

# **Espressione Genica II: la Traduzione**

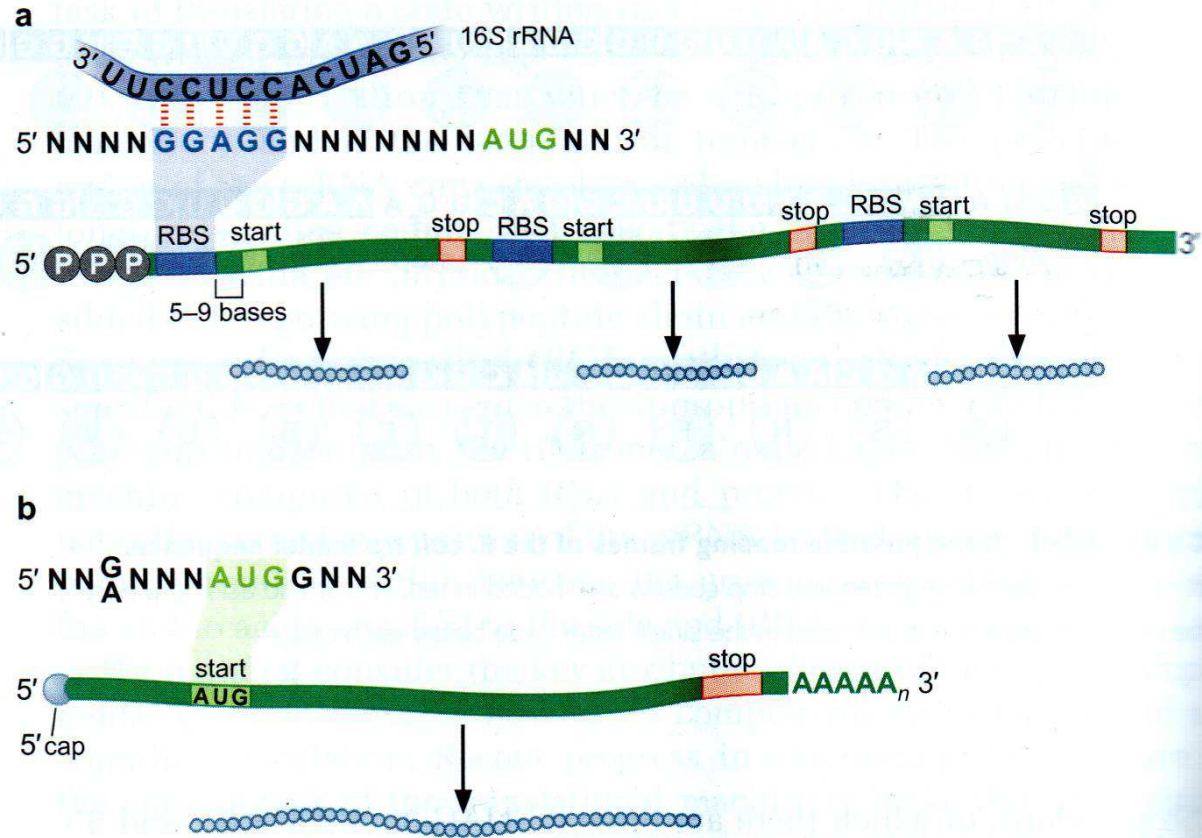
		Second letter							
		U	C	A	G				
U	UUU	Phe (F)	UCU		UAU	Tyr (Y)	UGU	Cys (C)	U C A G
	UUC		UCC	Ser (S)	UAC		UGC		
	UUA	Leu (L)	UCA		UAA	Stop	UGA	Stop	
	UUG		UCG		UAG	Stop	UGG	Trp (W)	
C	CUU		CCU		CAU	His (H)	CGU		U C A G
	CUC	Leu (L)	CCC	Pro (P)	CAC		CGC	Arg (R)	
	CUA		CCA		CAA	Gln (Q)	CGA		
	CUG		CCG		CAG		CGG		
A	AUU		ACU		AAU	Asn (N)	AGU	Ser (S)	U C A G
	AUC	Ile (I)	ACC	Thr (T)	AAC		AGC		
	AUA		ACA		AAA	Lys (K)	AGA	Arg (R)	
	AUG	Met (M)	ACG		AAG		AGG		
G	GUU		GCU		GAU	Asp (D)	GGU		U C A G
	GUC	Val (V)	GCC	Ala (A)	GAC		GGC	Gly (G)	
	GUA		GCA		GAA	Glu (E)	GGA		
	GUG		GCG		GAG		GGG		

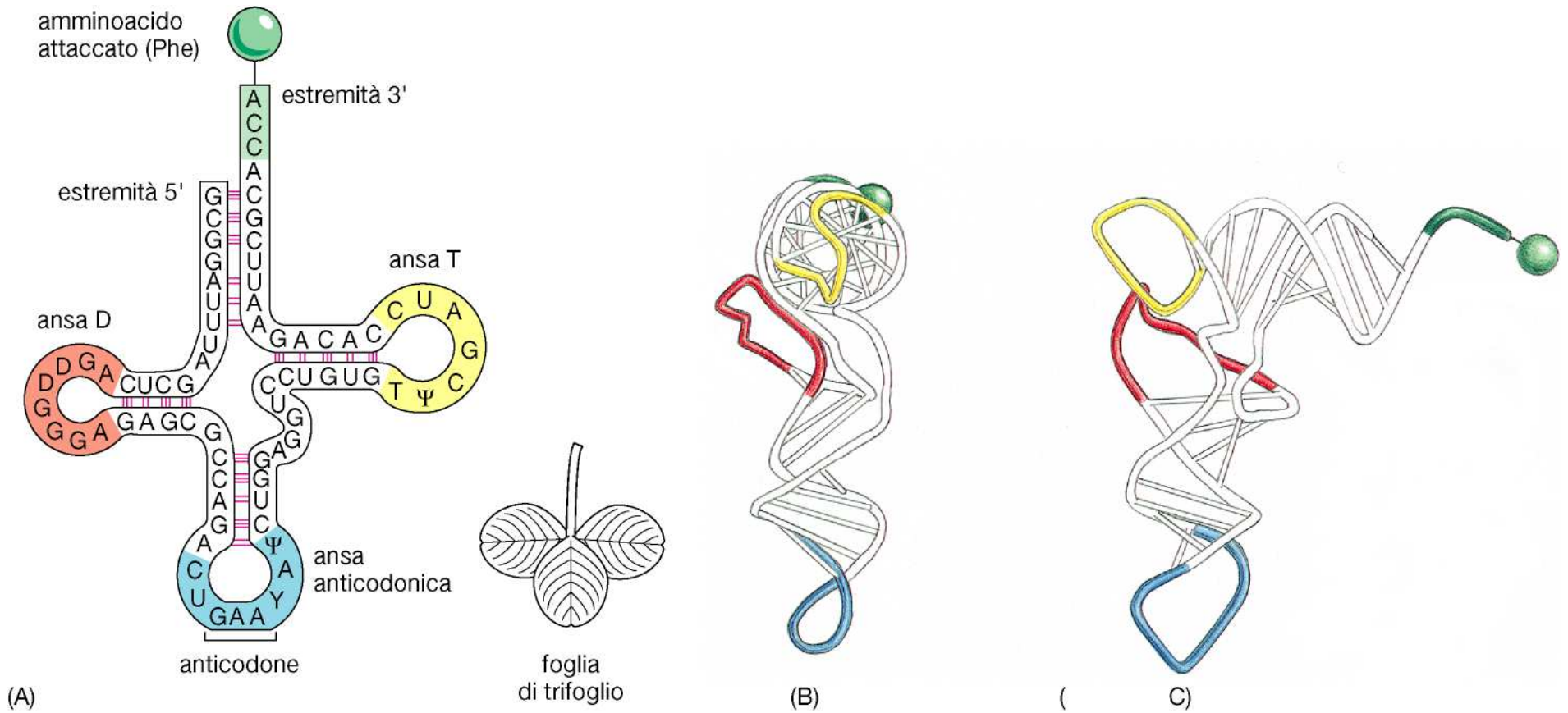
 = Chain termination codon (stop)

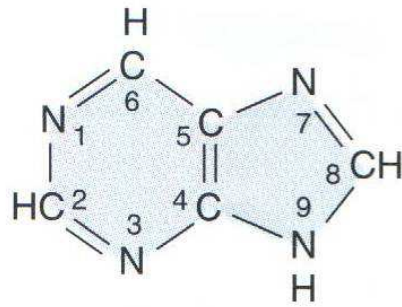
 = Initiation codon

**FIGURE 14-2 Structure of messenger RNA.**

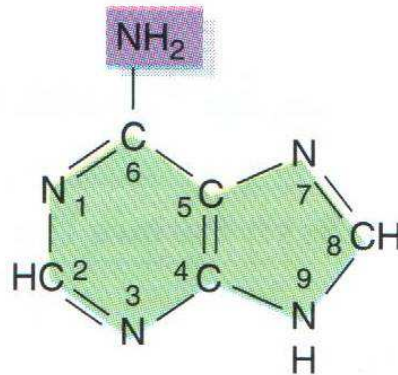
(a) A polycistronic prokaryotic message. The ribosome binding site is indicated by RBS. (b) A monocistronic eukaryotic message. The 5' cap is indicated by a "ball" at the end of the mRNA.



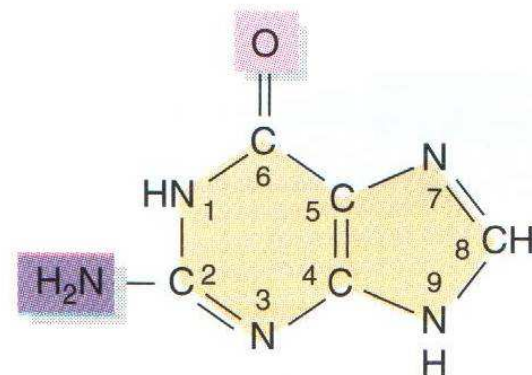




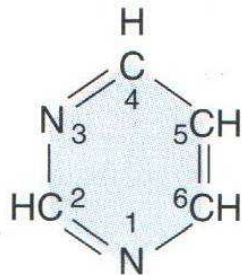
**Purine**  
(parent compound)



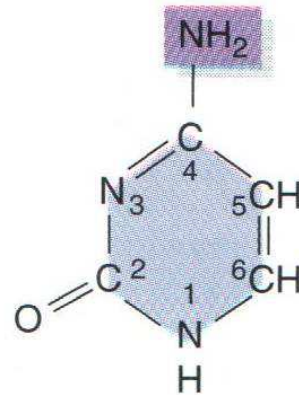
**Adenine (A)**



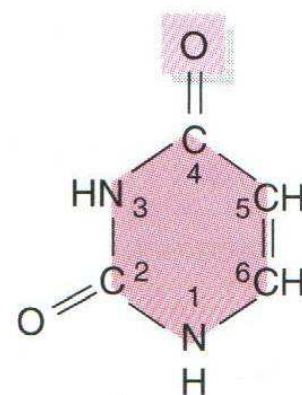
**Guanine (G)**



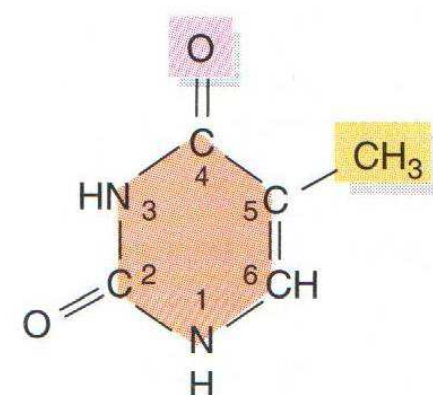
**Pyrimidine**  
(parent compound)



**Cytosine (C)**



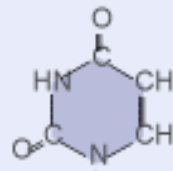
**Uracil (U)**  
(found in RNA)



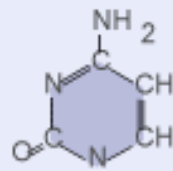
**Thymine (T)**  
(found in DNA)

## Base modifications in tRNA vary in complexity

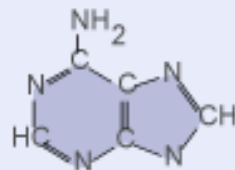
### Normal bases



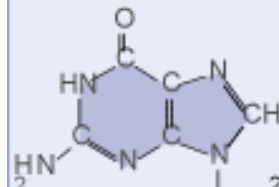
Uridine



Cytidine

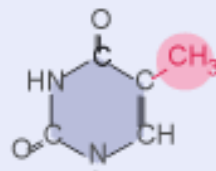


Adenosine

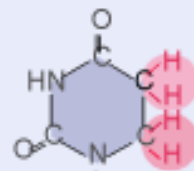


Guanosine

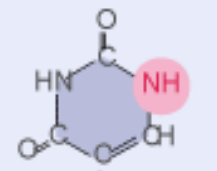
### Modified bases



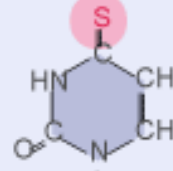
Ribothymidine (T)



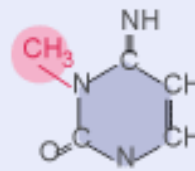
Dihydrouridine (D)



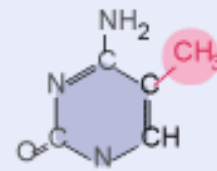
Pseudouridine (ψ)



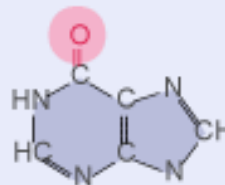
4-thiouridine



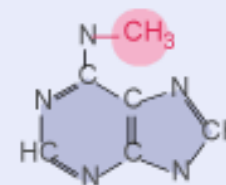
3-methylcytosine



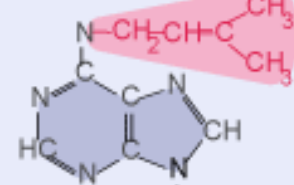
5-methylcytosine



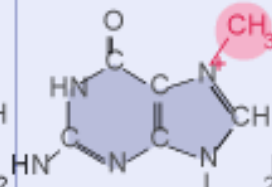
Inosine



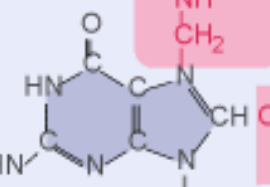
$N^6$  methyladenosine ( $m^6A$ )



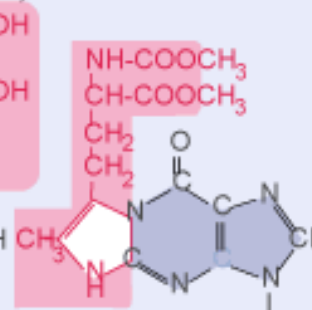
$N^6$  isopentenyladenosine



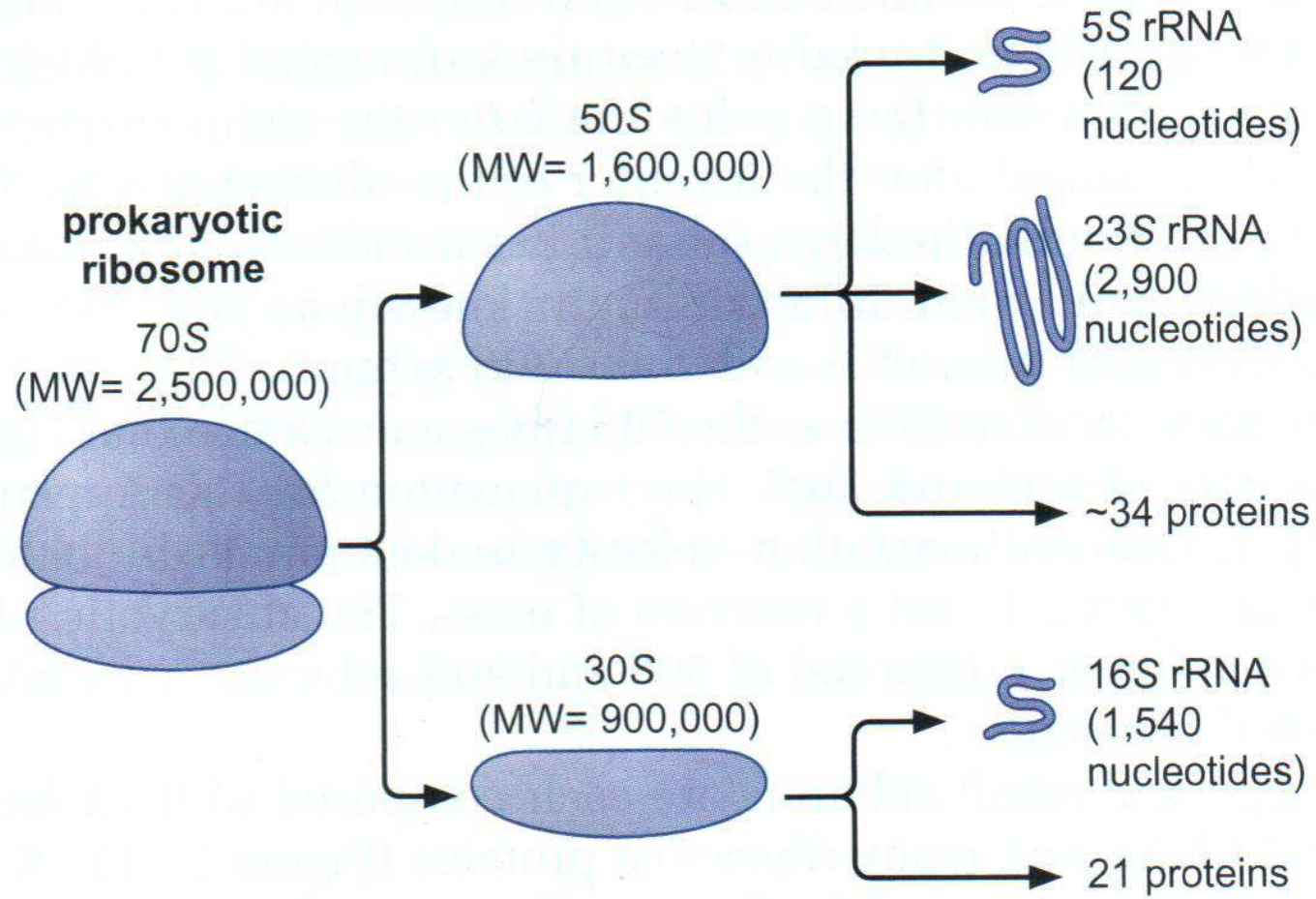
7-methylguanosine

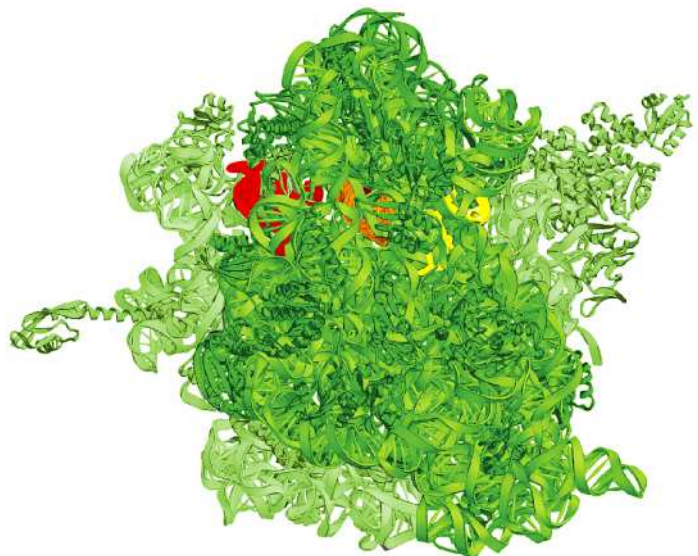


Queuosine (Q)

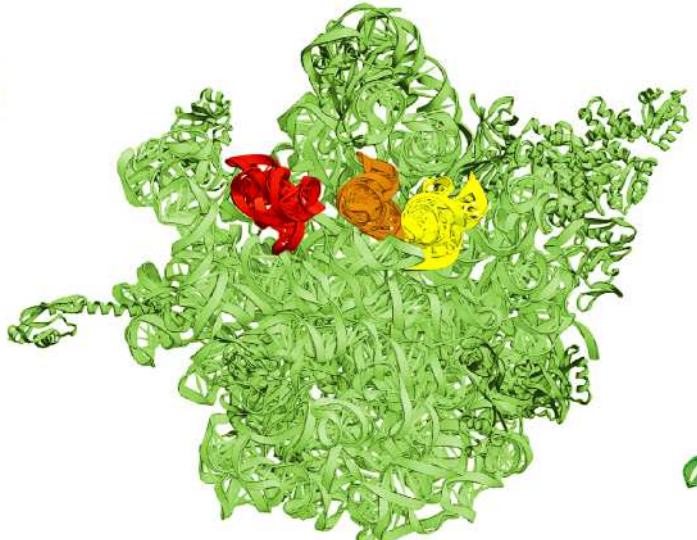


Wyosine (Y)

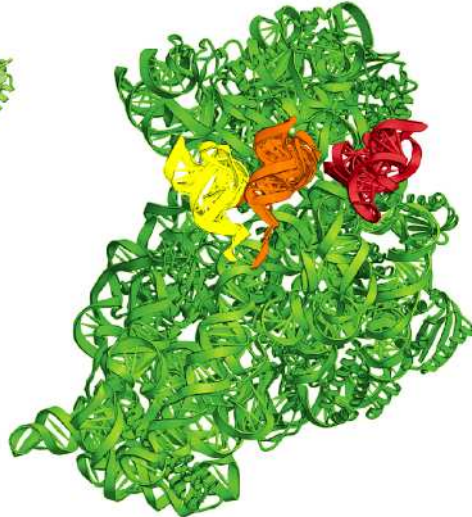




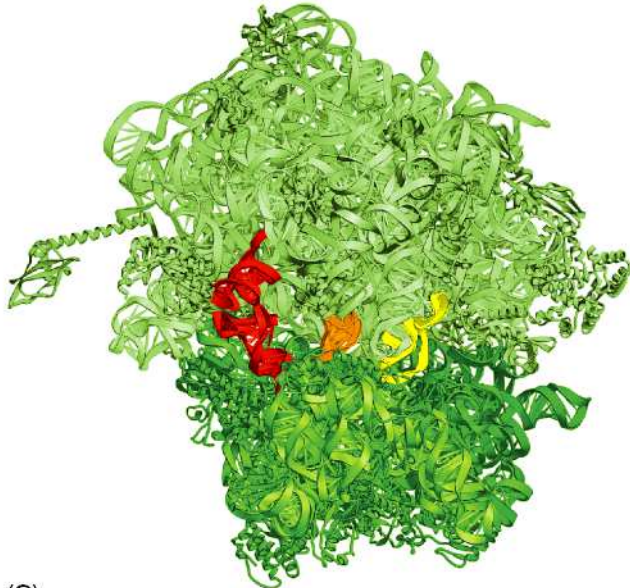
(A)



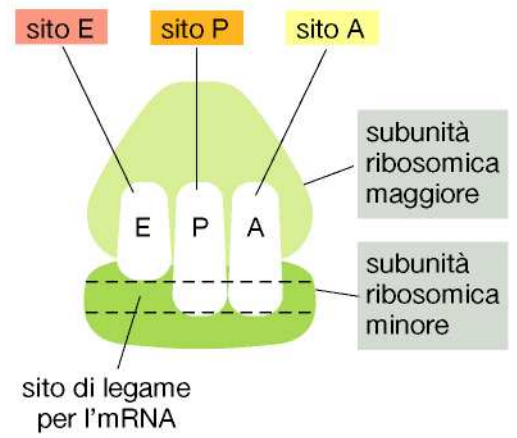
(B)



90°

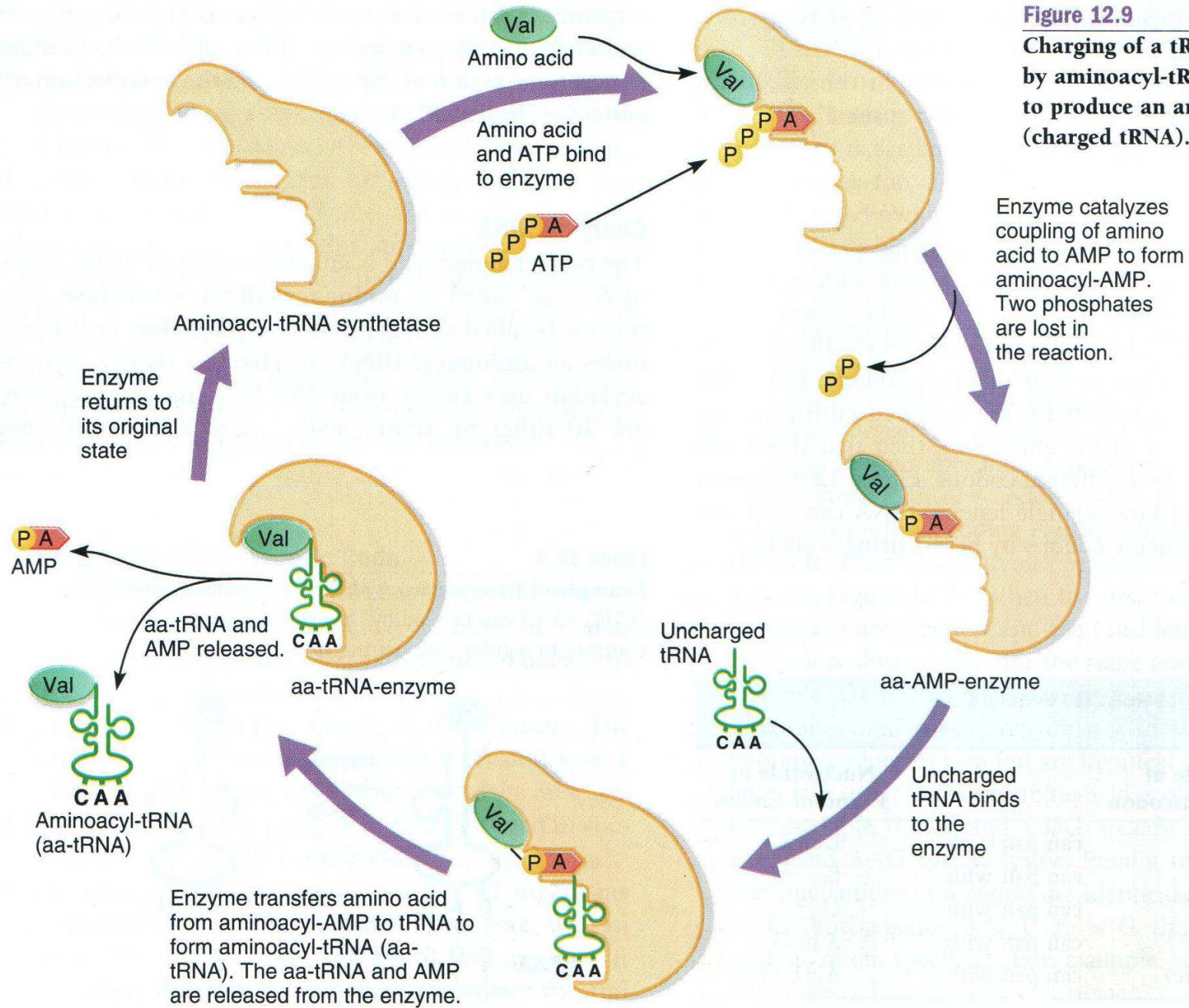


(C)



(D)





**Figure 12.9**  
**Charging of a tRNA molecule by aminoacyl-tRNA synthetase to produce an aminoacyl-tRNA (charged tRNA).**

Enzyme catalyzes coupling of amino acid to AMP to form aminoacyl-AMP. Two phosphates are lost in the reaction.

Enzyme returns to its original state

Enzyme transfers amino acid from aminoacyl-AMP to tRNA to form aminoacyl-tRNA (aa-tRNA). The aa-tRNA and AMP are released from the enzyme.

Uncharged tRNA  
 CAA

aa-AMP-enzyme

Uncharged tRNA binds to the enzyme

Val  
 Amino acid

Val  
 P P P A  
 ATP

Amino acid and ATP bind to enzyme

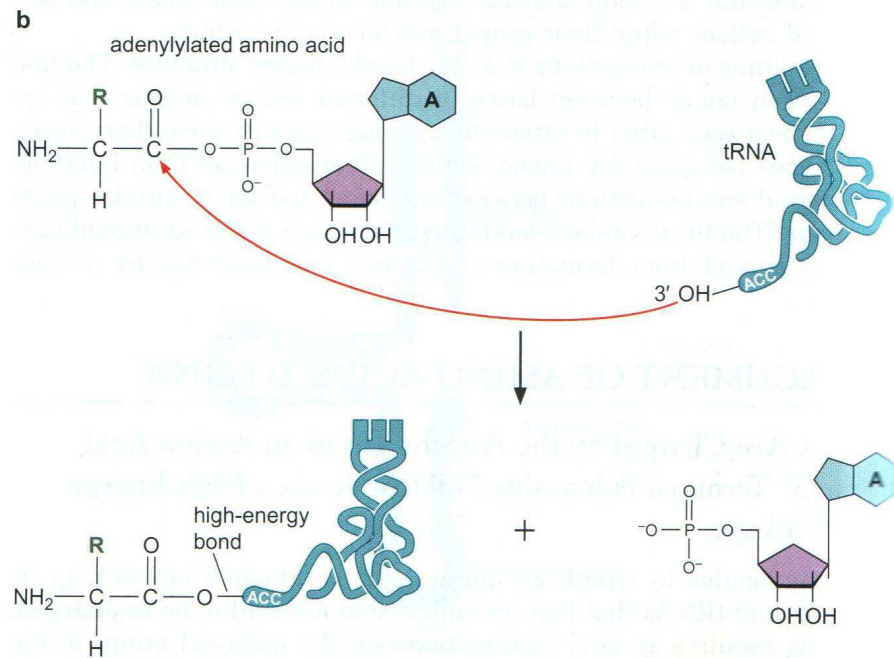
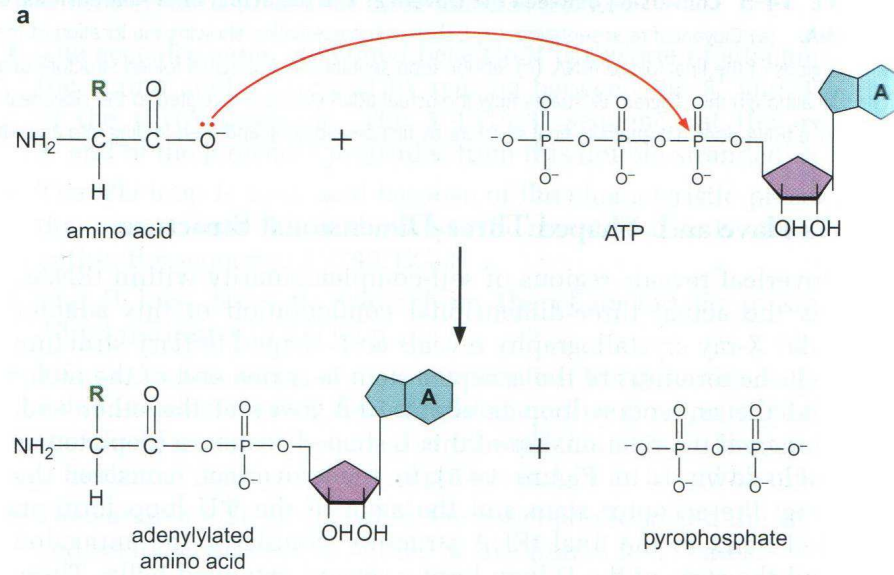
Aminoacyl-tRNA synthetase

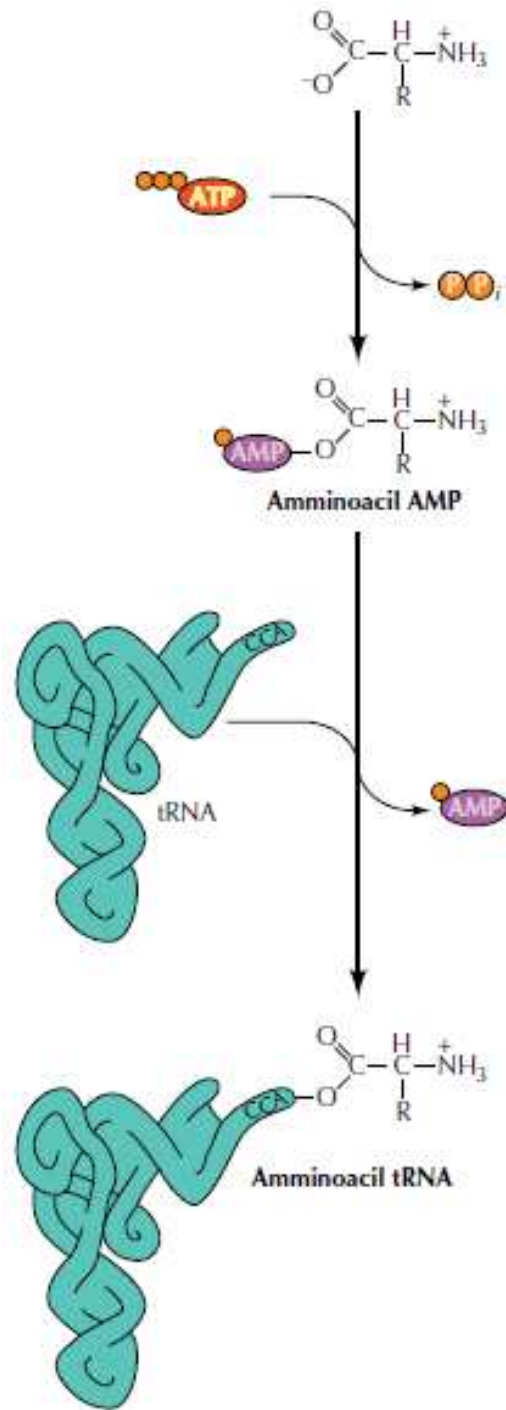
P A  
 AMP

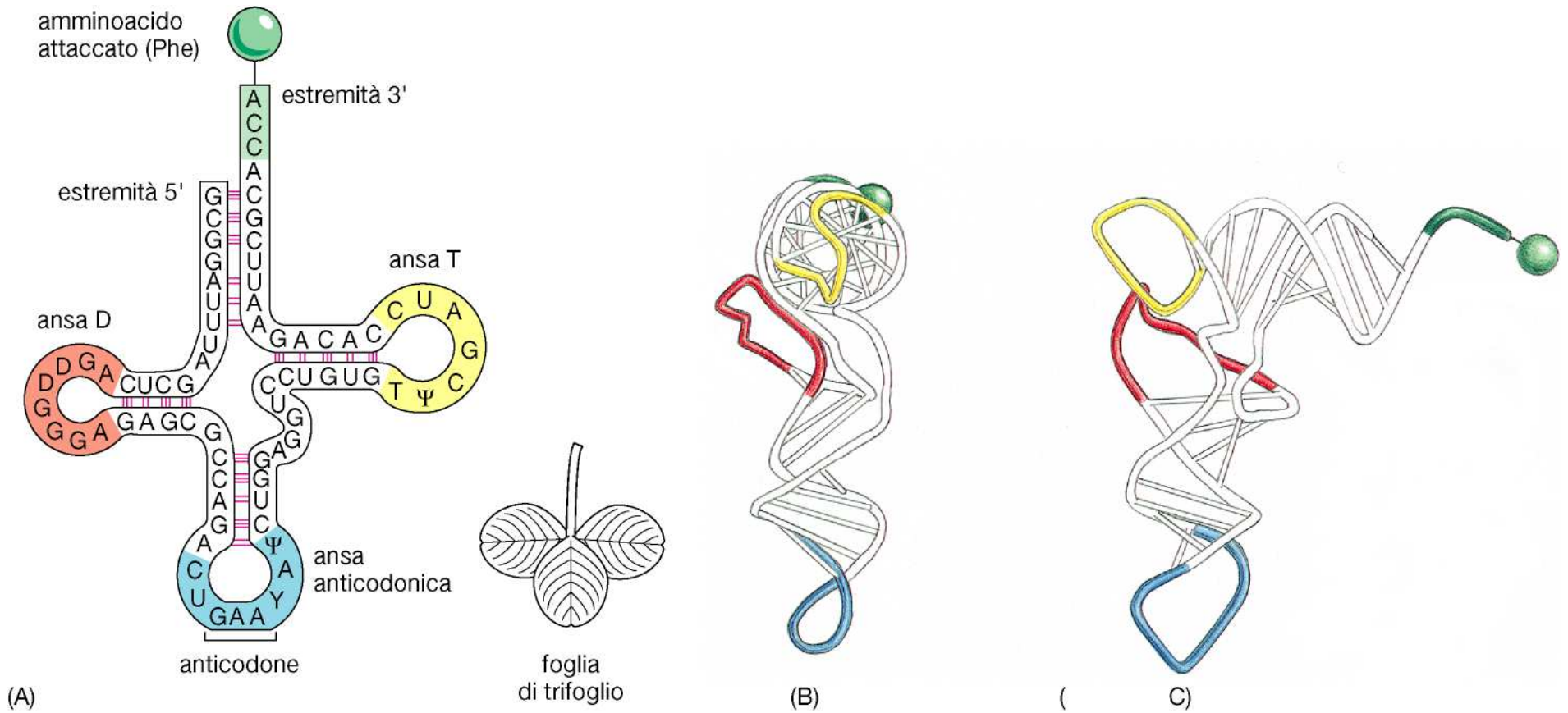
Val  
 CAA  
 Aminoacyl-tRNA (aa-tRNA)

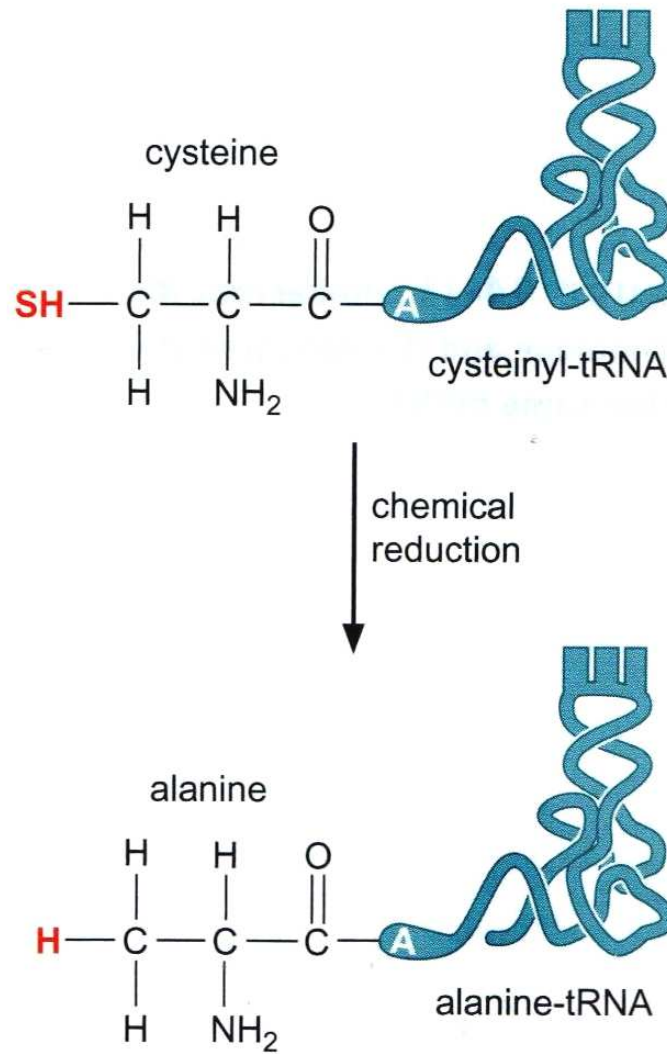
aa-tRNA-enzyme  
 CAA

aa-tRNA and AMP released.









**FIGURE 14-10 Cysteinyl-tRNA charged with C or A.** Chemical reductions of cysteine attached to cysteinyl-tRNA.

# Fase di Inizio

Fattori di inizio della traduzione (IF)

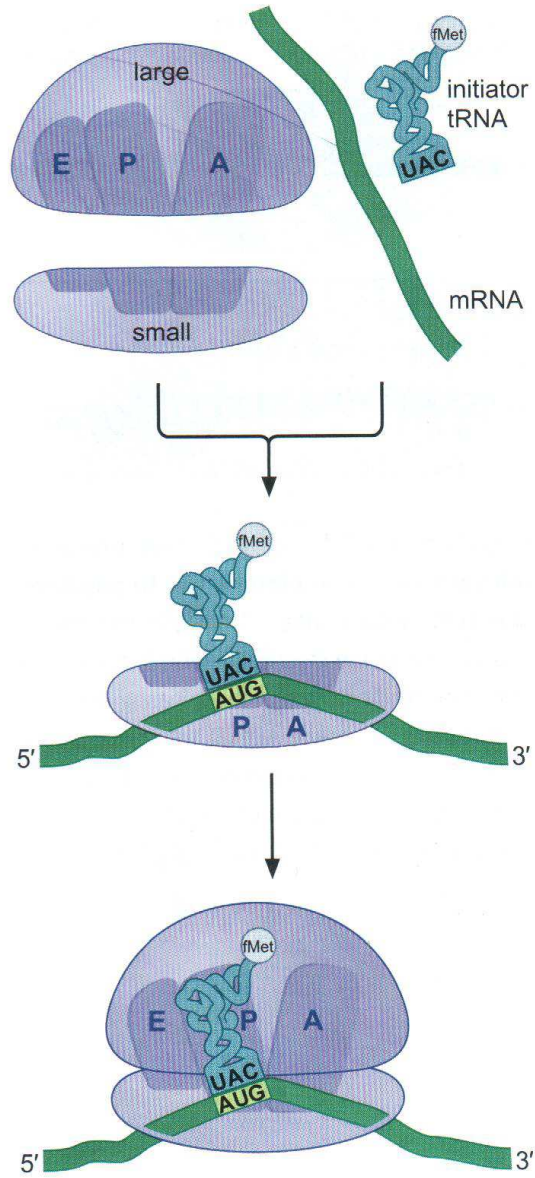
- IF1

- IF2 (GTP<sub>asi</sub>)

- IF3

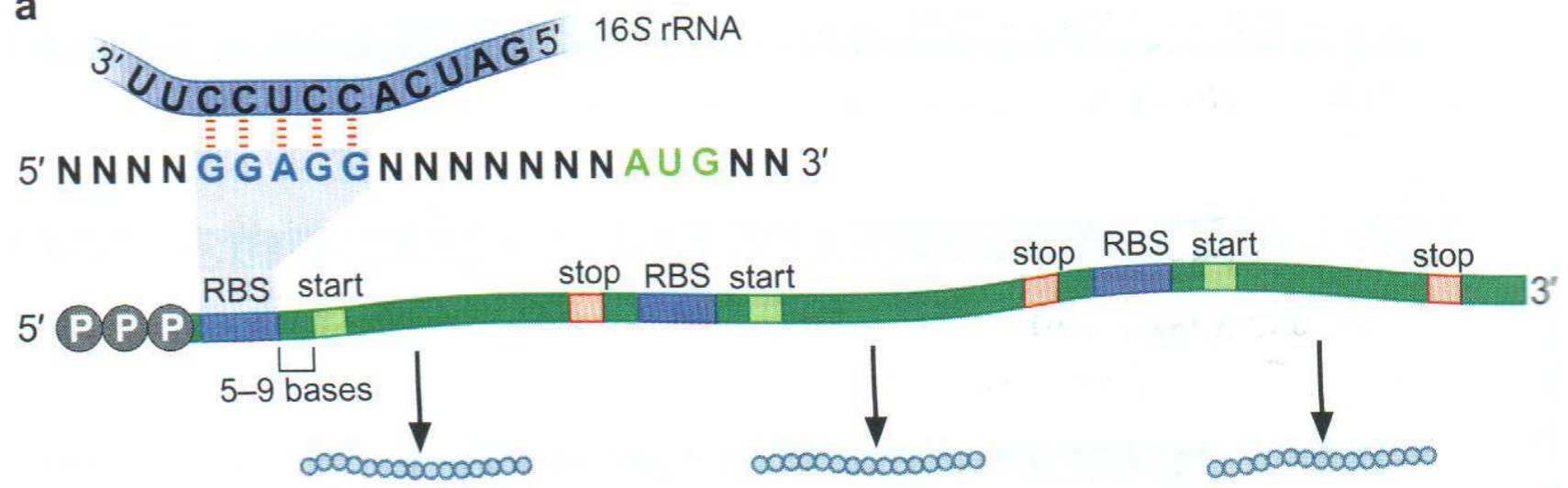
GTP

tRNA iniziatore



**FIGURE 14-22** An overview of the events of translation initiation.

a

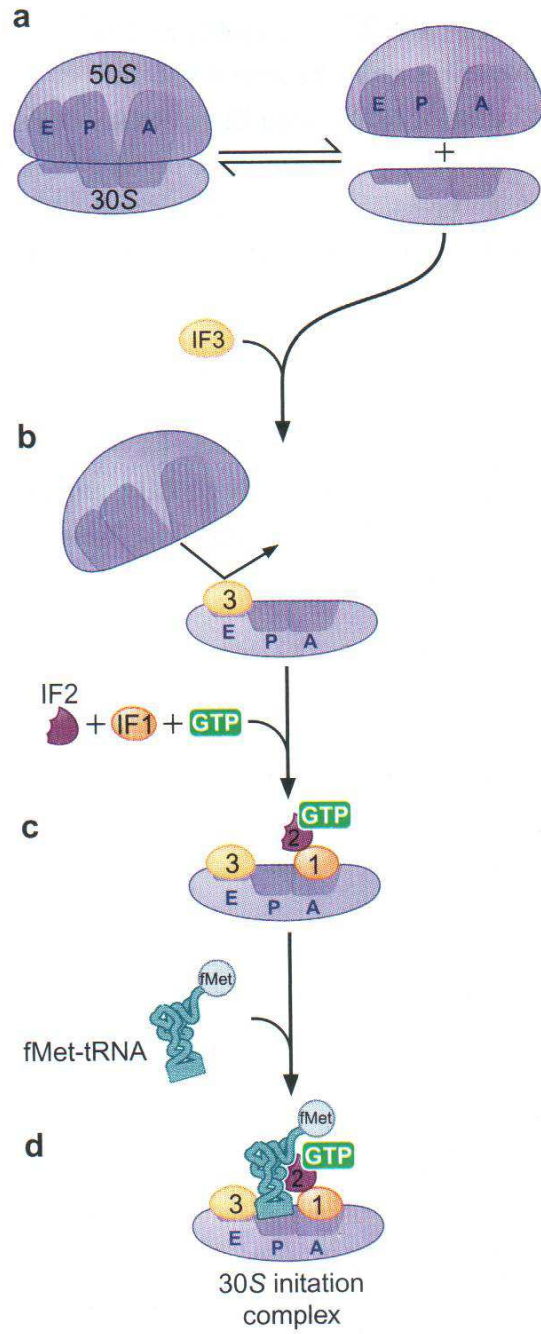




Sequenza di Shine-Dalgarno,  
solo nei procarioti

mRNA





## Initiator tRNA has distinct features

Formylated amino acid

formyl

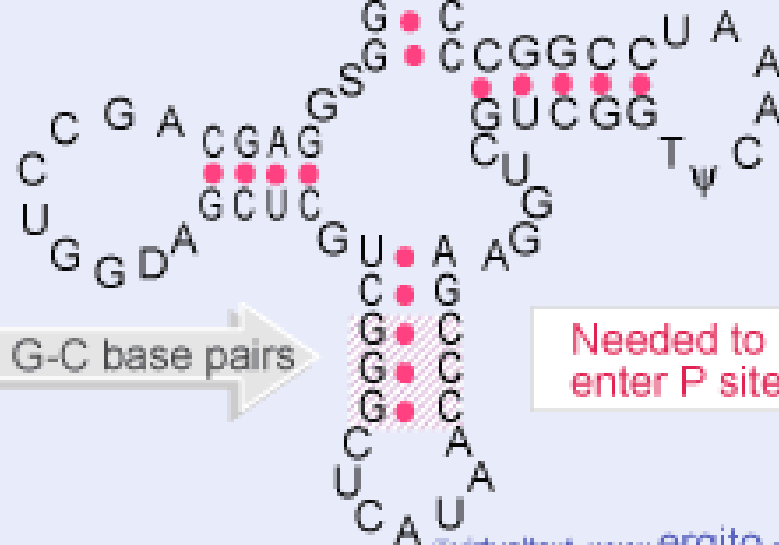
Met

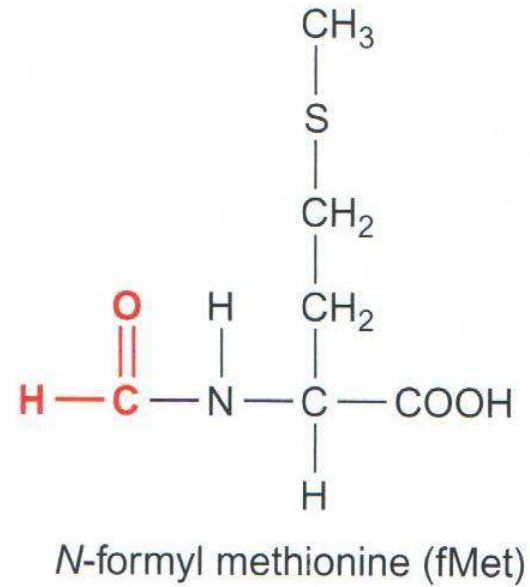
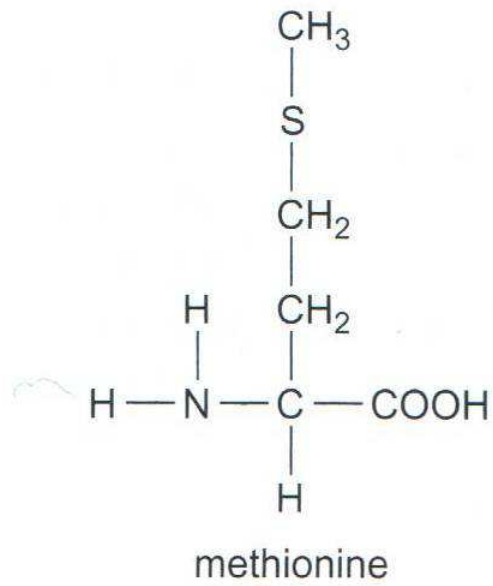
No base pairing

Needed for formylation

3 G-C base pairs

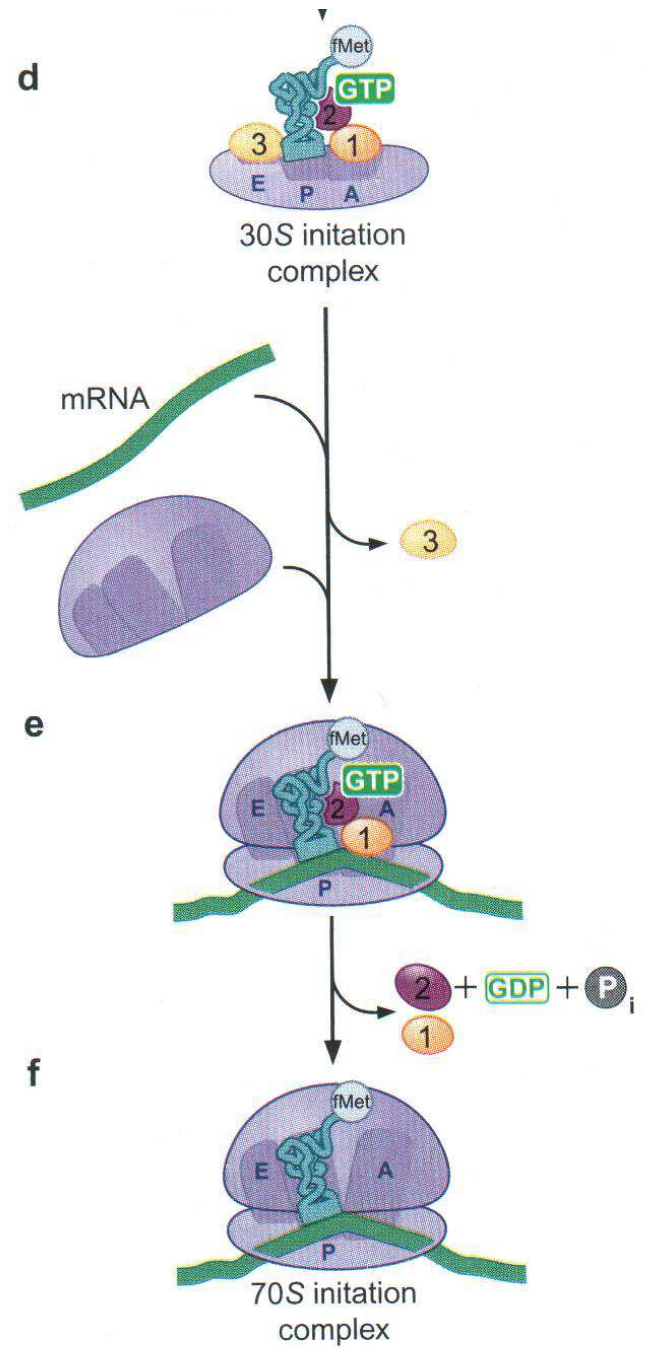
Needed to enter P site



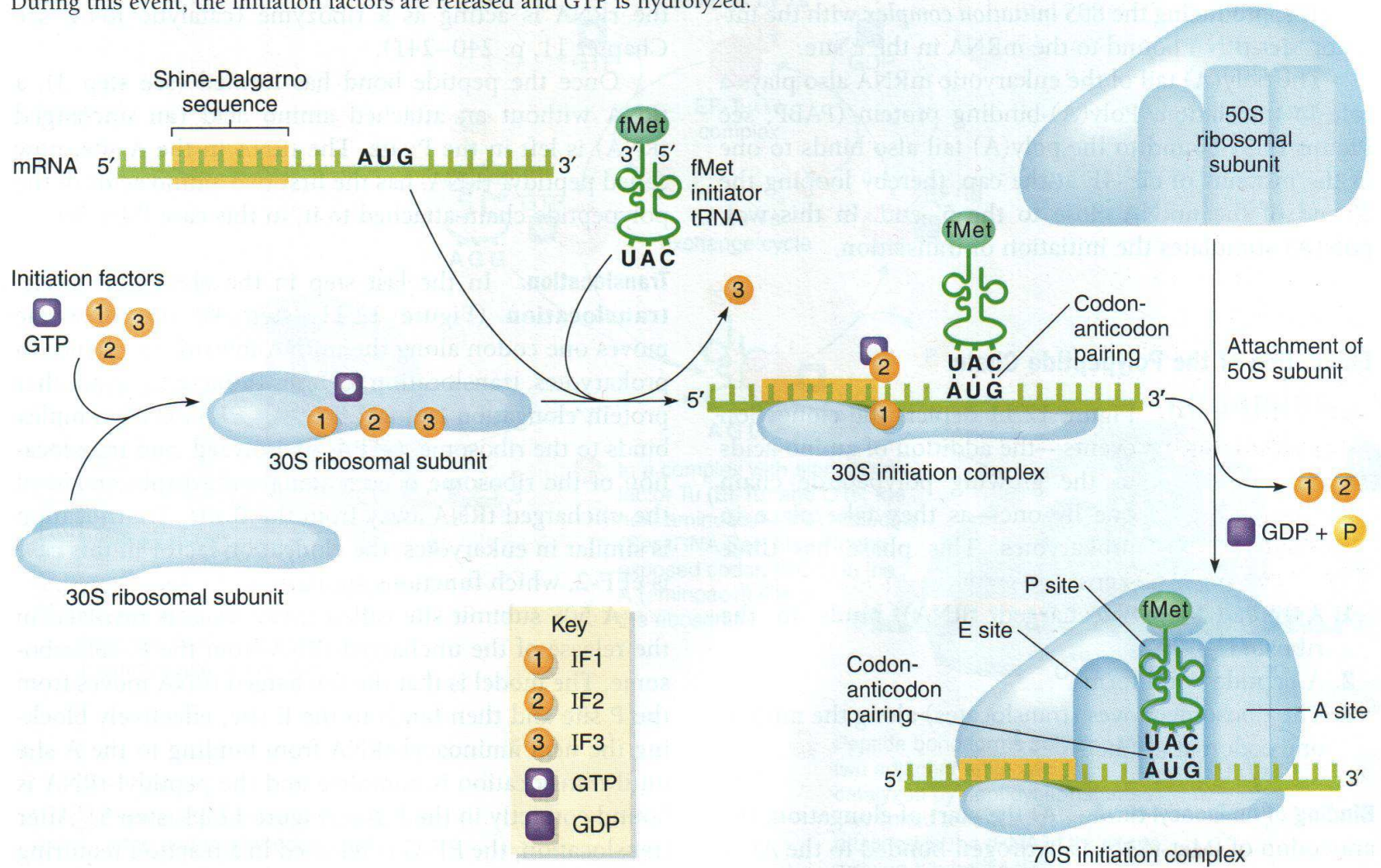


---

**FIGURE 14-24** Methionine and *N*-formyl methionine.



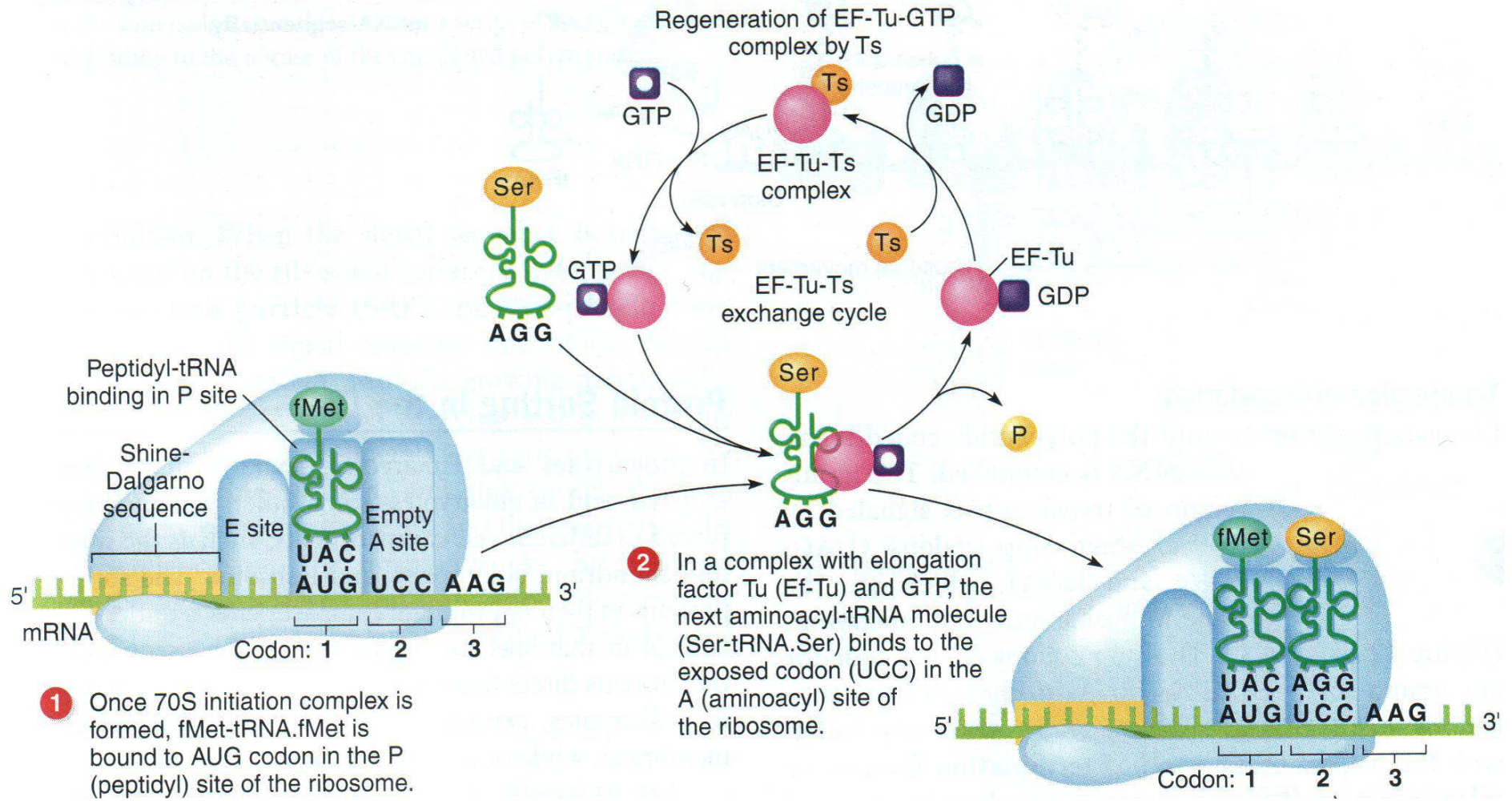
**Initiation of protein synthesis in prokaryotes.** A 30S ribosomal subunit, complexed with initiation factors and GTP, binds to mRNA and fMet-tRNA to form a 30S initiation complex. Next, the 50S ribosomal subunit binds, forming a 70S initiation complex. During this event, the initiation factors are released and GTP is hydrolyzed.



# Fase di Elongazione

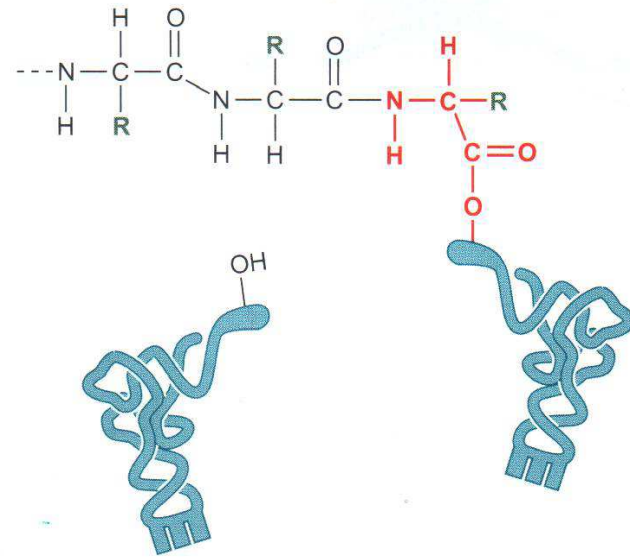
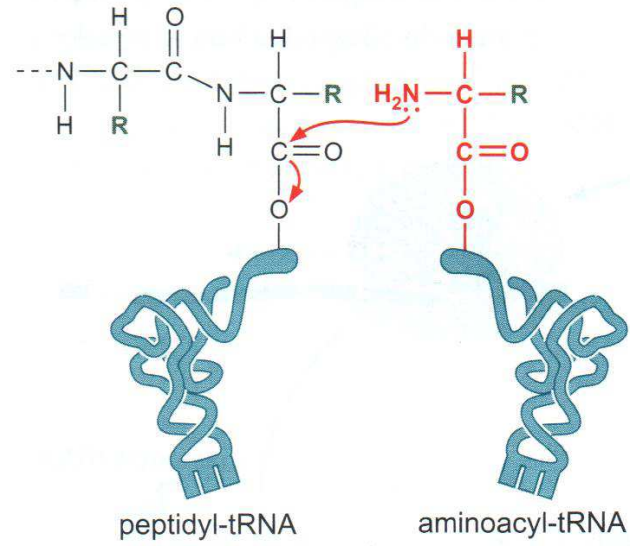
Fattori di elongazione (EF)

- EF-Tu ( $GTP_{asi}$ )      porta gli aa-tRNA al sito A del ribosoma
- EF-G ( $GTP_{asi}$ )      completa la **traslocazione** del ribosoma

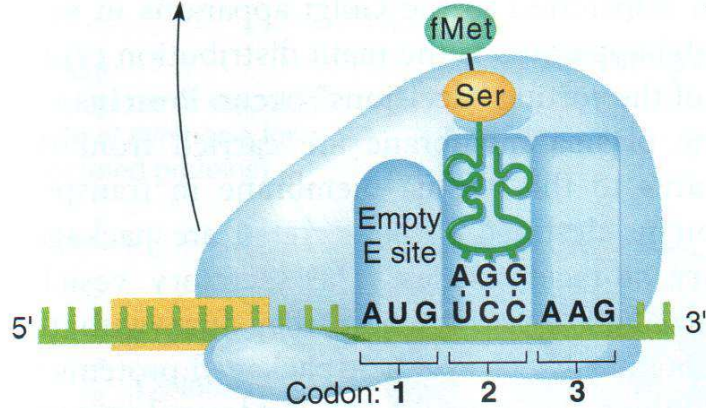




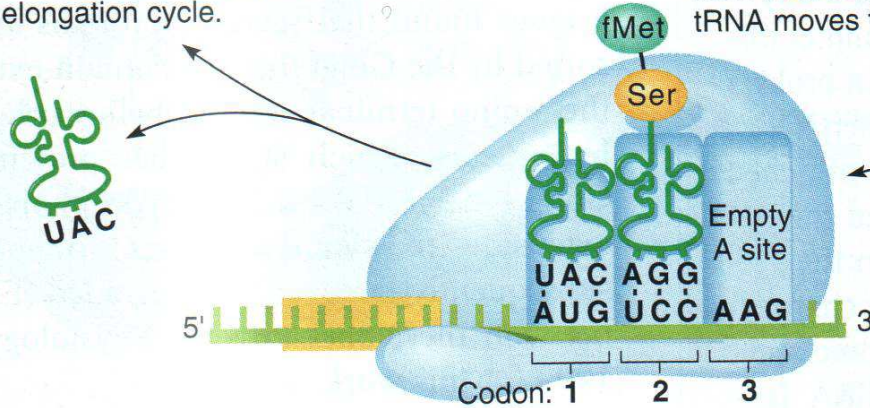
polypeptide chain



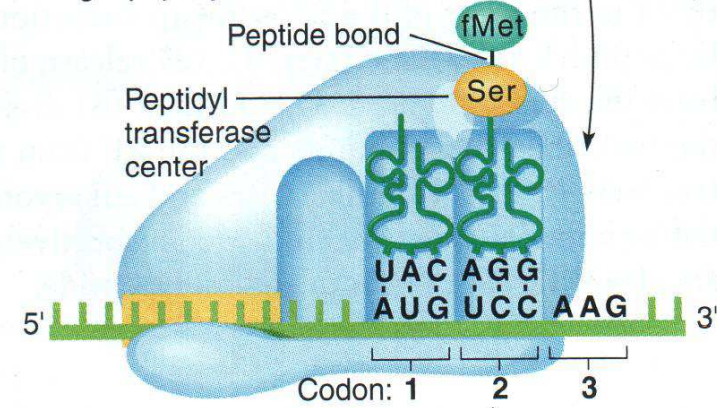
- 6 The elongation cycle repeats until stop codon is encountered.



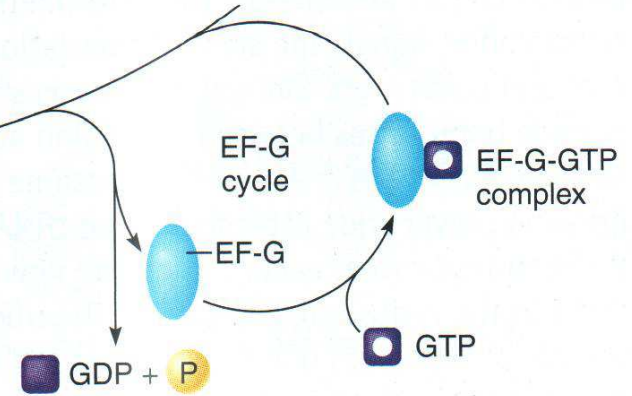
- 5 When translocation is complete and the peptidyl-tRNA is in the P site, uncharged tRNA is released from the E site and the ribosome is ready for another elongation cycle.



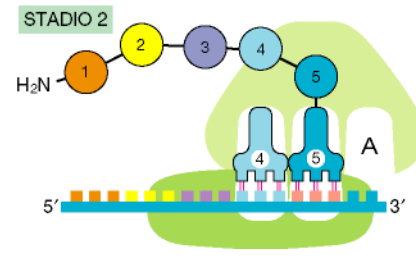
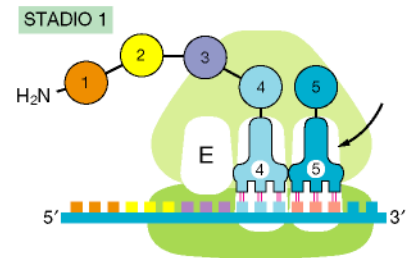
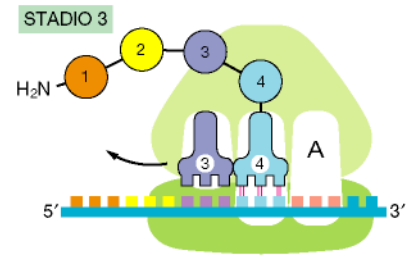
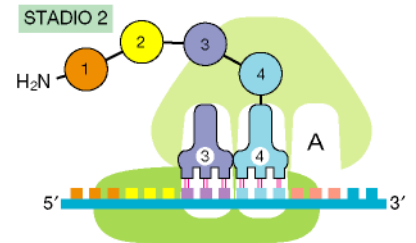
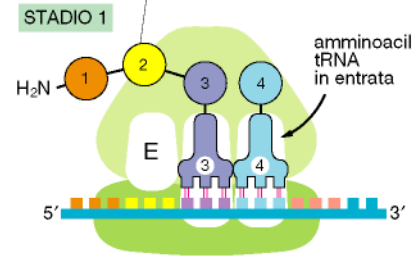
- 3 Peptide bond forms between the two adjacent amino acids, catalyzed by peptidyl transferase. The linked amino acids are attached to the tRNA in the A site, forming a peptidyl-tRNA.

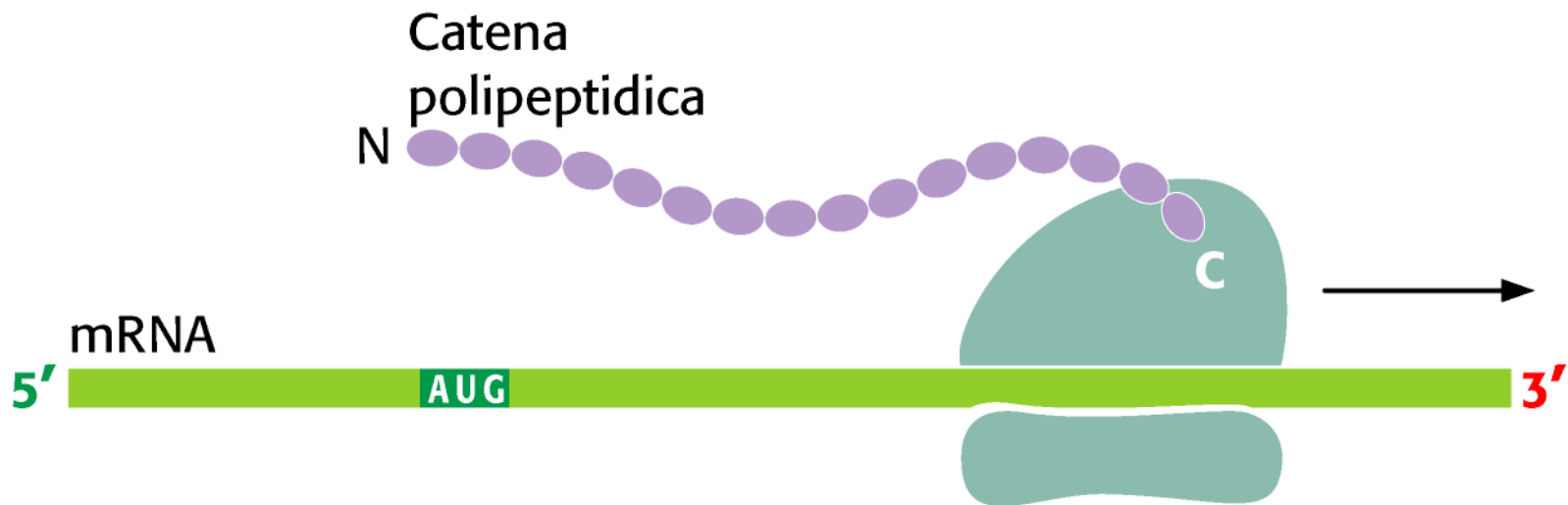
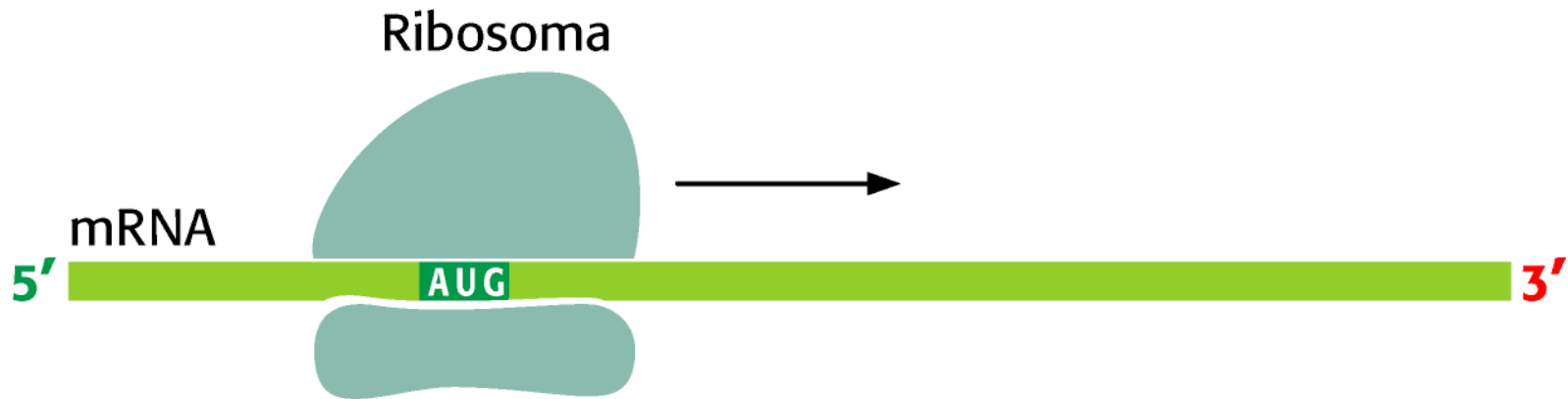


- 4 Translocation occurs as the ribosome moves one codon to the right, requiring EF-G and GTP, and peptidyl-tRNA moves from the A site to the P site. Uncharged tRNA moves from the P site to the E site.



catena polipeptidica in allungamento

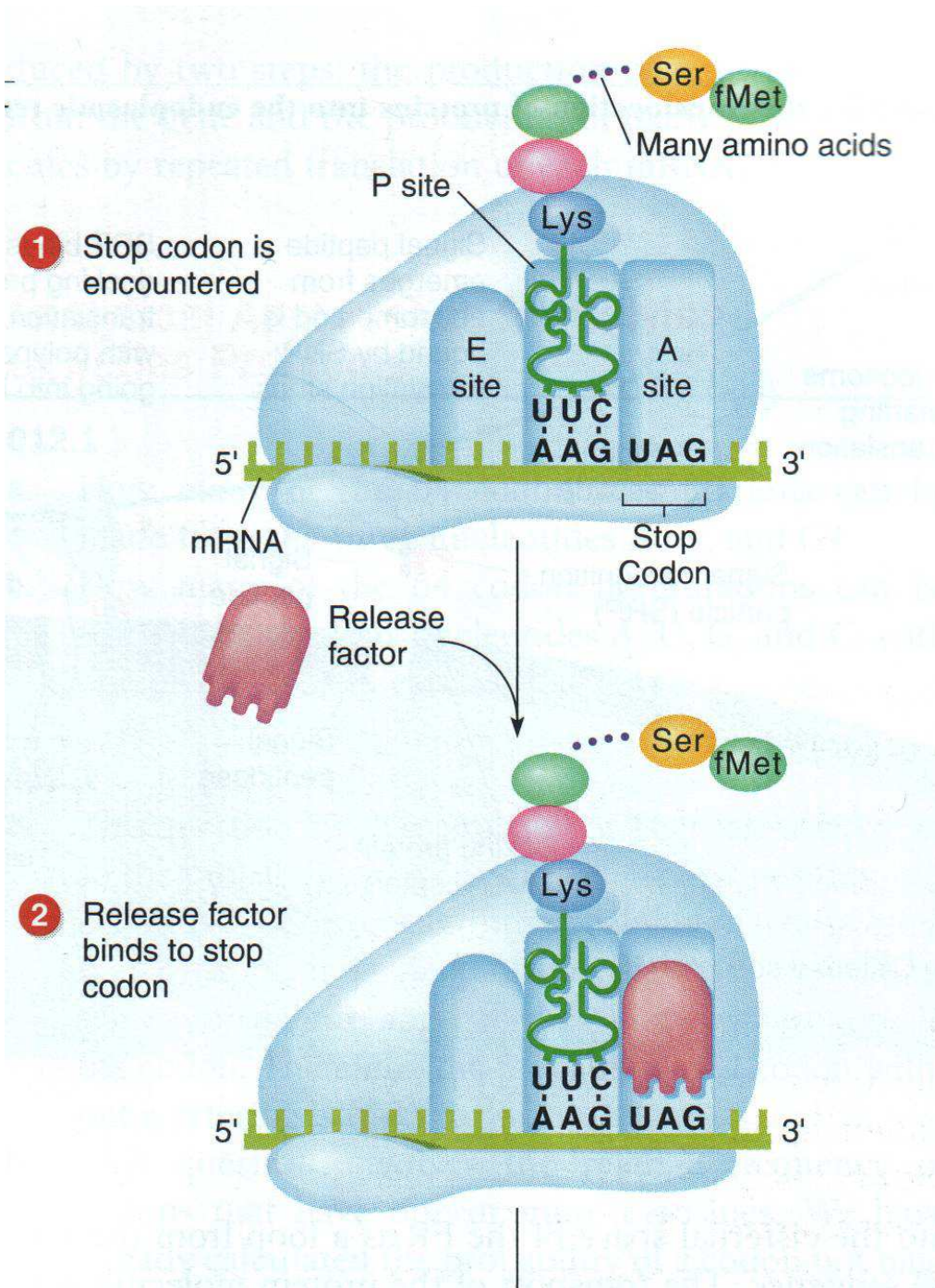


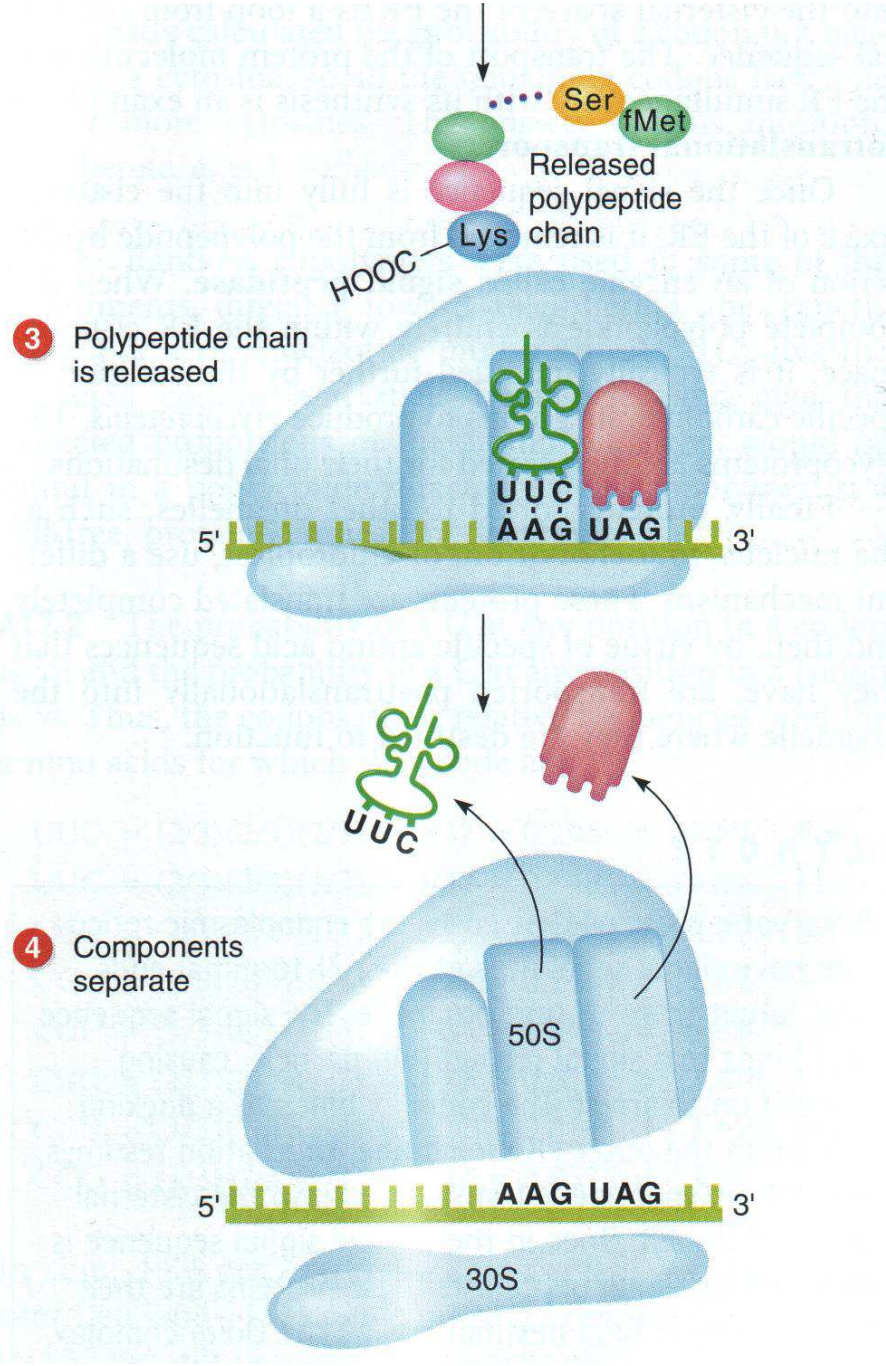


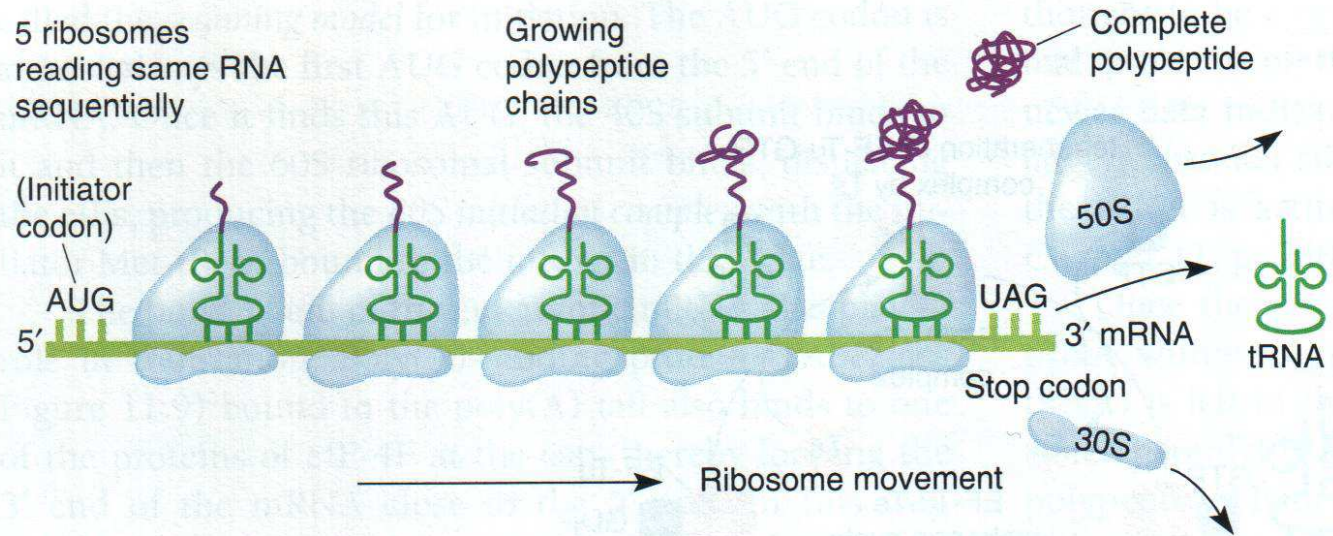
# Fase di Termine

## Fattori di rilascio (RF)

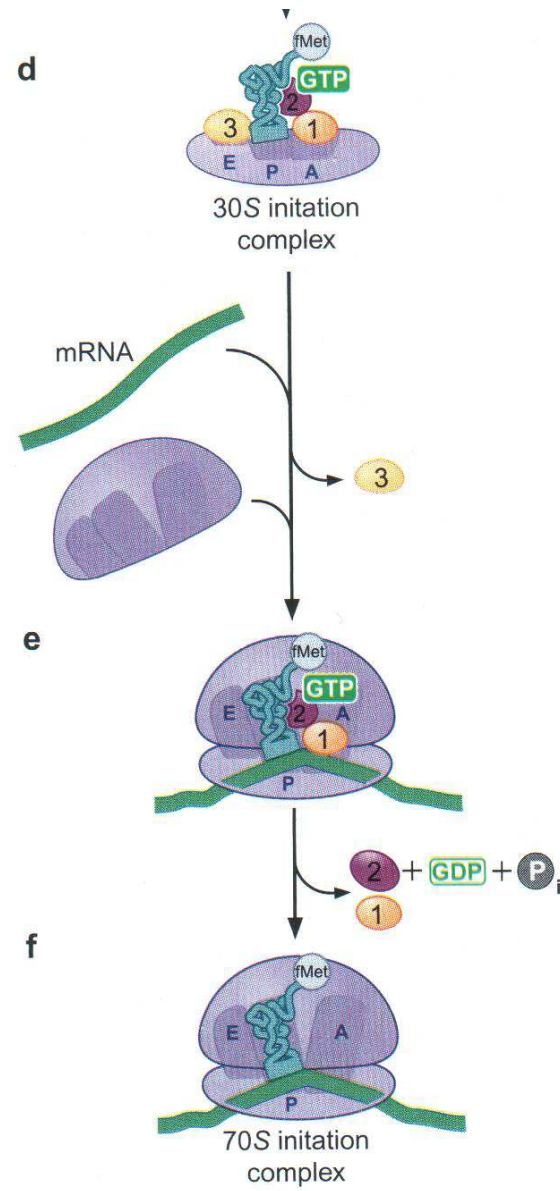
- RF di classe I riconoscono i codoni di stop e stimolano l'idrolisi del peptide dal tRNA nel sito P
- RF di classe II (GTPasi) stimolano la dissociazione dei RF di classe I dal ribosoma dopo il rilascio della catena polipeptidica



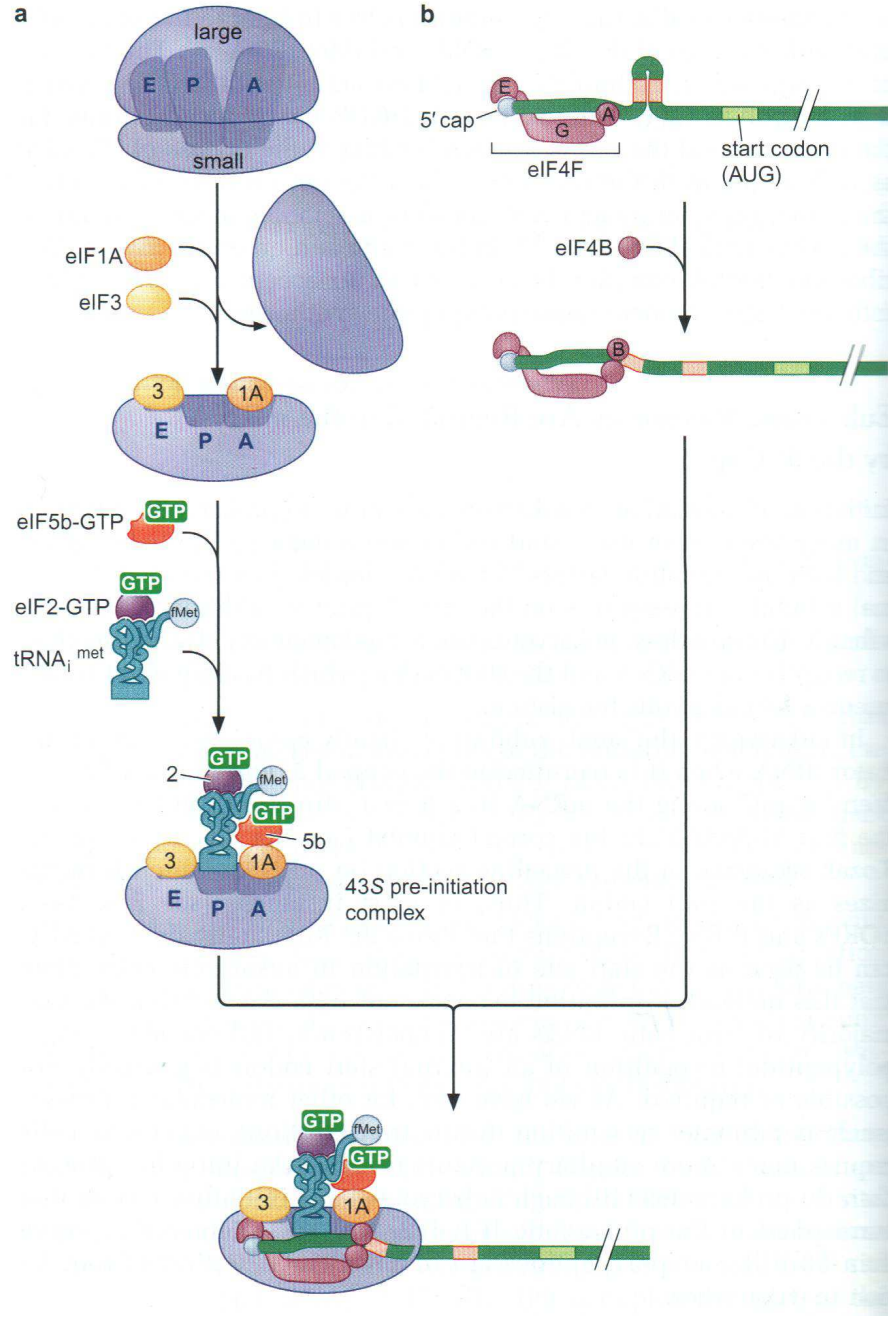


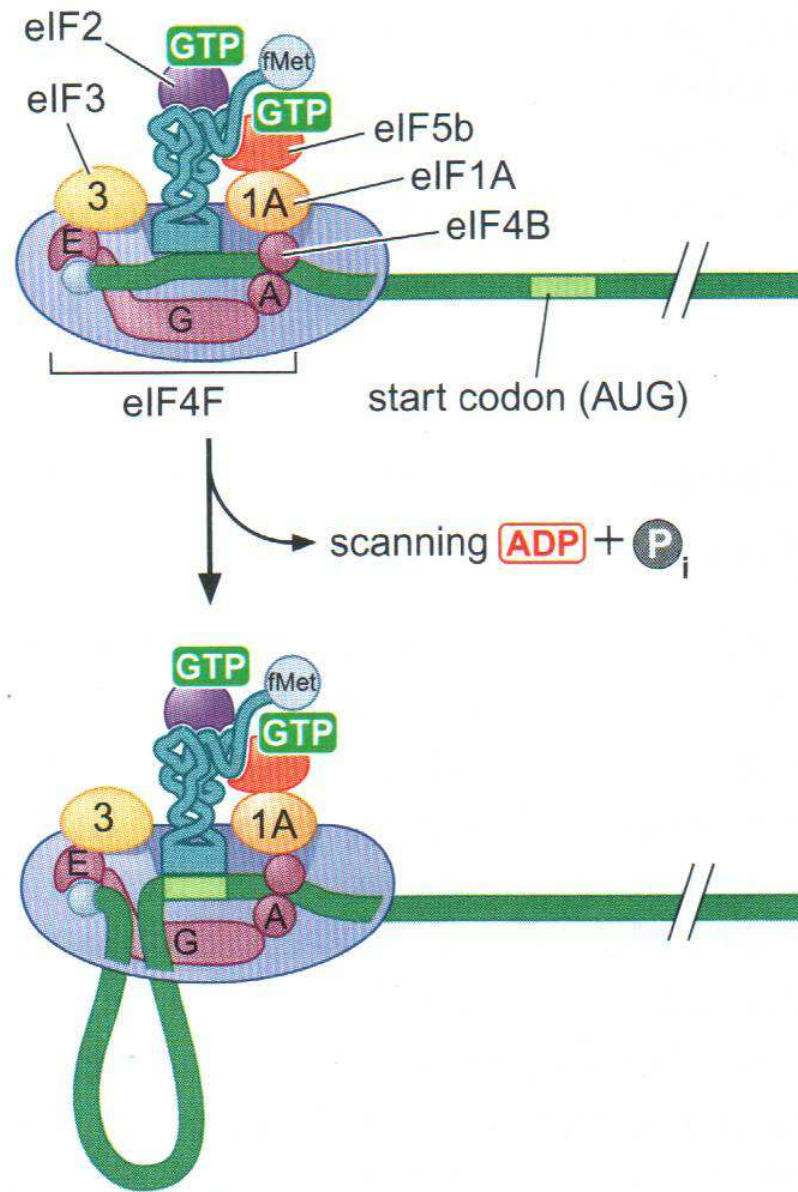






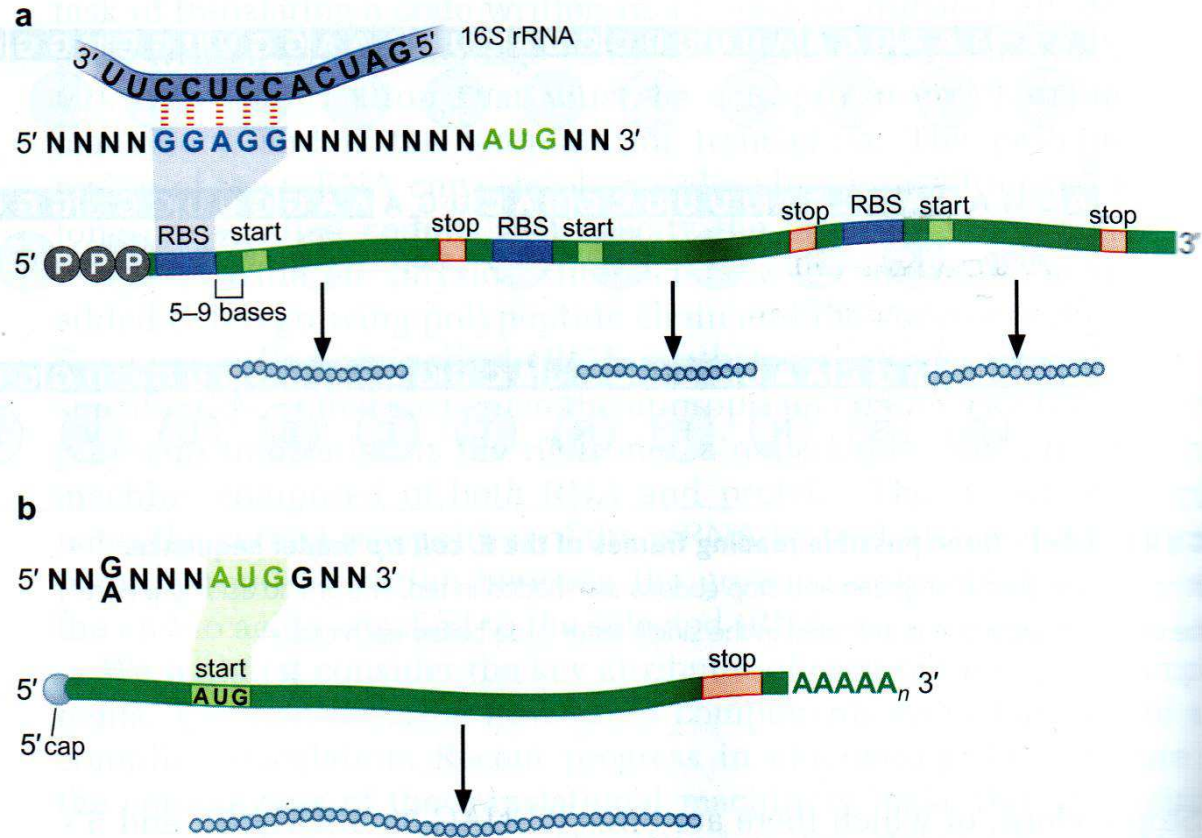
**FIGURE 14-26** A summary of translation initiation in prokaryotes.

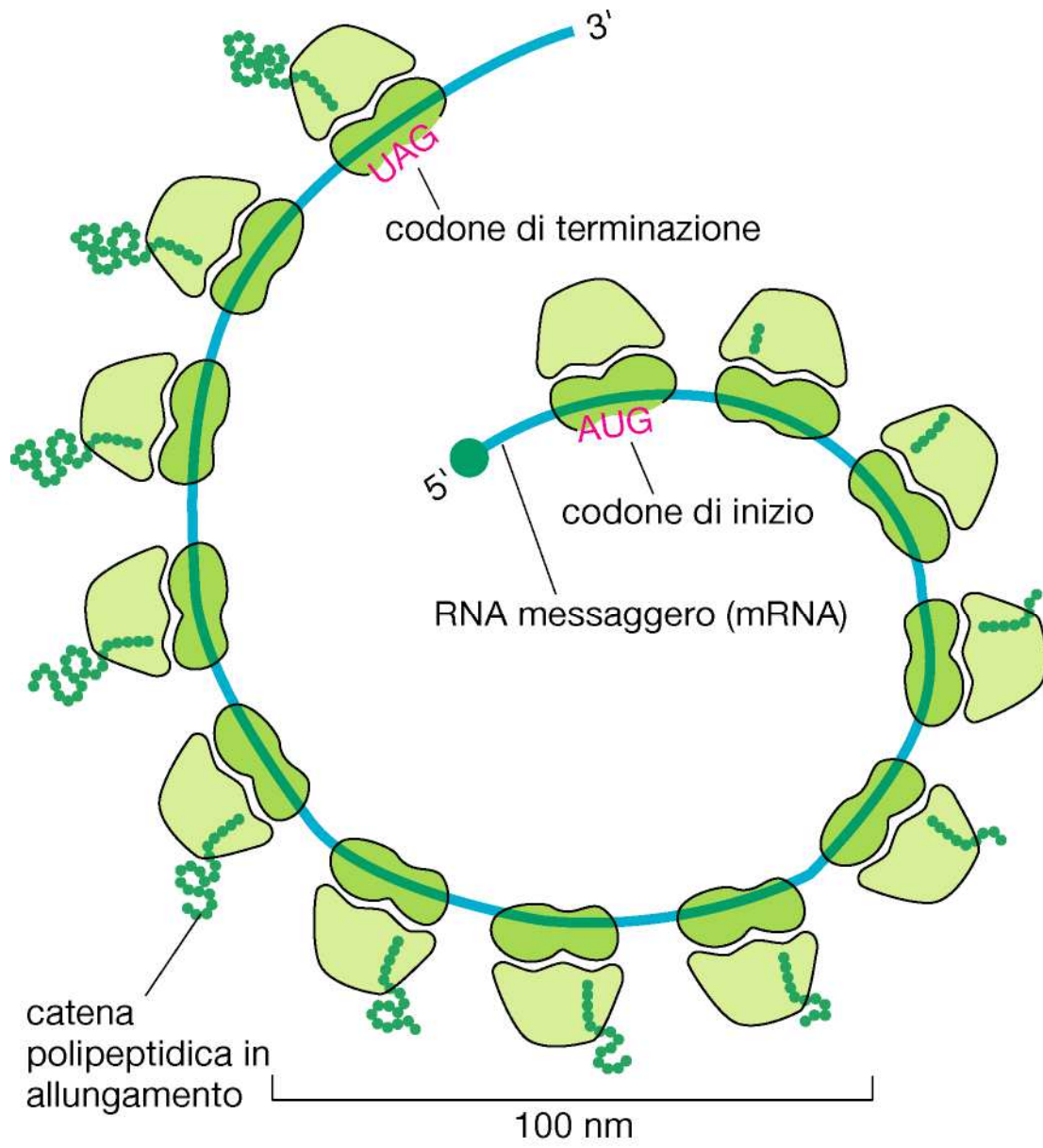




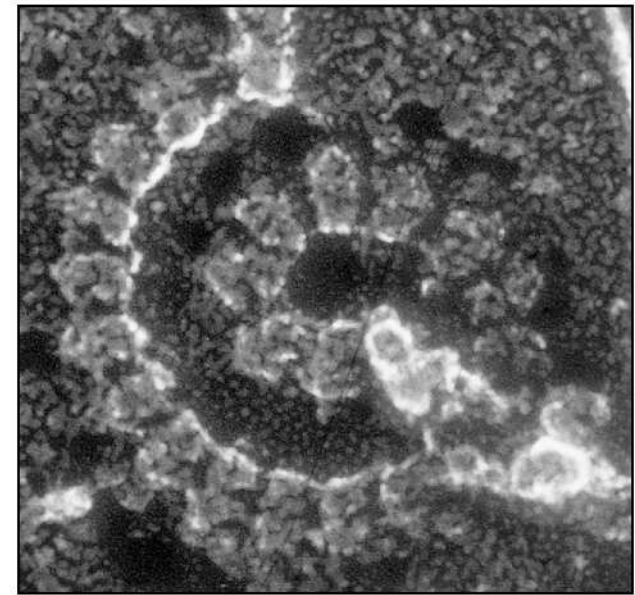
**FIGURE 14-2 Structure of messenger RNA.**

(a) A polycistronic prokaryotic message. The ribosome binding site is indicated by RBS. (b) A monocistronic eukaryotic message. The 5' cap is indicated by a "ball" at the end of the mRNA.

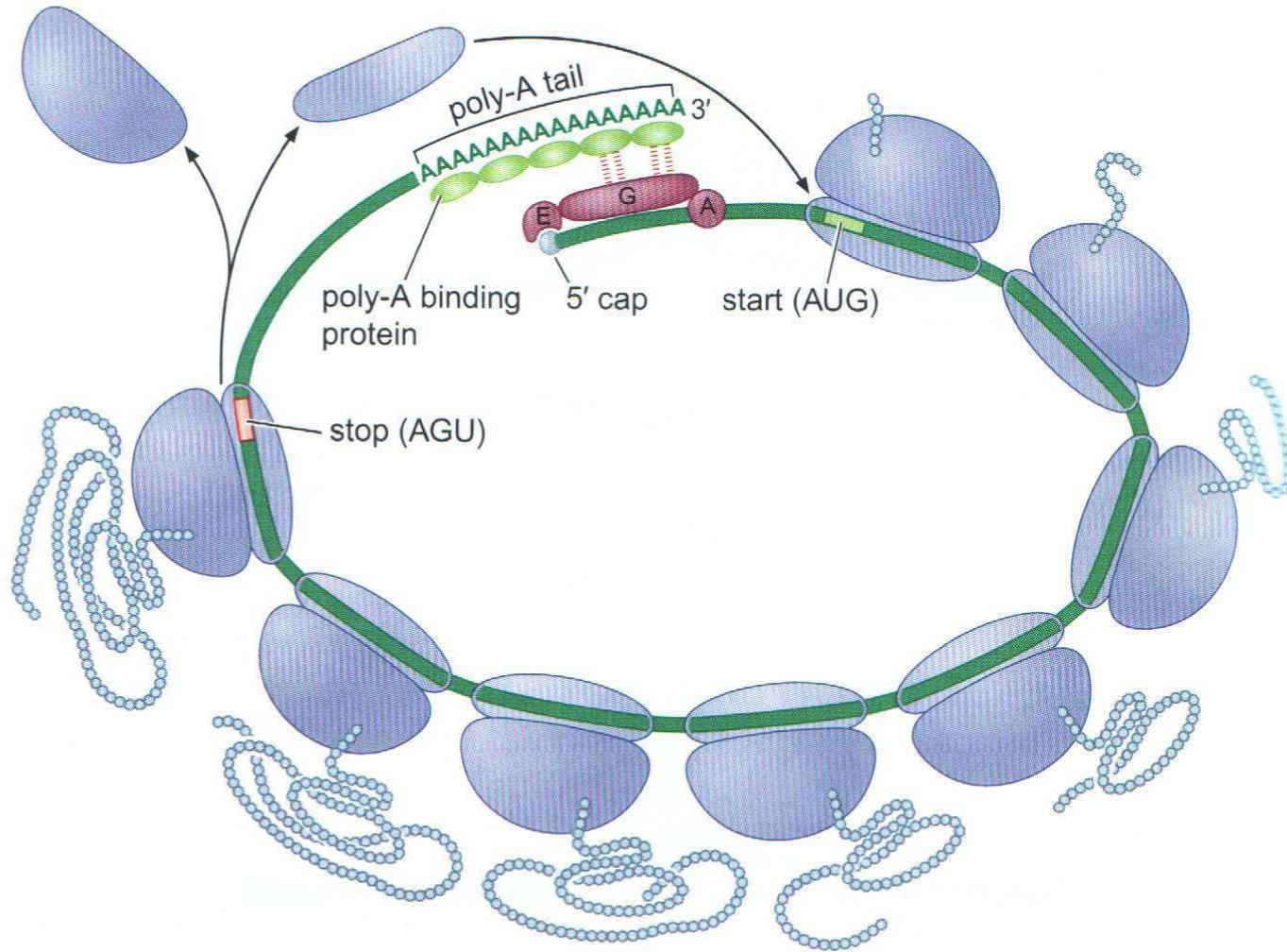




(A)

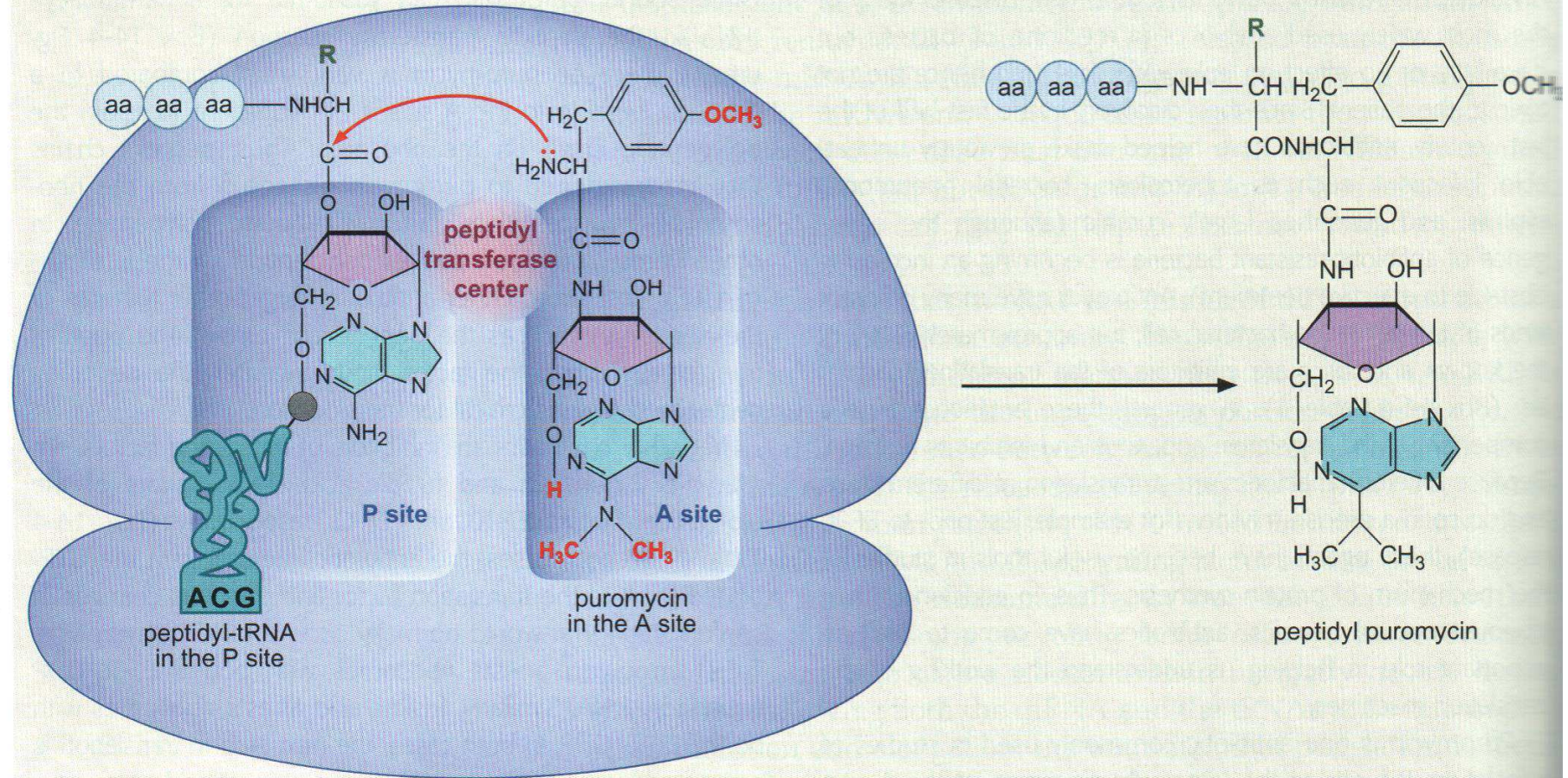


(B)



<b>Antibiotic/Toxin</b>	<b>Target Cells</b>	<b>Molecular Target</b>	<b>Consequence</b>
Tetracycline	Prokaryotic cells	A site of 30S subunit	Inhibits aminoacyl-tRNA binding to the A site
Hygromycin B	Prokaryotic and eukaryotic cells	Near the A site of 30S subunit	Prevents translocation of A-site tRNA to P site
Paromycin	Prokaryotic cells	Adjacent to the A site codon-anticodon interaction site in 30S subunit	Increases error rate during translation by decreasing selectivity of codon-anticodon pairing
Chloramphenicol	Prokaryotic cells	Peptidyl transferase center of 50S subunit	Blocks correct positioning of the A site aminoacyl-tRNA for peptidyl transfer reaction
Puromycin	Prokaryotic and eukaryotic cells	Peptidyl transferase center of large ribosomal subunit	Chain terminator; mimics the 3' end of aminoacyl-tRNA in A site and acts as acceptor for the nascent polypeptide chain
Erythromycin	Prokaryotic cells	Peptide exit tunnel of 50S subunit	Blocks exit of the growing polypeptide chain from the ribosome; arrests translation
Fusidic acid	Prokaryotic cells	EF-G	Prevents release of EF-G-GDP from the ribosome
Thiostrepton	Prokaryotic cells	Factor binding center of the 50S subunit	Interferes with the association of IF2 and EF-G with factor binding center
Kirromycin		EF-Tu	Prevents the conformational changes associated with GTP hydrolysis and, therefore, EF-Tu release
Ricin and $\alpha$ -Sarcin (protein toxins)	Prokaryotic and eukaryotic cells	Chemically modifies the RNA in the factor binding center of large ribosomal subunit	Prevents activation of translation factor GTPases
Diphtheria Toxin	Eukaryotic cells	Chemically modifies EF-Tu	Inhibits EF-Tu function
Cycloheximide	Eukaryotic cells	Peptidyl transferase center of the 60S subunit	Inhibits peptidyl transferase activity

**Box 14-4 (Continued)**



**BOX 14-4 FIGURE 1 Puromycin terminates translation by mimicking a tRNA in the A site.** Puromycin binds in the A site and participates in peptide bond formation. Once completed, puromycin and any associated polypeptide diffuses out of the ribosome.



		Second letter							
		U	C	A	G				
U	UUU	Phe (F)	UCU		UAU	Tyr (Y)	UGU	Cys (C)	U
	UUC		UCC	Ser (S)	UAC		UGC		C
	UUA	Leu (L)	UCA		UAA	Stop	UGA	Stop	A
	UUG		UCG		UAG	Stop	UGG	Trp (W)	G
C	CUU		CCU	Pro (P)	CAU	His (H)	CGU		U
	CUC	Leu (L)	CCC		CAC		CGC	Arg (R)	C
	CUA		CCA		CAA	Gln (Q)	CGA		A
	CUG		CCG		CAG		CGG		G
A	AUU		ACU		AAU	Asn (N)	AGU	Ser (S)	U
	AUC	Ile (I)	ACC	Thr (T)	AAC		AGC		C
	AUA		ACA		AAA	Lys (K)	AGA	Arg (R)	A
	AUG	Met (M)	ACG		AAG		AGG		G
G	GUU		GCU		GAU	Asp (D)	GGU		U
	GUC	Val (V)	GCC	Ala (A)	GAC		GGC	Gly (G)	C
	GUA		GCA		GAA	Glu (E)	GGA		A
	GUG		GCG		GAG		GGG		G

 = Chain termination codon (stop)

 = Initiation codon

**•Il Codice Genetico è un Codice a Triplette**

**•Il Codice Genetico è Continuo**

**•Il Codice Genetico non è Sovrapposto**

Sequenza  
nucleotidica

A U A C G A G U C

Codice non  
sovrapposto

A U A C G A G U C . . .  
1 2 3

Codice  
sovrapposto

A U A C G A G U C  
1  
U A C  
2  
A C G  
3

- **Il Codice Genetico ha Segnali di Inizio e di Fine**
- **Il Codice Genetico è Degenerato, ma non Ambiguo**

		Second letter							
		U	C	A	G				
U	UUU	Phe (F)	UCU		UAU	Tyr (Y)	UGU	Cys (C)	U
	UUC		UCC	Ser (S)	UAC		UGC		C
	UUA	Leu (L)	UCA		UAA	Stop	UGA	Stop	A
	UUG		UCG		UAG	Stop	UGG	Trp (W)	G
C	CUU		CCU	Pro (P)	CAU	His (H)	CGU		U
	CUC	Leu (L)	CCC		CAC		CGC	Arg (R)	C
	CUA		CCA		CAA	Gln (Q)	CGA		A
	CUG		CCG		CAG		CGG		G
A	AUU		ACU	Thr (T)	AAU	Asn (N)	AGU	Ser (S)	U
	AUC	Ile (I)	ACC		AAC		AGC		C
	AUA		ACA		AAA	Lys (K)	AGA	Arg (R)	A
	AUG	Met (M)	ACG		AAG		AGG		G
G	GUU		GCU	Ala (A)	GAU	Asp (D)	GGU		U
	GUC	Val (V)	GCC		GAC		GGC	Gly (G)	C
	GUA		GCA		GAA	Glu (E)	GGA		A
	GUG		GCG		GAG		GGG		G

 = Chain termination codon (stop)

 = Initiation codon

- **Il Codice Genetico è (quasi) Universale**

- **Il Codice Genetico Presenta il Fenomeno del Vacillamento della Terza Base (Wobbling)**

**TABLE 15-6 Genetic Code of Mammalian Mitochondria\***

		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) <b>UAA stop</b> <b>UAG stop</b>	UGU Cys UGC (GCA) <b>UGA Trp</b> UGG (UCA)	U C A G
	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 G
	A	AUU Ile AUC (GAU) <b>AUA Met</b> AUG (CAU) <sup>‡</sup>	ACU ACC Thr ACA (UGU) ACG	AAU Asn AAC (GUU) AAA Lys AAG (UUU)	AGU Ser AGC (GCU) <b>AGA stop</b> <b>AGG stop</b>	U C A G
	G	GUU GUC Val GUA (UAC) GUG	GCU GCC Ala GCA (UGC) GCG	GAU Asp GAC (GUC) GAA Glu GAG (UUC)	GGU GGC Gly GGA (UCC) GGG	U C A G

- **Il Codice Genetico è (quasi) Universale**

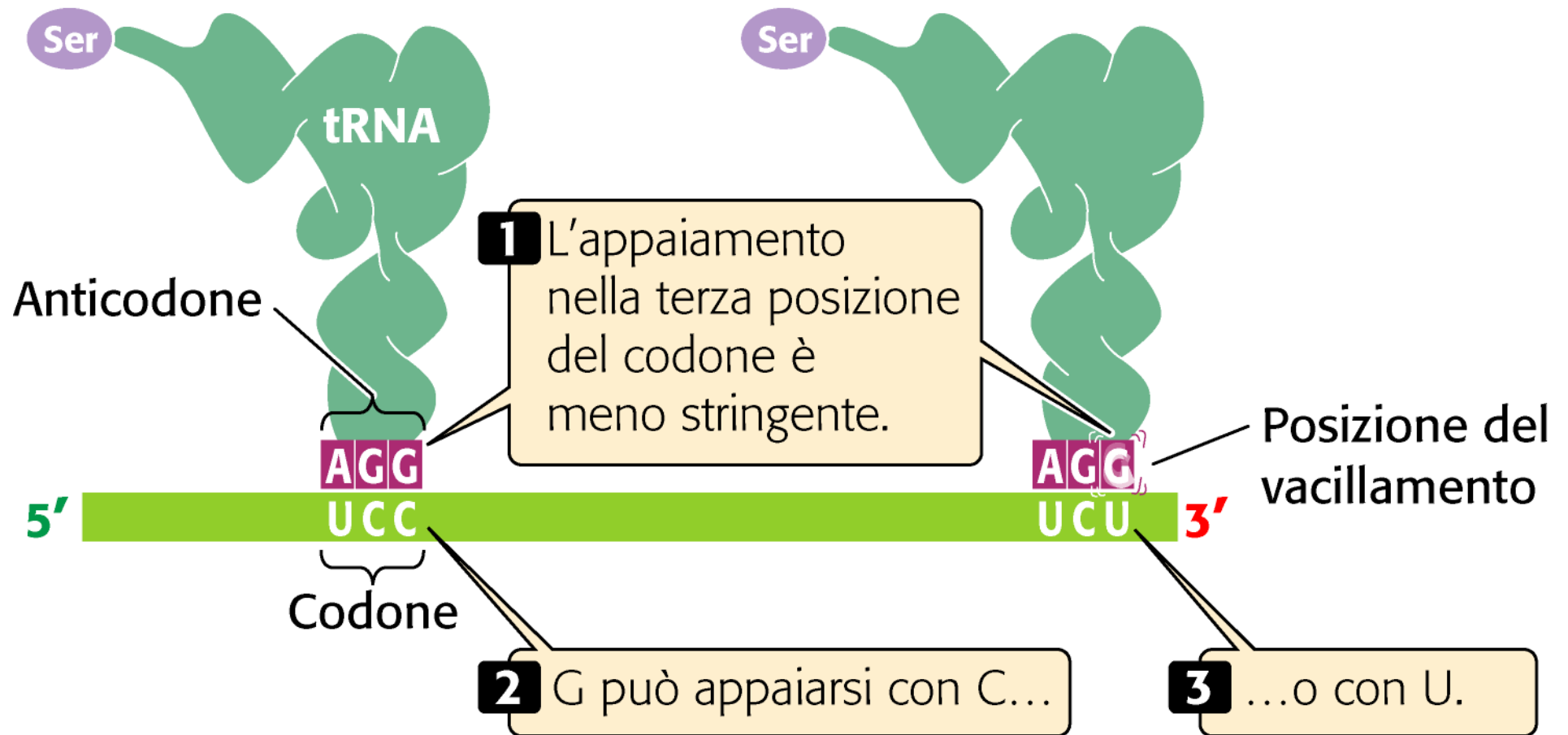
- **Il Codice Genetico Presenta il Fenomeno del Vacillamento della Terza Base (Wobbling)**

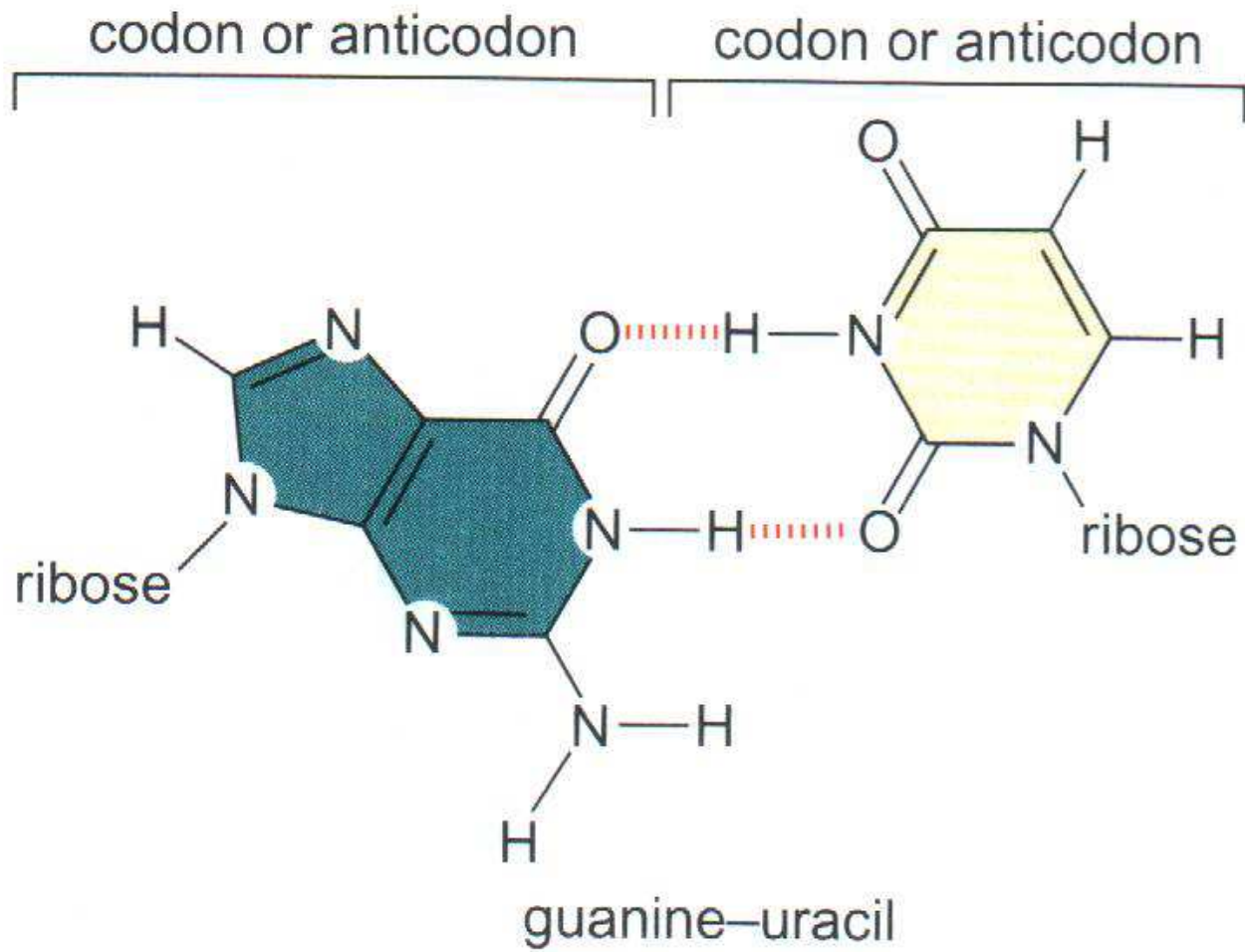


		Second letter							
		U	C	A	G				
U	UUU	Phe (F)	UCU		UAU	Tyr (Y)	UGU	Cys (C)	U
	UUC		UCC	Ser (S)	UAC		UGC		C
	UUA	Leu (L)	UCA		UAA	Stop	UGA	Stop	A
	UUG		UCG		UAG	Stop	UGG	Trp (W)	G
C	CUU		CCU	Pro (P)	CAU	His (H)	CGU		U
	CUC	Leu (L)	CCC		CAC		CGC	Arg (R)	C
	CUA		CCA	Gln (Q)	CAA		CGA		A
	CUG		CCG		CAG		CGG		G
A	AUU		ACU	Thr (T)	AAU	Asn (N)	AGU	Ser (S)	U
	AUC	Ile (I)	ACC		AAC		AGC		C
	AUA		ACA	Lys (K)	AAA		AGA	Arg (R)	A
	AUG	Met (M)	ACG		AAG		AGG		G
G	GUU		GCU	Ala (A)	GAU	Asp (D)	GGU		U
	GUC	Val (V)	GCC		GAC		GGC	Gly (G)	C
	GUA		GCA	Glu (E)	GAA		GGA		A
	GUG		GCG		GAG		GGG		G

 = Chain termination codon (stop)

 = Initiation codon

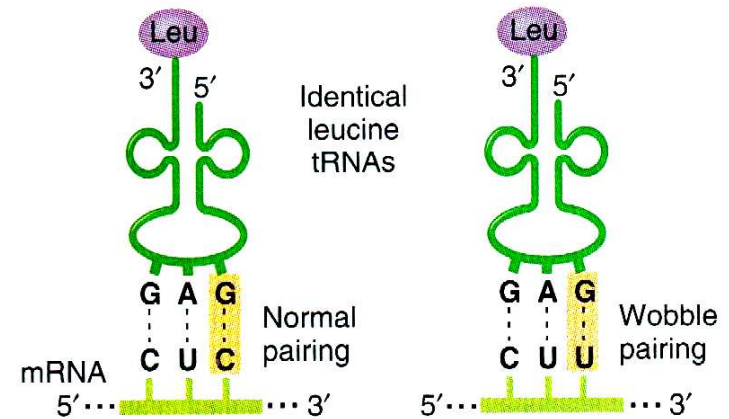




**Table 12.1 Wobble in the Genetic Code**

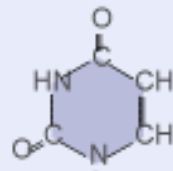
Nucleotide at 5' End of Anticodon		Nucleotide at 3' End of Codon
G	can pair with	U or C
C	can pair with	G
A	can pair with	U
U	can pair with	A or G
I (inosine)	can pair with	A, U, or C

**Example of base-pairing wobble.** Two different leucine codons (CUC, CUU) can be read by the same leucine tRNA molecule, contrary to regular base-pairing rules.

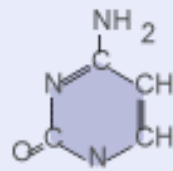


Base modifications in tRNA vary in complexity

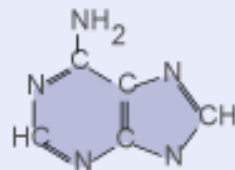
Normal bases



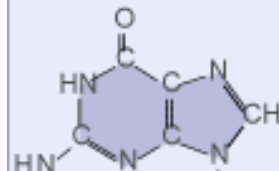
Uridine



Cytidine

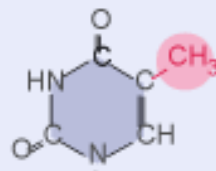


Adenosine

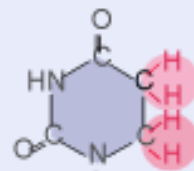


Guanosine

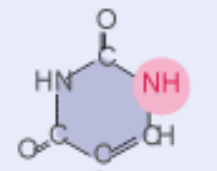
Modified bases



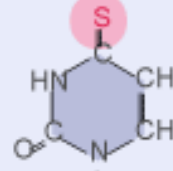
Ribothymidine (T)



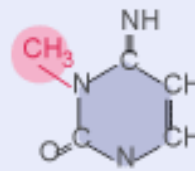
Dihydrouridine (D)



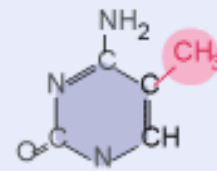
Pseudouridine (ψ)



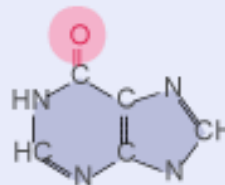
4-thiouridine



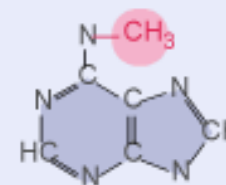
3-methylcytosine



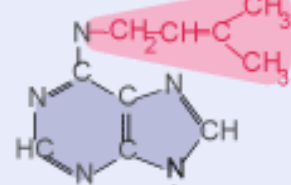
5-methylcytosine



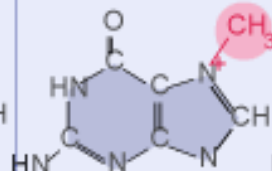
Inosine



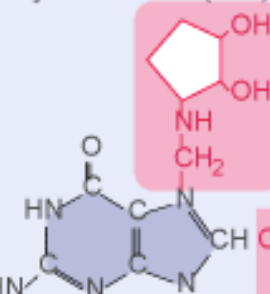
N<sup>6</sup> methyladenosine (m<sup>6</sup>A)



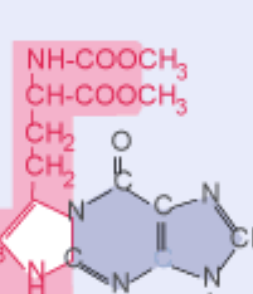
N<sup>6</sup> isopentenyladenosine



7-methylguanosine

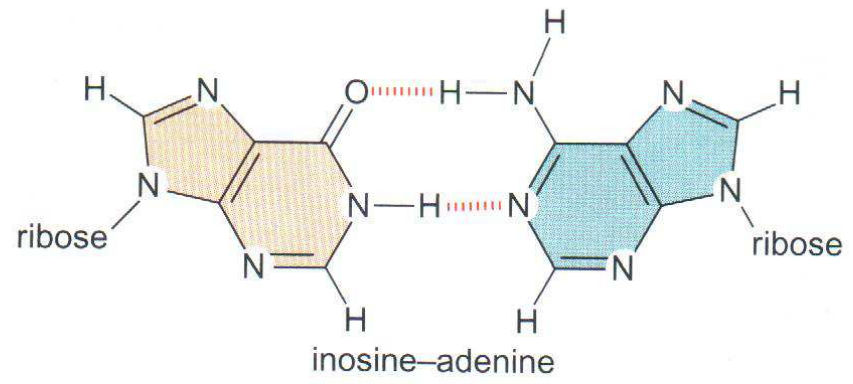
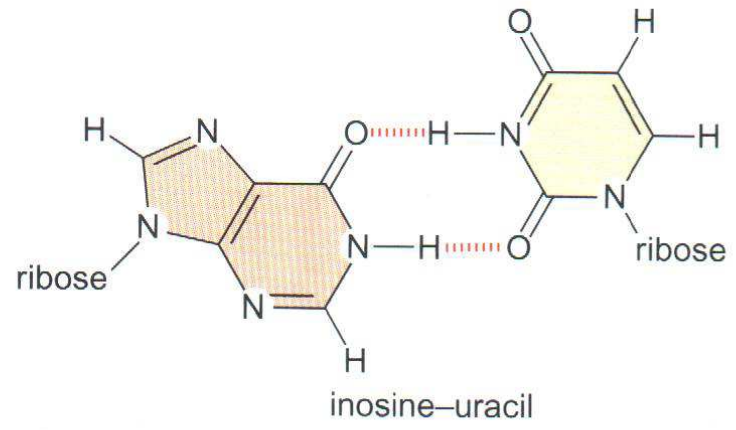
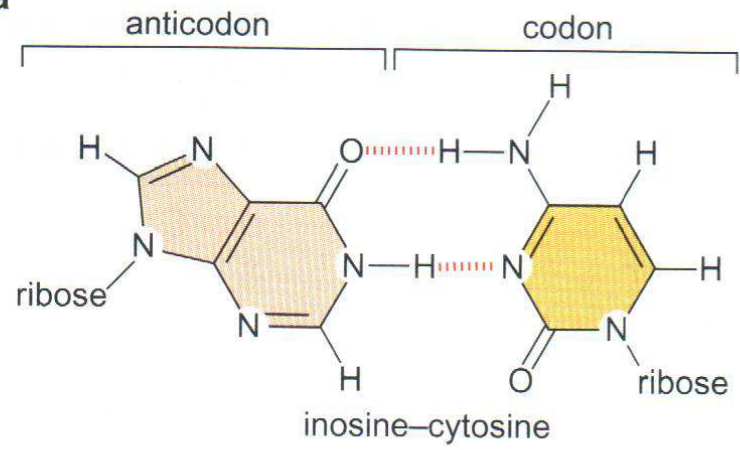


Queuosine (Q)



Wyosine (Y)

**a**

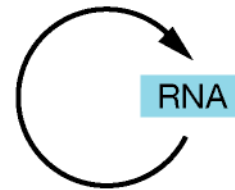


		Second letter							
		U	C	A	G				
U	UUU	Phe (F)	UCU		UAU	Tyr (Y)	UGU	Cys (C)	U
	UUC		UCC	Ser (S)	UAC		UGC		C
	UUA	Leu (L)	UCA		UAA	Stop	UGA	Stop	A
	UUG		UCG		UAG	Stop	UGG	Trp (W)	G
C	CUU		CCU	Pro (P)	CAU	His (H)	CGU		U
	CUC	Leu (L)	CCC		CAC		CGC	Arg (R)	C
	CUA		CCA	Gln (Q)	CAA		CGA		A
	CUG		CCG		CAG		CGG		G
A	AUU		ACU	Thr (T)	AAU	Asn (N)	AGU	Ser (S)	U
	AUC	Ile (I)	ACC		AAC		AGC		C
	AUA		ACA	Lys (K)	AAA		AGA	Arg (R)	A
	AUG	Met (M)	ACG		AAG		AGG		G
G	GUU		GCU	Ala (A)	GAU	Asp (D)	GGU		U
	GUC	Val (V)	GCC		GAC		GGC	Gly (G)	C
	GUA		GCA	Glu (E)	GAA		GGA		A
	GUG		GCG		GAG		GGG		G

 = Chain termination codon (stop)

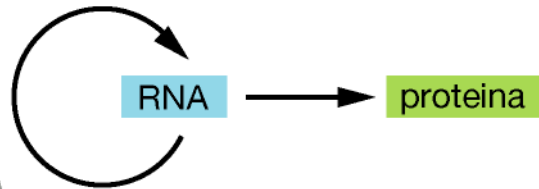
 = Initiation codon

sistemi basati sull'RNA



↓ EVOLUZIONE DI RNA  
CAPACI DI DIRIGERE  
LA SINTESI PROTEICA

sistemi basati su RNA e proteine



↓ EVOLUZIONE DI ENZIMI NUOVI  
CHE FORMANO IL DNA  
E LO COPIANO IN RNA

cellule attuali





**Table 7–3 Biochemical Reactions that Can Be Catalyzed by Ribozymes**

ACTIVITY

RNA cleavage, RNA ligation

DNA cleavage

Peptide bond formation in protein synthesis

DNA ligation

RNA splicing

RNA polymerization

RNA phosphorylation

RNA aminoacylation

RNA alkylation

Isomerization (C–C bond rotation)

RIBOZYMES

self-splicing RNAs

self-splicing RNAs

ribosomal RNA

*in vitro* selected RNA

RNAs of the spliceosome (?),  
self-splicing RNAs

*in vitro* selected RNA

*in vitro* selected RNA

*in vitro* selected RNA

*in vitro* selected RNA

*in vitro* selected RNA