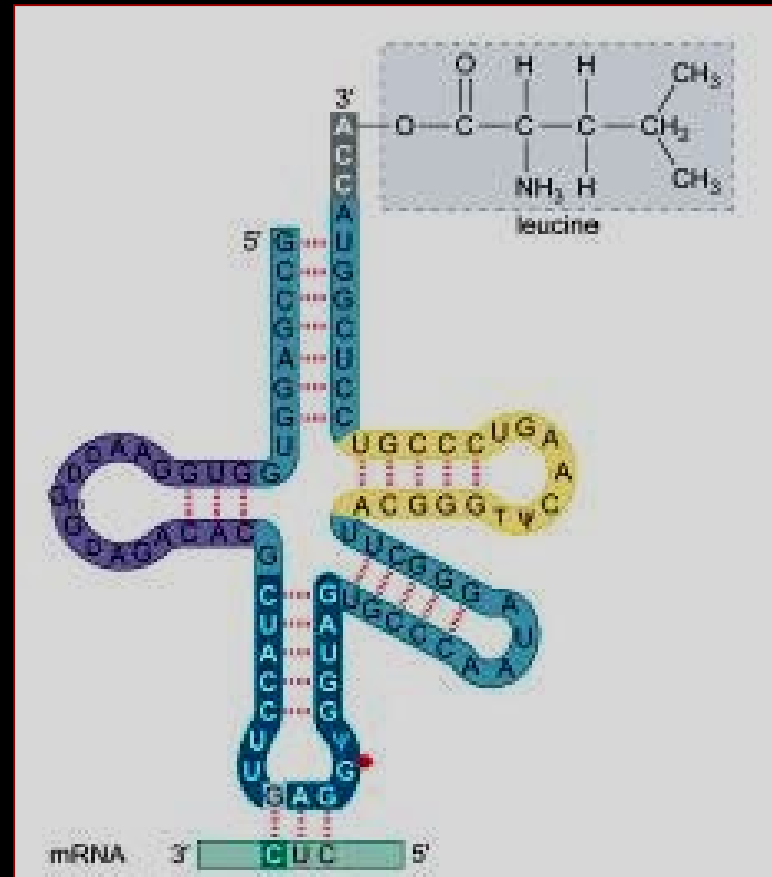
TABLE 7-1 The Genetic Code

# 7-1-1 Coding role #1-degeneracy

1. Often, when the first two nucleotides are identical, the third nucleotide can be either C or U without changing the code. A and G at the third position are interchangeable as well.
2. Transition in the third position of a codon specifies a same amino acid, while Transversion in this position changes the amino acid about half the time.



CUG



CUC

Figure 7-1 Codon-anticodon pairing of two tRNA Leu molecules

Code degeneracy explains how there can be a great variation in the AT/GC ratios in the DNA of various organisms without large changes in the proportion of amino acids in their proteins.



7-1-1 Coding role #2: The genetic code are arranged to minimize the deleterious effects of mutations. \*\*\*

1. The third position: Transition specifies a same amino acid, while Transversion changes the amino acid about half the time. If the first two positions are both occupied by G or C, each of the four nucleotides in the third position specifies the same amino acid.
2. The second position:
  - Pyrimidines-hydrophobic amino acids
  - Purines-polar amino acids

# Reasons for degeneracy

- Some tRNAs (a total of ~40) could recognize more than one different codons (a total of 61).
- The wobble feature of the base at the 5' end of the anticodon (also called the wobble position).

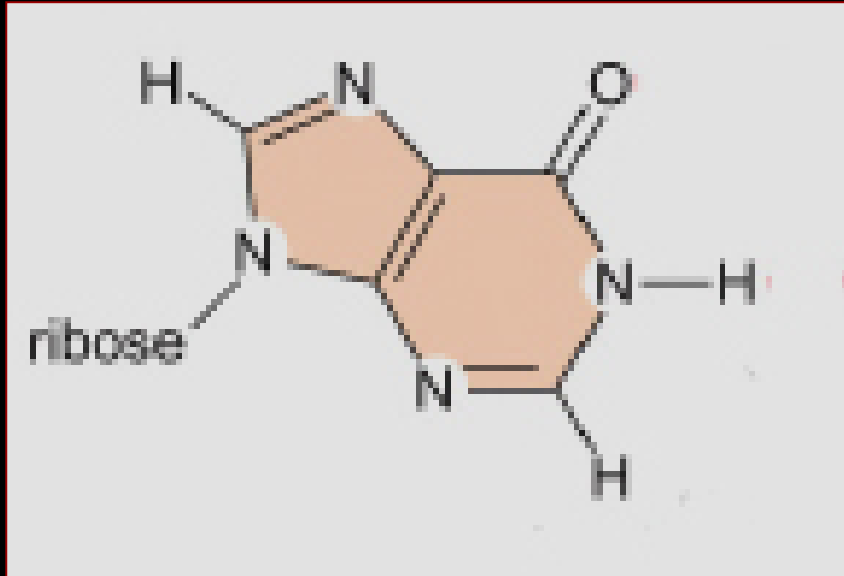
## 7-1-2 Wobble in the Anticodon (反密码子具有摇摆性)

In 1966, Francis Crick devised the wobble concept. It states that the base at the 5' end of the anticodon is not as spatially confined as the other two, allowing it to form hydrogen bonds with more than one bases located at the 3' end of a codon.

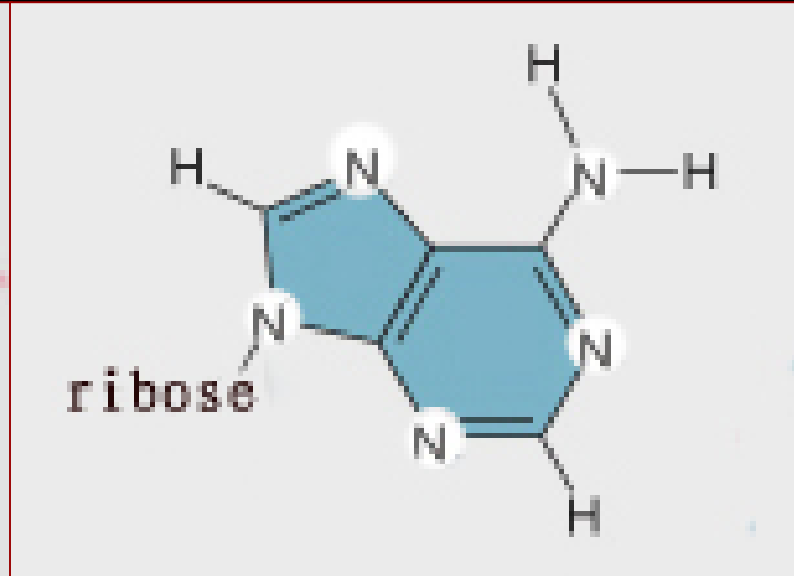
# Table 7-2 Pairing Combinations with the Wobble Concept

Base in 5' Anticodon	Base in 3' Codon
G	U or C
C	G
A	U
U	A or G
I	A, U, or C

Inosine is the fifth base in the anticodon



inosine

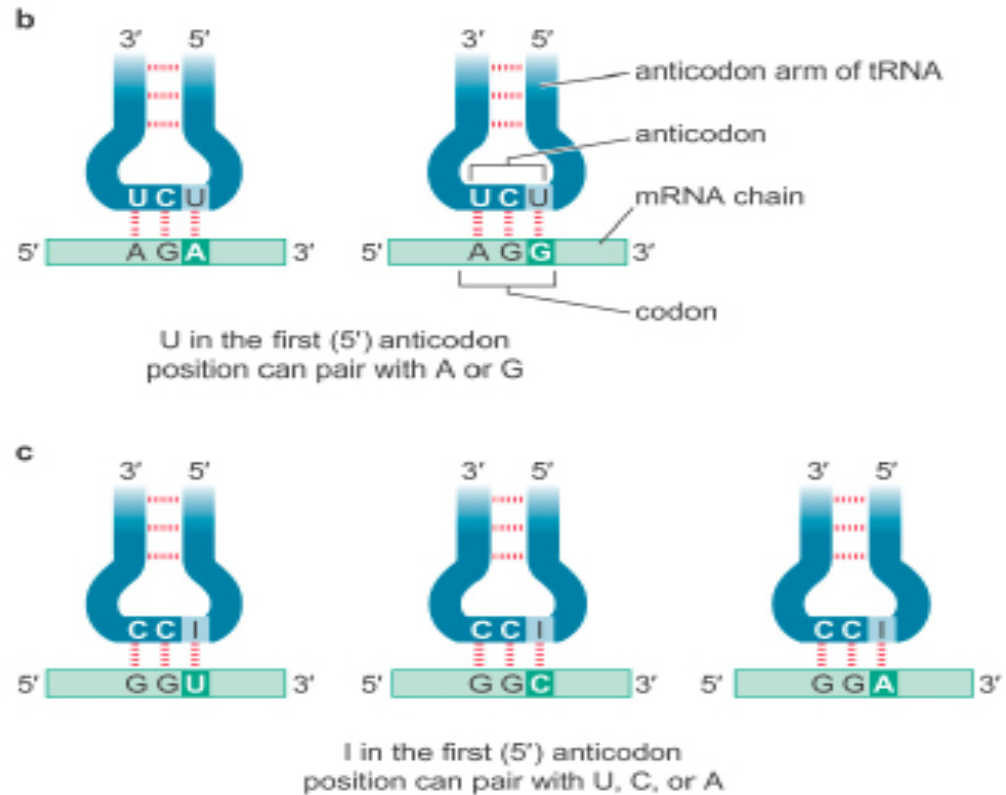
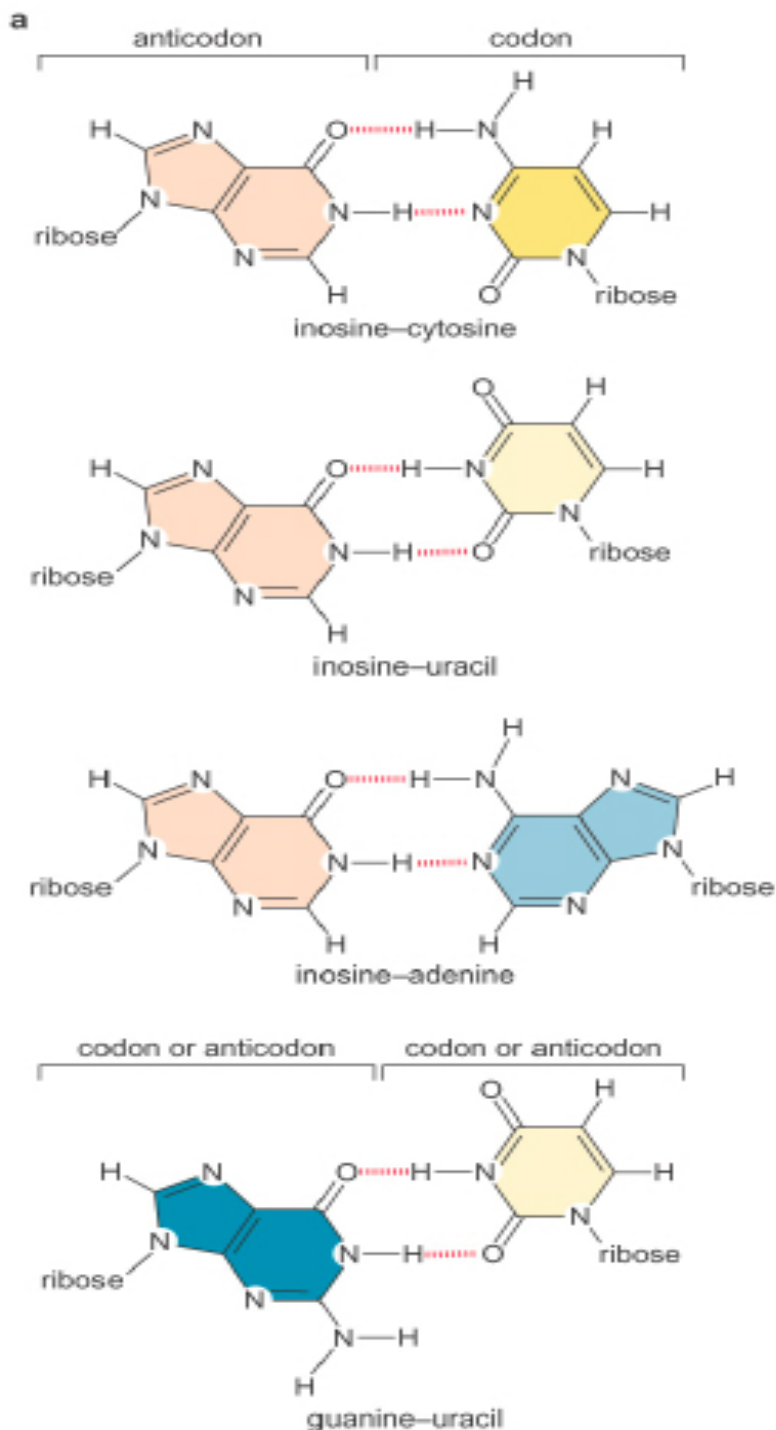


adenine

Inosine arises through enzymatic modification of adenine by ADAR

# The Wobble Rules

- The pairings permitted are those give ribose-ribose distances close to that of the standard A:U or G:C base pairs.



The ribose-ribose distances for the wobble pairs are close to those of A:U or G:C base pairs

Figure 7-2  
Wobble base pairing

# Critical Thinking\*\*\*\*\*

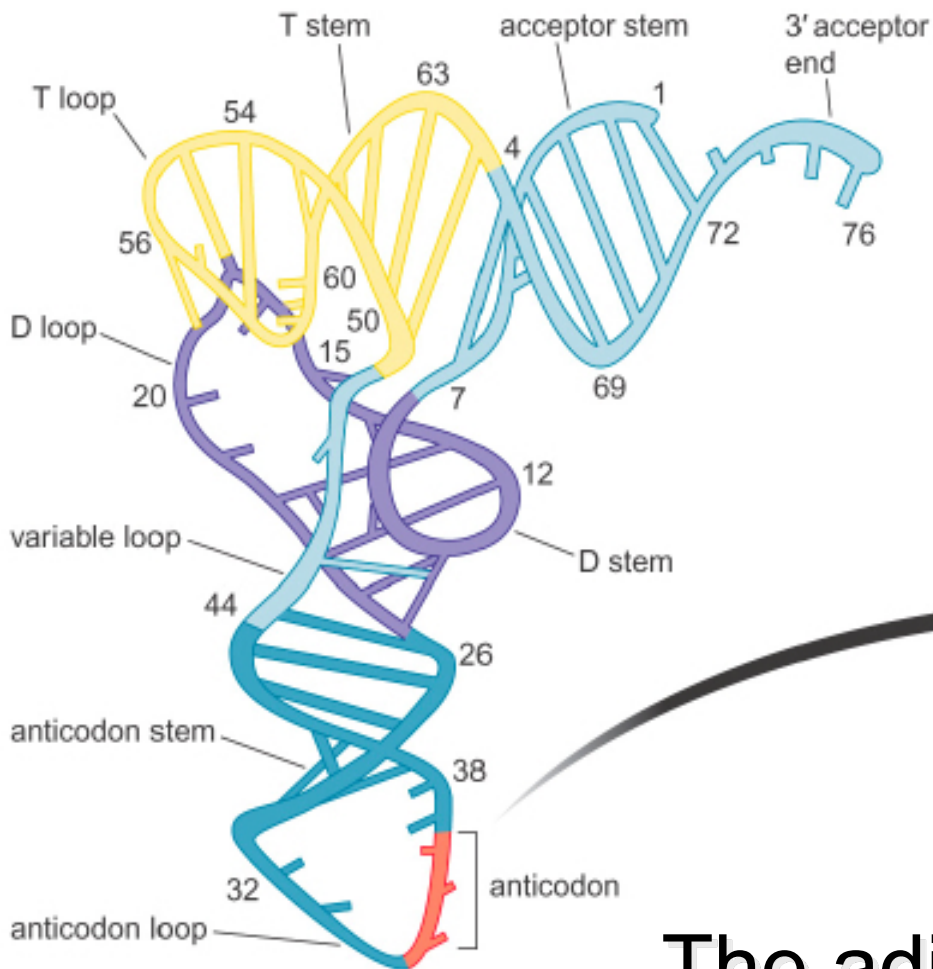
The wobble concept predicted that at least ? tRNAs exist for the six serine codons (UCU, UCC, UCA, UCG, AGU, and AGC).  
Why?



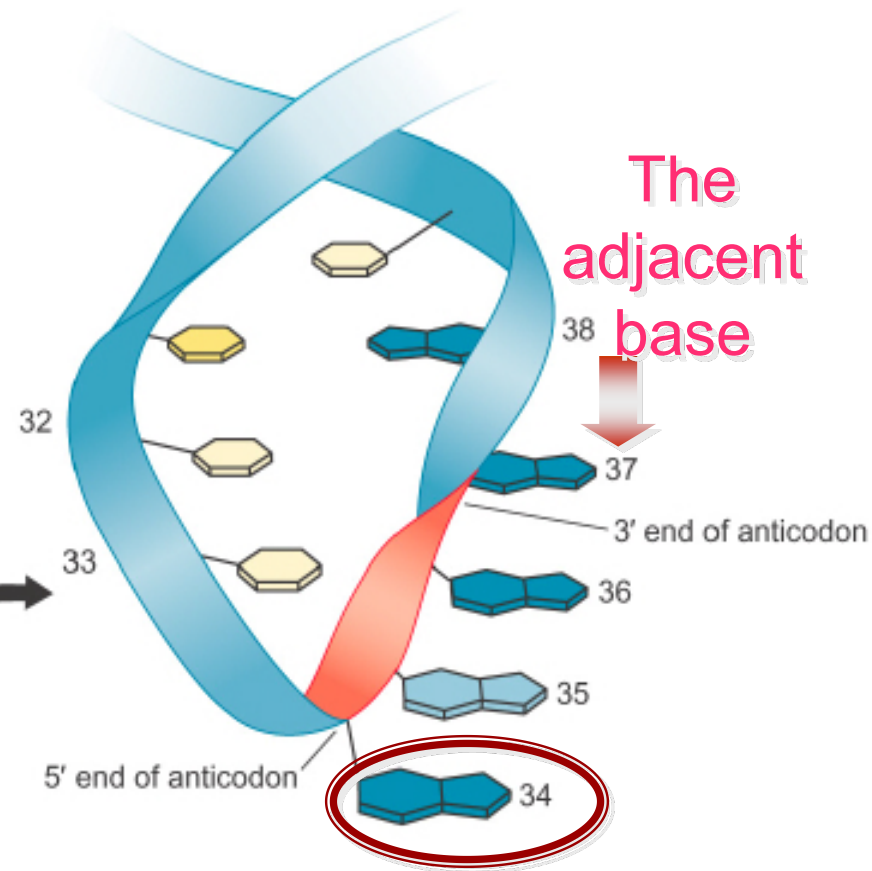
# Why wobble is allowed at the 5' anticodon? --the structural basis\*\*

- The 3-D structure of tRNA shows that the stacking interactions between the flat surfaces of the 3 anticodon bases + 2 followed bases, and the first (5') anticodon base is positioned at the end of the stack, thus less restricted in its movements.
- The 3' base appears in the middle of the stack, resulting in the restriction of its movements.

a



b



The adjacent base is always a bulky modified purine residue.

Figure 7-3 Structure of yeast tRNA(Phe)

### Topic 2:

Three rules govern the genetic code

## 7-2-1 Three Rules\*\*\*

- Codons are read in a 5' to 3' direction in units of three nucleotides.
- Codons are nonoverlapping and the message contains no gaps.
- The message is translated in a fixed reading frame which is set by the initiation codon.

## 7-2-2 Three Kinds of Point Mutations Alter the Genetic Code

1. Missense mutation: An alternation that changes a codon specific for one amino acid to a codon specific for another amino acid. [Sense mutations do not alter genetic code]
2. Nonsense or stop mutation: An alternation causing a change to a chain-termination codon.

3. Frameshift mutation: Insertions or deletions of one or a small number of base pairs that alter the reading frame.

### Topic 3:

Suppressor mutations can  
reside in the same or a different  
gene

# The harmful mutations can be reversed by a second genetic change

- Reverse (back) mutations: change an altered nucleotide sequence back to its original arrangement.
- Suppressor mutations: suppress the change due to mutation at site A by producing an additional genetic change at site B.
  - (1) Intragenic suppression (基因内抑制, site B与原突变同基因)
  - (2) Intergenic suppression (基因间抑制, site B与原突变异基因)

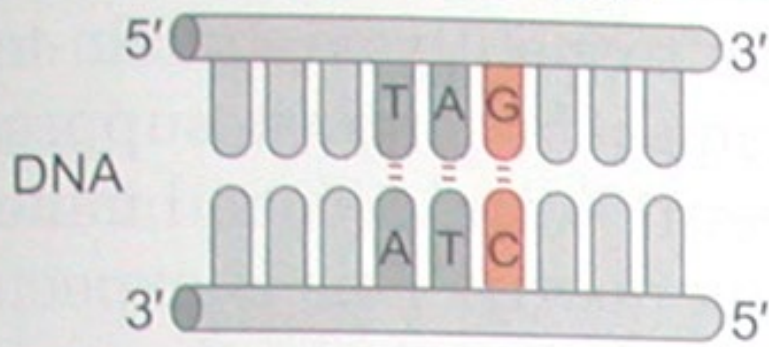


- Suppressor genes: genes that cause suppression of mutations in other genes.

## 7-3-1 Intergenic Suppression Involves Mutant tRNAs\*\*\*

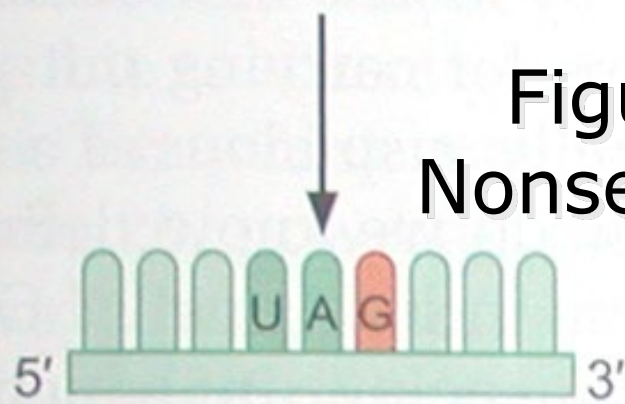
- Mutant tRNA genes suppress the effects of nonsense mutations in protein-coding genes.
- They act by reading a stop codon as if it were a signal for a specific amino acid.

a mutated gene containing  
nonsense codon

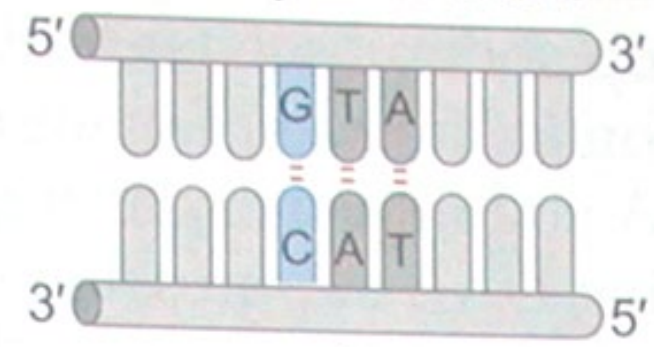


transcription

mutant mRNA containing  
nonsense codon read  
by a release factor  
to form a nonfunctional  
incomplete protein product



gene coding for a  
minor tyrosine tRNA



tyrosine tRNA  
recognizes the tyrosine  
codons 5'-UAC-3' and  
5'-UAU-3'

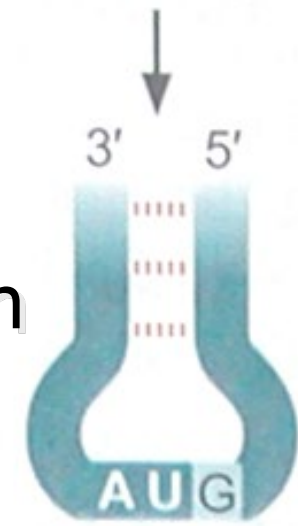
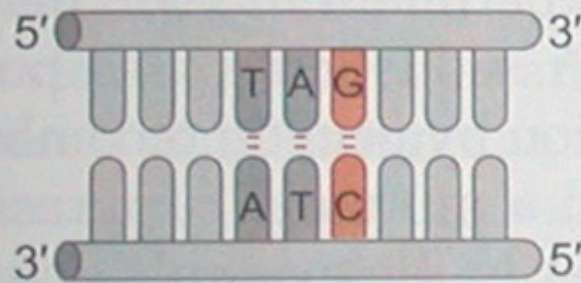


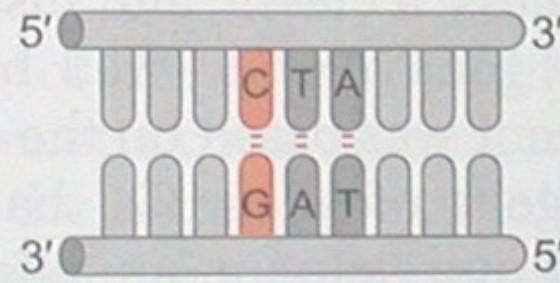
Figure 7-4a: A  
Nonsense mutation

b

mutated gene containing  
nonsense codon



mutated gene for  
minor tyrosine tRNA



transcription

recognizes  
the nonsense  
codon 5'-UAG-3'



the nonsense codon is suppressed;  
tyrosine is inserted at the position  
of the nonsense codon to allow  
the formation of a complete  
polypeptide chain.

Figure 7-4b

## 7-3-2 Nonsense Suppressors also Read Normal Termination Signals

- The act of nonsense suppression is a competition between the suppressor tRNA and the release factor.
- In *E. coli*, suppression of UAG codons is efficient, and suppression of UAA codon average is inefficient. Why? (*Because UAG is a less frequent stop codon in E. coli*)

### Topic 4:

The code is nearly universal



The results of large-scale sequencing of genomes have confirmed the universality of the genetic code.\*\*\*

### Benefits of the universal codes

- Allow us to directly compare the protein coding sequences among all organisms (comparative genomics).
- Make it possible to express cloned copies of genes encoding useful protein in different host organism. Example: Human insulin expression in bacteria)

However, in certain subcellular organelles, the genetic code is slightly different from the standard code.

- Mitochondrial tRNAs are unusual in the way that they decode mitochondrial messages.
- Only 22 tRNAs are present in mammalian mitochondria. The U in the 5' wobble position of a tRNA is capable of recognizing all four bases in the 3' of the codon.



		second position					
		U	C	A	G		
first position (5' end)	U	UUU Phe UUC (GAA) <sup>†</sup> UUA Leu UUG (UAA)	UCU UCC Ser UCA (UGA) UCG	UAU Tyr UAC (GUA) UAA stop UAG stop	UGU Cys UGC (GCA) UGA Trp UGG (UCA)	U	C
	C	CUU CUC Leu CUA (UAG) CUG	CCU CCC Pro CCA (UGG) CCG	CAU His CAC (GUG) CAA Gln CAG (UUG)	CGU CGC Arg CGA (UCG) CGG	U	C
	A	AUU Ile AUC (GAU) AUA Met AUG (CAU) <sup>‡</sup>	ACU ACC Thr ACA (UGU) ACG	AAU Asn AAC (GUU) AAA Lys AAG (UUU)	AGU Ser AGC (GCU) AGA stop AGG stop	U	C
	G	GUU GUC Val GUA (UAC) GUG	GCU GCC Ala GCA (UGC) GCG	GAU Asp GAC (GUC) GAA Glu GAG (UUC)	GGU GGC Gly GAA (UCC) GGG	U	C
						third position (3' end)	
		U	C	A	G	U	C
		A	G	U	C	A	G

**Table 7-3 Genetic Code of Mammalian Mitochondria**

# Key points of the chapter

1. What is the degeneracy of genetic code? what is its importance?
2. What are the three roles governing the genetic code? What are the best known intergenic suppressor genes?
3. What are the benefits of the code universality?