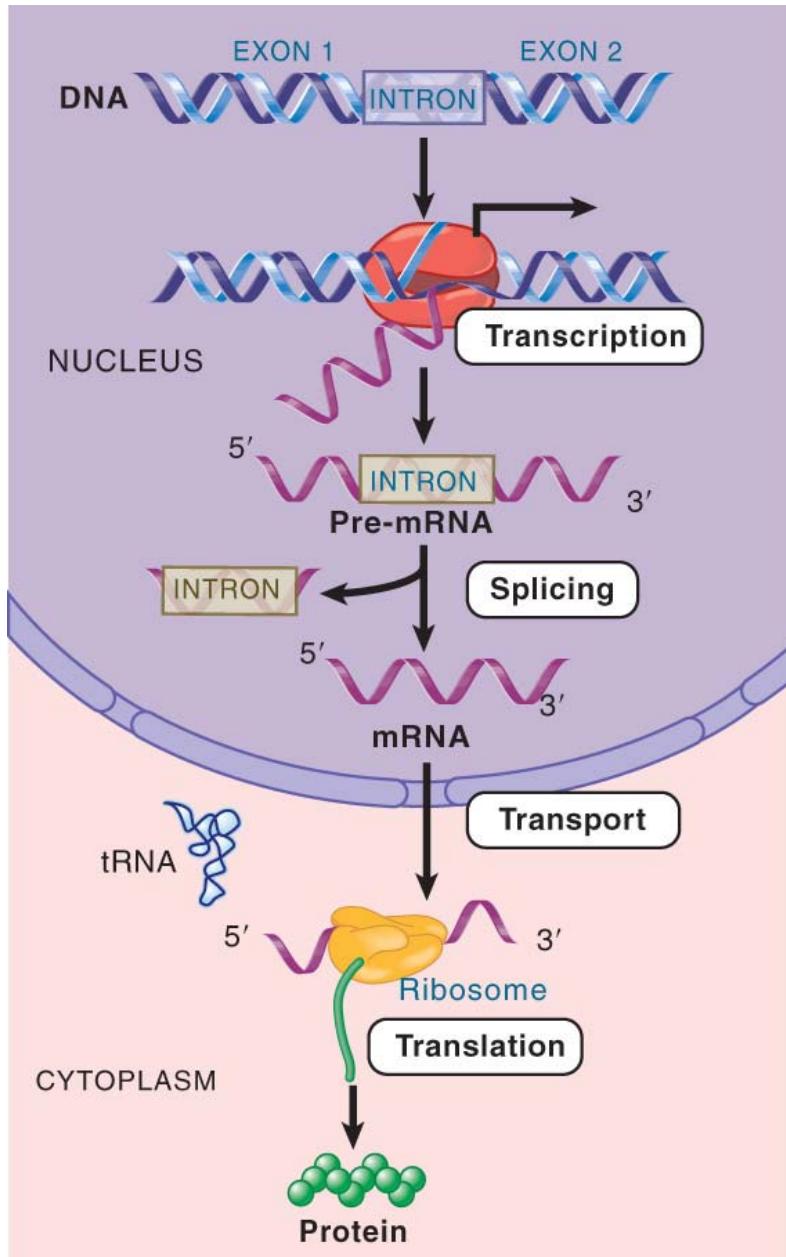


# **Protein Metabolism**

# RNA → Protein (translation)

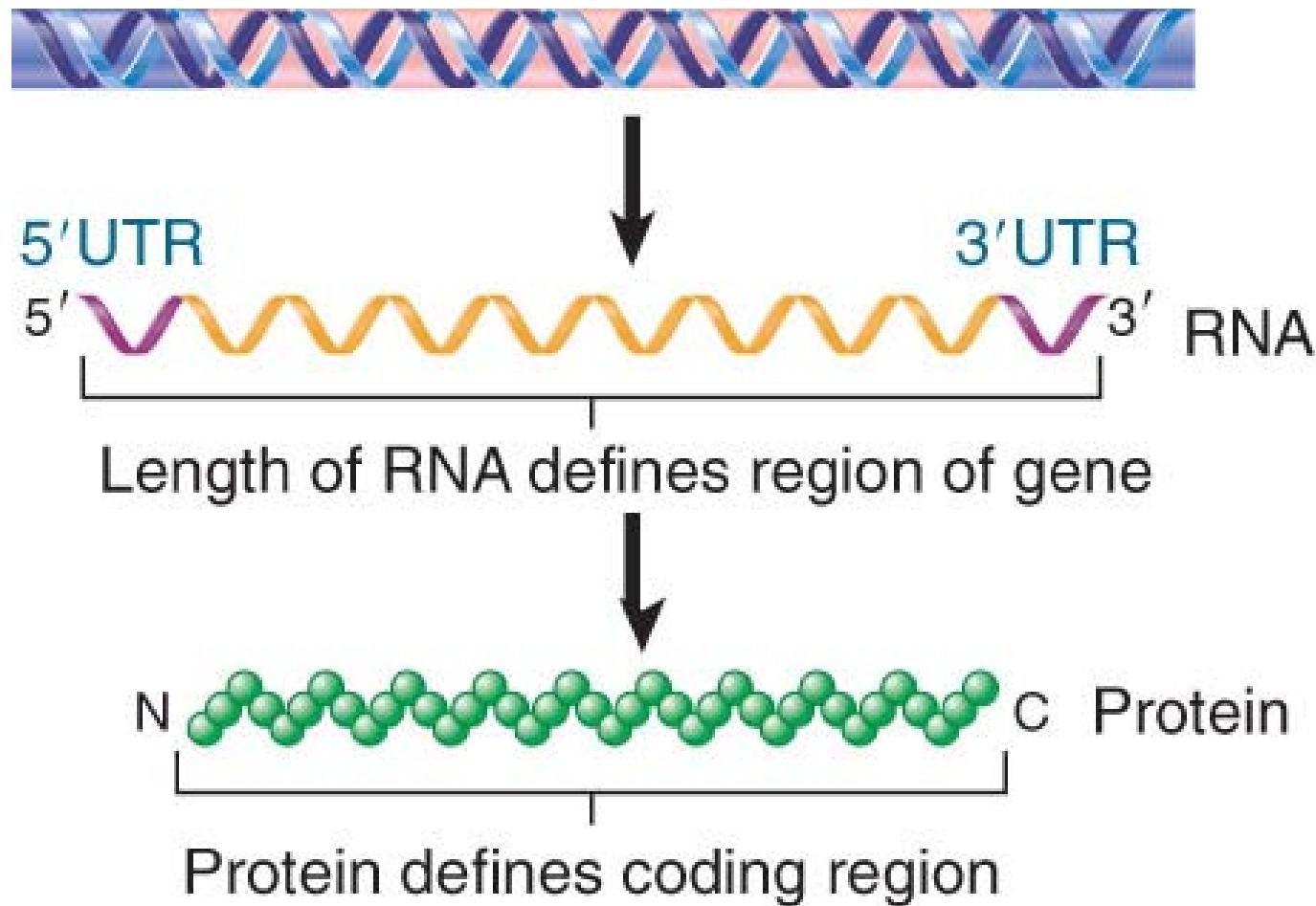


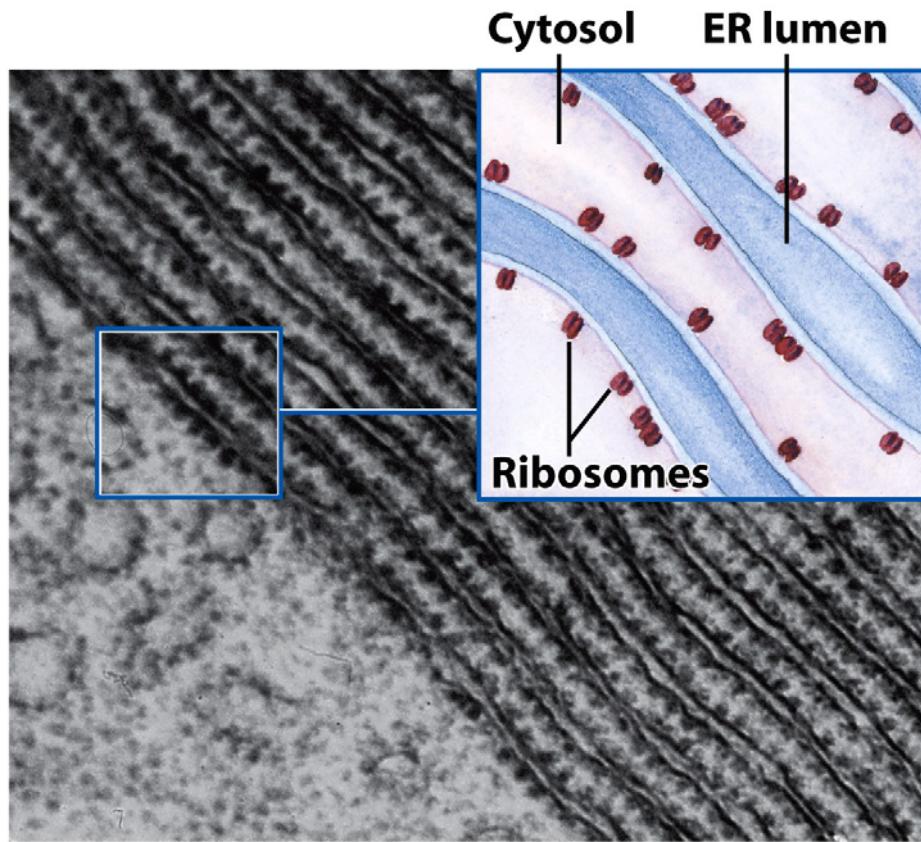
- In eukaryotes, a gene may contain internal regions, or **introns**, that are not represented in protein.
- Introns are removed from the pre-mRNA transcript by **RNA splicing** to give an mRNA.

Three major kinds of RNA:

- Messenger RNA (mRNA)
  - a **template** for translation
- Transfer RNA (tRNA)
  - to **read** the information of mRNA
- Ribosomal RNA (rRNA)
  - a **machinery** for synthesizing protein

Each mRNA consists of a untranslated 5' region (**5'-UTR**), a **coding region**, and an untranslated **3'-UTR**.





- **Ribosome** – A large assembly of RNA and proteins that synthesizes proteins under direction from an mRNA template.
- **rRNAs** – A major component of the ribosome.
- **Ribonucleoproteins**
- **Ribosomes** attach to the outer membrane (cytosolic) face of the endoplasmic reticulum (ER)

## Genetic code

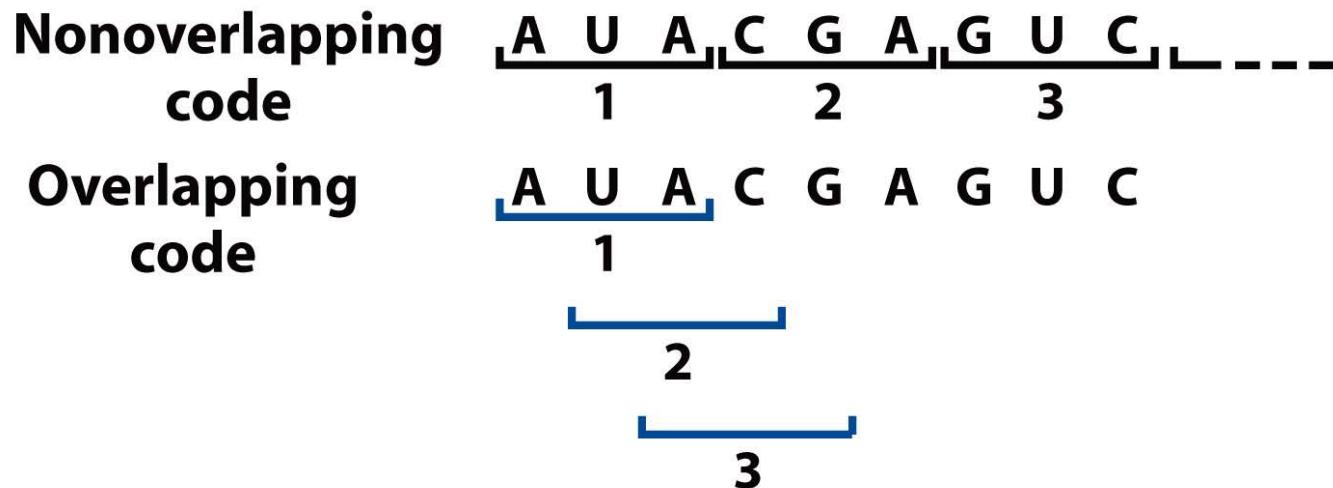
**4-letter** language of nucleic acids (ATCG/AUCG)



**20-letter** language of proteins (20 types of amino acids)

$4^2 \rightarrow 16 < 20$  (ATCG/AUCG)

$4^3 \rightarrow 64 > 20$  (ATCG/AUCG)



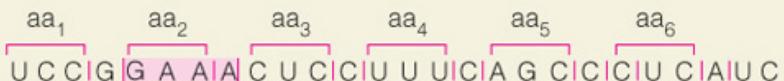
**Overlapping or Non-overlapping**

**FIGURE 28.3**

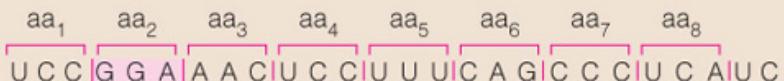
Three conceivable kinds of genetic codes. Early research on the nature of the code quickly showed that a nonoverlapping, unpunctuated code (c) fit all experimental observations.



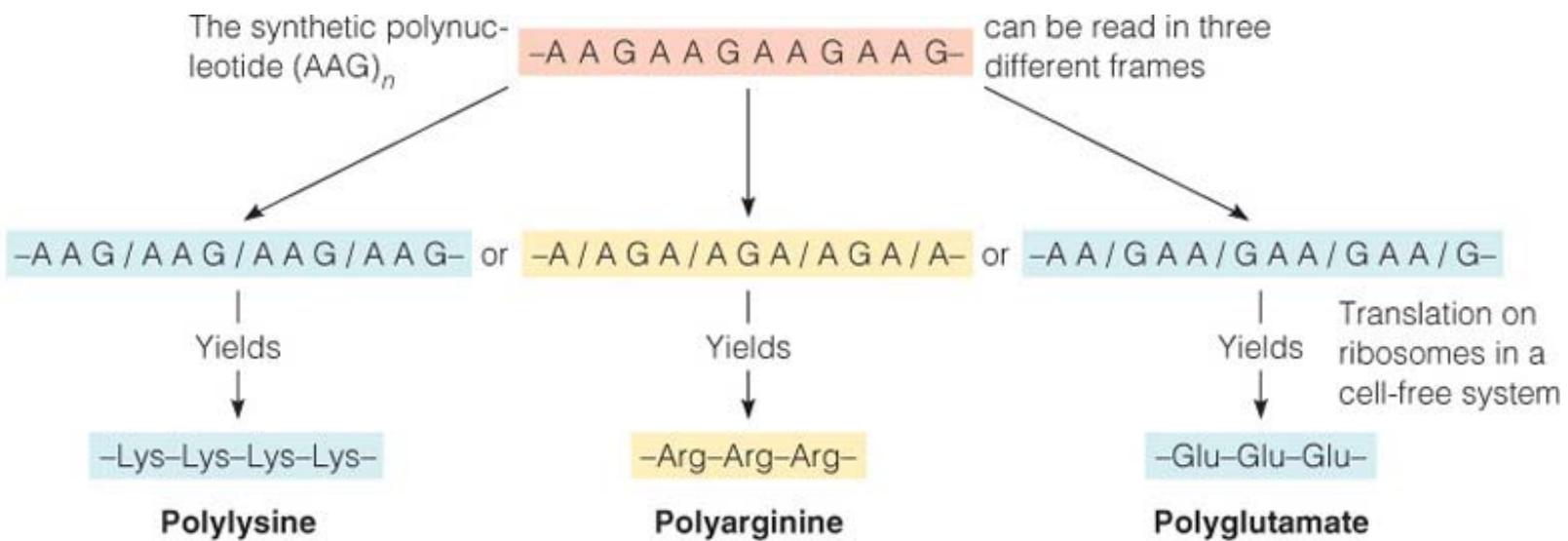
**(a)** Overlapping code. There will be statistical regularities between adjacent amino acid residues. Point mutations (magenta) will be able to change two amino acid residues.



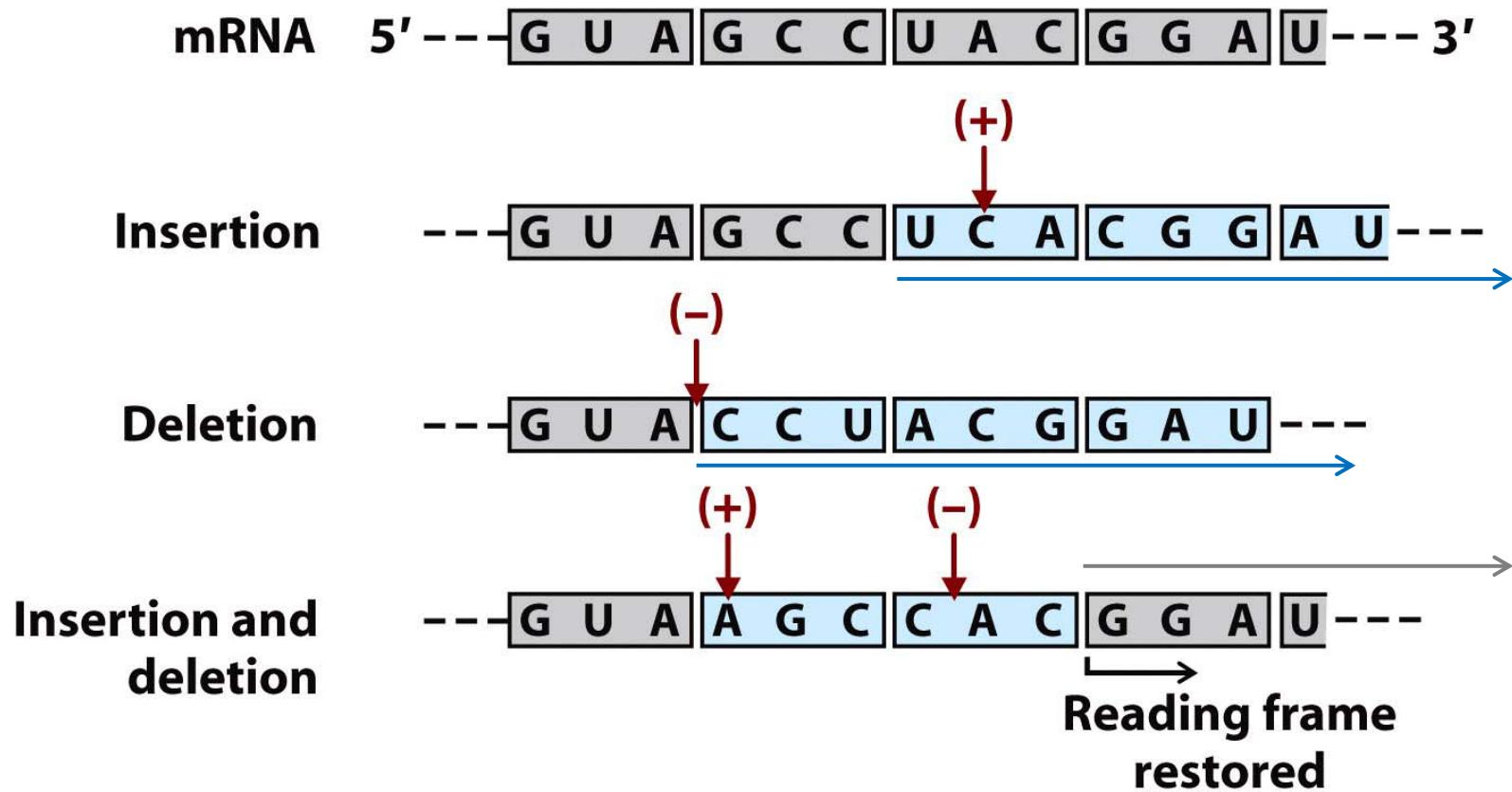
**(b)** Punctuated code. Deletions of four nucleotides (or multiples thereof) will restore the reading frame.



**(c)** Unpunctuated code. Deletions of three nucleotides (or multiples thereof) will restore the reading frame. This is the actual form of the code.



The genetic code used in is now known to be **nonoverlapping & triplet**.



# Three reading frames in the genetic code

Reading frame 1    5'---[U U C] [U C G] [G A C] [C U G] [G A G] [A U U] [C A C] [A G U]---3'

Reading frame 2    ---[U] [U C U] [C G G] [A C C] [U G G] [A G A] [U U C] [A C A G U]---

Reading frame 3    ---[U U] [C U C] [G G A] [C C U] [G G A] [G A U] [U U C] [A C A G U]---

## **Effect of a termination codon on reading frames**

**Reading frame 1** 5' --- **G** U A A **G** U A A **A** **G** U A A **G** U A A **A** **G** U A A A **G** U A A --- 3'

**Reading frame 2** --- **G** **U** A A **G** U A A **A** **G** U A A **A** **G** U A A **A** **G** U A A ---

**Reading frame 3** --- **G** **U** **A** A **G** **U** A A **G** U A A **A** **G** U A A **A** **G** U A A ---

↑

## **Startpoint or termination**

**4<sup>3</sup>** → 64 codons > 20 amino acids (start signal; termination signal)

**First letter of codon (5' end)**

**Second letter  
of codon**

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

- The codons are written in the  $5' \rightarrow 3'$ .
- **AUG** is the initiation codon (Met).
- **UAA, UAG, and UGA** are the termination codons (stop codons).
- The **first two bases** of each codon play the role in specifying an amino acid.
- Met and Trp have one codon.

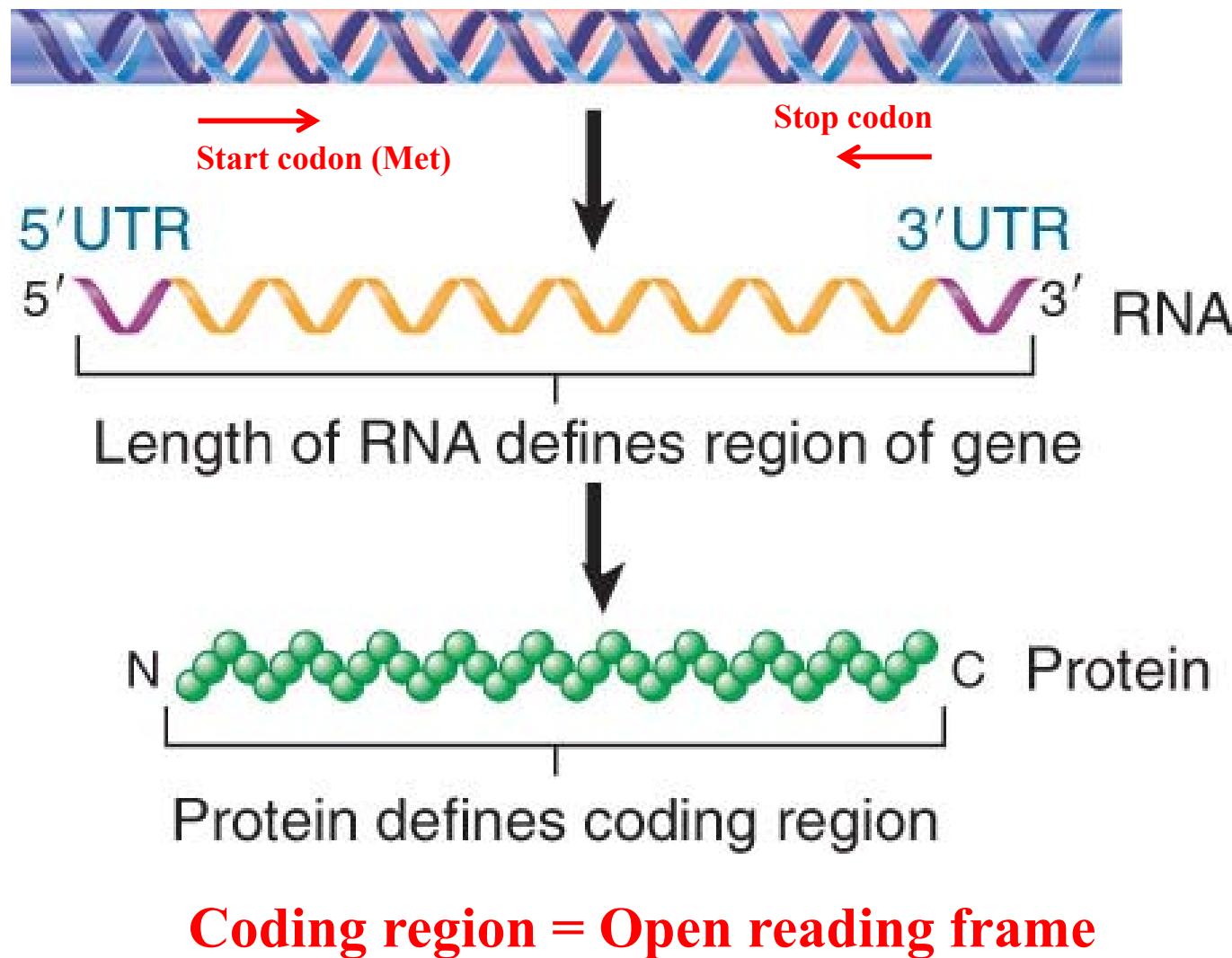
Amino acid	Number of codons	Amino acid	Number of codons
Met	1	Tyr	2
Trp	1	Ile	3
Asn	2	Ala	4
Asp	2	Gly	4
Cys	2	Pro	4
Gln	2	Thr	4
Glu	2	Val	4
His	2	Arg	6
Lys	2	Leu	6
Phe	2	Ser	6

**TABLE 28.1** Modifications of the genetic code

Codon	Usual Use	Alternate Use	Where Alternate Use Occurs
AGA	Arg	Stop, Ser	Some animal mitochondria, some protozoans
AGG			
AUA	Ile	Met	Mitochondria
CGG	Arg	Trp	Plant mitochondria
CUU	Leu	Thr	Yeast mitochondria
CUC			
CUA			
CUG			
AUU	Ile	Start ( <i>N</i> -fMet)	Some prokaryotes <sup>a</sup>
GUG	Val		
UUG	Leu		
UAA	Stop	Glu	Some protozoans
UAG	Stop	Pyrrolysine Glu	Various archaea Some protozoans
UGA	Stop	Trp Selenocysteine Selenocysteine and Cys	Mitochondria, mycoplasmas Widespread <sup>a</sup> <i>Euplotes</i>

<sup>a</sup>Depends on context of message, other factors.

Each mRNA consists of a untranslated 5' region (**5'-UTR**), a **coding region (start codon to stop codon)**, and an untranslated **3'-UTR**.



# Pairing relationship of codon and anticodon

Alanine:

GCU, GCC, GCA, and GCG

CGT, CGG, CGT, and CGC

64 codons → 64 tRNAs

Alanine:

GCU, GCC, GCA, and GCG

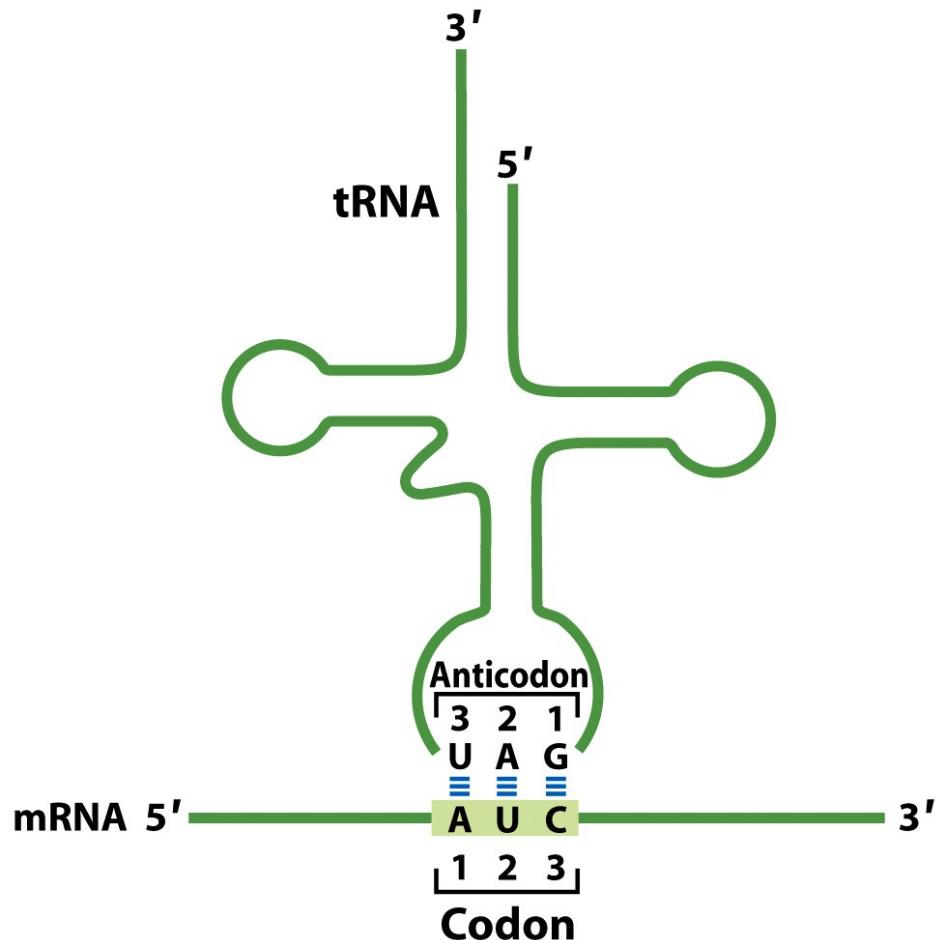
CGI, CGI, CGI, and CGC

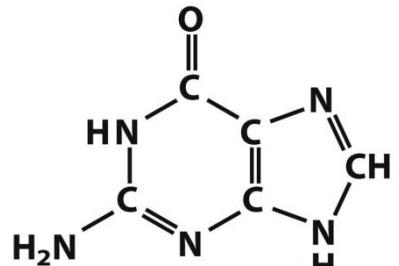
I: Inosinate == Guanosine

I complementary to A, C, and U

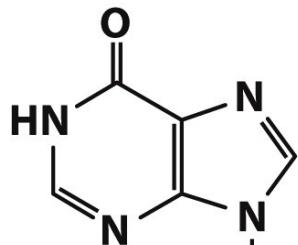
64 codons → 32 tRNAs

	3	2	1		3	2	1		3	2	1	
Anticodon	(3')	G-C-I	G-C-I	(5')	G-C-I	G-C-I	(5')	(3')	U-A-G	U-A-G	U-A-G	(5')
Codon	(5')	C-G-A	C-G-U		C-G-C	C-G-C		(3')	A-U-C	A-U-C	A-U-C	

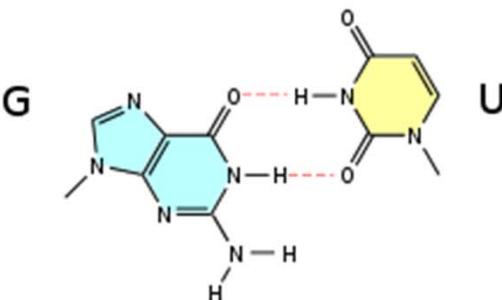
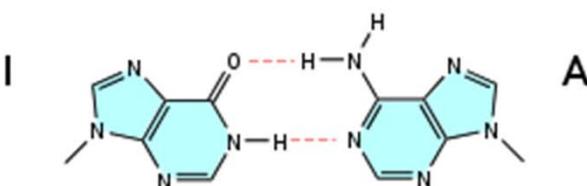
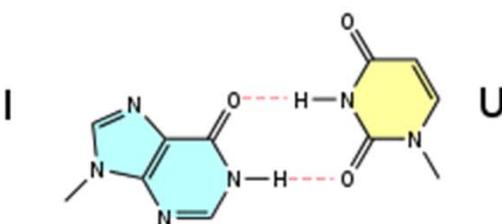
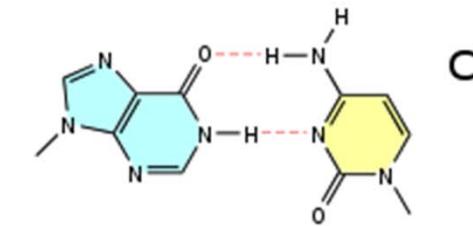




**Guanine**



**Inosine**



**TABLE 27–4** How the Wobble Base of the Anticodon Determines the Number of Codons a tRNA Can Recognize

**1. One codon recognized:**

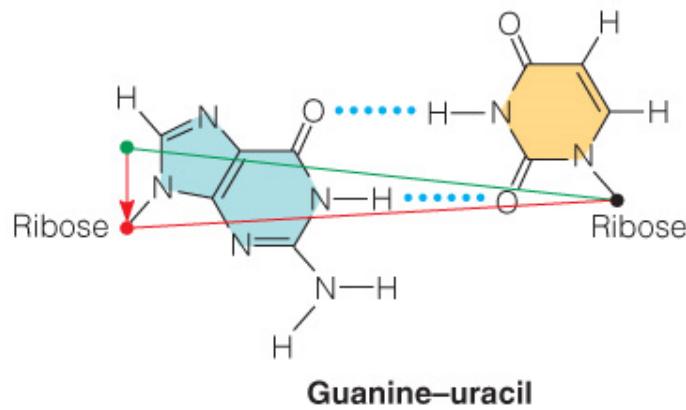
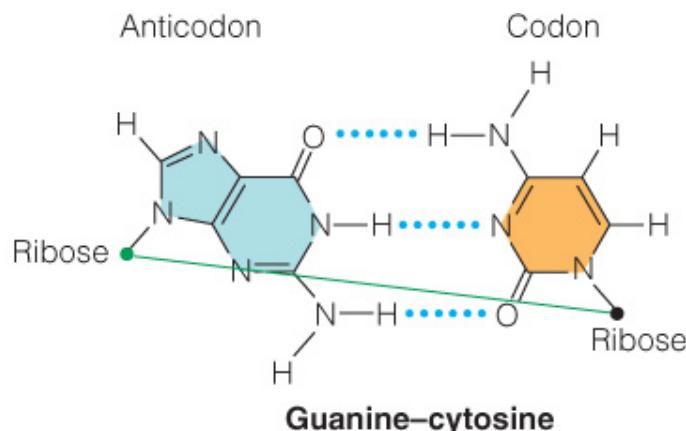
Anticodon	(3') X - Y - <b>C</b> (5')	(3') X - Y - <b>A</b> (5')
Codon	(5') X' - Y' - <b>G</b> (3')	(5') X' - Y' - <b>U</b> (3')

**2. Two codons recognized:**

Anticodon	(3') X - Y - <b>U</b> (5')	(3') X - Y - <b>G</b> (5')
Codon	(5') X' - Y' - <b>A</b> (3')	(5') X' - Y' - <b>C</b> (3')

**3. Three codons recognized:**

Anticodon	(3') X - Y - <b>I</b> (5')
Codon	(5') X' - Y' - <b>A</b> (3')



**FIGURE 28.7**

**The wobble hypothesis.** As an example, we show how the anticodon base G can pair with either C or U in a codon. Movement (“wobble”) of the base in the 5' anticodon position is necessary for this capability (see arrow).

**TABLE 28.2** Base-pairing capabilities in wobble pairs

Base at 5' Position in Anticodon		Base at 3' Position in Codon
G	pairs with	C or U
C	pairs with	G
A	pairs with	U
U	pairs with	A or G
I	pairs with	A, U, or C

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# Protein synthesis

## ■ Three major stages:

Initiation

Elongation

Termination

## ■ Two additional stages:

Activation of precursor

Postsynthetic processing

TABLE 27–5 Components Required for the Five Major Stages of Protein Synthesis in *E. coli*

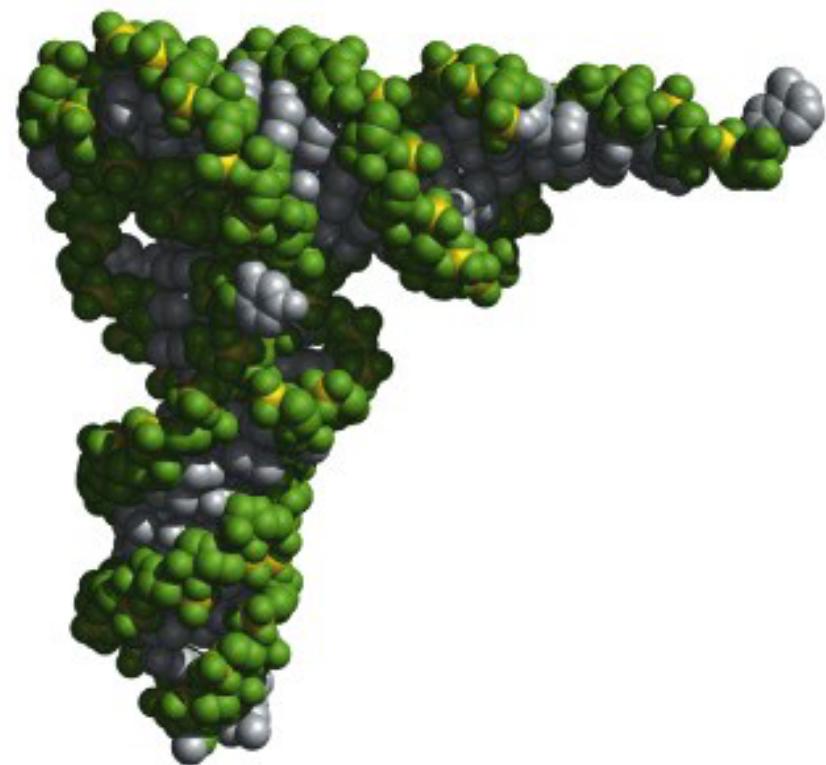
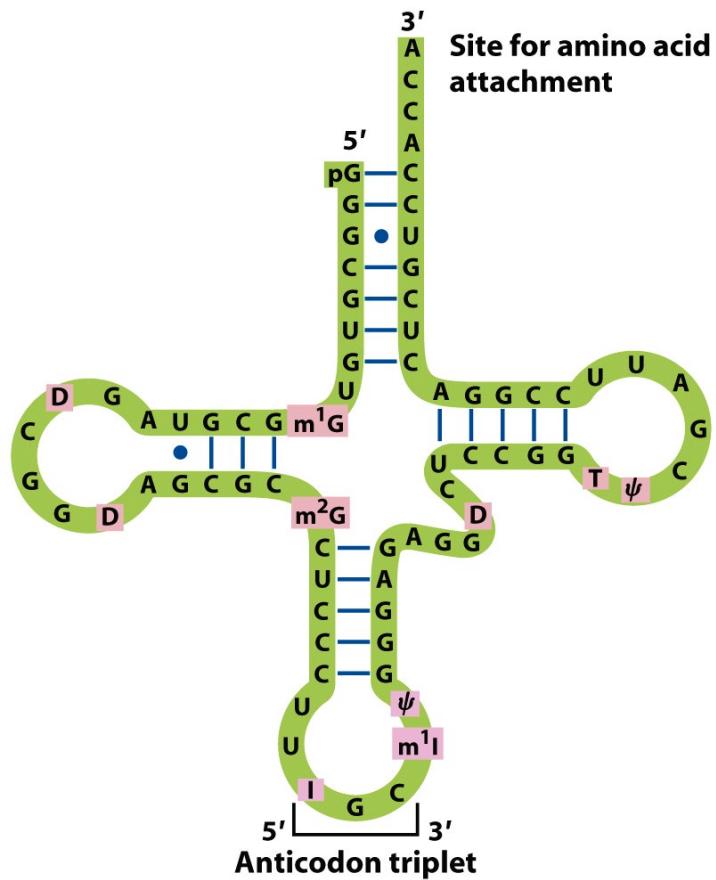
Stage	Essential components
1. Activation of amino acids	20 amino acids 20 aminoacyl-tRNA synthetases 32 or more tRNAs ATP $Mg^{2+}$
2. Initiation	mRNA <i>N</i> -Formylmethionyl-tRNA <sup>fMet</sup> Initiation codon in mRNA (AUG) 30S ribosomal subunit 50S ribosomal subunit Initiation factors (IF-1, IF-2, IF-3) GTP $Mg^{2+}$
3. Elongation	Functional 70S ribosome (initiation complex) Aminoacyl-tRNAs specified by codons Elongation factors (EF-Tu, EF-Ts, EF-G) GTP $Mg^{2+}$
4. Termination and ribosome recycling	Termination codon in mRNA Release factors (RF-1, RF-2, RF-3, RRF) EF-G IF-3
5. Folding and posttranslational processing	Specific enzymes, cofactors, and other components for removal of initiating residues and signal sequences, additional proteolytic processing, modification of terminal residues, and attachment of acetyl, phosphoryl, methyl, carboxyl, carbohydrate, or prosthetic groups

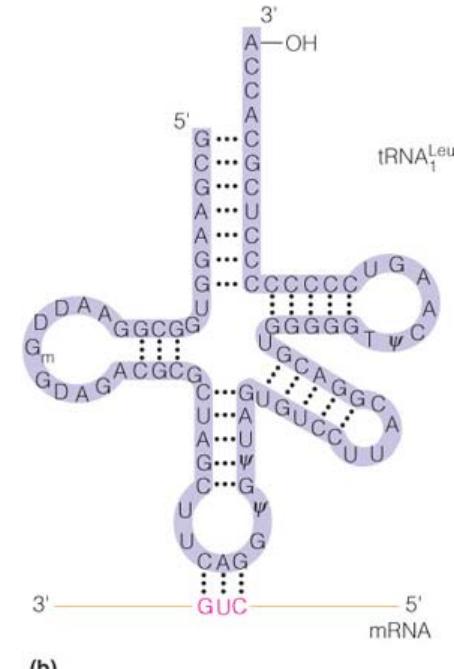
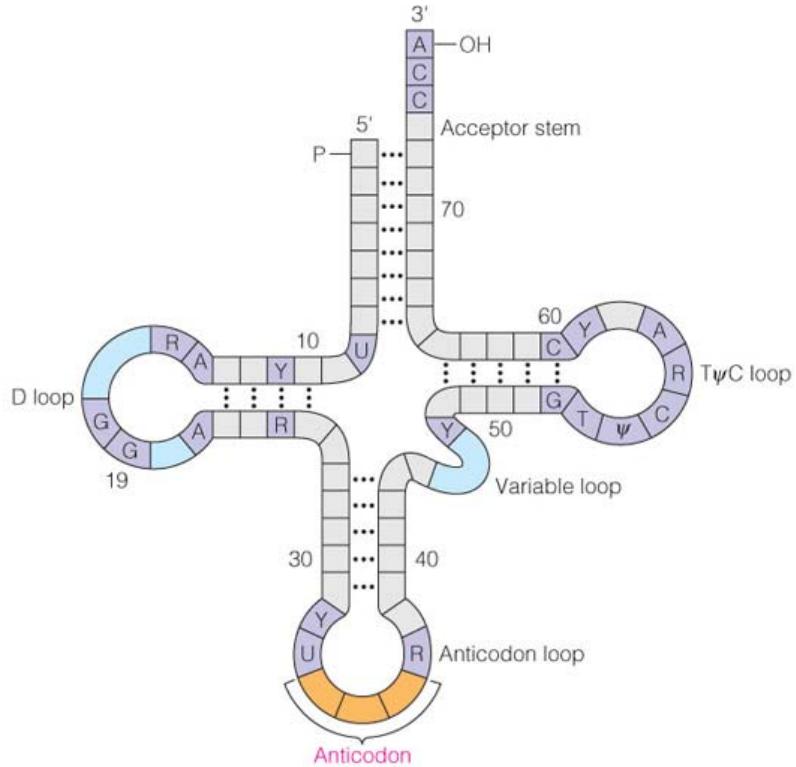
TABLE 27–6 RNA and Protein Components of the *E. coli* Ribosome

Subunit	Number of different proteins	Total number of proteins	Protein designations	Number and type of rRNAs
30S	21	21	S1–S21	1 (16S rRNA)
50S	33	36	L1–L36*	2 (5S and 23S rRNAs)

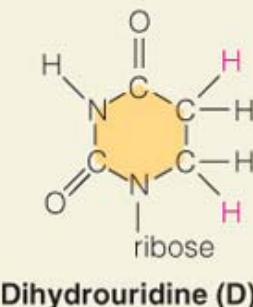
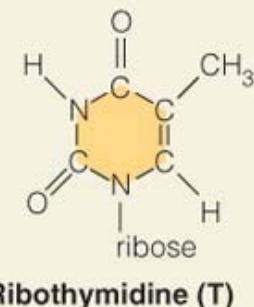
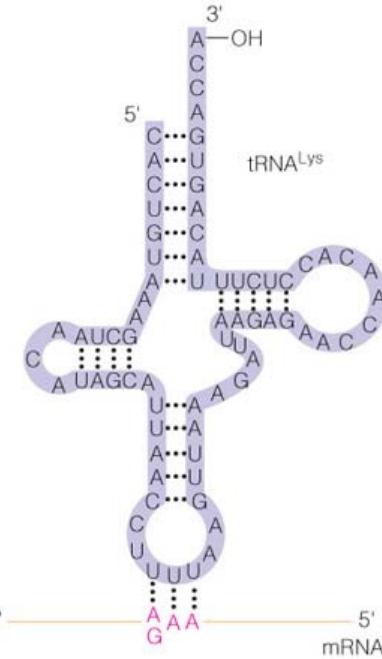
# tRNA

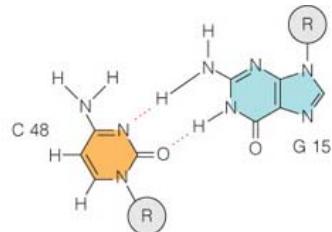
- A single strand of RNA
- 73 to 93 nucleotide residues
- Folding to 3-D structure
- > 32 tRNAs for translation



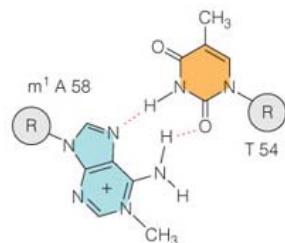


(b)

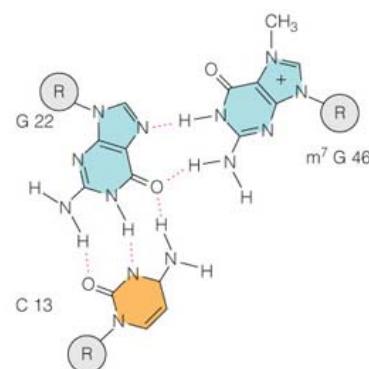




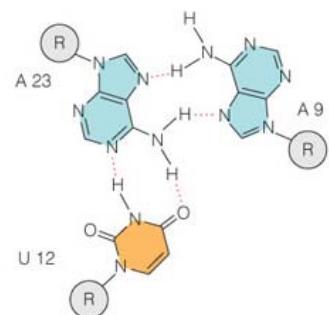
(a)



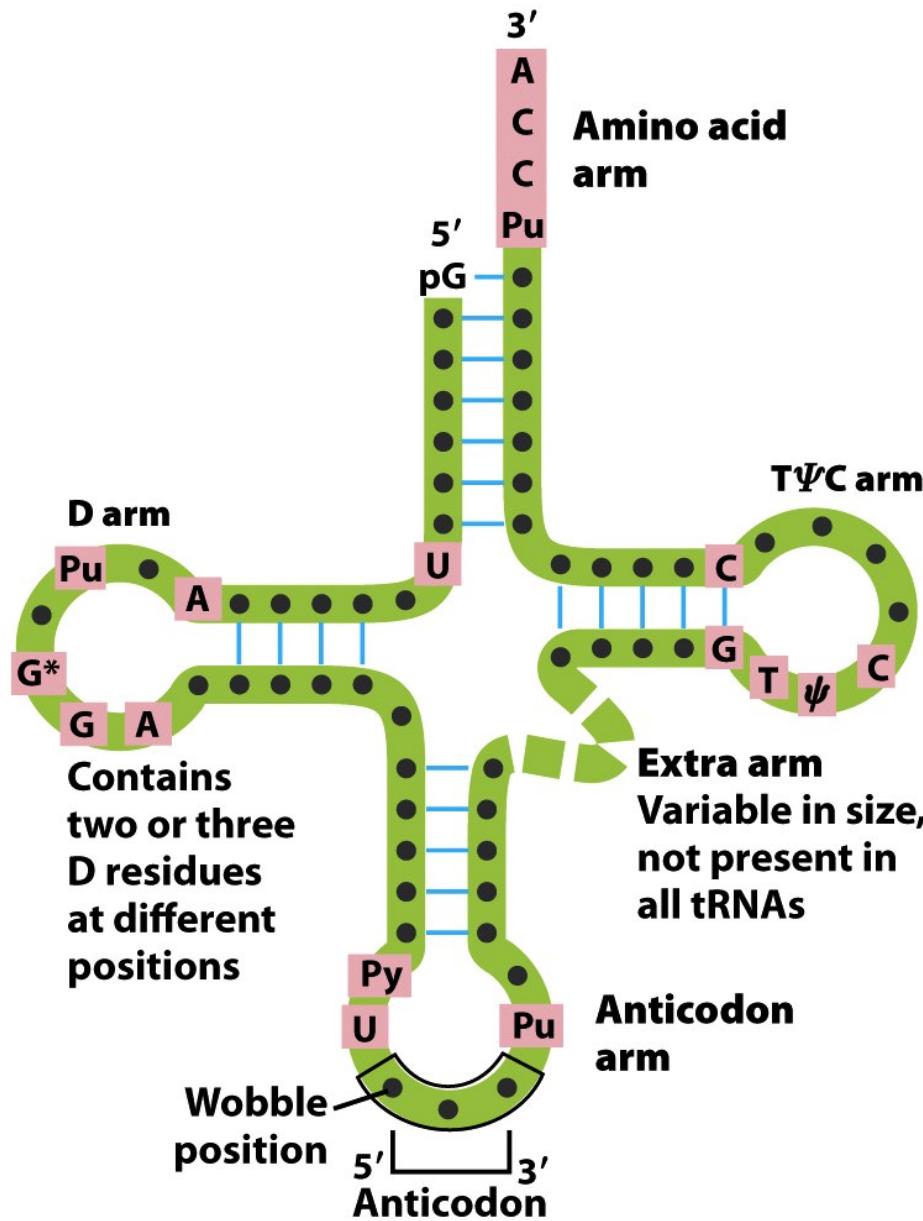
(b)



(c)



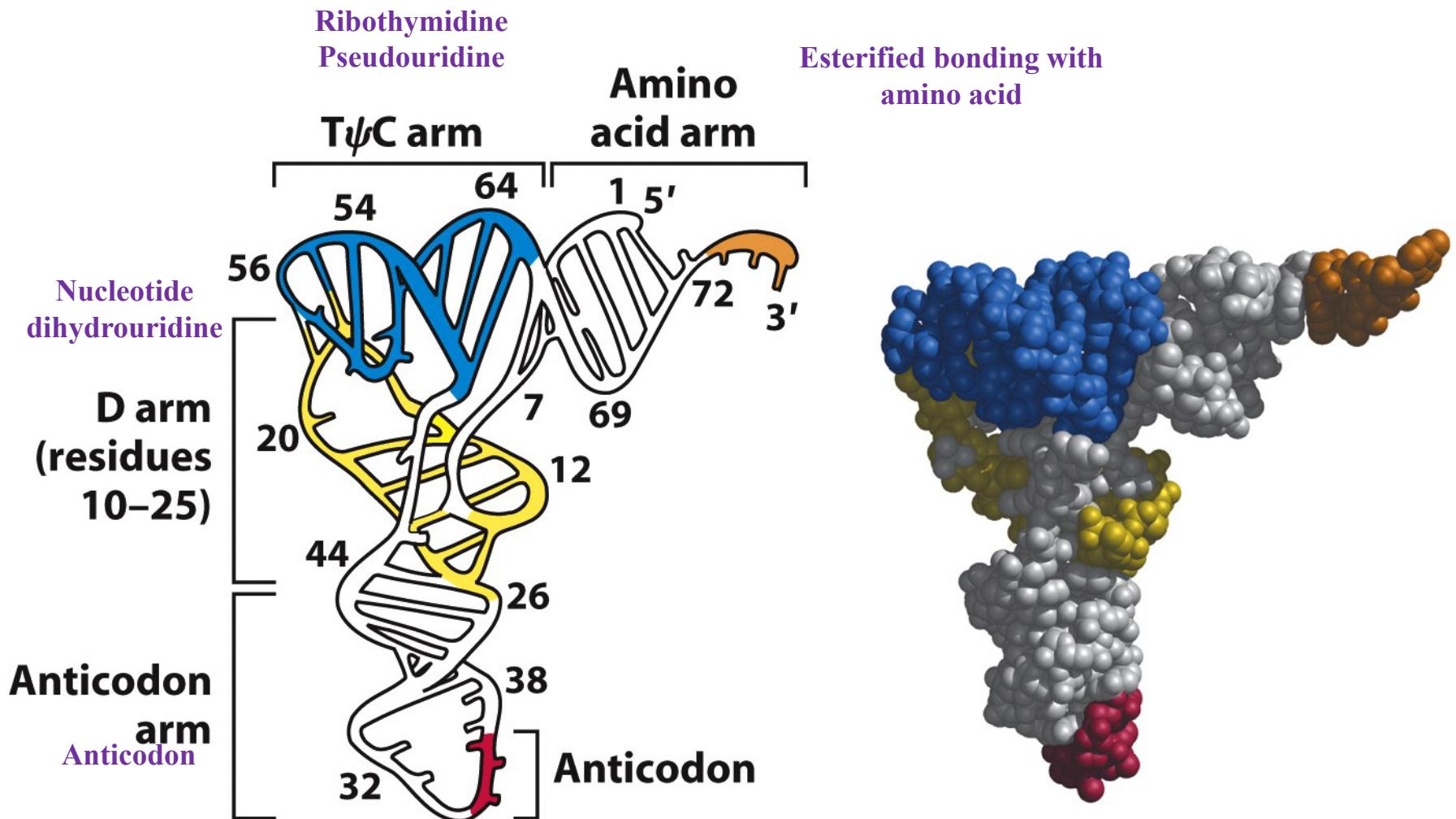
(d)



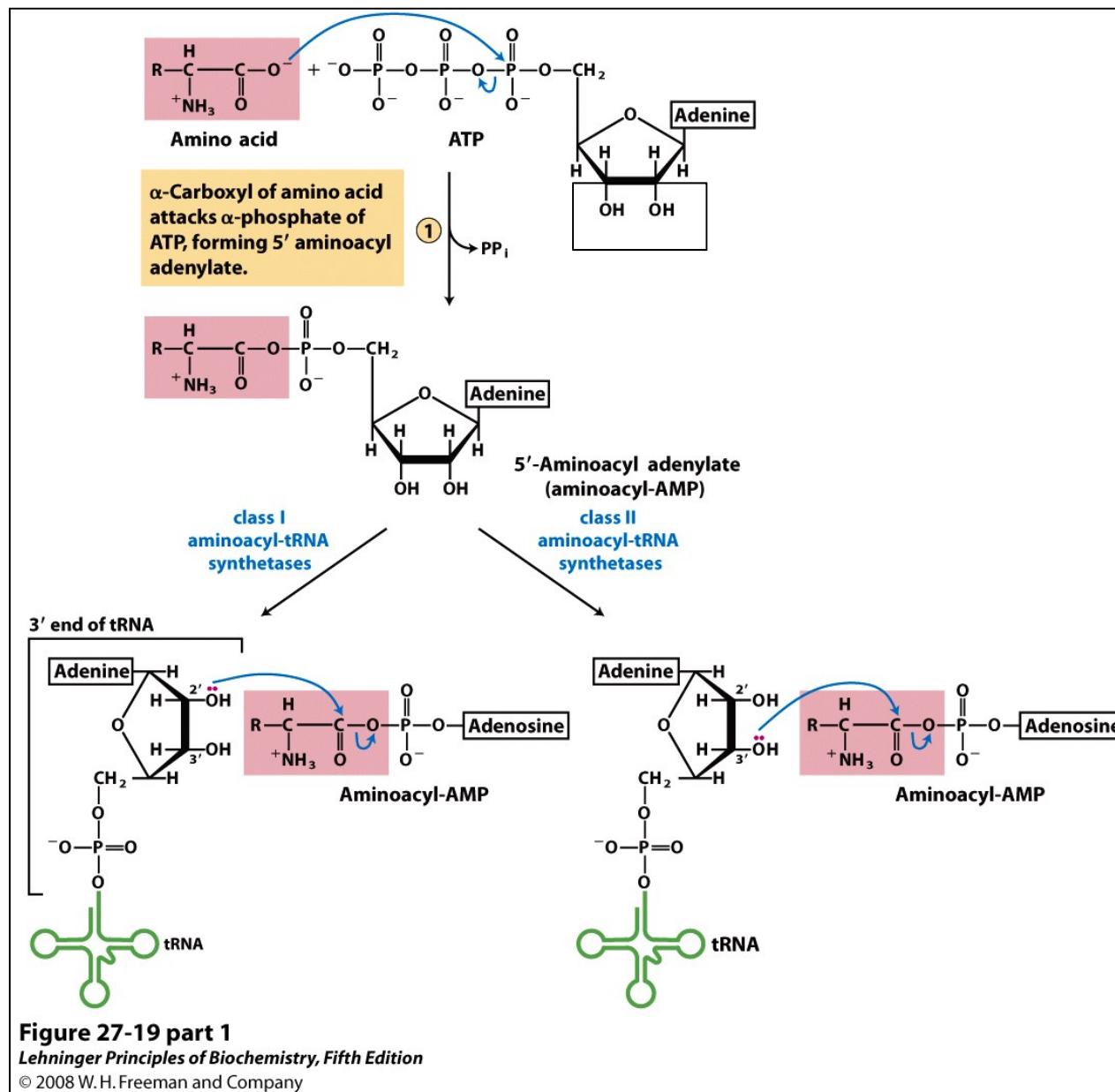
## Yeast alanine tRNA

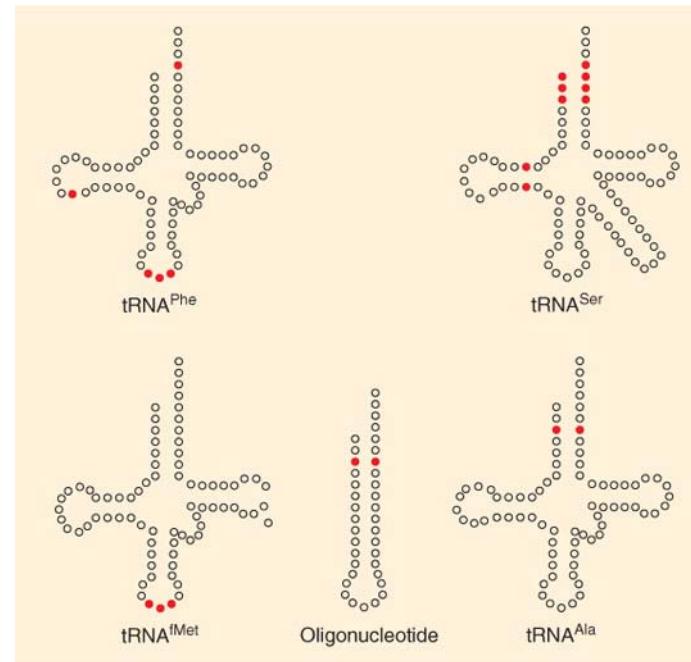
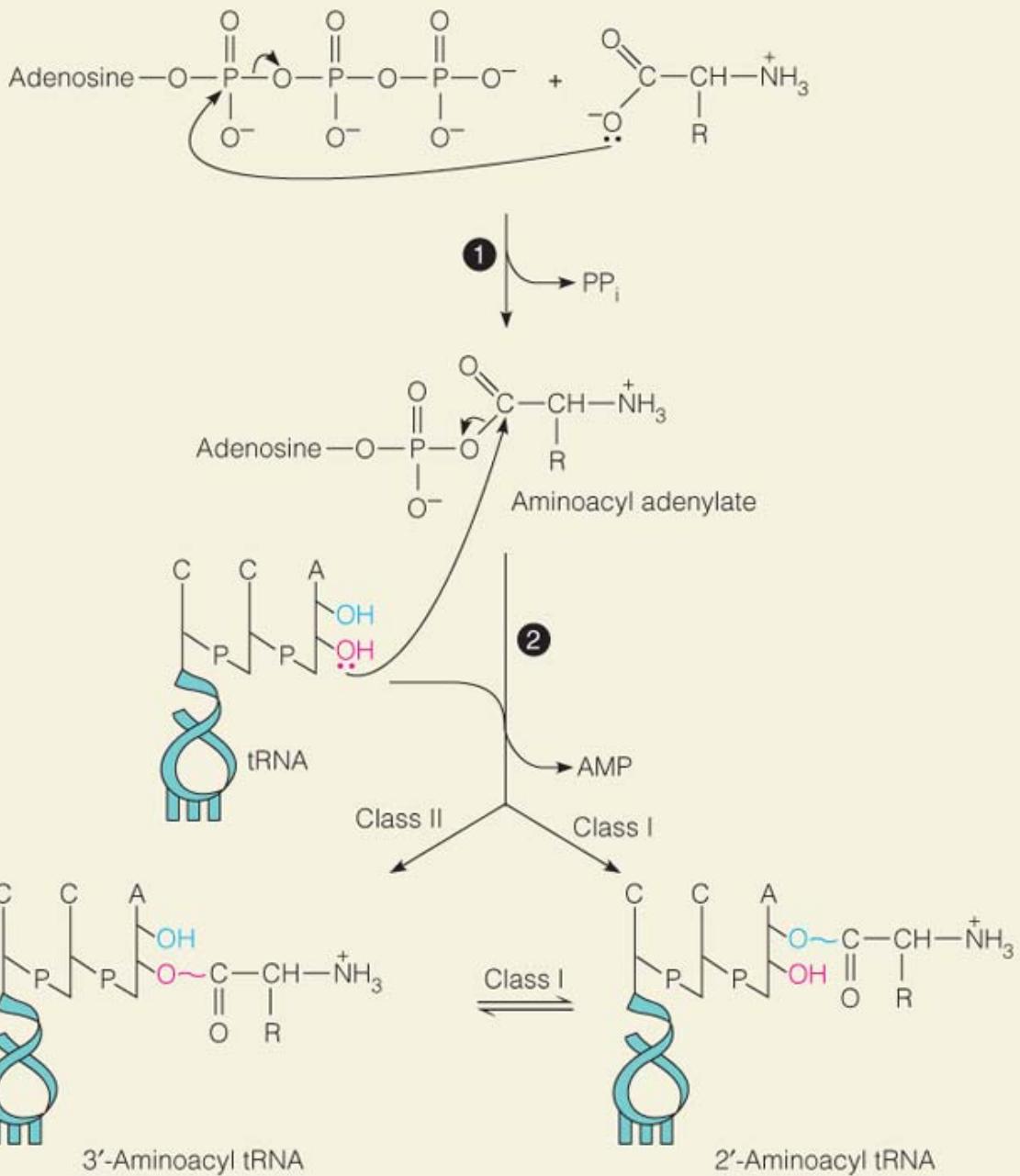
- 73 nucleotide residues
- 10 modified bases
- Guanylate (pG) residue at the 5'-end
- CCA residues at the 3'-end
- Four arms:
  - Amino acid arm (ACG)
  - Anticodon arm  
(Inosine/wobble position)
  - D arm (D residues)
  - T $\Psi$ C arm  
(Ribothymidine; Pseudouridine)

# Twisted L form of 3-D tRNA



# Aminoacylation of tRNA by aminoacyl-tRNA synthetases





# Aminoacylation of tRNA by aminoacyl-tRNA synthetases

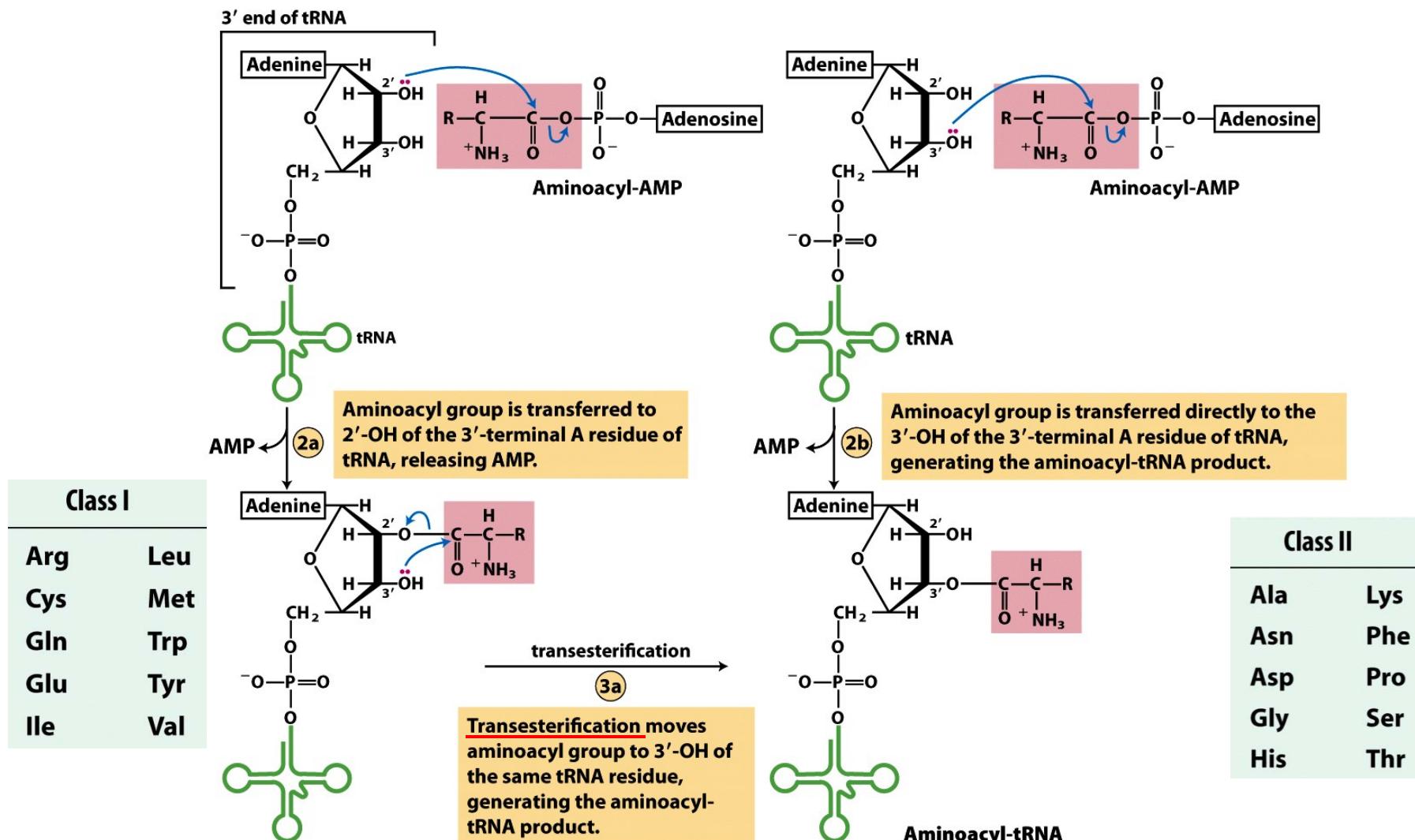
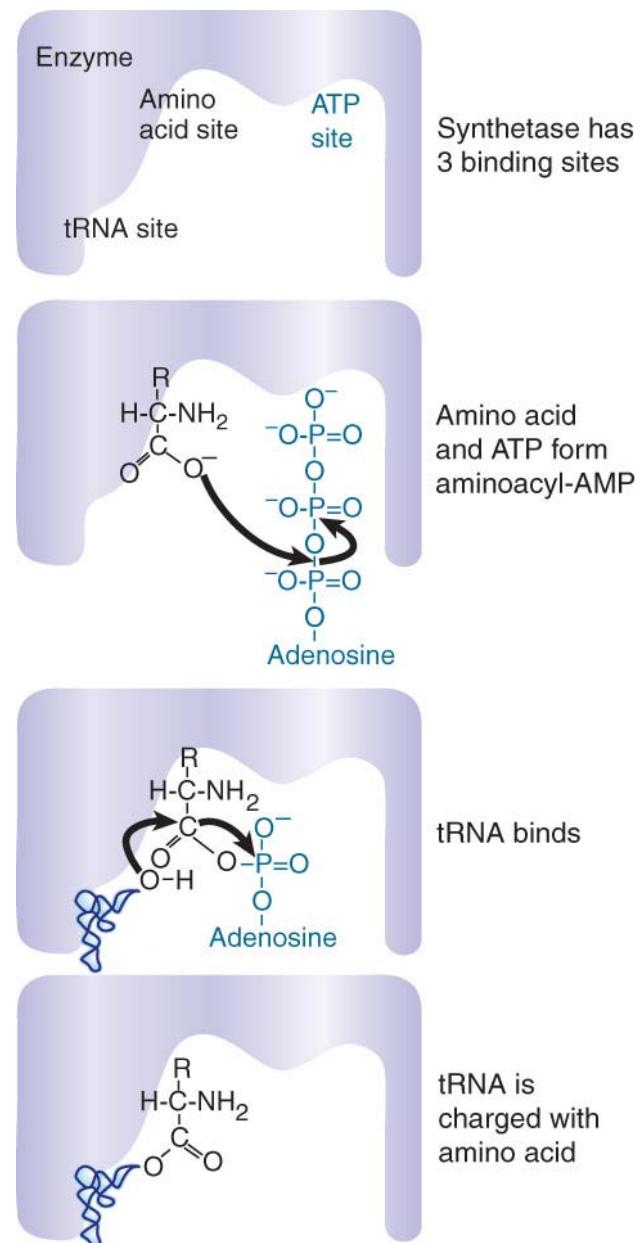


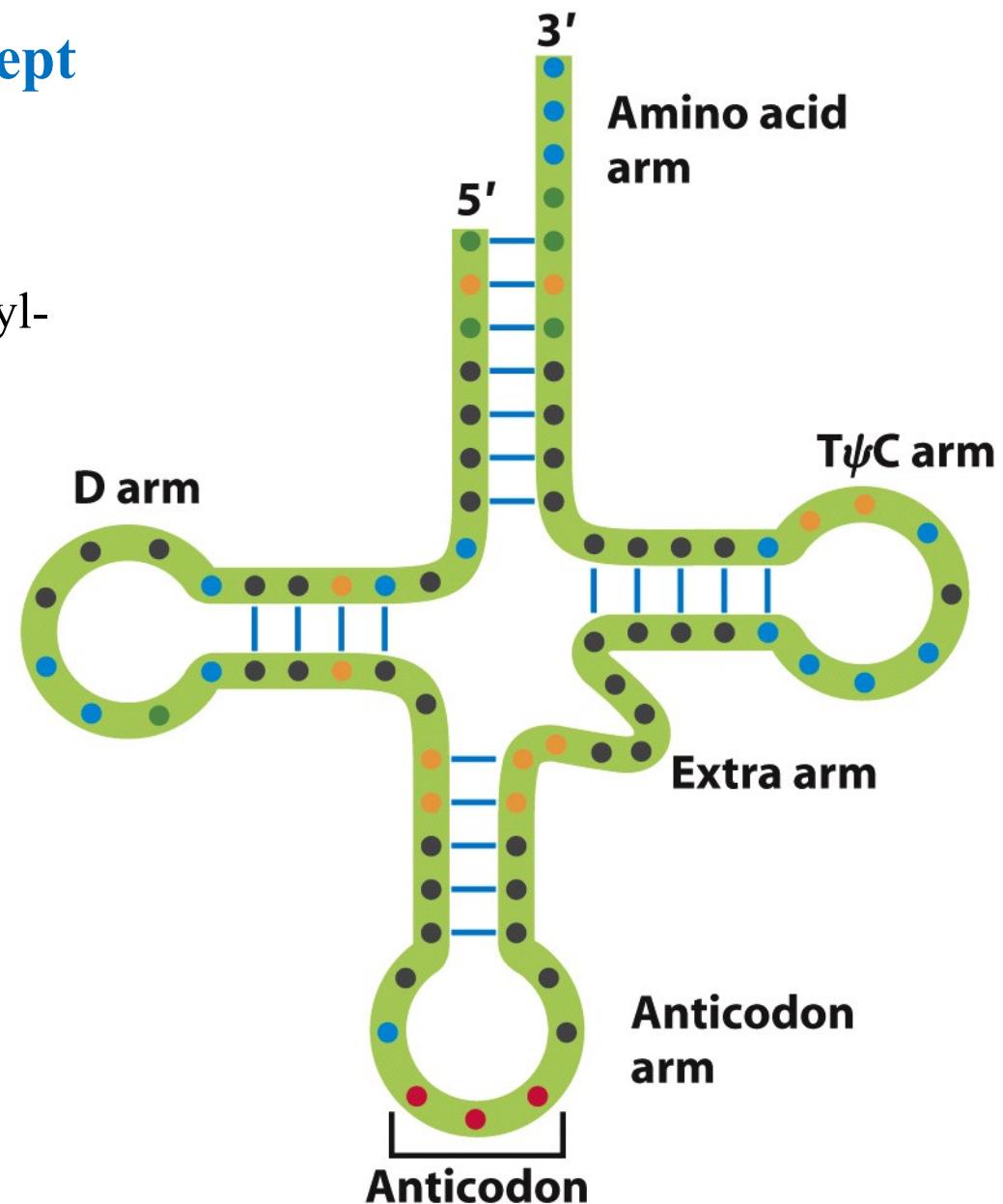
Figure 27-19 part 2  
*Lehninger Principles of Biochemistry, Fifth Edition*  
 © 2008 W.H. Freeman and Company

# tRNAs are selectively paired with amino acids by aminoacyl-tRNA synthetases

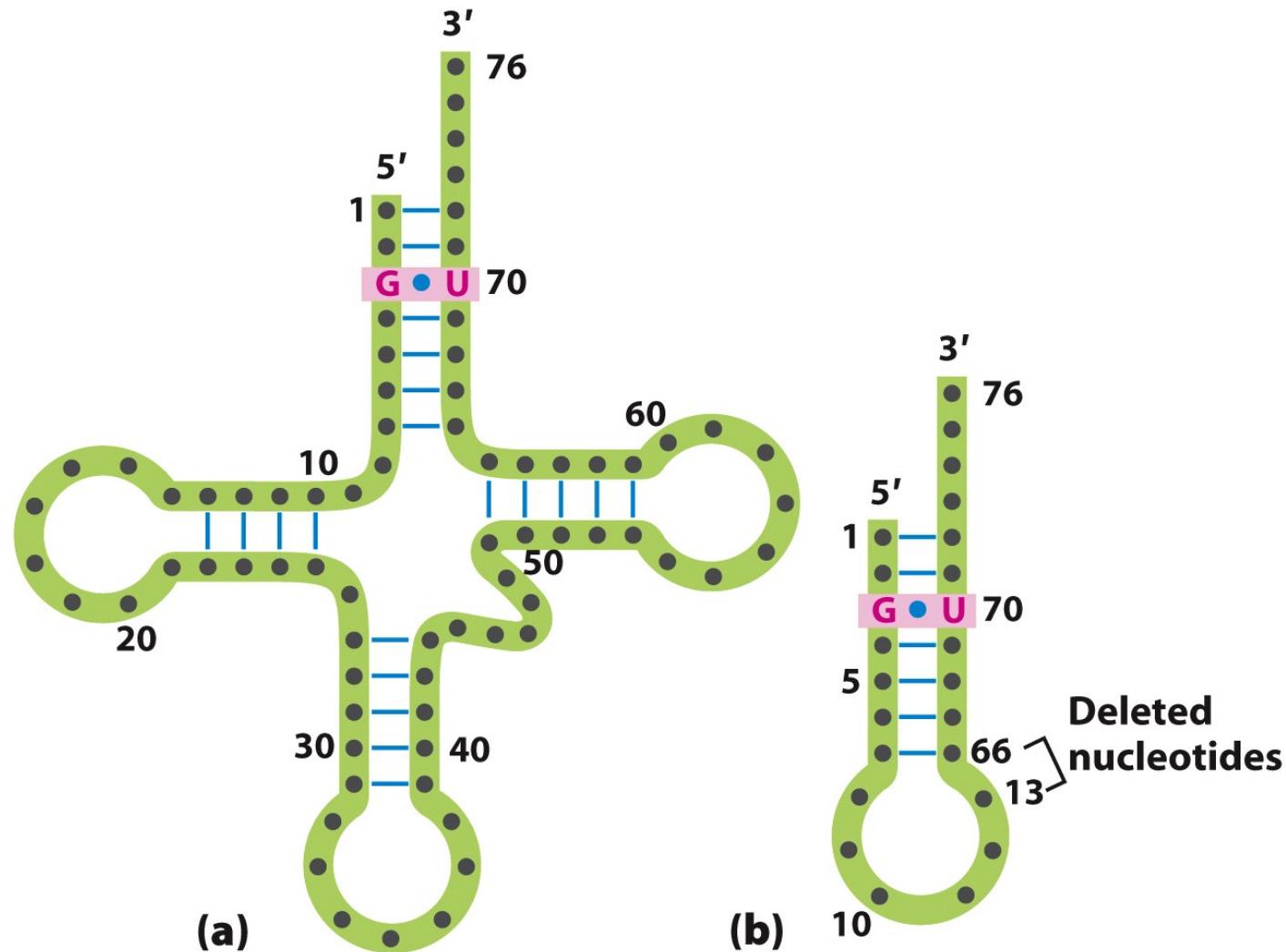


## Second Genetic Code Concept

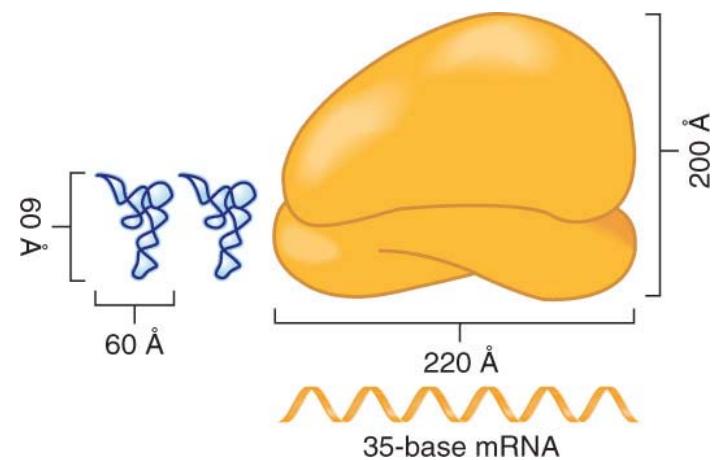
- Conserved residues in all tRNAs
- Recognition points
- > 10 nucleotides involved in recognition of a tRNA by aminoacyl-tRNA synthetase



## Structural elements of tRNA<sup>Ala</sup> that are required for recognition by Ala-tRNA synthetase

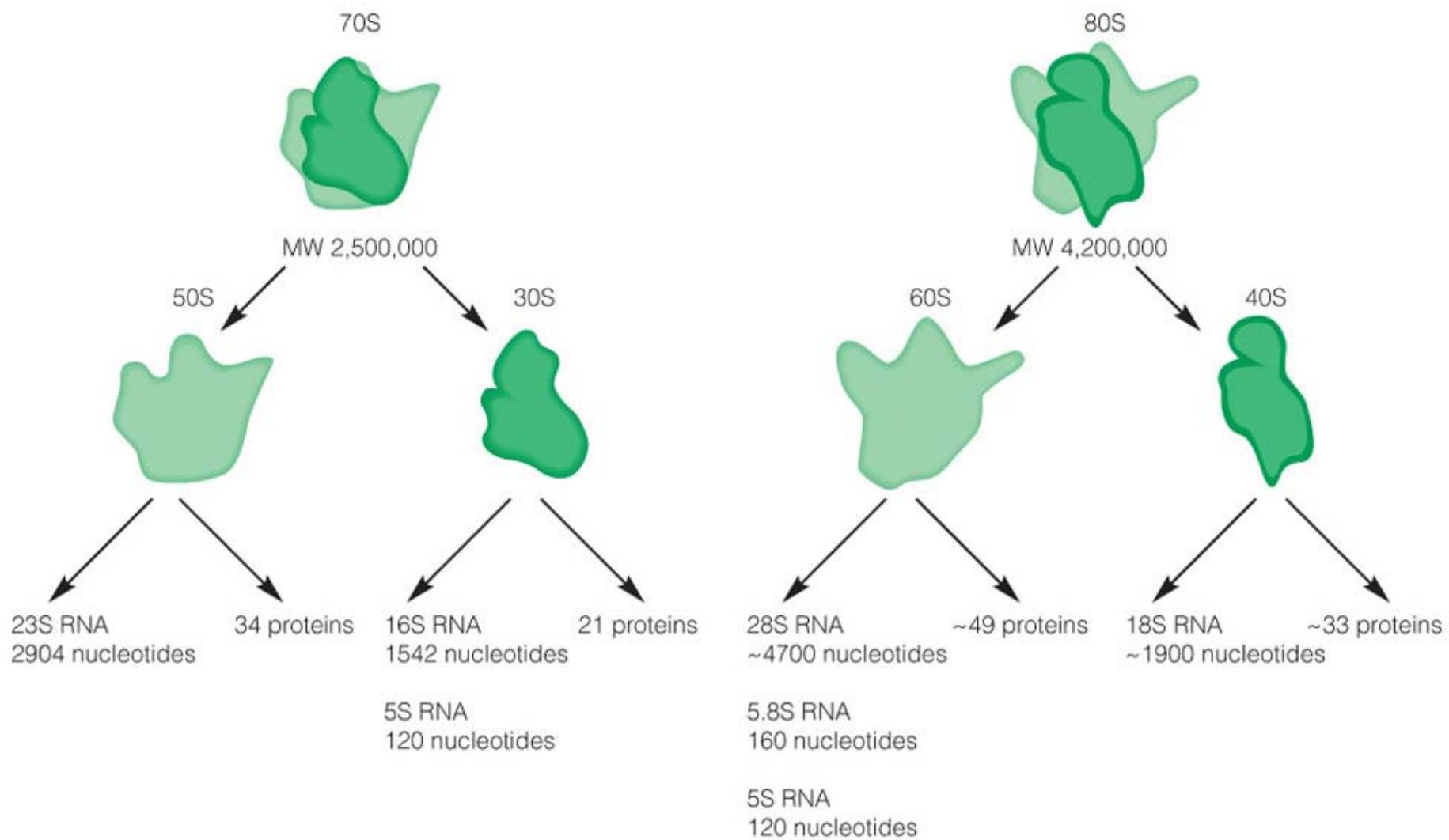


## A ribosome binds mRNA and tRNAs.



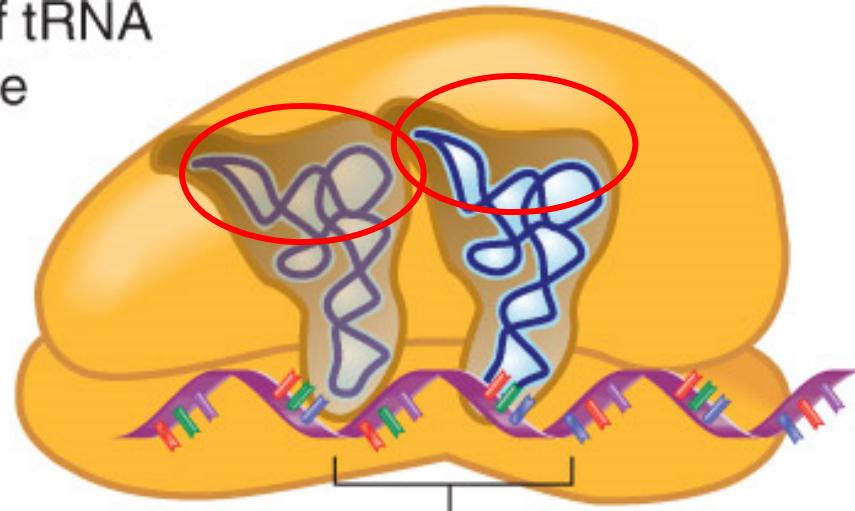
	Ribosomes	rRNAs	r-proteins
Bacterial (70S) mass: 2.5 MDa 66% RNA	50S 30S	23S = 2904 bases 5S = 120 bases 16S = 1542 bases	31 21
Mammalian (80S) mass: 4.2 MDa 60% RNA	60S 40S	28S = 4718 bases 5.8S = 160 bases 5S = 120 bases 18S = 1874 bases	49 33

Ribosomes are ribonucleoprotein particles.



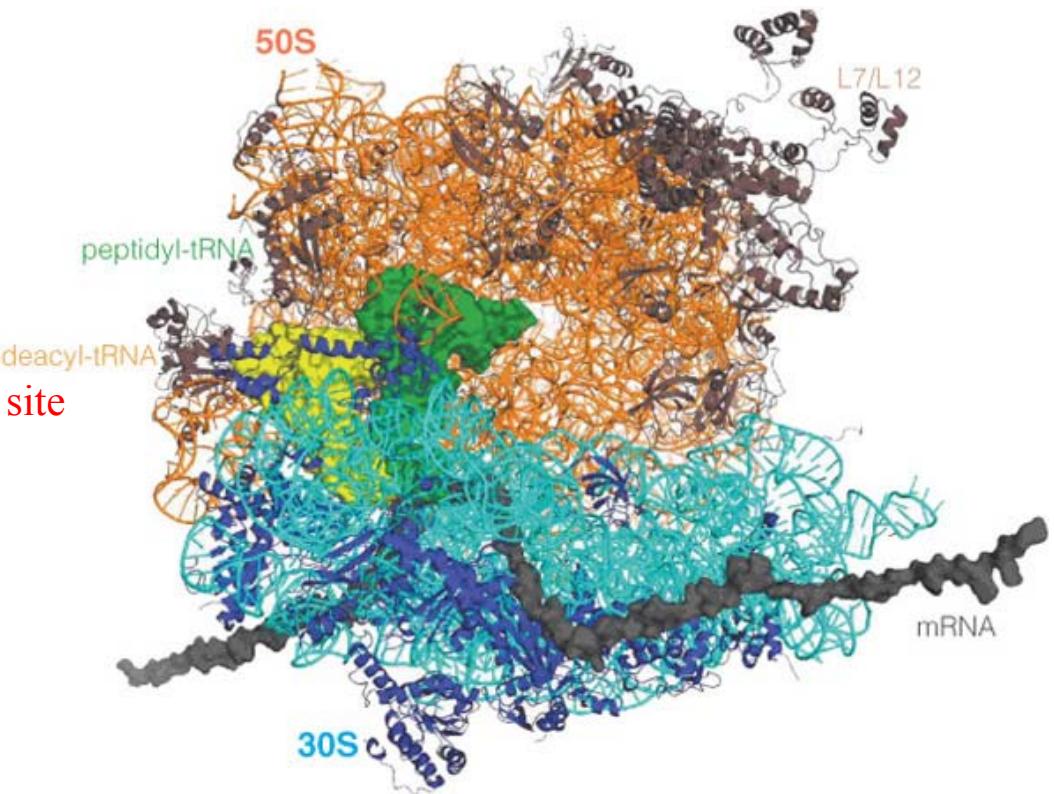
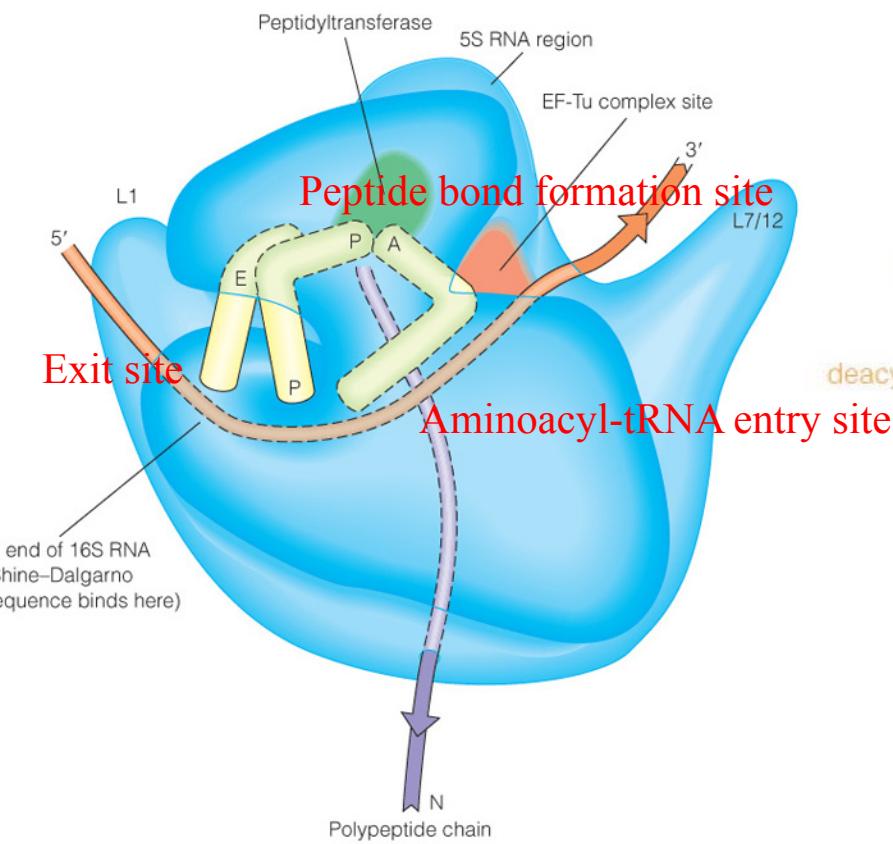
## Amino acid ; T<sub>Ψ</sub>C arms

Aminoacyl-ends of tRNA  
interact within large  
ribosome subunit

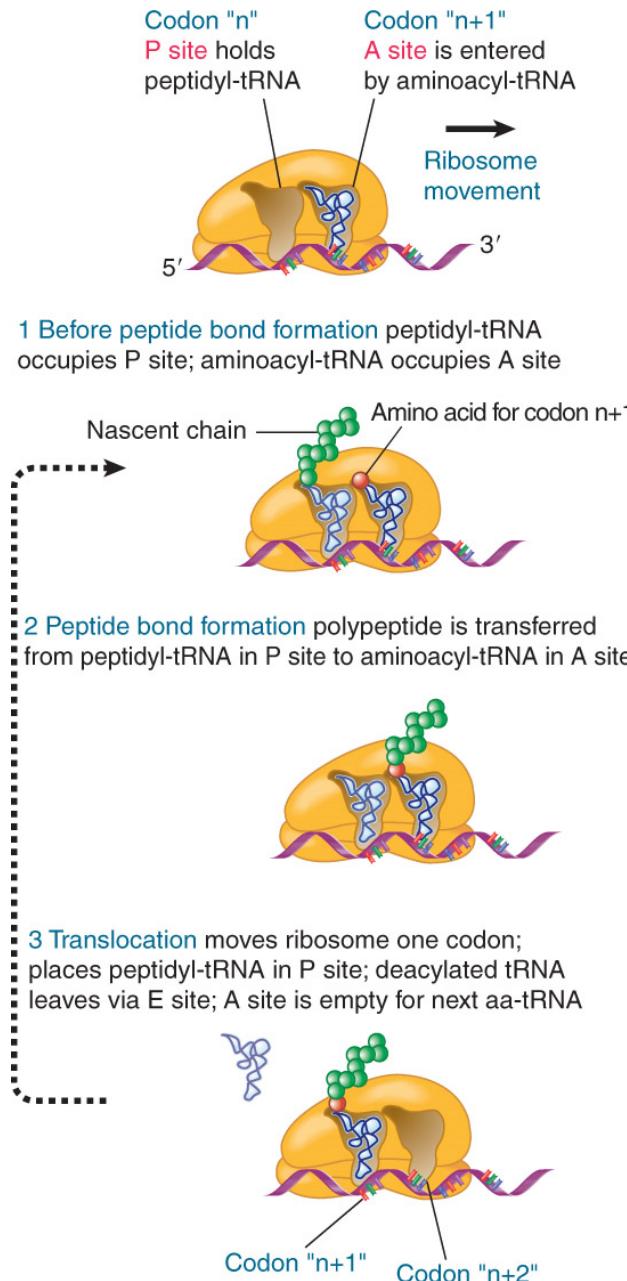


Anticodons are bound  
to adjacent triplets on mRNA  
in small ribosome subunit

**Anticodon arm**



# Translation Occurs by Initiation, Elongation, and Termination



The ribosome has three tRNA-binding sites:

Charged tRNA

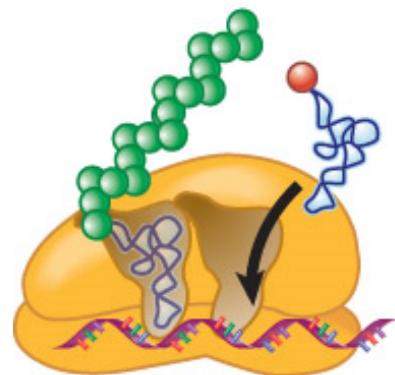
- An aminoacyl-tRNA enters the **A site**
- **Peptidyl-tRNA** is bound in the **P site**

Uncharged tRNA

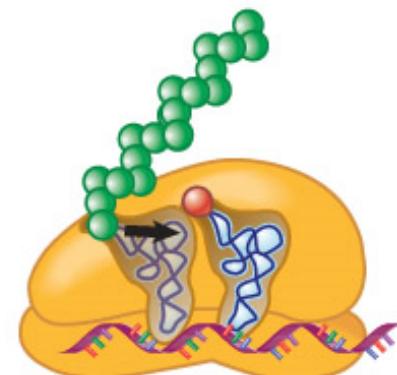
- **Deacylated tRNA** exits via the **E (exit) site**

## Aminoacyl-tRNA enters the A site

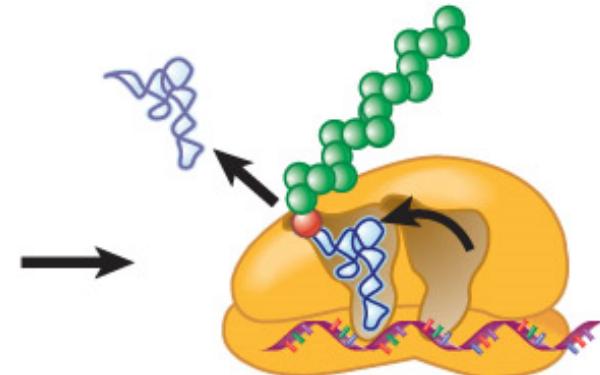
Aminoacyl-tRNA  
enters the A site



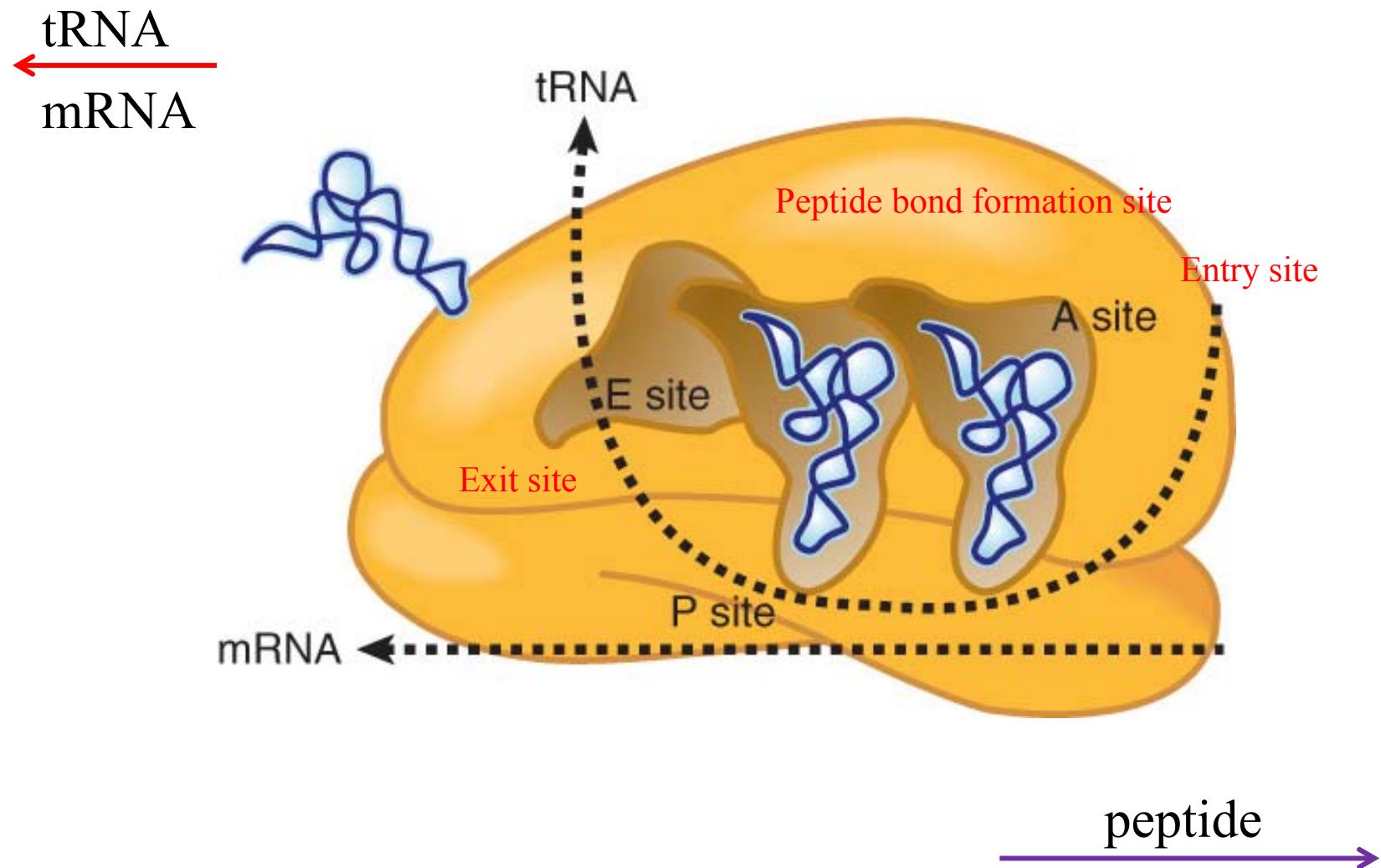
Polypeptide is transferred to  
aminoacyl-tRNA



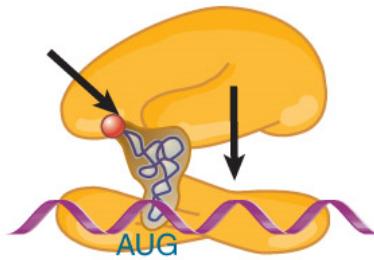
Translocation moves  
peptidyl-tRNA into P site



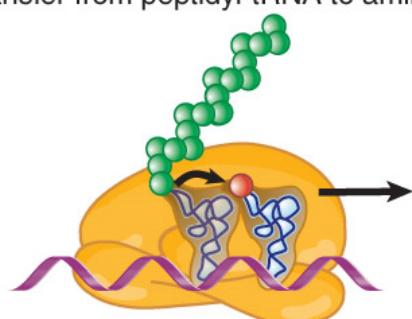
## tRNA and mRNA move through the ribosome in the same direction



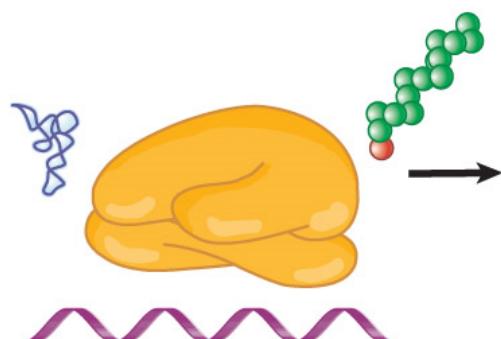
**Initiation** small subunit on mRNA binding site is joined by large subunit and aminoacyl-tRNA binds



**Elongation** Ribosome moves along mRNA, extending protein by transfer from peptidyl-tRNA to aminoacyl-tRNA



**Termination** Polypeptide chain is released from tRNA, and ribosome dissociates from mRNA

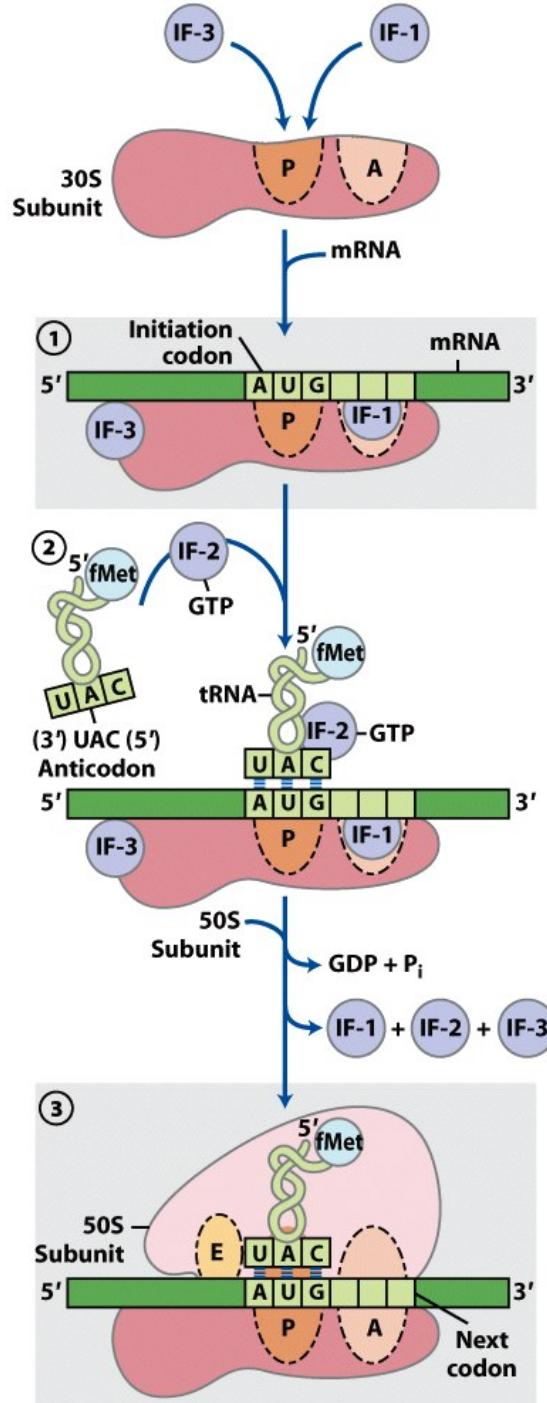
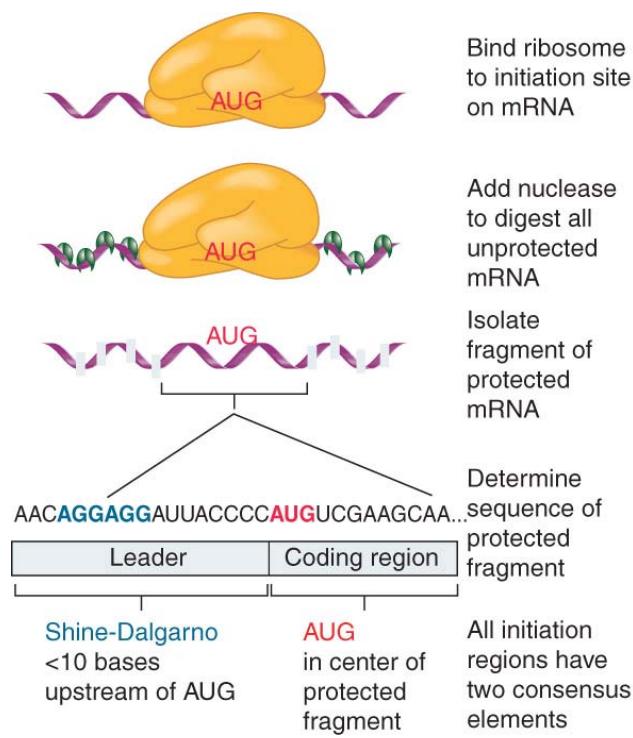


## Three major stages:

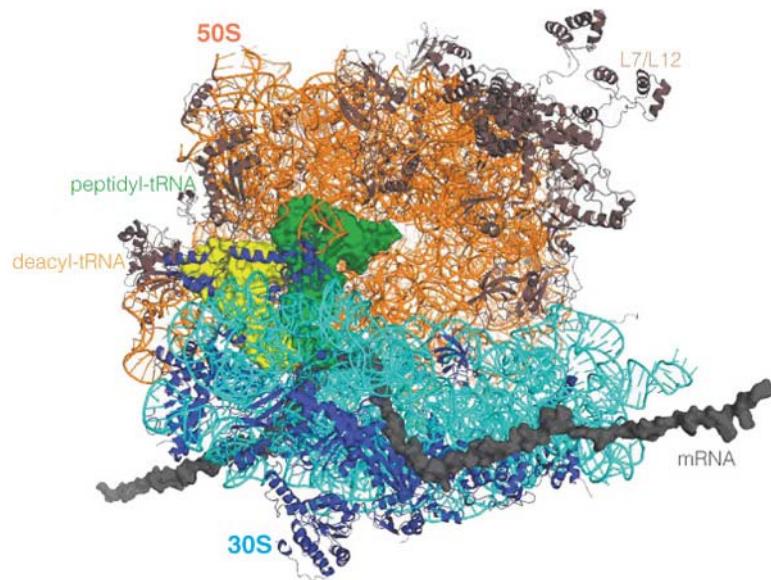
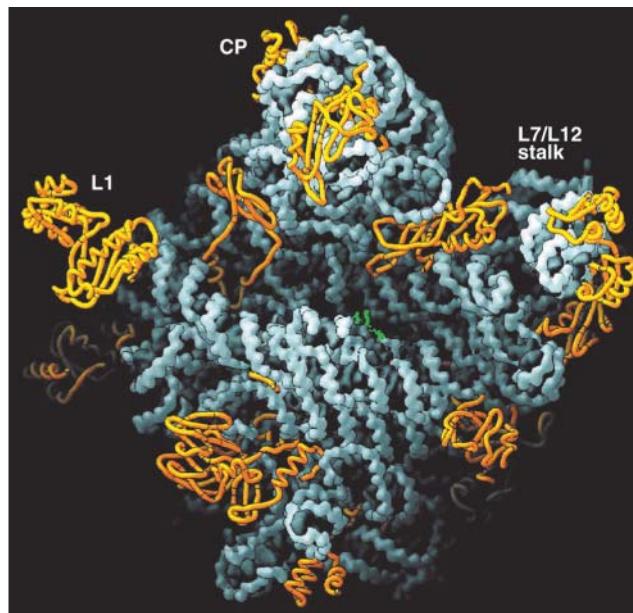
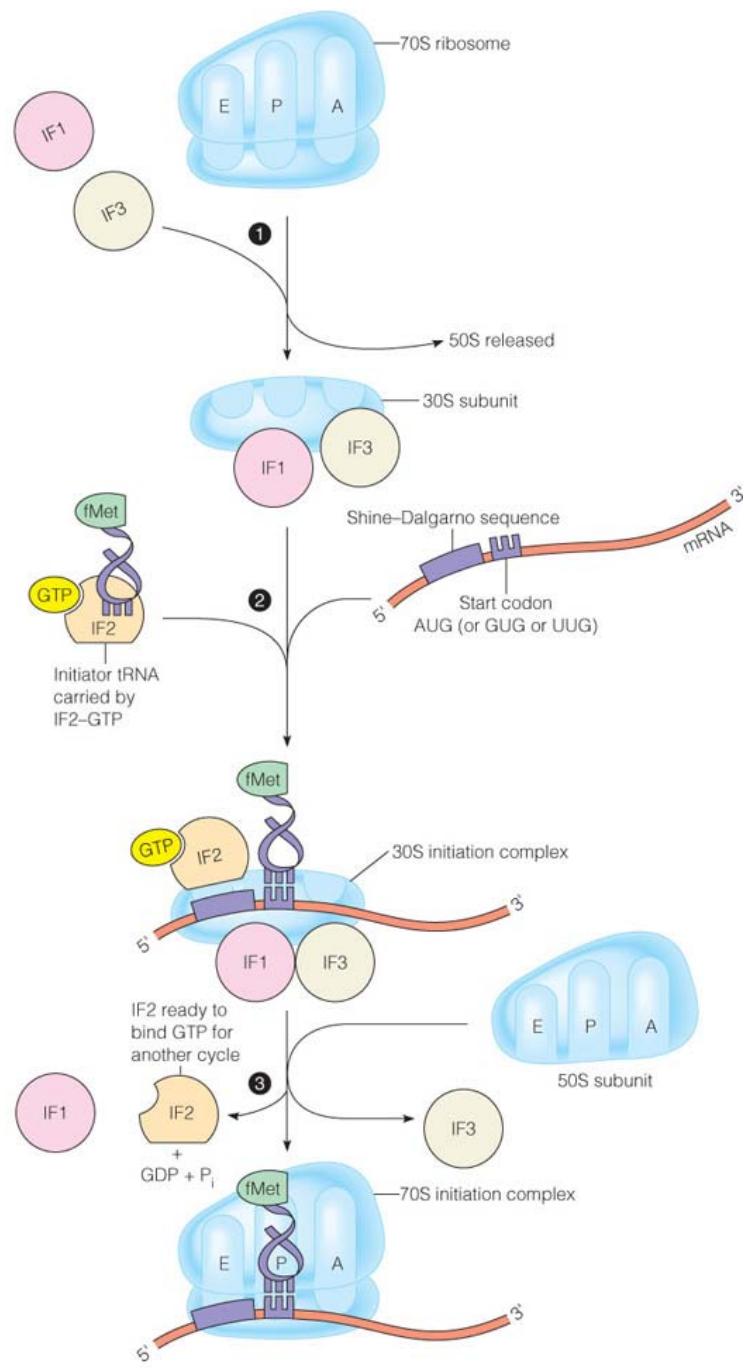
- **Initiation** – The stages of translation up to synthesis of the first peptide bond of the polypeptide. (GTP)
- **Elongation** – The stage of translation in which the polypeptide chain is extended by the addition of individual subunits. (GTP)
- **Termination** – A separate reaction that ends translation by stopping the addition of subunits and (typically) causing disassembly of the synthetic apparatus.

# Initiation

- 30S ribosomal subunit
- The mRNA template
- The initiating fMet-tRNA
- Three initiation factors:  
IF1, IF2, and IF3
- GTP
- 50S ribosomal subunit
- Mg<sup>2+</sup>



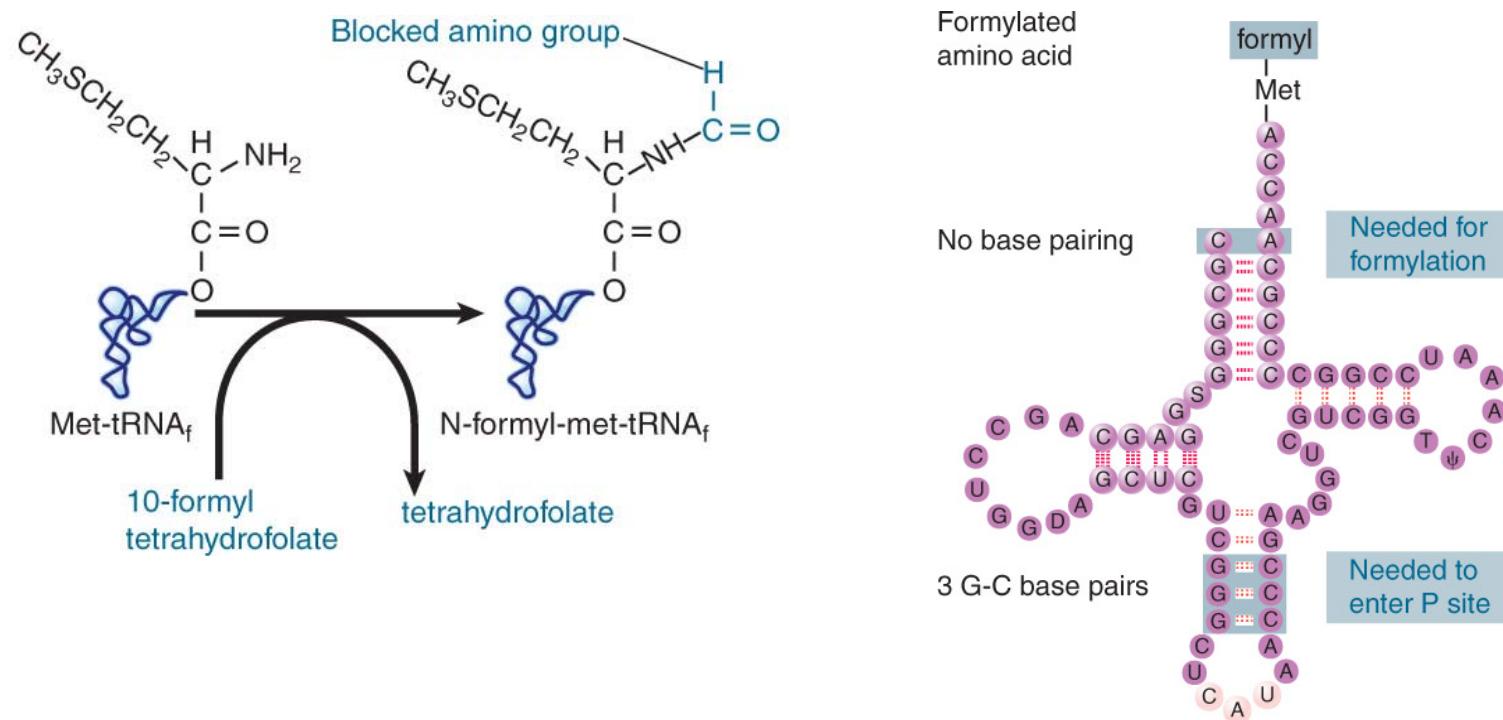
- IF1 and IF3 bind to 30S
- IF3 prevents the premature formation of 30S & 50S
- mRNA binds to 30S
- AUG is guided by **Shine-Dalgarno sequence** (9 purine residues complementary to 3'-end of 16s rRNA of 30S)
- fMet-tRNA binds to P site (only)
- IF1 binding to A site prevents tRNA binding
- Initiation of fMet-tRNA binding to P site requires **GTP-bound IF2**
- 50S binding; GTP-bound IF2 → GDP-bound IF2



**TABLE 28.3 Representative Shine–Dalgarno sequences**

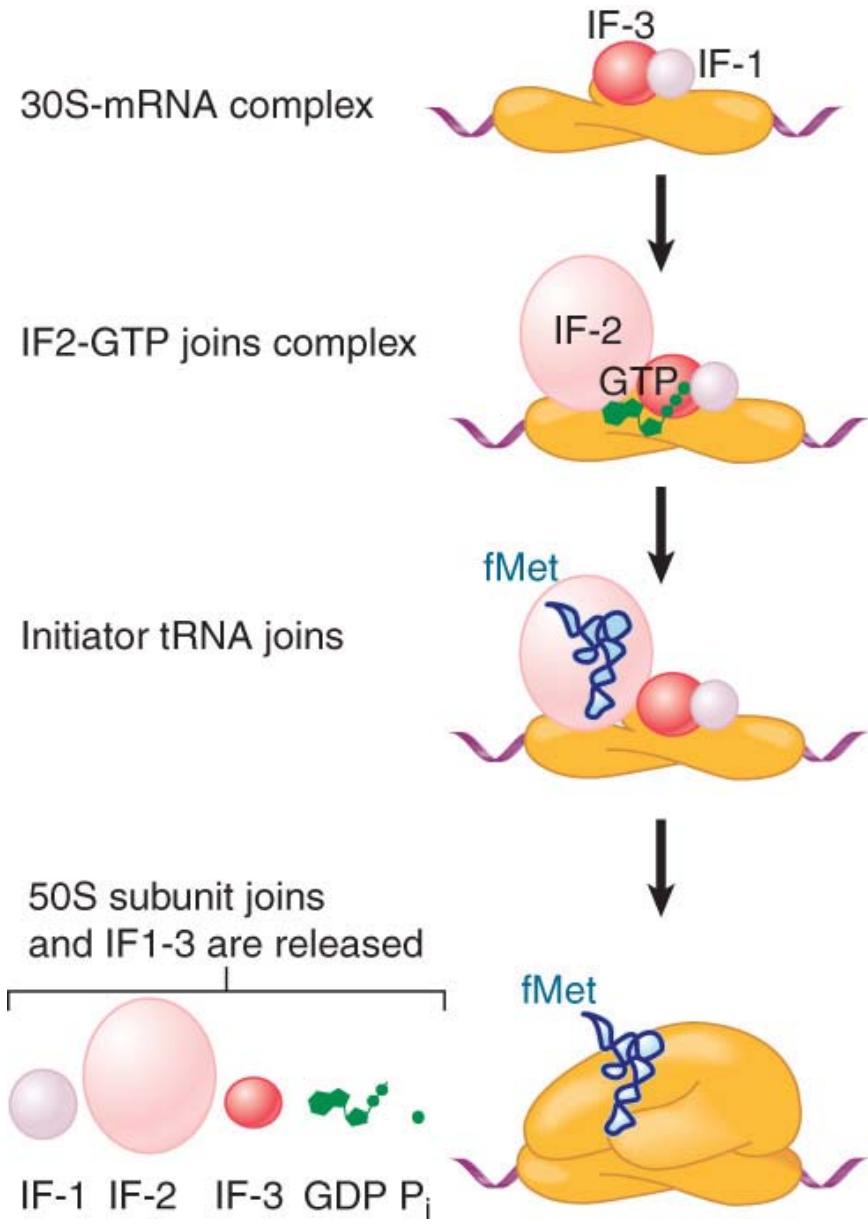
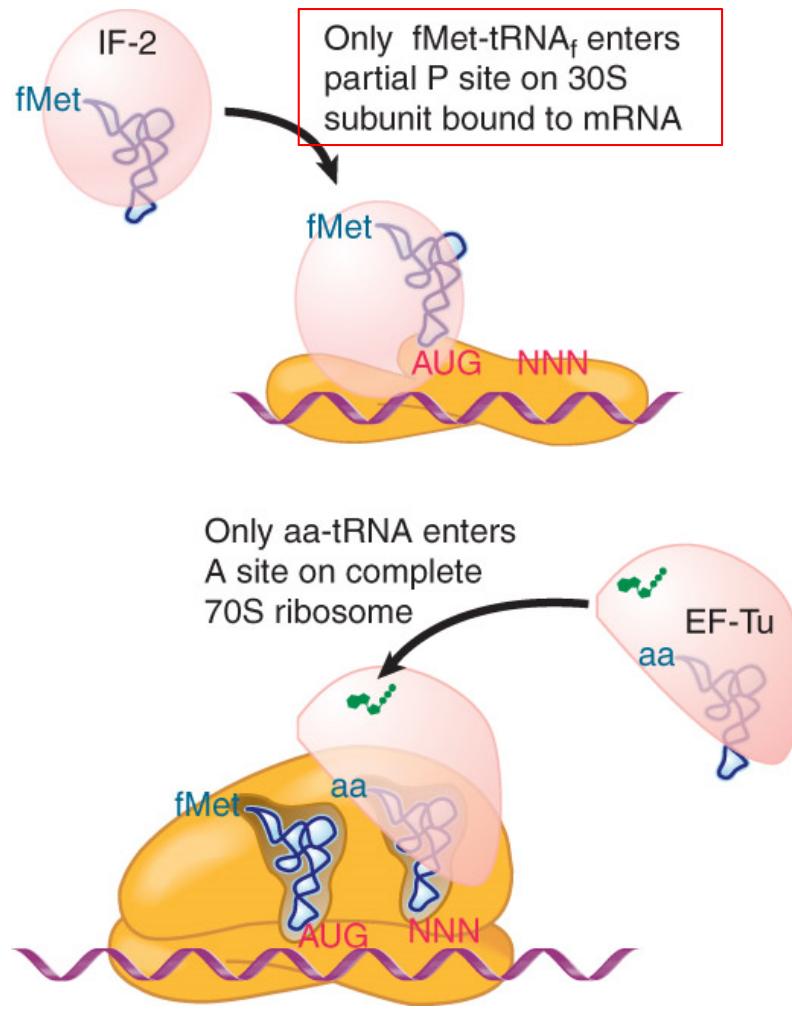
Message for	Shine–Dalgarno Sequence	SD sequence	Start
Ribosomal protein L10	5' AGGAGCAAAGCUA AUG 3' 3' AUUCCUCCCA 5'		mRNA
<i>E. coli lac z</i>	5' AGGAAACAGCUA AUG 3' 3' AUUCCUCCCA 5'		Complementary 3' end of 16S ribosomal RNA
$\lambda$ phage Cro	5' UAAGGAGGUUGUAUG 3' 3' AUUCCUCCCA 5'		

- **N-formyl-methionyl-tRNA (fMet-tRNA)** – The aminoacyl-tRNA that initiates bacterial polypeptide translation.
- The amino group of the methionine is formylated.

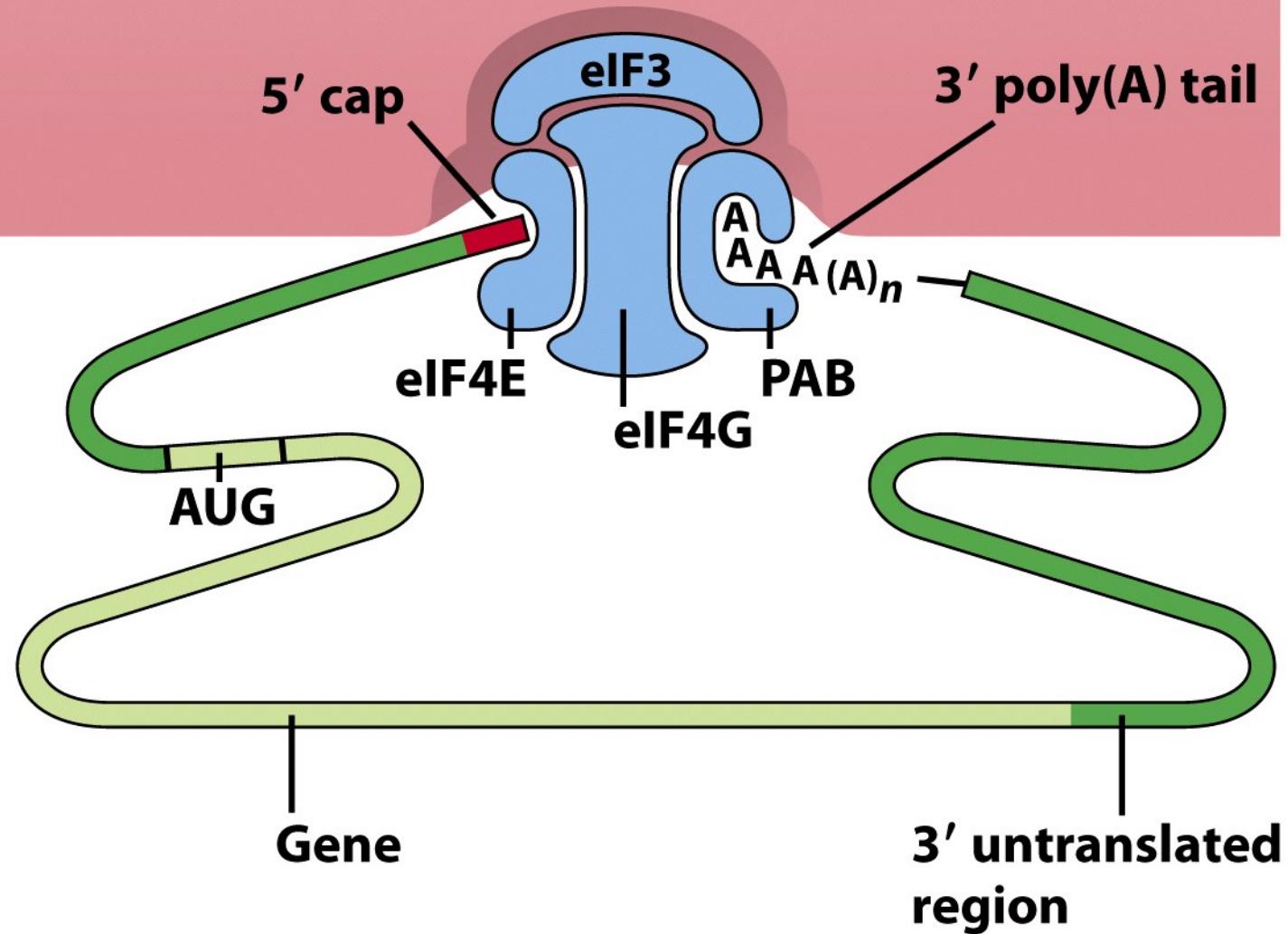


- **tRNA<sub>m</sub>Met** – The bacterial tRNA that inserts methionine at internal AUG codons.
- The initiator tRNA has unique structural features that distinguish it from all other tRNAs.
- The  $\text{NH}_2$  group of the methionine bound to bacterial initiator tRNA is formylated.

## IF2 recruits fMet-tRNA<sub>f</sub> to P site



## 40S ribosomal subunit

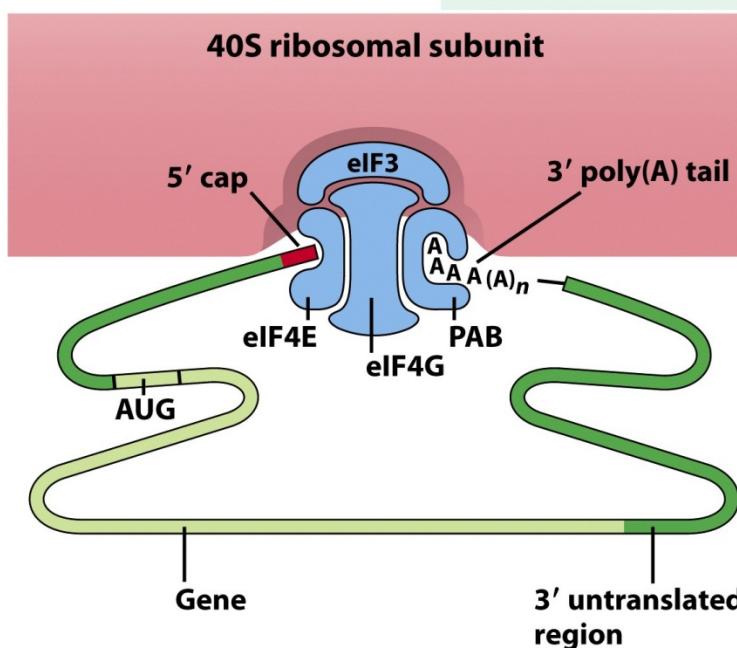


# Similar

**TABLE 27–8** Protein Factors Required for Initiation of Translation in Bacterial and Eukaryotic Cells

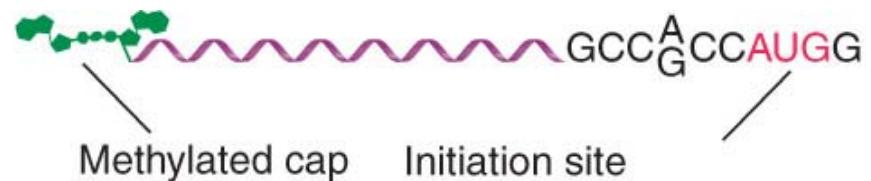
Factor	Function
<b>Bacterial</b>	
IF-1	Prevents premature binding of tRNAs to A site
IF-2	Facilitates binding of fMet-tRNA <sup>fMet</sup> to 30S ribosomal subunit
IF-3	Binds to 30S subunit; prevents premature association of 50S subunit; enhances specificity of P site for fMet-tRNA <sup>fMet</sup>
<b>Eukaryotic</b>	
elf2	Facilitates binding of initiating Met-tRNA <sup>Met</sup> to 40S ribosomal subunit
elf2B, elf3	First factors to bind 40S subunit; facilitate subsequent steps
elf4A	RNA helicase activity removes secondary structure in the mRNA to permit binding to 40S subunit; part of the elf4F complex
elf4B	Binds to mRNA; facilitates scanning of mRNA to locate the first AUG
elf4E	Binds to the 5' cap of mRNA; part of the elf4F complex
elf4G	Binds to elf4E and to poly(A) binding protein (PAB); part of the elf4F complex
elf5	Promotes dissociation of several other initiation factors from 40S subunit as a prelude to association of 60S subunit to form 80S initiation complex
elf6	Facilitates dissociation of inactive 80S ribosome into 40S and 60S subunits

elf4F



- elf4A: a RNA helicase to eliminate the secondary structure of 5'UTR
- elf4F may participate in the recognition of the first AUG.

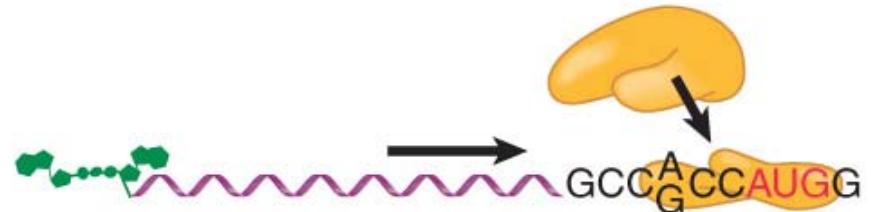
- Eukaryotic 40S ribosomal subunits bind to the 5' end of mRNA and scan the mRNA until they reach an initiation site.
- A eukaryotic initiation site consists of a ten-nucleotide sequence that includes an AUG codon (Kozak consensus sequence).
- 60S ribosomal subunits join the complex at the initiation site.
- Prokaryotic 30S ribosomal subunits directly binds to initiation site.
- A prokaryotic initiation site that includes an AUG codon is guided by Shine-Dalgarno sequence.



- Small subunit binds to methylated cap



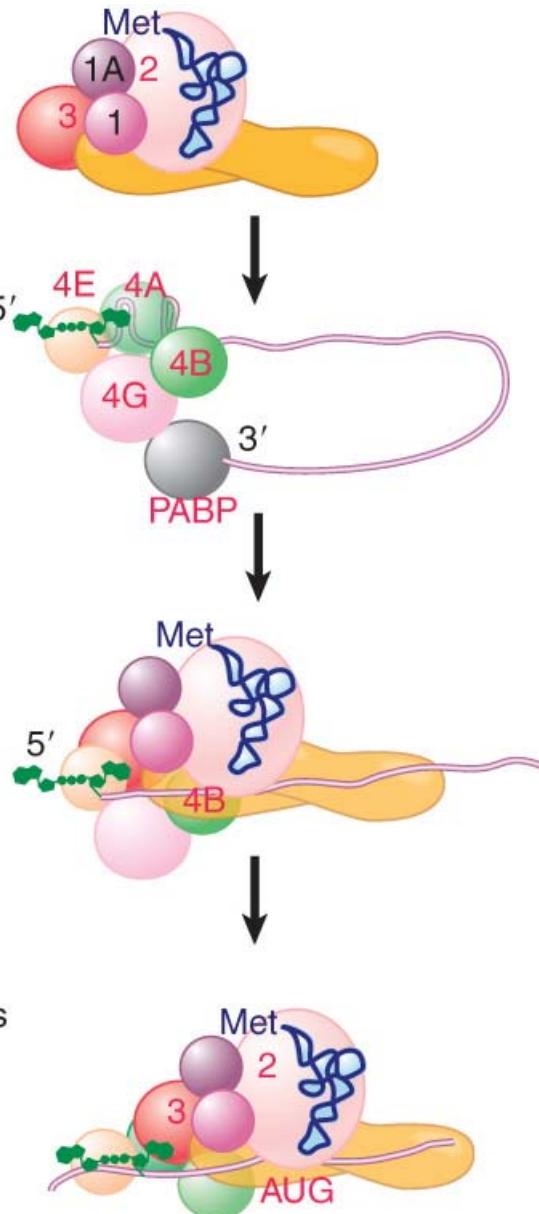
- Small subunit migrates to initiation site



- If leader is long, subunits may form queue

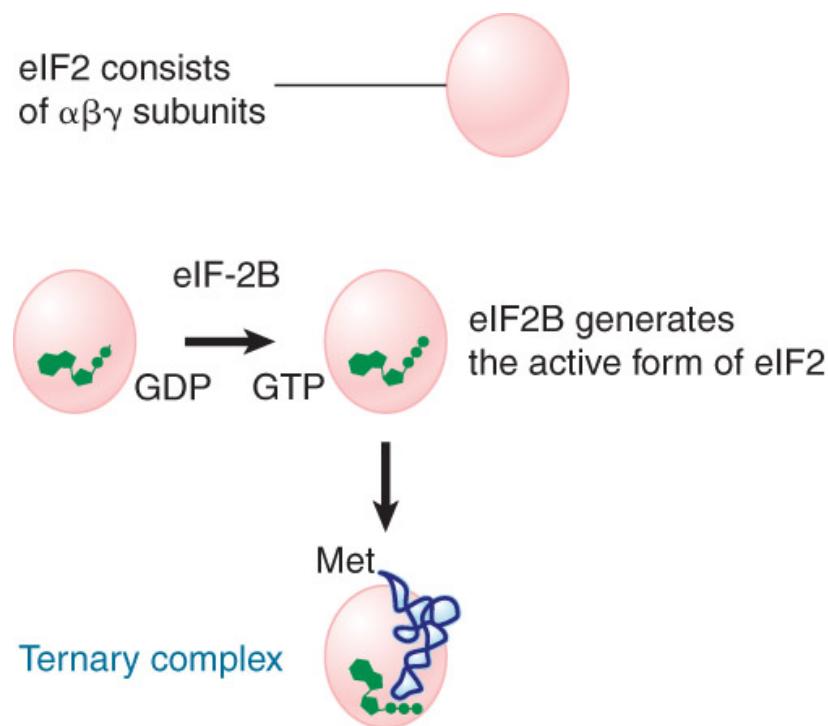


43S preinitiation complex eIF2, eIF3, Met-tRNA<sub>i</sub>, eIF1, eIF1A

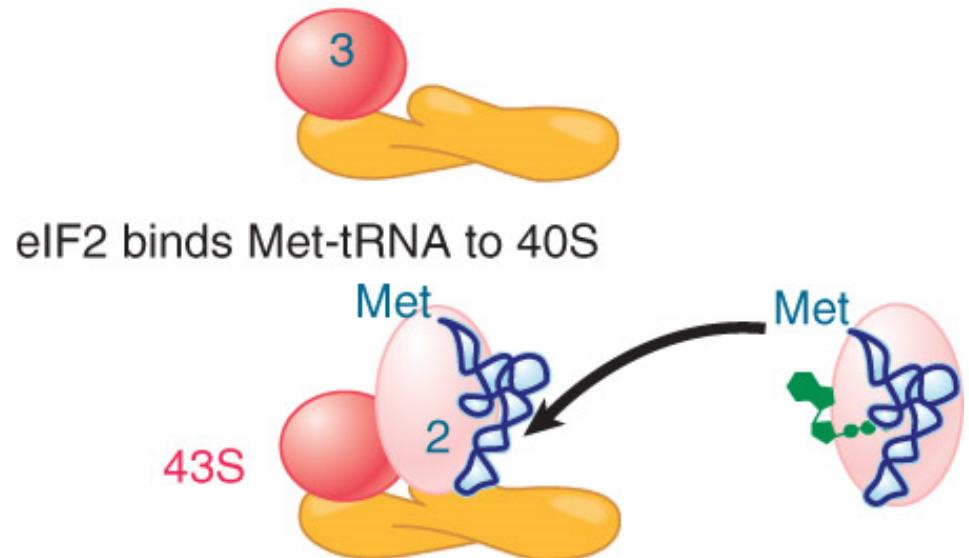


- Initiation factors are required for all stages of initiation, including binding the initiator tRNA, **40S subunit attachment to mRNA, movement along the mRNA**, and joining of the 60S subunit.
- Eukaryotic initiator tRNA is a **Met-tRNA<sub>i</sub>** that is different from the Met-tRNA used in elongation, but the methionine is not formylated.

## A ternary complex of eIF2



eIF3 maintains free 40S subunits



eIF2 is a GTPase  
eIF2B is the exchange factor



**43S complex = 40S subunit + factors +tRNA**

## 43S complex binds to mRNA-factor complex

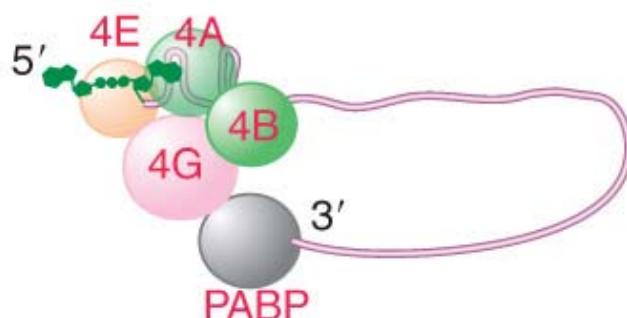
### Initiation factors bind the 5'-end & 3'-end

eIF4F is a heterotrimer consisting of:

eIF4G is a scaffold protein

eIF4E binds the 5' methyl cap

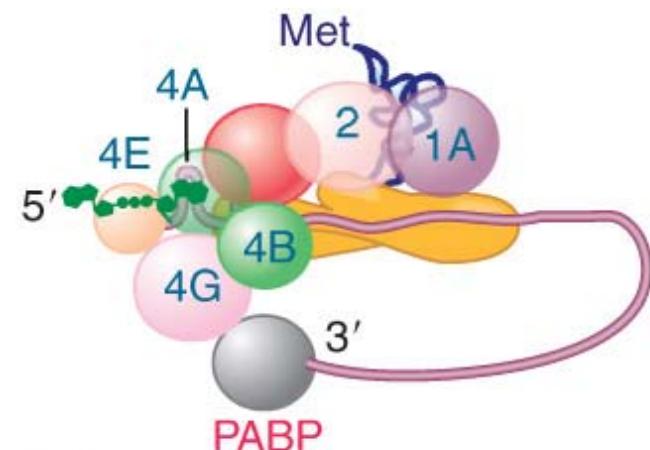
eIF4A is a helicase that unwinds the 5' structure



eIF4G binds two further factors

eIF4B stimulates eIF4A helicase

PABP binds 3' poly(A)

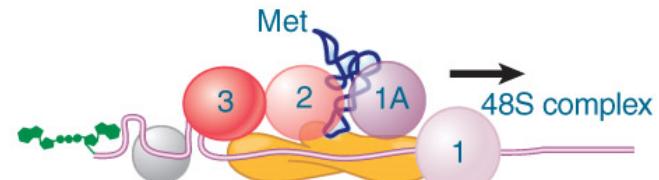


Possible interactions:

eIF4G binds to eIF3

mRNA binds eIF4G, eIF3, and 40S subunit

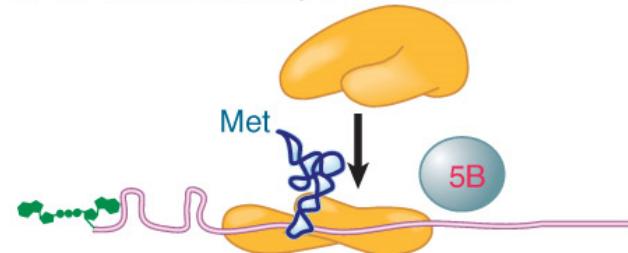
eIF1 and eIF1A enable scanning



eIF5 induces GTP hydrolysis by eIF2

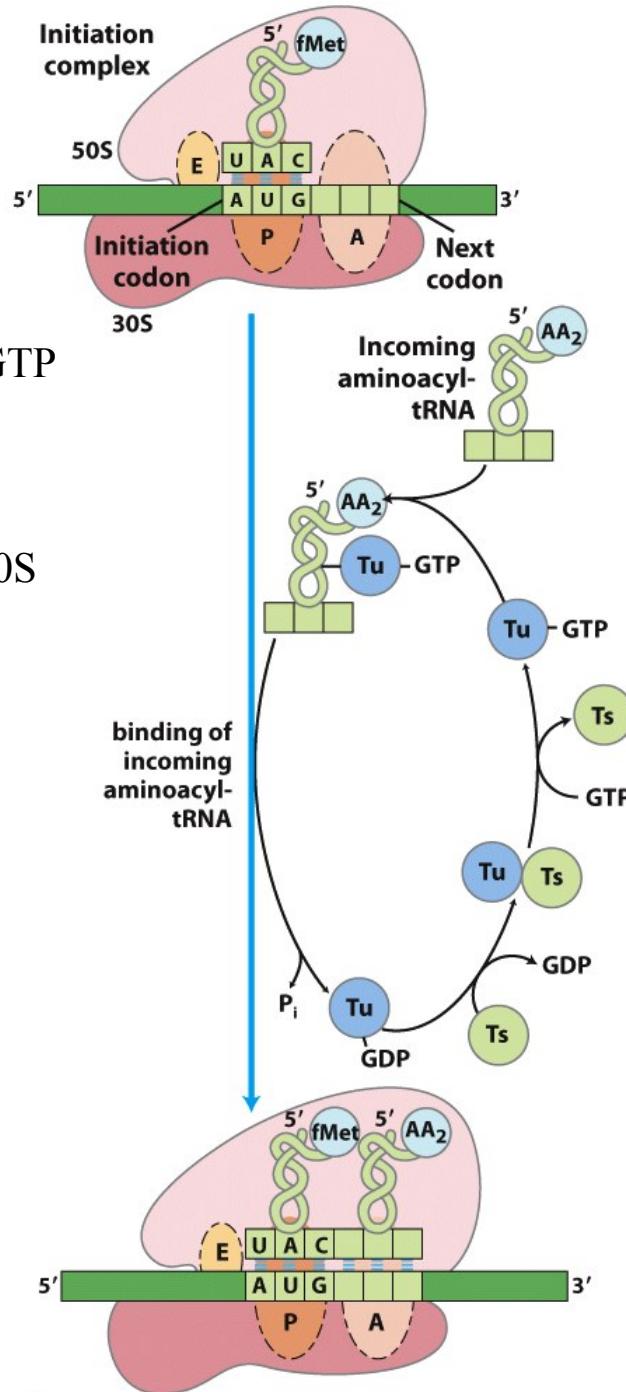
eIF2 and eIF3 are released

eIF5B mediates joining of 60S subunit



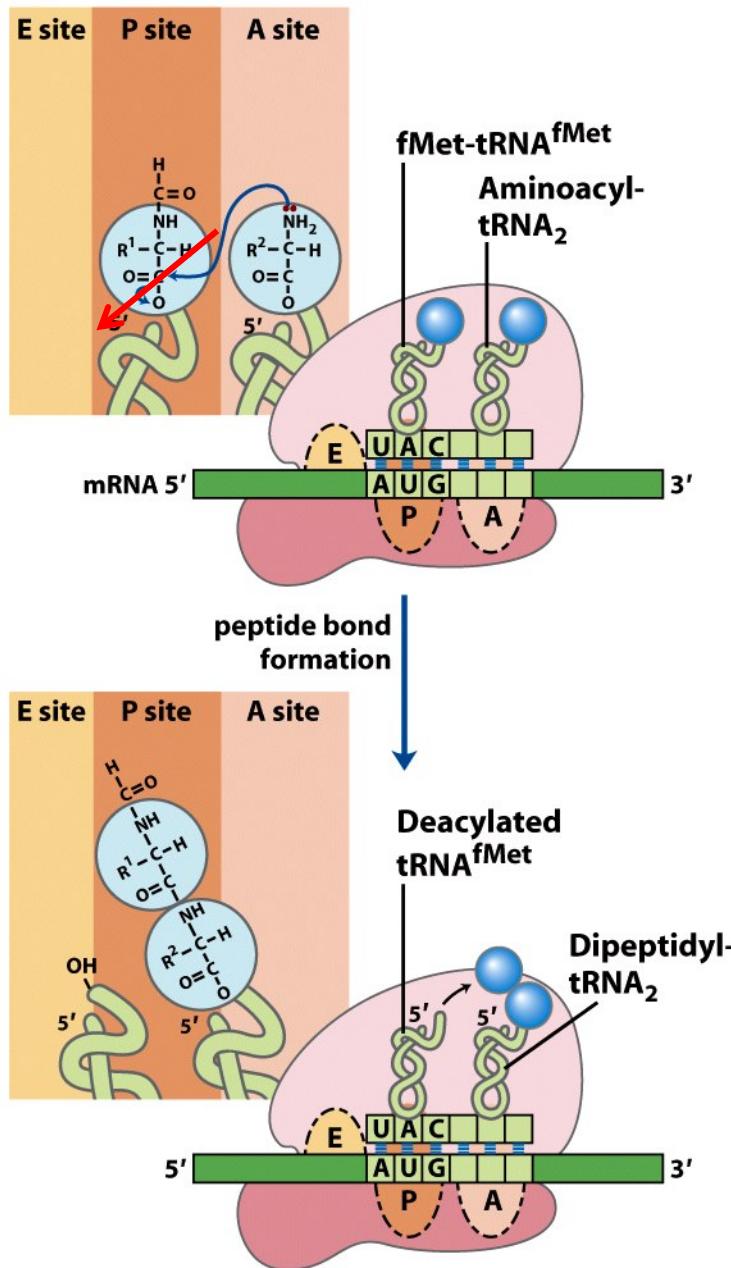
## Binding of incoming aminoacyl-tRNA

- GTP-bound EF-Tu binds to aminoacyl-tRNA
- The aminoacyl-tRNA-EF-Tu-GTP complex binds to A site
- GTP is hydrolyzed and EF-Tu-GDP complex is released from 70S
- EF-Ts: exchange GDP to GTP



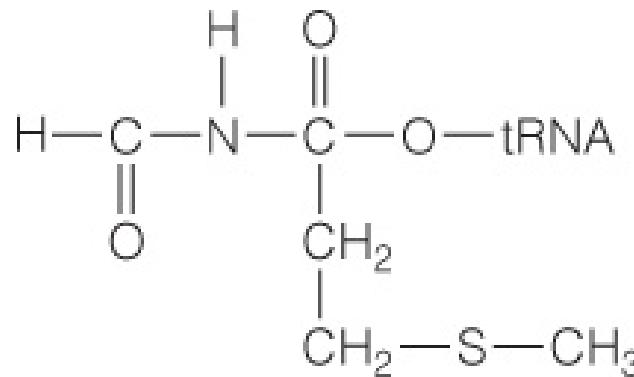
## Elongation

- The initiation complex
- Aminoacyl-tRNA
- Three elongation factors:
  - EF-Tu, EF-Ts, and EF-G
  - GTP
  - Mg<sup>2+</sup>



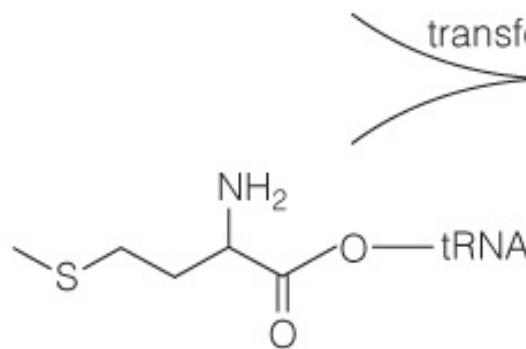
## Peptide bond formation

- The transfer of the initiating N-formylmethionyl group from fMet-tRNA to the amino group of second amino acid
- To displace the tRNA in the P site to form the peptide bond
- Formation of **dipeptidyl tRNA**
- Peptidyl transferase: 23s rRNA



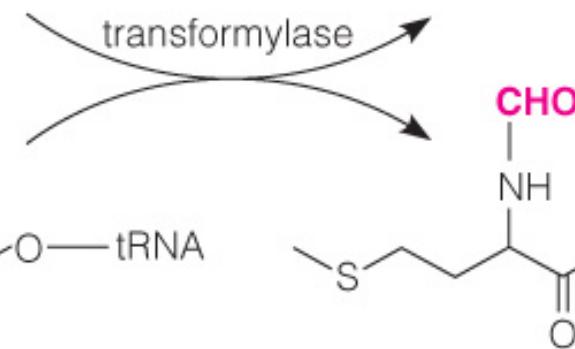
**N-formylmethionyl-tRNA**

**10-Formyl-tetrahydrofolate**

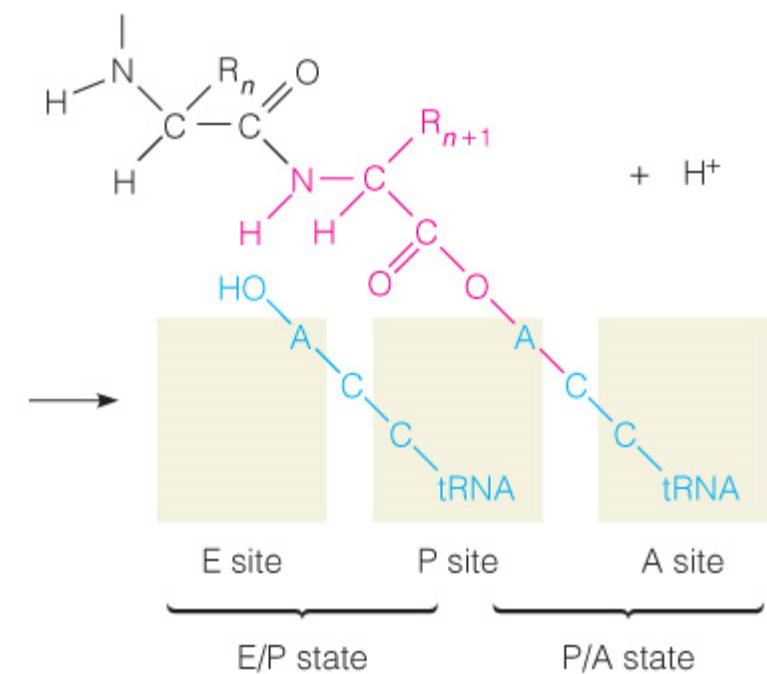
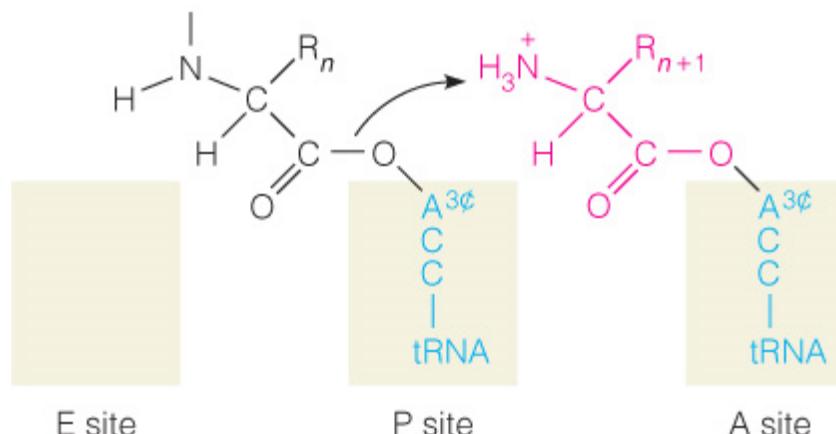


**Met-tRNA<sup>fMet</sup>**

**Tetrahydrofolate**



**fMet-tRNA<sup>fMet</sup>**

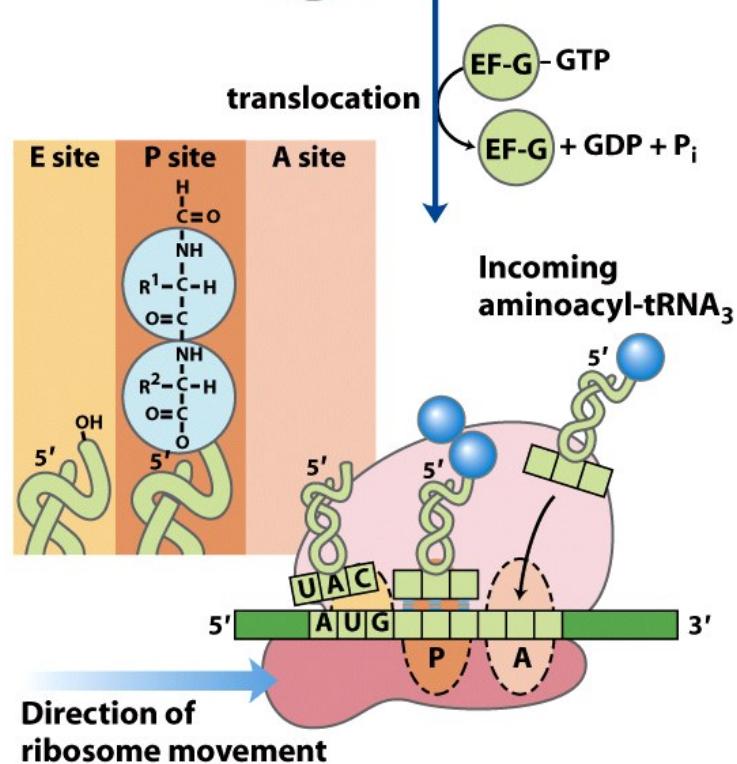
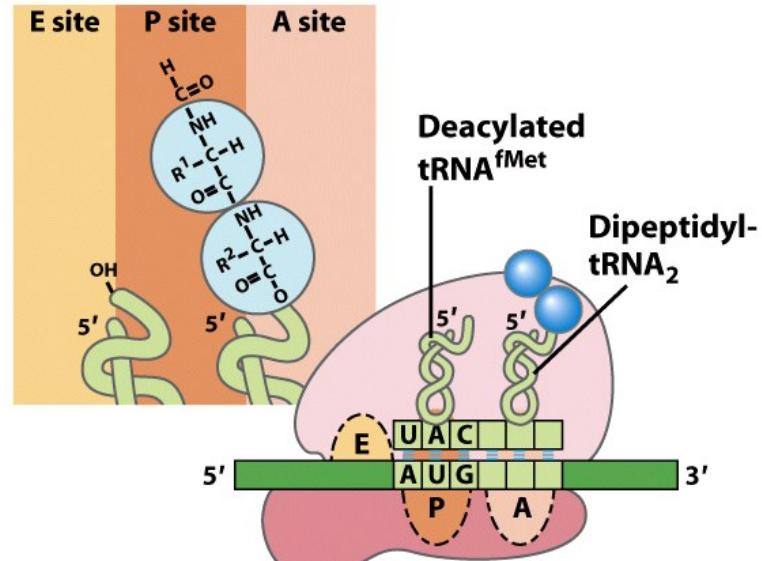


## Translocation

- Movement of **dipeptidyl tRNA** from A site to P site
- Shift of **deacylated tRNA** from P site to E site
- The third codon of mRNA lies to A site
- Movement of ribosome along with mRNA requires EF-G-GTP

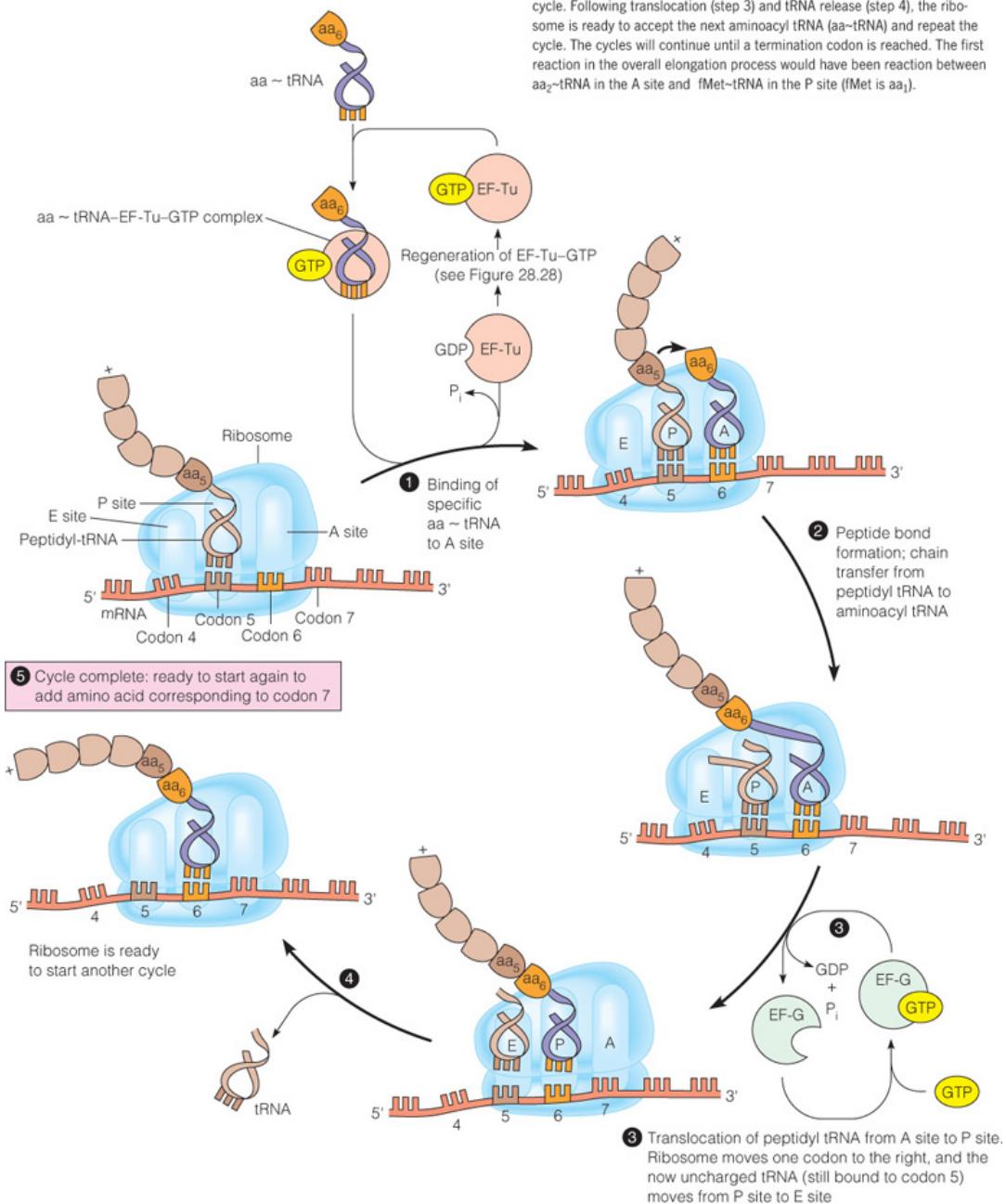
## Eukaryotic cells:

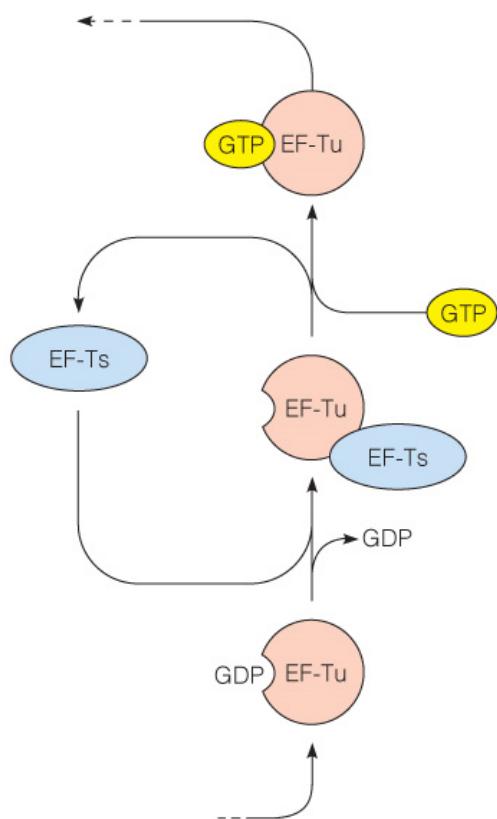
- eEF1 $\alpha$  = EF-Tu GTP binding
- eEF1 $\beta$ , eEF1 $\gamma$  = EF-Ts GDP exchange
- eEF2 = EF-G Ribosome translocation



**FIGURE 28.26**

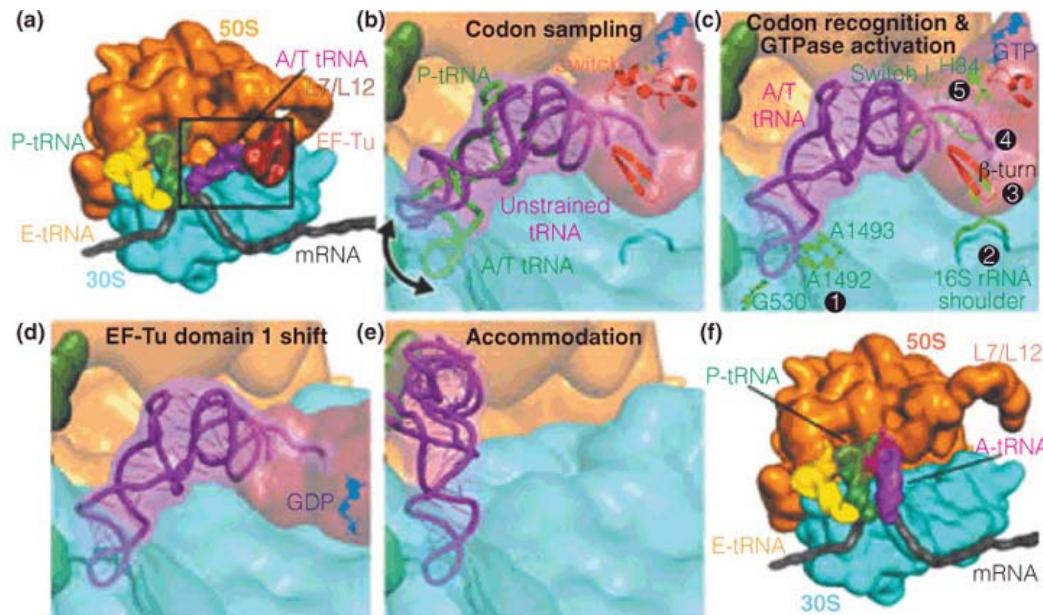
Chain elongation in prokaryotic translation. The process is depicted as a cycle. Following translocation (step 3) and tRNA release (step 4), the ribosome is ready to accept the next aminoacyl tRNA ( $\text{aa}_2\text{-tRNA}$ ) and repeat the cycle. The cycles will continue until a termination codon is reached. The first reaction in the overall elongation process would have been reaction between  $\text{aa}_2\text{-tRNA}$  in the A site and fMet-tRNA in the P site (fMet is  $\text{aa}_1$ ).

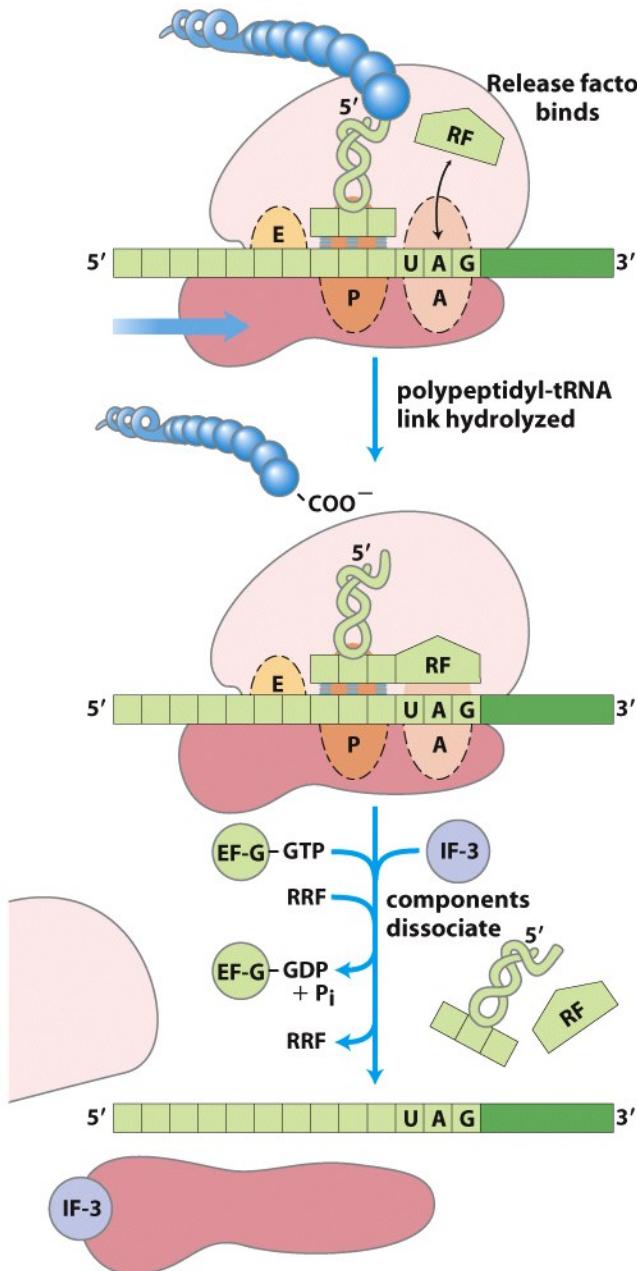




**FIGURE 28.28**

Regeneration of EF-Tu-GTP by Tu-Ts exchange. This figure gives details of the regeneration cycle shown at the top of Figure 28.26. Binding of the factor EF-Ts to EF-Tu allows the release of GDP and binding of a new GTP to prepare EF-Tu for another cycle.

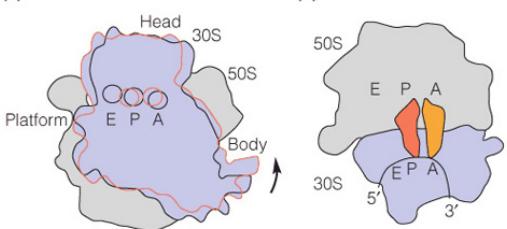




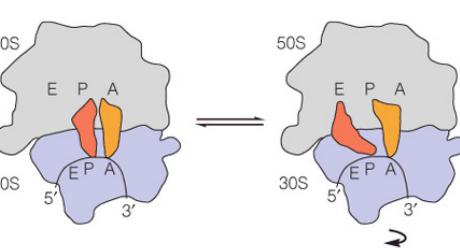
## Termination

- Stop codons: UAA, UAG, and UGA
- Three termination (release) factors:
  - RF1, EF2, and EF-3
  - RF1 binds to UAG and UAA
  - RF2 binds to UGA and UAA
- RF similar to EF-G: mimics the structural of tRNA and binds to A site
- Hydrolysis of terminal peptidyl-tRNA bond
- Release of the free peptide and the last tRNA
- Dissociation of 70S rRNA to 30S and 50S rRNAs
  - EF-G-GTP and ribosome recycling factor (RRF)
  - leads to dissociation of 50S to 30S-tRNA-mRNA complex
- IF3 replaces EF-G and RFF; promotes the dissociation of 30S to tRNA

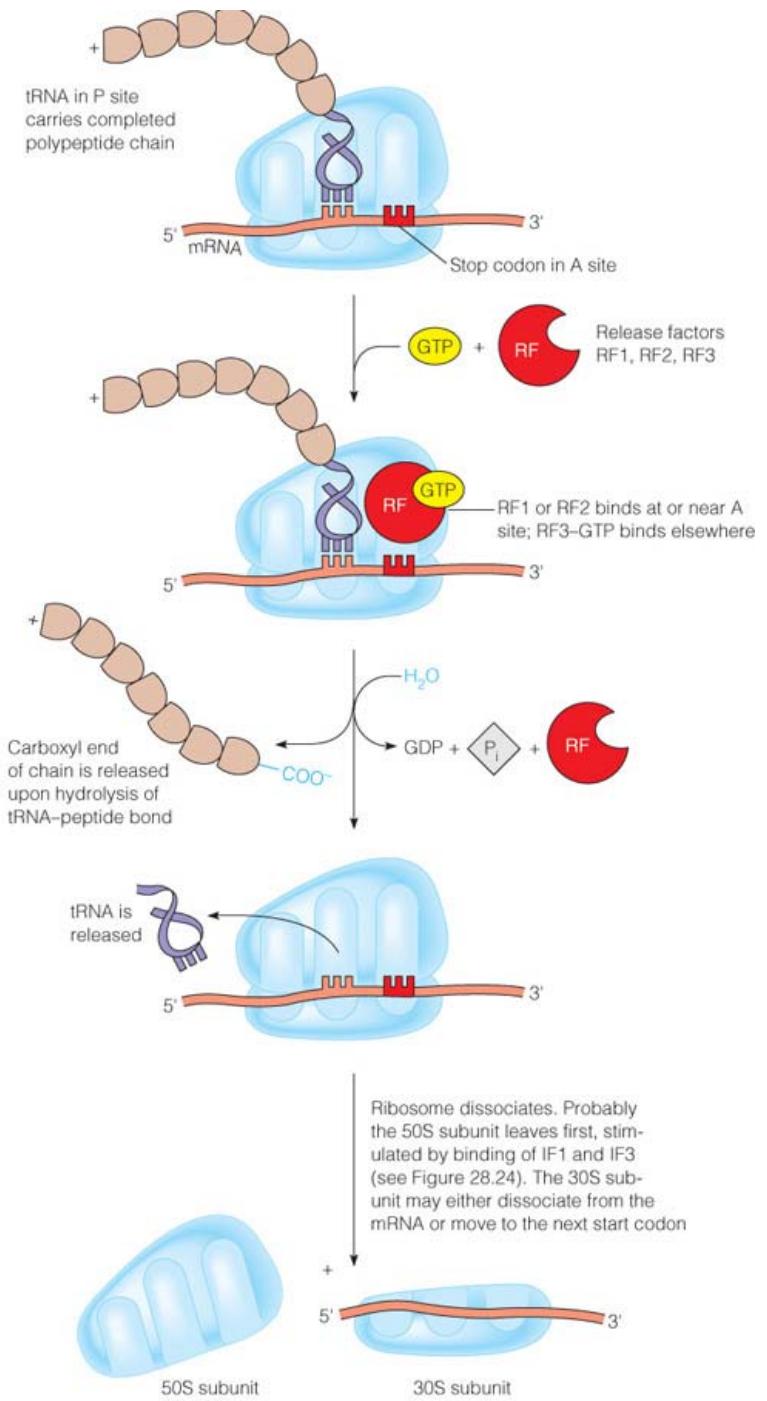
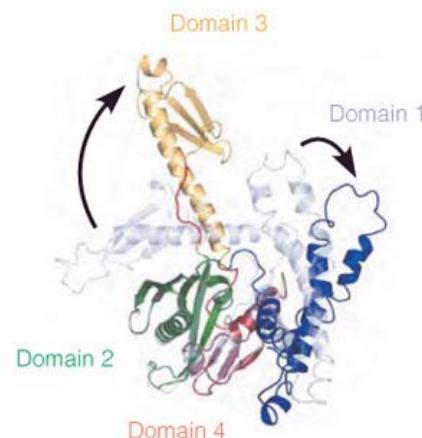
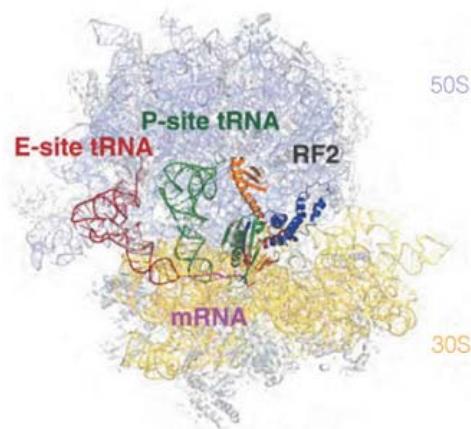
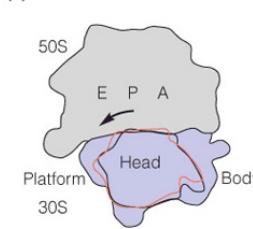
(a)

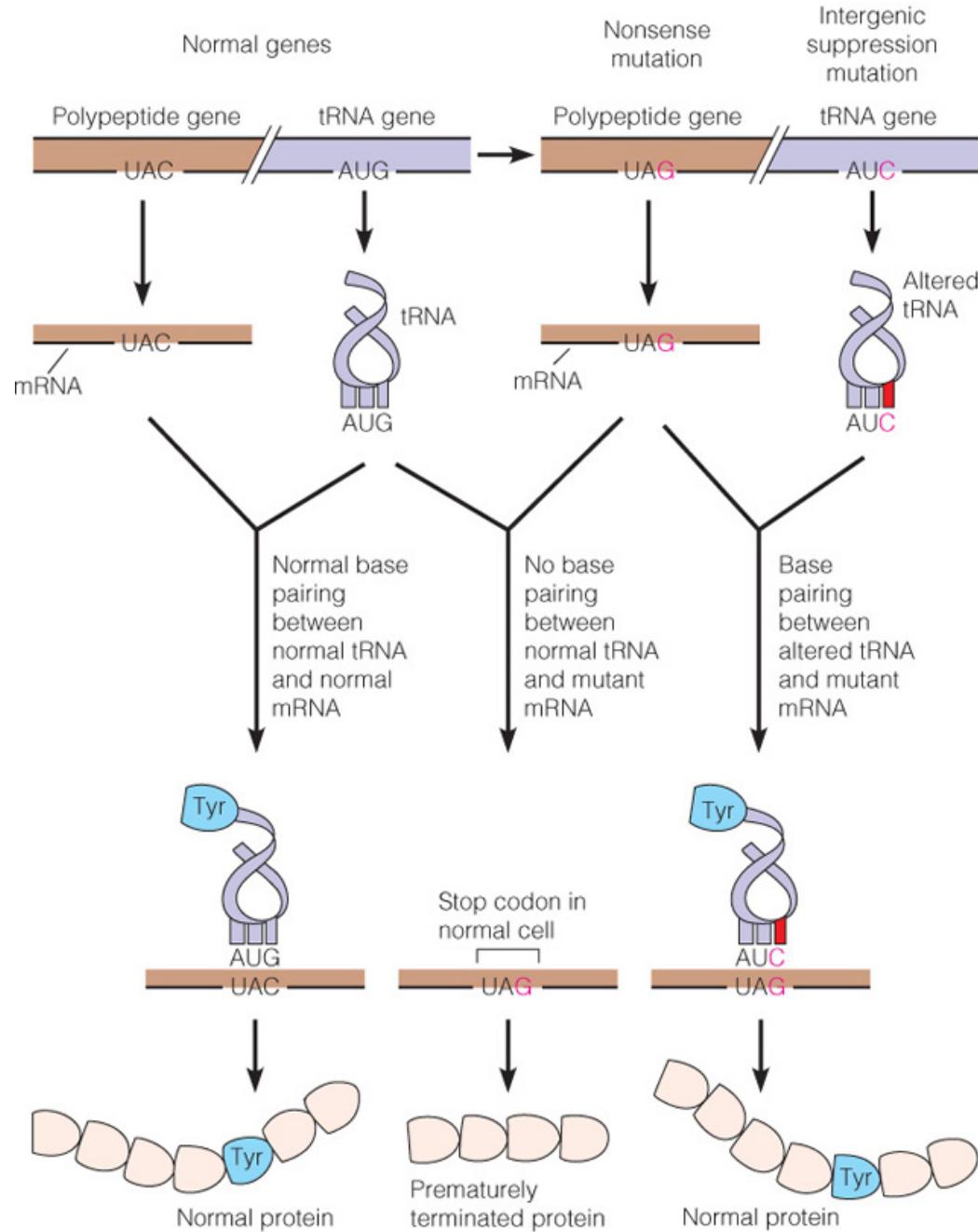


(b)



(c)





**FIGURE 28.34**

**How an intergenic suppression mutation can overcome a nonsense mutation.** A nonsense mutation in a protein-coding gene changes a codon for an amino acid into a stop codon, causing translation to terminate prematurely. Another mutation, in a tRNA gene, can circumvent the first mutation by altering the tRNA anticodon so that it will base-pair with the mutant mRNA. A functional protein is produced in this situation, even though suppression might not restore the original amino acid at that site.

# Functional homologies of prokaryotic and eukaryotic translation factors

Initiation Factors			
Prokaryotic	Eukaryotic	General Function	Notes
IF-1	eIF1A	Blocks A site	eIF1A assists eIF2 in promoting Met-tRNA <sub>i</sub> <sup>Met</sup> to binding to 40S; also promotes subunit dissociation
IF-2*†	eIF2, eIF3, eIF5B*	Entry of initiator tRNA	eIF2 is a GTPase eIF3 stimulates formation of the ternary complex, its binding to 40S, and binding and scanning of mRNA eIF5B is involved in initiator tRNA entry and is a GTPase
IF-3	eIF1, eIF4 complex, eIF3	Small subunit binding to mRNA	eIF4 complex functions in cap binding
Elongation Factors			
Prokaryotic	Eukaryotic	General Function	
EF-Tu <sup>†‡</sup> , EF-G <sup>†</sup> EF-Ts EF-G <sup>§</sup>	eEF1 $\alpha$ <sup>‡</sup> eEF1 $\beta$ , eEF1 $\gamma$ eEF2 <sup>§</sup>	GTP-binding GDP-exchanging Ribosome translocation	
Release Factors			
Prokaryotic	Eukaryotic	General Function	
RF1 RF2 RF3 <sup>†</sup>	eRF1 eRF1 eRF3	UAA/UAG recognition UAA/UGA recognition Stimulation of other RF(s)	

\* IF-2 and eIF5B have sequence homology.

† IF-2, EF-Tu, EF-G, and RF3 have sequence homology.

‡ EF-Tu and eEF1 $\alpha$  have sequence homology.

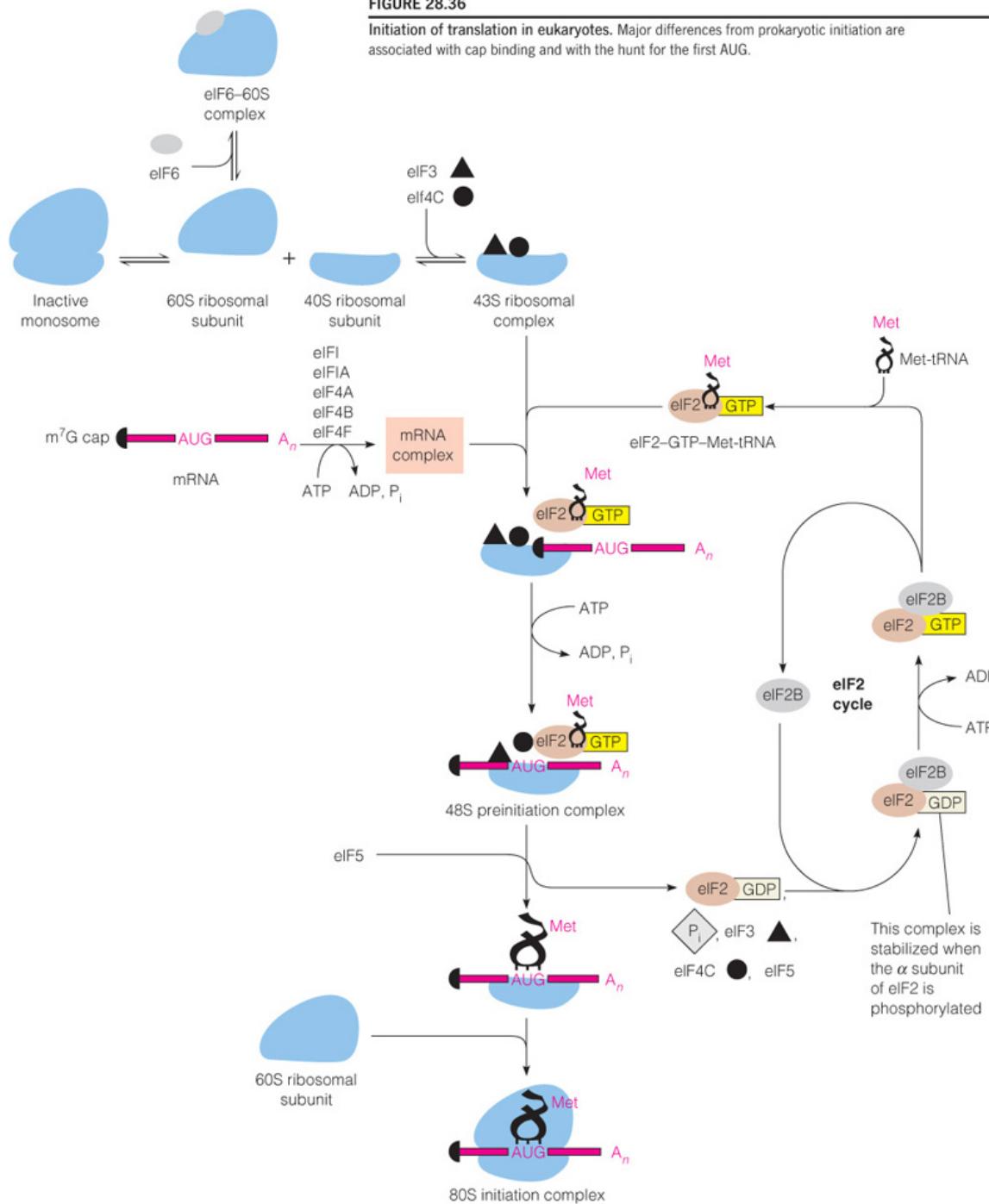
§ EF-G and eEF2 have sequence homology.

**TABLE 28.4 Soluble protein factors in translation**

Function	Factor (Bacteria)	Factor (Eukaryotes)	Role in Translation
<b>Initiation</b>	IF1	eIF1, eIF1A	Promotes dissociation of preexisting 70S ribosome
	IF2	eIF2, eIF2B	Helps attach initiator tRNA
	IF3	eIF3, eIF4C	Similar to IF1; prepares mRNA for ribosome binding
		eIF4A, eIF4B, eIF4F	Same as eIF1, eIF1A
		eIF5	Helps dissociate eIF2, eIF3, eIF4C
		eIF6	Helps dissociate 60S subunit from inactive ribosomes
<b>Elongation</b>	EF-Tu	eEF1 $\alpha$	Helps deliver aminoacyl-tRNA to ribosomes
	EF-Ts	eEF1 $\beta\gamma$	Helps recharge EF-Tu with GTP
	EF-G	eEF2	Facilitates translocation
<b>Termination</b>	RF1	eRF	Release factor (UAA, UAG)
	RF2		Release factor (UAA, UGA)
	RF3		A GTPase that promotes release

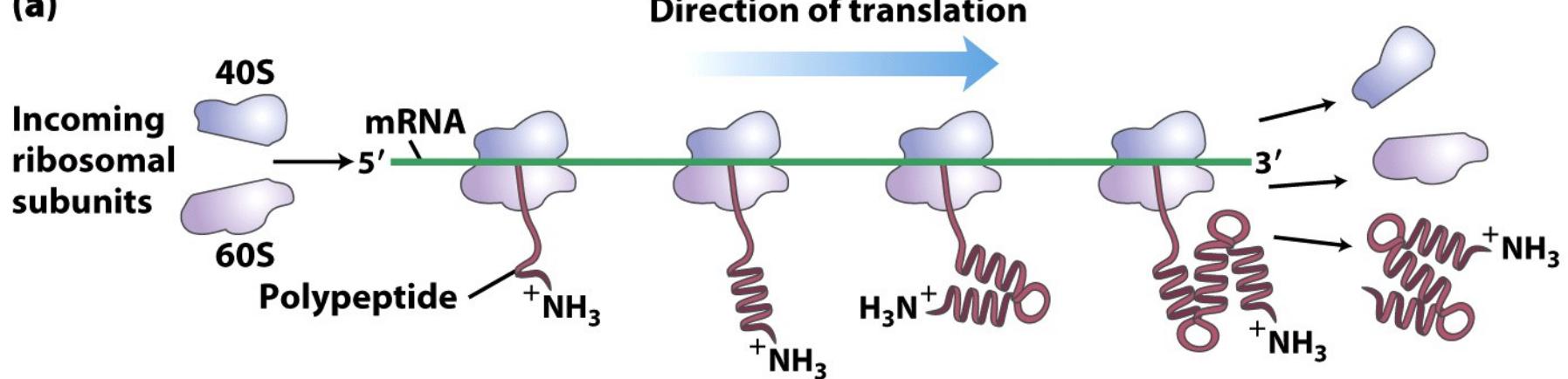
**FIGURE 28.36**

Initiation of translation in eukaryotes. Major differences from prokaryotic initiation are associated with cap binding and with the hunt for the first AUG.

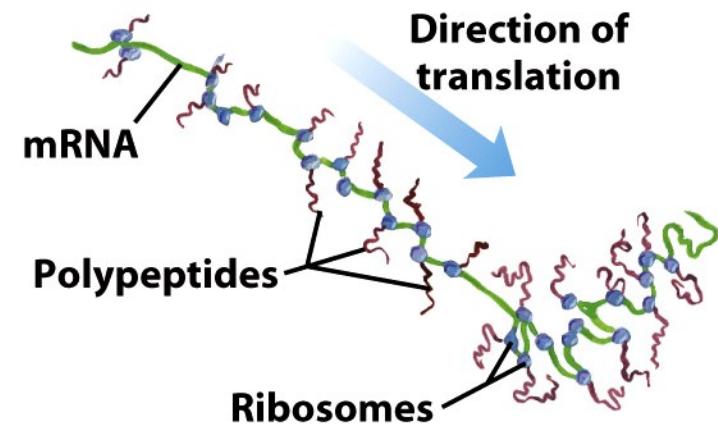
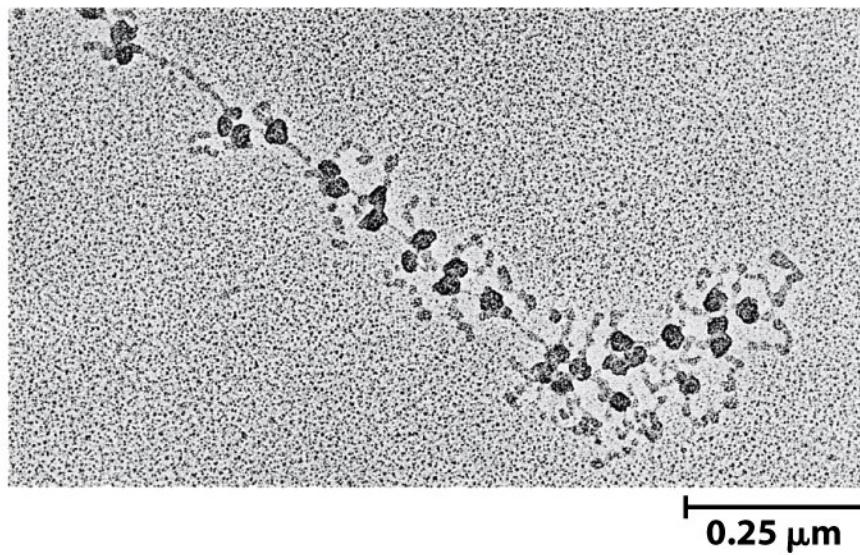


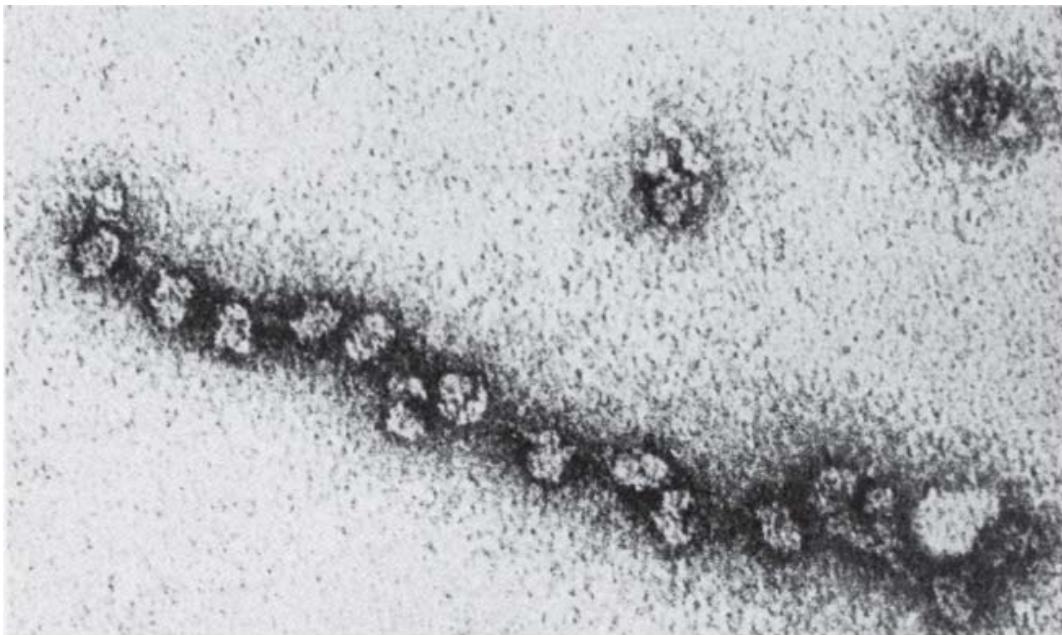
# Polysome

(a)

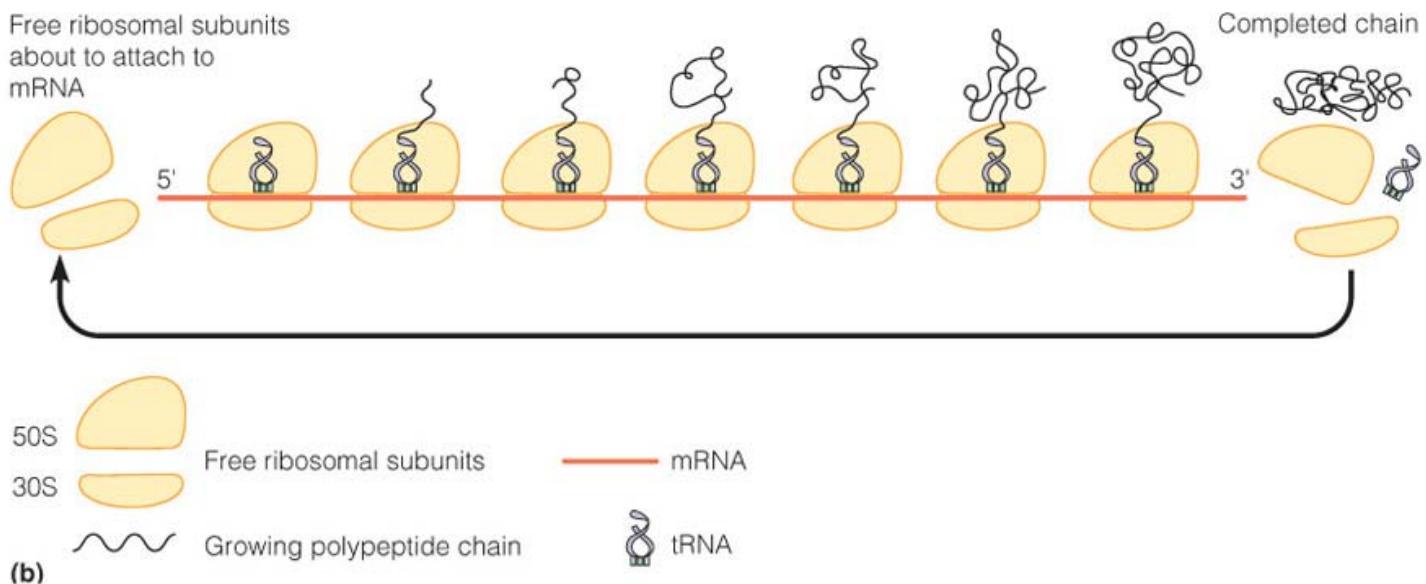


(b)





(a)



# Post-translational modification:

## ■ N-terminal & C-terminal modification:

N-acetylation

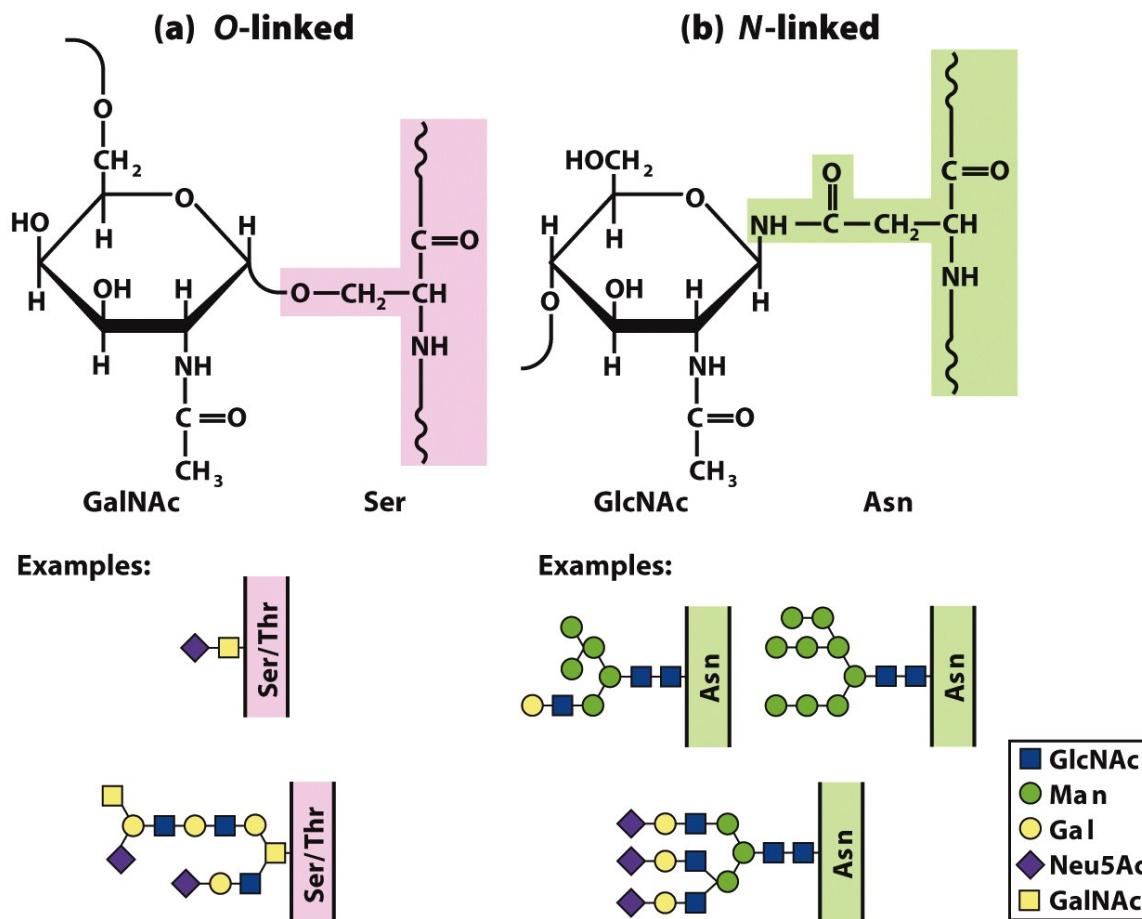
## ■ Loss of signal sequence:

Signal sequence directs protein to final destination; signal peptidase

Human influenza virus A	Human proinsulin	Bovine growth hormone	Bee promellitin	Drosophila glue protein	<small>cleavage site</small> 
Met Lys Ala Lys Leu Leu Val Leu Leu Tyr Ala Phe Val Ala Gly Asp Gln --	Met Ala Leu Trp Met Arg Leu Leu Pro Leu Leu Ala Leu Leu Ala Leu Trp Gly Pro Asp Pro Ala Ala Ala Phe Val --	Met Met Ala Ala Gly Pro Arg Thr Ser Leu Leu Leu Ala Phe Ala Leu Leu Cys Leu Pro Trp Thr Gln Val Val Gly Ala Phe --	Met Lys Phe Leu Val Asn Val Ala Leu Val Phe Met Val Val Tyr Ile Ser Tyr Ile Tyr Ala Ala Pro --	Met Lys Leu Leu Val Val Ala Val Ile Ala Cys Met Leu Ile Gly Phe Ala Asp Pro Ala Ser Gly Cys Lys --	

# Post-translational modification:

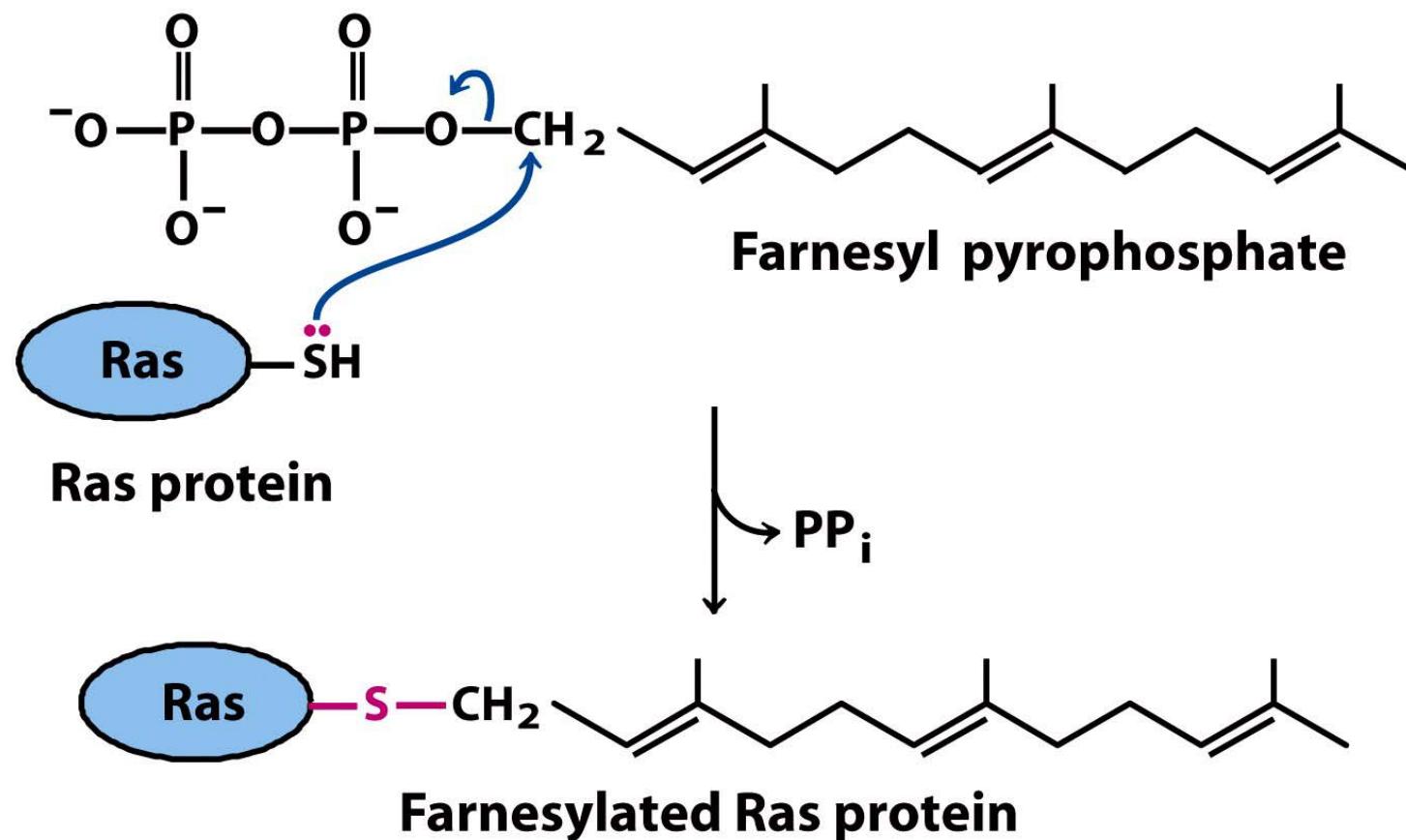
- Modification of individual amino acid:  
Attachment of carbohydrate side chain



**Figure 7-29**  
*Lehninger Principles of Biochemistry, Fifth Edition*  
© 2008 W.H. Freeman and Company

# Post-translational modification:

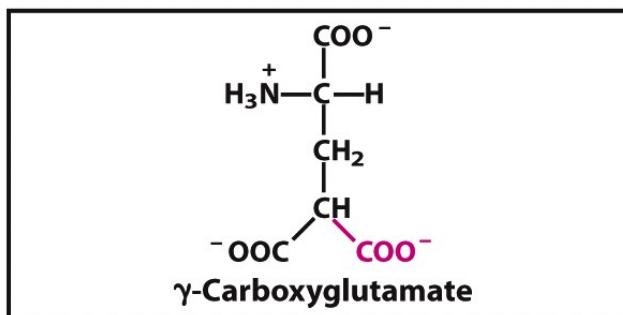
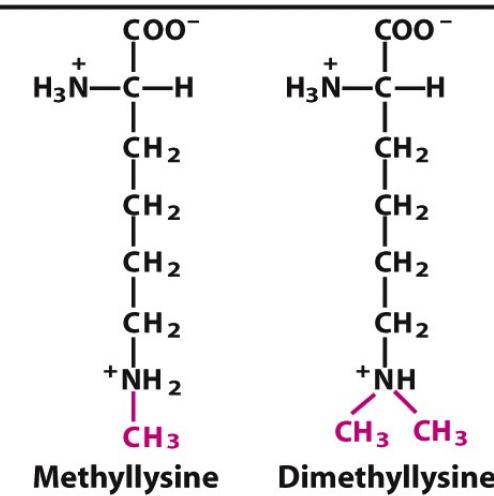
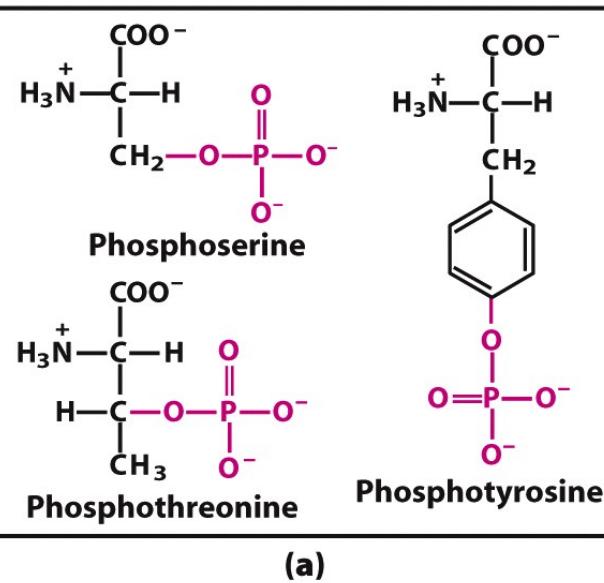
- Modification of individual amino acid:  
Addition of isoprenyl group



# Post-translational modification:

## ■ Modification of individual amino acid:

Phosphorylation, carboxylation, and methylation



(c)

# Post-translational modification:

## ■ Ubiquitination & degradation

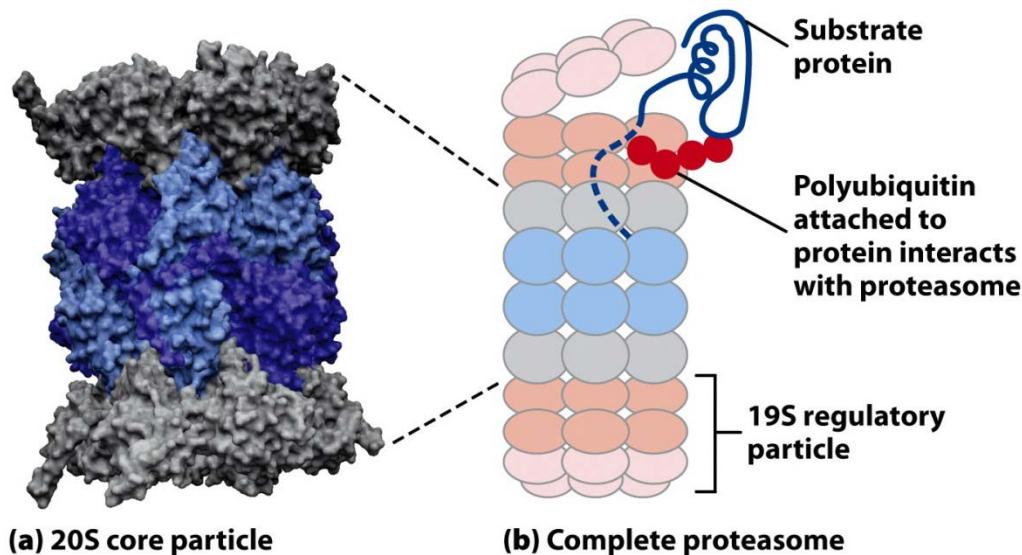


TABLE 27–9

Relationship between Protein Half-Life and Amino-Terminal Amino Acid Residue

Amino-terminal residue	Half-life*
<b>Stabilizing</b>	
Met, Gly, Ala, Ser, Thr, Val	>20 h
<b>Destabilizing</b>	
Ile, Gln	~30 min
Tyr, Glu	~10 min
Pro	~7 min
Leu, Phe, Asp, Lys	~3 min
Arg	~2 min

