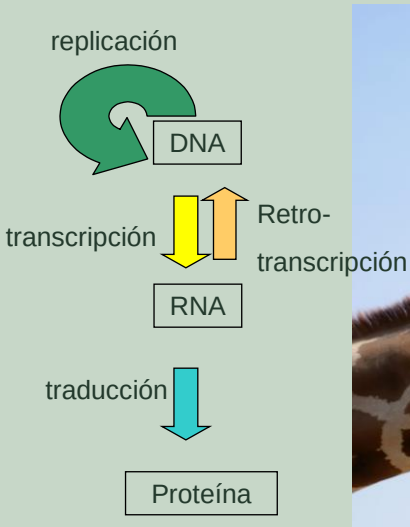
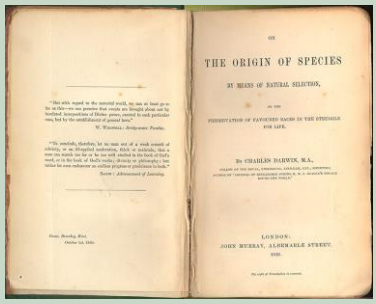
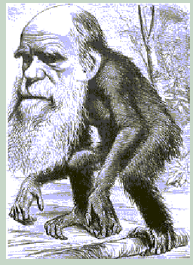
INTRODUCCION A LA BIOLOGIA CELULAR Y MOLECULAR

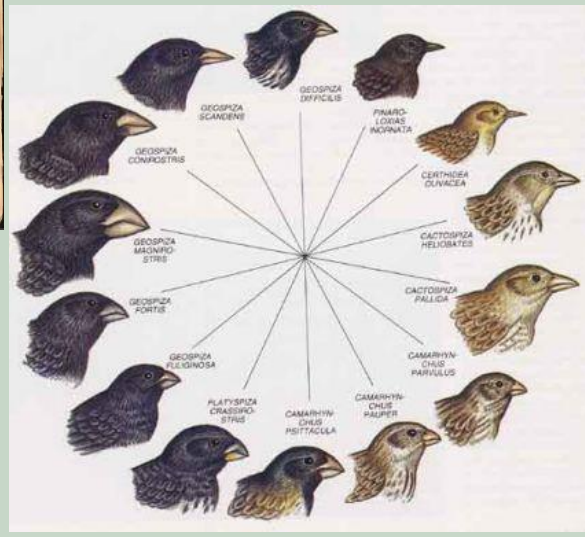
- Transcripción Genética -

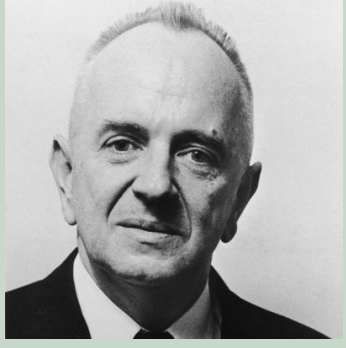
El Dogma Central de la Biología Molecular











Theodosius Dobzhansky (Jan. 25, 1900, Nemirov, Ukraine, Russian Empire - Dec. 18, 1975, Davis, Calif., U.S.)

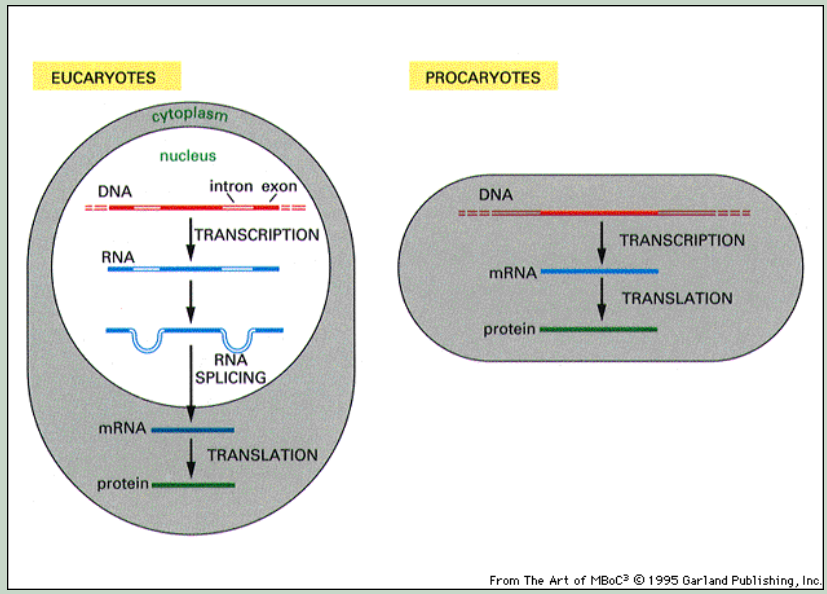
Nothing in biology makes sense except in the light of evolution

ARN

TABLE 6–1 Principal Types of RNAs Produced in Cells

Type of RNA	Function
mRNAs	Messenger RNAs, code for proteins
rRNAs	Ribosomal RNAs, form the basic structure of the ribosome and catalyze protein synthesis
tRNAs	Transfer RNAs, central to protein synthesis as adaptors between mRNA and amino acids
snRNAs	Small nuclear RNAs, function in a variety of nuclear processes, including the splicing of pre-mRNA
snoRNAs	Small nucleolar RNAs, help to process and chemically modify rRNAs
miRNAs	MicroRNAs, regulate gene expression by blocking translation of specific mRNAs and cause their degradation
siRNAs	Small interfering RNAs, turn off gene expression by directing the degradation of selective mRNAs and the establishment of compact chromatin structures
piRNAs	Piwi-interacting RNAs, bind to piwi proteins and protect the germ line from transposable elements
lncRNAs	Long noncoding RNAs, many of which serve as scaffolds; they regulate diverse cell processes, including X-chromosome inactivation

Eucariotas vs. Procariotas



Genes

“Secuencia completa de ADN que está involucrada en la formación de una cadena polipeptidica o de un RNA funcional”

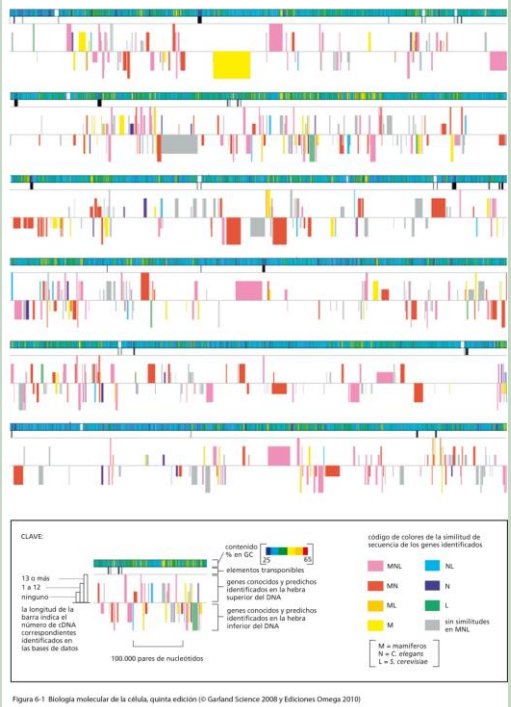
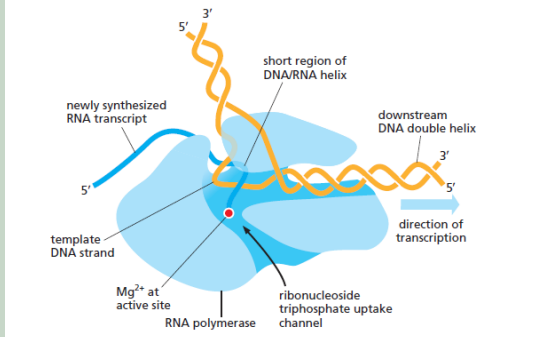


Figura 6-1 Biología molecular de la célula, quinta edición (© Garland Science 2008 y Ediciones Omega 2010)



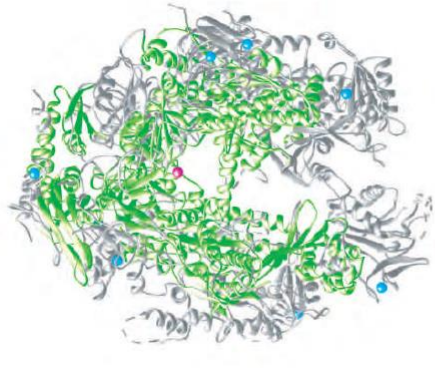
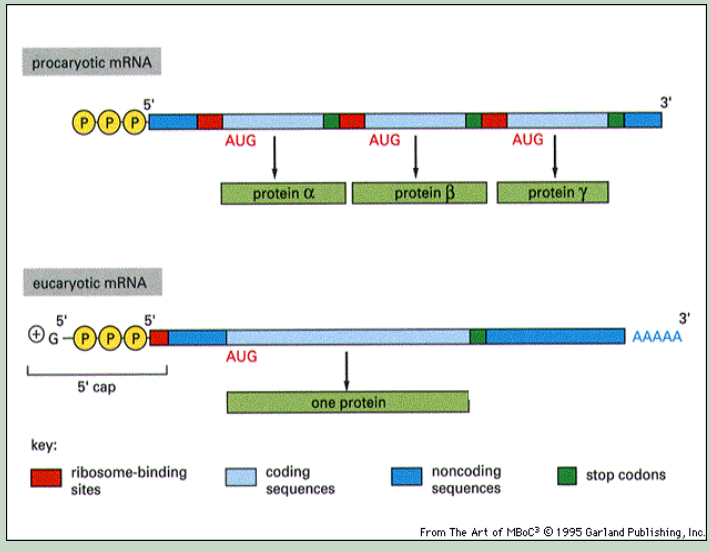
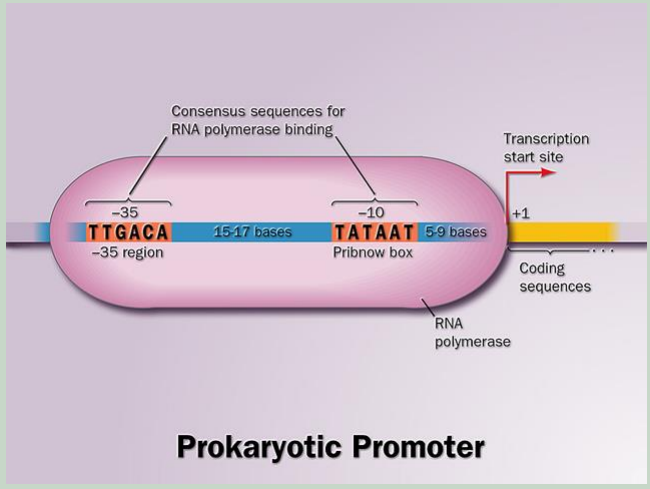


Figure 6–14 Structural similarity between a bacterial RNA polymerase and a eukaryotic RNA polymerase II. Regions of the two RNA polymerases that have similar structures are indicated in *green*. The eukaryotic polymerase is larger than the bacterial enzyme (12 subunits instead of 5), and some of the additional regions are shown in *gray*. The *blue* spheres represent Zn atoms that serve as structural components of the polymerases, and the *red* sphere represents the Mg atom present at the active site, where polymerization takes place. The RNA polymerases in all modern-day cells (bacteria, archaea, and eukaryotes) are closely related, indicating that the basic features of the enzyme were in place before the divergence of the three major branches of life. (Courtesy of P. Cramer and R. Kornberg.)

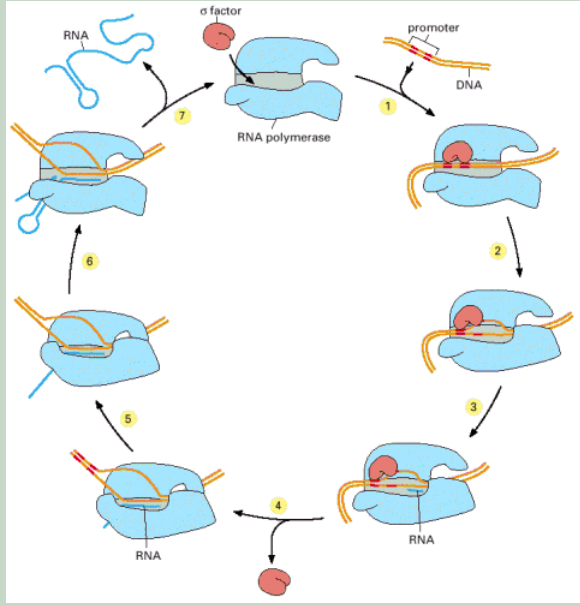
Genes



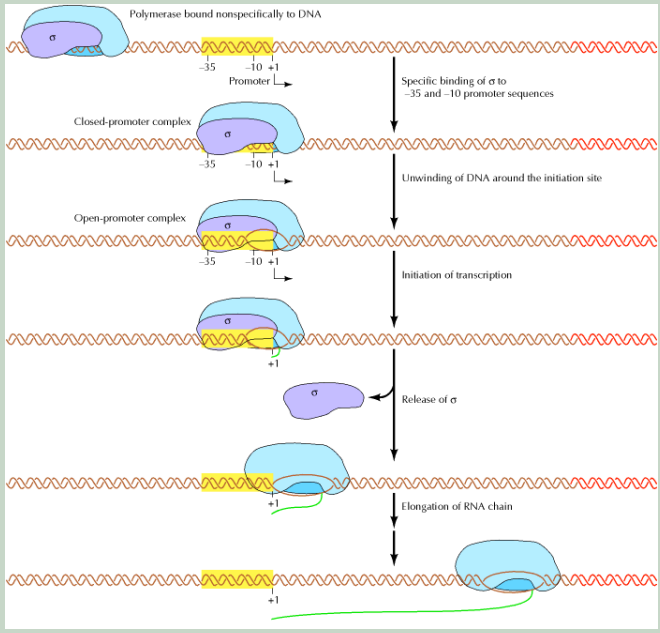
Promotor - PROCARIOTAS



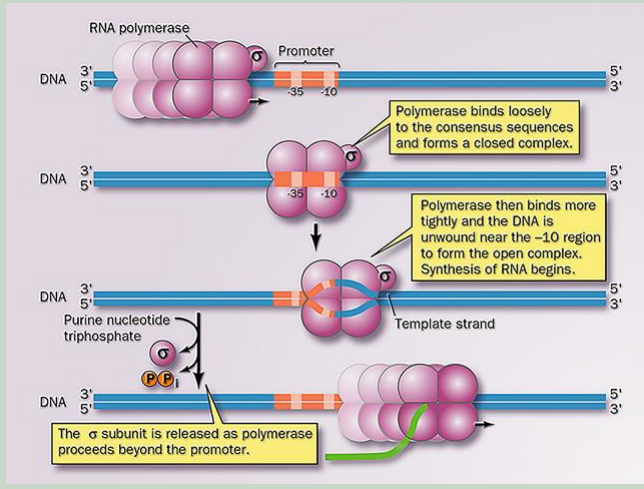
Ciclo de transcripción - PROCARIOTAS



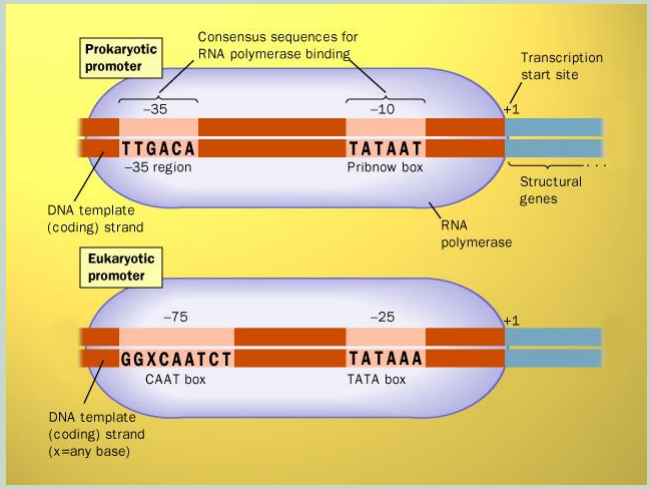
Comienzo de la transcripción- PROCARIOTAS



Inicio de la transcripción - Procariotas



Promotores – Procariotas vs Eucariotas



Polimerasas eucariotas

Eukaryotic RNA Polymerases

Type	Localization	Cellular transcripts
I	Nucleolus	18S, 5.8S, and 28S ribosomal RNAs (rRNA)
II	Nucleoplasm	mRNA precursors and small nuclear RNAs (snRNA)
III	Nucleoplasm	tRNAs and 5S rRNAs

Inicio de la transcripción – ARNpol II (Eucariotas)

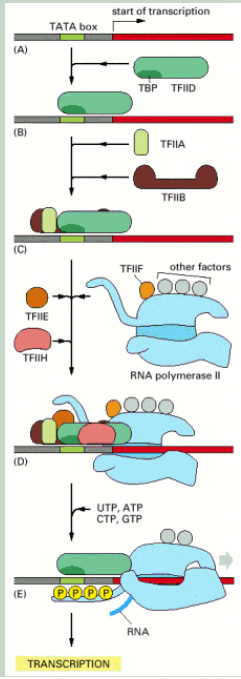
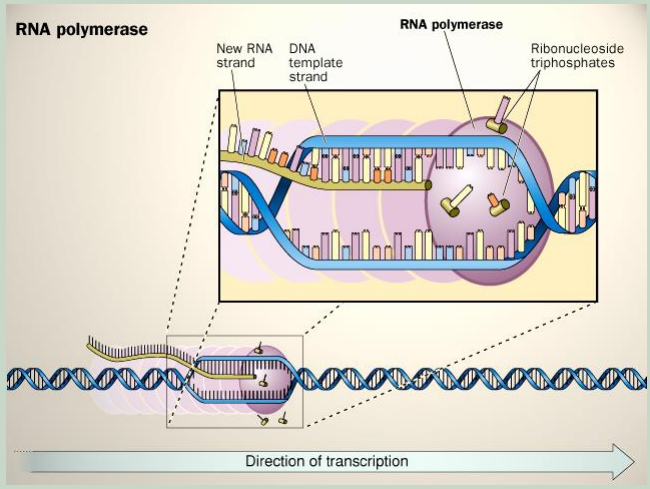


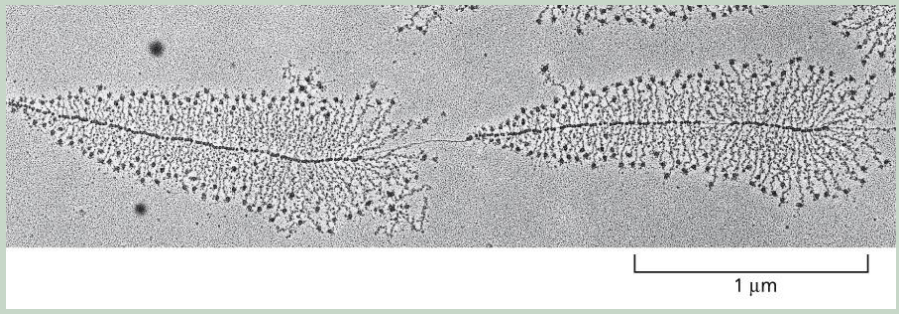
TABLE 6–3 The General Transcription Factors Needed for Transcription Initiation by Eukaryotic RNA Polymerase II

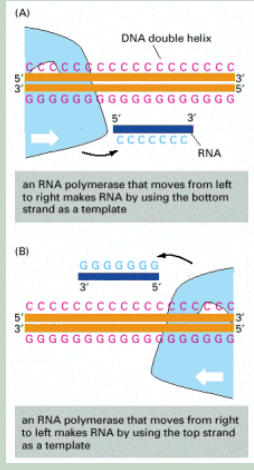
Name	Number of subunits	Roles in transition initiation
TFIID TBP subunit TAF subunits	1 ~11	Recognizes TATA box Recognizes other DNA sequences near the transcription start point; regulates DNA-binding by TBP
TFIIB	1	Recognizes BRE element in promoters; accurately positions RNA polymerase at the start 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

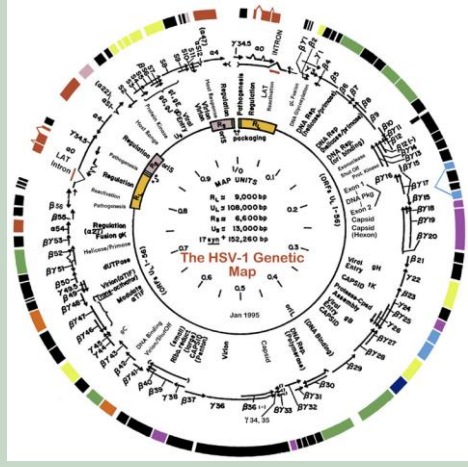
TFIID is composed of TBP and ~11 additional subunits called TAFs (TBP-associated factors); CTD, C-terminal domain.

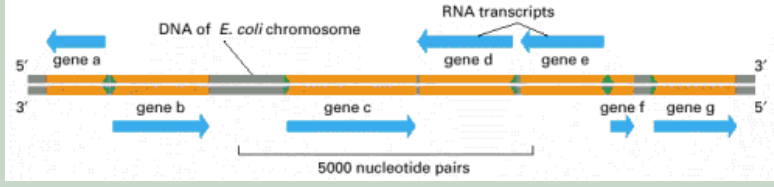
ARN Polimerasa




1 µm


(A)
DNA double helix
5′
3′
3′
5′
5′
3′
RNA
an RNA polymerase that moves from left to right makes RNA by using the bottom strand as a template
(B)
3′
5′
5′
3′
3′
5′
an RNA polymerase that moves from right to left makes RNA by using the top strand as a template

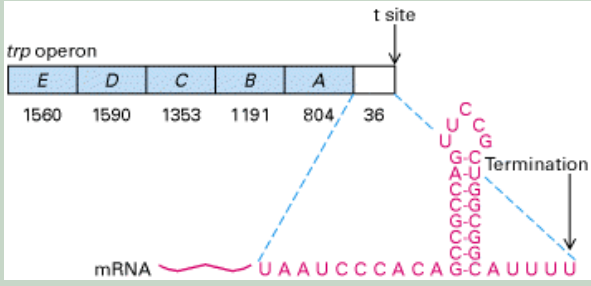

The HSV-1 Genetic Map
Jan 1995


DNA of E. coli chromosome
RNA transcripts
5′
gene a
gene d
gene e
3′
3′
gene b
gene c
gene f
gene g
5′
5000 nucleotide pairs

Fin de la transcripción - PROCARIOTAS

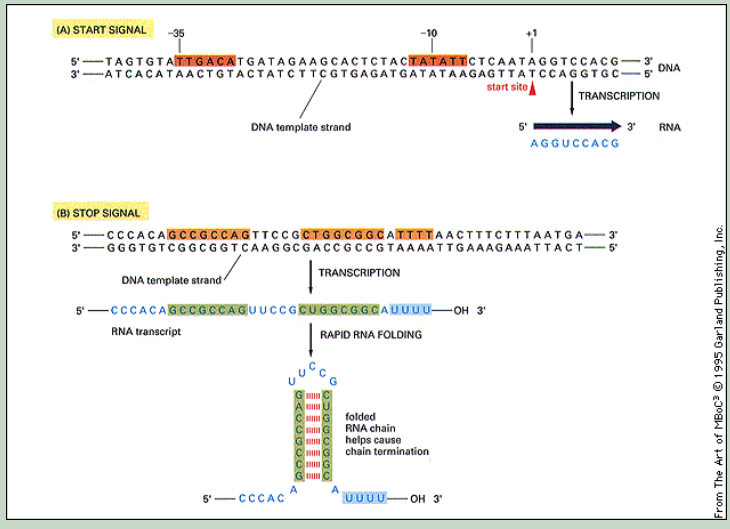
En procariontes se conocen dos sistemas de terminación de la transcripción que involucran a la misma RNA polimerasa, denominados: terminación Rho-independiente (la mayoría de los operones) y terminación Rho dependiente

Terminación Rho-independiente: Estas secuencias de terminación poseen dos características típicas, una serie de residuos U en el RNA transcripto, y, antes de estos, una región autocomplementaria rica en GC.

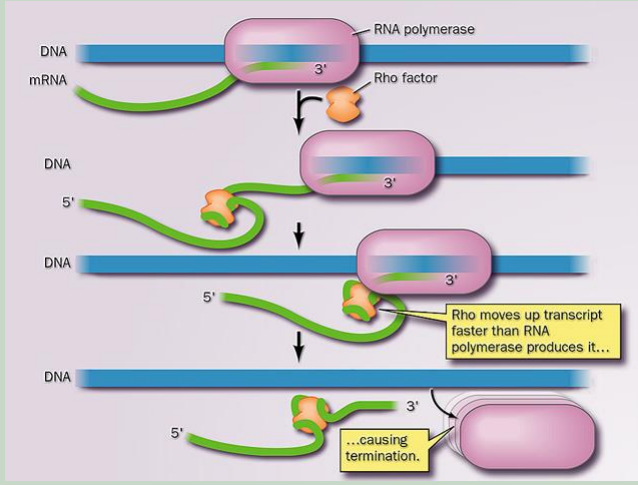


Esta estructura tallo-asa obliga a hacer una pausa a la RNA polimerasa. Además los pares de bases entre los residuos U en el extremo 3´ de la hebra de RNA naciente y los residuos de A en la hebra de DNA plantilla son muy inestables en comparación con otros tipos de apareamientos de Watson-Crick

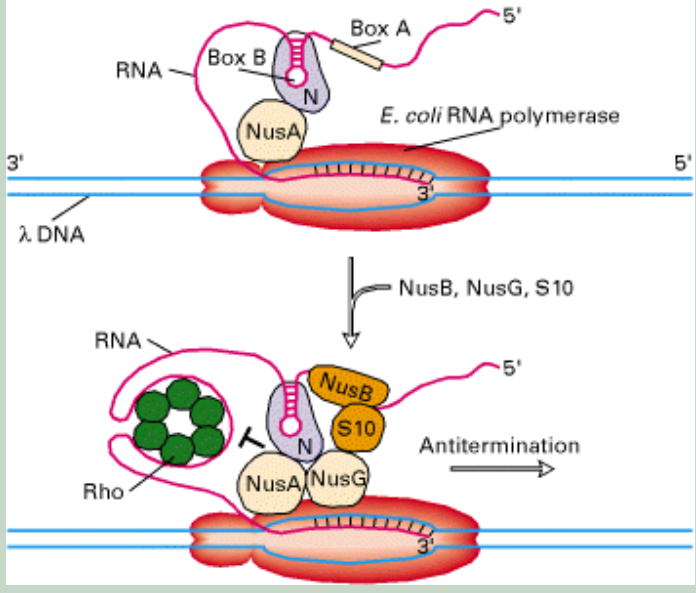
Fin de la transcripción Rho independiente



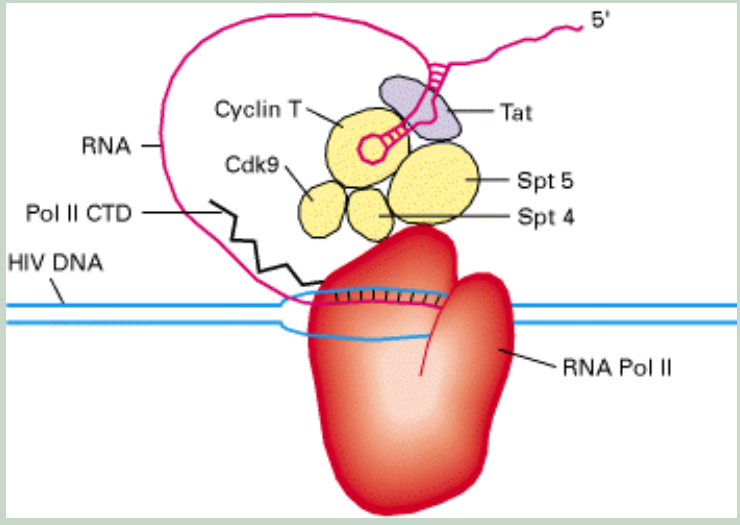
Fin de la transcripción RHO dependiente - PROCARIOTAS



Fin de la transcripción RHO dependiente - PROCARIOTAS

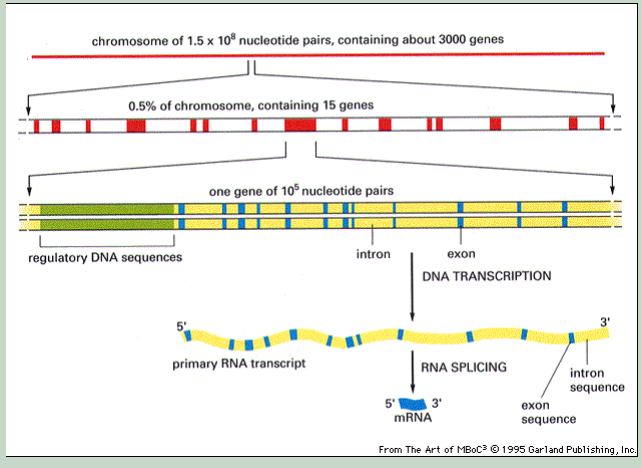


Fin de la transcripción – HIV RNA pol II

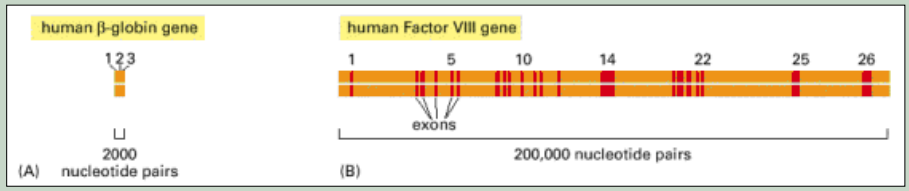


Complejo de antiterminación compuesto por la proteína Tat de HIV y varias proteínas celulares eucariontes. El elemento TAR en el transcripto de HIV contiene secuencias reconocidas por la TAT y la proteína celular ciclina. La ciclina T, activa y contribuye a ubicar la Cdk9, una quinasa, cerca de su sustrato, el CTD de la RNA polimerasa II, el cual es hiperfosforilado por esta quinasa.

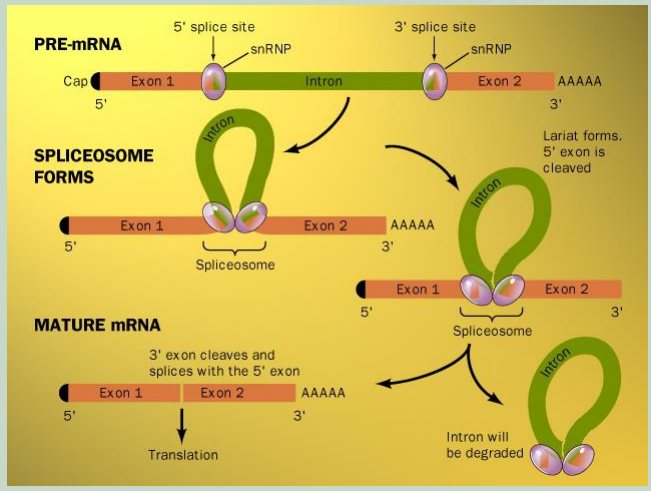
Intrones y exones



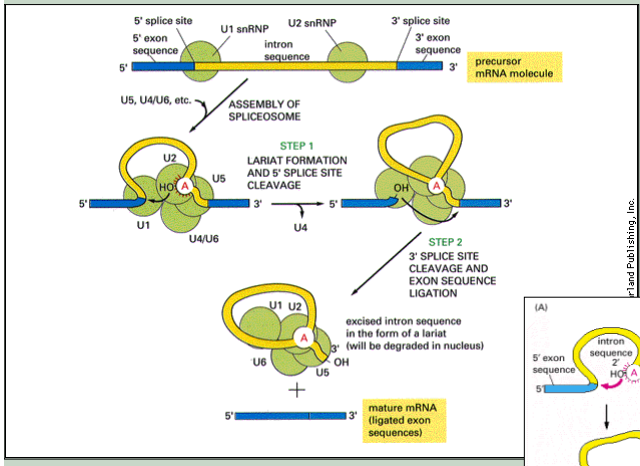
Intrones y exones

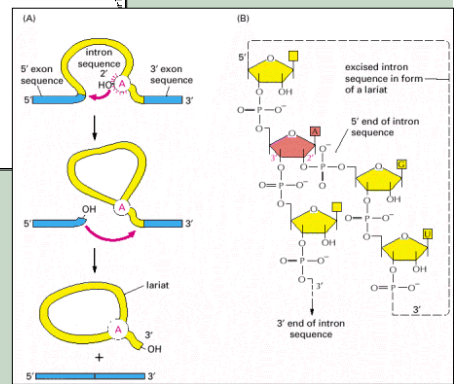

human β-globin gene
1 2 3
2000
nucleotide pairs
(A)
human Factor VIII gene
1
5
10
14
22
25
26
exons
200,000 nucleotide pairs
(B)

Splicing

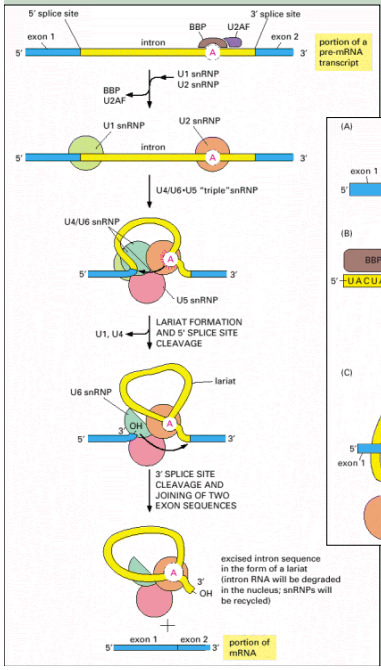

PRE-mRNA
5' splice site
3' splice site
snRNP
snRNP
Cap
Exon 1
Intron
Exon 2
AAAAA
5'
3'
SPLICEOSOME FORMS
Intron
Lariat forms. 5' exon is cleaved
Exon 1
Exon 2
AAAAA
5'
3'
Spliceosome
Intron
Exon 1
Exon 2
5'
3'
Spliceosome
MATURE mRNA
3' exon cleaves and splices with the 5' exon
Exon 1
Exon 2
AAAAA
5'
3'
Translation
Intron
Intron will be degraded

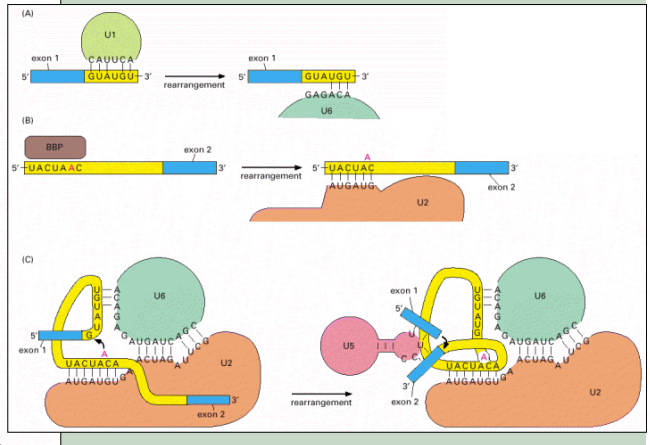
Splicing



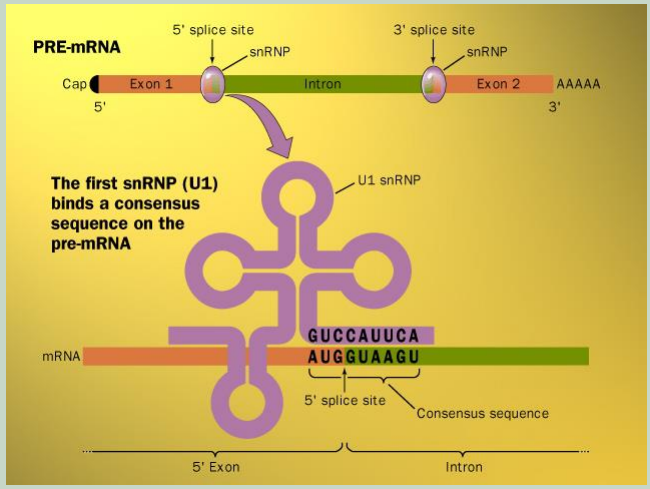


Intrones de tipo III

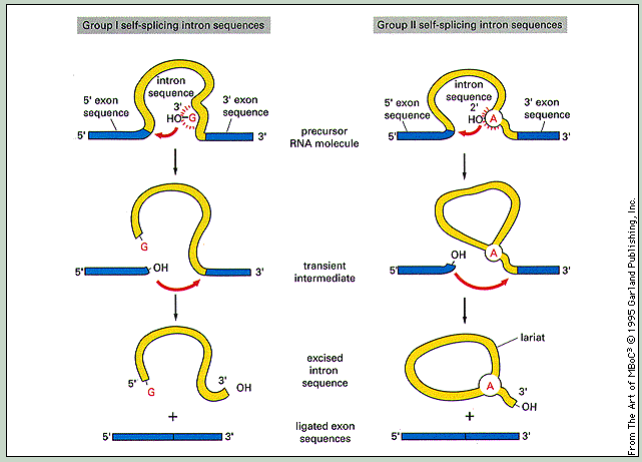




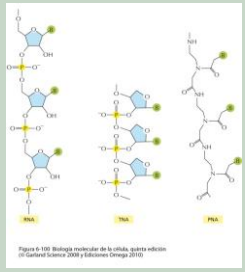
Splicing



Autosplicing – RNA catalitico



Introns de tipo I y II



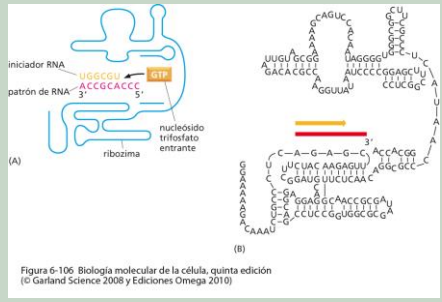


Figura 6-106 Biología molecular de la célula, quinta edición (© Garland Science 2008 y Ediciones Omega 2010)

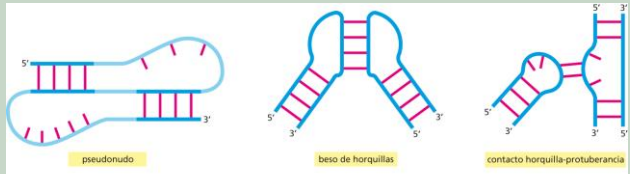


Figura 6-102 Biología molecular de la célula, quinta edición (© Garland Science 2008 y Ediciones Omega 2010)

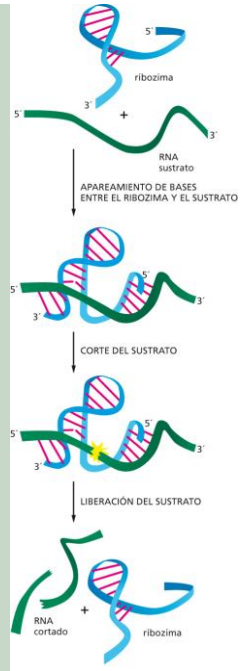


Figura 6-103 Biología molecular de la célula, quinta edición (© Garland Science 2008 y Ediciones Omega 2010)

Splicing alternativo

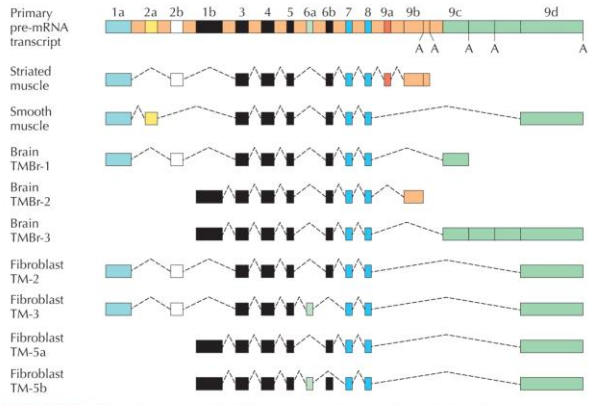
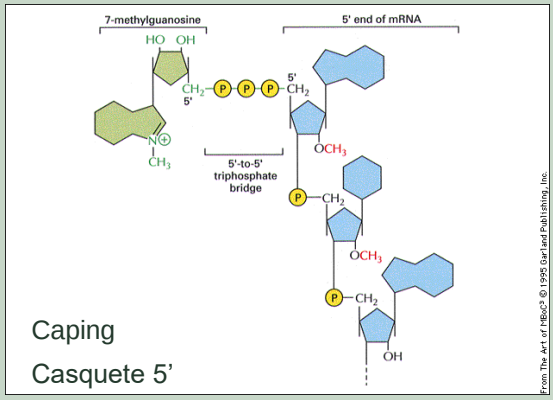


FIGURE 8.22. Alternative splicing. Multiple proteins are known to be made from the α-tropomyosin gene by alternatively splicing in different cell types. The *orange boxes* in the primary transcript represent introns; all other boxes are exons. For each tissue type the splicing form is shown by *lines* connecting the exons that are used.

8.22, modified from Lees-Miller J.P. et al., *Mol. Cell. Biol.* **10:** 1729–1742, © 1990 American Society for Microbiology

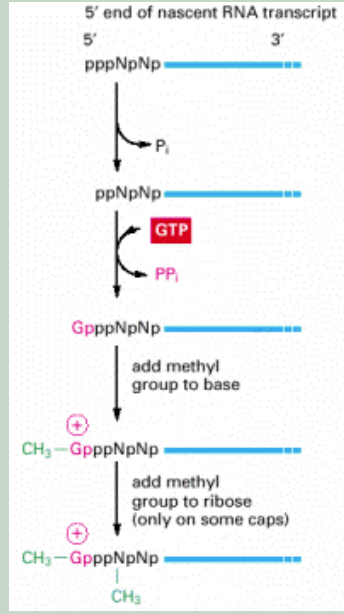
Evolution © 2007 Cold Spring Harbor Laboratory Press

Maduración del transcripto primario. CAP

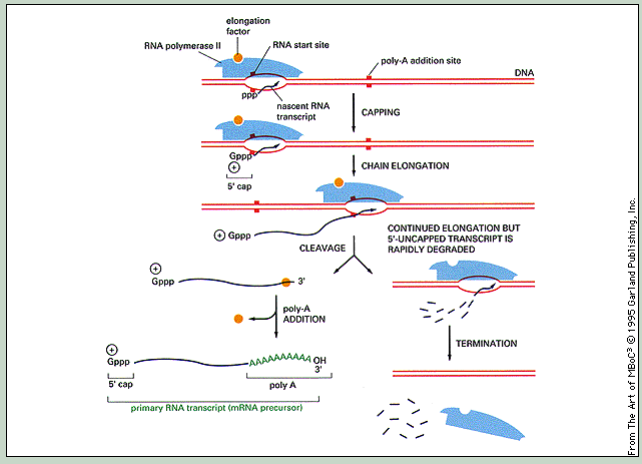


Caping

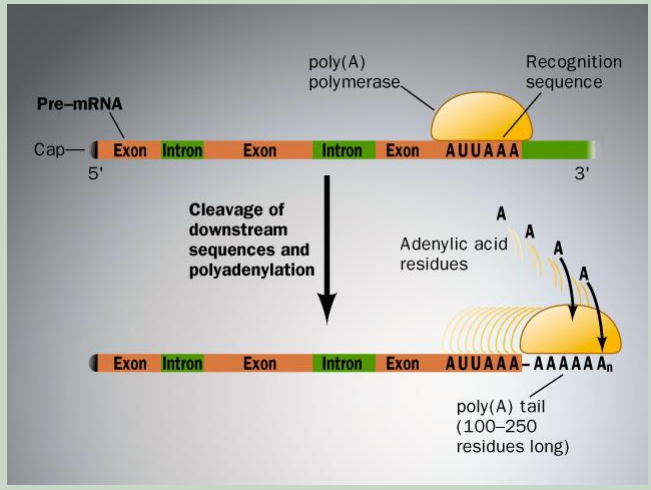
Casquete 5’



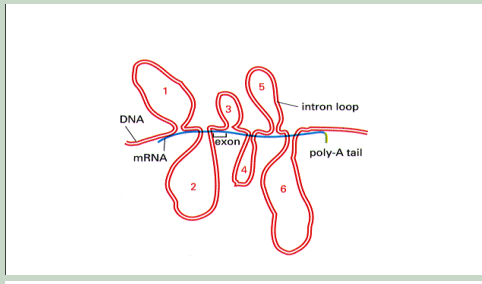
ARNm

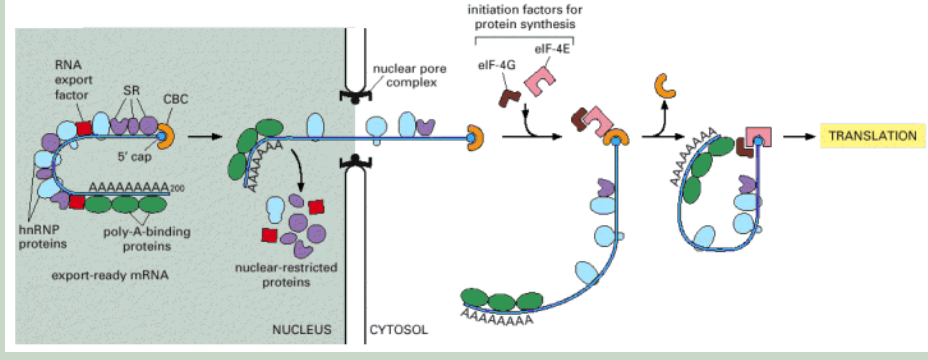


Poliadenilación

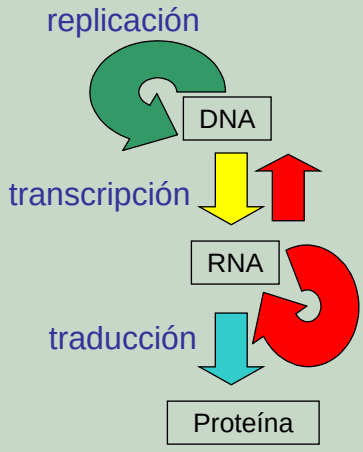


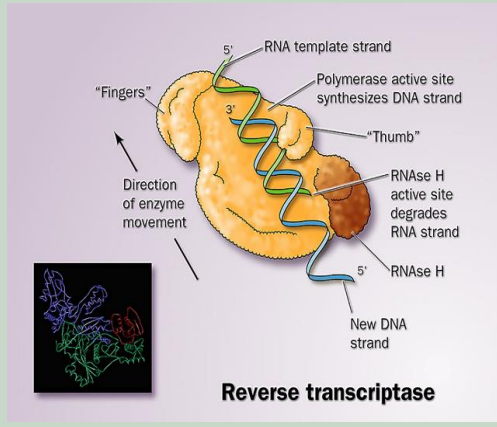
DNA vs. mRNA maduro



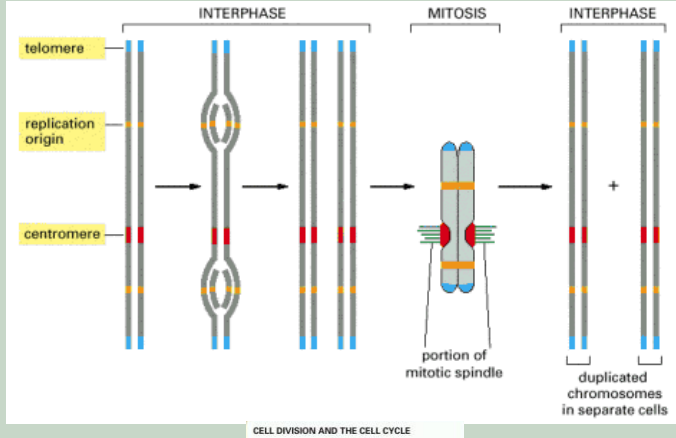


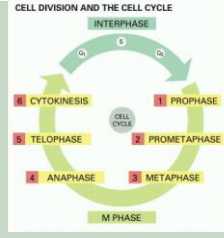
Retrotranscripción y replicación de RNA



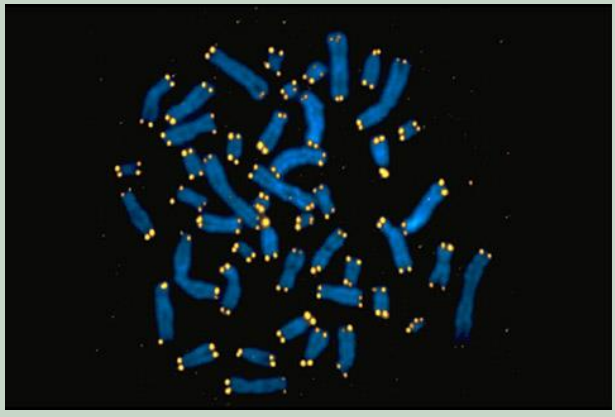


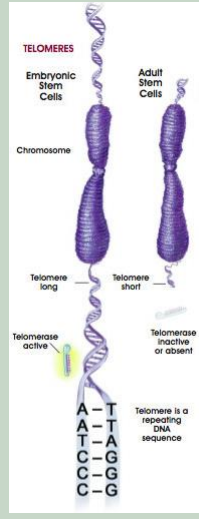
ADN





Cromosomas y Telómeros

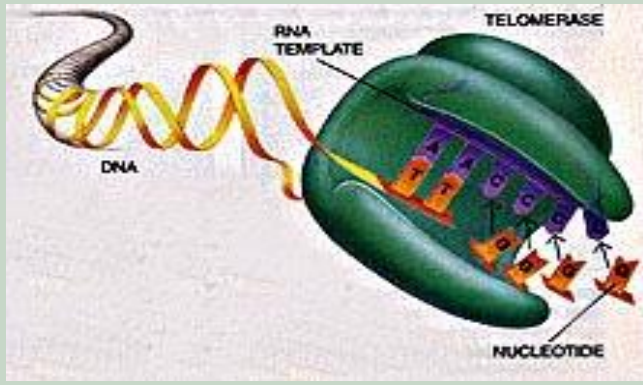




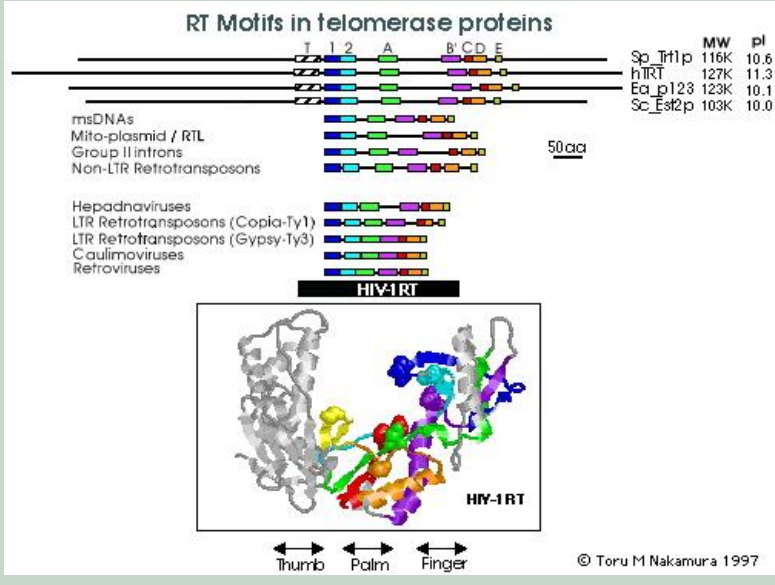
TELOMERASA

Es la enzima responsable de la replicación del ADN telomérico. Es una ribonucleoproteína, que contiene el templado de ARN con el que se impide la perdida de secuencias que se produciría normalmente en cada división celular.

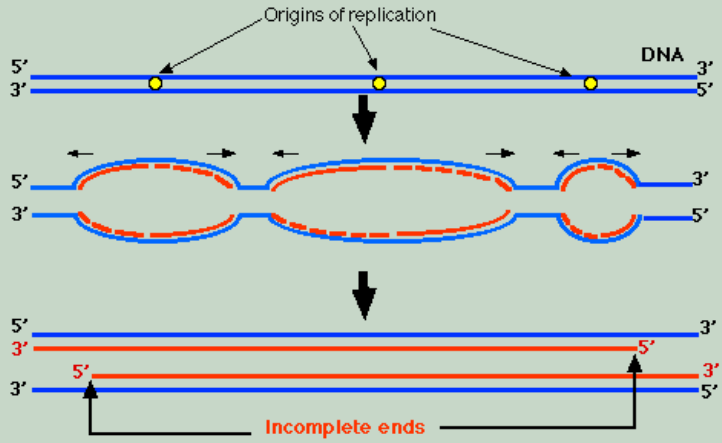
TELOMERASA

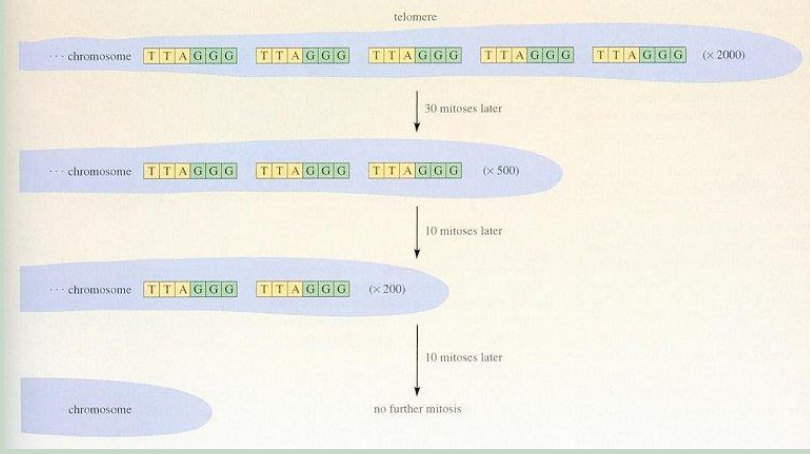


HOMOLOGIA DE LA TELOMERASA



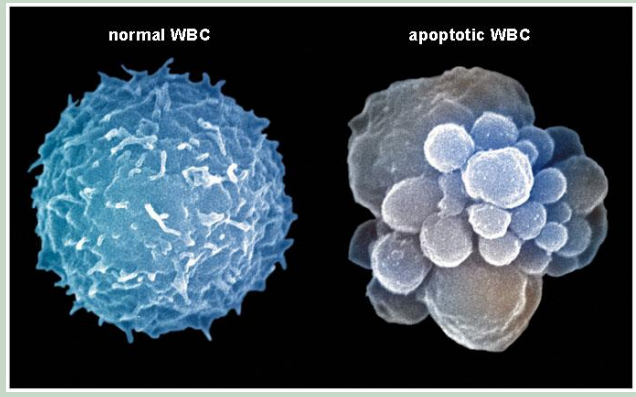
Acortamiento telomérico

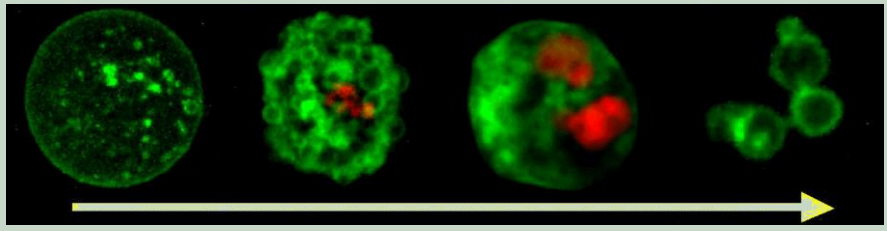




Senescencia Replicativa

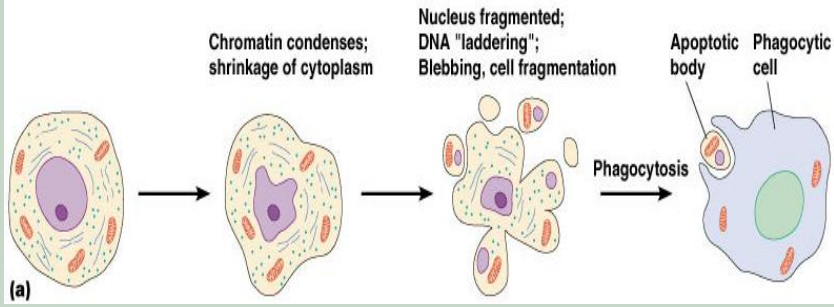
Apoptosis





APOPTOSIS VS. NECROSIS

- ACHICAMIENTO CELULAR
- CONDENSACIÓN DE LA CROMATINA
- FRAGMENTACION DEL ADN
- VACUOLIZACION CITOPLASMÁTICA
- LISIS CELULAR



Research article

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Potential involvement of oxidative stress in cartilage senescence and development of osteoarthritis: oxidative stress induces chondrocyte telomere instability and downregulation of chondrocyte function

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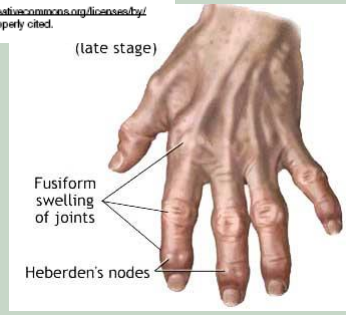

Progeria