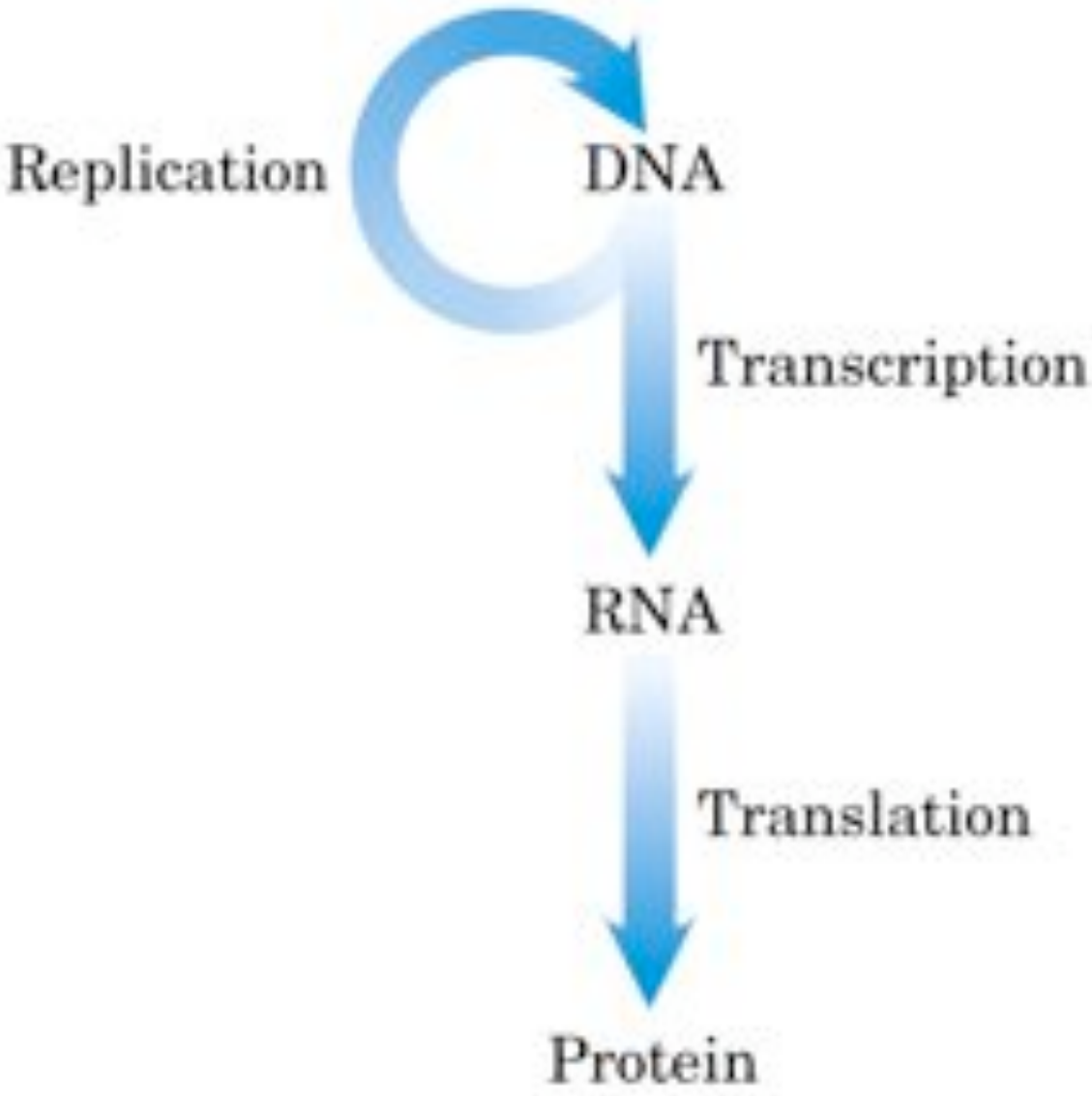
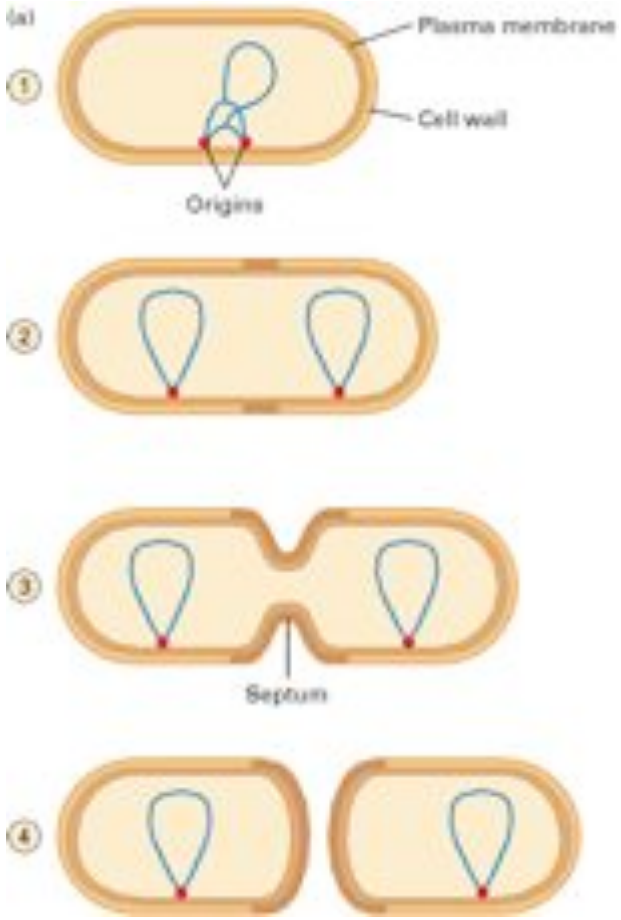
Del Genotipo al Fenotipo

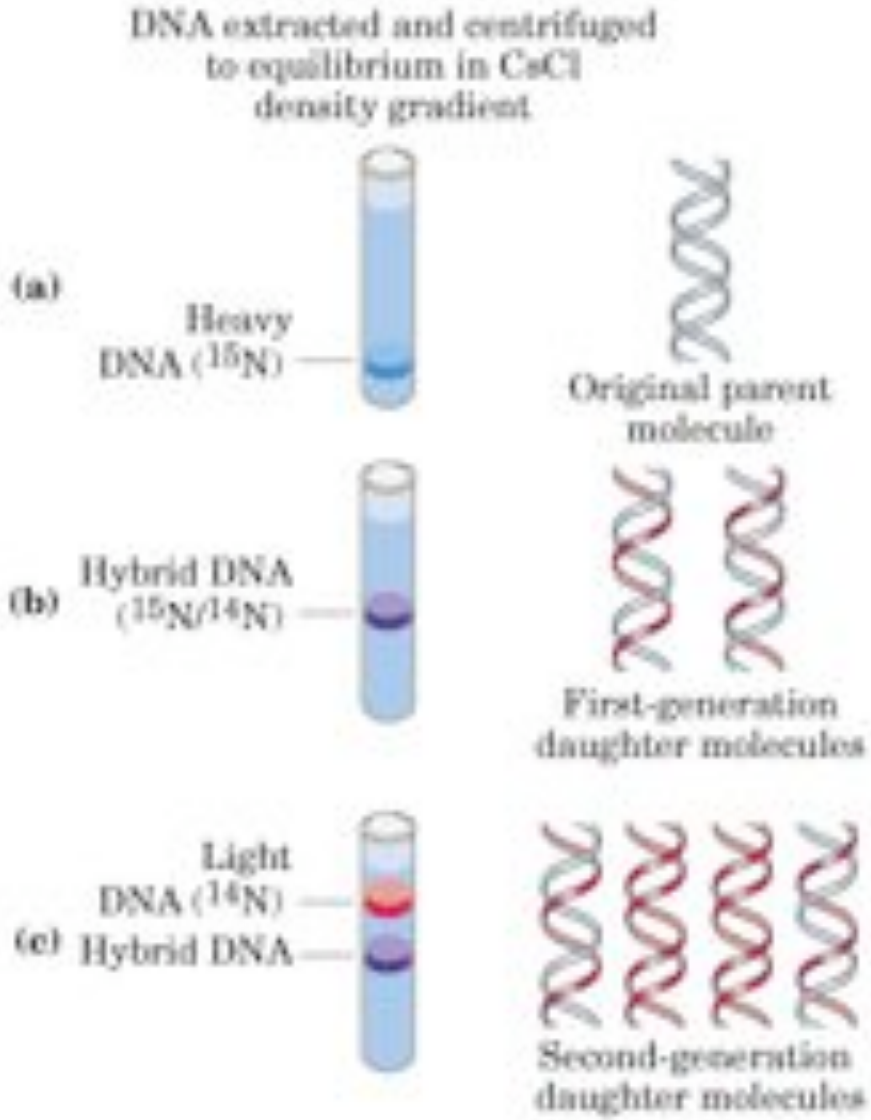

Replication
DNA
Transcription
RNA
Translation
Protein

DNA → RNA → Proteínas



Pro y eucariontes difieren en la coordinación de la síntesis del DNA y la división celular asegurando la continuidad del DNA genómico. En procariontes hay una sola molécula de DNA que se replica a medida que se sintetizan los otros componentes celulares. No hay condensación y decondensación del cromosoma

Una propiedad de todas las células que crecen (pro y eucarióticas), es que pueden duplicar su DNA genómico y pasarlo en copias idénticas a cada célula hija. Las actividades de células que crecen y se dividen se describen en términos del ciclo de vida de la célula o “ciclo celular”.


DNA extracted and centrifuged to equilibrium in CsCl density gradient
(a)
Heavy DNA (^{15}N)
Original parent molecule
(b)
Hybrid DNA (^{15}N/^{14}N)
First-generation daughter molecules
Light DNA (^{14}N)
(c)
Hybrid DNA
Second-generation daughter molecules

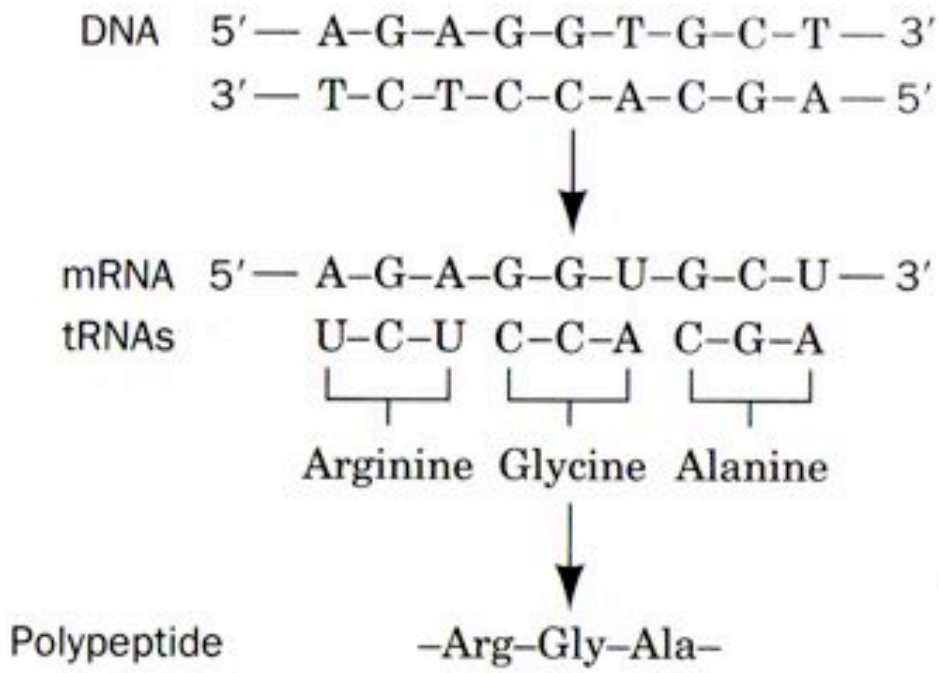
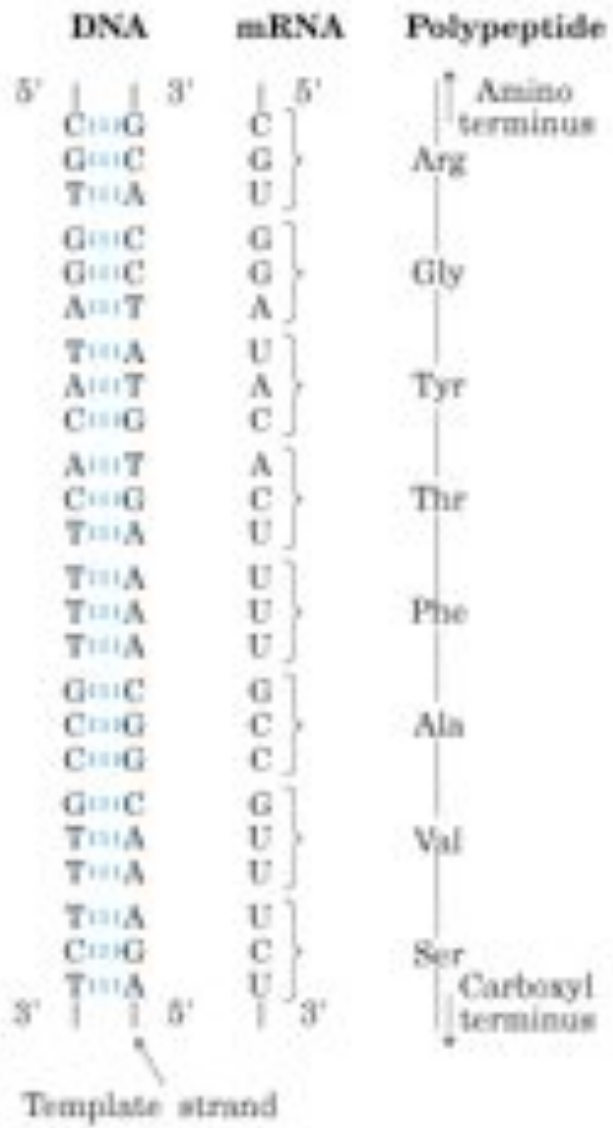


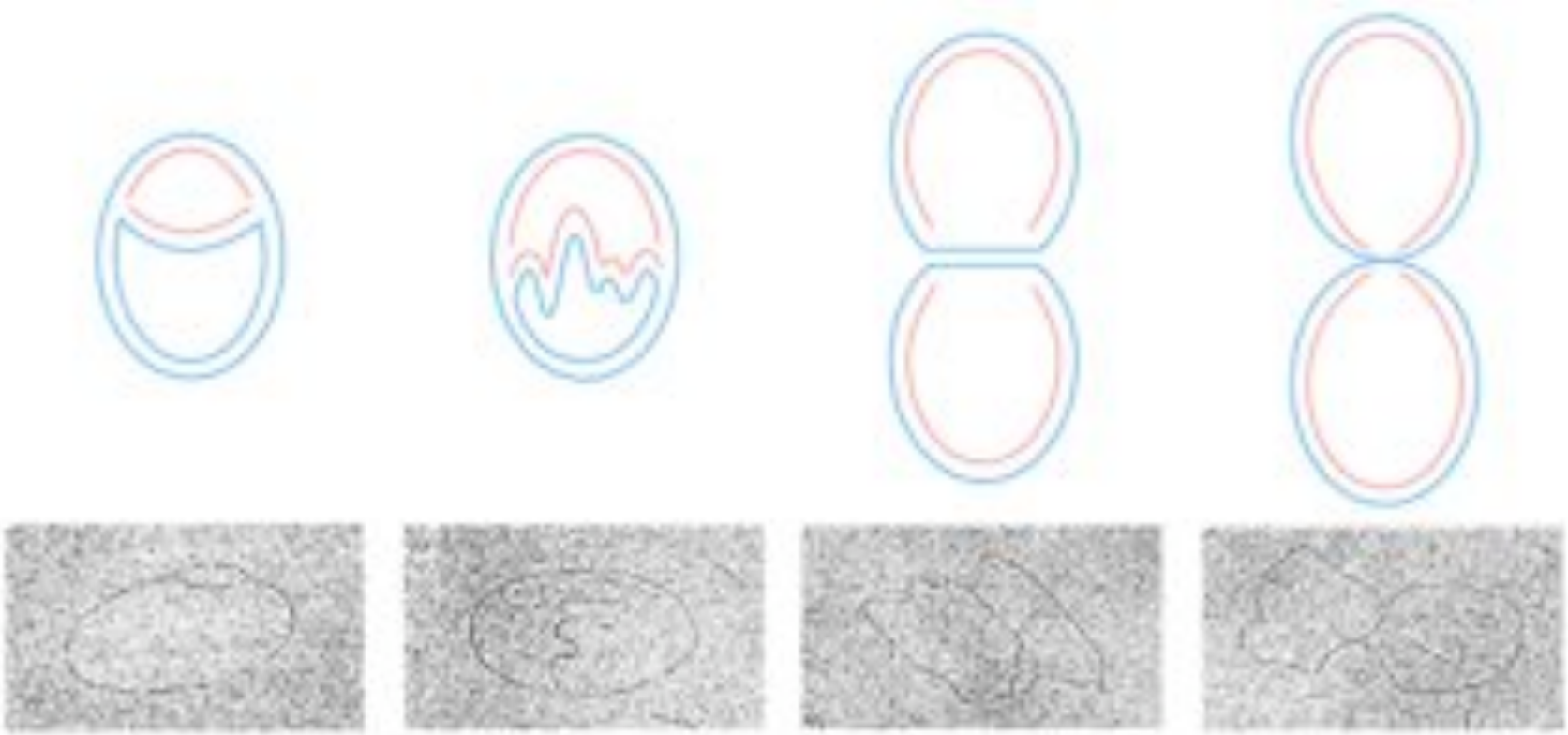
FIGURE 5-22 Gene expression. One strand of DNA directs the synthesis of RNA, a process known as transcription. The base sequence of the transcribed RNA is complementary to that of the DNA strand. The RNAs known as **messenger RNAs (mRNAs)** are translated when molecules of **transfer RNA (tRNA)** align with the mRNA via complementary base pairing between 3-nucleotide segments known as codons. Each type of tRNA carries a specific amino acid. These amino acids are covalently joined by the ribosome to form a polypeptide. Thus, the sequence of bases in DNA specifies the sequence of amino acids in a protein.

1.ª posición (extremo 5')	2.ª posición U	2.ª posición C	2.ª posición A	2.ª posición G	3.ª posición (extremo 3')
U	Phe	Ser	Tyr	Cys	U
	Phe	Ser	Tyr	Cys	C
	Leu	Ser	STOP	STOP	A
	Leu	Ser	STOP	Trp	G
C	Leu	Pro	His	Arg	U
	Leu	Pro	His	Arg	C
	Leu	Pro	Gln	Arg	A
	Leu	Pro	Gln	Arg	G
A	Ile	Thr	Asn	Ser	U
	Ile	Thr	Asn	Ser	C
	Ile	Thr	Lys	Arg	A
	Met	Thr	Lys	Arg	G
G	Val	Ala	Asp	Gly	U
	Val	Ala	Asp	Gly	C
	Val	Ala	Glu	Gly	A
	Val	Ala	Glu	Gly	G

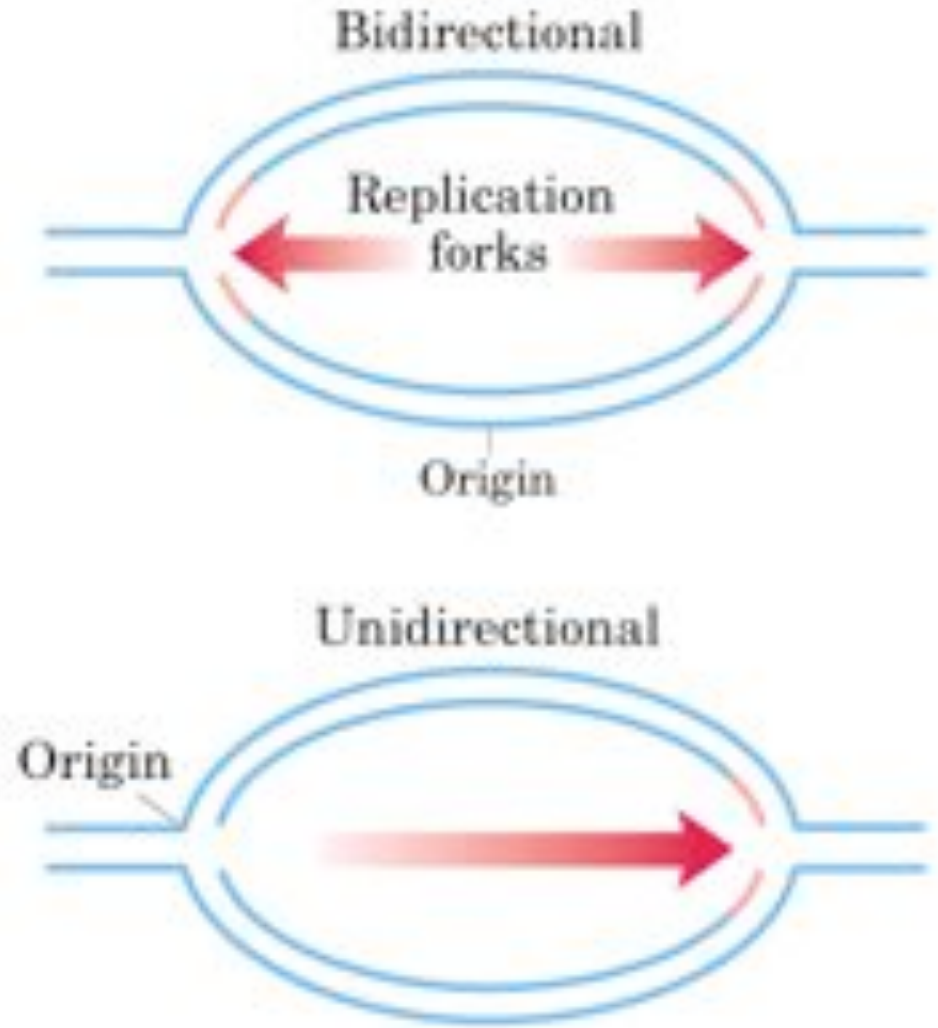
Figura 3-16 El código genético. En el transcurso de la síntesis proteica, los grupos de tres nucleótidos (*codones*) de una molécula de mRNA son traducidos a aminoácidos de acuerdo con las reglas indicadas aquí. Los codones GUG y GAG, por ejemplo, se traducen a valina y a ácido glutámico respectivamente. Obsérvese que los codones que presentan U o C como segundo nucleótido tienden a codificar los aminoácidos más hidrofóbicos (compárese con el Panel 2-5, págs. 58-59).


DNA
mRNA
Polypeptide
5'
3'
C G
G C
T A
G C
G C
A T
T A
A T
C G
A T
C G
T A
T A
T A
T A
G C
C G
C G
G C
T A
T A
T A
T A
C G
T A
3'
5'
Template strand
5'
3'
Amino terminus
Arg
Gly
Tyr
Thr
Phe
Ala
Val
Ser
Carboxyl terminus

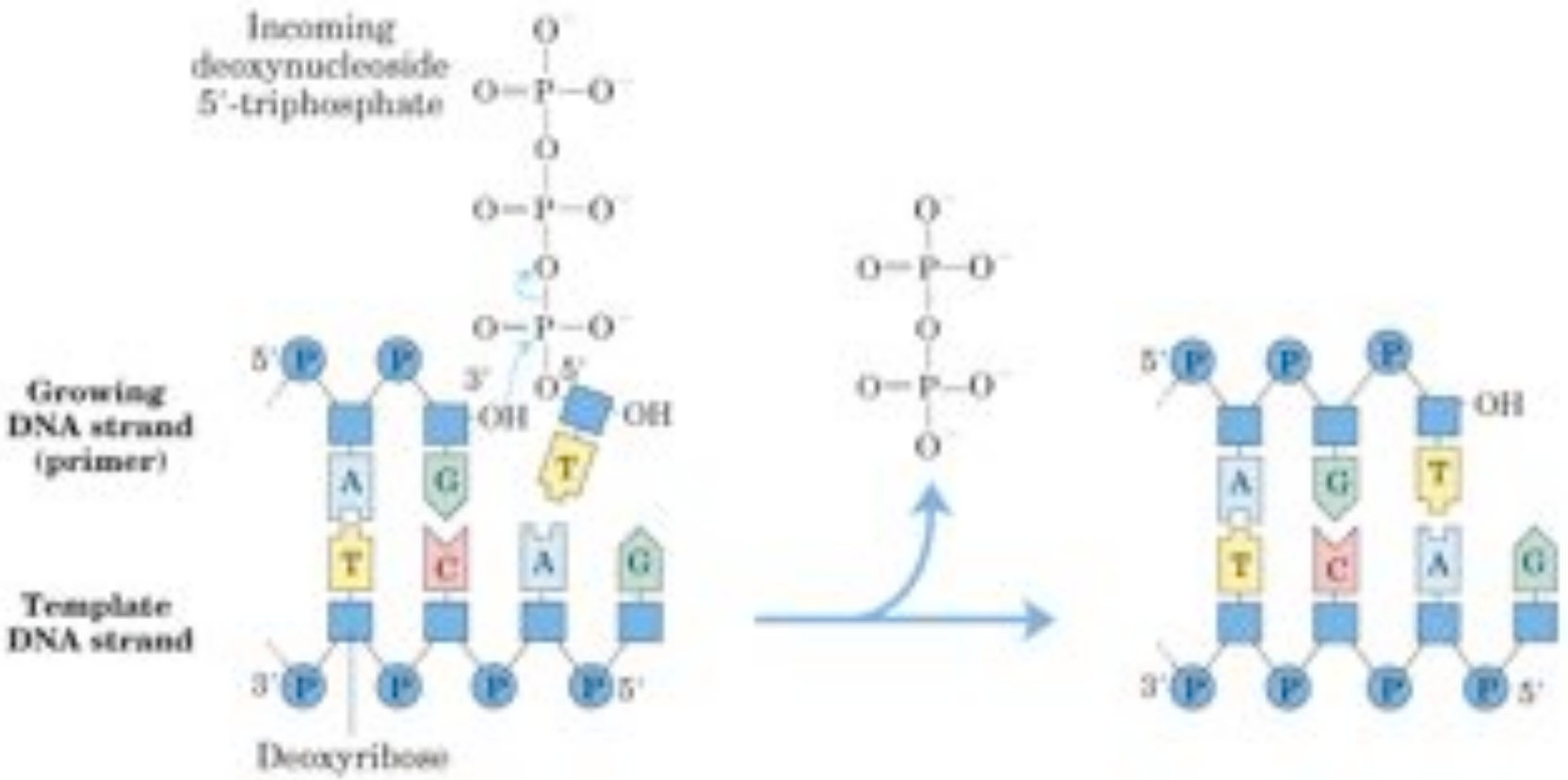
Replicación del DNA

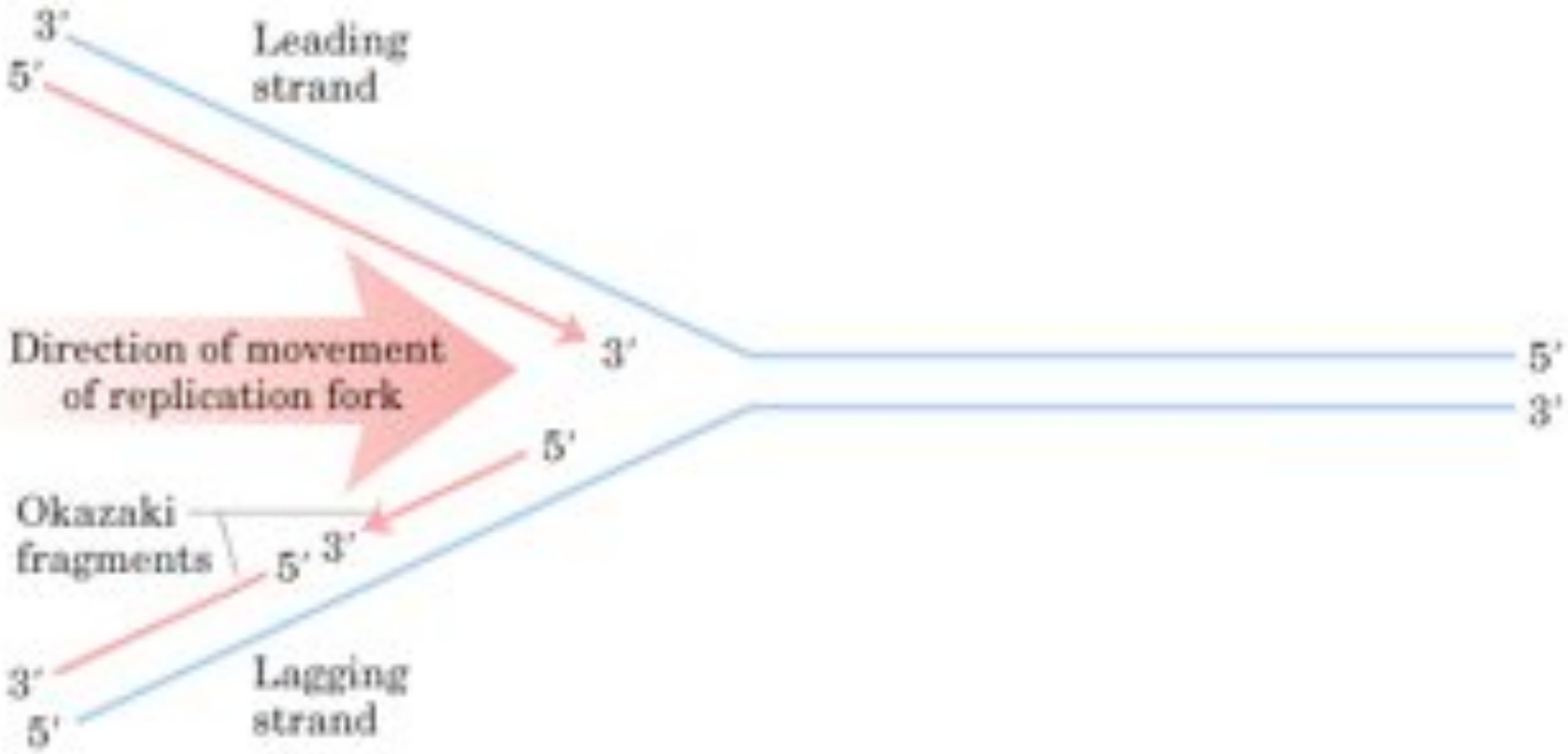


(a)

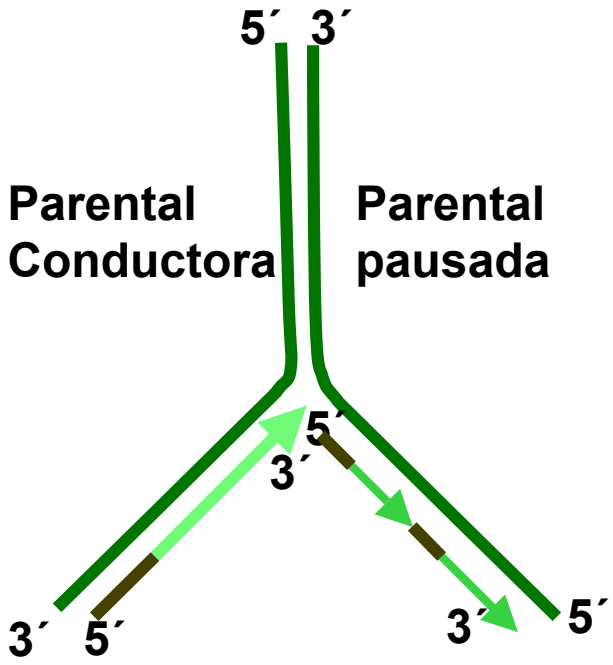

Bidirectional
Replication forks
Origin
Unidirectional
Origin

(b)

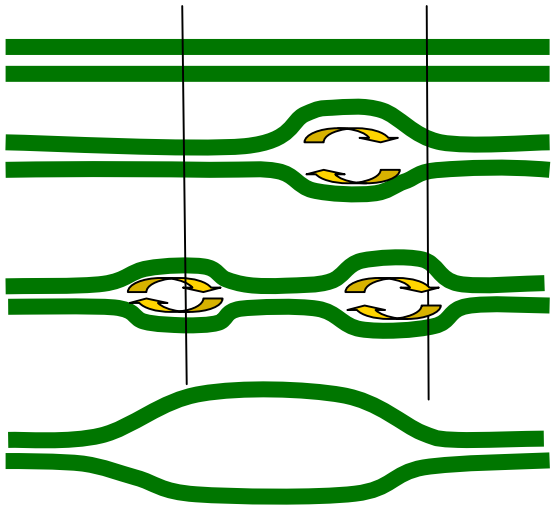

Incoming
deoxynucleoside
5'-triphosphate
Growing
DNA strand
(primer)
Template
DNA strand
Deoxyribose
OH
A
G
T
C


3′
5′
Leading strand
Direction of movement of replication fork
3′
5′
3′
5′
Okazaki fragments
5′
3′
3′
5′
Lagging strand

Las células eucariontes tienen un gran número de moléculas de DNA polimerasas. La enzima inicia la síntesis bidireccional del DNA, desde varios sitios de origen de replicación, ubicados de 5 a 300 kb de distancia en el cromosoma, según la célula y la especie. Estos sitios se llaman horquillas de iniciación. El segmento entre ellas es un replicon.



La DNA polimerasa no puede iniciar la síntesis de la cadena de DNA, sólo puede alargar una hebra partidora pre-existente de RNA o DNA. Todas las DNA polimerasas agregan nucleótidos al extremo 3´OH del partidor, dirigiendo el crecimiento en la dirección 5´→3´. La replicación del DNA está ligada con la reparación.



La replicación se inicia en las secuencias de replicación autónomas (SRA), a las que se unen proteínas para formar el complejo de origen de replicación (COR) que ayuda a desenrollar el DNA. Otras proteínas estabilizan la forma desenrollada y entra la DNA polimerasa. La copia se inicia en cientos de distintos orígenes, algunos al inicio de S y otros mas tarde.

Durante la replicación hay disociación incompleta y ordenada de la cromatina y reasociación del DNA con octámeros de histona para formar nucleosomas.

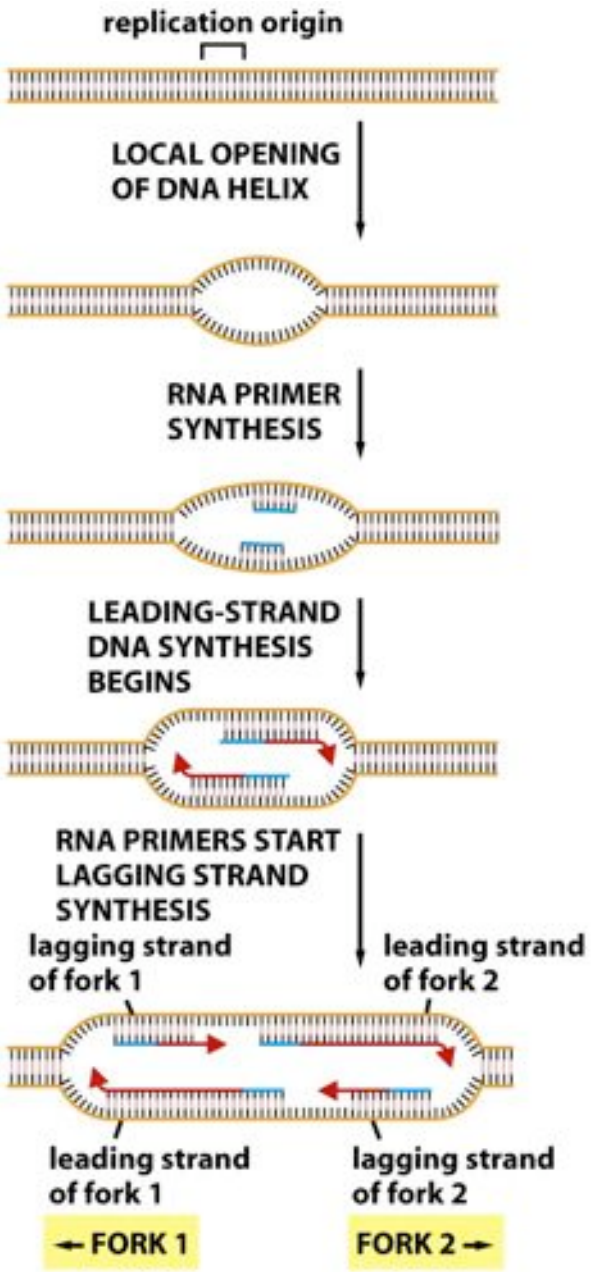


Figure 5-25 *Molecular Biology of the Cell* (© Garland Science 2008)

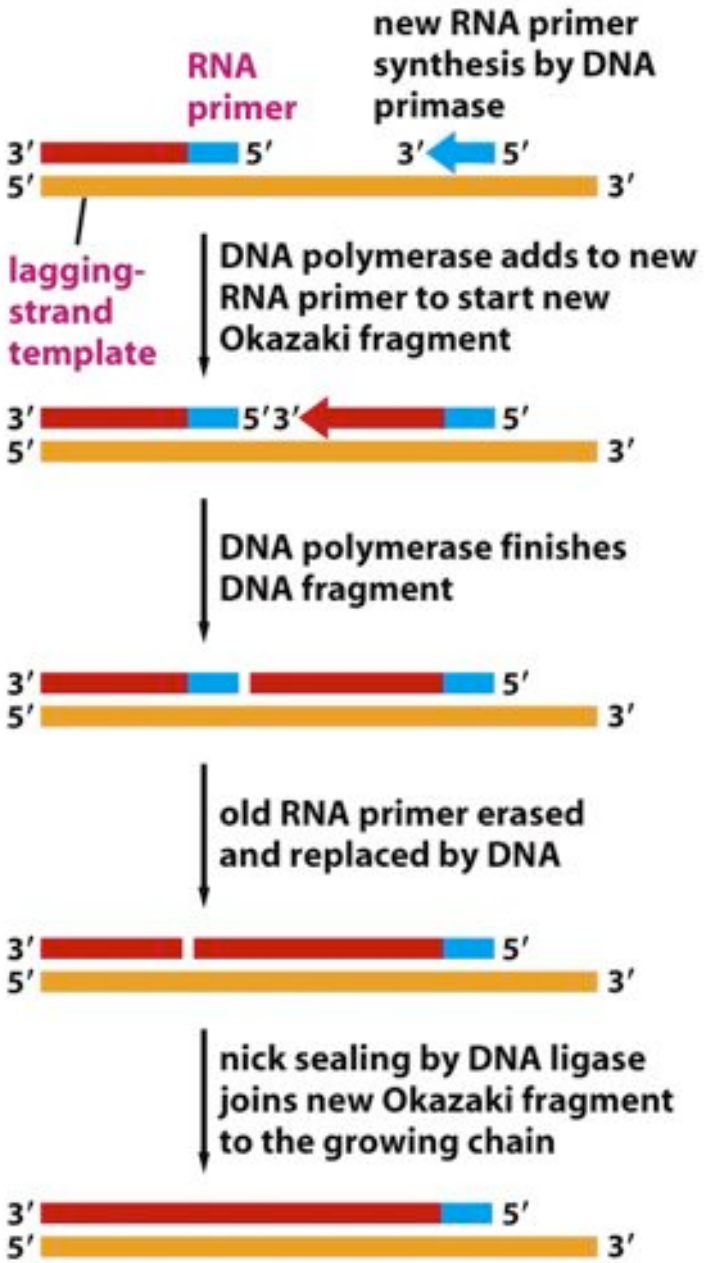
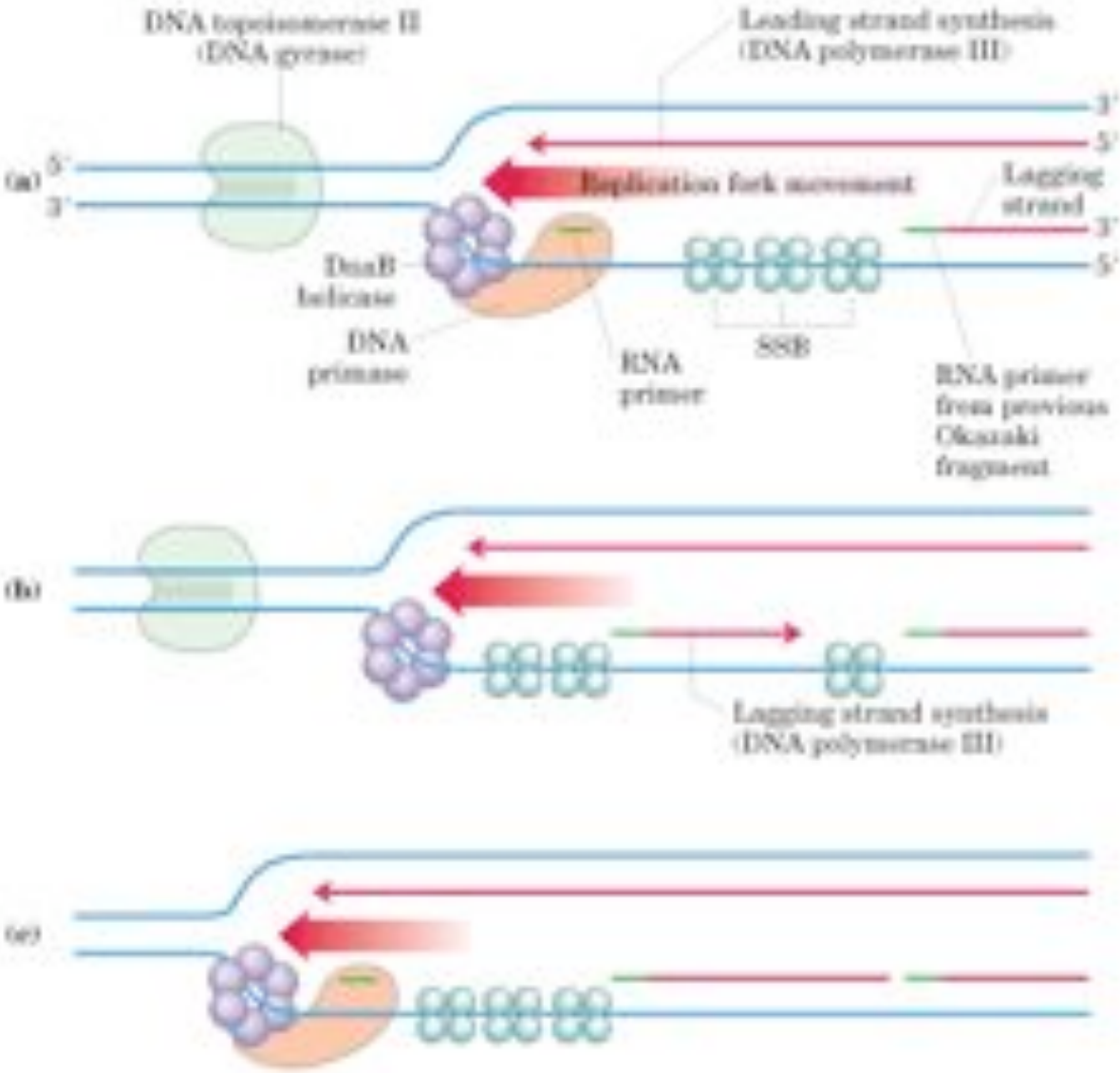
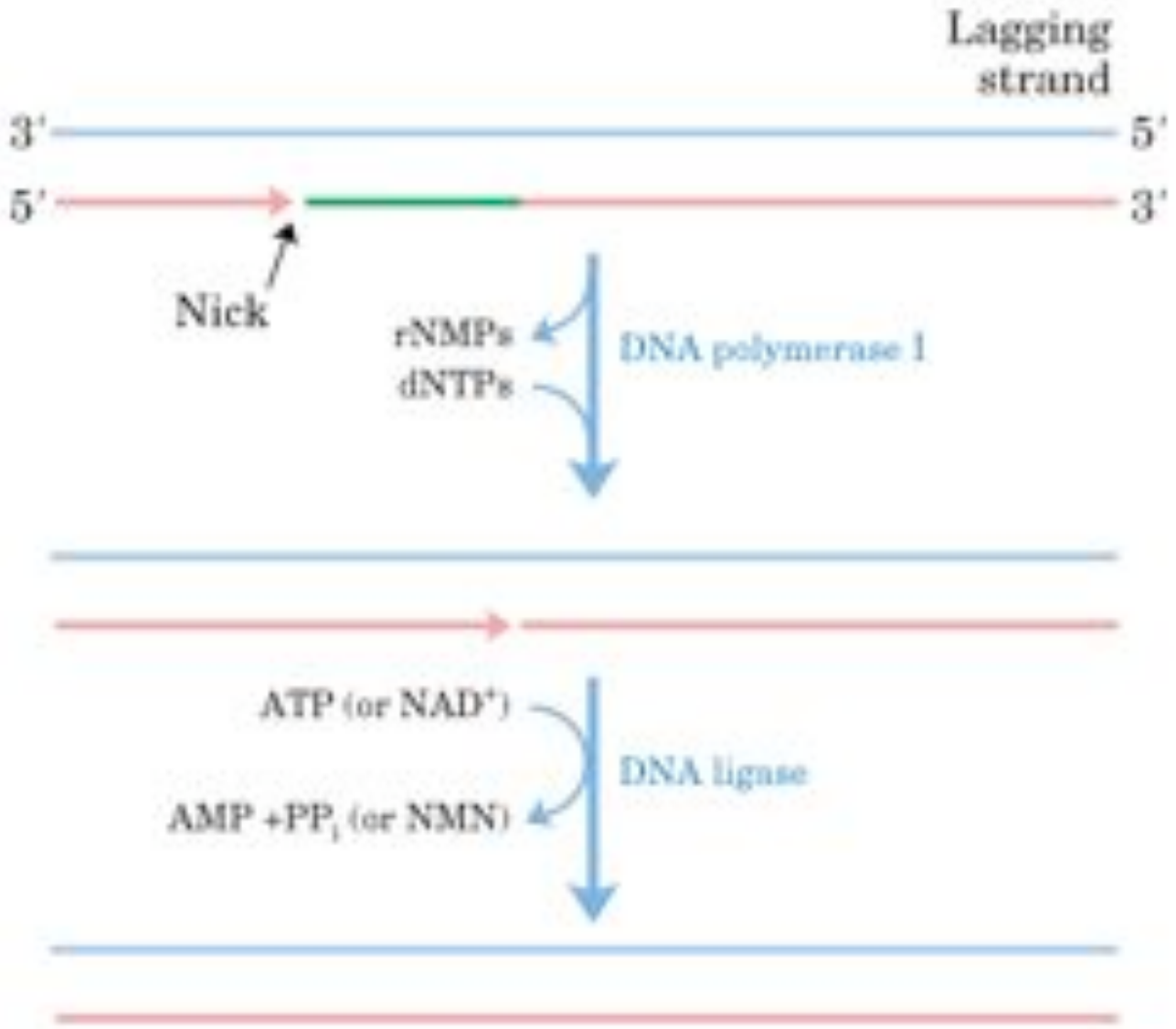


Figure 5-12 *Molecular Biology of the Cell* (© Garland Science 2008)


DNA topoisomerase II
(DNA gyrase)
Leading strand synthesis
(DNA polymerase III)
3'
5'
(a) 5'
3'
Replication fork movement
Lagging
strand
3'
5'
DnaB
helicase
DNA
primase
RNA
primer
SSB
RNA primer
from previous
Okazaki
fragment
(b)
Lagging strand synthesis
(DNA polymerase III)
(c)


Lagging strand
3'
5'
5'
3'
Nick
rNMPs
dNTPs
DNA polymerase I
ATP (or NAD+)
AMP +PPi (or NMN)
DNA ligase

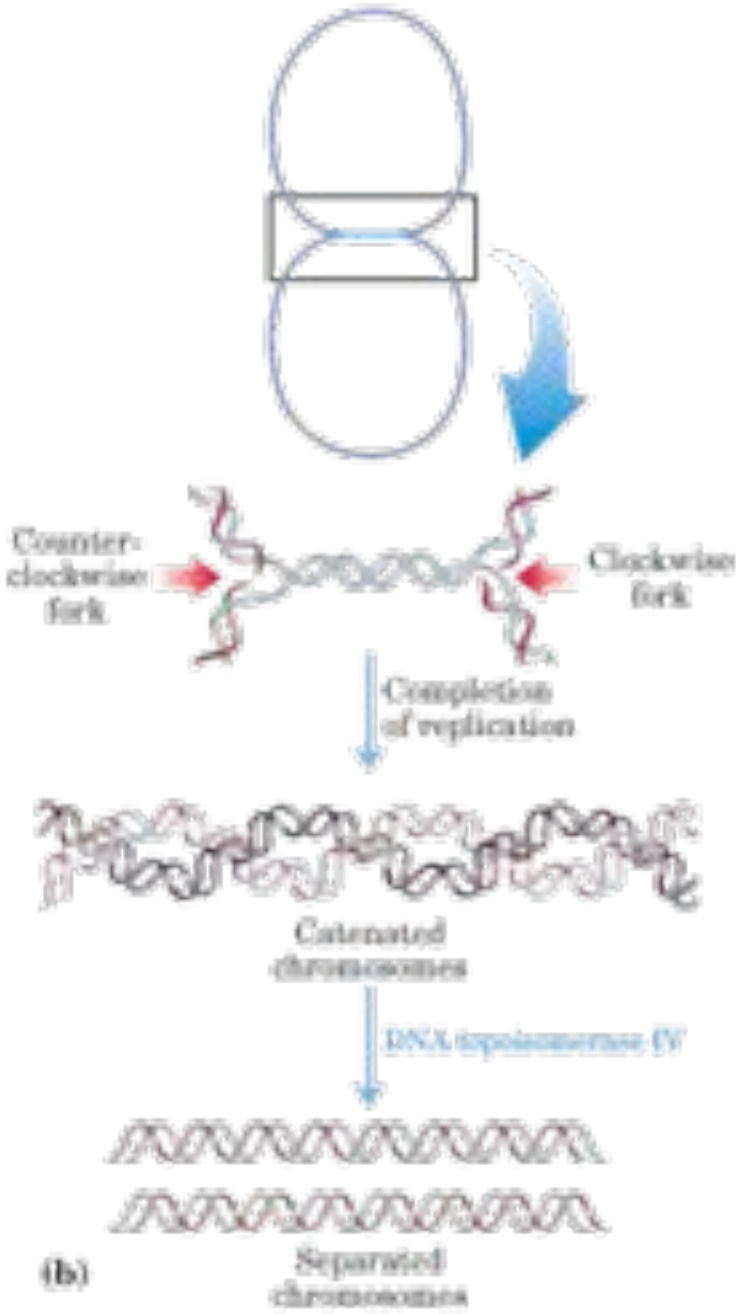

Counter-clockwise fork
Clockwise fork
Completion of replication
Catenated chromosomes
DNA topoisomerase IV
Separated chromosomes
(b)

table 25–3

Proteins Required to Initiate Replication at the *E. coli* Origin

Protein	M_r	Number of subunits	Function
DnaA protein	52,000	1	Recognizes origin sequence; opens duplex at specific sites in origin
DnaB protein (helicase)	300,000	6*	Unwinds DNA
DnaC protein	29,000	1	Required for DnaB binding at origin
HU	19,000	2	Histonelike protein; DNA bending protein; stimulates initiation
Primase (DnaG protein)	60,000	1	Synthesizes RNA primers
Single-stranded DNA-binding protein (SSB)	75,600	4*	Binds single-stranded DNA
RNA polymerase	454,000	5	Facilitates DnaA activity
DNA gyrase (DNA topoisomerase II)	400,000	4	Relieves torsional strain generated by DNA unwinding
Dam methylase	32,000	1	Methylates (5′)GATC sequences at *ori*C

*Subunits in these cases are identical.

table 25–5

Types of DNA Repair Systems in *E. coli*

Enzymes/proteins	Type of damage
Mismatch repair	
Dam methylase	Mismatches
MutH, MutL, MutS proteins	
DNA helicase II	
SSB	
DNA polymerase III	
Exonuclease I	
Exonuclease VII	
RecJ nuclease	
Exonuclease X	
DNA ligase	
Base-excision repair	
DNA glycosylases	Abnormal bases (uracil, hypoxanthine, xanthine); alkylated bases; pyrimidine dimers in some other organisms
AP endonucleases	
DNA polymerase I	
DNA ligase	
Nucleotide-excision repair	
ABC excinuclease	DNA lesions that cause large structural changes (e.g., pyrimidine dimers)
DNA polymerase I	
DNA ligase	
Direct repair	
DNA photolyases	Pyrimidine dimers
O^6-Methylguanine-DNA methyltransferase	O^6-Methylguanine

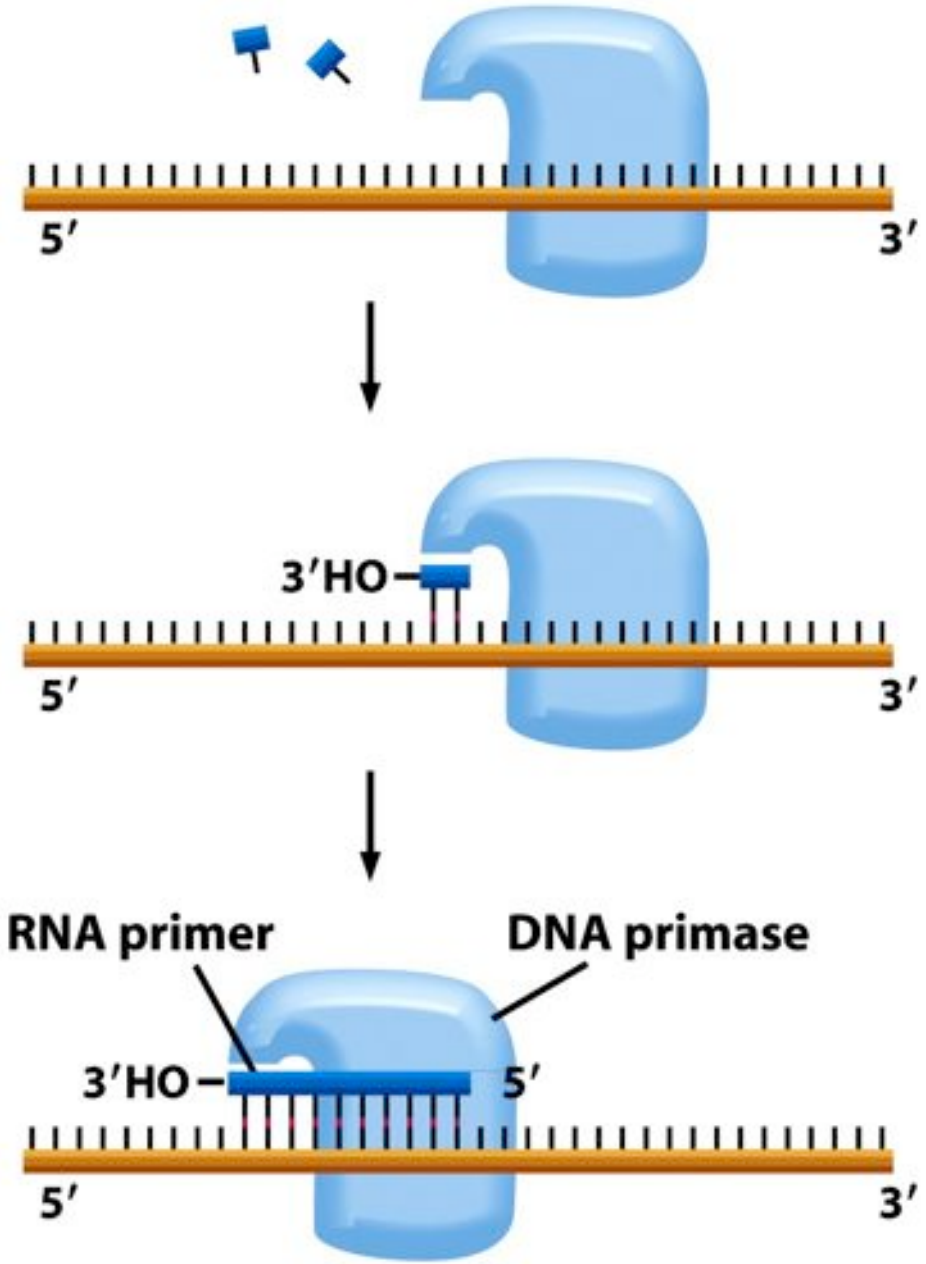


Figure 5-11 *Molecular Biology of the Cell* (© Garland Science 2008)

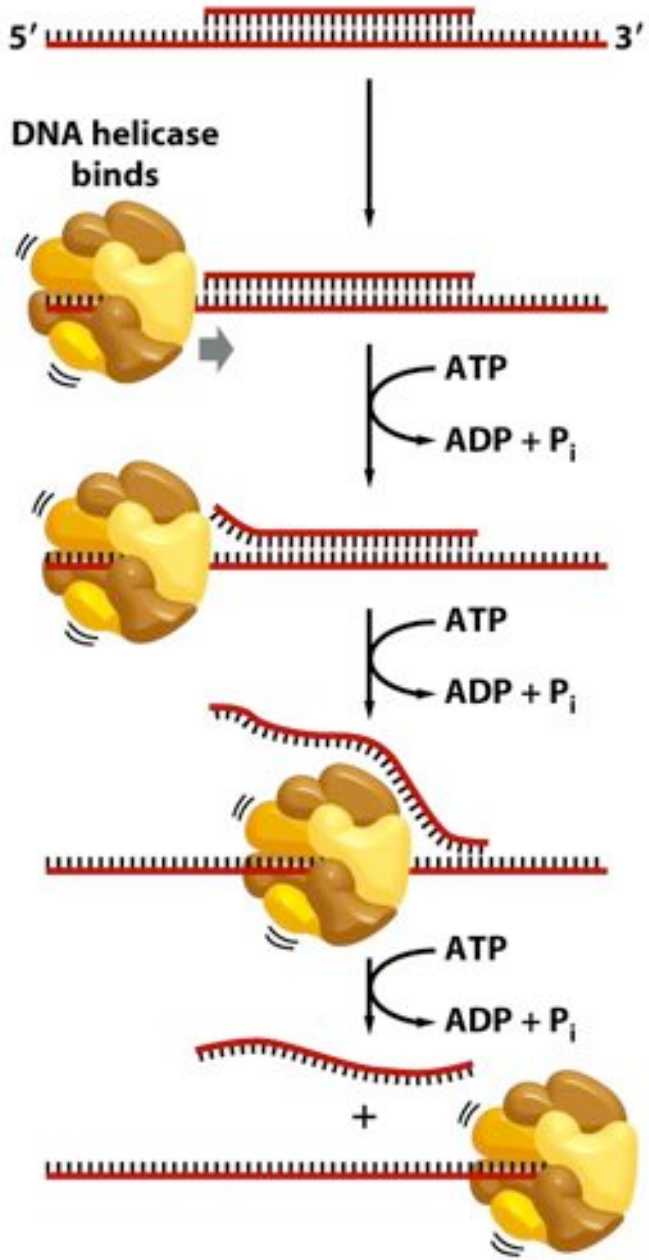


Figure 5-14 *Molecular Biology of the Cell* (© Garland Science 2008)

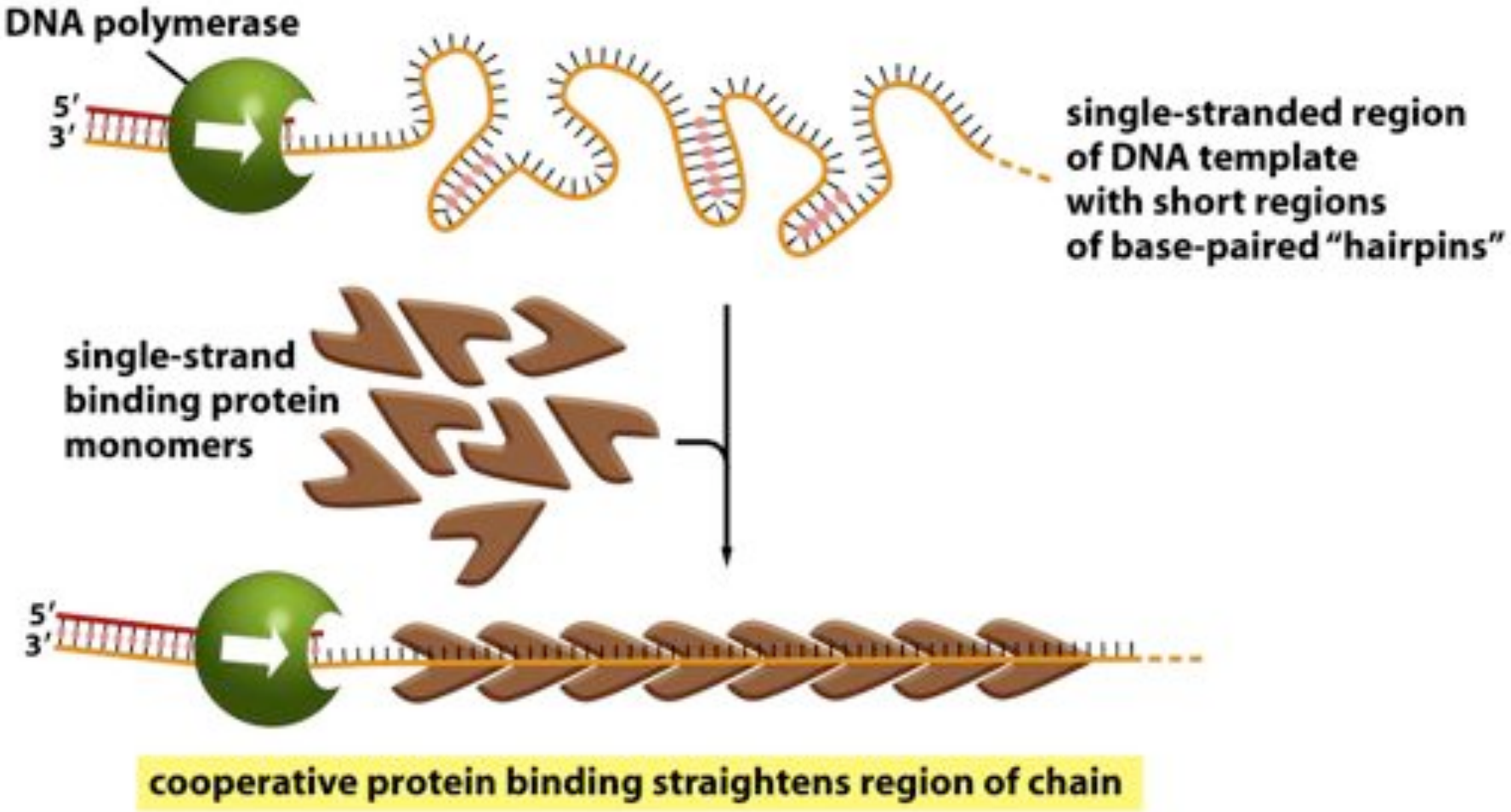


Figure 5-16 *Molecular Biology of the Cell* (© Garland Science 2008)

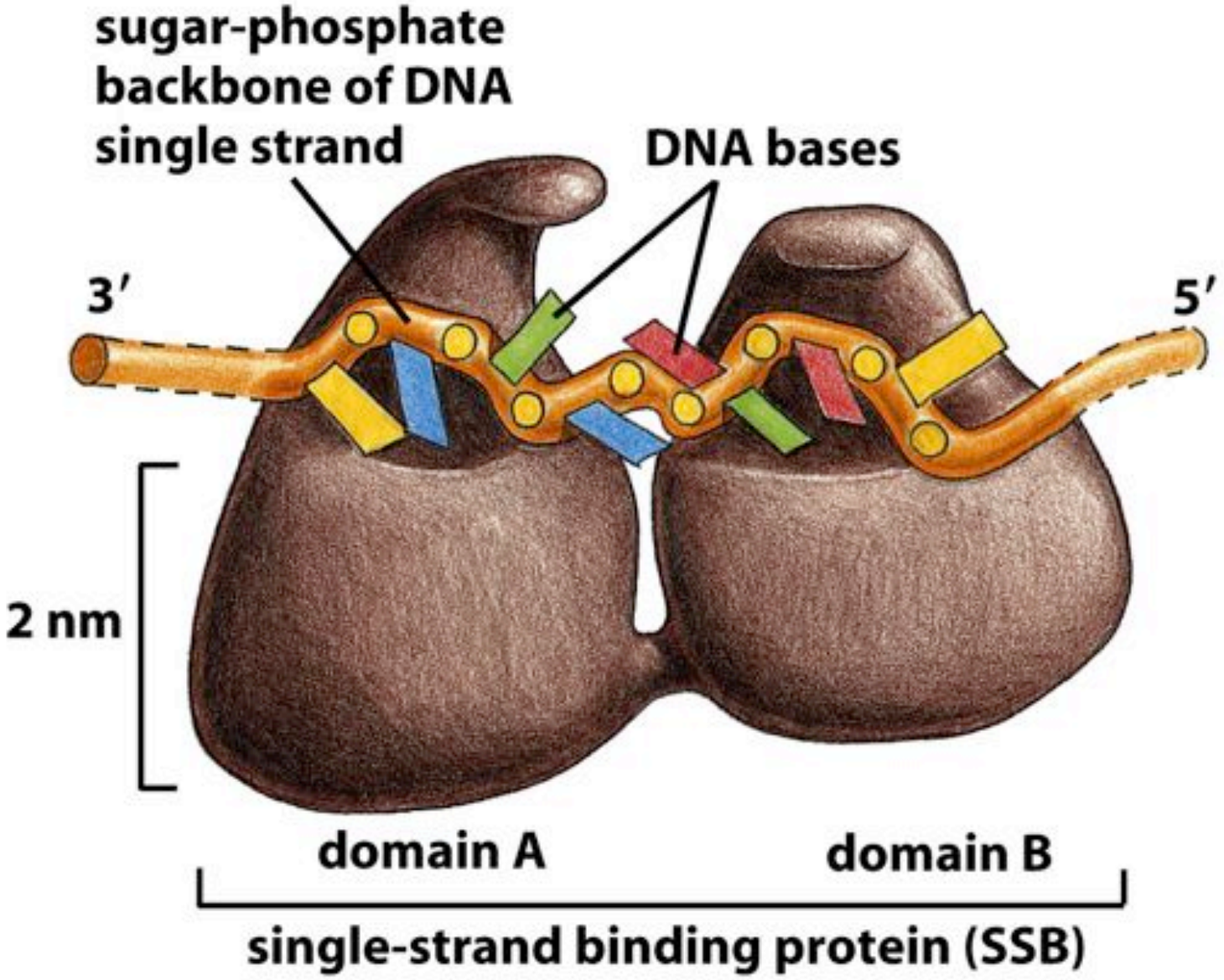


Figure 5-17a *Molecular Biology of the Cell* (© Garland Science 2008)

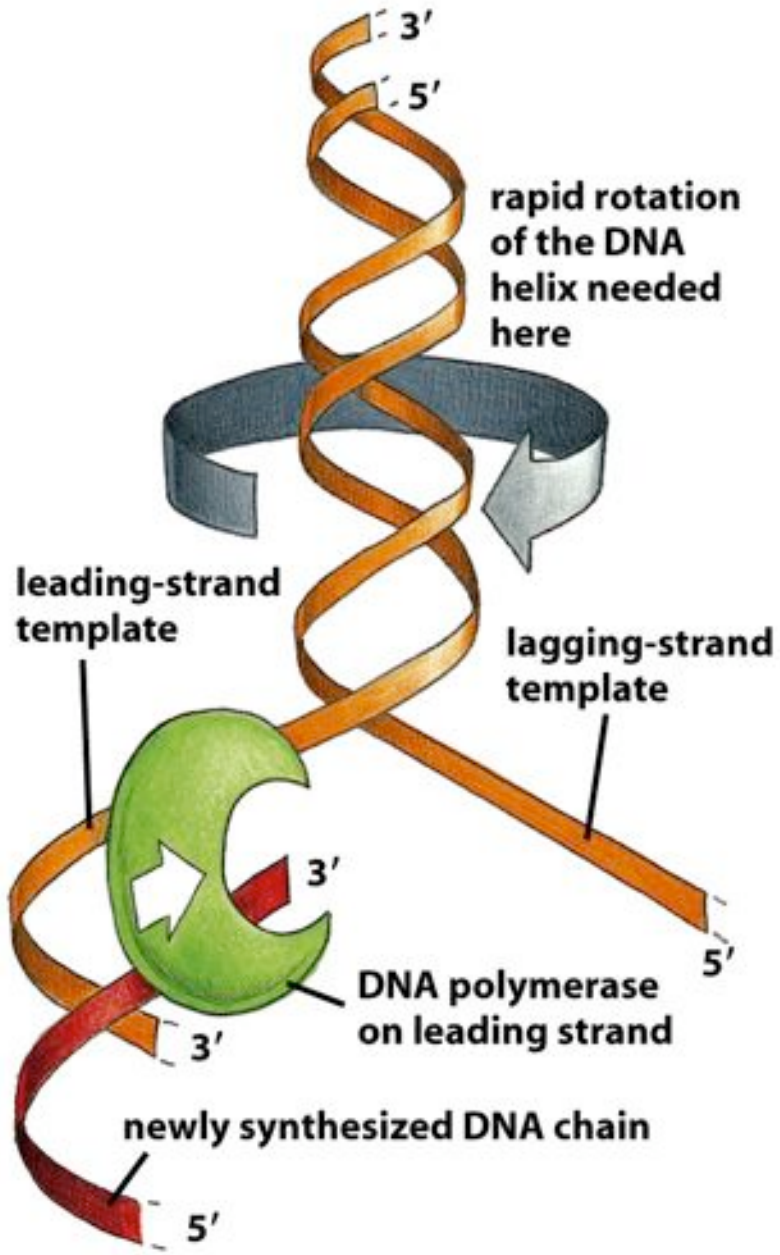
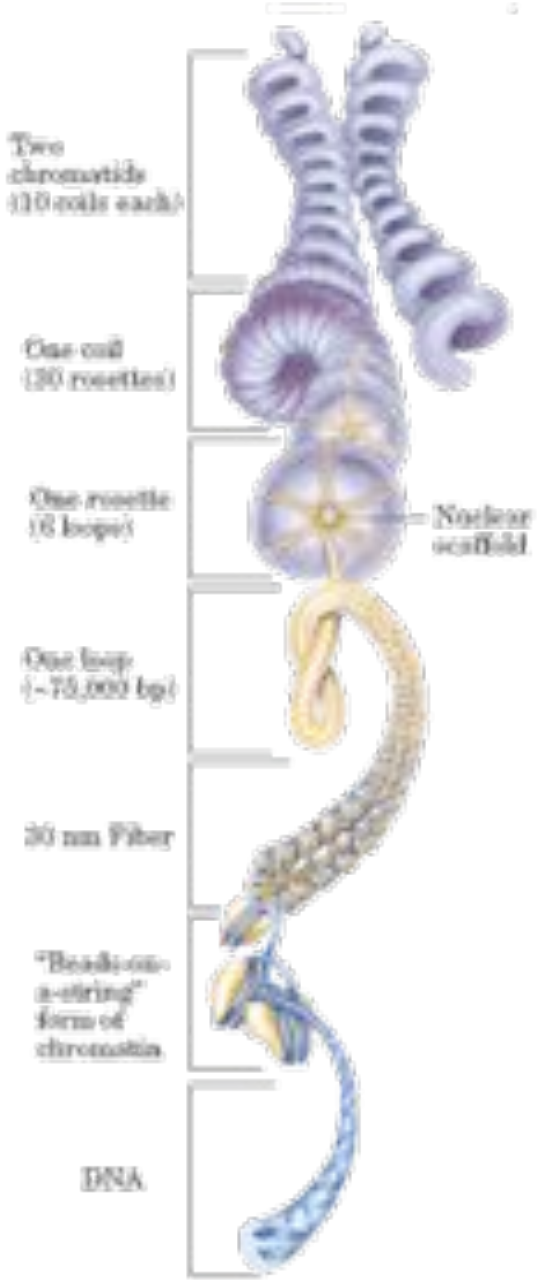


Figure 5-21 *Molecular Biology of the Cell* (© Garland Science 2008)

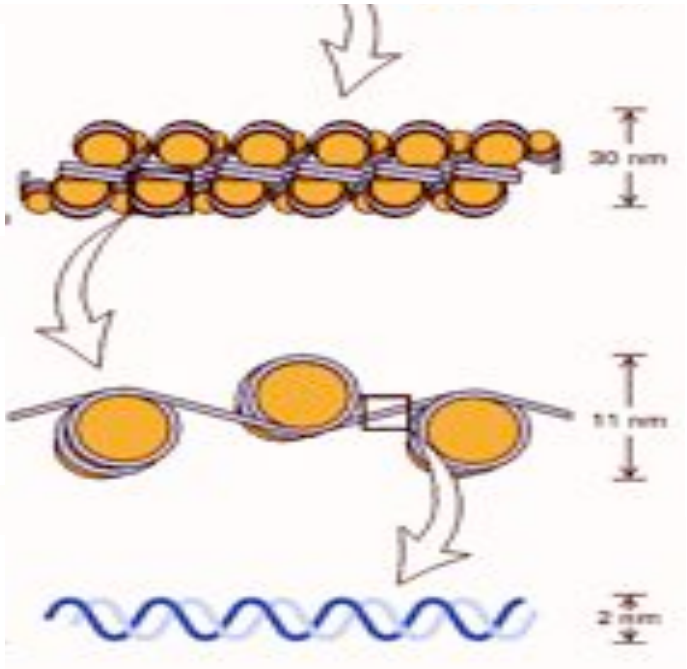

Two chromatids (10 coils each)
One coil (20 rosettes)
One rosette (6 loops)
Nuclear scaffold
One loop (~75,000 bp)
30 nm Fiber
"Beads-on-a-string" form of chromatin
DNA

Organización estructural de cromosomas molécula de DNA, nucleosoma, solenoide (cromatina, eucromatina).

Fibra de 30 nm: cromatina en nucleosomas en espiral o solenoide

Cromatina en cuentas de collar, nucleosomas.

Región corta de doble hélice de DNA.



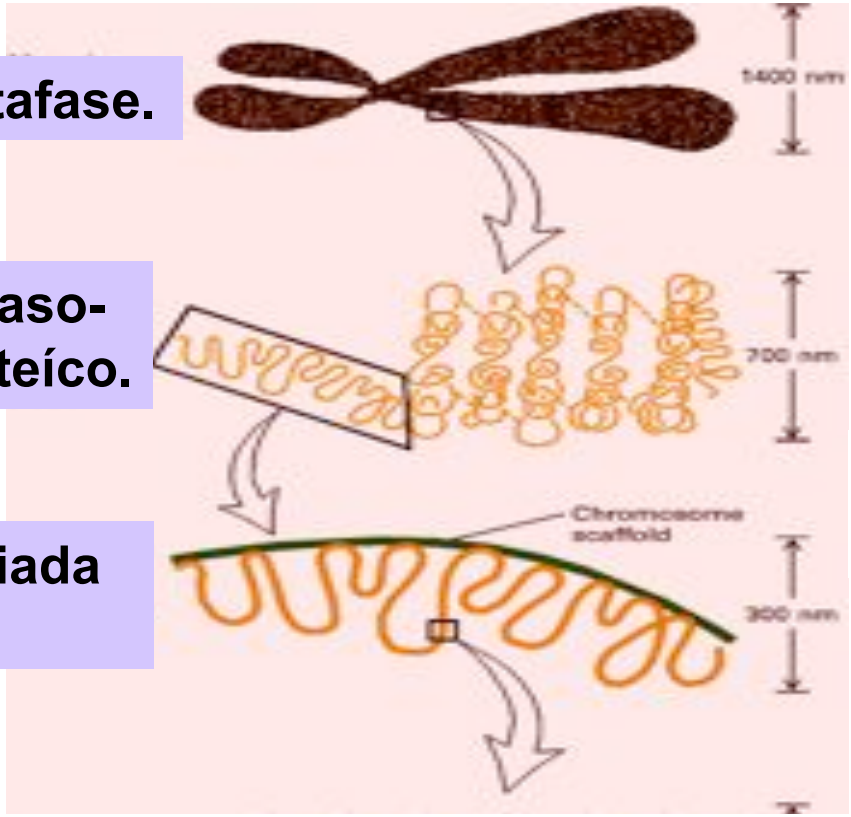
Proteínas: Histonas. H1, H2A, H2B, H3 y H4

Octámero de 2 copias de. H2A, H2B, H3 y H4

Cromosoma en metafase.

Forma condensada, aso-
ciada a andamio proteíco.

Forma extendida asociada
a andamio proteíco.



Proteínas no
histonas

Estructura de cromosoma en metafase.

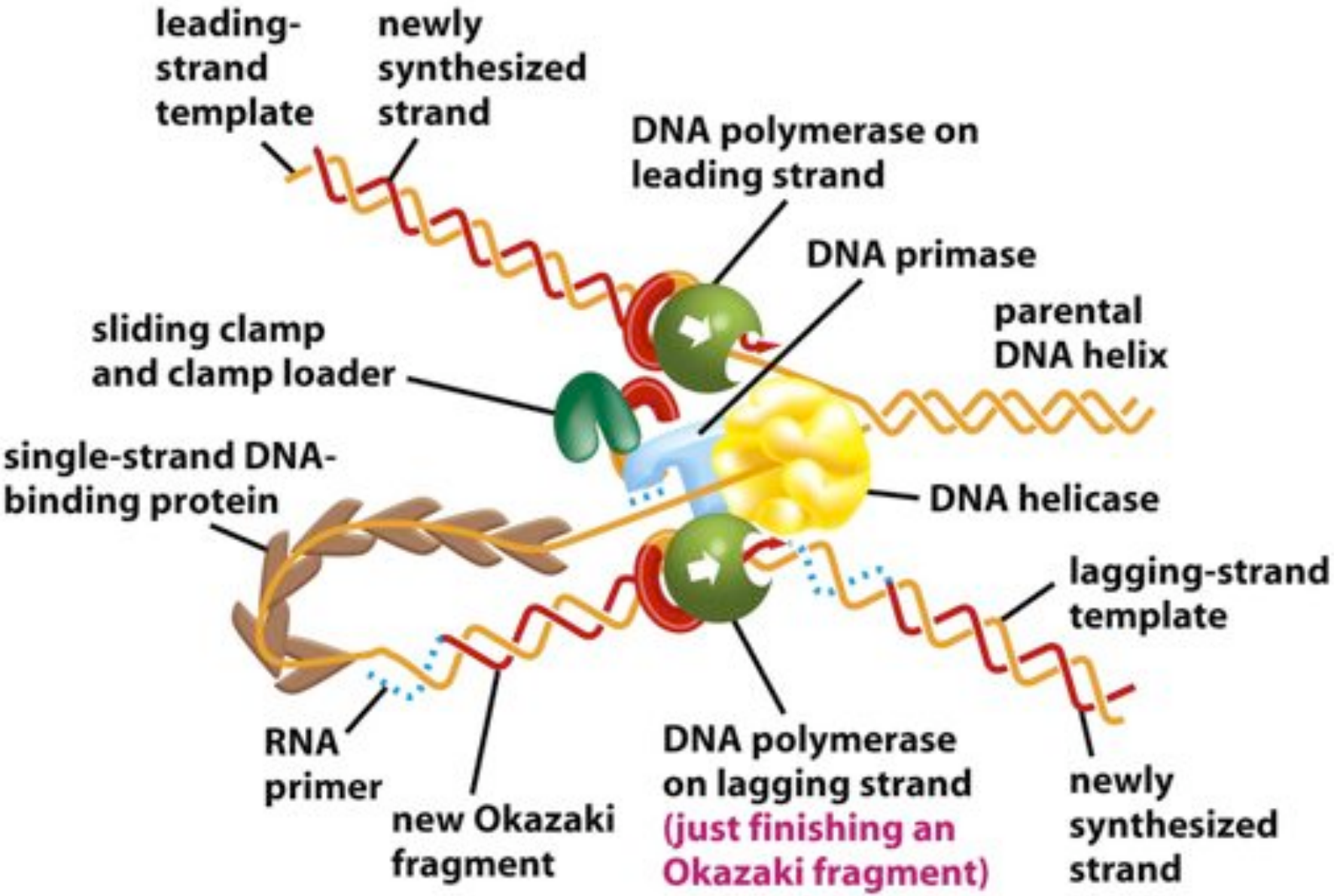


Figure 5-19a *Molecular Biology of the Cell* (© Garland Science 2008)

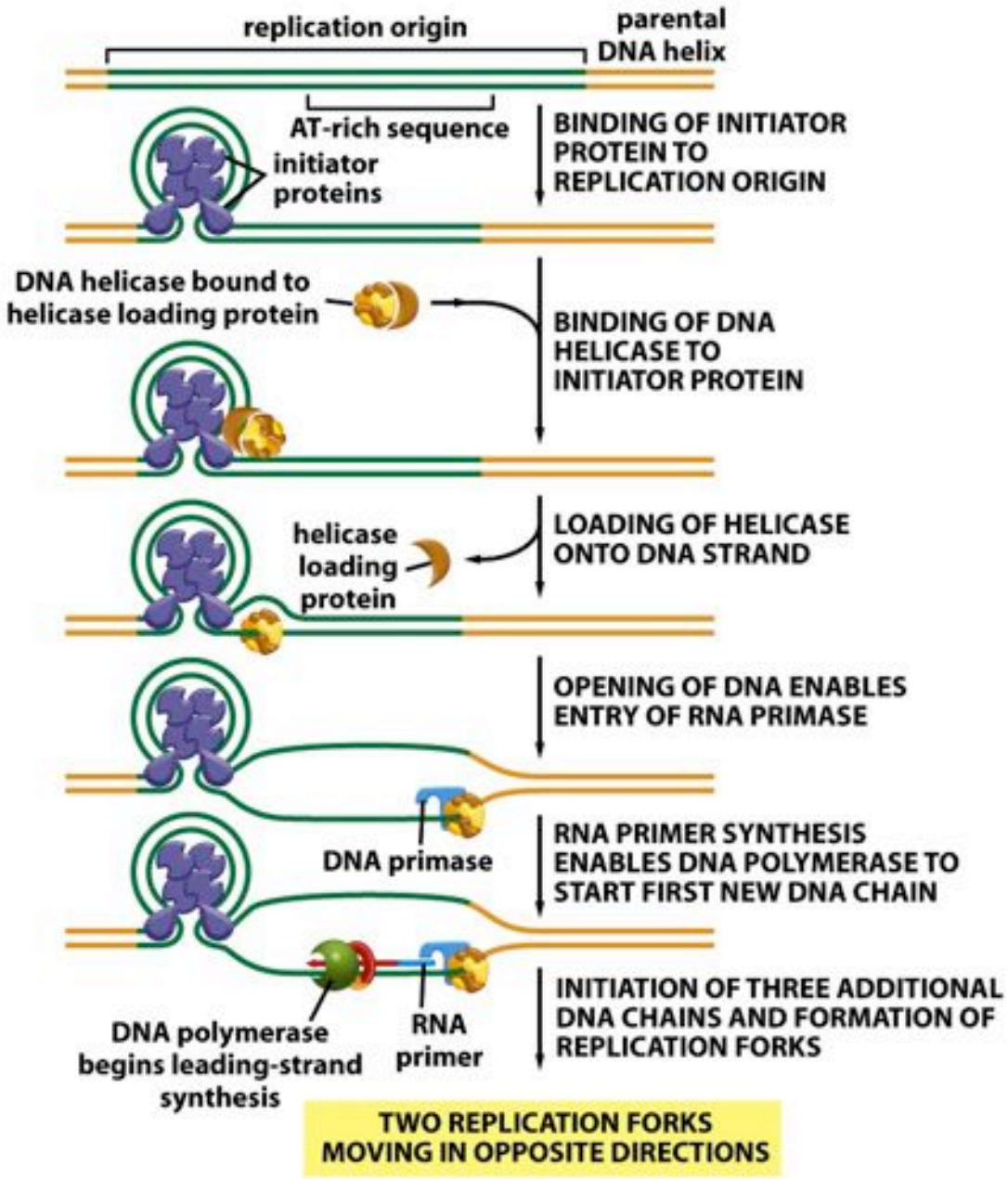


Figure 5-27 *Molecular Biology of the Cell* (© Garland Science 2008)

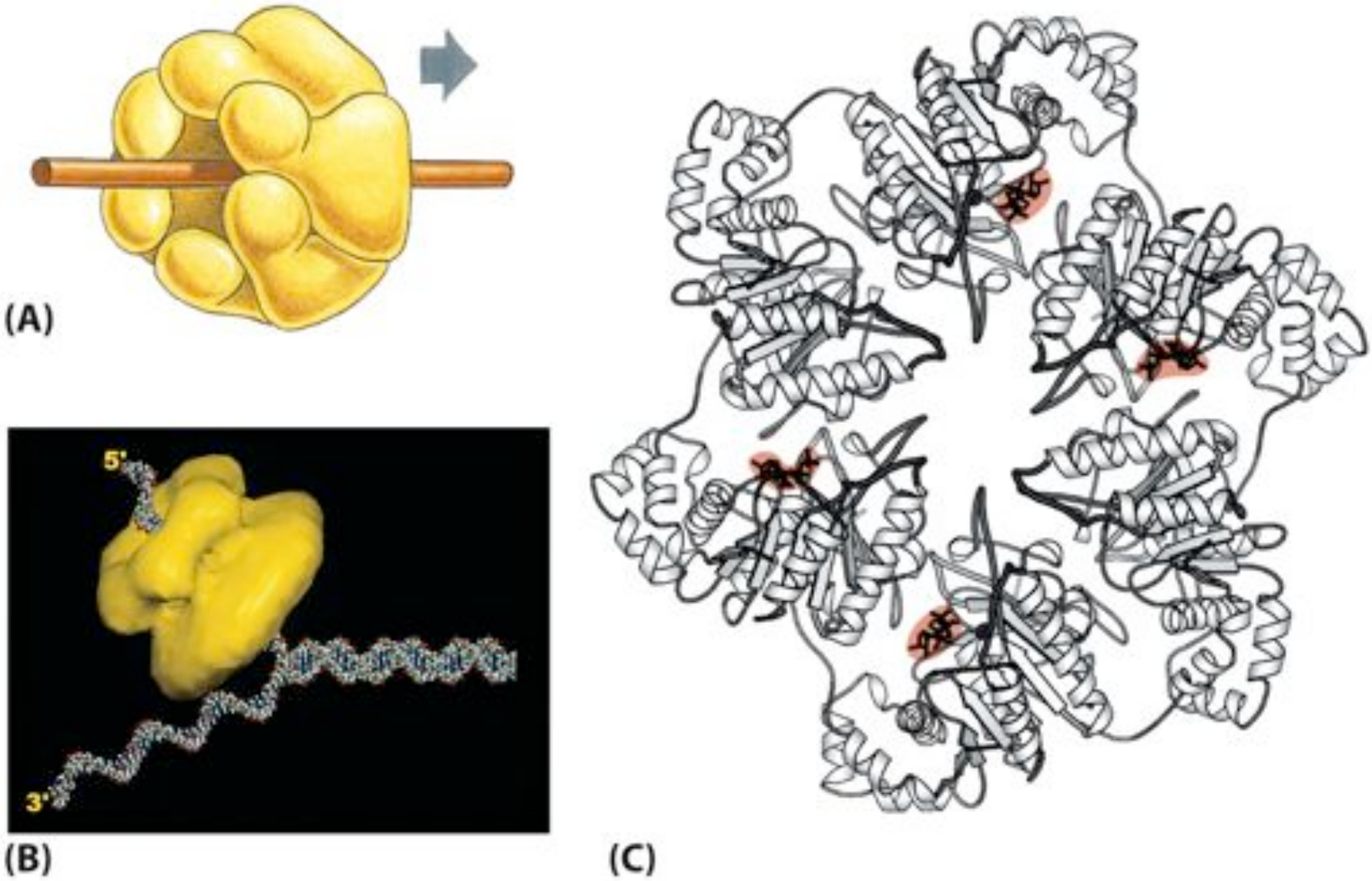


Figure 5-15 *Molecular Biology of the Cell* (© Garland Science 2008)

Transcripción

La síntesis de RNA se llama transcripción, a partir de un molde o templado de DNA. Las enzimas que catalizan este proceso se llaman RNA polimerasas. En eucariontes el proceso ocurre en el núcleo (RNAm), nucléolo (RNAribosomal), mitocondrias (RNA mitocondrial) y cloroplastos (RNA de cloroplastos).
A medida que ocurre la transcripción la RNA polimerasa separa las dos hebras del DNA e incorpora ribonucleotidos complementarios al molde de DNA.

Las RNA polimerasas, inician cadenas nuevas de RNA desde sitios apropiados en el DNA. Los procariontes tienen una RNA polimerasa, y los eucariontes 3 (I, II y III) que catalizan la síntesis de RNA r (ribosomal), RNAm (mensajero) y RNAt (transferencia), respectivamente. Los RNA transcritos pueden ser modificados luego de la transcripción

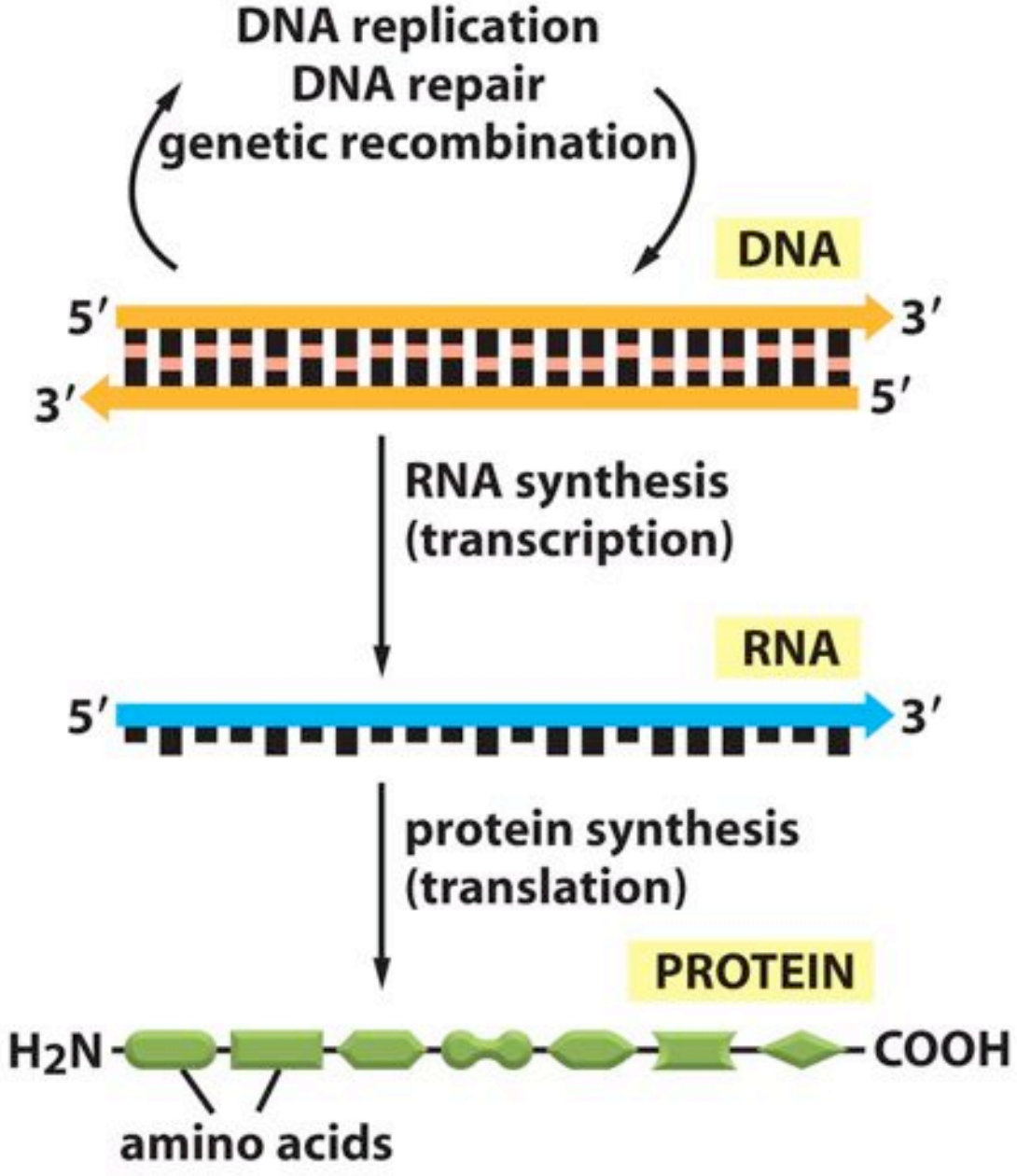
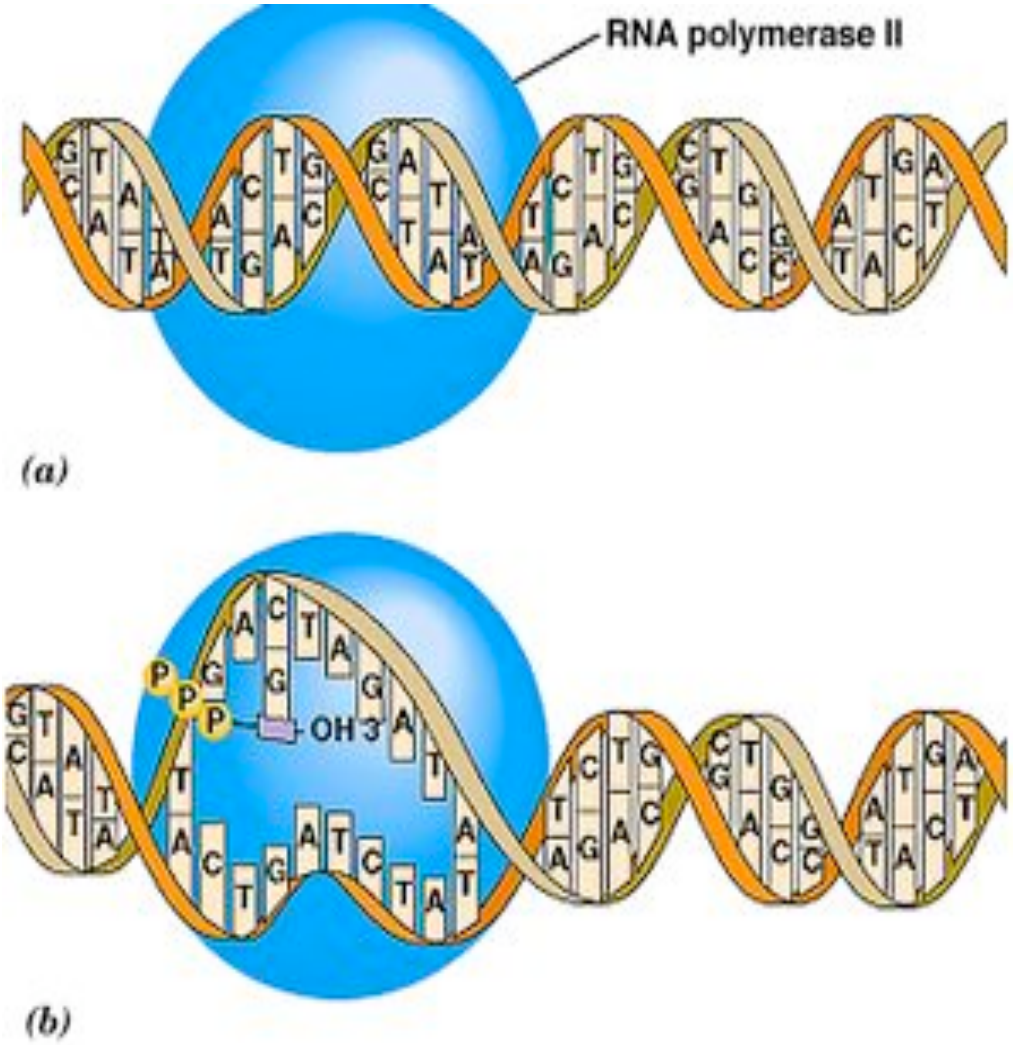


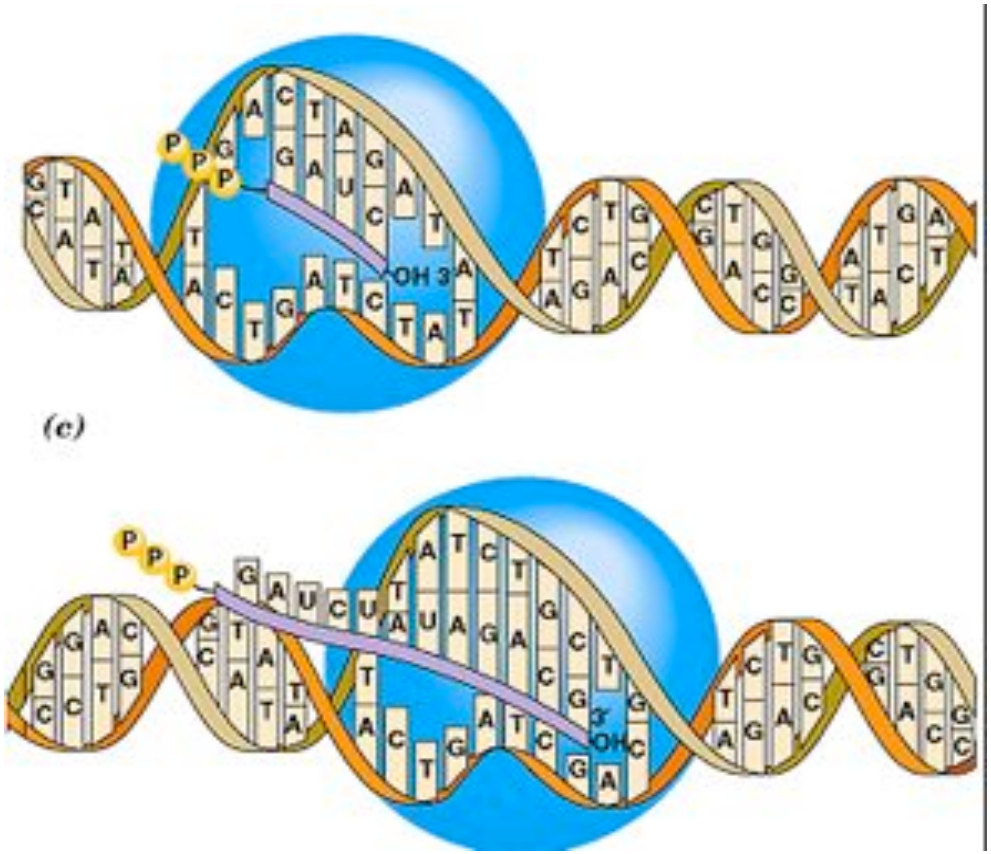
Figure 6-2 *Molecular Biology of the Cell* (© Garland Science 2008)



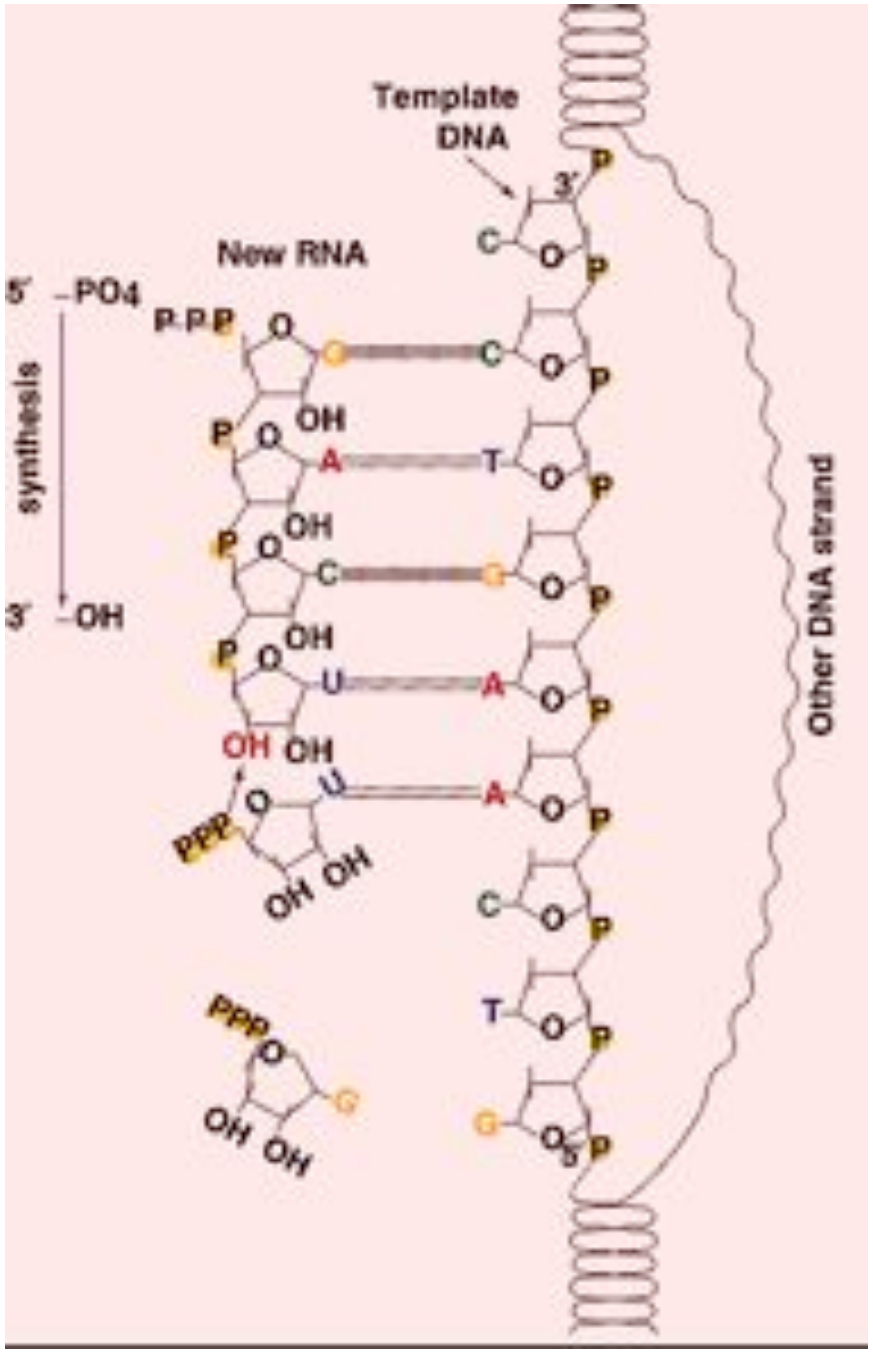
Reconocimiento del sitio de iniciación de transcripción por la RNA polimerasa, en el promotor del gen que se transcribe

Ubicación del primer nucleotido transcrito.

c) Formación del primer enlace fosfodiéster.



d) Prosigue la síntesis con movimiento de la RNA polimerasa a lo largo del DNA. Se reorganiza la doble hélice.



Biosíntesis de RNA mostrando la asimetría en la transcripción. El Nuevo RNA se forma desde su extremo 5´ hacia el extremo 3´.

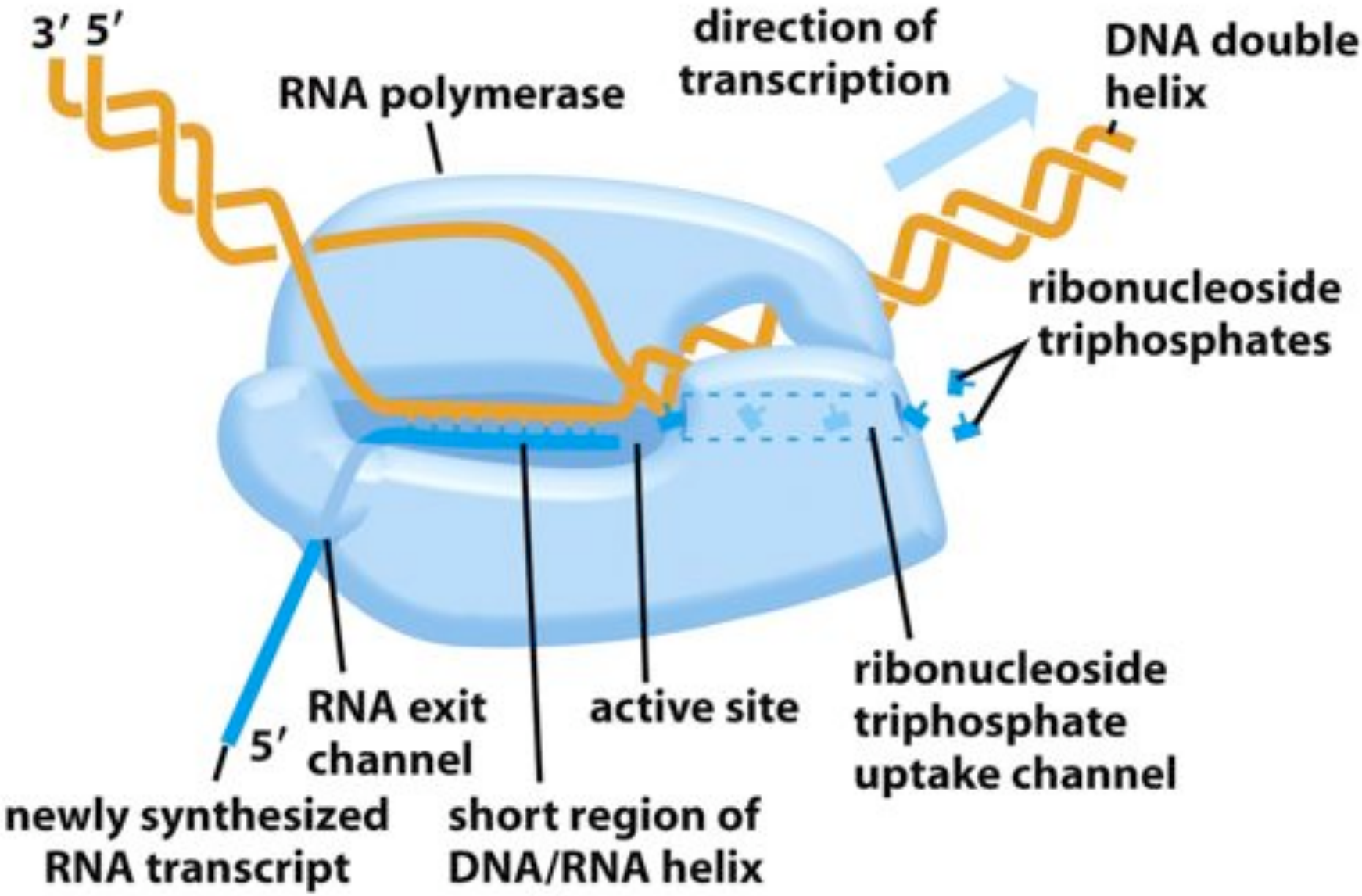


Figure 6-8a *Molecular Biology of the Cell* (© Garland Science 2008)

Table 6–2 The Three RNA Polymerases in Eucaryotic Cells

TYPE OF POLYMERASE	GENES TRANSCRIBED
RNA polymerase I	5.8S, 18S, and 28S rRNA genes
RNA polymerase II	all protein-coding genes, plus snoRNA genes, miRNA genes, siRNA genes, and most snRNA genes
RNA polymerase III	tRNA genes, 5S rRNA genes, some snRNA genes and genes for other small RNAs

The rRNAs are named according to their "S" values, which refer to their rate of sedimentation in an ultracentrifuge. The larger the S value, the larger the rRNA.

Table 6-2 *Molecular Biology of the Cell* (© Garland Science 2008)

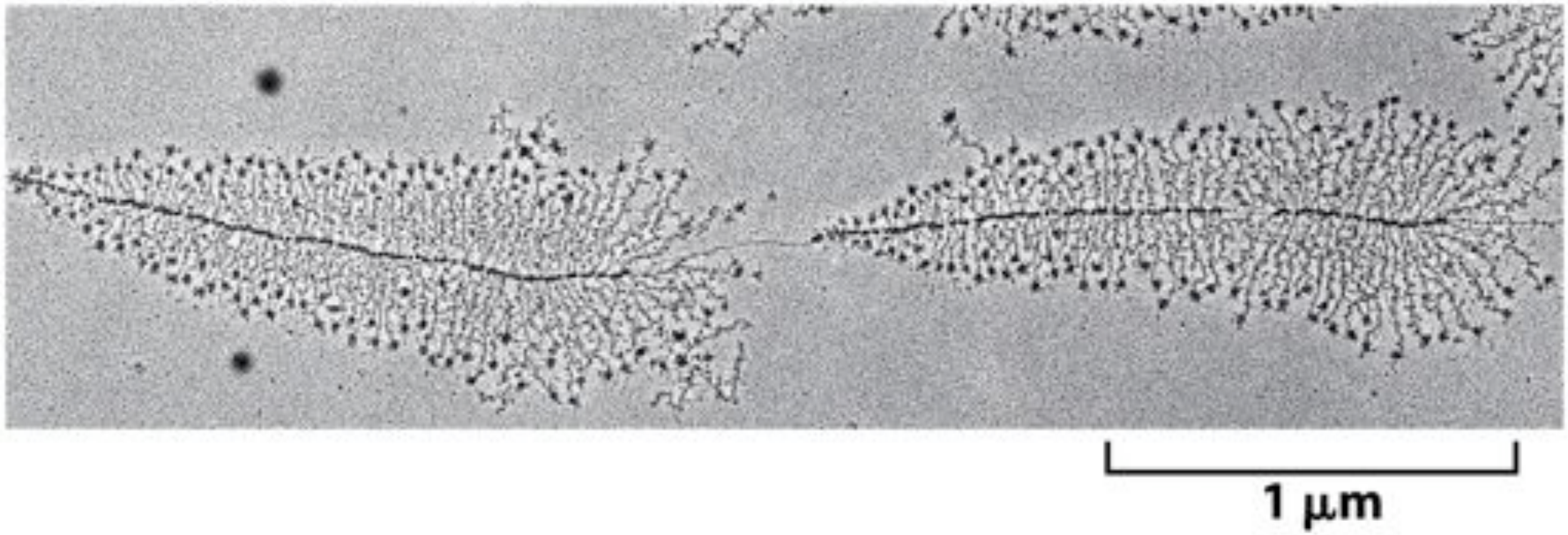


Figure 6-9 *Molecular Biology of the Cell* (© Garland Science 2008)

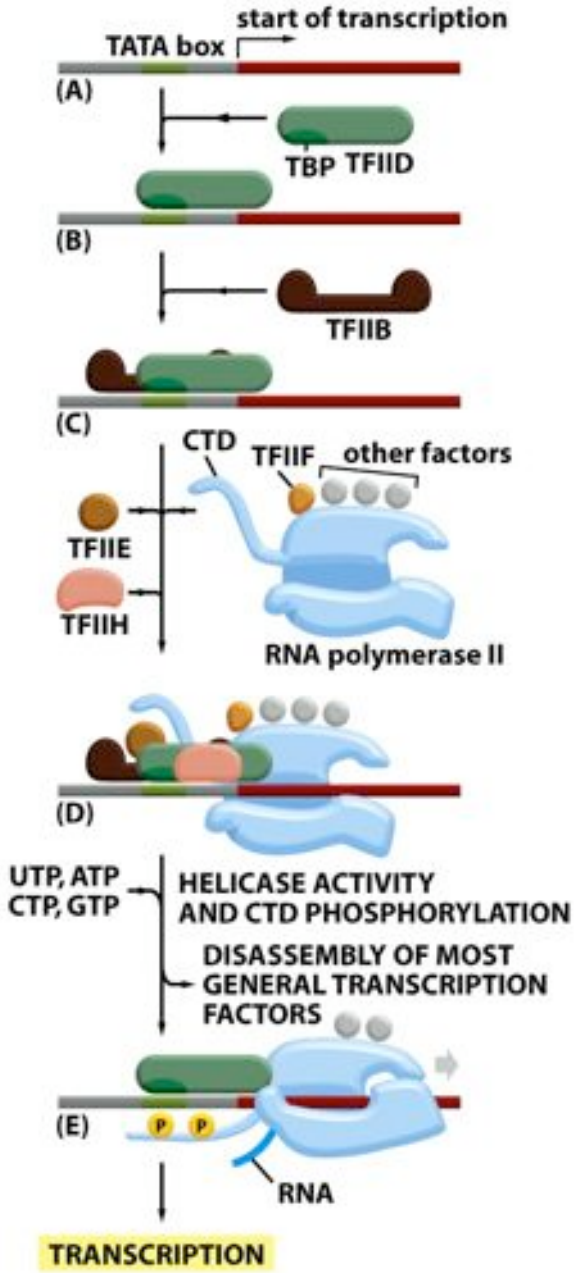


Figure 6-16 *Molecular Biology of the Cell* (© Garland Science 2008)

Table 6–3 The General Transcription Factors Needed for Transcription Initiation by Eucaryotic RNA Polymerase II

NAME	NUMBER OF SUBUNITS	ROLES IN TRANSITION INITIATION
TFIID		
TBP subunit	1	recognizes TATA box
TAF subunits	~11	recognizes other DNA sequences near the transcription start point; regulates DNA-binding by TBP
TFIIB	1	recognizes BRE element in promoters; accurately positions RNA polymerase at the start site of transcription
TFIIF	3	stabilizes RNA polymerase interaction with TBP and TFIIB; helps attract TFIIE and TFIIH
TFIIE	2	attracts and regulates TFIIH
TFIIH	9	unwinds DNA at the transcription start point, phosphorylates Ser5 of the RNA polymerase CTD; releases RNA polymerase from the promoter

TFIID is composed of TBP and ~11 additional subunits called TAFs (TBP-associated factors); CTD, C-terminal domain.

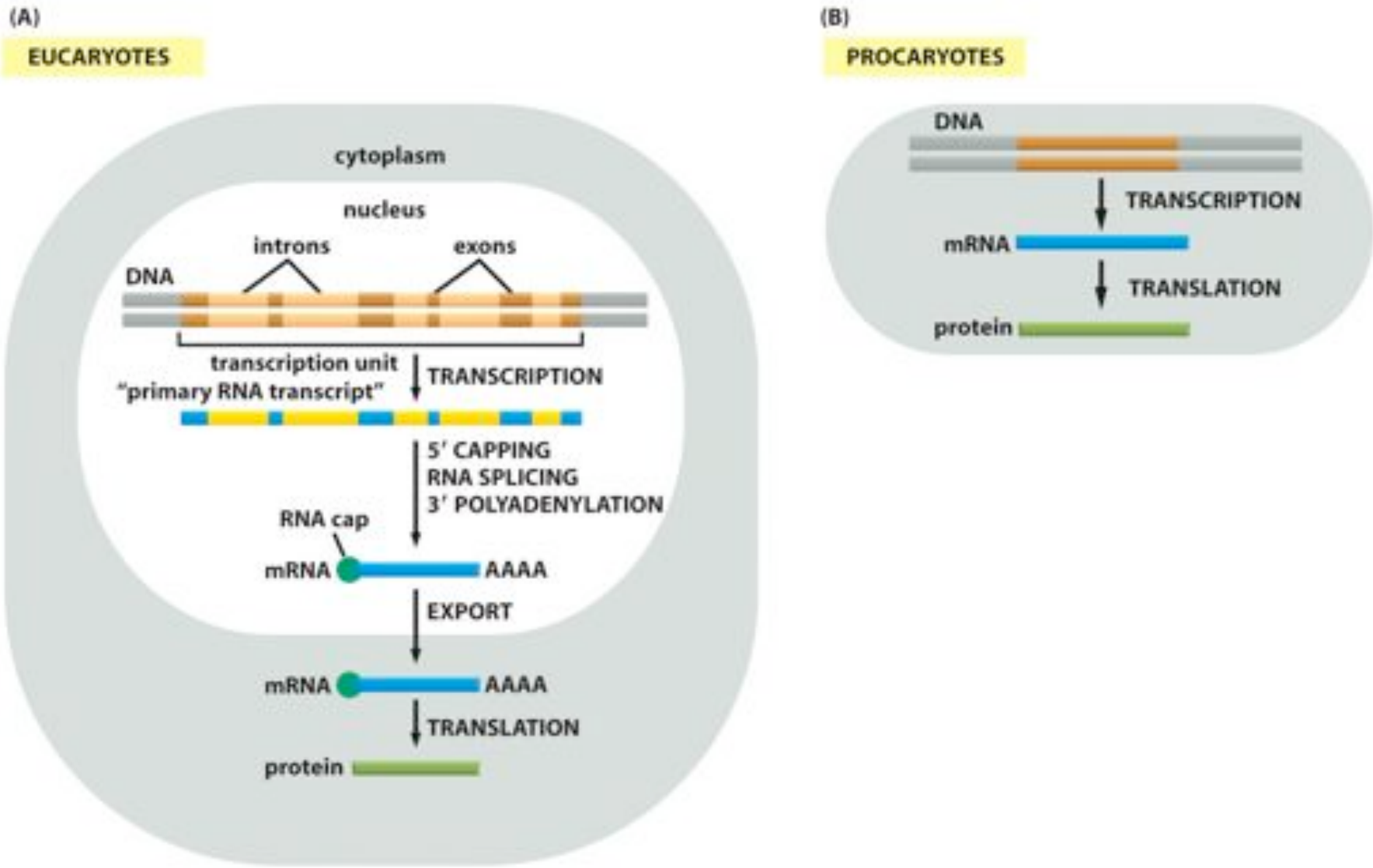


Figure 6-21 *Molecular Biology of the Cell* (© Garland Science 2008)

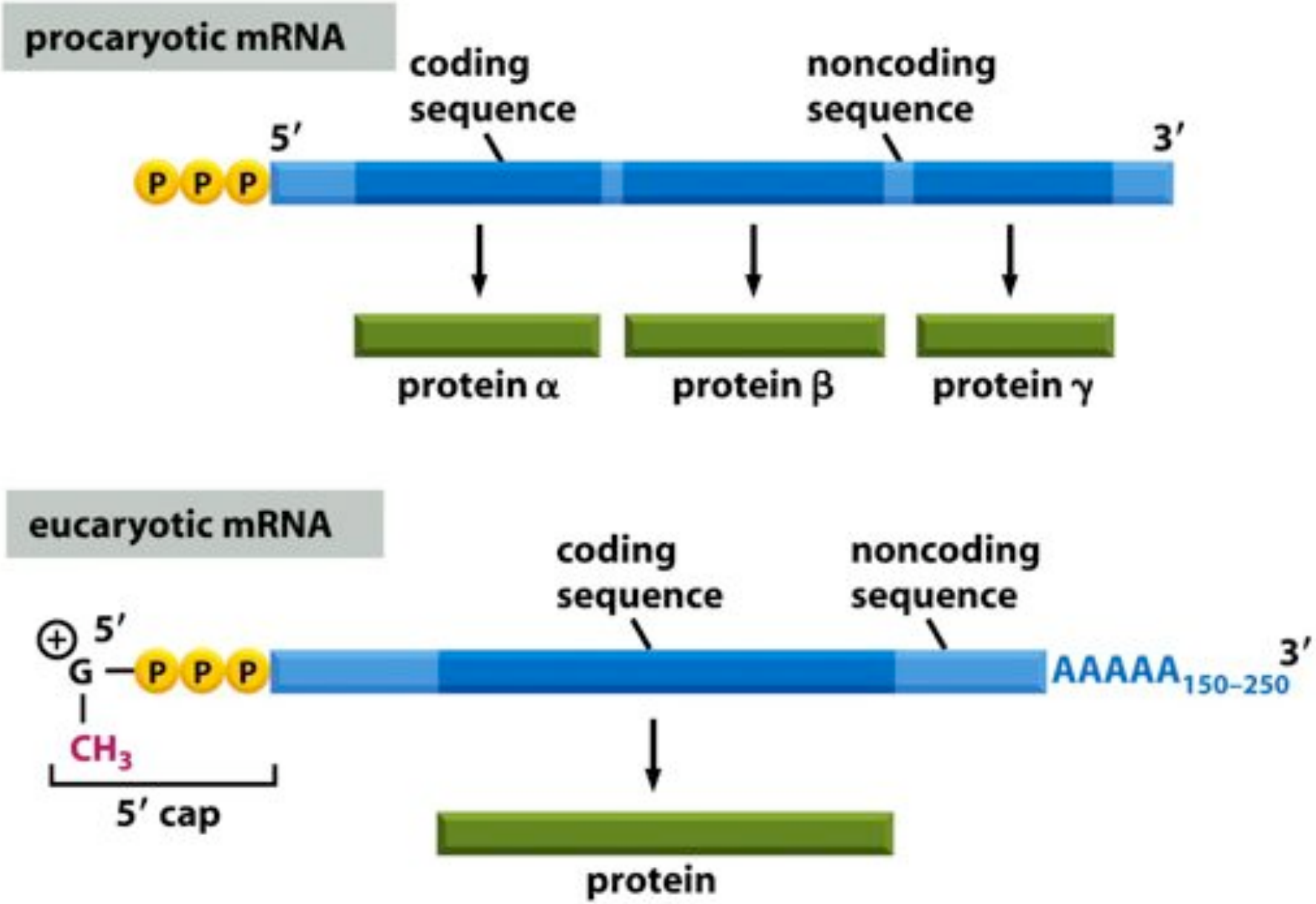


Figure 6-22a *Molecular Biology of the Cell* (© Garland Science 2008)

El DNA tiene dos tipos de secuencia: sitios de control y la región codificante. Los sitios de control son reconocidos por proteínas específicas.

Un gen típico (transcrito por la RNA polimerasa II) tiene un promotor que se extiende río arriba del sitio en que se inicia la transcripción. El promotor tiene varios elementos de secuencia cortos (< 10 pb) que unen factores de transcripción, estos pueden extenderse por mas de 200 pb.

El DNA puede estar doblado o reordenado de modo que el sitio de iniciación no es accesible, los factores de transcripción en el promotor y en sitios enhancer (potenciadores) interactúan para formar un gran complejo de proteínas que facilitan el reconocimiento del inicio.

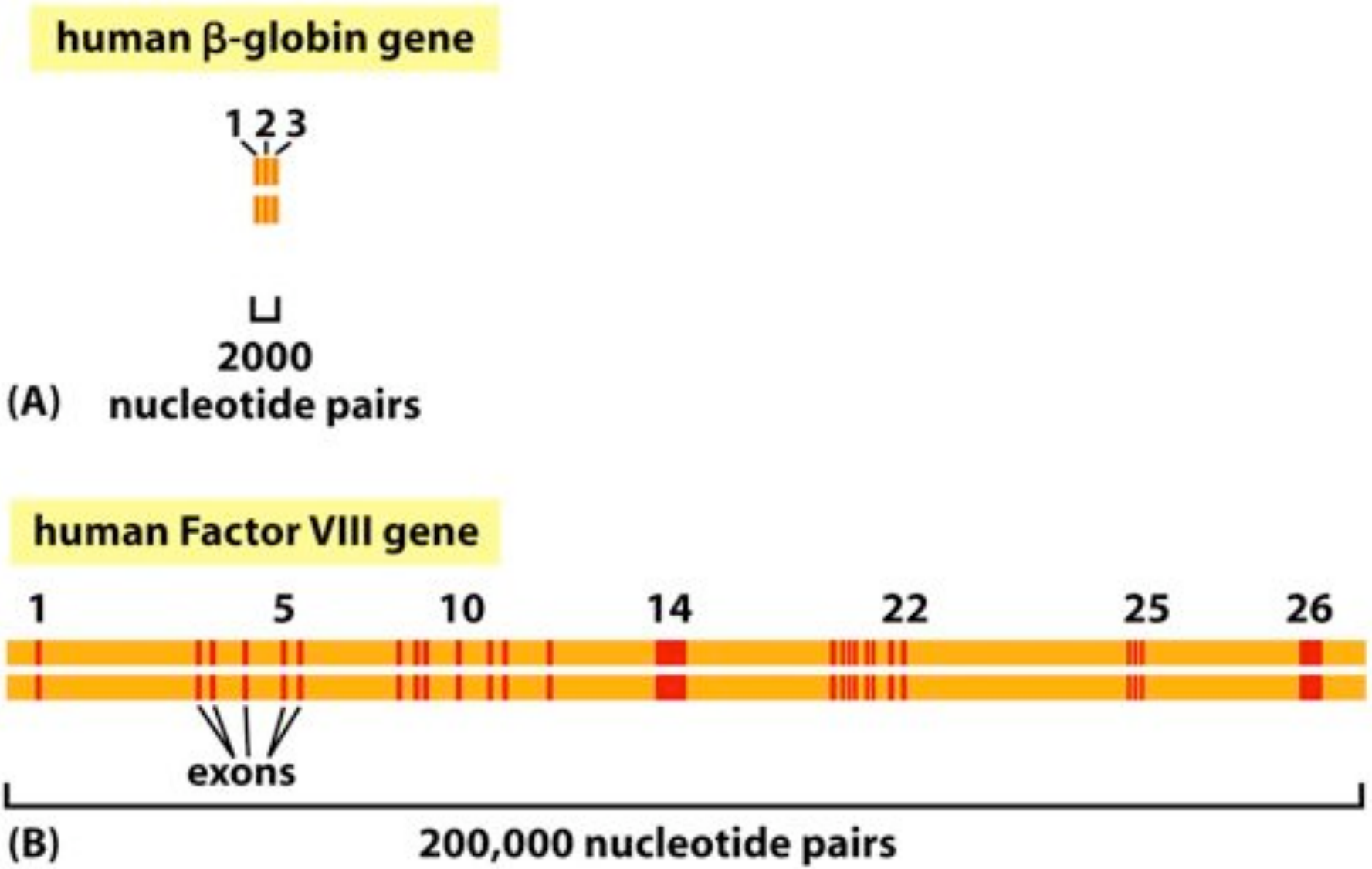


Figure 6-25 *Molecular Biology of the Cell* (© Garland Science 2008)

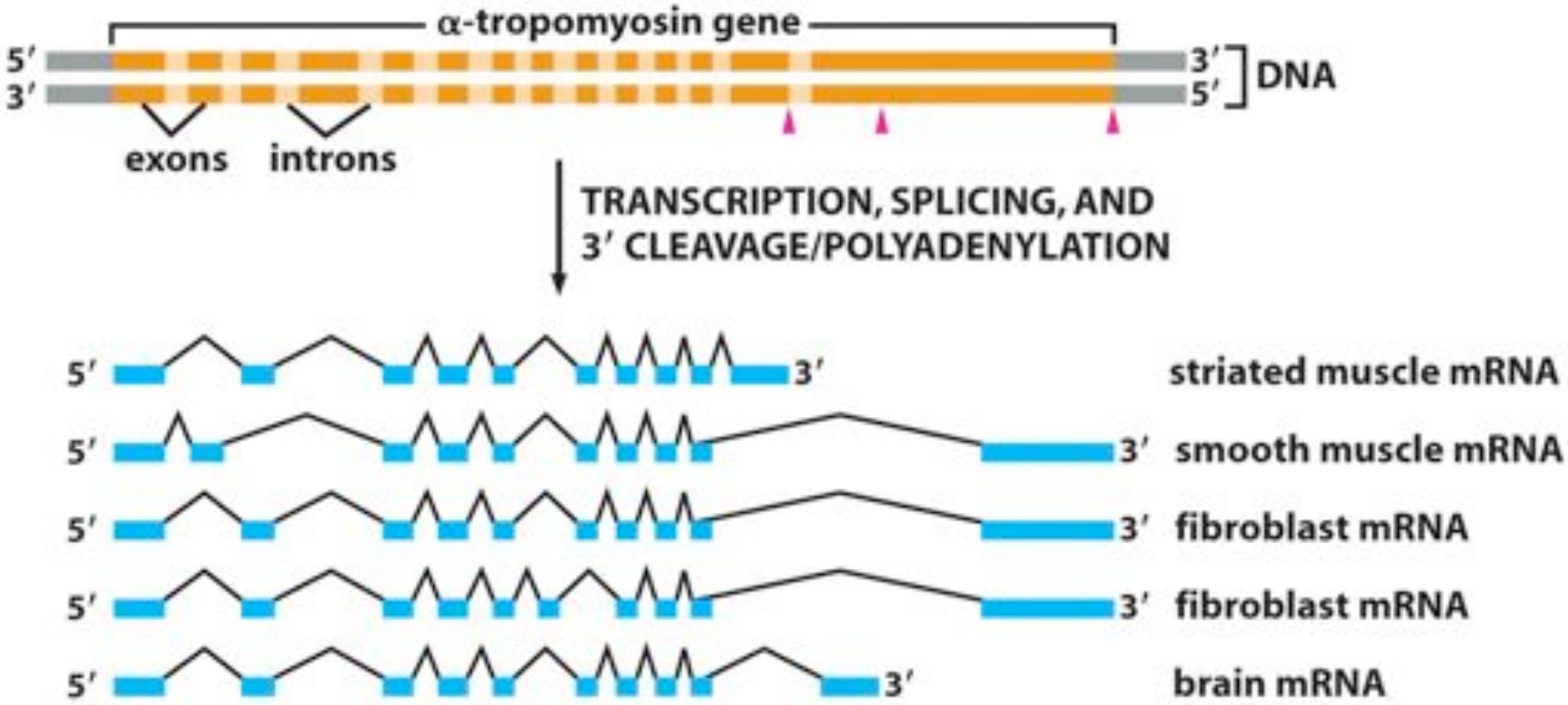


Figure 6-27 *Molecular Biology of the Cell* (© Garland Science 2008)

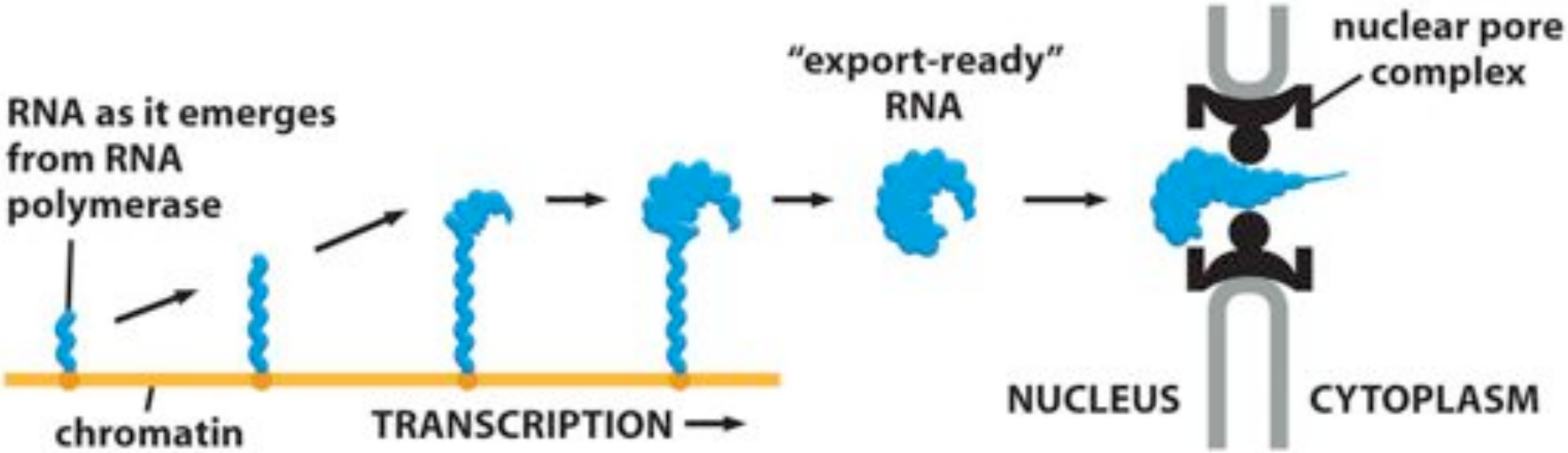


Figure 6-39a *Molecular Biology of the Cell* (© Garland Science 2008)

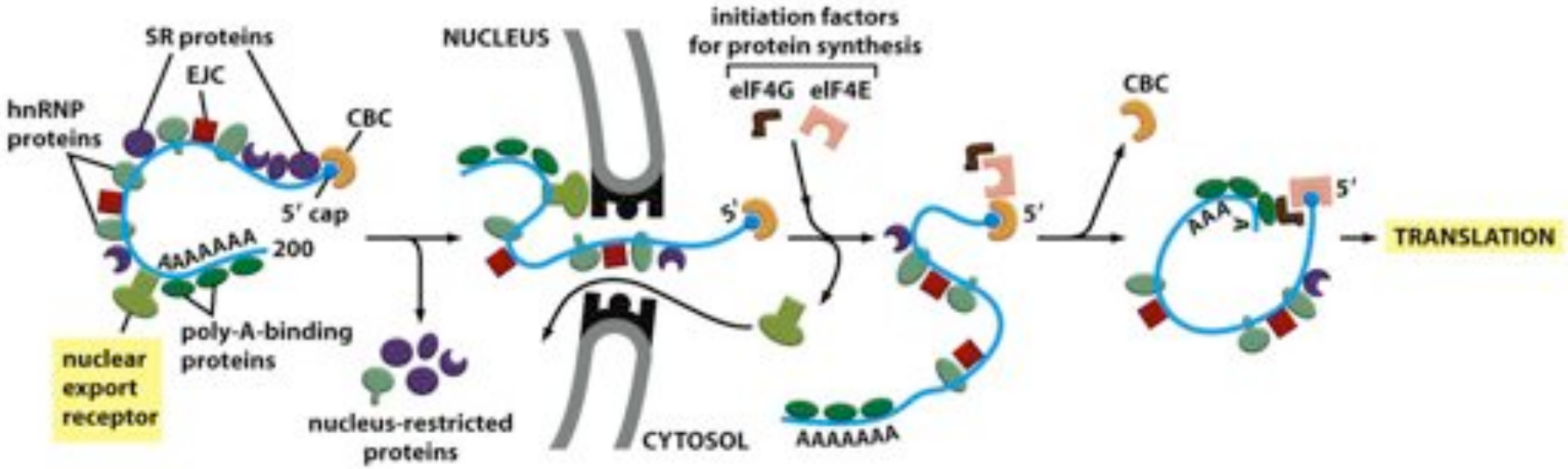


Figure 6-40 *Molecular Biology of the Cell* (© Garland Science 2008)

Traducción

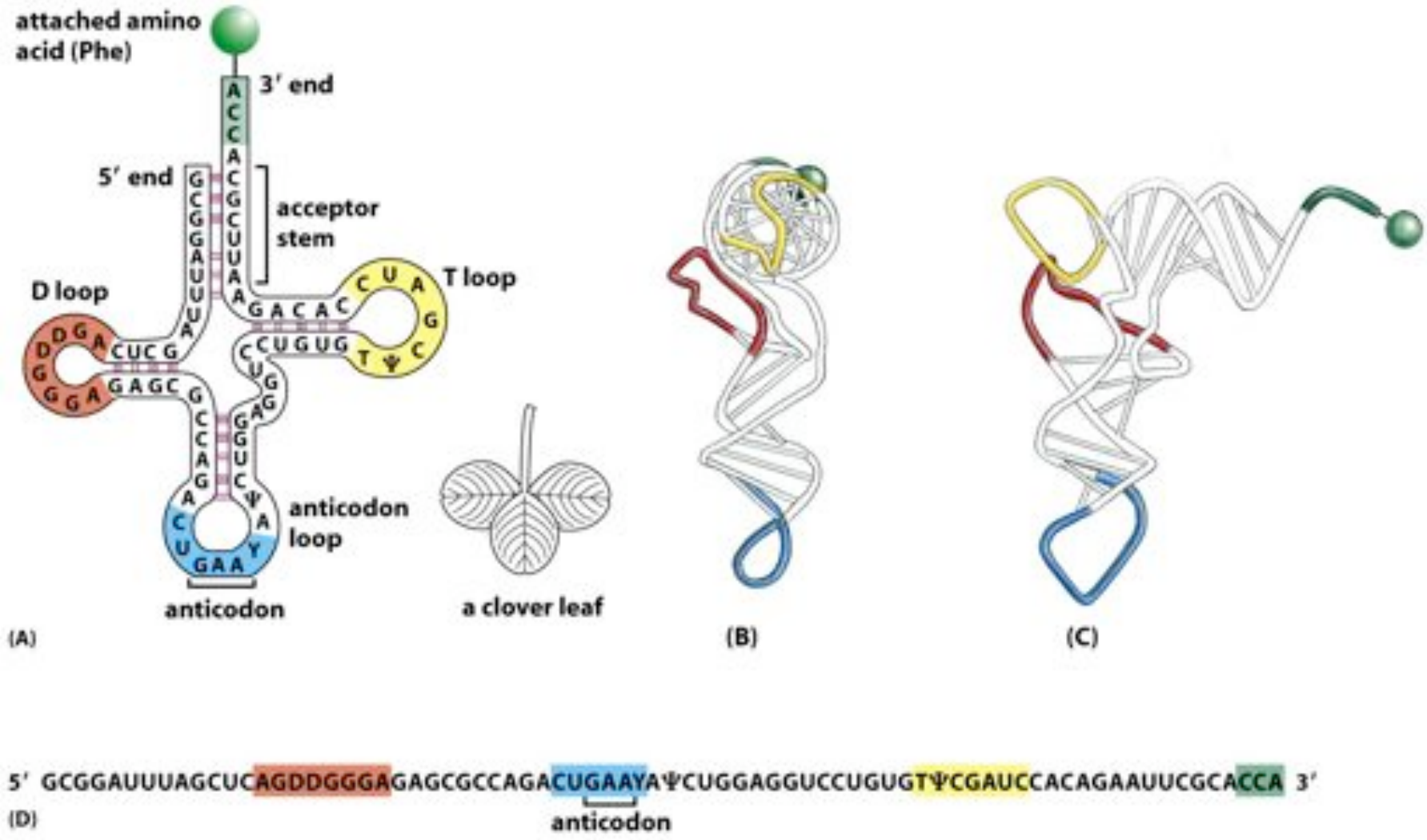
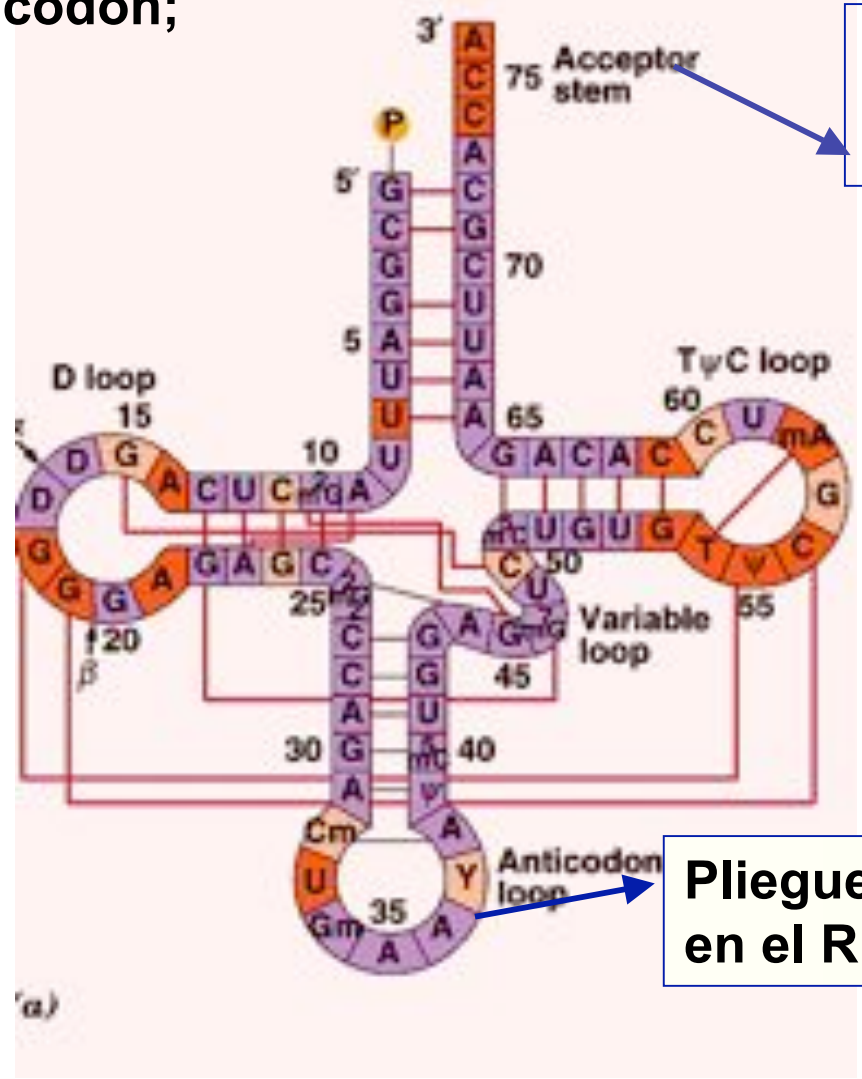


Figure 6-52 *Molecular Biology of the Cell* (© Garland Science 2008)

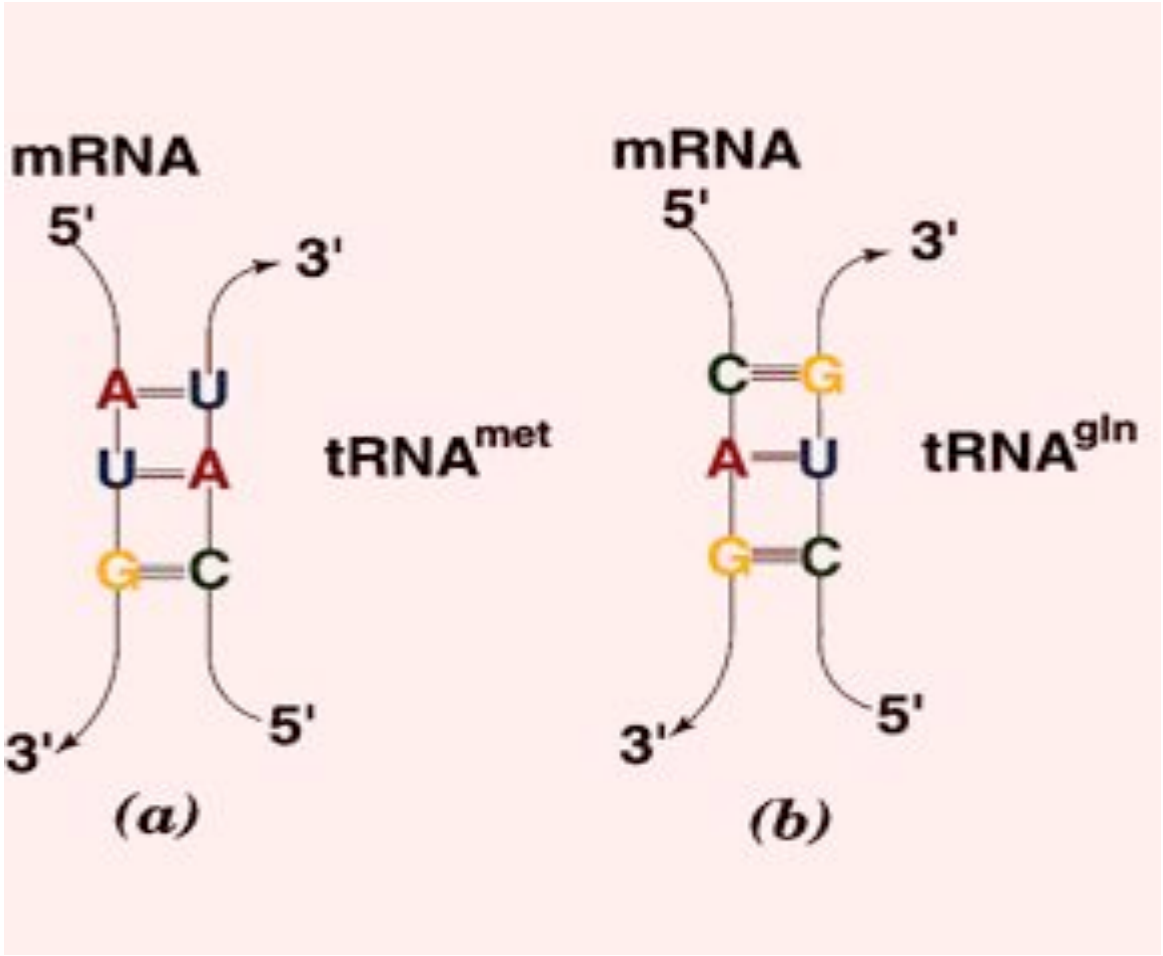
Los RNAt son moléculas pequeñas (70-80 nucleótidos), y hay varias para los distintos aminoácidos. Son moléculas adaptadoras, reconocen: un codón en el RNAm y al aminoácido que corresponde al codón;



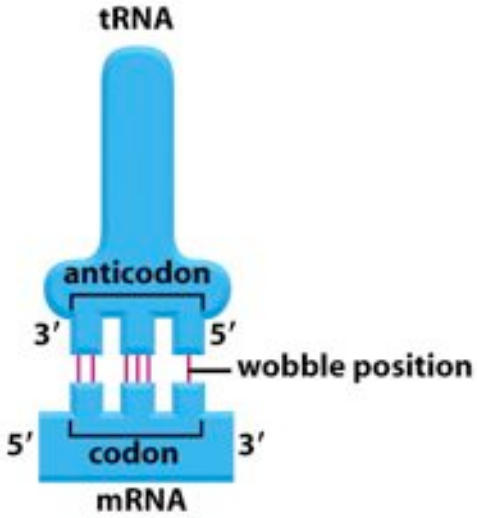
El extremo 3´, aceptor, reconoce y une al aminoácido correspondiente

La enzima que cataliza la unión de los RNAt con el aminoácido correspondiente es la aminoacil-tRNA- sintetasa.

Pliegue anticodón, reconoce y une al codón en el RNAm, con bases complementarias.



Interacciones codón anticodón. a) Interacción entre el codón AUG y su anti codón CAU. b) El codón CAG (glutamina) y su anticodón (CUG). Hay interacciones complementarias de apareamiento anti paralelo entre mRNA y tRNA. Este reconocimiento ocurre en los ribosomas.



bacteria

wobble codon base	possible anticodon bases
U	A, G, or I
C	G or I
A	U or I
G	C or U

eucaryotes

wobble codon base	possible anticodon bases
U	A, G, or I
C	G or I
A	U
G	C

Figure 6-53 *Molecular Biology of the Cell* (© Garland Science 2008)

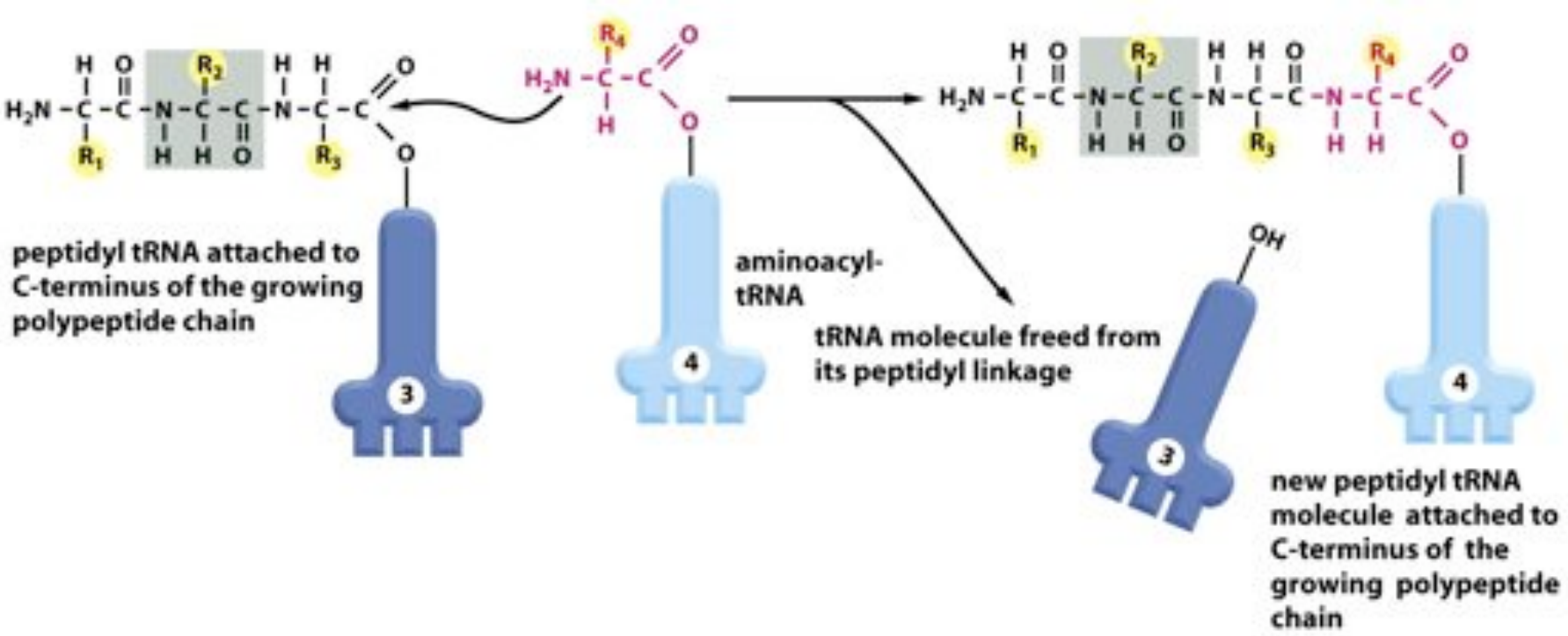
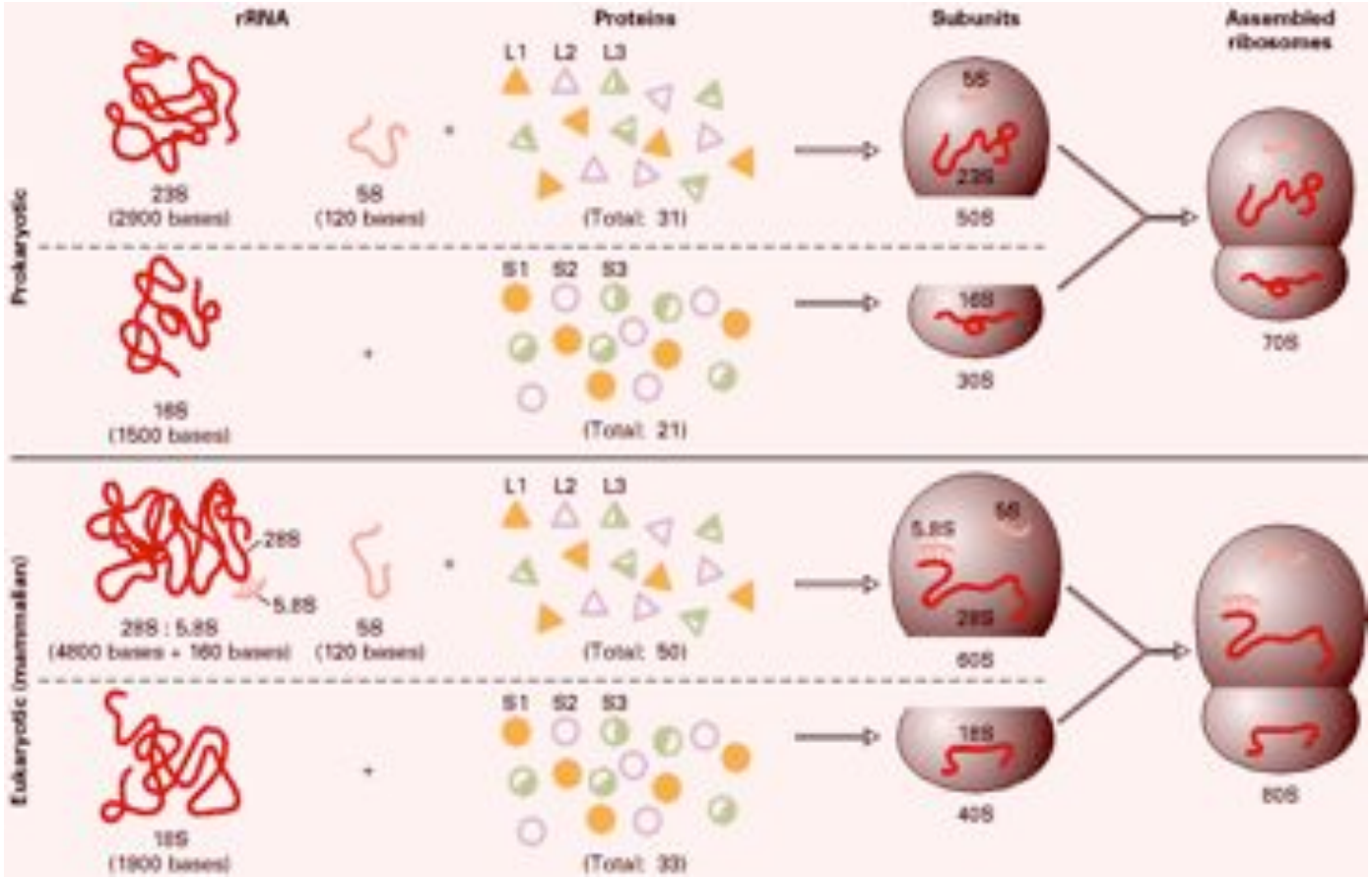


Figure 6-61 *Molecular Biology of the Cell* (© Garland Science 2008)

Composición de ribosomas de procariontes y eucariontes, cada uno con una sub-unidad pequeña y otra grande



Los ribosomas son organizaciones macromoleculares que sintetizan proteínas. Un ribosoma es una partícula compuesta de moléculas de RNA individuales (contienen un tercio del RNA celular) y mas de 50 proteínas, organizadas en una sub unidad pequeña y otra grande.

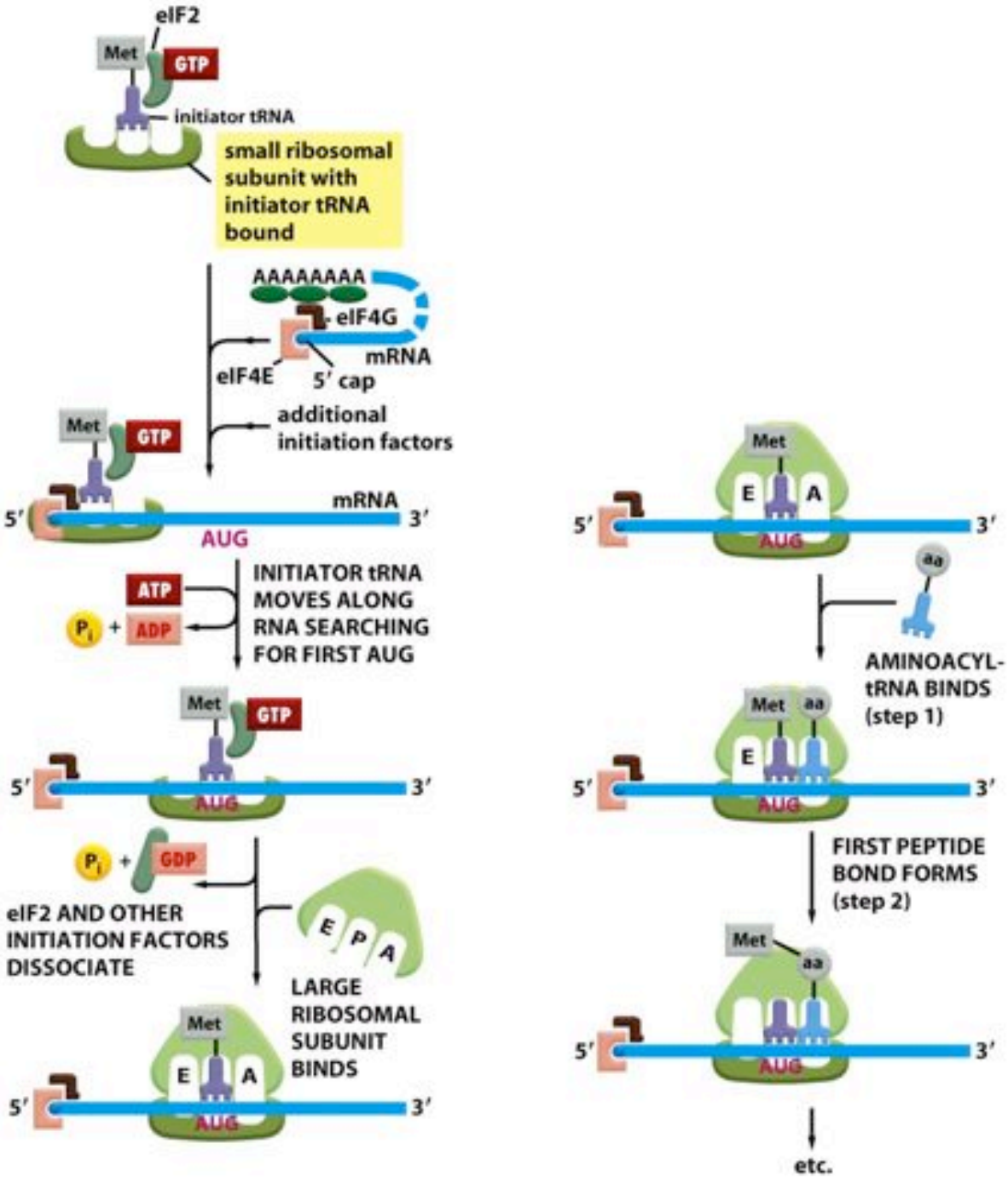


Figure 6-72 *Molecular Biology of the Cell* (© Garland Science 2008)

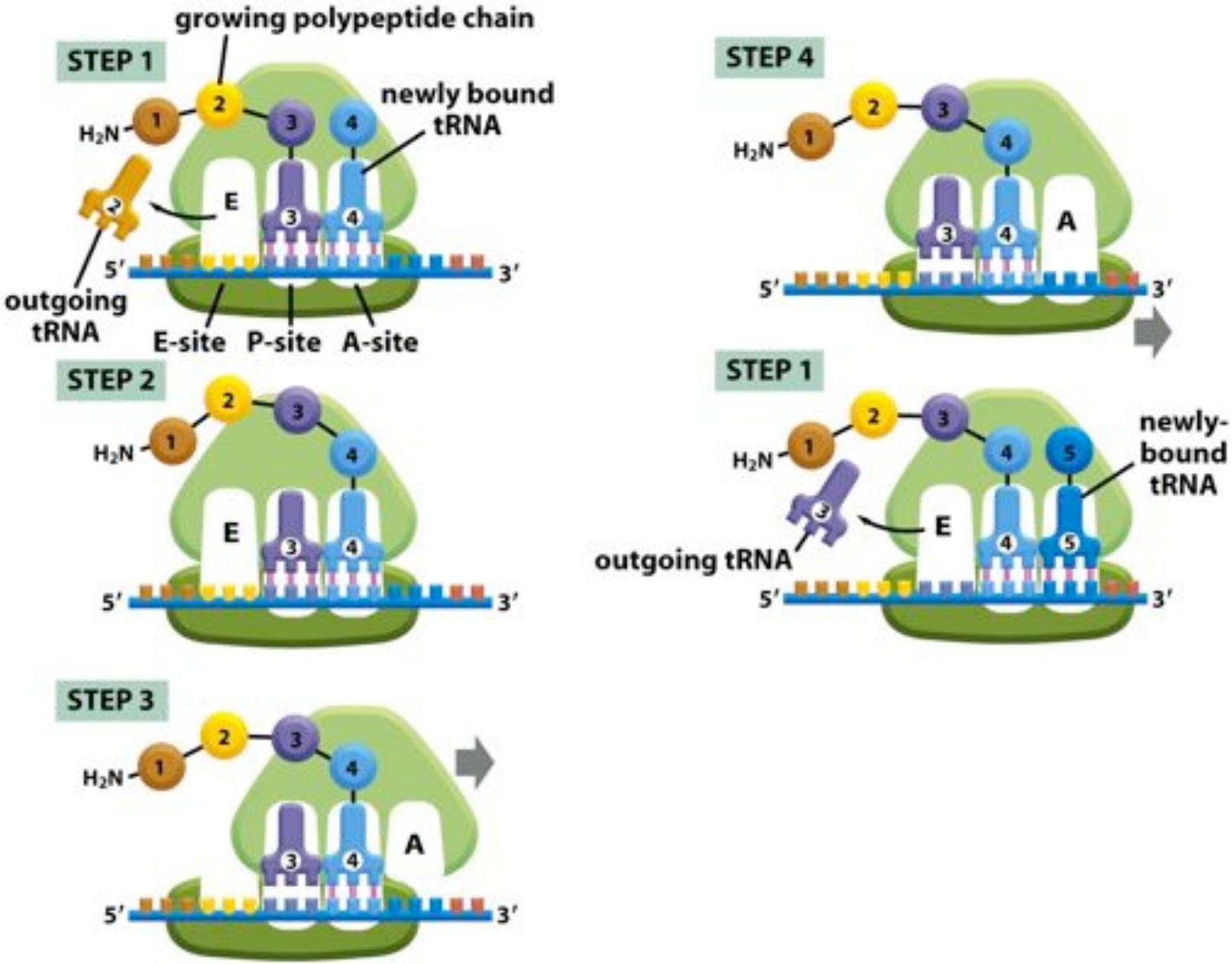


Figure 6-66 *Molecular Biology of the Cell* (© Garland Science 2008)

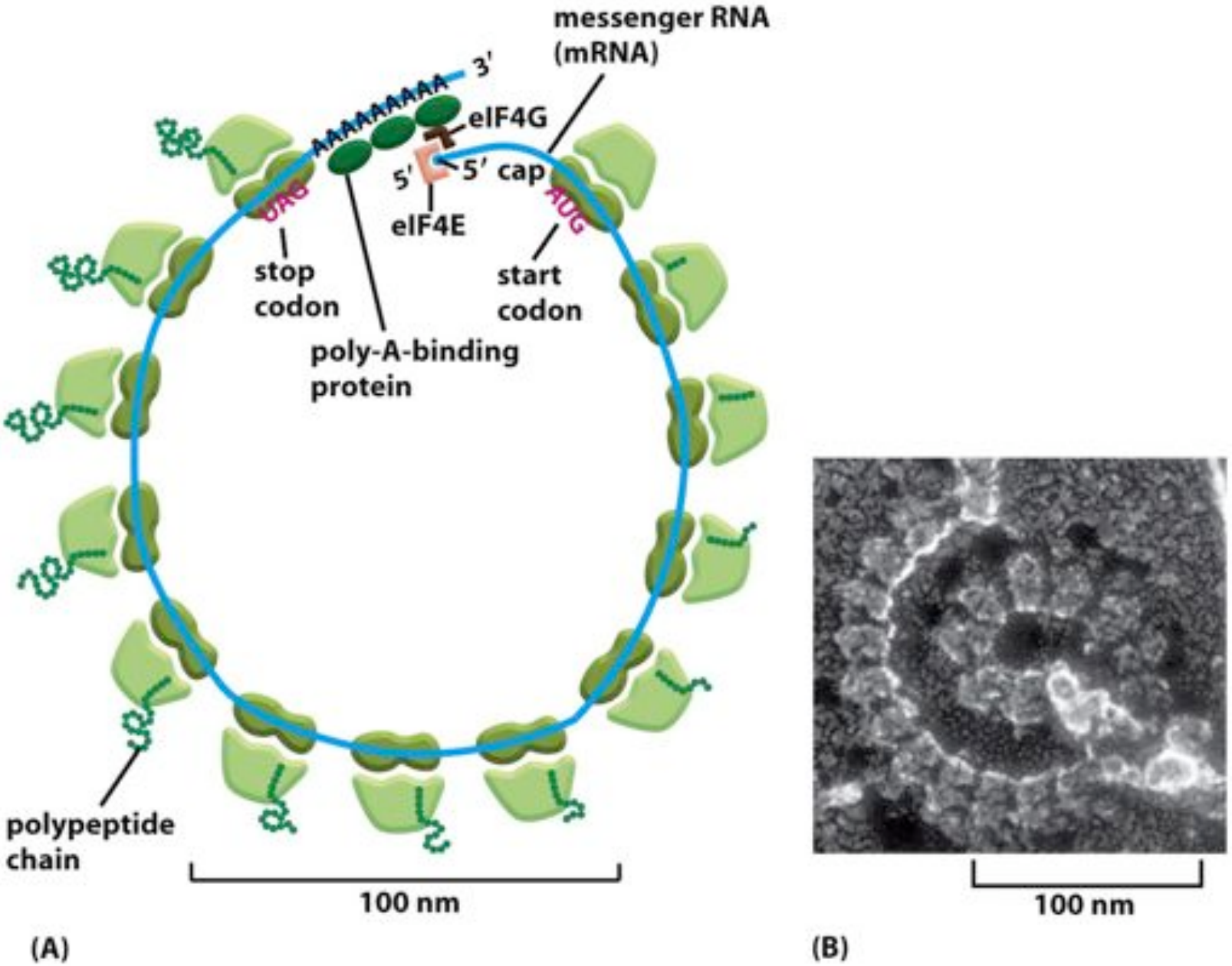


Figure 6-76 *Molecular Biology of the Cell* (© Garland Science 2008)

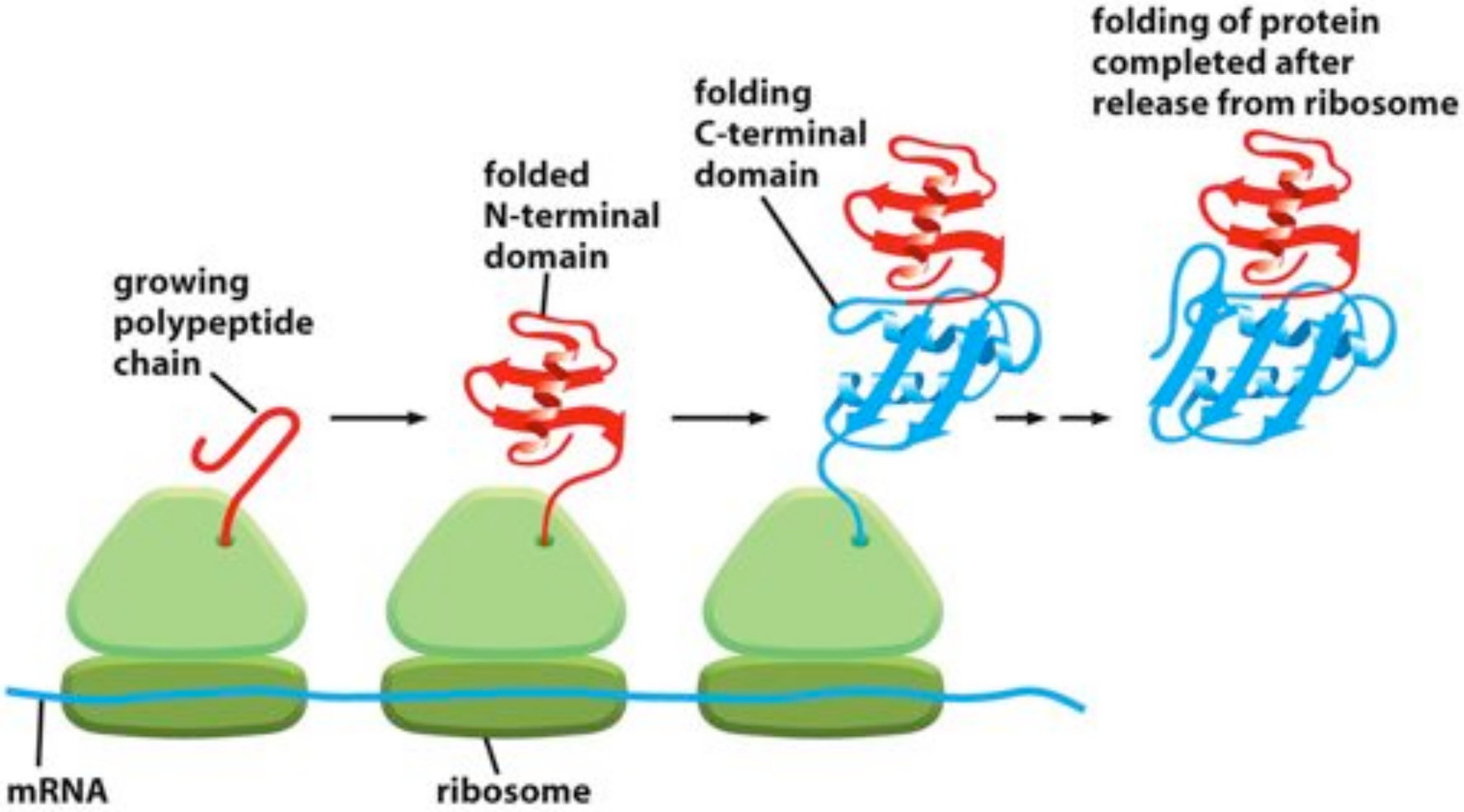


Figure 6-84 *Molecular Biology of the Cell* (© Garland Science 2008)

Table 6–4 Inhibitors of Protein or RNA Synthesis

INHIBITOR	SPECIFIC EFFECT
Acting only on bacteria	
Tetracycline	blocks binding of aminoacyl-tRNA to A-site of ribosome
Streptomycin	prevents the transition from translation initiation to chain elongation and also causes miscoding
Chloramphenicol	blocks the peptidyl transferase reaction on ribosomes (step 2 in Figure 6–66)
Erythromycin	binds in the exit channel of the ribosome and thereby inhibits elongation of the peptide chain
Rifamycin	blocks initiation of RNA chains by binding to RNA polymerase (prevents RNA synthesis)
Acting on bacteria and eucaryotes	
Puromycin	causes the premature release of nascent polypeptide chains by its addition to the growing chain end
Actinomycin D	binds to DNA and blocks the movement of RNA polymerase (prevents RNA synthesis)
Acting on eucaryotes but not bacteria	
Cycloheximide	blocks the translocation reaction on ribosomes (step 3 in Figure 6–66)
Anisomycin	blocks the peptidyl transferase reaction on ribosomes (step 2 in Figure 6–66)
α-Amanitin	blocks mRNA synthesis by binding preferentially to RNA polymerase II

The ribosomes of eucaryotic mitochondria (and chloroplasts) often resemble those of bacteria in their sensitivity to inhibitors. Therefore, some of these antibiotics can have a deleterious effect on human mitochondria.

Table 6-4 *Molecular Biology of the Cell* (© Garland Science 2008)

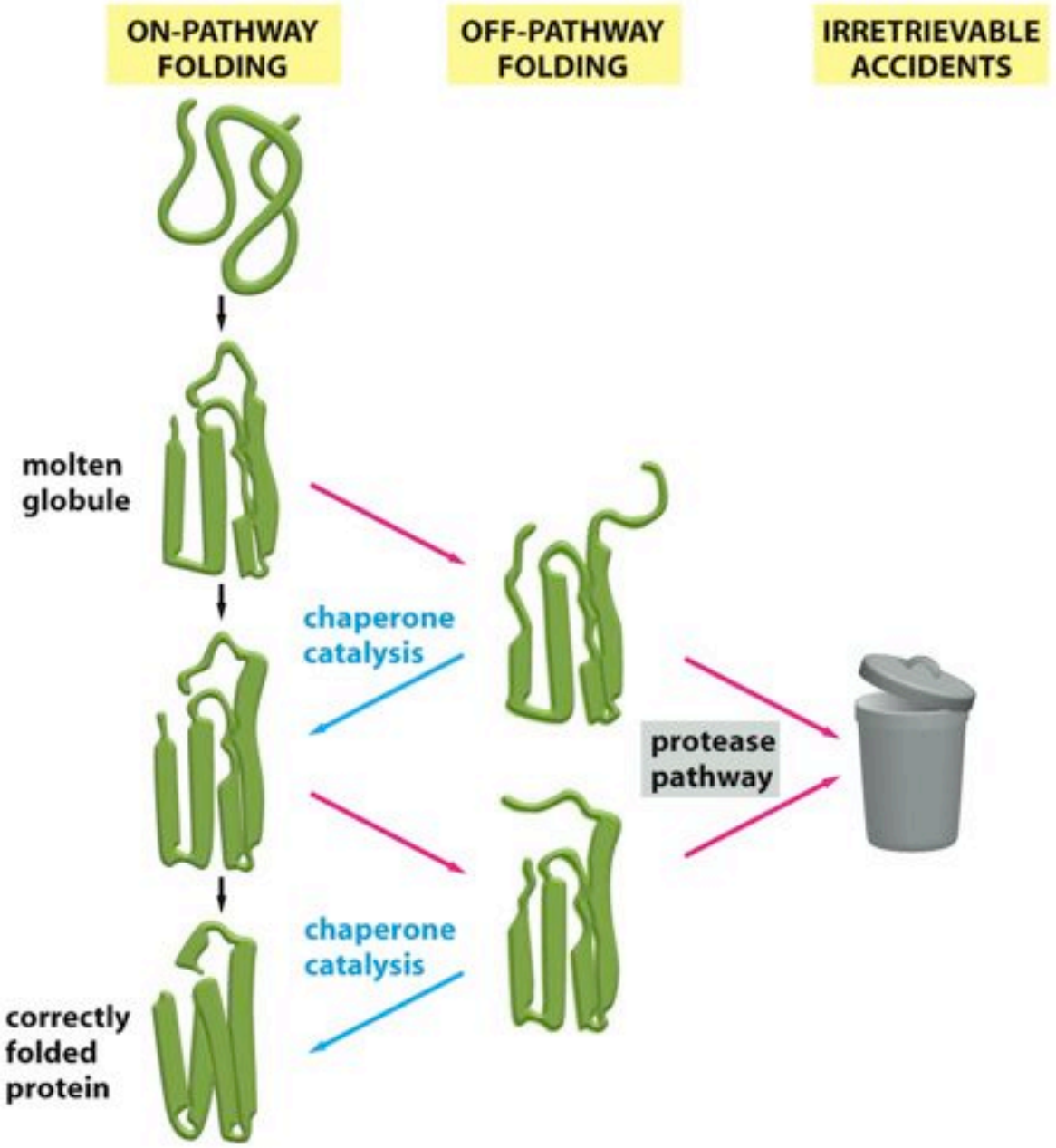


Figure 6-85 *Molecular Biology of the Cell* (© Garland Science 2008)

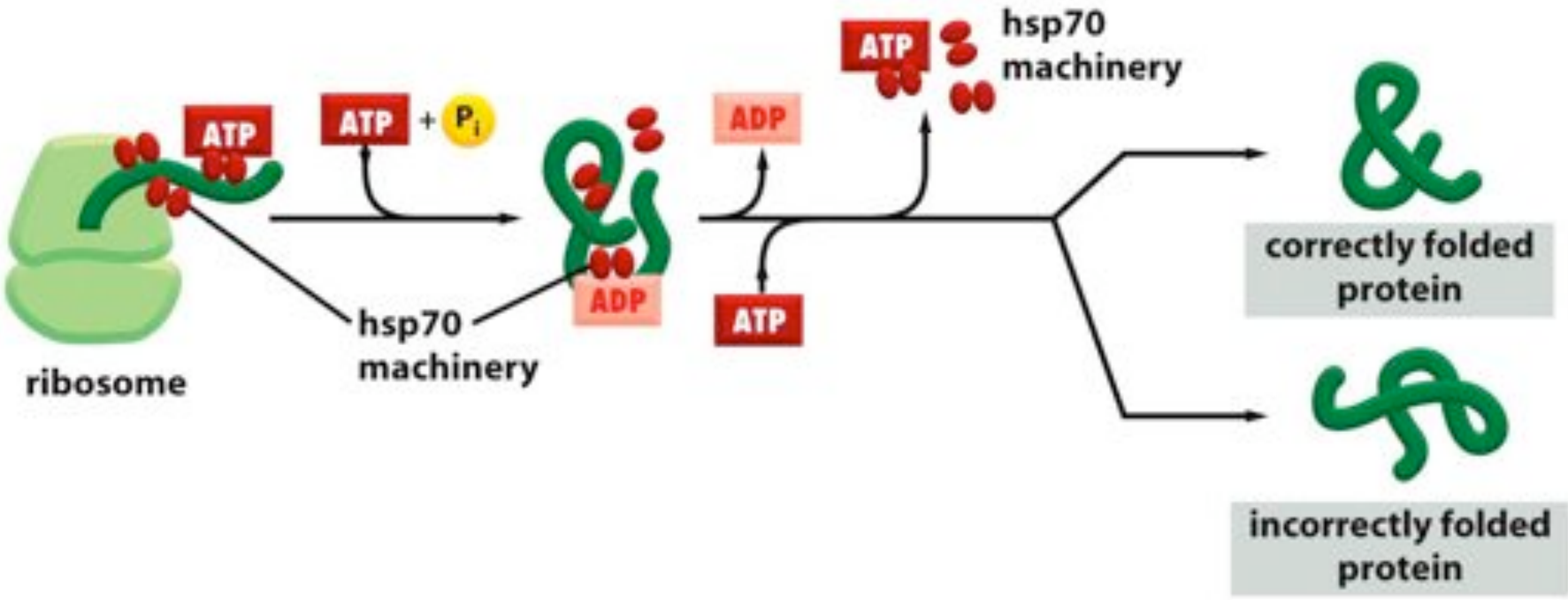


Figure 6-86 *Molecular Biology of the Cell* (© Garland Science 2008)

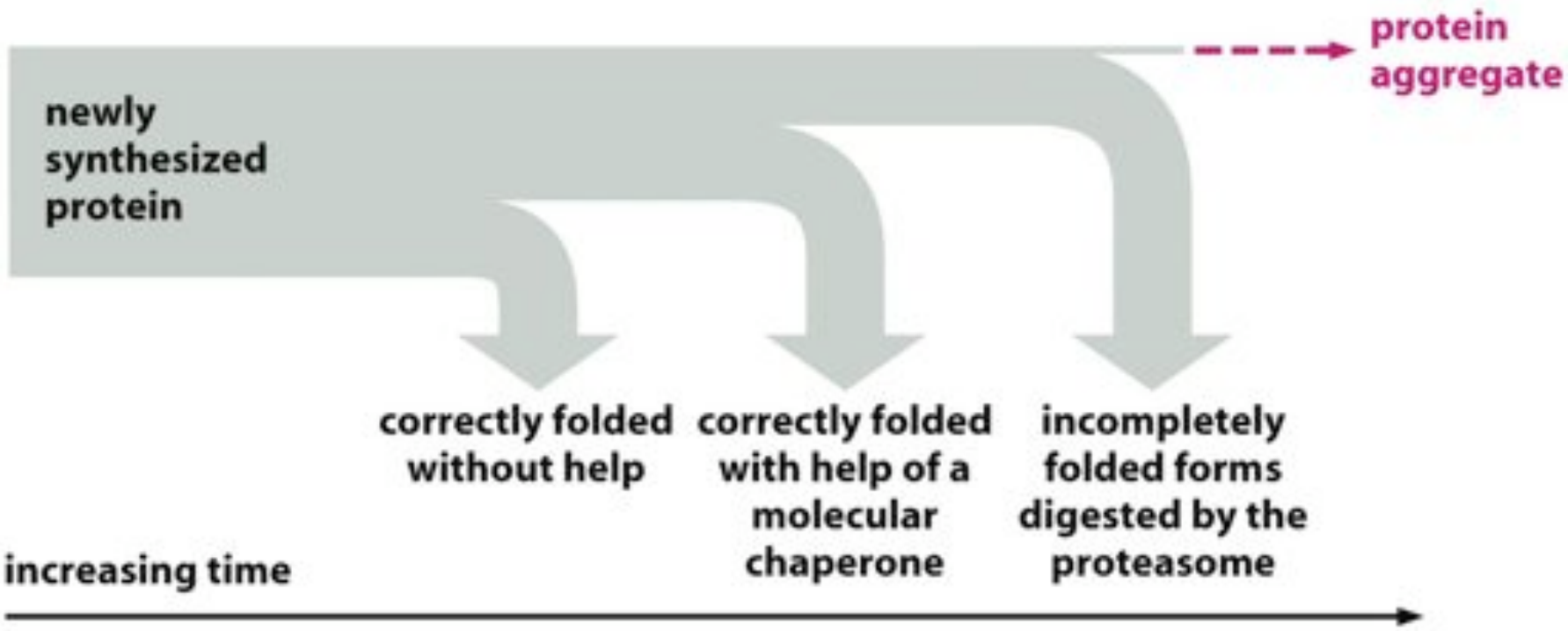


Figure 6-88 *Molecular Biology of the Cell* (© Garland Science 2008)

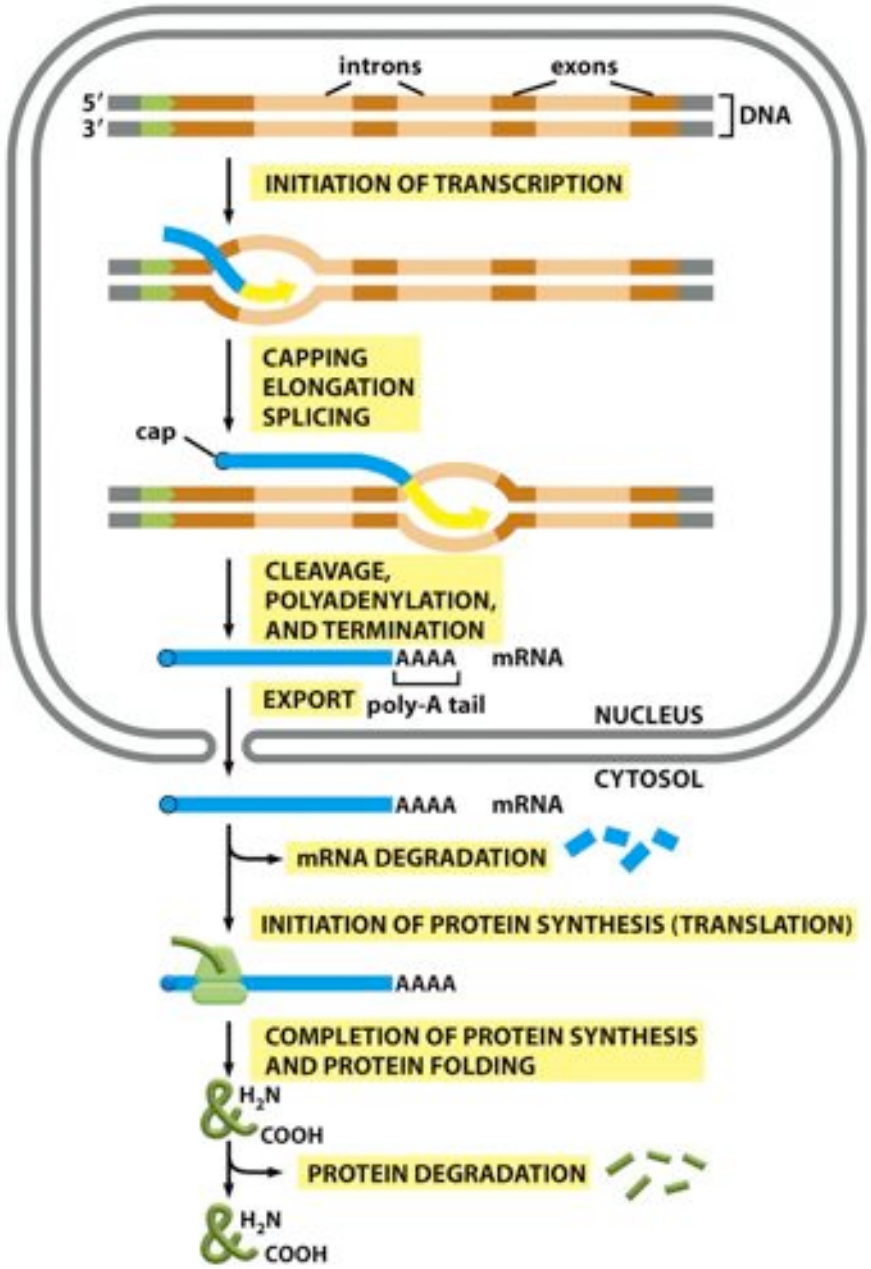


Figure 6-97 *Molecular Biology of the Cell* (© Garland Science 2008)