تولید پروتئین از RNA

زیست شناسی مولکولی

منبع: بیوشیمی لنینجر، The cell: Alberts

Ribosome

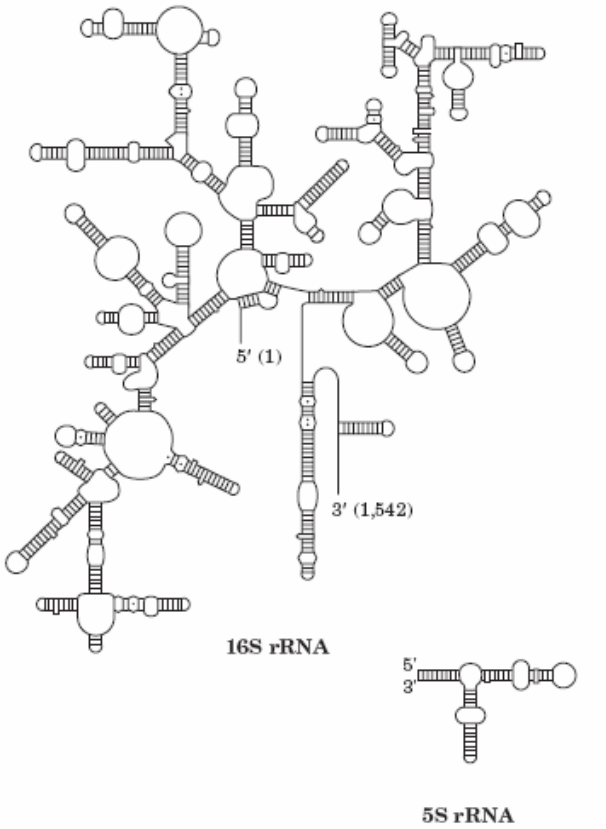
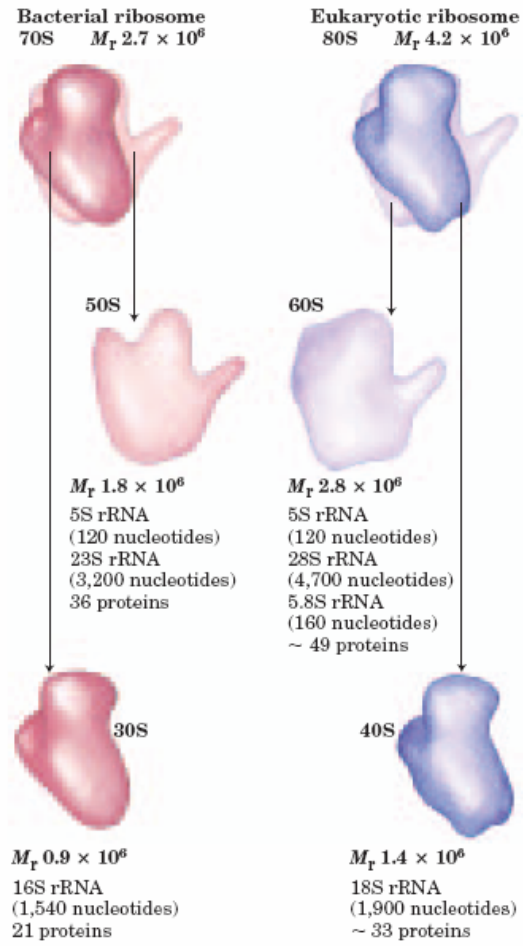


FIGURE 27–10 **Bacterial rRNAs.** Diagrams of the secondary structure of *E. coli* 16S and 5S rRNAs. The first (5′ end) and final (3′ end) ribonucleotide residues of the 16S rRNA are numbered.



tRNA

۷۳ تا ۹۳ نوکلئوتید دارند
گوانیلات در سمت ′۵
CCA در سمت ′۳

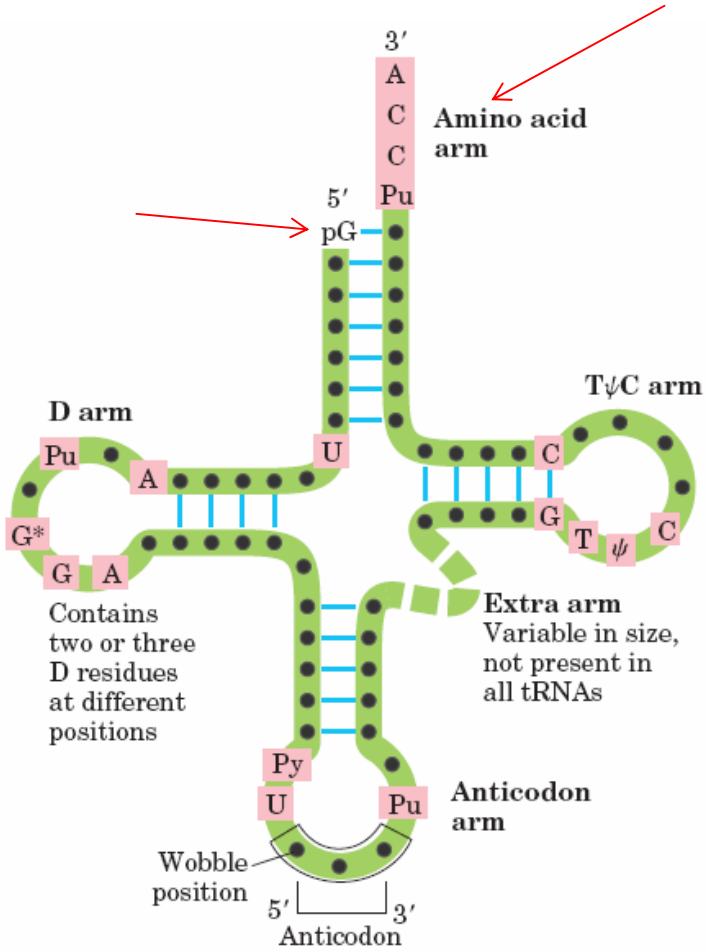
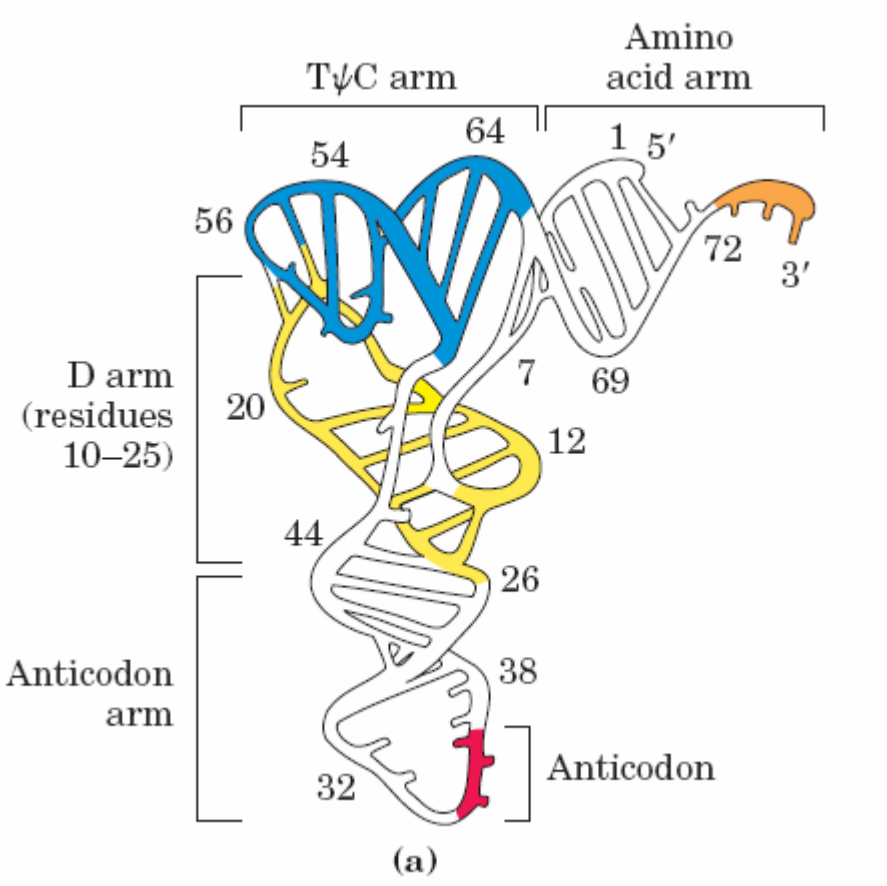


FIGURE 27–12 General cloverleaf secondary structure of tRNAs. The large dots on the backbone represent nucleotide residues; the blue lines represent base pairs. Characteristic and/or invariant residues common to all tRNAs are shaded in pink. Transfer RNAs vary in length from 73 to 93 nucleotides. Extra nucleotides occur in the extra arm or in the D arm. At the end of the anti-codon arm is the anticodon loop, which always contains seven unpaired nucleotides. The D arm contains two or three D (5,6-dihydrouridine) residues, depending on the tRNA. In some tRNAs, the D arm has only three hydrogen-bonded base pairs. In addition to the symbols explained in Figure 27–11: Pu, purine nucleotide; Py, pyrimidine nucleotide; G*, guanylate *or* 2′-*O*-methylguanylate.

tRNA


TψC arm
Amino acid arm
64
54
1
5′
56
72
3′
D arm (residues 10–25)
7
69
20
12
44
26
Anticodon arm
38
32
Anticodon
(a)

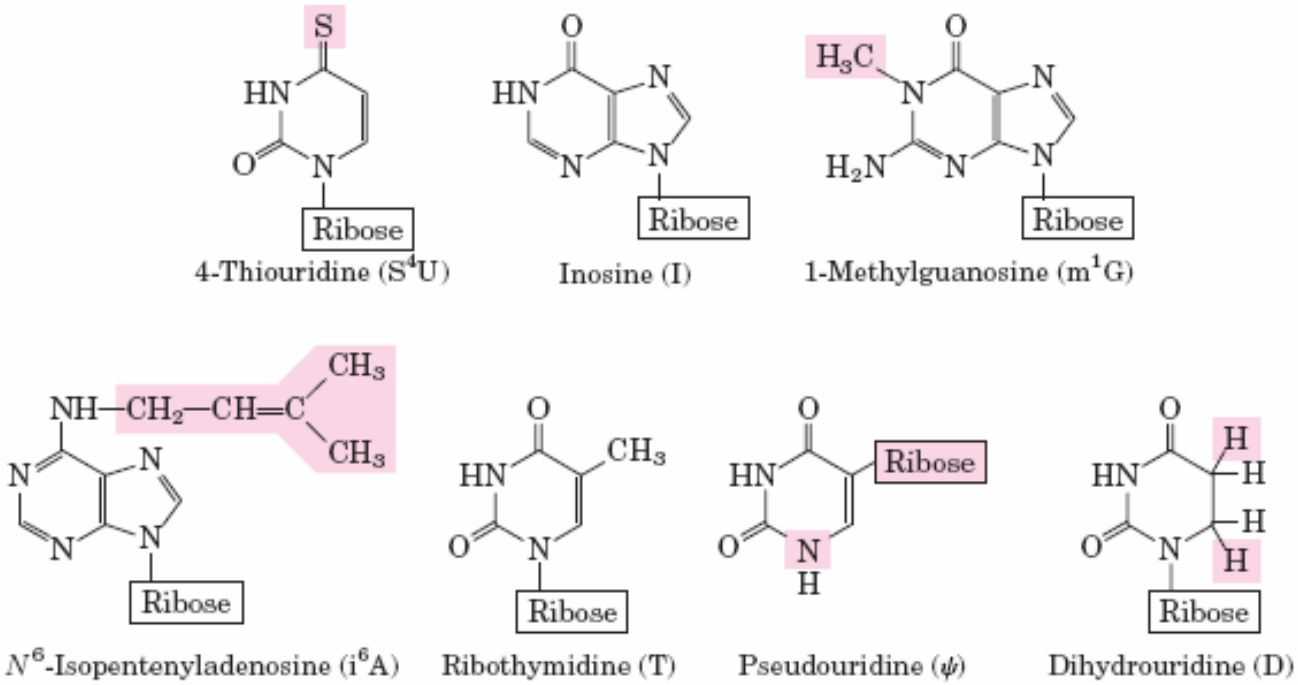
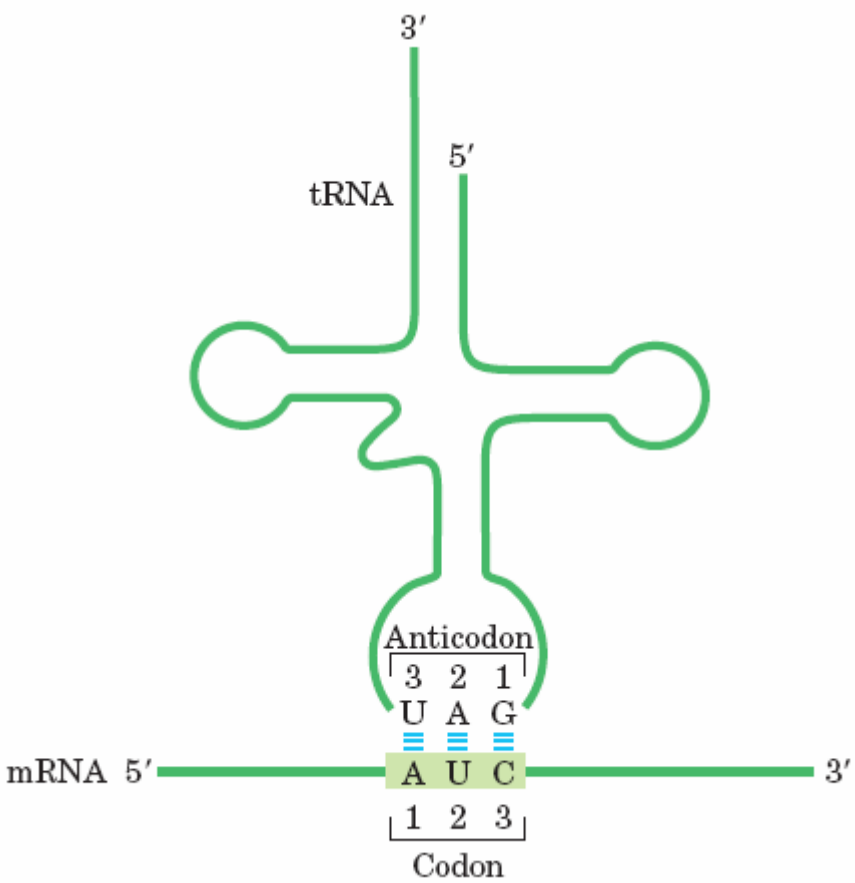


FIGURE 26–24 **Some modified bases of tRNAs, produced in posttranscriptional reactions.** The standard symbols (used in Fig. 26–23) are shown in parentheses. Note the unusual ribose attachment point in pseudouridine.


3′
5′
tRNA
Anticodon
3 2 1
U A G
mRNA 5′
A U C
3′
1 2 3
Codon

کد ژنتیکی

First letter of codon (5′ end)

Second letter of codon

	U		C		A		G	
U	UUU	Phe	UCU	Ser	UAU	Tyr	UGU	Cys
	UUC	Phe	UCC	Ser	UAC	Tyr	UGC	Cys
	UUA	Leu	UCA	Ser	UAA	Stop	UGA	Stop
	UUG	Leu	UCG	Ser	UAG	Stop	UGG	Trp
C	CUU	Leu	CCU	Pro	CAU	His	CGU	Arg
	CUC	Leu	CCC	Pro	CAC	His	CGC	Arg
	CUA	Leu	CCA	Pro	CAA	Gln	CGA	Arg
	CUG	Leu	CCG	Pro	CAG	Gln	CGG	Arg
A	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
G	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

FIGURE 27–7 "Dictionary" of amino acid code words in mRNAs. The codons are written in the 5′⟶3′ direction. The third base of each codon (in bold type) plays a lesser role in specifying an amino acid than the first two. The three termination codons are shaded in pink, the initiation codon AUG in green. All the amino acids except methionine and tryptophan have more than one codon. In most cases, codons that specify the same amino acid differ only at the third base.

TABLE 27–3 Degeneracy of the Genetic Code

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

کدون شروع

کدون ختم

تکرار پذیری یا **Degeneracy**

عمومیت کد ژنتیکی

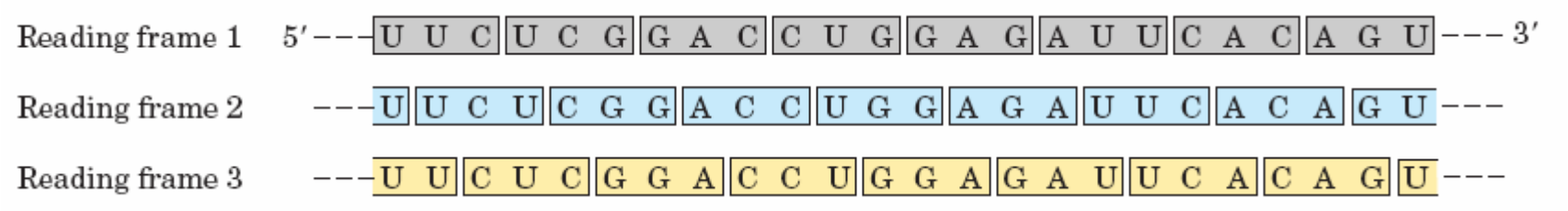
TABLE 4-2 Known Deviations from the Universal Genetic Code

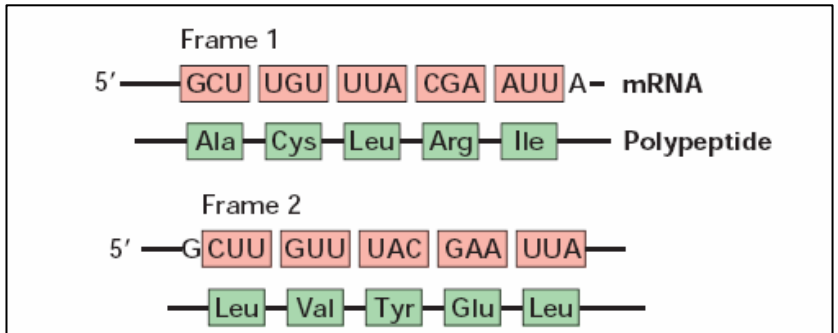
Codon	Universal Code	Unusual Code*	Occurrence
UGA	Stop	Trp	*Mycoplasma, Spiroplasma,* mitochondria of many species
CUG	Leu	Thr	Mitochondria in yeasts
UAA, UAG	Stop	Gln	*Acetabularia, Tetrahymena,* Paramecium, etc.
UGA	Stop	Cys	*Euplotes*

*"Unusual code" is used in nuclear genes of the listed organisms and in mitochondrial genes as indicated.
SOURCE: S. Osawa et al., 1992, *Microbiol. Rev.* **56**:229.

Reading frame

- عدم وجود فاصله بین کدون ها
- سه قالب خواندن





▲ FIGURE 4-20 Example of how the genetic code—a non-overlapping, comma-less triplet code—can be read in different frames. If translation of the mRNA sequence shown begins at two different upstream start sites (not shown), then two overlapping reading frames are possible. In this example, the codons are shifted one base to the right in the lower frame. As a result, the same nucleotide sequence specifies different amino acids during translation. Although they are rare, many

باز سوم آنتی کدون

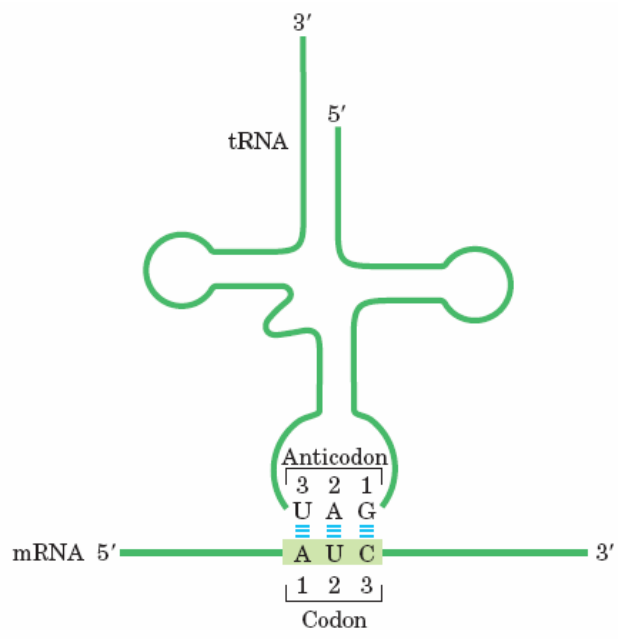
Degeneracy

GGU	Gly
GGC	Gly
GGA	Gly
GGG	Gly

$XY\begin{matrix}A\\G\end{matrix}$

$XY\begin{matrix}U\\C\end{matrix}$

AAU	Asn
AAC	Asn
AAA	Lys
AAG	Lys
GAU	Asp
GAC	Asp
GAA	Glu
GAG	Glu
CAU	His
CAC	His
CAA	Gln
CAG	Gln



آیا برای شناسایی کدون های متفاوت یک اسید آمینه tRNA های مختلف مورد نیاز است؟

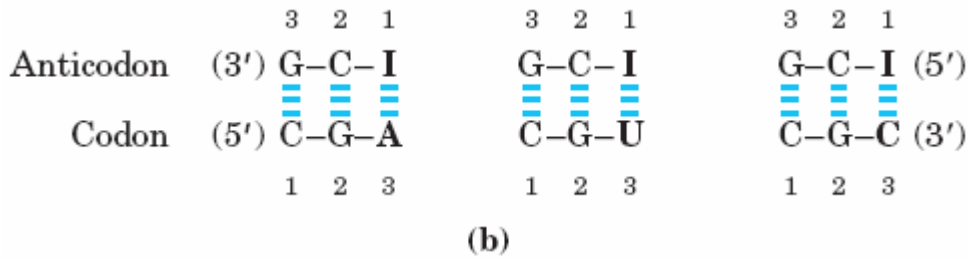
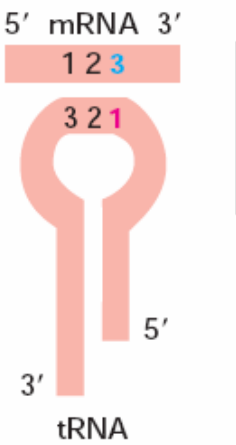


FIGURE 27–8 **Pairing relationship of codon and anticodon.** (a) Alignment of the two RNAs is antiparallel. The tRNA is shown in the traditional cloverleaf configuration. (b) Three different codon pairing relationships are possible when the tRNA anticodon contains inosinate.

نوکلئوتید اینوزینات دارای باز غیر معمول هیپوگزانتین پیوند هیدروژنی ضعیف ایجاد می کند.

فرضیه لرزش باز سوم

- ۱) دو باز ابتدائی کدون mRNA همیشه ایجاد جفت-های قوی واتسون- کریک با بازهای مربوط بر روی آنتی-کدون tRNA نموده و بیشترین ویژگی کدشدن را سبب می-شوند.



If these bases are in third, or wobble, position of codon of an mRNA

C	A	G	U	then the codon may be recognized by a tRNA having these bases in first position of anticodon
G I	U I	C U	A G I	

فرضیه لرزش باز سوم

- ۲) اولین باز در آنتی کدون (در جهت '۵ به '۳ بخوانید؛ با باز سوم کدون جفت می شود) تعیین کننده تعداد کدون هایی است که توسط tRNA شناسایی می گردد. وقتی اولین باز آنتی کدون A یا C است، ایجاد جفت باز اختصاصی بوده و تنها یک کدون توسط tRNA شناسایی می گردد. وقتی این باز U یا G می باشد، ایجاد جفت باز کمتر اختصاصی بوده و ممکن است دو کدون مختلف خوانده شود. اما وقتی اینوزینات اولین نوکلئوتید (لرزان) یک آنتی کدون است، سه کدون مختلف (حداکثر تعداد ممکن برای هر tRNA) قابل شناسایی خواهد بود.

فرضیه لرزش باز سوم

- ۳)وقتی یک اسید آمینه توسط چندین کدون مشخص می گردد. کدون هایی که در یکی از دو باز ابتدایی متفاوتند، نیاز به ملکول مختلف tRNA برای شناسایی دارند.
- ۴)برای ترجمه تمامی ۶۱ کدون، نیاز به حداقل ۳۲ ملکول tRNA است.

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

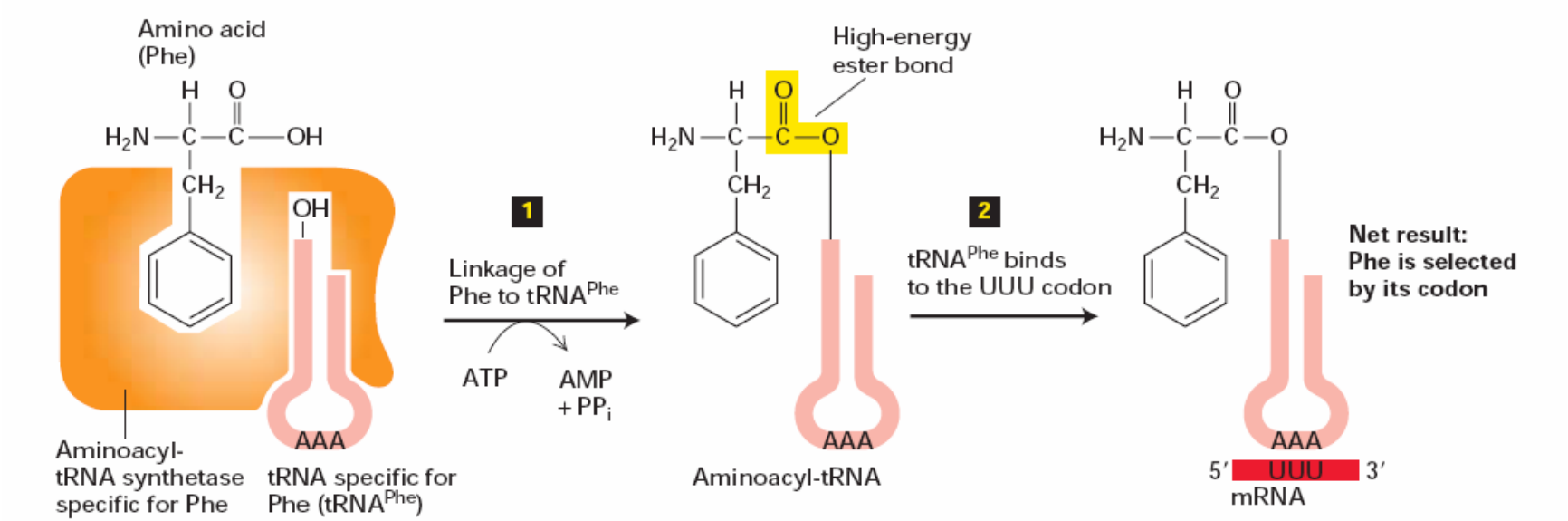
1. One codon recognized:
   1. Anticodon (3′) X–Y–**C** (5′) | (3′) X–Y–**A** (5′)
      Codon (5′) Y–X–**G** (3′) | (5′) Y–X–**U** (3′)
2. Two codons recognized:
   1. Anticodon (3′) X–Y–**U** (5′) | (3′) X–Y–**G** (5′)
      Codon (5′) Y–X–**A G** (3′) | (5′) Y–X–**C U** (3′)
3. Three codons recognized:
   1. Anticodon (3′) X–Y–**I** (5′)
      Codon (5′) Y–X–**A U C** (3′)

Note: X and Y denote bases complementary to and capable of strong Watson-Crick base pairing with X′ and Y′, respectively. Wobble bases—in the 3′ position of codons and 5′ position of anticodons—are shaded in pink.

If these bases are in third, or wobble, position of codon of an mRNA

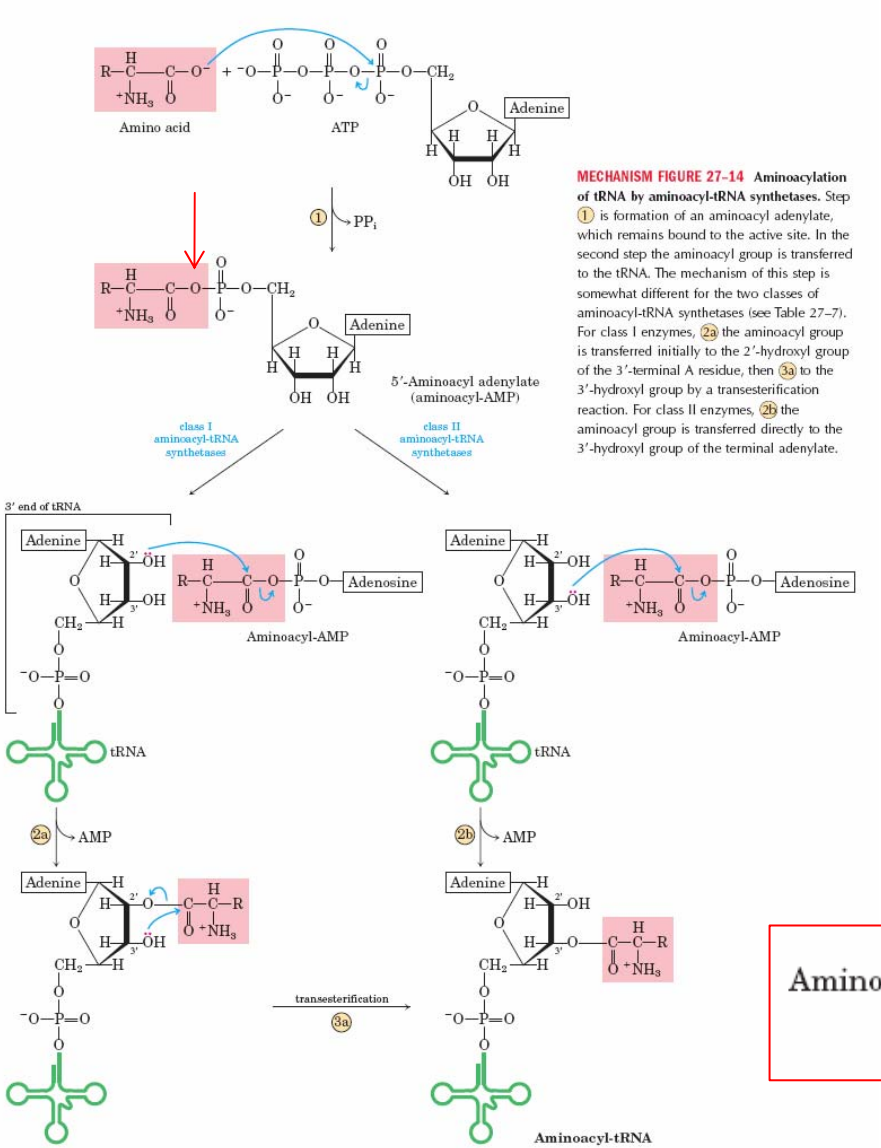
C	A	G	U	
G I	U I	C U	A G I	then the codon may be recognized by a tRNA having these bases in first position of anticodon

فعال شدن tRNA



▲ FIGURE 4-21 Two-step decoding process for translating nucleic acid sequences in mRNA into amino acid sequences in proteins. Step 1: An aminoacyl-tRNA synthetase first couples a specific amino acid, via a high-energy ester bond (yellow), to either the 2′ or 3′ hydroxyl of the terminal adenosine in the corresponding tRNA. Step 2: A three-base sequence in the tRNA (the anticodon) then base-pairs with a codon in the mRNA specifying the attached amino acid. If an error occurs in either step, the wrong amino acid may be incorporated into a polypeptide chain. Phe = phenylalanine.

اتصال اسید آمینه به tRNA



MECHANISM FIGURE 27–14 Aminoacylation of tRNA by aminoacyl-tRNA synthetases. Step (1) is formation of an aminoacyl adenylate, which remains bound to the active site. In the second step the aminoacyl group is transferred to the tRNA. The mechanism of this step is somewhat different for the two classes of aminoacyl-tRNA synthetases (see Table 27–7). For class I enzymes, (2a) the aminoacyl group is transferred initially to the 2′-hydroxyl group of the 3′-terminal A residue, then (3a) to the 3′-hydroxyl group by a transesterification reaction. For class II enzymes, (2b) the aminoacyl group is transferred directly to the 3′-hydroxyl group of the terminal adenylate.

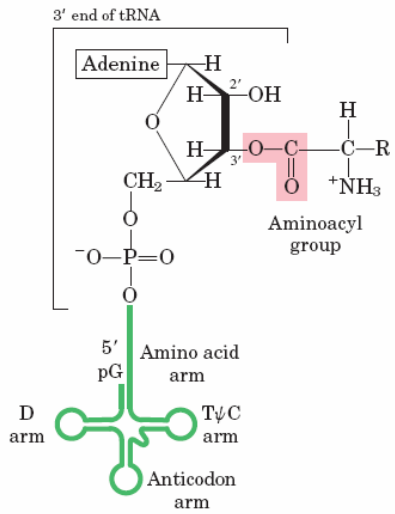


FIGURE 27–15 General structure of aminoacyl-tRNAs. The aminoacyl group is esterified to the 3′ position of the terminal A residue. The ester linkage that both activates the amino acid and joins it to the tRNA is shaded pink.

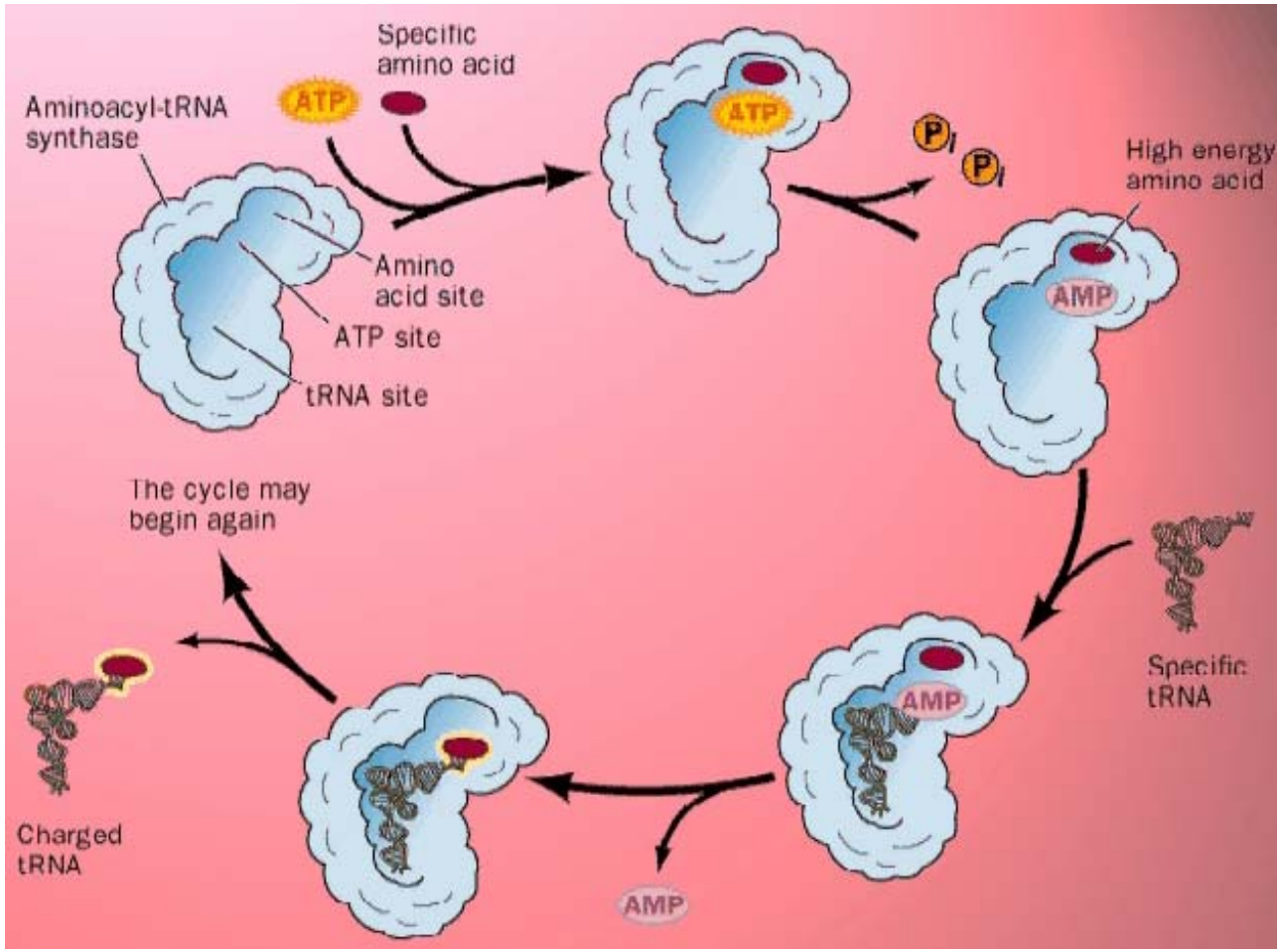
$$\text{Amino acid} + \text{tRNA} + \text{ATP} \xrightleftharpoons{Mg^{2+}} \text{aminoacyl-tRNA} + \text{AMP} + PP_i$$

TABLE 27–7 The Two Classes of Aminoacyl-tRNA Synthetases

Class I		*Class II*	
Arg	Leu	Ala	Lys
Cys	Met	Asn	Phe
Gln	Trp	Asp	Pro
Glu	Tyr	Gly	Ser
Ile	Val	His	Thr

Note: Here, Arg represents arginyl-tRNA synthetase, and so forth. The classification applies to all organisms for which tRNA synthetases have been analyzed and is based on protein structural distinctions and on the mechanistic distinction outlined in Figure 27–14.

شارژ کردن tRNA



کد ژنتیکی دوم

- آبی در تمام tRNA ها یکسان
- نارنجی در یک tRNA
- سبز در چند tRNA

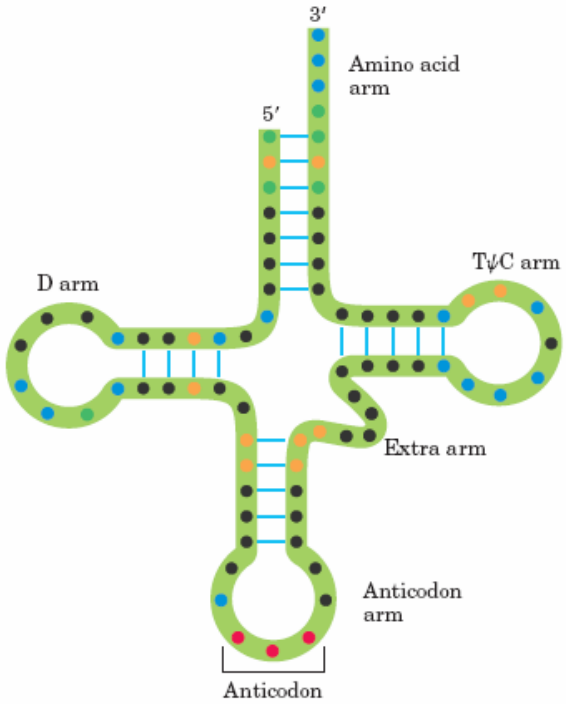


FIGURE 27-16 Nucleotide positions in tRNAs that are recognized by aminoacyl-tRNA synthetases. Some positions (blue dots) are the same in all tRNAs and therefore cannot be used to discriminate one from another. Other positions are known recognition points for one (orange) or more (green) aminoacyl-tRNA synthetases. Structural features other than sequence are important for recognition by some of the synthetases.

کد ژنتیکی دوم

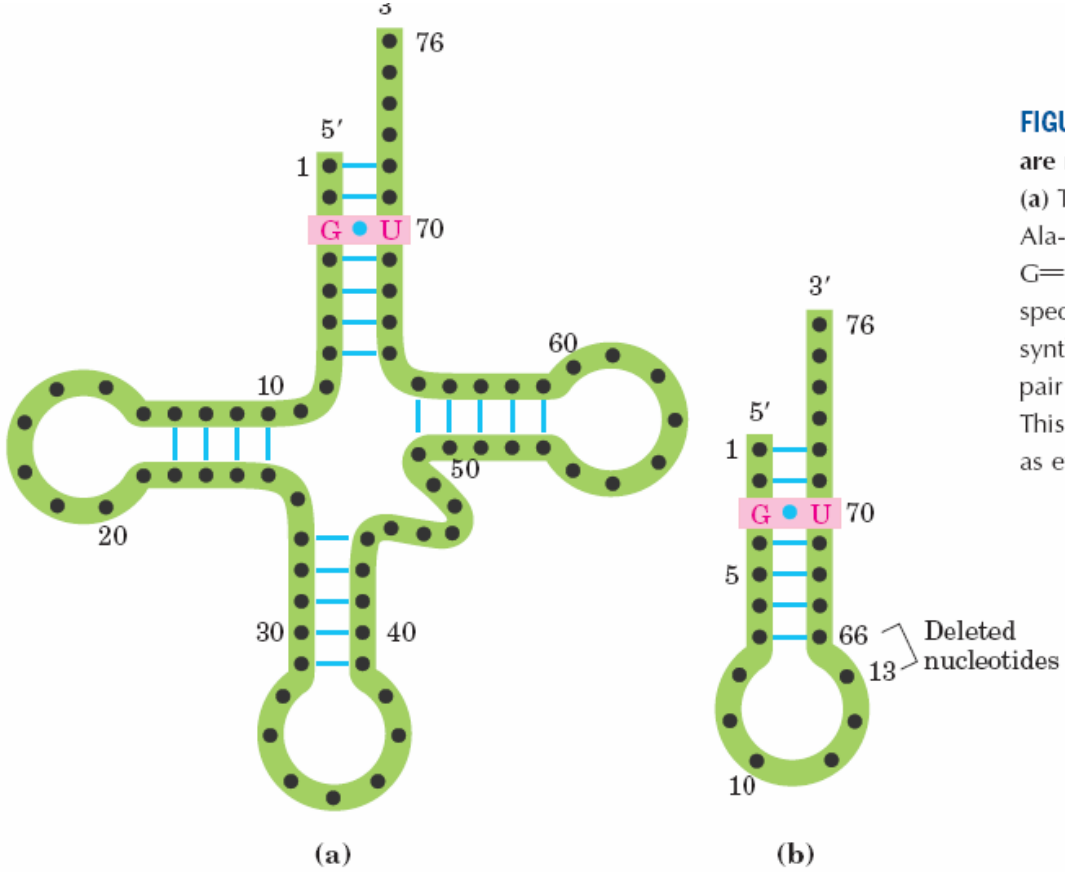


FIGURE 27-18 **Structural elements of $tRNA^{Ala}$ that are required for recognition by Ala-tRNA synthetase.** **(a)** The $tRNA^{Ala}$ structural elements recognized by the Ala-tRNA synthetase are unusually simple. A single G═U base pair (pink) is the only element needed for specific binding and aminoacylation. **(b)** A short synthetic RNA minihelix, with the critical G═U base pair but lacking most of the remaining tRNA structure. This is specifically aminoacylated with alanine almost as efficiently as the complete $tRNA^{Ala}$.

توالی شاین–دالگارنو

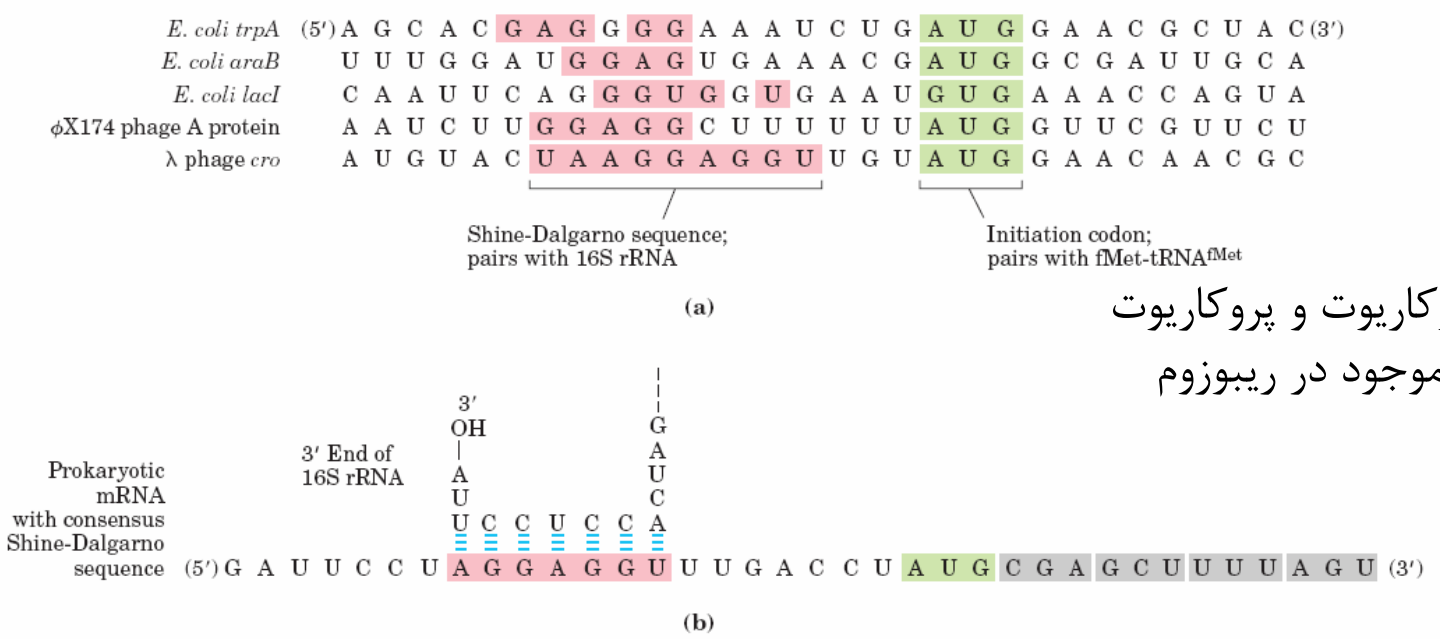


FIGURE 27-21 **Messenger RNA sequences that serve as signals for initiation of protein synthesis in bacteria.** **(a)** Alignment of the initiating AUG (shaded in green) at its correct location on the 30S ribosomal subunit depends in part on upstream Shine-Dalgarno sequences (pink). Portions of the mRNA transcripts of five prokaryotic genes are shown. Note the unusual example of the *E. coli* LacI protein, which initiates with a GUG (Val) codon (see Box 27–2). **(b)** The Shine-Dalgarno sequence of the mRNA pairs with a sequence near the 3′ end of the 16S rRNA.

- tRNA آغازی در یوکاریوت و پروکاریوت
- جایگاه های مختلف موجود در ریبوزوم
- فاکتور های آغازی

مرحله آغازی

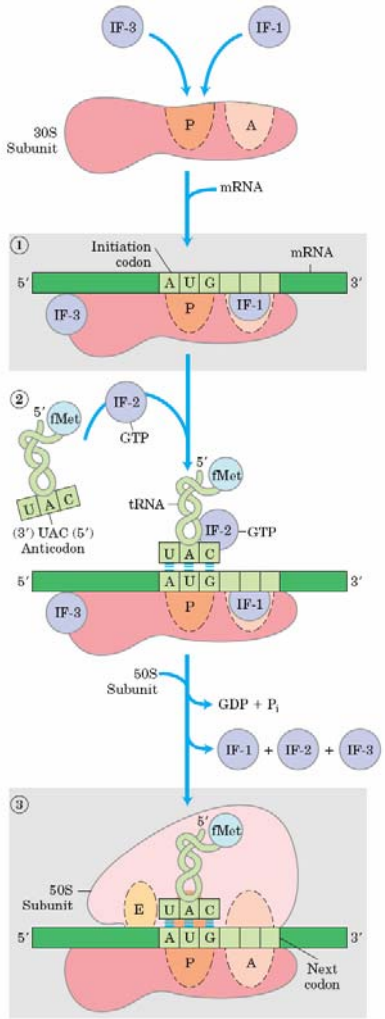


FIGURE 27-20 Formation of the initiation complex in bacteria. The complex forms in three steps (described in the text) at the expense of the hydrolysis of GTP to GDP and P_i. IF-1, IF-2, and IF-3 are initiation factors. P designates the peptidyl site, A the aminoacyl site, and E the exit site. Here the anticodon of the tRNA is oriented 3′ to 5′, left to right, as in Figure 27-8 but opposite to the orientation in Fig-

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

Factor	*Function*
Bacterial	
IF-1	Prevents premature binding of tRNAs to A site
IF-2	Facilitates binding of fMet-tRNA^{fMet} to 30S ribosomal subunit
IF-3	Binds to 30S subunit; prevents premature association of 50S subunit; enhances specificity of P site for fMet-tRNA^{fMet}
Eukaryotic*	
eIF2	Facilitates binding of initiating Met-tRNA^{Met} to 40S ribosomal subunit
eIF2B, eIF3	First factors to bind 40S subunit; facilitate subsequent steps
eIF4A	RNA helicase activity removes secondary structure in the mRNA to permit binding to 40S subunit; part of the eIF4F complex
eIF4B	Binds to mRNA; facilitates scanning of mRNA to locate the first AUG
eIF4E	Binds to the 5′ cap of mRNA; part of the eIF4F complex
eIF4G	Binds to eIF4E and to poly(A) binding protein (PAB); part of the eIF4F complex
eIF5	Promotes dissociation of several other initiation factors from 40S subunit as a prelude to association of 60S subunit to form 80S initiation complex
eIF6	Facilitates dissociation of inactive 80S ribosome into 40S and 60S subunits

*The prefix "e" identifies these as eukaryotic factors.

مرحله طویل شدن

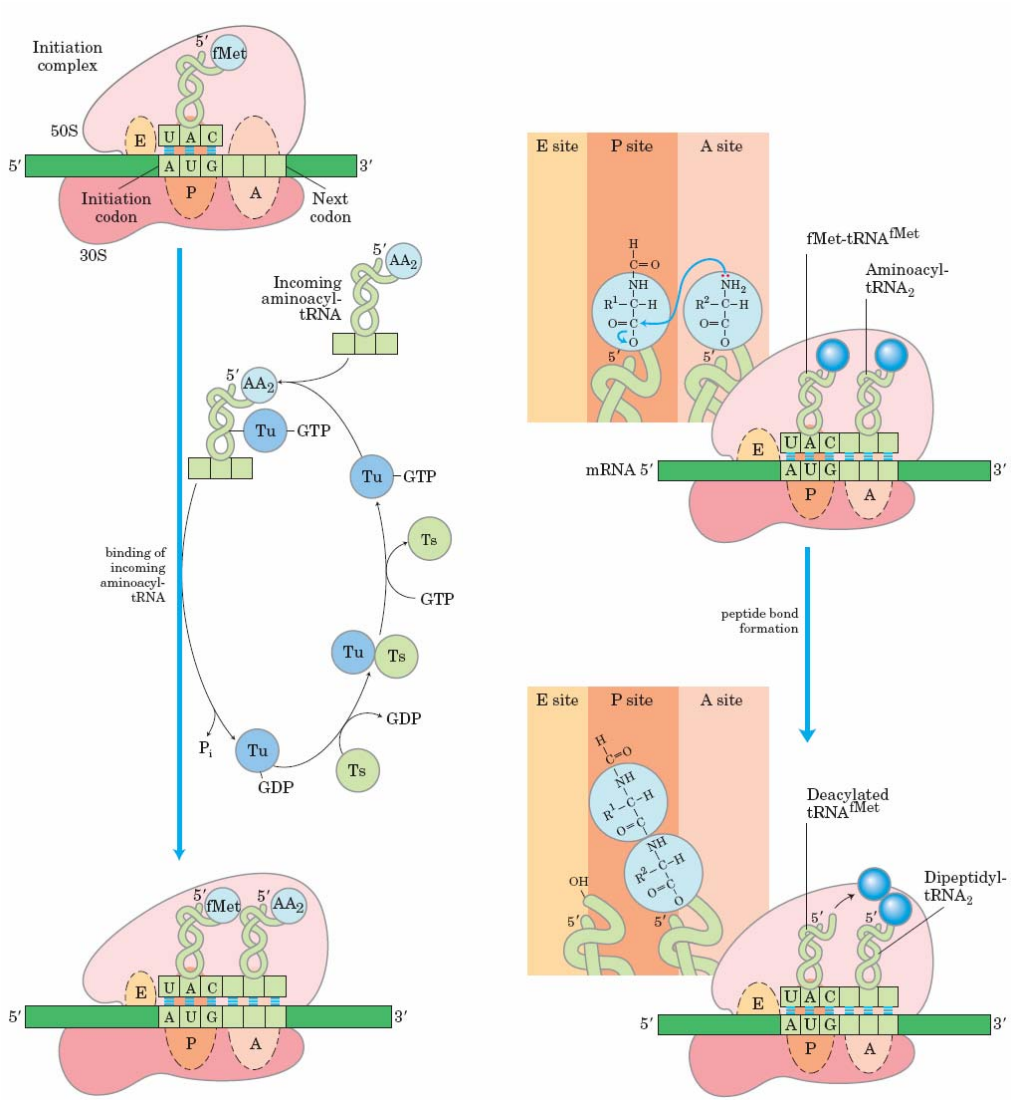
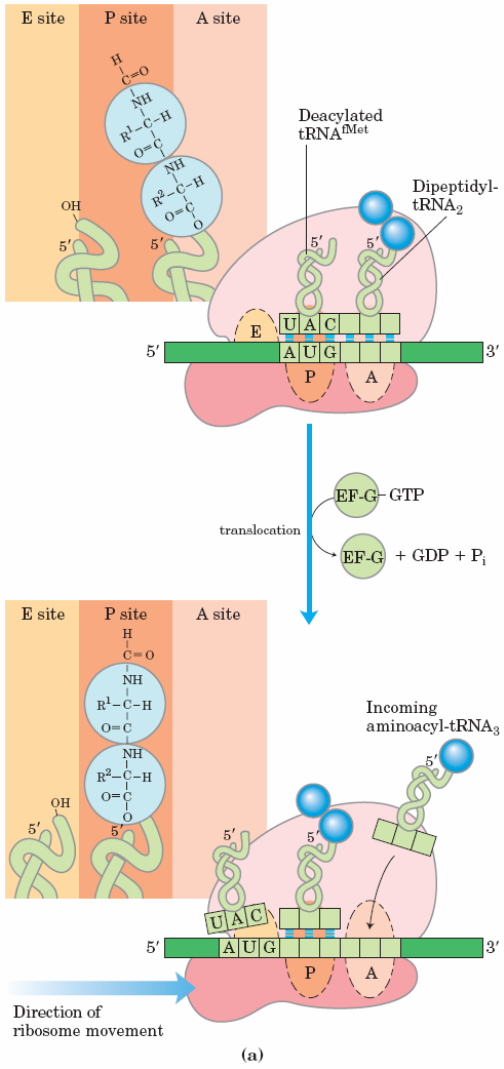


FIGURE 27-23 First elongation step in bacteria: binding of the sec-

FIGURE 27-24 Second elongation step in bacteria: formation of the

مرحله طویل شدن



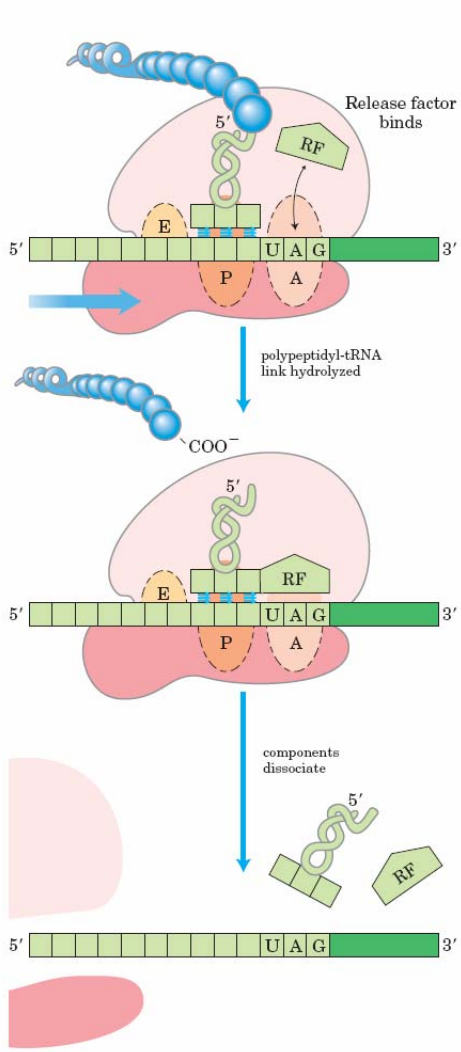
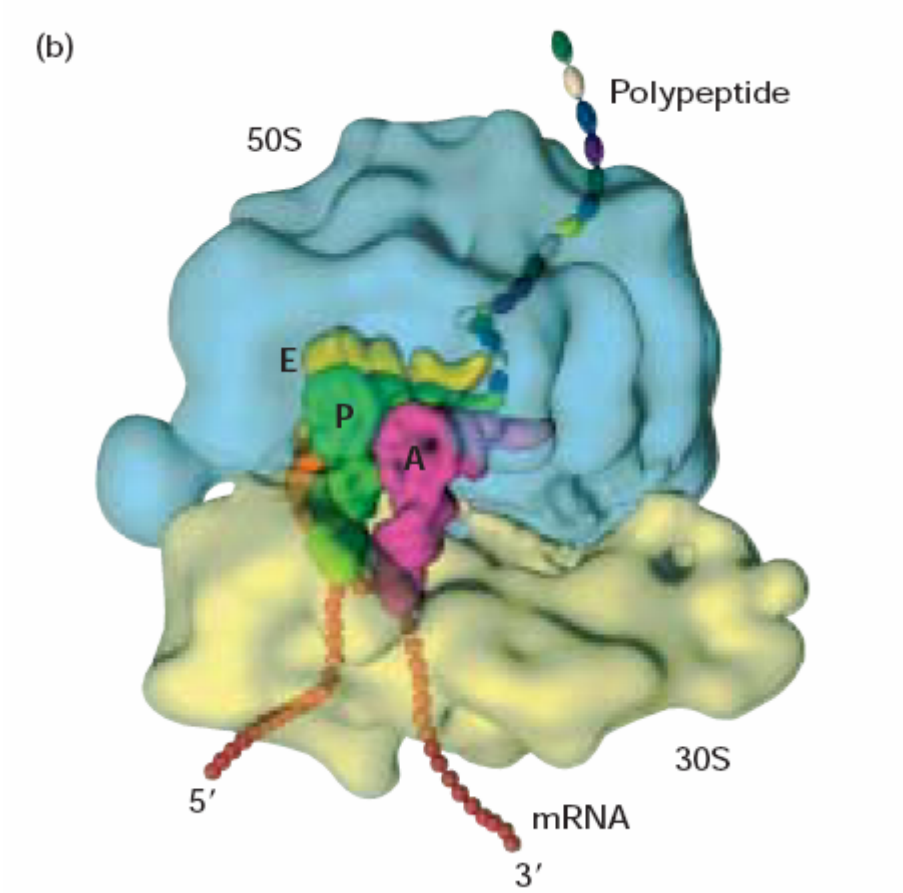


FIGURE 27-26 **Termination of protein synthesis in bacteria.** Termination occurs in response to a termination codon in the A site. First, a release factor, RF (RF-1 or RF-2, depending on which termination


(b)
Polypeptide
50S
E
P
A
30S
5′
mRNA
3′

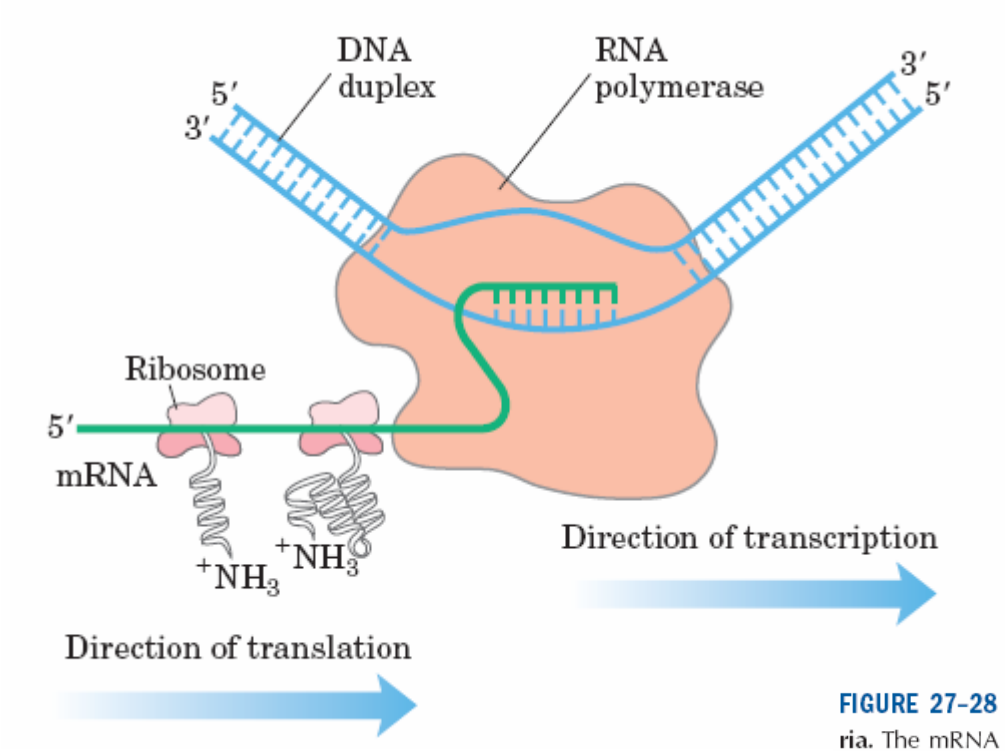
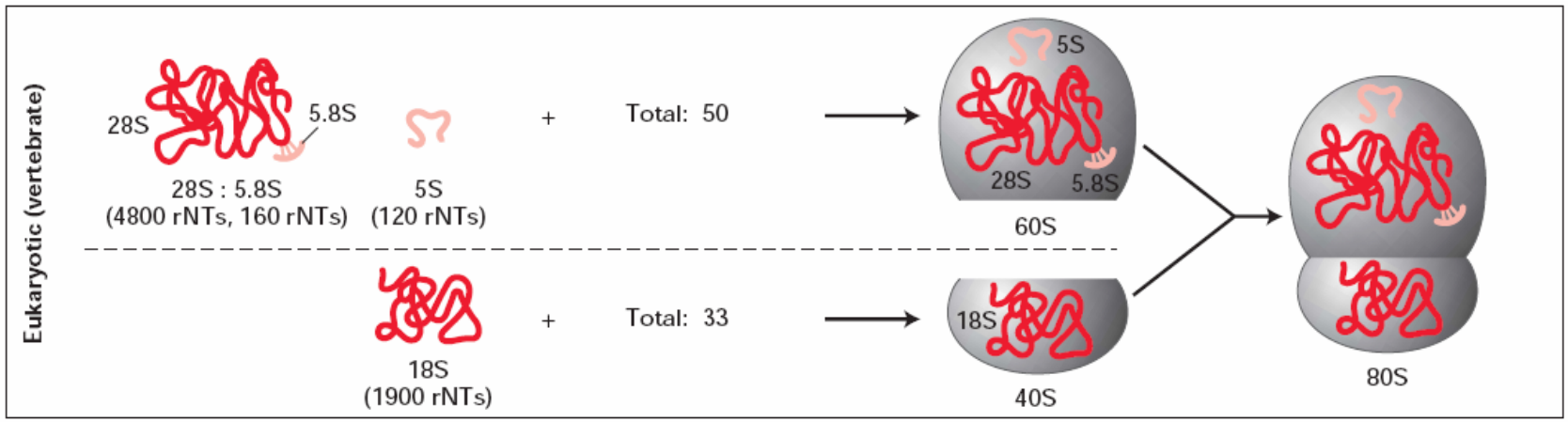
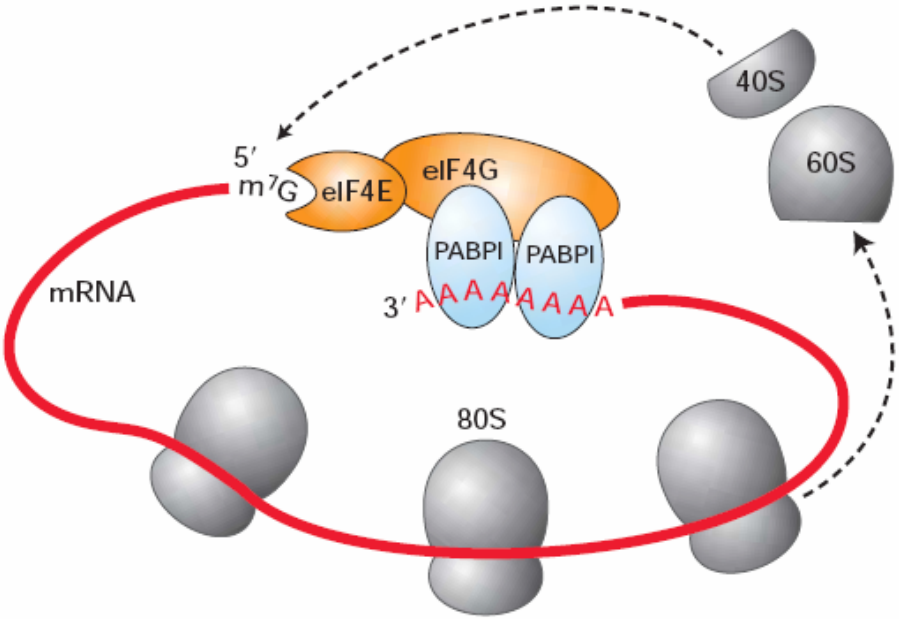


FIGURE 27–28 Coupling of transcription and translation in bacteria. The mRNA is translated by ribosomes while it is still being transcribed from DNA by RNA polymerase. This is possible because the mRNA in bacteria does not have to be transported from a nucleus to the cytoplasm before encountering ribosomes. In this schematic diagram the ribosomes are depicted as smaller than the RNA polymerase. In reality the ribosomes (M_r 2.7×10^6) are an order of magnitude larger than the RNA polymerase (M_r 3.9×10^5).



▲ FIGURE 4-24 The general structure of ribosomes in prokaryotes and eukaryotes. In all cells, each ribosome consists of a large and a small subunit. The two subunits contain rRNAs (red) of different lengths, as well as a different set of proteins. All ribosomes contain two major rRNA molecules (23S and 16S rRNA in bacteria; 28S and 18S rRNA in vertebrates) and a 5S rRNA. The large subunit of vertebrate ribosomes also contains a 5.8S rRNA base-paired to the 28S rRNA. The number of ribonucleotides (rNTs) in each rRNA type is indicated.



◀ **FIGURE 4-31 Model of protein synthesis on circular polysomes and recycling of ribosomal subunits.** Multiple individual ribosomes can simultaneously translate a eukaryotic mRNA, shown here in circular form stabilized by interactions between proteins bound at the 3′ and 5′ ends. When a ribosome completes translation and dissociates from the 3′ end, the separated subunits can rapidly find the nearby 5′ cap (m^7G) and initiate another round of synthesis.

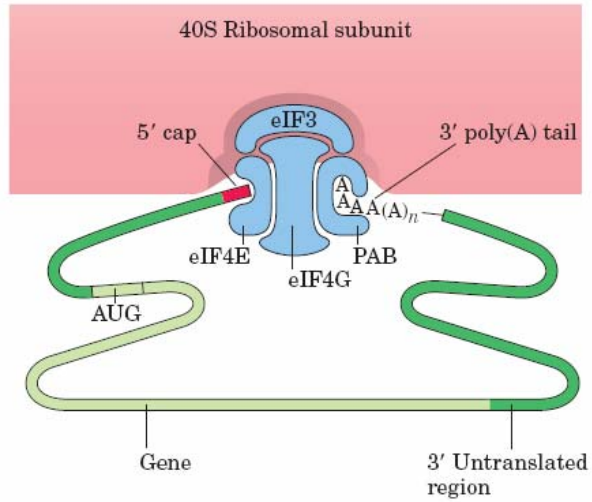
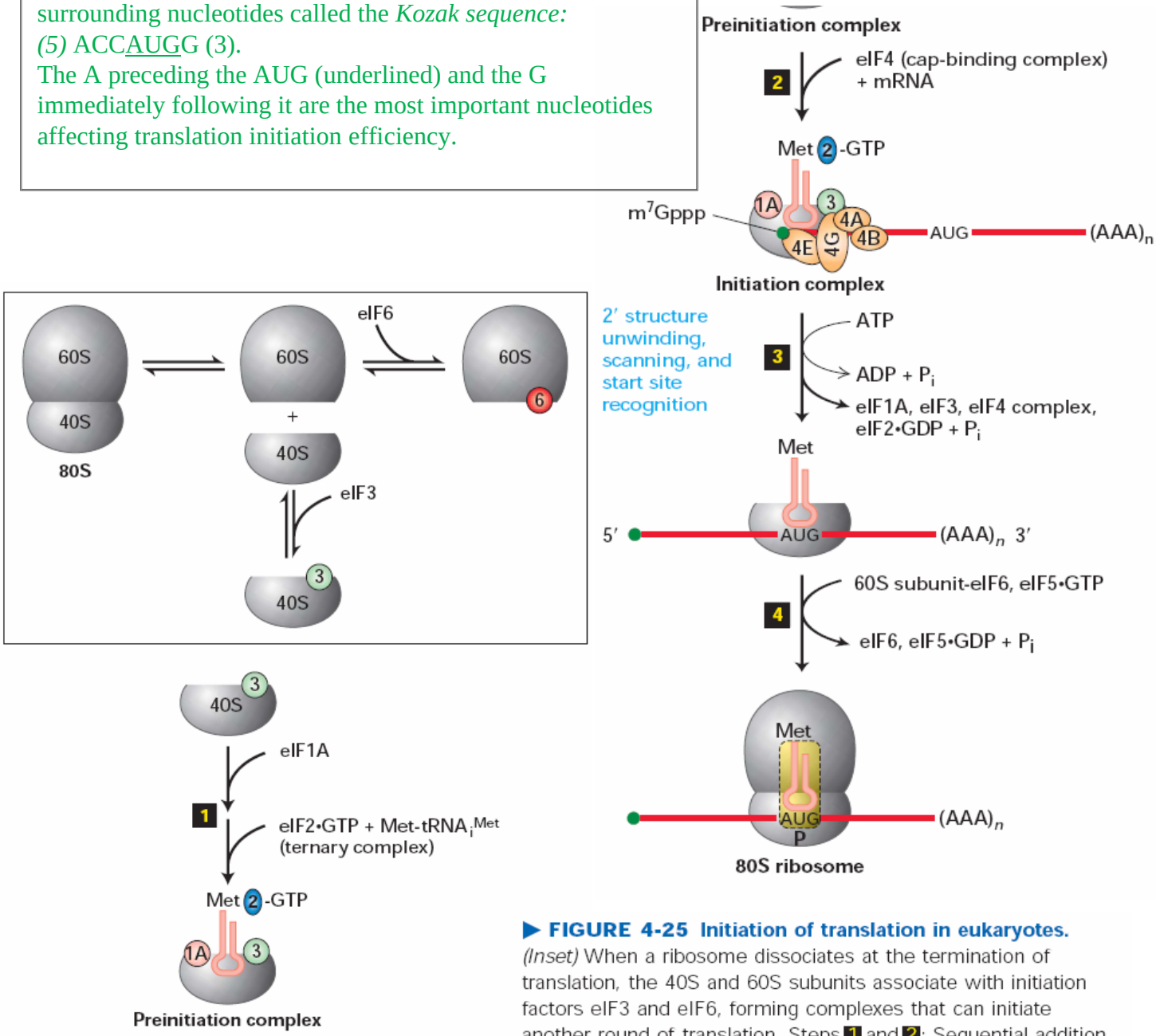
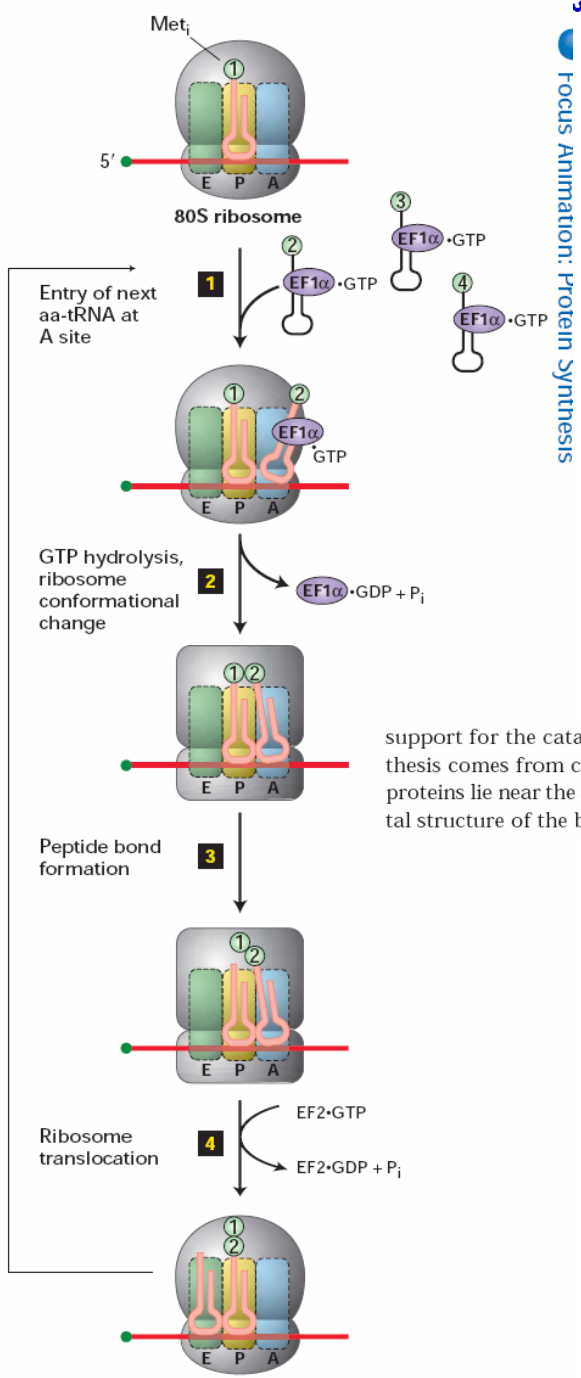


FIGURE 27-22 Protein complexes in the formation of a eukaryotic initiation complex. The 3′ and 5′ ends of eukaryotic mRNAs are linked by a complex of proteins that includes several initiation factors and the poly(A) binding protein (PAB). The factors eIF4E and eIF4G are part of a larger complex called eIF4F. This complex binds to the 40S ribosomal subunit.

Selection of the initiating AUG is facilitated by specific surrounding nucleotides called the *Kozak sequence:*
(5) ACCAUGG (3).
The A preceding the AUG (underlined) and the G immediately following it are the most important nucleotides affecting translation initiation efficiency.



▶ **FIGURE 4-25 Initiation of translation in eukaryotes.**
(Inset) When a ribosome dissociates at the termination of translation, the 40S and 60S subunits associate with initiation factors eIF3 and eIF6, forming complexes that can initiate another round of translation. Steps 1 and 2: Sequential addition



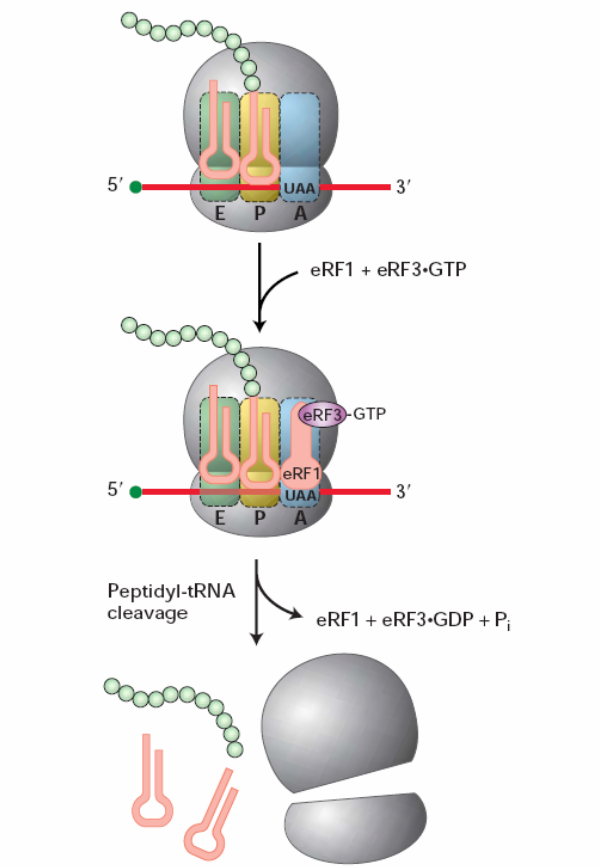
► **FIGURE 4-26 Cycle of peptidyl chain elongation during translation in eukaryotes.** Once the 80S ribosome with Met-tRNA$_i^{Met}$ in the ribosome P site is assembled *(top)*, a ternary complex bearing the second amino acid (aa_2) coded by the mRNA binds to the A site (step 1). Following a conformational change in the ribosome induced by hydrolysis of GTP in EF1α·GTP (step 2), the large rRNA catalyzes peptide bond formation between Met$_i$ and aa_2 (step 3). Hydrolysis of GTP in EF2·GTP causes another conformational change in the ribosome that results in its translocation one codon along the mRNA and shifts the unacylated tRNA$_i^{Met}$ to the E site and the tRNA with the bound peptide to the P site (step 4). The cycle can begin again with binding of a ternary complex bearing aa_3 to the now-open A site. In the second and subsequent elongation cycles, the tRNA at the E site is ejected during step 2 as a result of the conformational change induced by hydrolysis of GTP in EF1α·GTP. See the text for details. [Adapted from K. H. Nierhaus et al., 2000, in R. A. Garrett et al., eds., *The Ribosome: Structure, Function, Antibiotics, and Cellular Interactions*, ASM Press, p. 319.]

support for the catalytic role of large rRNA in protein synthesis comes from crystallographic studies showing that no proteins lie near the site of peptide bond synthesis in the crystal structure of the bacterial large subunit.

تناقض

Lehninger 4th Ed.

The elongation cycle in eukaryotes is quite similar to that in prokaryotes. Three eukaryotic elongation factors (eEF1α, eEF1$\beta\gamma$, and eEF2) have functions analogous to those of the bacterial elongation factors (EF-Tu, EF-Ts, and EF-G, respectively). Eukaryotic ribosomes do not have an E site; uncharged tRNAs are expelled directly from the P site.



▲ FIGURE 4-29 Termination of translation in eukaryotes. When a ribosome bearing a nascent protein chain reaches a stop codon (UAA, UGA, UAG), release factor eRF1 enters the ribosomal complex, probably at or near the A site together with eRF3•GTP. Hydrolysis of the bound GTP is accompanied by cleavage of the peptide chain from the tRNA in the P site and release of the tRNAs and the two ribosomal subunits.

پوروماسین

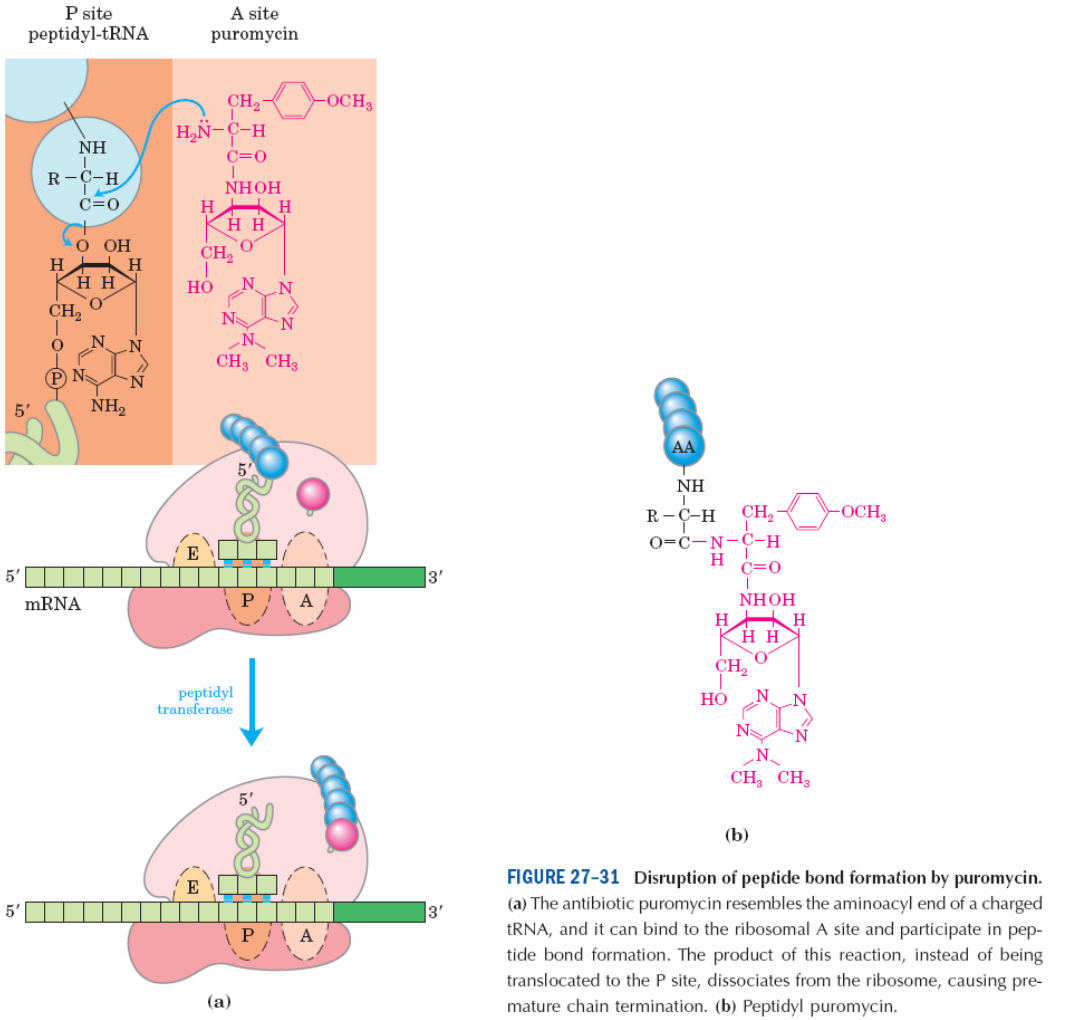
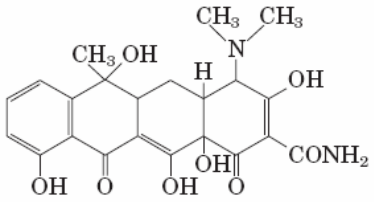
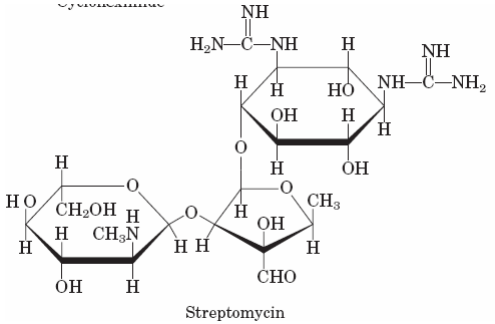
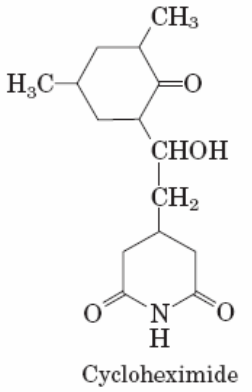


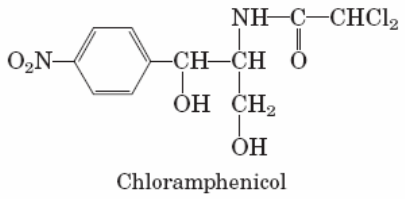
FIGURE 27-31 Disruption of peptide bond formation by puromycin. **(a)** The antibiotic puromycin resembles the aminoacyl end of a charged tRNA, and it can bind to the ribosomal A site and participate in peptide bond formation. The product of this reaction, instead of being translocated to the P site, dissociates from the ribosome, causing premature chain termination. **(b)** Peptidyl puromycin.

آنتی بیوتیک ها









- استرپتومایسین ← 30S
- تتراسیکلین ← 30S ← tRNA-aa
- کلرآمفنیکل ← 50S ← PT
- سیکلوهگزیمید ← 60S ← PT
- اریترومایسین ← 50S ← EF-G
- سم دیفتری ← eEF2

تغییر در پروتئین ها