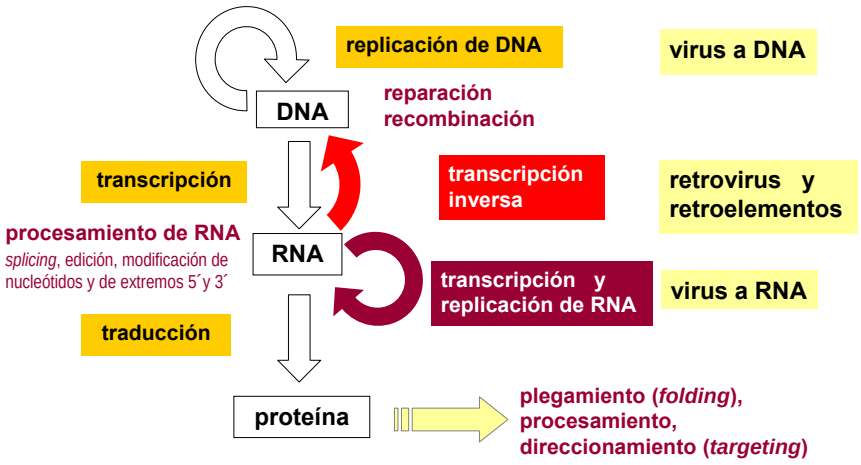
traducción

síntesis de proteínas (1)

Víctor Romanowski, 2013

"Dogma central de la biología molecular"

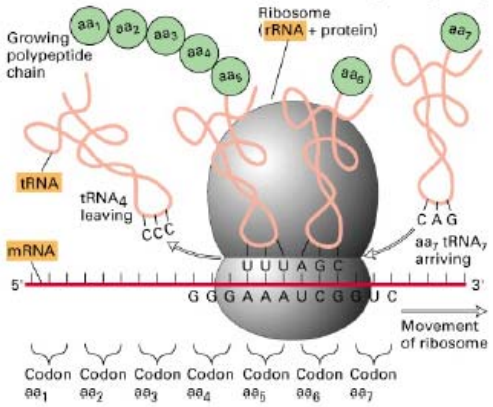


Víctor Romanowski

Protein translation – a gathering of RNAs, ribosomal proteins, and translation factors

- **mRNA** carries the genetic information
  - transcribed by RNA Pol II
- **tRNA** decodes the genetic information
  - transcribed by RNA Pol III
  - folds and then undergoes splicing before it is exported from nucleus
  - as many as 50 chemical modifications affecting ~10% of nucleotides (e.g., inosine, pseudouridine, dihydrouridine)
- **rRNA** interacts with amino-acylated ends of tRNAs and catalyzes peptide bond formation
  - transcribed by RNA Pol I (and Pol III)

Fig 4-20 (Lodish)



Ribosomal RNAs and ribosomes

- ~2/3 of ribosomal mass is rRNA
- prokaryotes (70S)
  - 50S = 23S rRNA + 5S rRNA + 34 proteins
  - 30S = 16S rRNA + 21 proteins
- eukaryotes (80S)
  - 60S = 28S rRNA + 5.8S rRNA + 5S rRNA + 49 proteins
  - 40S = 18S rRNA + 33 proteins
- rRNA sequences vary, yet 2° and 3° structures are conserved across all species

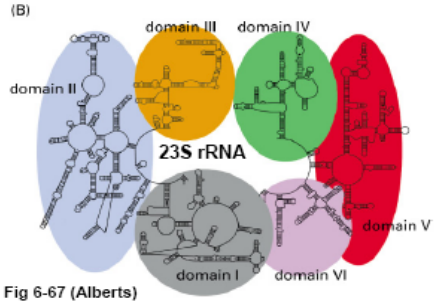
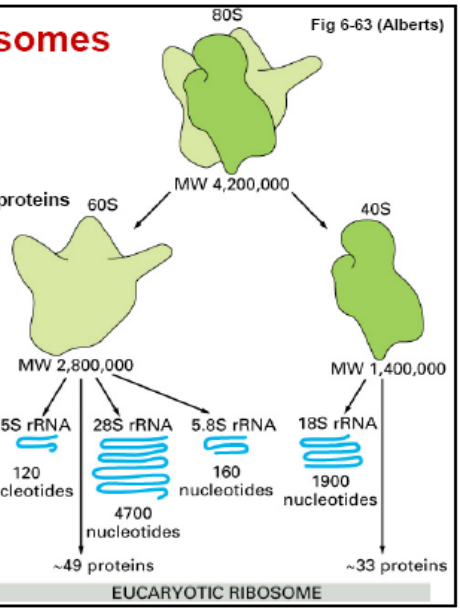


Fig 6-67 (Alberts)

Fig 6-63 (Alberts)



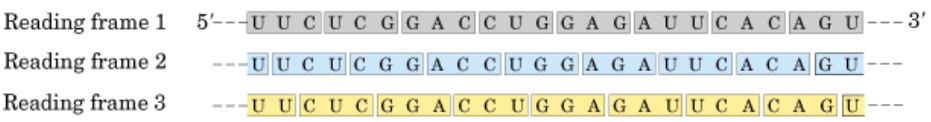
Código genético = diccionario
para traducir el lenguaje de ácidos nucleicos
al lenguaje de proteínas

- secuencia de tres nucleótidos = codón
- lectura no superpuesta de codones
- sin espacios ni signos de puntuación

3 nucleótidos = 1 codón = 1 aminoácido

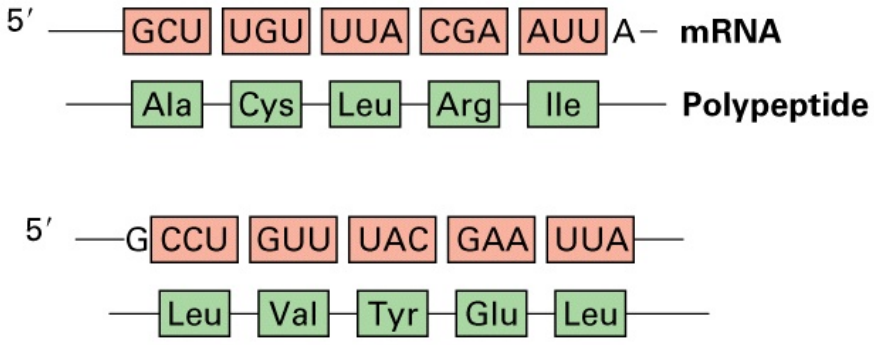
El código genético
puede ser leído en diferentes fases
o marcos (*reading frames*)

RNA

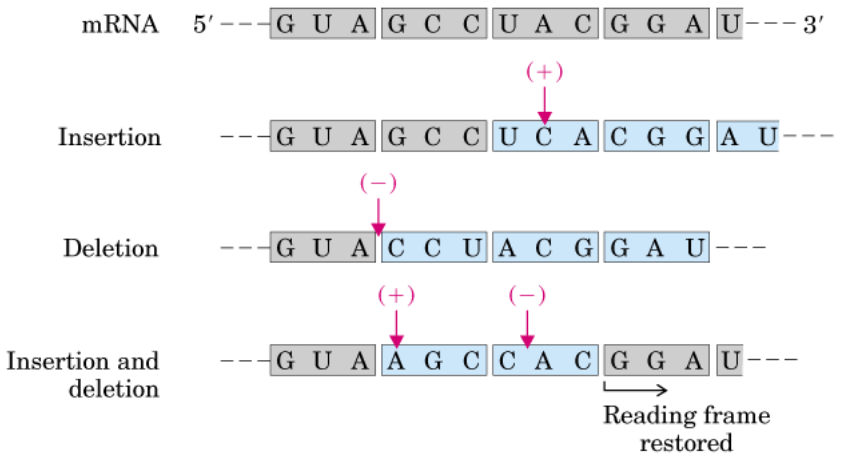


ds**DNA**

El código genético puede ser leído en diferentes fases o marcos
(una secuencia nucleotídica puede ser traducida teóricamente a una secuencia de aminoácidos, que depende de la fase de lectura)



La inserción o deleción de nucleótidos cambia el marco de lectura



Second letter of codon

First letter of codon (5′ end)	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

¿cómo se dedujo el código genético?

- Momento histórico: 1960s (pocas secuencias de proteínas conocidas, ninguna secuencia de DNA, no se podían purificar mRNAs)
- Sistema de traducción libre de células o sistema *in vitro* (Matthei and Nirenberg): OJO! El sistema funciona sin necesidad de reconocer un AUG.
- Incorporación de aminoácidos radiactivos a polipéptidos (dirigidos por el agregado de RNAs sintéticos)
- Síntesis de polinucleótidos (RNAs artificiales): poli-U, poli-A, poli-C… (polinucleótido fosforilasa: RNAn +NDP = RNAn+1 + Pi). Poli-U dirige la incorporación de Phe (UUU=Phe, AAA=Lys, CCC=Pro)
- La polinucleótido fosoforilasa copolimeriza los NDPs que se pongan en la mezcla de reacción: % de nucleótidos, frecuencia de tripletes, % de cada aa en el polipéptido…
- Síntesis orgánica de tripletes. Ensayos de unión a filtro (aa-tRNA+ribosoma+triplete). UUU=Phe
- Polímeros alternados: ej. (CACACACACACA– a partir de CA) produce un polipéptido alternado HisThrHisThrHisThr--, entonces CAC y ACA codifican para His y Thr, o viceversa.
- CAACAACAACAACAACAA– (a partir de CAA) produce poly(Gln), poly(Asn) y poly(Thr), entonces ACA=Thr y CAC=His; CAA=Gln o Asn y AAC=Asn o Gln

Descifrando el código genético
ensayo de unión a filtro de nitrocelulosa

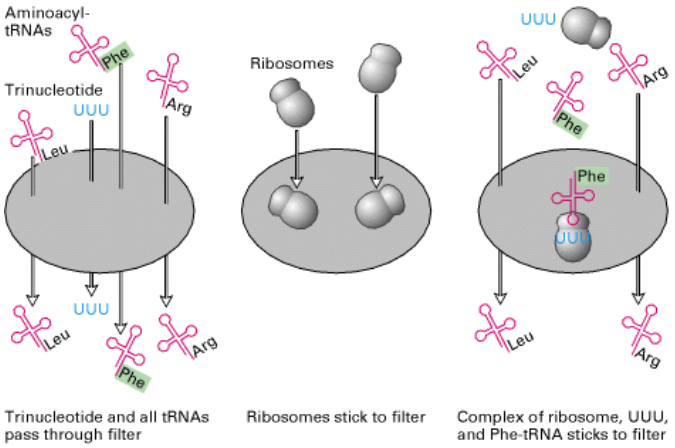
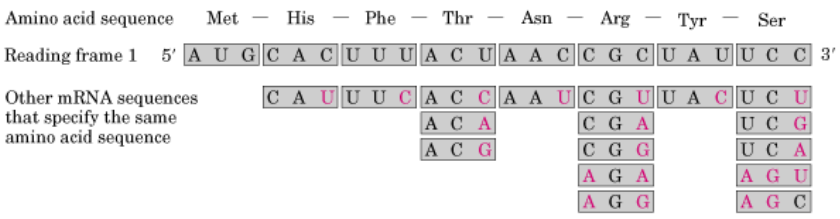


table 27–4

Degeneracy of the Genetic Code

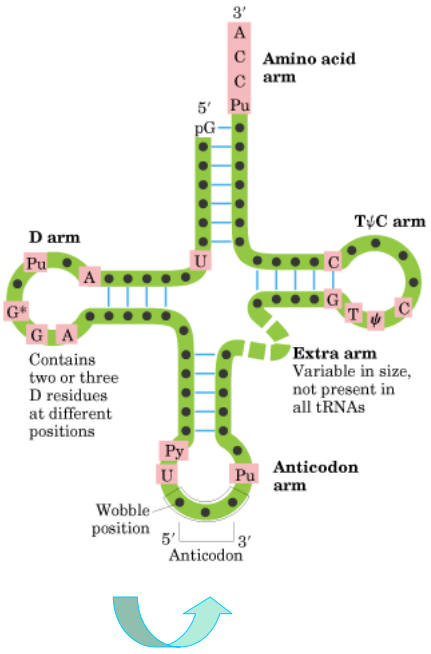
Amino acid	Number of codons
Ala	4
Arg	6
Asn	2
Asp	2
Cys	2
Gln	2
Glu	2
Gly	4
His	2
Ile	3
Leu	6
Lys	2
Met	1
Phe	2
Pro	4
Ser	6
Thr	4
Trp	1
Tyr	2
Val	4



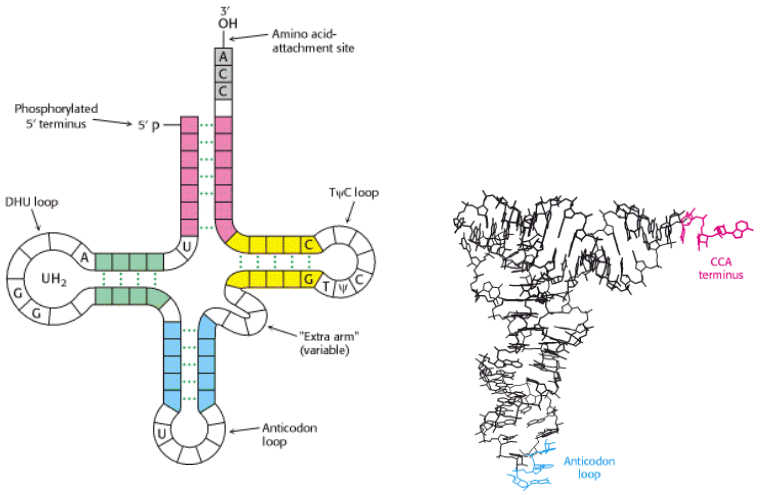
una secuencia de aminoácidos (N→C)

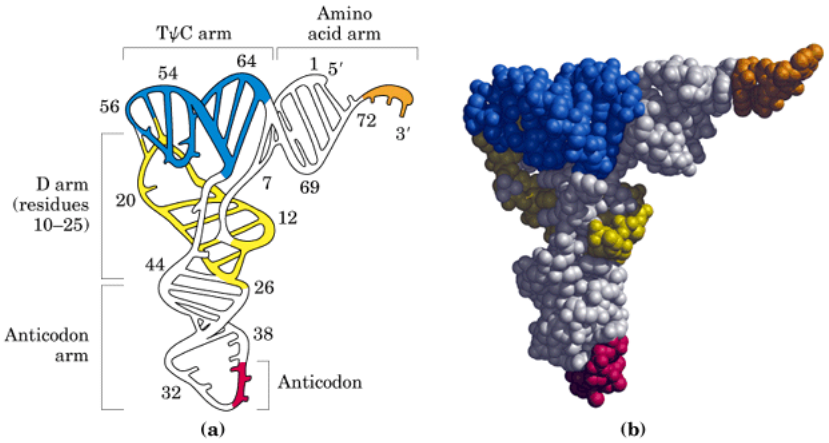
varias secuencias de nucleótidos alternativas (5'→3')

tRNA



Estructura de tRNAs

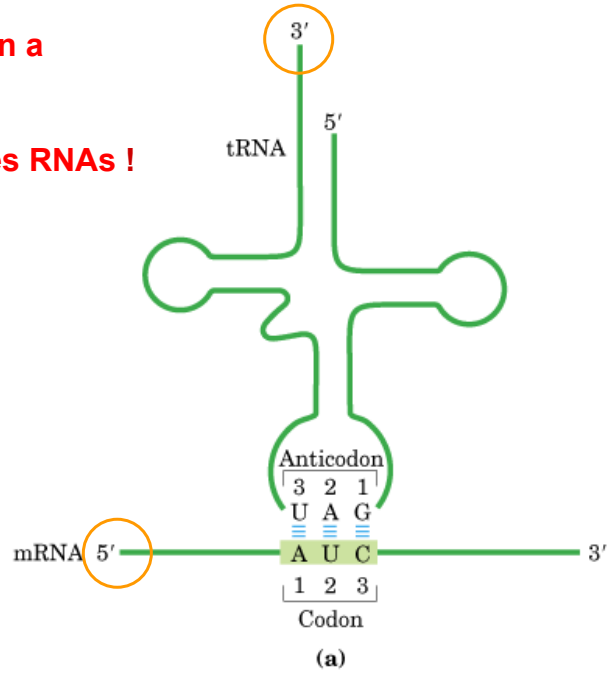




Prestar atención a

las polaridades

de los diferentes RNAs !

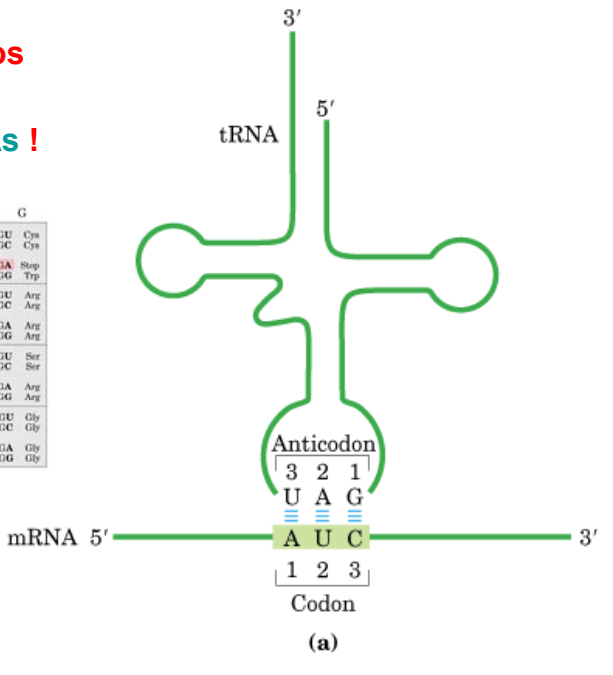


hay 61 codones
para aminoácidos

no hay 61 tRNAs !

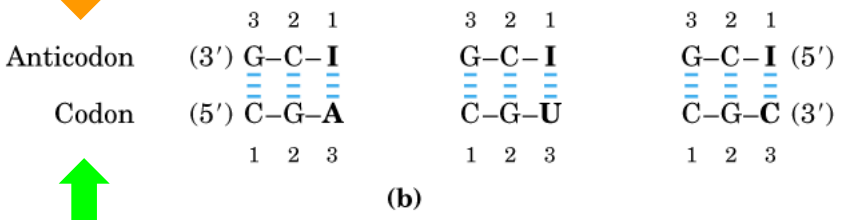
Second letter of codon

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



tRNA

un tRNA puede reconocer más de un codón



(b)

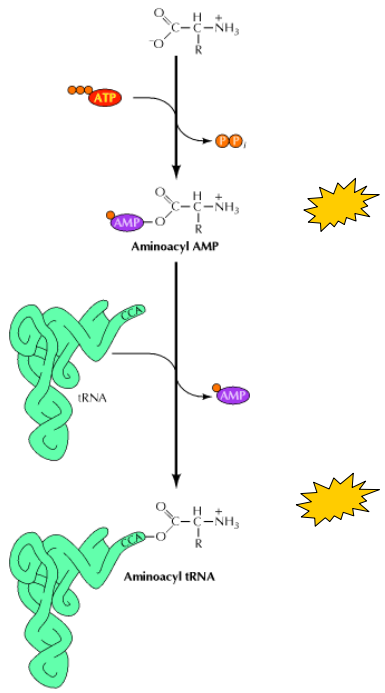
mRNA

table 27–5

How the Wobble Base of the Anticodon Determines the Number of Codons a tRNA Can Recognize*

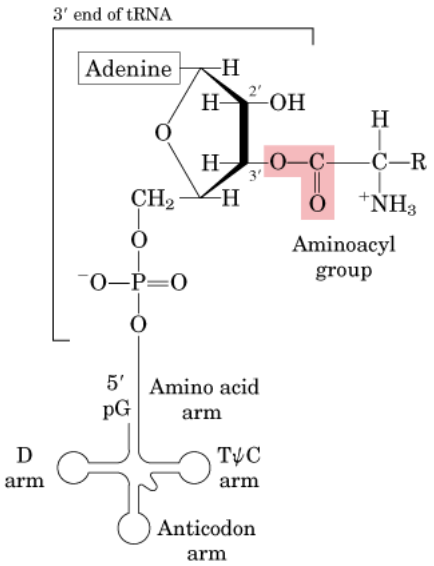
1. One codon recognized:			
	Anticodon	(3′) X–Y–C (5′)	(3′) X–Y–A (5′)
	Codon	(5′) Y–X–G (3′)	(5′) Y–X–U (3′)
2. Two codons recognized:			
	Anticodon	(3′) X–Y–U (5′)	(3′) X–Y–G (5′)
	Codon	(5′) Y–X–A/G (3′)	(5′) Y–X–C/U (3′)
3. Three codons recognized:			
	Anticodon	(3′) X–Y–I (5′)	
	Codon	(5′) Y–X–A/U/C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

*X and Y denote complementary bases capable of strong Watson-Crick base pairing with each other. The bases in the wobble positions—the 3′ position of codons and 5′ position of anticodons—are shaded in red.



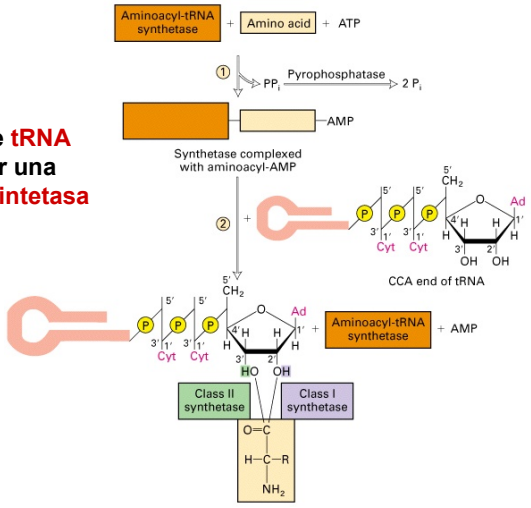
Activación del aminoácido

aminoacil-tRNA-sintetasa



Las aminoacil-tRNA sintetasas activan aminoácidos uniéndolos a tRNAs

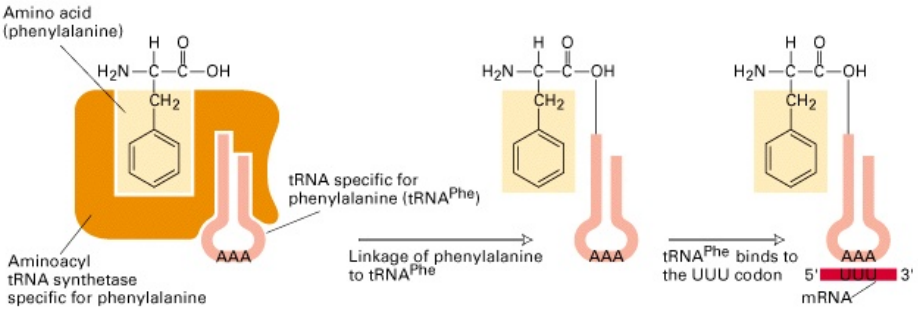
Cada molécula de tRNA es reconocida por una aminoacil-tRNA sintetasa específica



La traducción es un proceso de decodificación en dos etapas

etapa 1 = aminoacil-tRNA-sintetasa

etapa 2 = reconocimiento codón-anticodón



Net Result: Phenylalanine Is Selected by Its Codon

Especificidad de las aminoacil-tRNA sintetasas

1. $tRNA^{Xxx}$ (anticodón, brazo aceptor)
2. aminoácido **Xxx** (tamaño, hidrofobicidad, estereoquímica)

⇩

3. **Xxx-** $tRNA^{Xxx}$

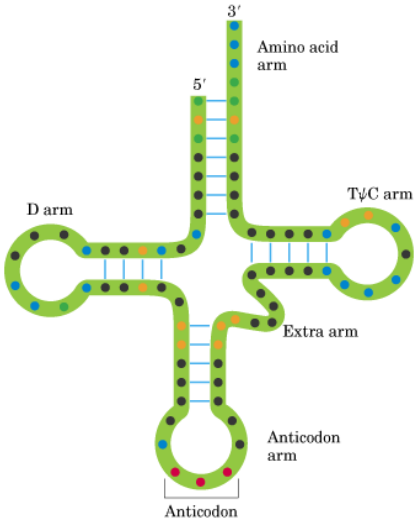
Ejemplo:

1. $tRNA^{Phe}$

2. Phe

3. Phe-$tRNA^{Phe}$

"Segundo código genético"



ejemplos

Especificidad de las aminoacil-tRNA sintetasas

para el **tRNA**

$tRNA^{Xxx}$ (anticodón y brazo aceptor) — Gln-tRNA sintetasa

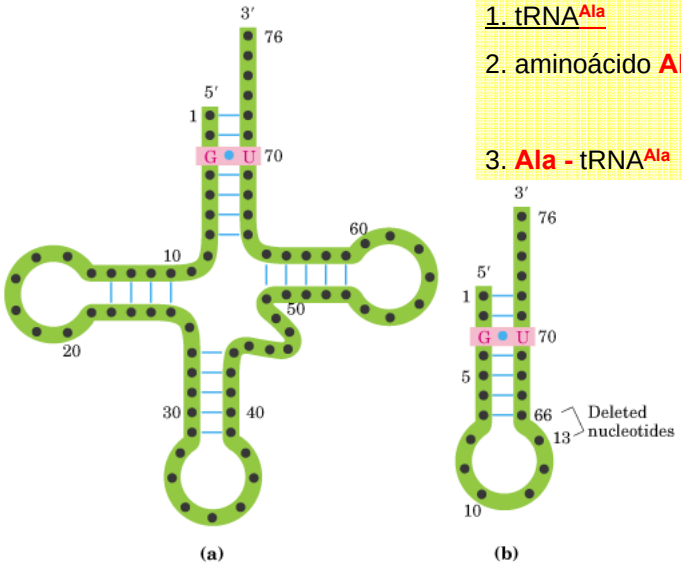
$tRNA^{Xxx}$ (anticodón) — Met-tRNA sintetasa

Si se muta el gen del $tRNA^{Val}$ (anticodón **UAC**) de manera que el anticodón sea **CAU**, este $tRNA^{Val}$*mut* será cargado con **Met**)

$tRNA^{Xxx}$ (brazo aceptor) — Ala-tRNA sintetasa

Un **mini** $tRNA^{Ala}$ que solamente tiene el brazo aceptor es cargado con **Ala** por la Ala-tRNA sintetasa

tRNA^{Ala}



Especificidad de la alanil - tRNA sintetasa

1. tRNA^{Ala}
2. aminoácido **Ala**
3. **Ala -** tRNA^{Ala}

Especificidad de las aminoacil-tRNA sintetasas ejemplos

Para el **aminoácido** (tamaño, hidrofobicidad, estereoquímica)

Edición (*proofreading*) o corrección de errores

Tyr-tRNA sintetasa

Sitio activo de acilación muy específico, sin edición: Tyr

Thr-tRNA sintetasa

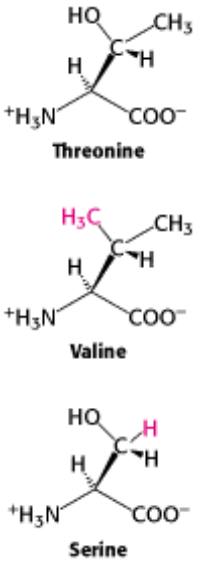
Sitio de acilación excluye aa de mayor tamaño
Sitio de acilación excluye aa de mayor hidrofobicidad (Val>Thr)
Edición: Sitio de hidrólisis hidroliza aa-tRNA de menor tamaño (Ser<Thr)

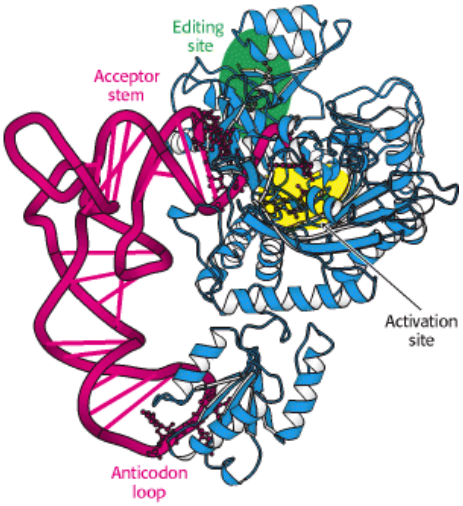
Ile-tRNA sintetasa

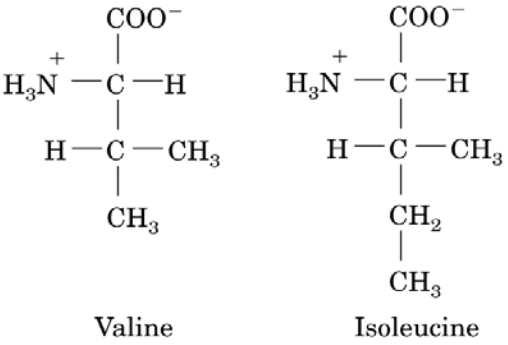
Sitio de acilación no excluye aa de menor tamaño (Val)
Edición: Sitio de hidrólisis hidroliza Val-AMP de menor tamaño (Val<Ile)
Ile-AMP no entra en el sitio de hidrólisis; sigue hacia la formación de Ile-tRNA

La edición (*proofreading*) de las aminoacil tRNA sintetasas aumenta la fidelidad de la síntesis de proteínas

Threonyl-tRNA synthetase.





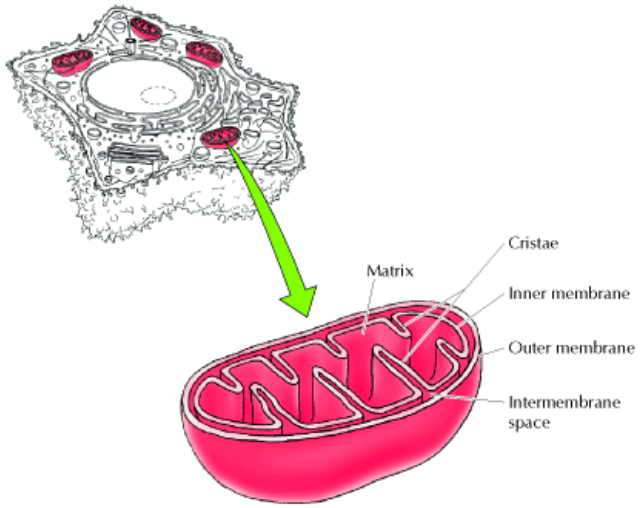


Código casi universal

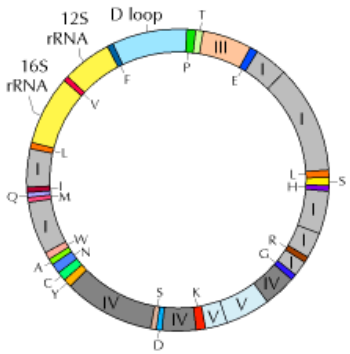
- Código genético en mitocondrias
  - Más de 20 aminoácidos

Second letter of codon

First letter of codon (5′ end)	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



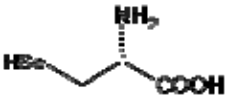
código genético en genomas mitocondriales



Differences between the Universal and Mitochondrial Genetic Codes		
Codon	Universal code	Human mitochondrial code
UGA	STOP	Trp
AGA	Arg	STOP
AGG	Arg	STOP
AUA	Ile	Met

Figure 10.3. The human mitochondrial genome The genome contains 13 protein coding sequences, which are designated as components of respiratory complexes I, III, IV, or V. In addition, the genome contains genes for 12S and 16S rRNAs and for 22 tRNAs, which are designated by the one-letter code for the corresponding amino acid. The region of the genome designated "D loop" contains an origin of DNA replication and transcriptional promoter sequences .

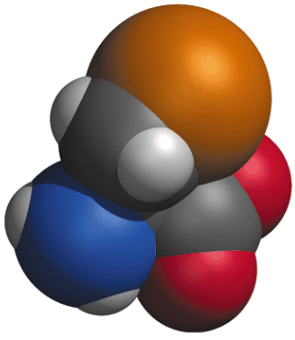
código genético = 20 aa ?

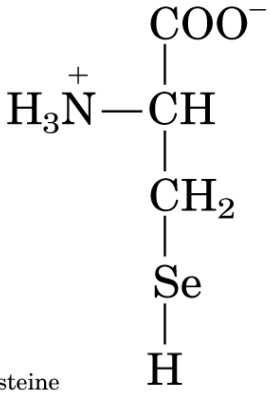


aminoácido número 21: **Sec** (selenocisteína)

codon **UGA** en un contexto de estructura secundaria del mRNA:

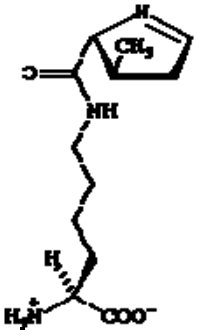
cis-acting selenocysteine insertion sequence - SECIS





Selenocysteine

aminoácido número 22: Pyl **Pirrolisina**

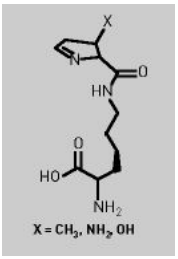


(codon **UAG** en un contexto
de estructura secundaria del mRNA)

*N*6-[(2*R*,3*R*)-3-methyl-3,4-dihydro-2*H*-pyrrol-2-ylcarbonyl]-L-lysine

lysine—tRNA Pyl ligase

ATP + L-lysine + tRNA Pyl =
AMP + PPi + L-lysyl-tRNAPyl



Science 24 May 2002: Vol. 296. no. 5572, pp. 1459 – 1462
Pyrrolysine Encoded by UAG in Archaea: Charging of a UAG-Decoding Specialized tRNA
Gayathri Srinivasan, Carey M. James, Joseph A. Krzycki*
Pyrrolysine is a lysine derivative encoded by the UAG codon in methylamine methyltransferase genes of *Methanosarcina barkeri*. Near a methyltransferase gene cluster is the *pylT* gene, which encodes an unusual transfer RNA (tRNA) with a CUA anticodon. The adjacent *pylS* gene encodes a class II aminoacyl-tRNA synthetase that charges the *pylT*-derived tRNA with lysine but is not closely related to known lysyl-tRNA synthetases. Homologs of *pylS* and *pylT* are found in a Gram-positive bacterium. Charging a tRNACUA with lysine is a likely first step in translating UAG amber codons as pyrrolysine in certain methanogens. Our results indicate that pyrrolysine is the 22nd genetically encoded natural amino acid.
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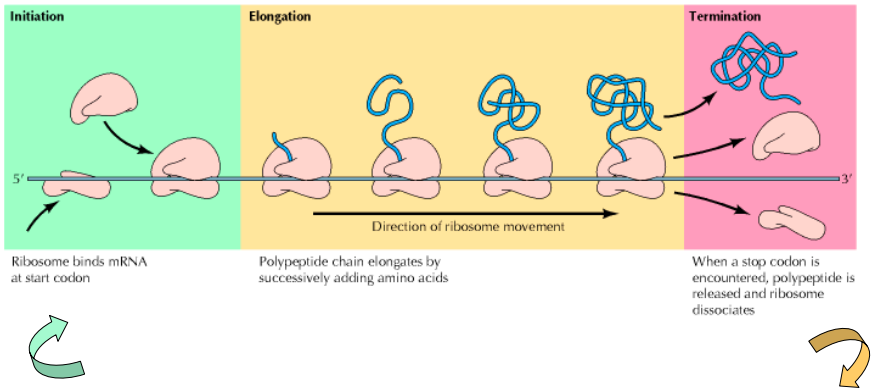
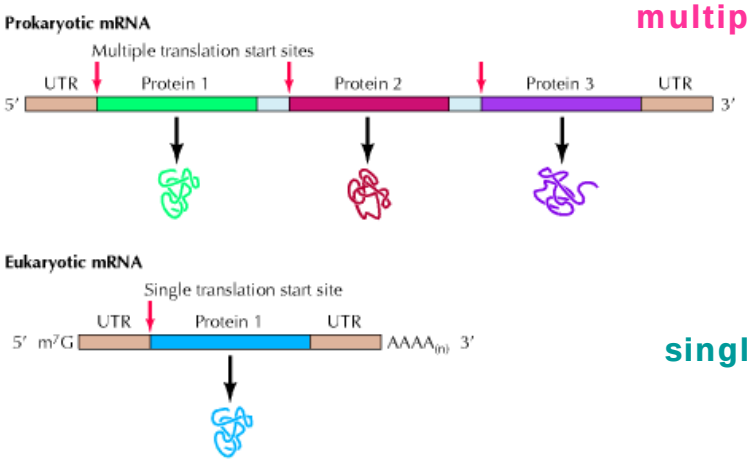
Traducción en etapas:
iniciación, elongación, terminación



Activación de aminoácidos

Plegamiento

multiple ORFs



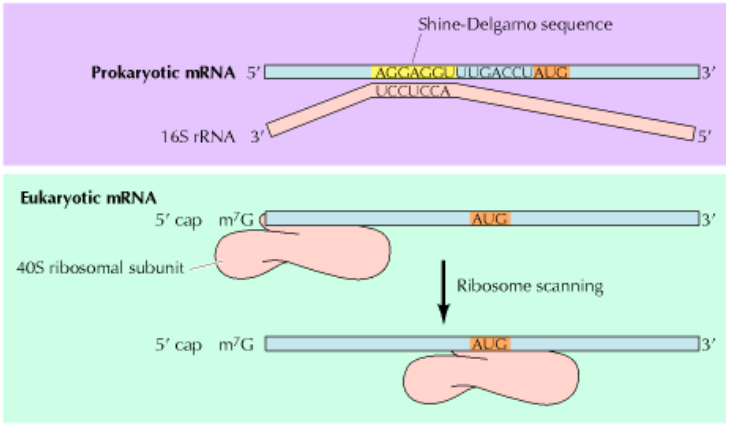
single ORF

Prokaryotic and eukaryotic mRNAs

Both prokaryotic and eukaryotic mRNAs contain untranslated regions (UTRs) at their 5´ and 3´ ends. Eukaryotic mRNAs also contain **5**´ 7-methylguanosine (m7G) caps and **3**´ poly-A tails. Prokaryotic mRNAs are frequently polycistronic: They encode multiple proteins, each of which is translated from an independent start site. Eukaryotic mRNAs are usually monocistronic, encoding only a single protein

iniciación de la traducción

procariotas

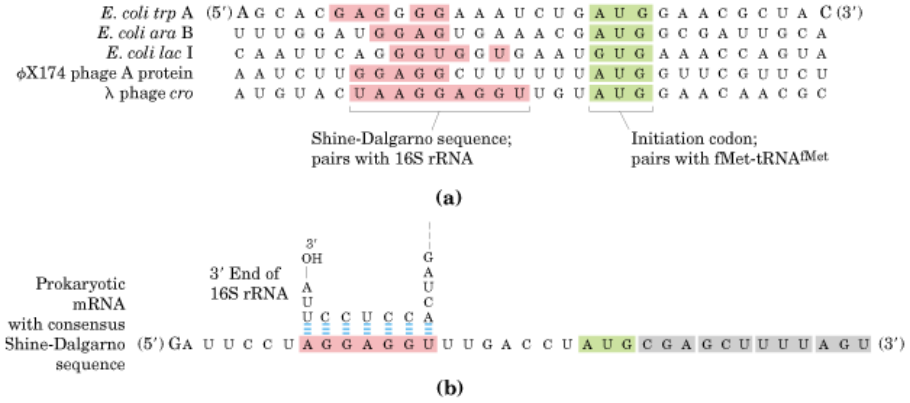


eucariotas

Signals for translation initiation Initiation sites in prokaryotic mRNAs are characterized by a Shine-Delgarno sequence that precedes the AUG initiation codon. Base pairing between the Shine-Delgarno sequence and a complementary sequence near the 3´ terminus of 16S rRNA aligns the mRNA on the ribosome. In contrast, eukaryotic mRNAs are bound to the 40S ribosomal subunit by their 5´ 7-

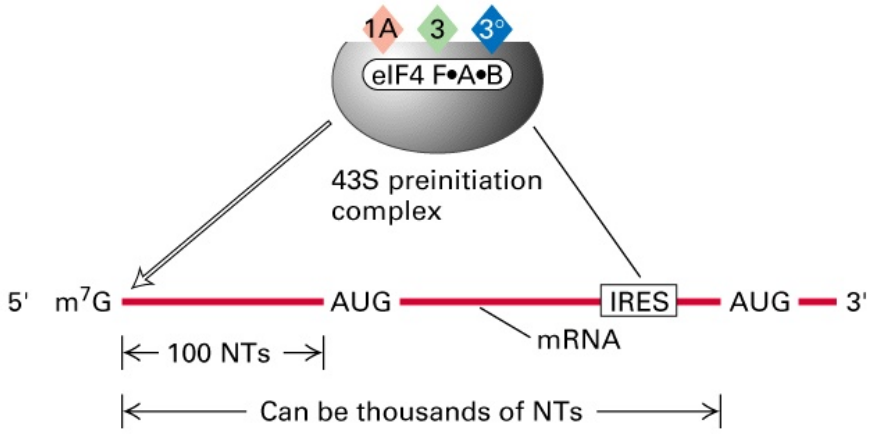
methylguanosine caps. The ribosome then scans along the RNA until it encounters an AUG initiation codon

RBS = Ribosome Binding Site = Shine-Dalgarno sequence (SD)



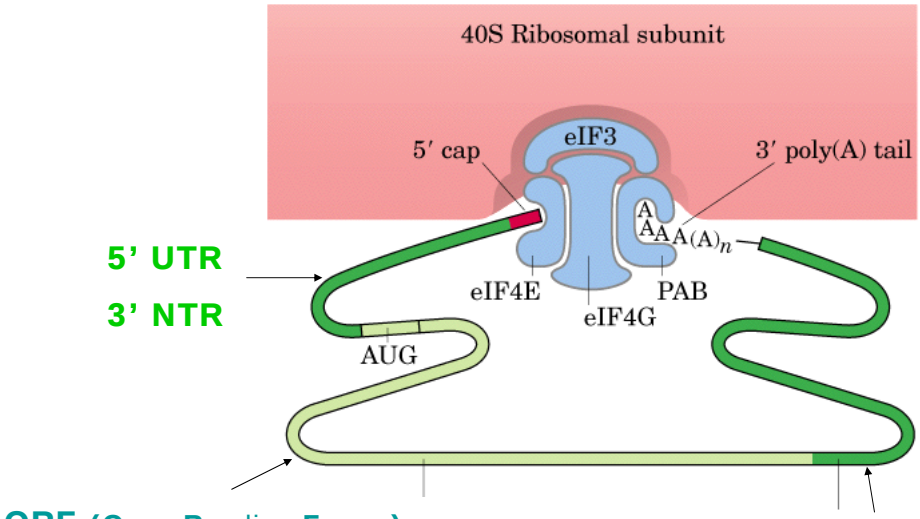
procariotas

Initiation of eukaryotic protein synthesis generally occurs at the **5' end of mRNA** but may occasionally occur at **internal sites**



eucariotas

eucariotas



ORF (**O**pen **R**eading **F**rame)

CDS (**Co**ding **S**equence)

3' UTR (**UnT**ranslated **R**egion)

3' NTR (**N**on**T**ranslated **R**egion)

The **AUG start** codon is recognized by **methionyl-$tRNA_i^{Met}$**

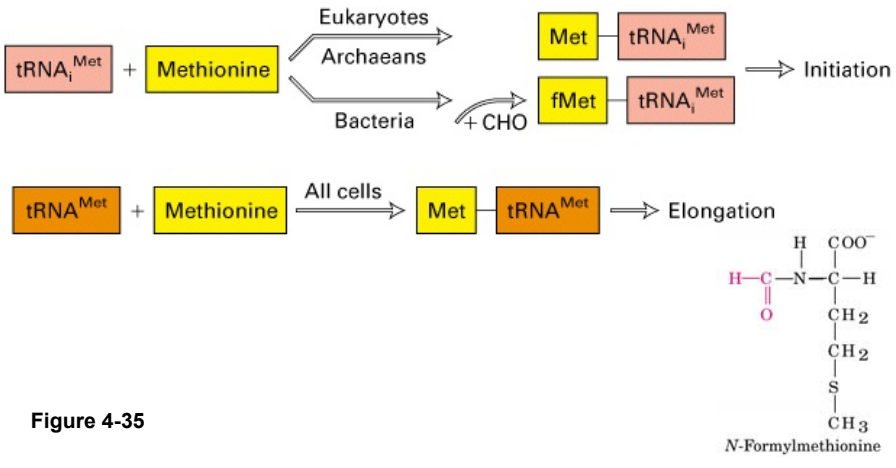
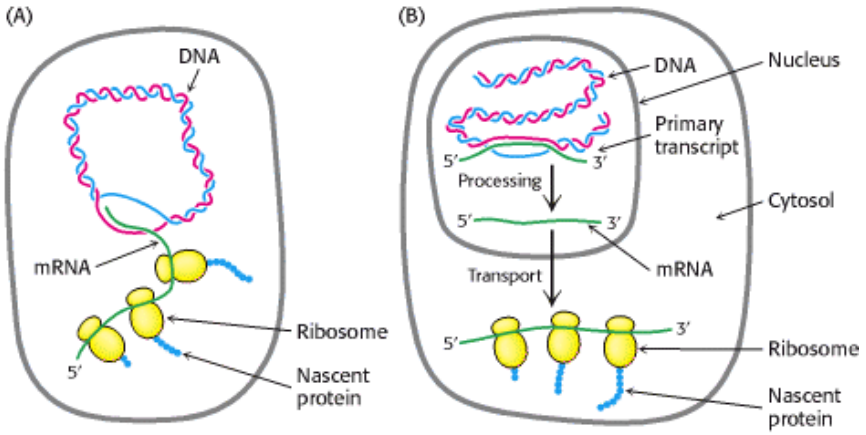


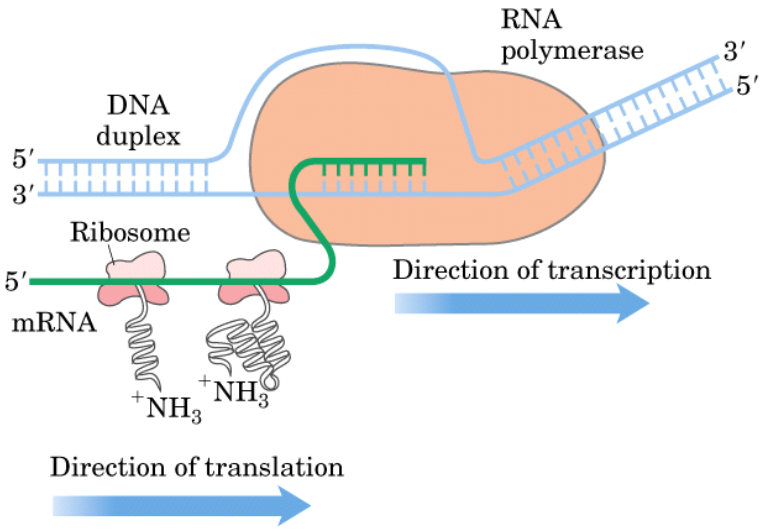
Figure 4-35

transcripción y traducción
en el mismo o en diferentes compartimientos



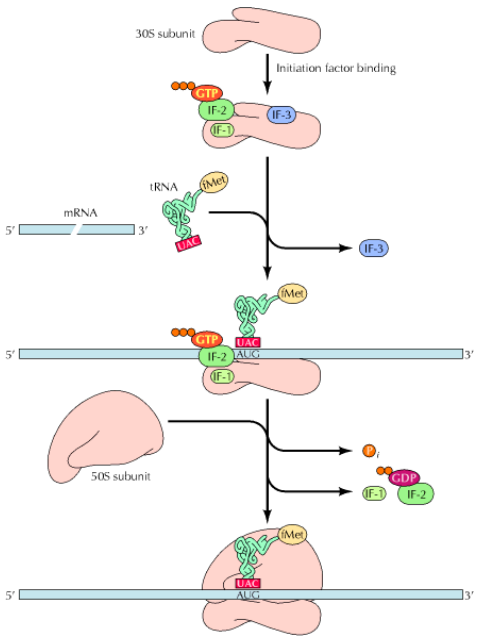
procariotas **eucariotas**

coupled transcription and translation

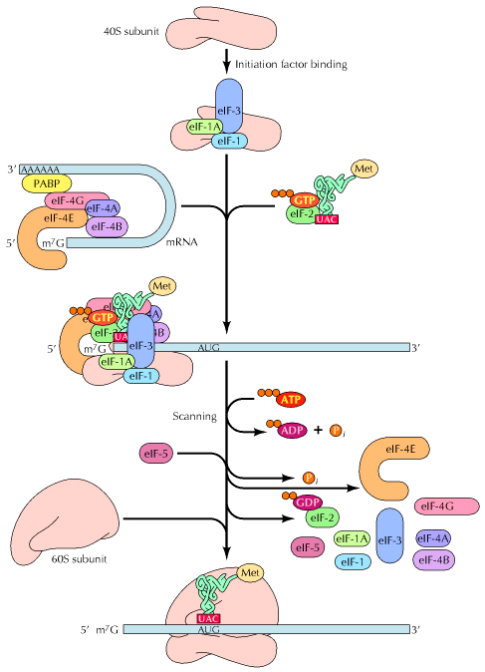


Translation Factors

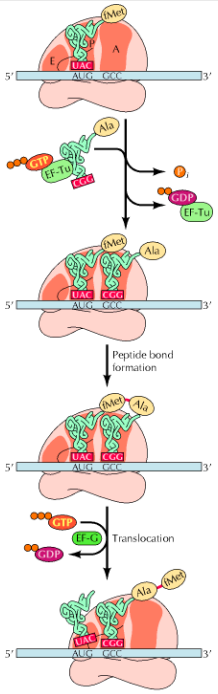
Role	Prokaryotes	Eukaryotes
Initiation	IF-1, IF-2, IF-3	eIF-1, eIF-1A, eIF-2, eIF-2B, eIF-3, eIF-4A, eIF-4B, eIF-4E, eIF-4G, eIF-5
Elongation	EF-Tu, EF-Ts, EF-G	eEF-1α, eEF-1$\beta\gamma$, eEF-2
Termination	RF-1, RF-2, RF-3	eRF-1, eRF-3



Initiation of translation in bacteria Three initiation factors (IF-1, IF-2, and IF-3) first bind to the 30S ribosomal subunit. This step is followed by binding of the mRNA and the initiator *N*-formylmethionyl (fMet) tRNA, which is recognized by IF-2 bound to GTP. IF-3 is then released, and a 50S subunit binds to the complex, triggering the hydrolysis of bound GTP, followed by the release of IF-1 and IF-2 bound to GDP

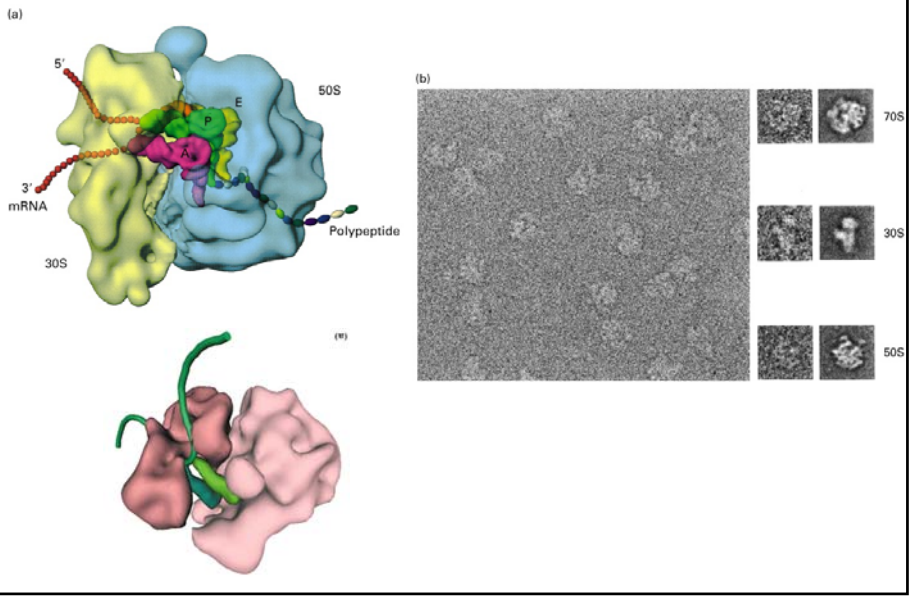


Initiation of translation in eukaryotic cells Initiation factors eIF-3, eIF-1, and eIF-1A bind to the 40S ribosomal subunit. The initiator methionyl tRNA is brought to the ribosome by eIF-2 (complexed to GTP), and the mRNA by eIF-4E (which binds to the 5´ cap), eIF-4G (which binds to both eIF-4E at the 5' cap and PABP at the 3' poly-A tail), eIF-4A, and eIF-4B. The ribosome then scans down the mRNA to identify the first AUG initiation codon. Scanning requires energy and is accompanied by ATP hydrolysis. When the initiating AUG is identified, eIF-5 triggers the hydrolysis of GTP bound to eIF-2, followed by the release of eIF-2 (complexed to GDP) and other initiation factors. The 60S ribosomal subunit then joins the 40S complex.

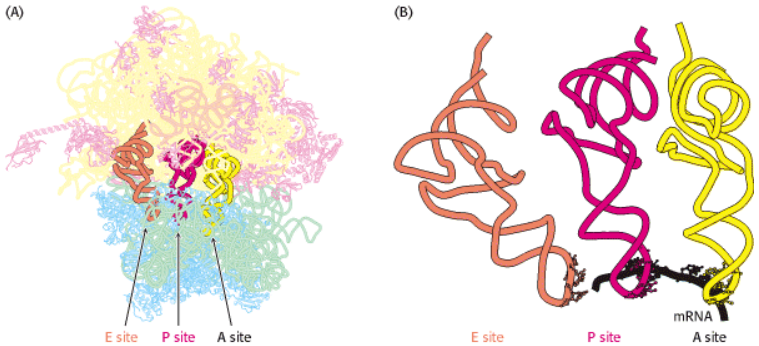


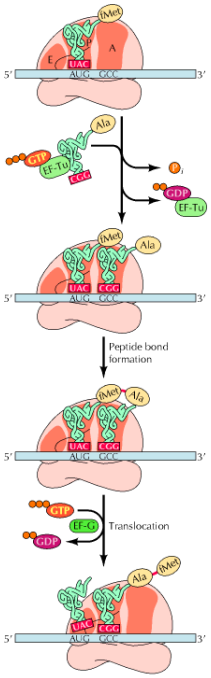
Elongation stage of translation The ribosome has three tRNA-binding sites, designated P (peptidyl), A (aminoacyl), and E (exit). The initiating *N*-formylmethionyl tRNA is positioned in the P site, leaving an empty A site. The second aminoacyl tRNA (e.g., alanyl tRNA) is then brought to the A site by EF-Tu (complexed with GTP). Following GTP hydrolysis, EF-Tu (complexed with GDP) leaves the ribosome, with alanyl tRNA inserted into the A site. A peptide bond is then formed, resulting in the transfer of methionine to the aminoacyl tRNA at the A site. The ribosome then moves three nucleotides along the mRNA. This movement translocates the peptidyl (Met-Ala) tRNA to the P site and the uncharged tRNA to the E site, leaving an empty A site ready for addition of the next amino acid. Translocation is mediated by EF-G, coupled to GTP hydrolysis. The process, illustrated here for prokaryotic cells, is very similar in eukaryotes. (Table 7.1 gives the names of the eukaryotic elongation factors.)

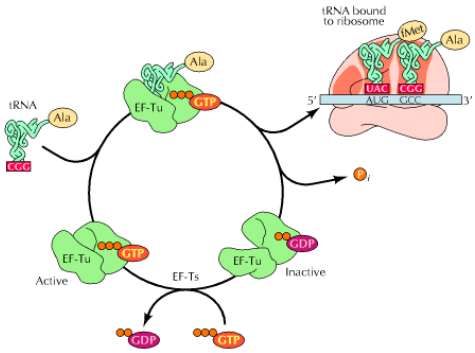
Image reconstruction of an *E. coli* ribosome



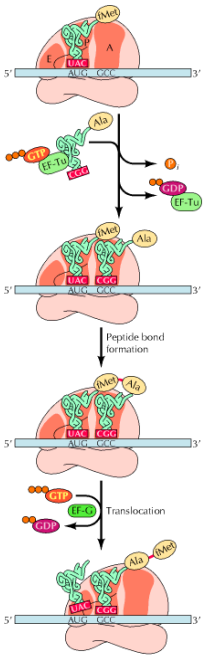
Transfer RNA-Binding Sites. (A) Three tRNA-binding sites are present on the 70S ribosome. They are called the **A** (for **aminoacyl**), **P** (for **peptidyl**), and **E** (for **exit**) sites. Each tRNA molecule contacts both the 30S and the 50S subunit. (B) The tRNA molecules in sites A and P are base paired with mRNA

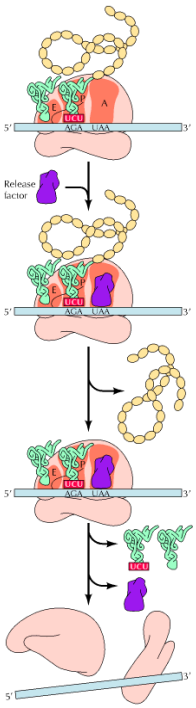






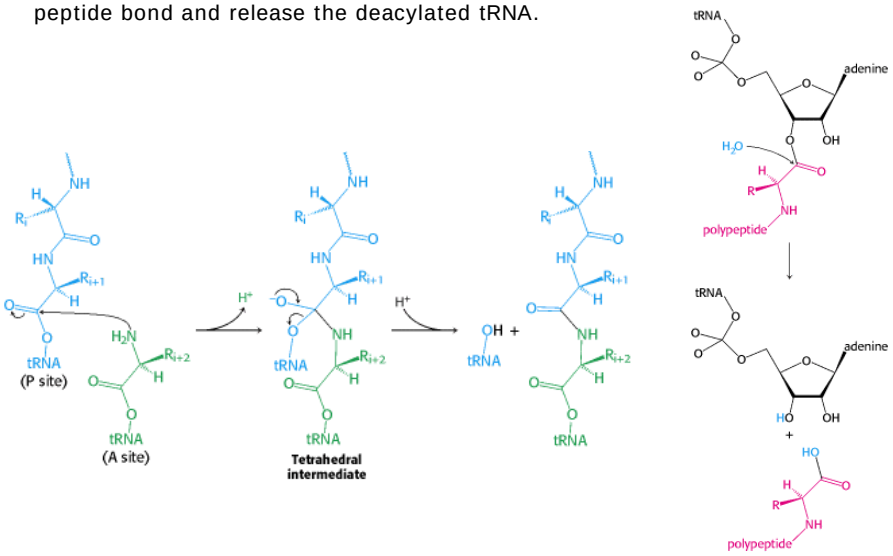
Regeneration of EF-Tu/GTP EF-Tu complexed to GTP escorts the aminoacyl tRNA to the ribosome. The bound GTP is hydrolyzed as the correct tRNA is inserted, so EF-Tu complexed to GDP is released. The EF-Tu/GDP complex is inactive and unable to bind another tRNA. In order for translation to continue, the active EF-Tu/GTP complex must be regenerated by another factor, EF-Ts, which stimulates the exchange of the bound GDP for free GTP.



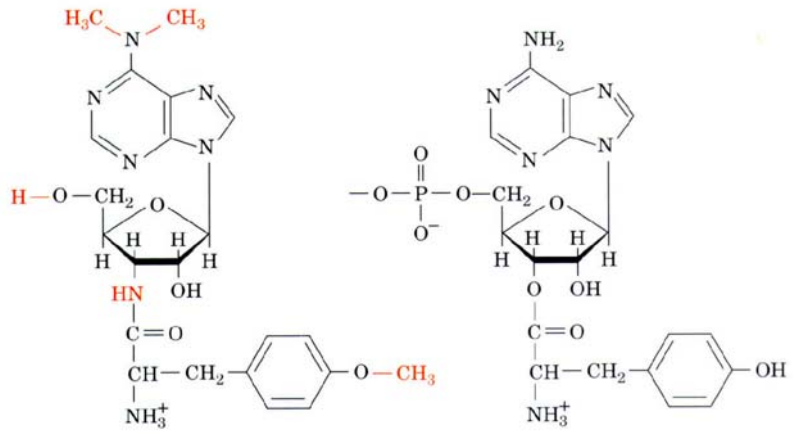


Termination of translation A termination codon (e.g., UAA) at the A site is recognized by a release factor rather than by a tRNA. The result is the release of the completed polypeptide chain, followed by the dissociation of tRNA and mRNA from the ribosome.

Peptide-Bond Formation. The amino group of the aminoacyl-tRNA attacks the carbonyl group of the ester linkage of the peptidyl-tRNA to form a tetrahedral intermediate. This intermediate collapses to form the peptide bond and release the deacylated tRNA.

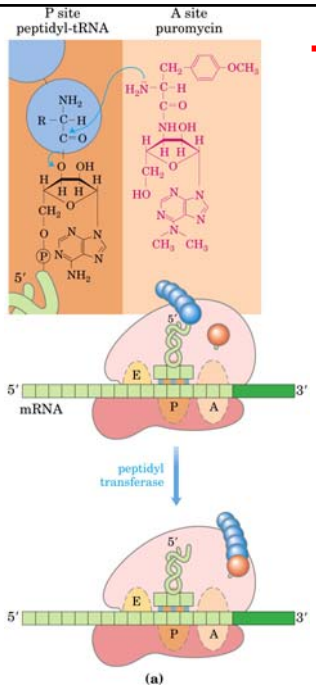


distintos antibióticos y toxinas inhiben la traducción

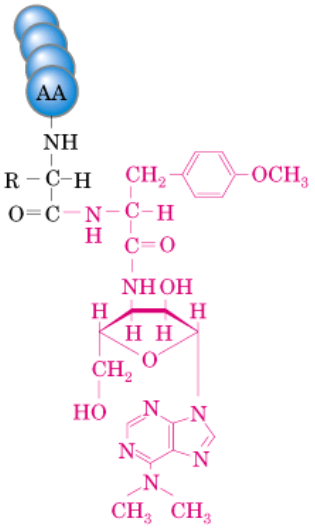


Puromycin

Tyrosyl–tRNA



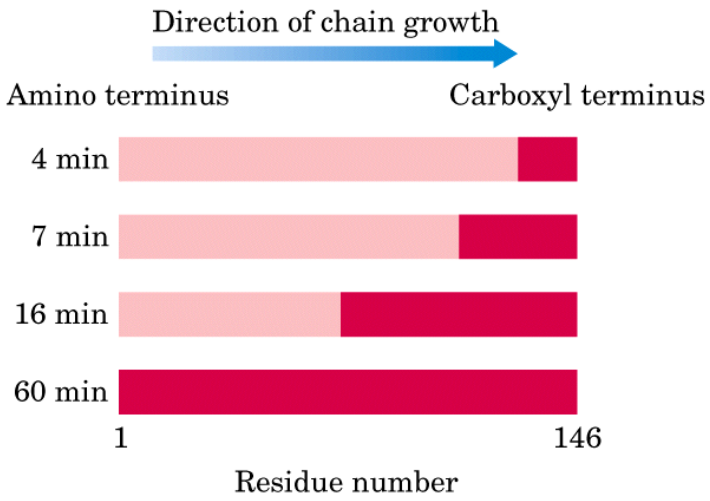
➔ **premature chain termination**



puromycin

Several Antibiotic and Toxin inhibitors of Translation

Inhibitor	Comments
Chloramphenicol	inhibits prokaryotic **peptidyl transferase**
Streptomycin	inhibits prokaryotic peptide chain **initiation**, also induces **mRNA misreading**
Tetracycline	inhibits prokaryotic **aminoacyl-tRNA** binding to the ribosome small subunit
Neomycin	similar in activity to streptomycin
Erythromycin	inhibits prokaryotic **translocation** through the ribosome large subunit
Fusidic acid	similar to erythromycin (translocation) only by preventing EF-G from dissociating from the large subunit
Puromycin	resembles an aminoacyl-tRNA, interferes with peptide transfer resulting in premature termination in both **prokaryotes and eukaryotes**
Diptheria toxin	catalyzes **ADP-ribosylation of and inactivation of eEF-2**
Ricin	found in castor beans, catalyzes **cleavage of the eukaryotic large subunit rRNA**
Cycloheximide	inhibits **eukaryotic peptidyltransferase**



Experimento de Dintzis: Reticulocitos incubados con ^{3}H-Leu.
Aislamiento a diferentes tiempos de cadenas α-globina completas (o sea, las que ya abandonaron los polisomas).
Medida de radiactividad en diferentes regiones de la cadena peptídica

*ASSEMBLY OF THE PEPTIDE CHAINS OF HEMOGLOBIN**

By Howard M. Dintzis

DEPARTMENT OF BIOLOGY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY

Proc. Natl. Acad. Sci. USA, **47**, 247-261 (1961)

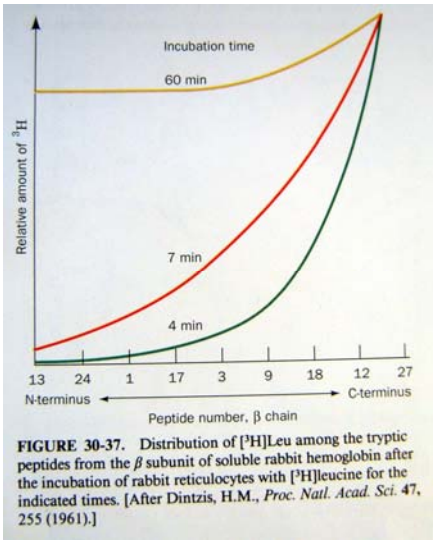
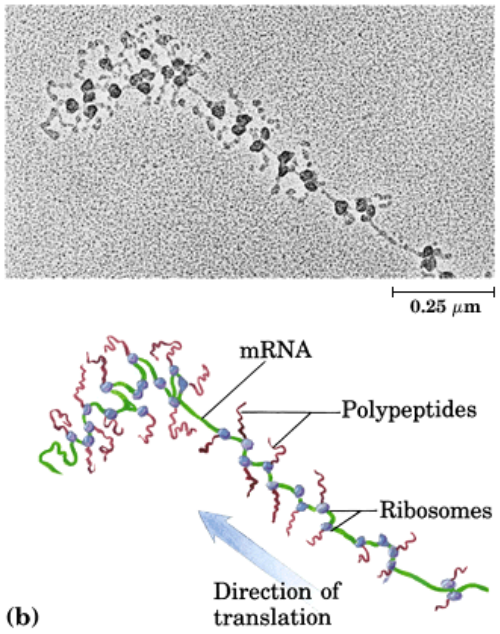
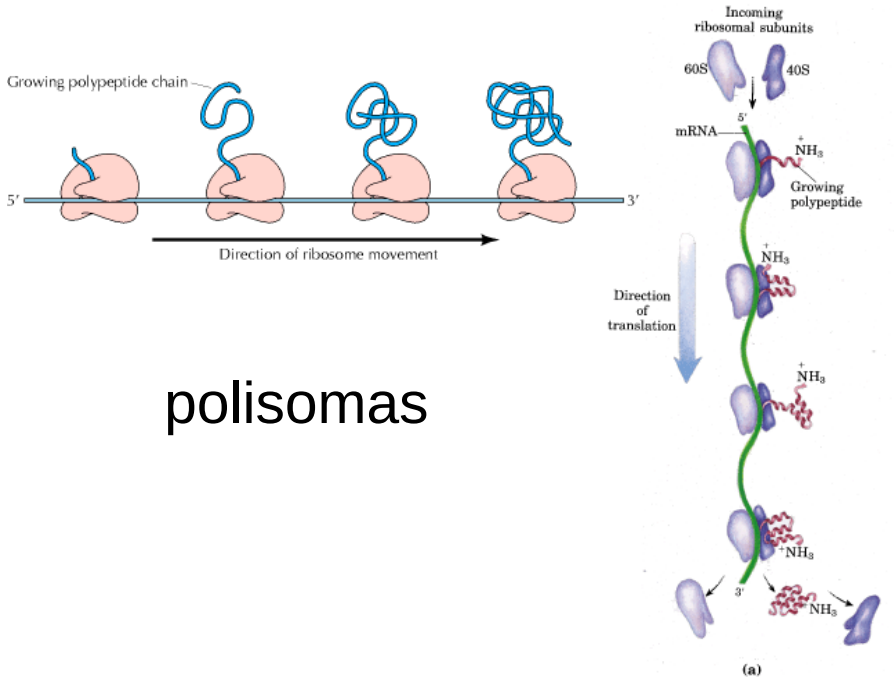


FIGURE 30-37. Distribution of [^{3}H]Leu among the tryptic peptides from the β subunit of soluble rabbit hemoglobin after the incubation of rabbit reticulocytes with [^{3}H]leucine for the indicated times. [After Dintzis, H.M., *Proc. Natl. Acad. Sci.* **47**, 255 (1961).]

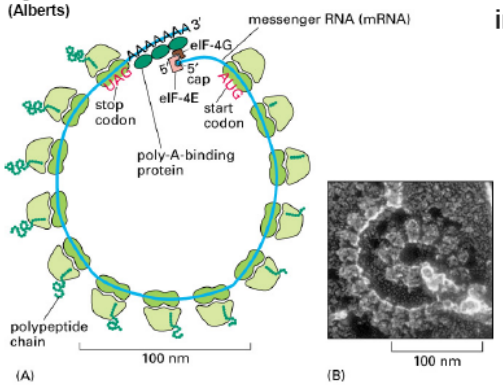

0.25 μm
mRNA
Polypeptides
Ribosomes
Direction of translation
(b)


Growing polypeptide chain
5′
3′
Direction of ribosome movement
Incoming ribosomal subunits
60S
40S
mRNA
5′
NH3
Growing polypeptide
Direction of translation
3′
(a)

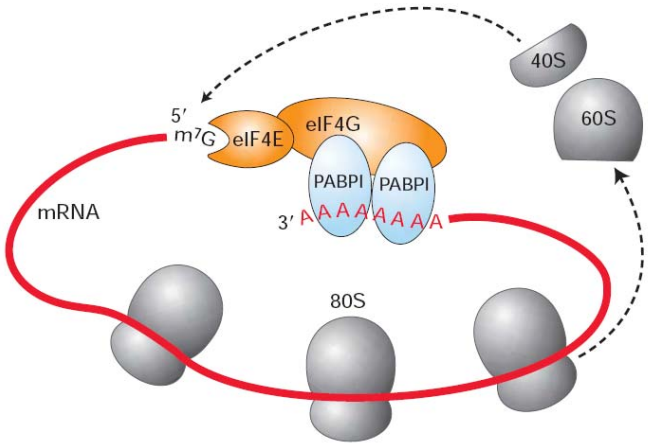
polisomas

Multiple ribosomes may engage a single mRNA transcript

Fig 6-75
(Alberts)

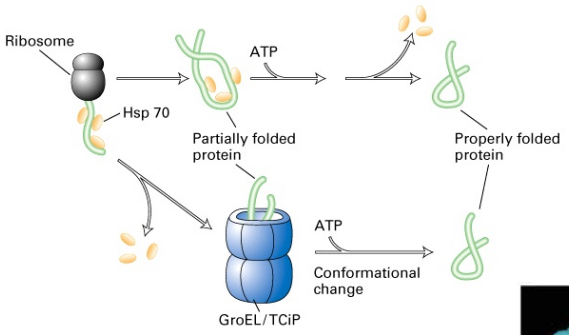


- synthesis rates may be increased by…
  - multiple ribosomes binding and translating single mRNA
    - evident by EM as polyribosomes (aka polysomes)
  - rapid recycling of ribosomal subunits after they finish a translation cycle
    - some polysomes appeared circular
    - complex forms between PABI, EF-4G, and EF-4E to circularize mRNAs



◄ **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.

Folding of proteins in vivo is promoted by chaperones



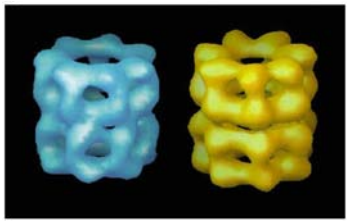
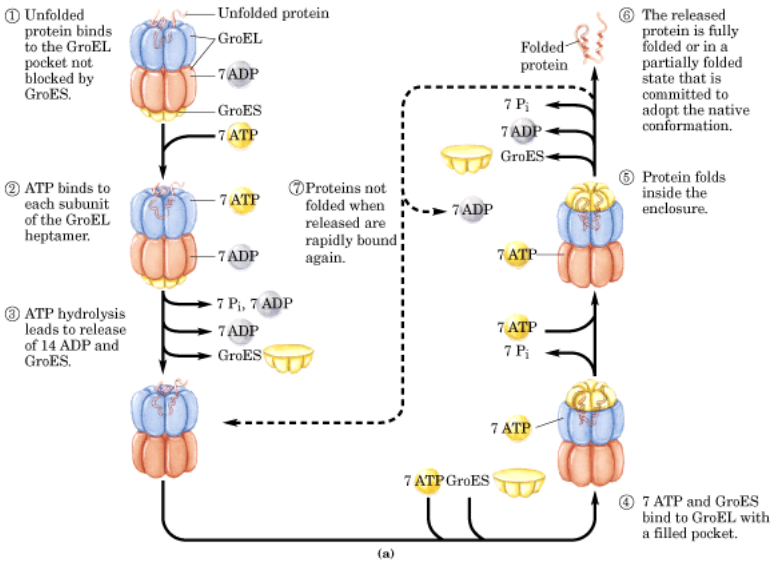
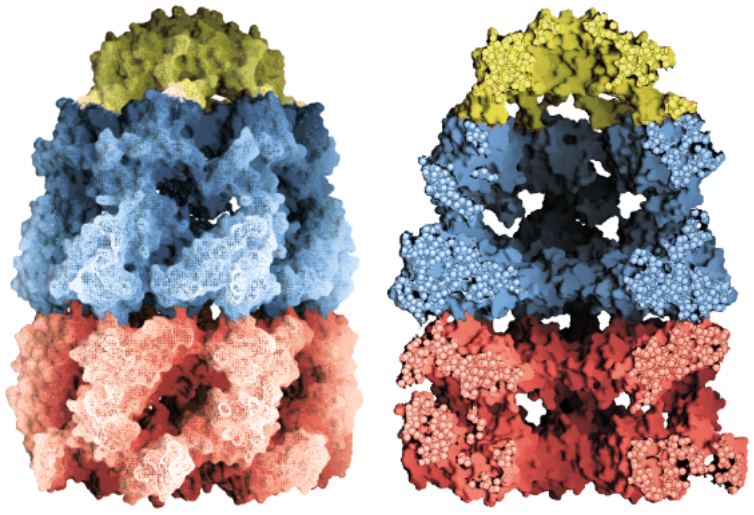


Figure 3-15





(b)

Aberrantly folded proteins are implicated in slowly developing diseases

An amyloid plaque in Alzheimer's disease is a tangle of protein filaments

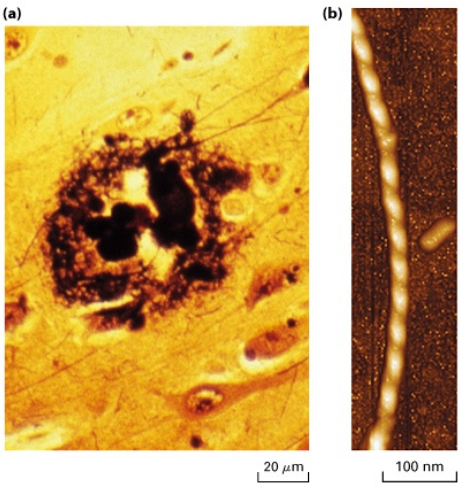


Figure 3-19

Encefalitis espongiforme