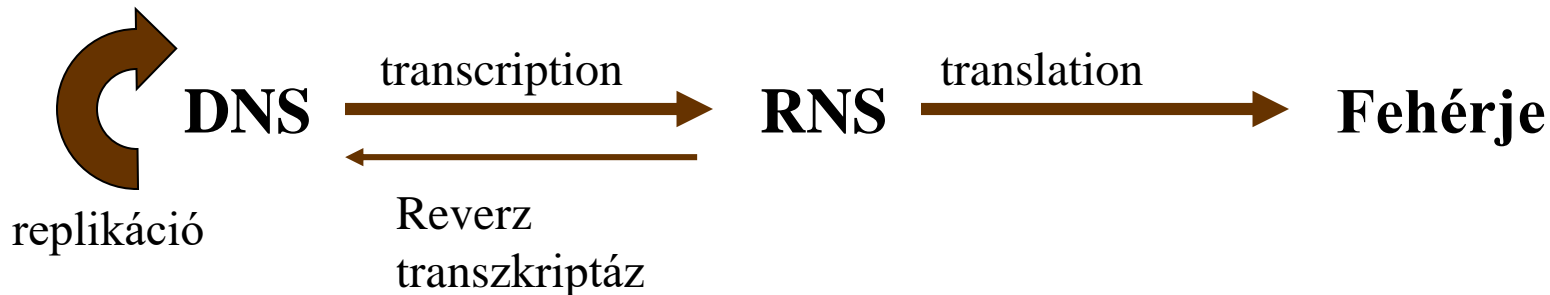


DNA replikáció

A molekuláris biológia centrális dogmája



A DNS-ben tárolt információ:

- fehérje szerkezet
- a gének kifejeződésének szabályozása

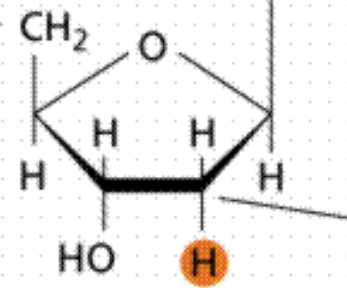
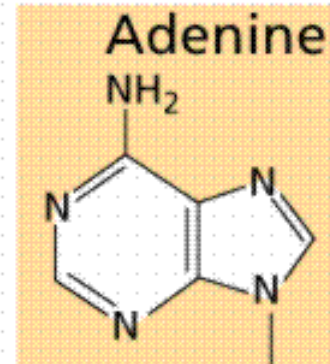
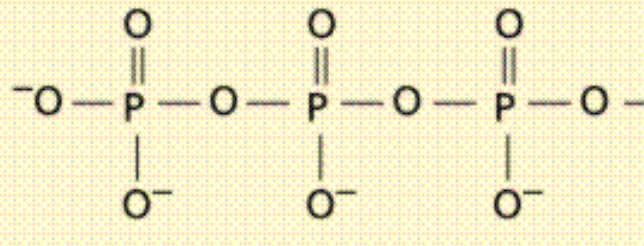
Nukleinsavak: nukleotid monomerekből álló polimerek

RNS: adenin, guanin, citozin, uracil bázisok and ribóz

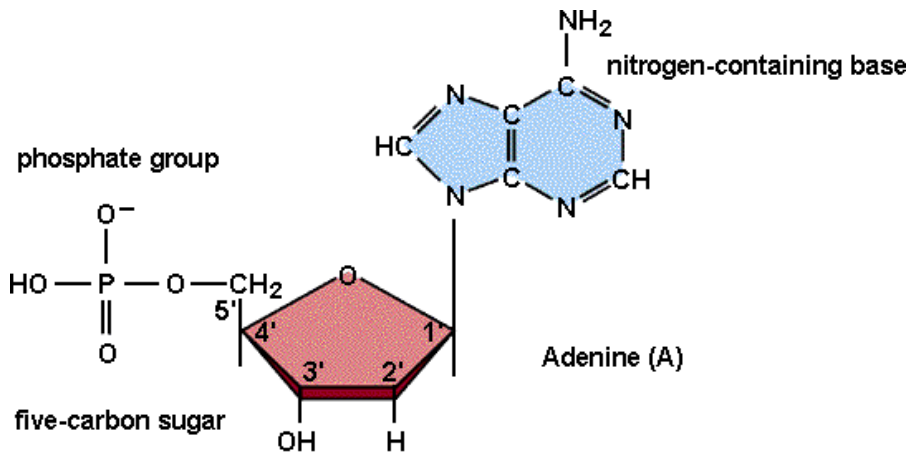
DNS: adenin, guanin, citozin, thimin bázisok és dezoxi ribóz

Deoxy-ATP
(deoxyadenosine
triphosphate)

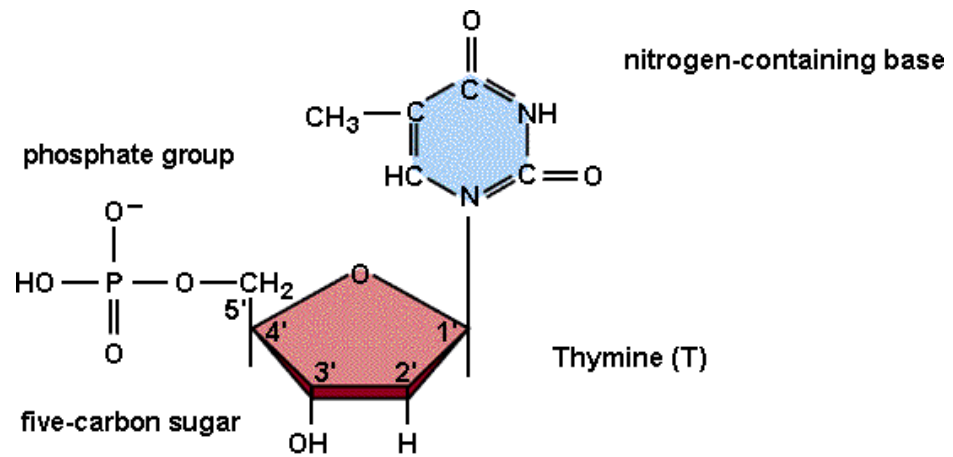
Phosphate groups



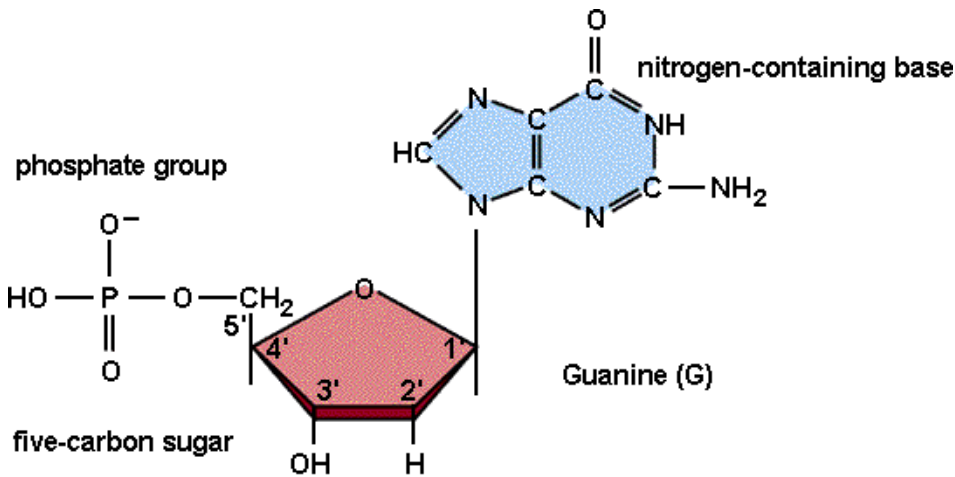
Deoxy-
ribose
sugar



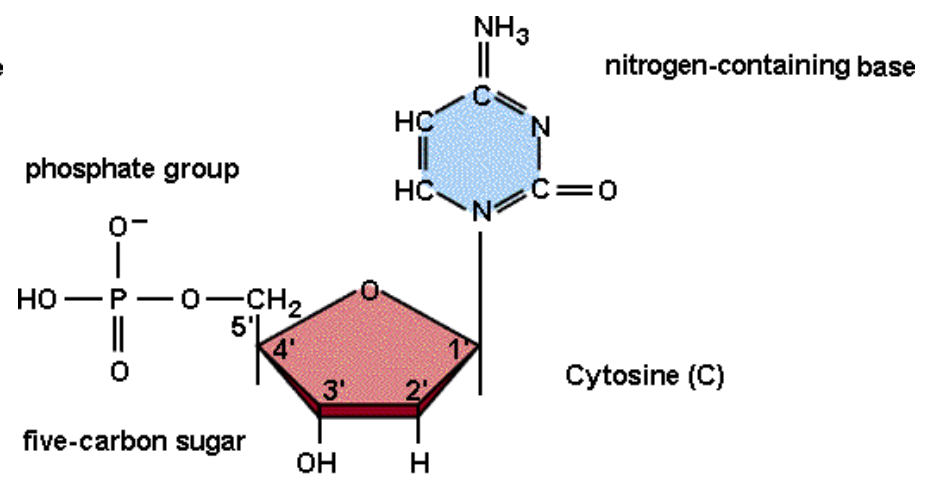
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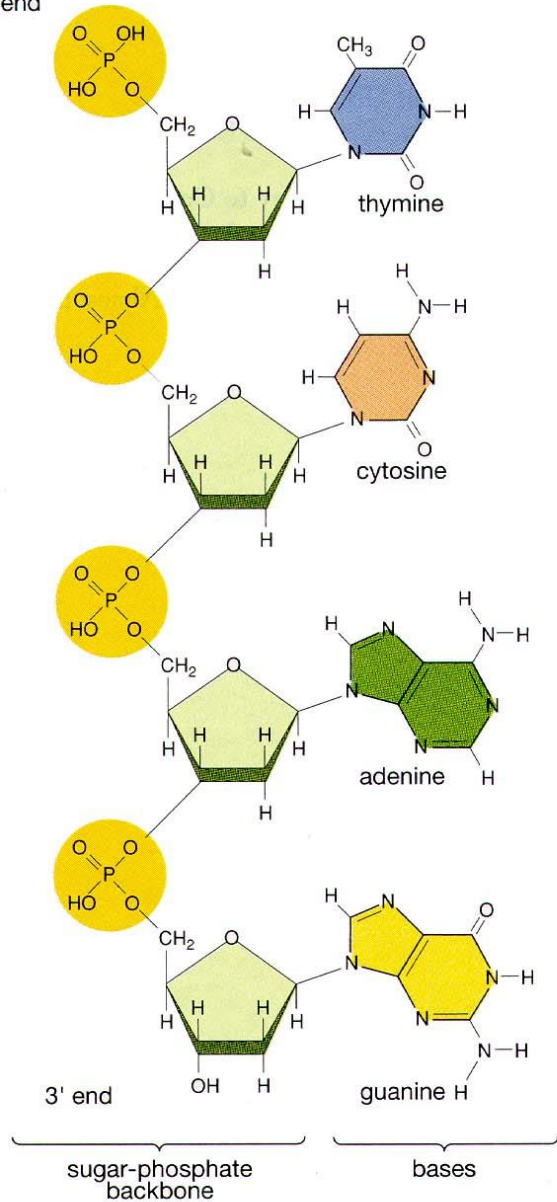
© 1997 Wadsworth Publishing Company/ITP



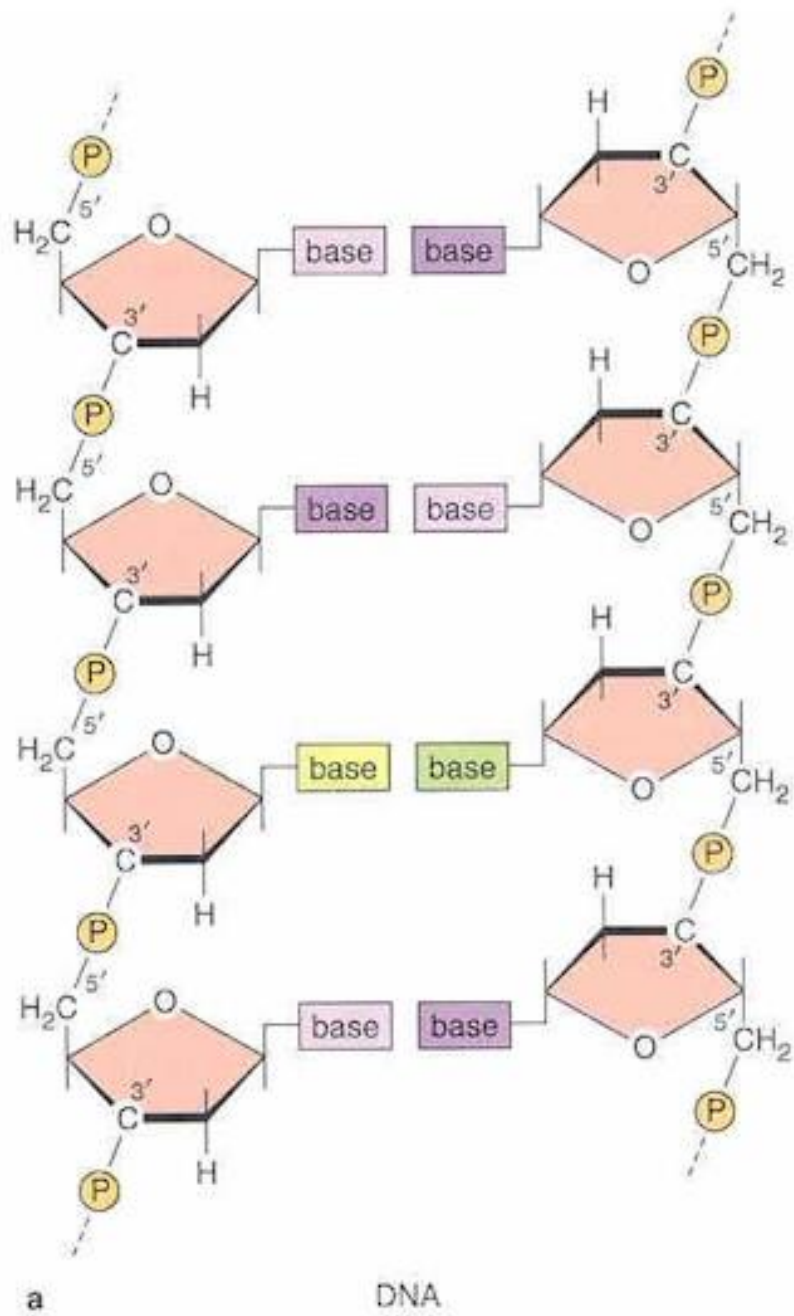
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Single strand of DNA:

5' end

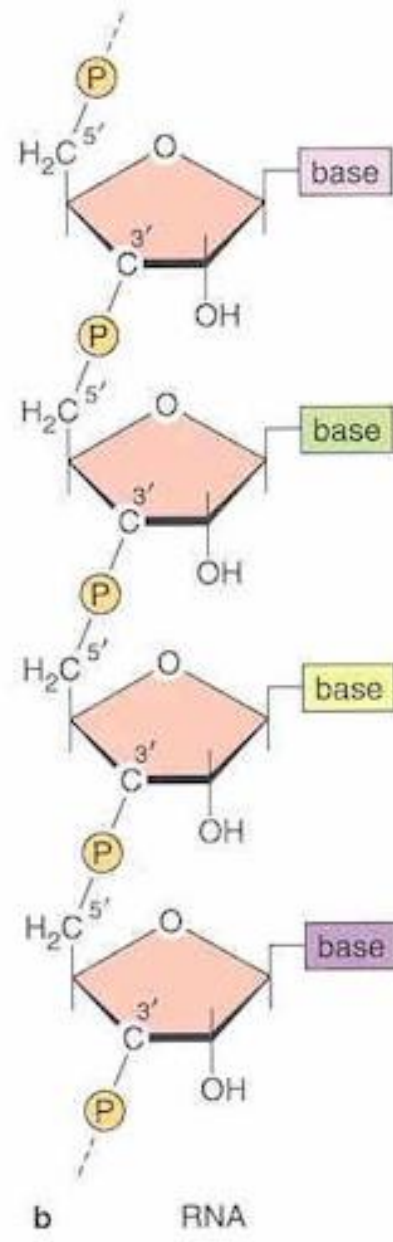


Információ: a dezoxiribonukleotidok sorrendje



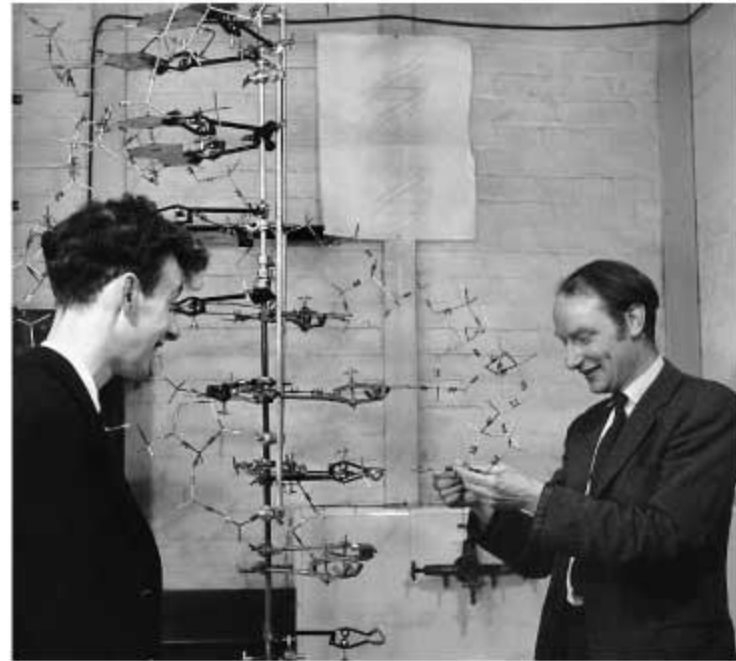
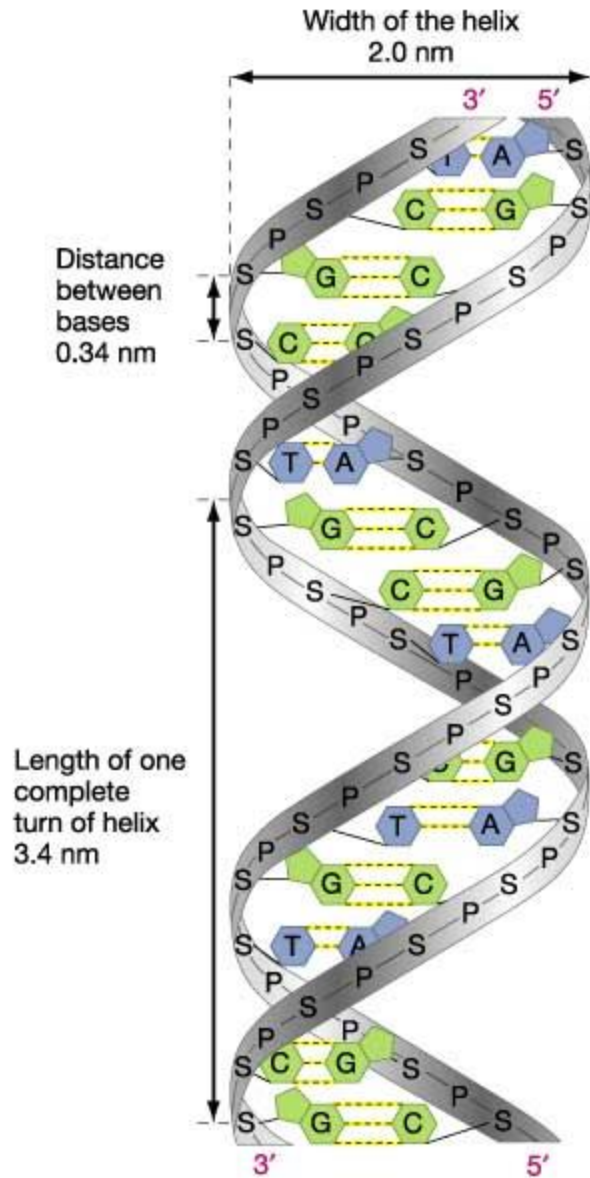
a

DNA



b

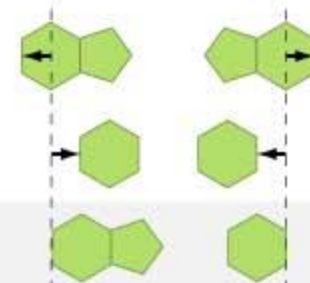
RNA



Purine-purine pair
TOO WIDE

Pyrimidine-pyrimidine pair
TOO NARROW

Purine-pyrimidine pair
JUST RIGHT



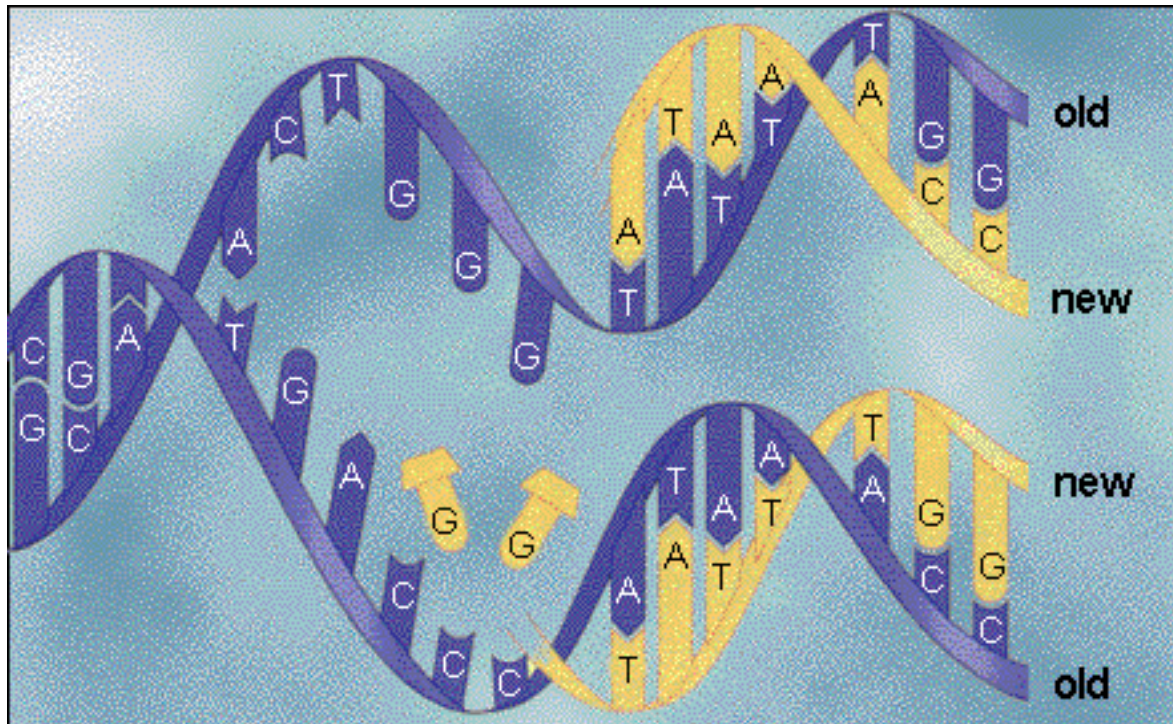
Space inside sugar-phosphate backbones

DNS replikációnak le kell játszódnia mielőtt a sejt két genetikailag megegyező sejté osztódik.

A DNS replikáció szemikonzervatív

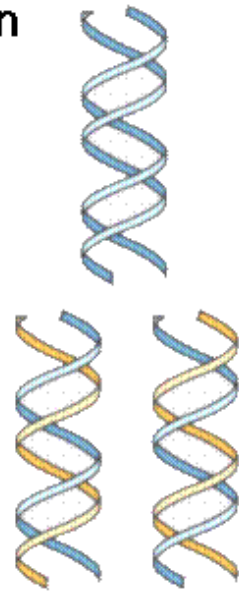
Mindkét DNS szál templátként szolgál egy új szál szintéziséhez, az eredmény 2 DNS molekula, amely egy régi (templát) és egy újonnan szintetizált szálból áll.

Semiconservative replication

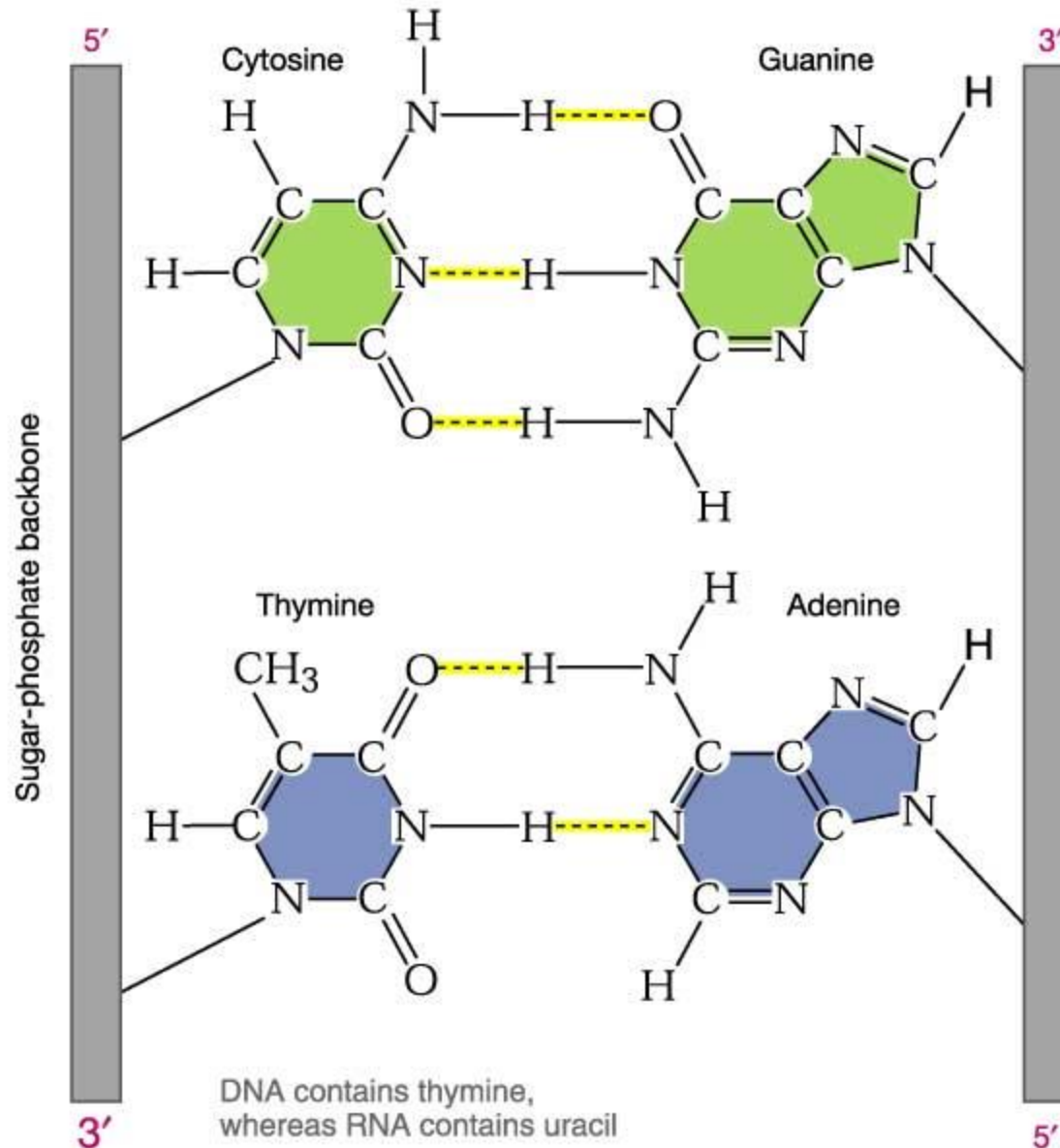


**Original DNA
Helix**

**DNA helices
after one round
of replication**



The hydrogen bonds between complementary bases and the common geometry of the standard A=T and G≡C base pairs provide the correct pairing



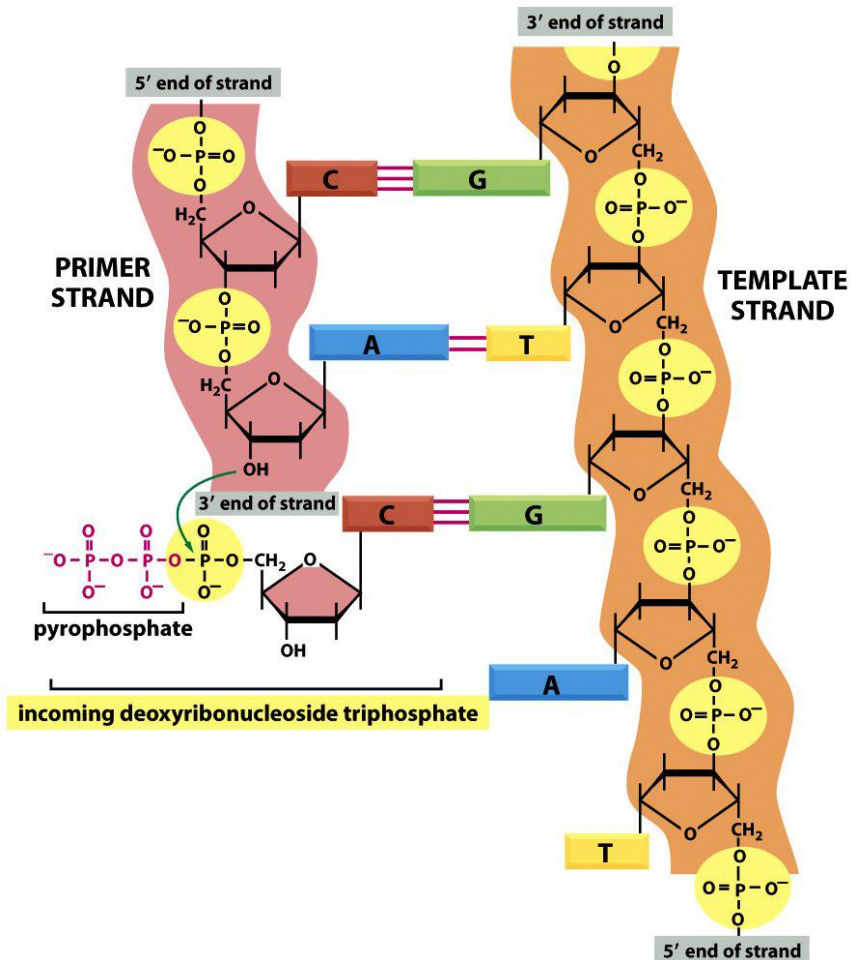
DNS polimerizációnak két követelménye van:

1. Templát
2. Primer

A primer egy száldarabka (a templáttal komplementer) szabad 3'-hidroxil csoporttal

A DNS polimerázok csak már egy meglévő szálat tudnak meghosszabbítani

Sok primer RNS oligonukleotid



The replication of DNA in prokaryotes

The enzymes of the process

DNA polymerase I: the first known enzyme DNA polymerase, consist of one polipeptide chain, 3 different activity:

- synthetic activity
- correction 3'-5' exonuclease
- correction 5'-3' exonuclease activity

The main function of DNA polymerase I is repair.

DNA polymerase III: this enzyme responsible for the replication, consist of many subunits, 2 different enzyme activity:

- synthetic activity
- correction 3'-5' exonuclease activity

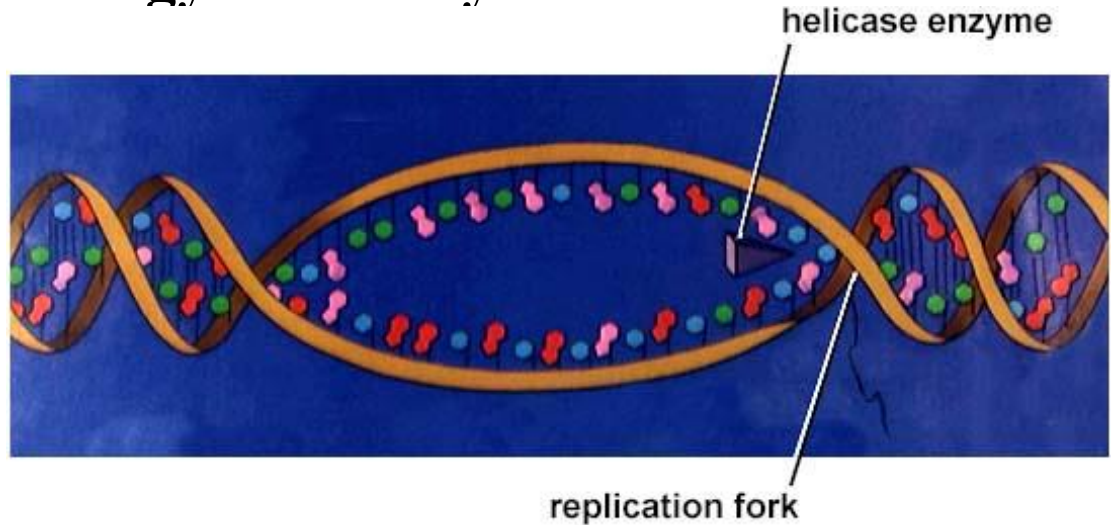
DNA polymerase III is the principal replication enzyme

The process of DNA replication

A DNS szintézis iránya: 5' végtől a 3' végig.

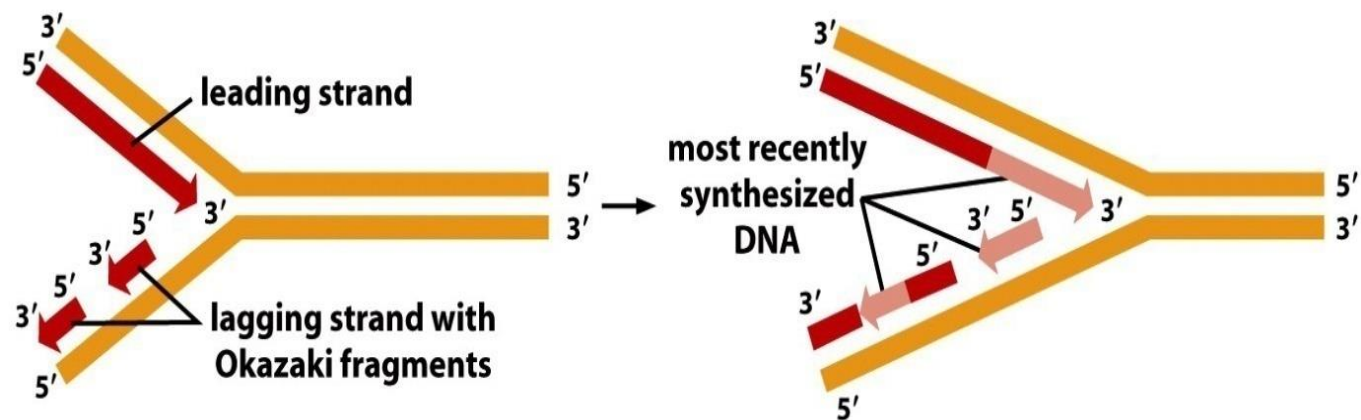
A replikáció mindkét szálon egyszerre folyik

A templát szál és a szintetizálódó leányszál antiparalel lefutású.

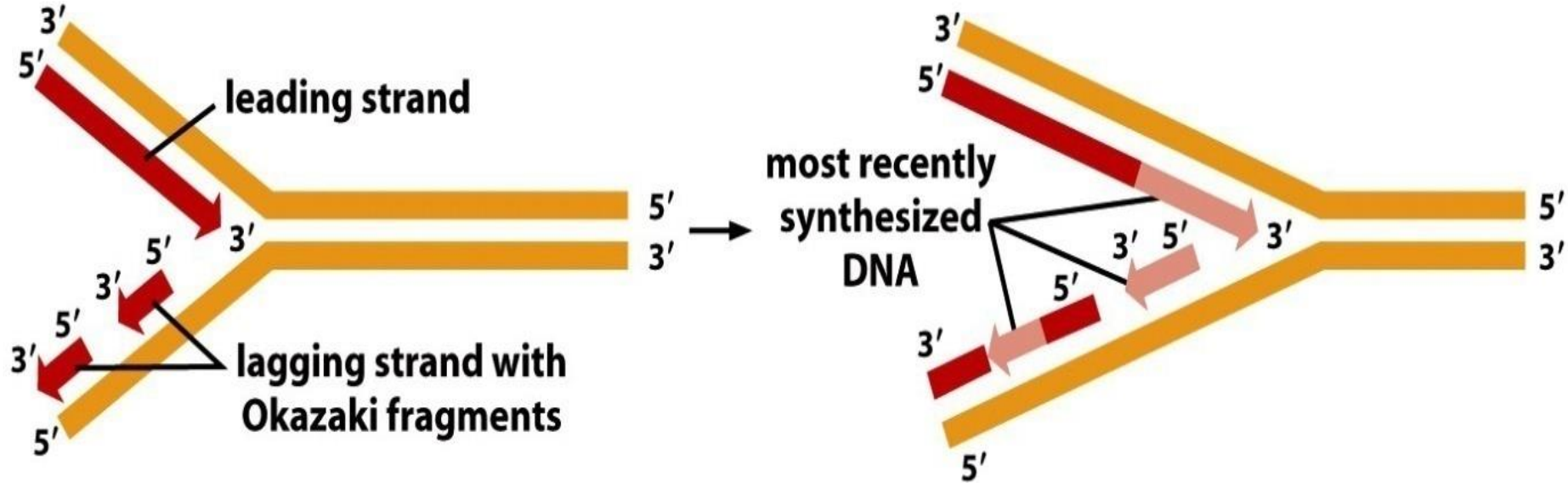


szintézis 5' → 3'

olvasás 3' → 5'



Ha mind a két szál folyamatosan szintetizálná miközben replikációs villa felnyílik, halad, akkor az egyik szálnak $3' \rightarrow 5'$ irányban kellene szintetizálnia



Vezető szál

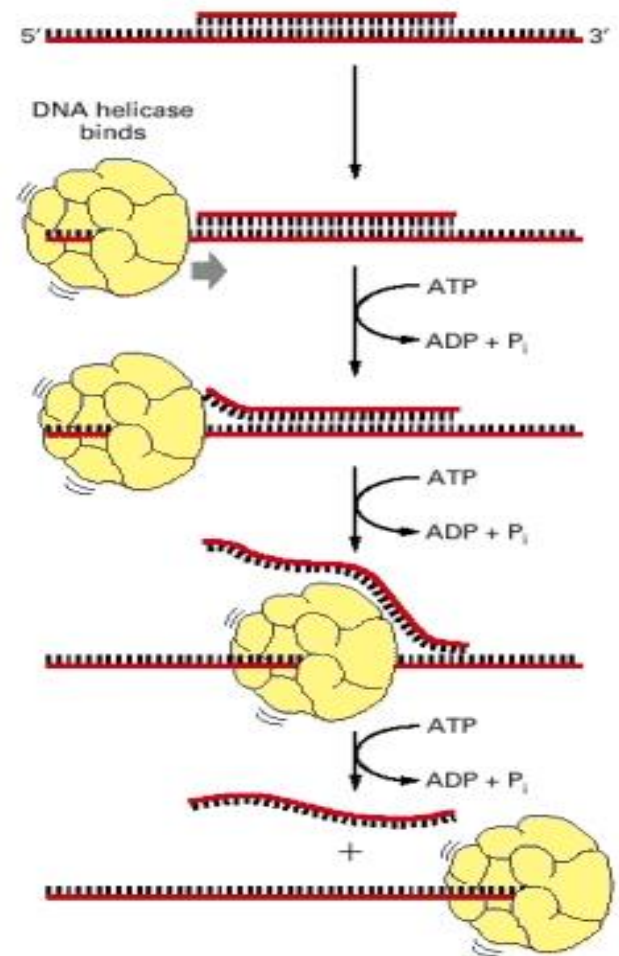
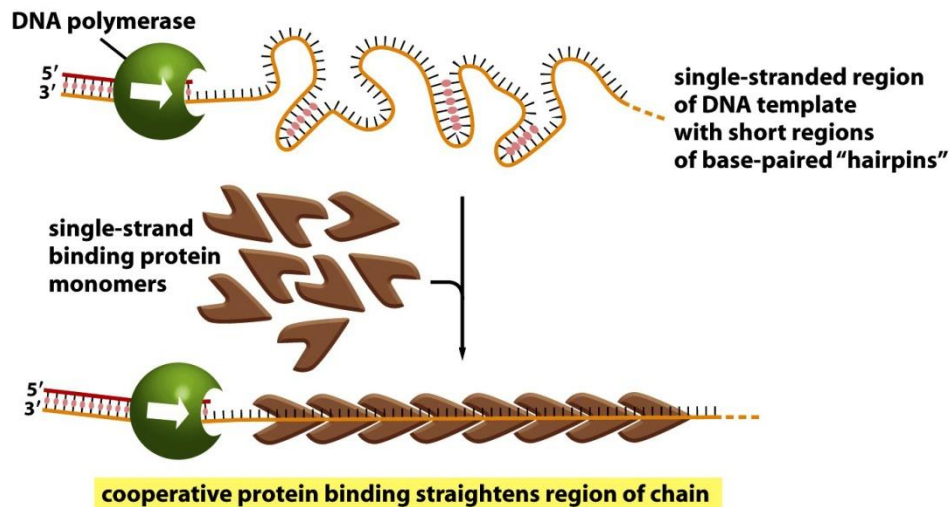
Követő szál

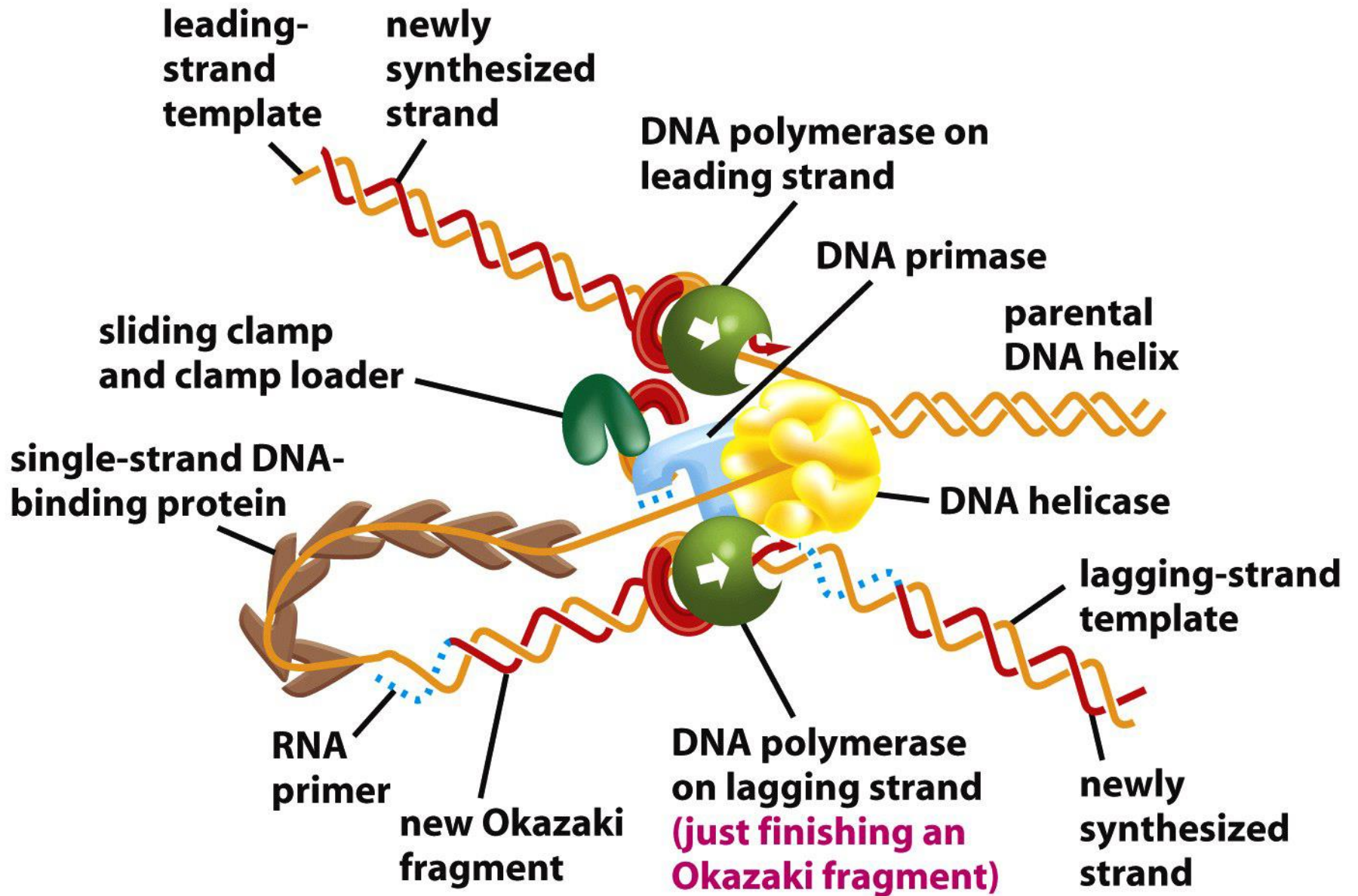
A kettős hélixnek fel kell nyílnia a replikációs villa előtt

A DNS polimerázok és a DNS primáz csak akkor képesek a DNS megkettőzésére, amennyiben az nyitott állapotban van.

A DNS felnyitásában 2 fehérje vesz részt:

- DNS helikázok
- Egyszálú DNS kötő fehérjék: segítenek a helikázoknak stabilizálni a kitekert egyszálú DNS-t





- 1. A vezető szál szintézise egy rövid RNS primer primáz általi szintézisével kezdődik a replikációs origónál.**
- 2. A dezoxiribonukleotidokat a DNS polimeráz III ehhez a primerhez adja.**
- 3. A vezető szál szintézise folyamatosan halad a replikációs villa felnyílásával.**
- 4. A követő szál szintézise Okazaki fragmensek formájában történik.**
- 5. Amikor egy Okazaki fragmens szintézise befejeződik, az RNS primer levágódik és a helyét a DNS polimeráz I DNS pótolja egy rövid DNS szakasszal. A fentmaradó rövidke szakadást (nick) a DNS ligáz foltozza be.**

Hibajavítás

A nem komplementer bázisok beépülését meg kell akadályozni. A hibajavítást maga a DNS polimeráz végzi → korrekciós 3'-5' exonukleáz aktivitás.

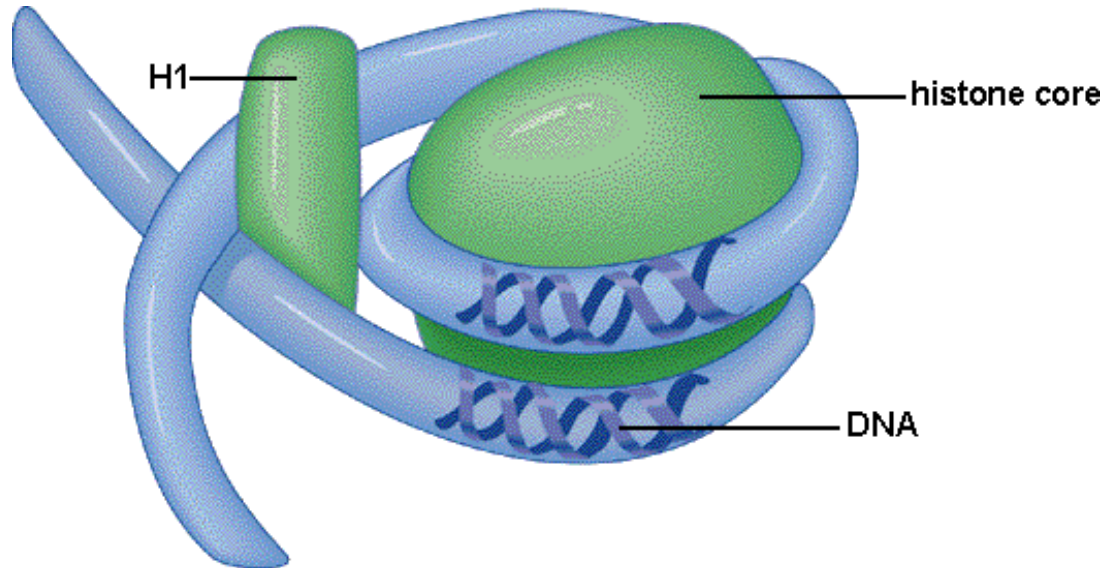
Komplementer kettősszálú régiókban a DNS polimeráz I 5'-3' exonukleáz aktivitása válik fontossá.

DNS-ligáz

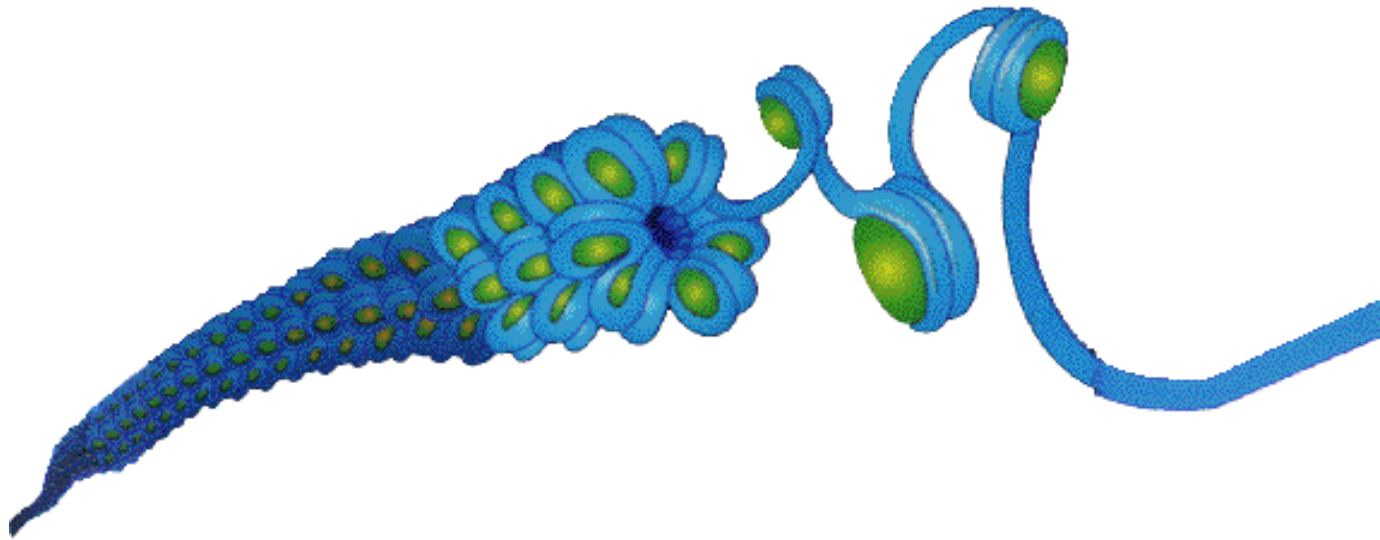
Két DNS szál összekötését végzi. A reakció energiaigényét prokariótákban a NAD hidrolízise, eukariótákban az ATP hidrolízise fedezi.

The organisation of eukaryotic chromosome

nucleosome



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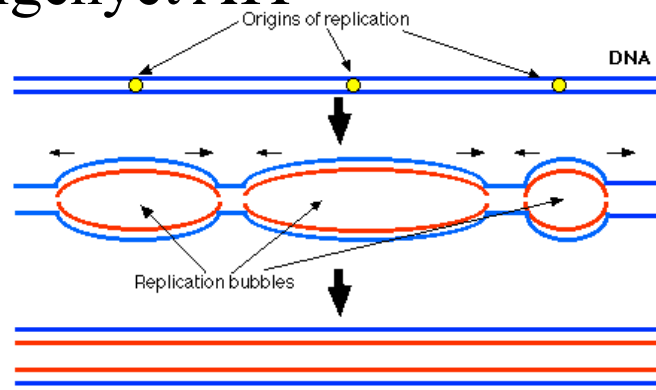
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Az eukarióta DNS replikáció sajátosságai

A replikáció a hosszú lineáris DNS molekula mentén egyszerre sok startponton indul meg.

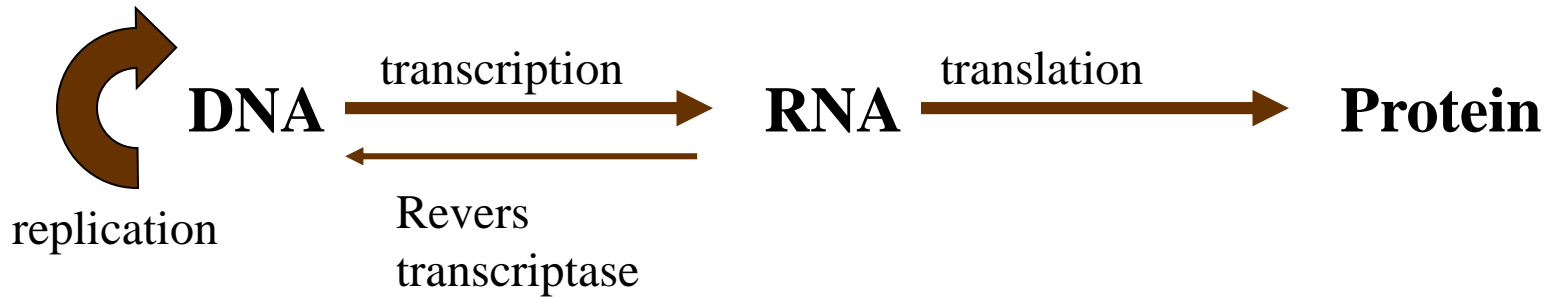
A vezető szál és a késlekedő szál szintézisét nem ugyanaz a polimeráz végzi:

- α -DNS polimeráz: késlekedő szál
- δ -polimeráz: vezető szál
- nincs saját exonukleáz aktivitásuk, ezt külön enzim végzi (a polimerázhoz asszociálódva)
- az eukarióta DNS-ligáz energiaigényét ATP hidrolízisével fedezi



Transcription: the synthesis of ribonucleic acids

The central dogma of molecular biology

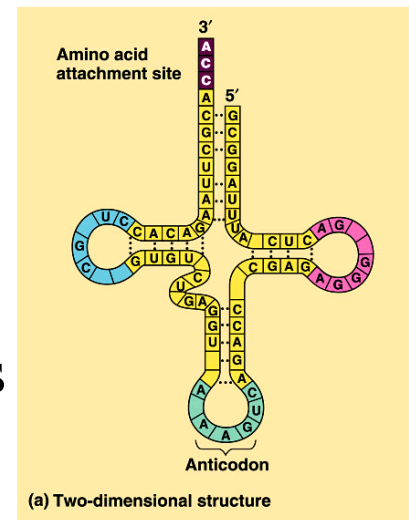


Three major kinds of RNA are produced.

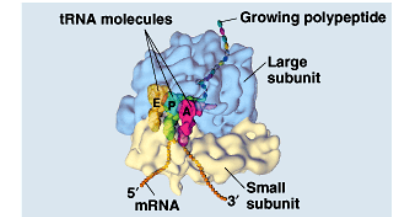
mRNA: carries the genetic information from DNA to the place of protein synthesis (ribosomes).

rRNA: a component of the protein synthesizing machinery (ribosomes).

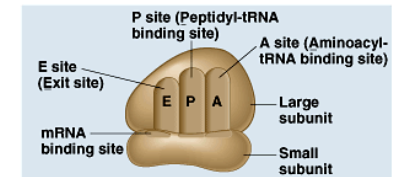
tRNA: an adapter molecule, translates the genetic code to amino acids.



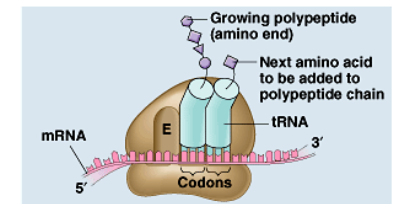
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(a) Computer model of functioning ribosome



(b) Schematic model showing binding sites



(c) Schematic model with mRNA and tRNA

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During transcription, an enzyme system converts the genetic information in a segment of **double-stranded DNA into an RNA strand** with a **base sequence complementary** to one of the DNA strands.

Only **particular part of DNA** (genes or groups of genes) **are transcribed**

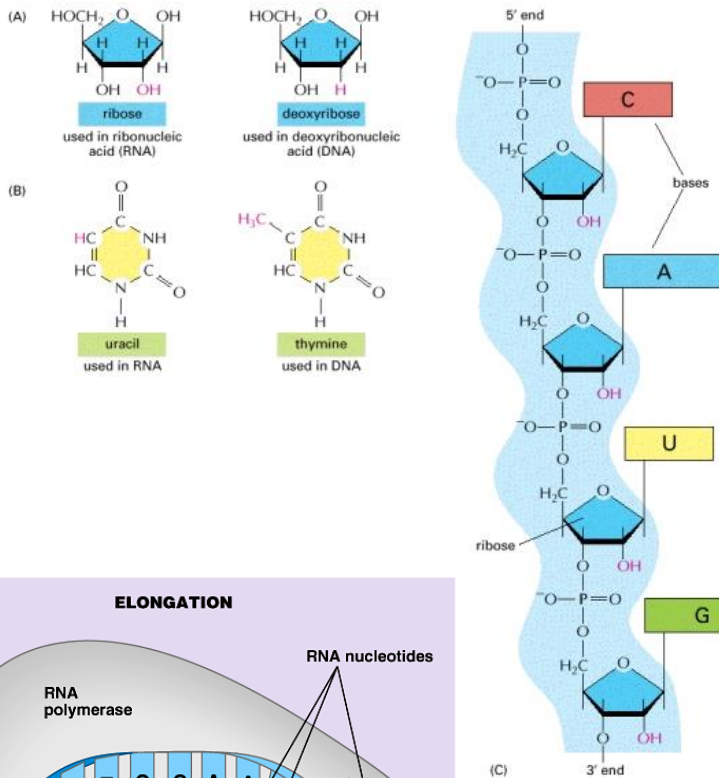
Specific regulatory sequences mark the beginning and end of the DNA segments to be transcribed and designate which strand in duplex DNA is to be used as the template.

Transcription resembles replication in its fundamental chemical mechanism direction of synthesis, and its use of a template.

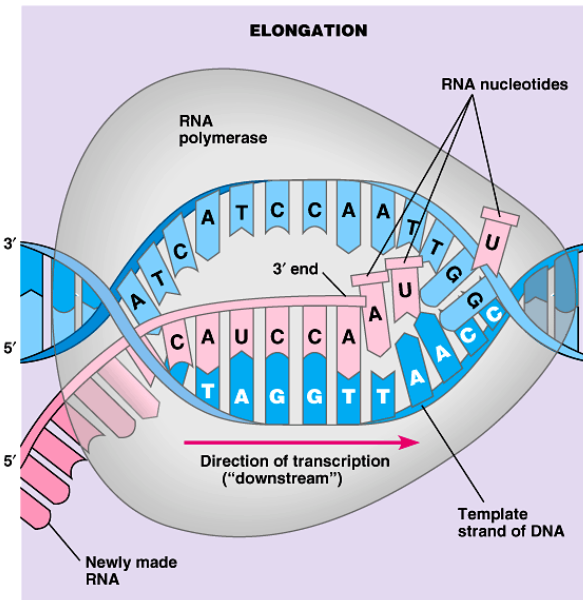
Transcription differs from replication in that it does not require a primer and involves only limited segments of a DNA molecule.

Transcription has three phases, initiation, elongation, and termination.

DNA-dependent RNA polymerase requires a DNA template and all four NTPs of the nucleotide units of RNA.



RNA polymerase elongates an RNA strand by adding ribonucleotide units to the 3'-hydroxyl end, building RNA in the 5' → 3' direction.



Each nucleotide in the newly formed RNA is selected by base-pairing interactions:
U=A, G≡C.

Transcription has three phases, **initiation**, elongation, and termination.

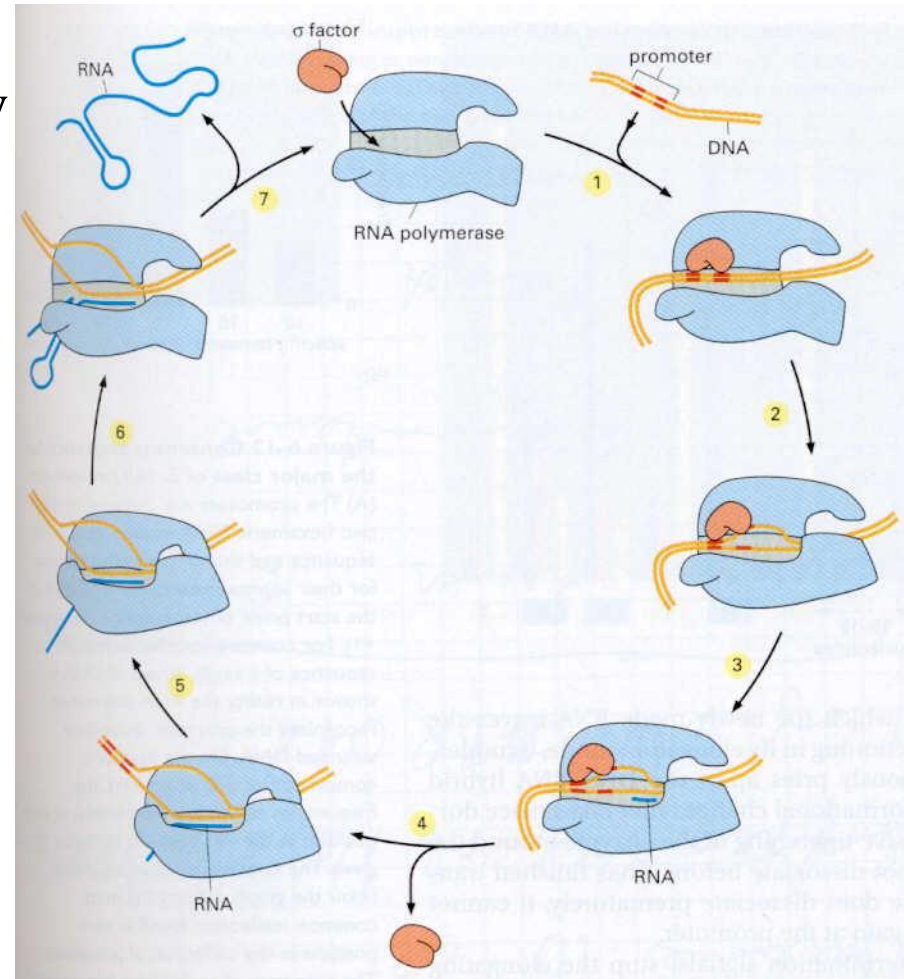
Initiation occurs when RNA polymerase binds at specific DNA sequences called promoters

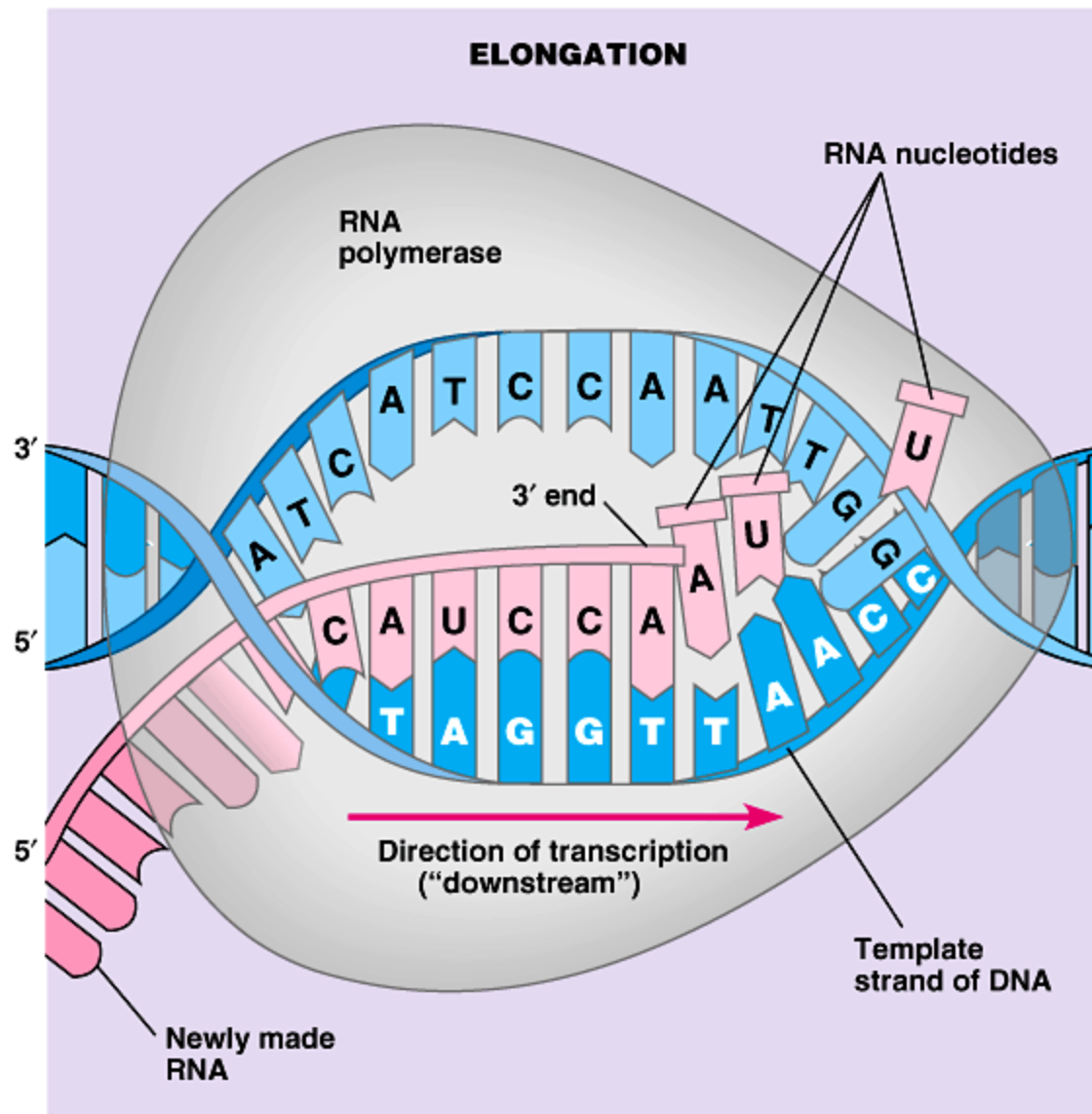
The role of the promoter region in transcription

The promoter region is recognised by the σ factor of the RNA polymerase

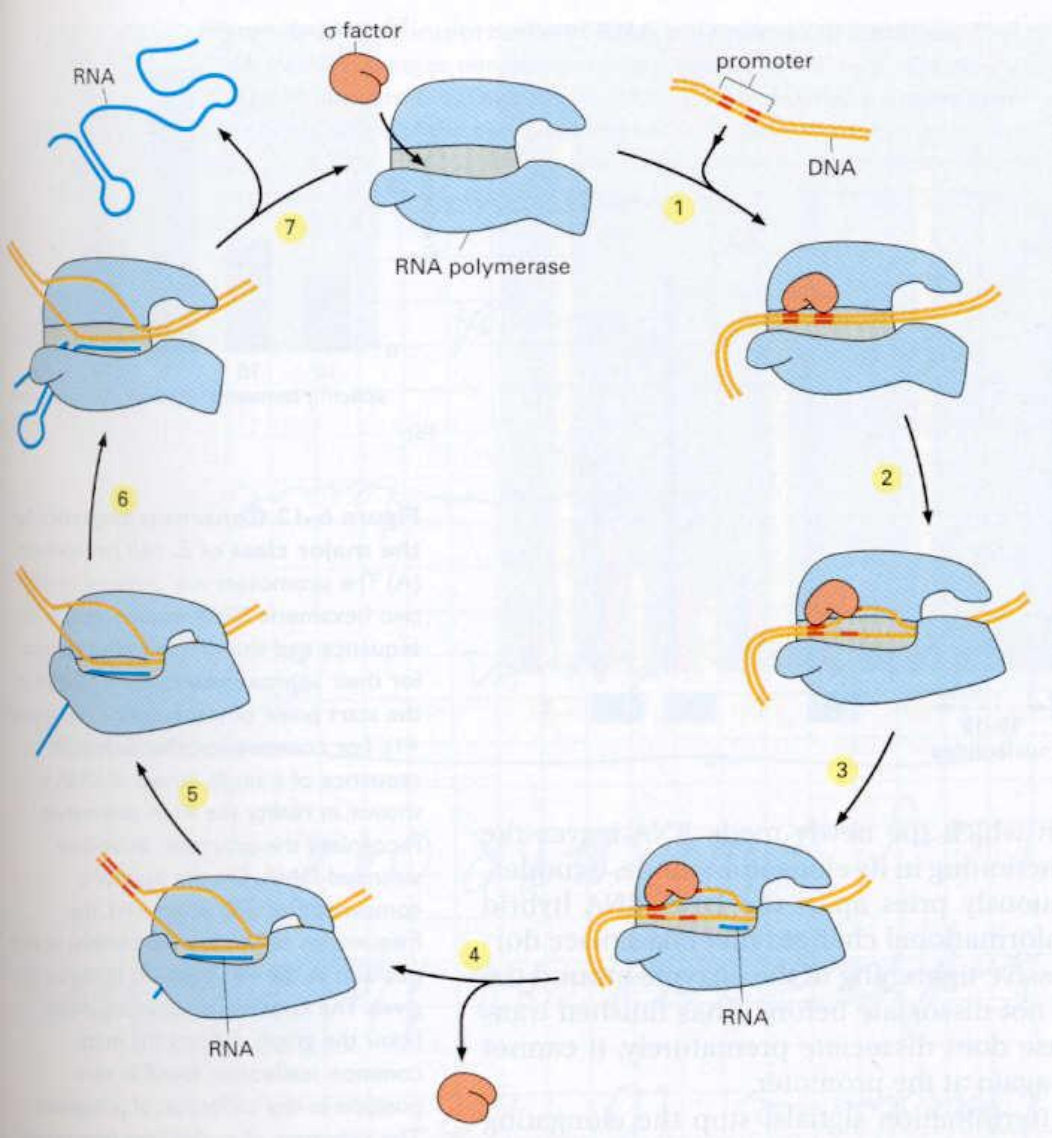
The DNA duplex must unwind over a short distance, forming a transcription bubble.

During the elongation phase of transcription, the growing end of the RNA strand forms an 8 bp long hybrid RNA-DNA double helix with the DNA template.

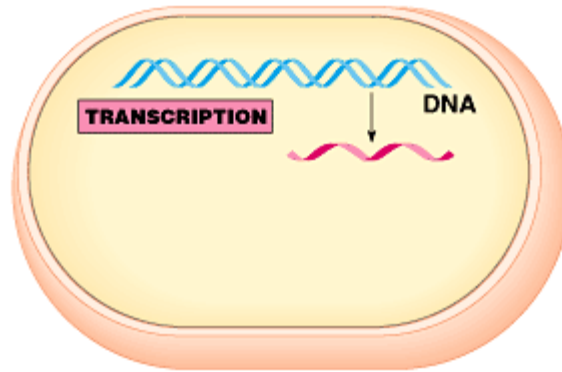




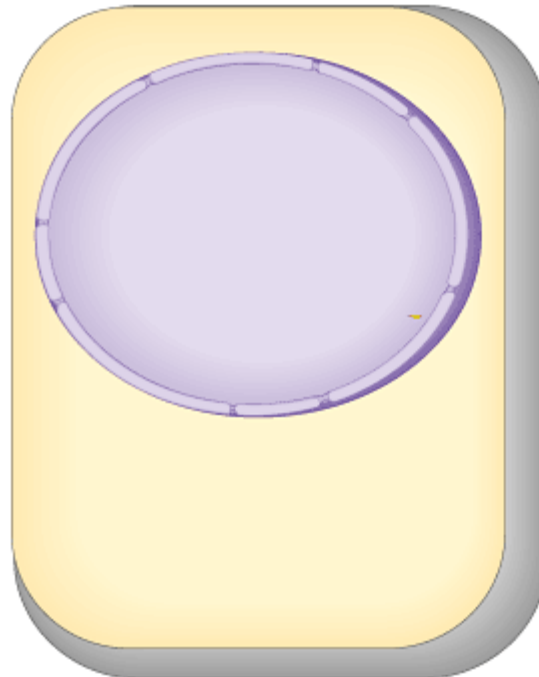
When RNA polymerase reaches a terminator sequence, RNA synthesis halts, and the RNA polymerase dissociates from the DNA.



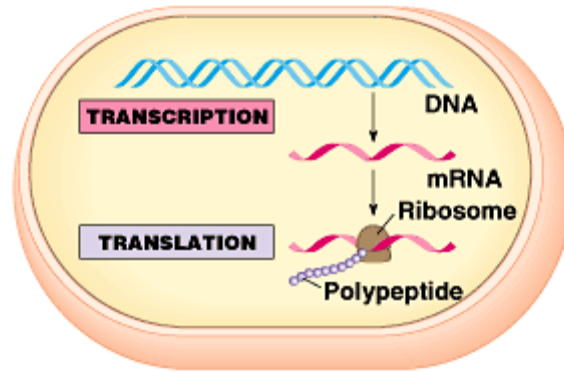
Transcription



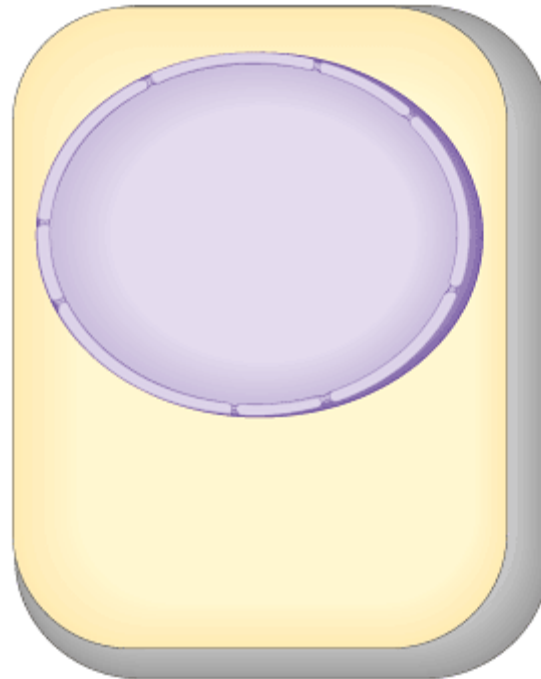
(a) Prokaryotic cell



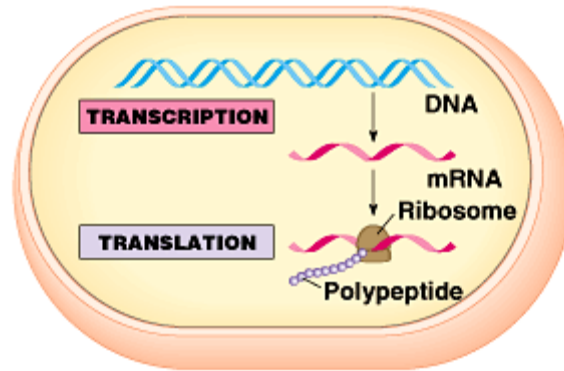
(b) Eukaryotic cell



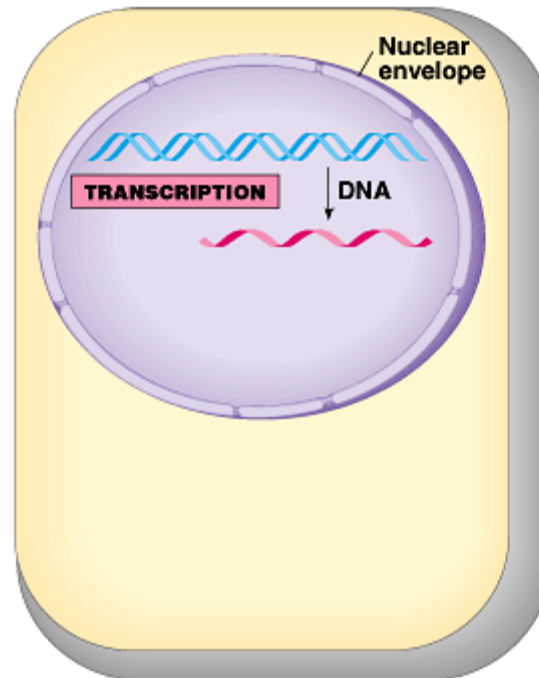
(a) Prokaryotic cell



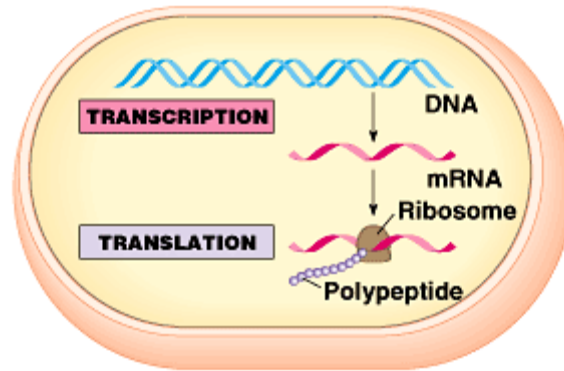
(b) Eukaryotic cell



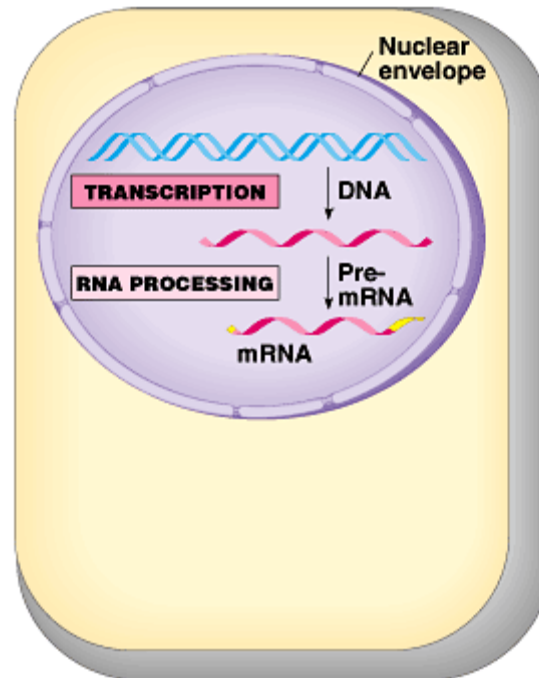
(a) Prokaryotic cell



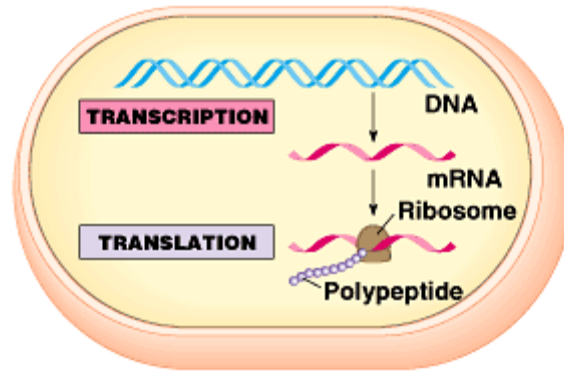
(b) Eukaryotic cell



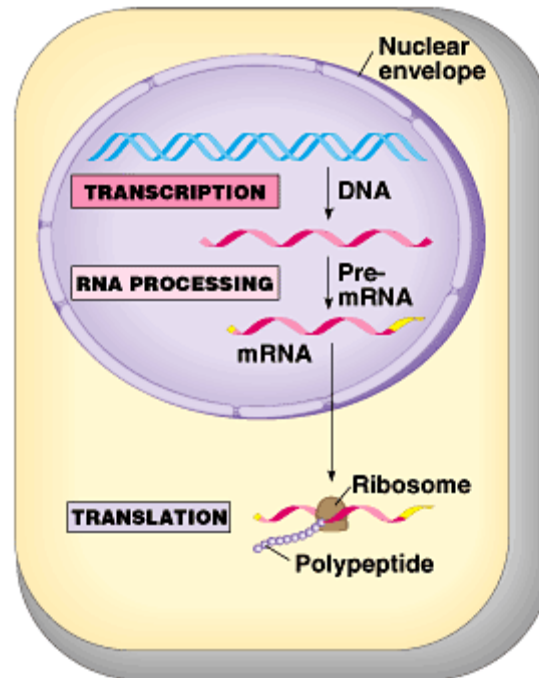
(a) Prokaryotic cell



(b) Eukaryotic cell



(a) Prokaryotic cell



(b) Eukaryotic cell

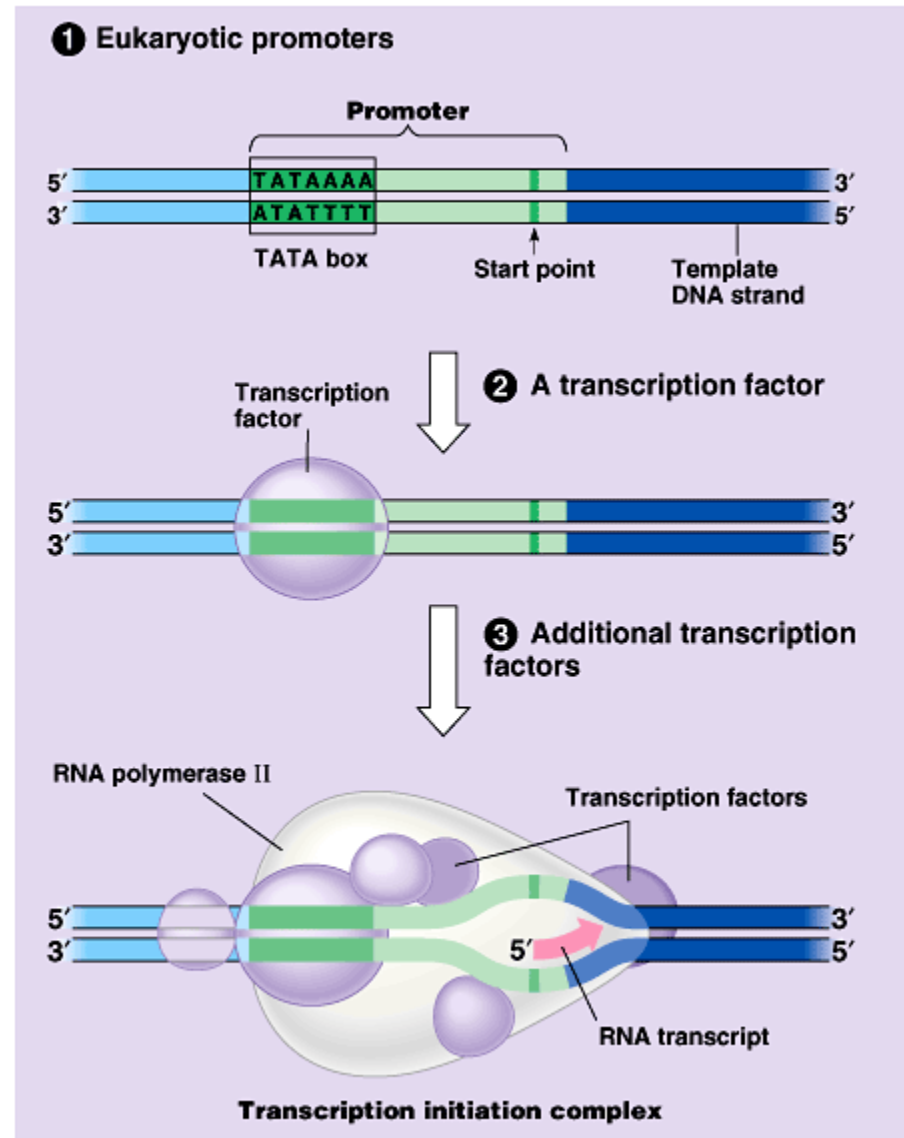
The transcription in a eukaryotic cell is much more complex than that in bacteria.

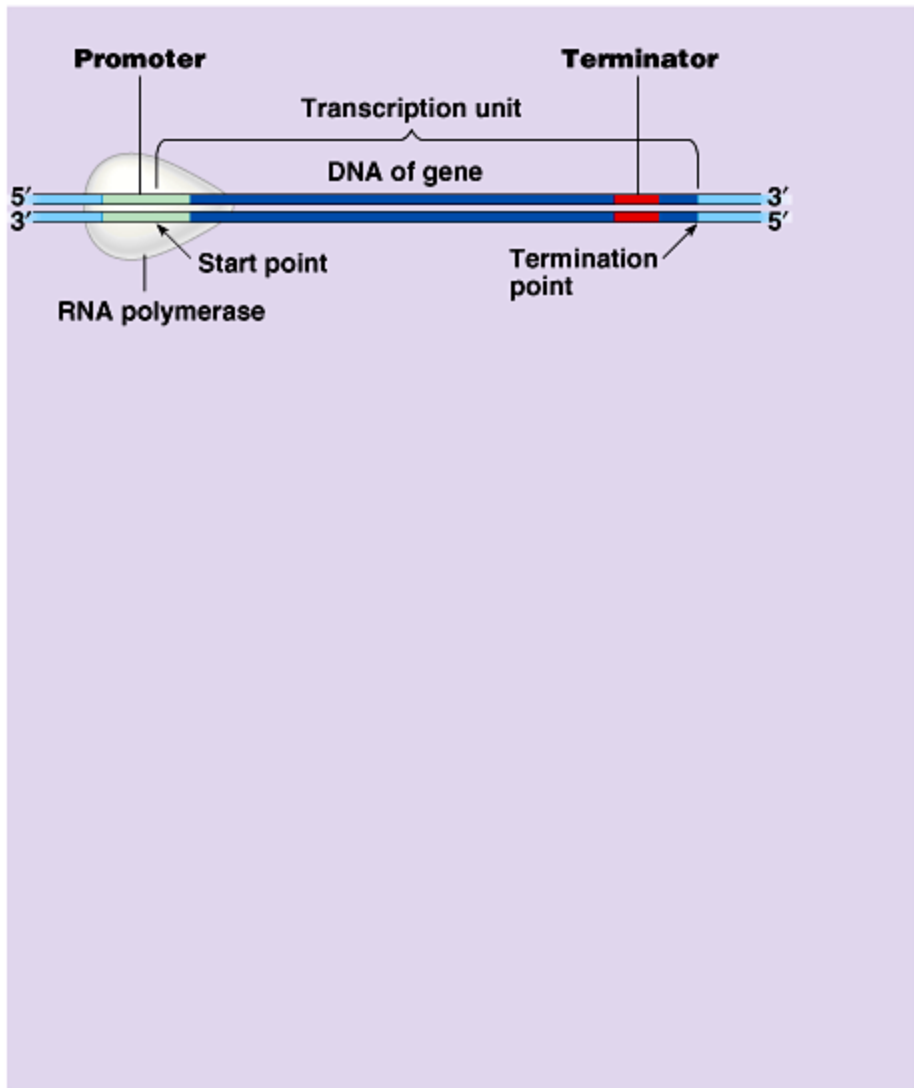
Eukaryotes have three RNA polymerases, designated I, II, and III

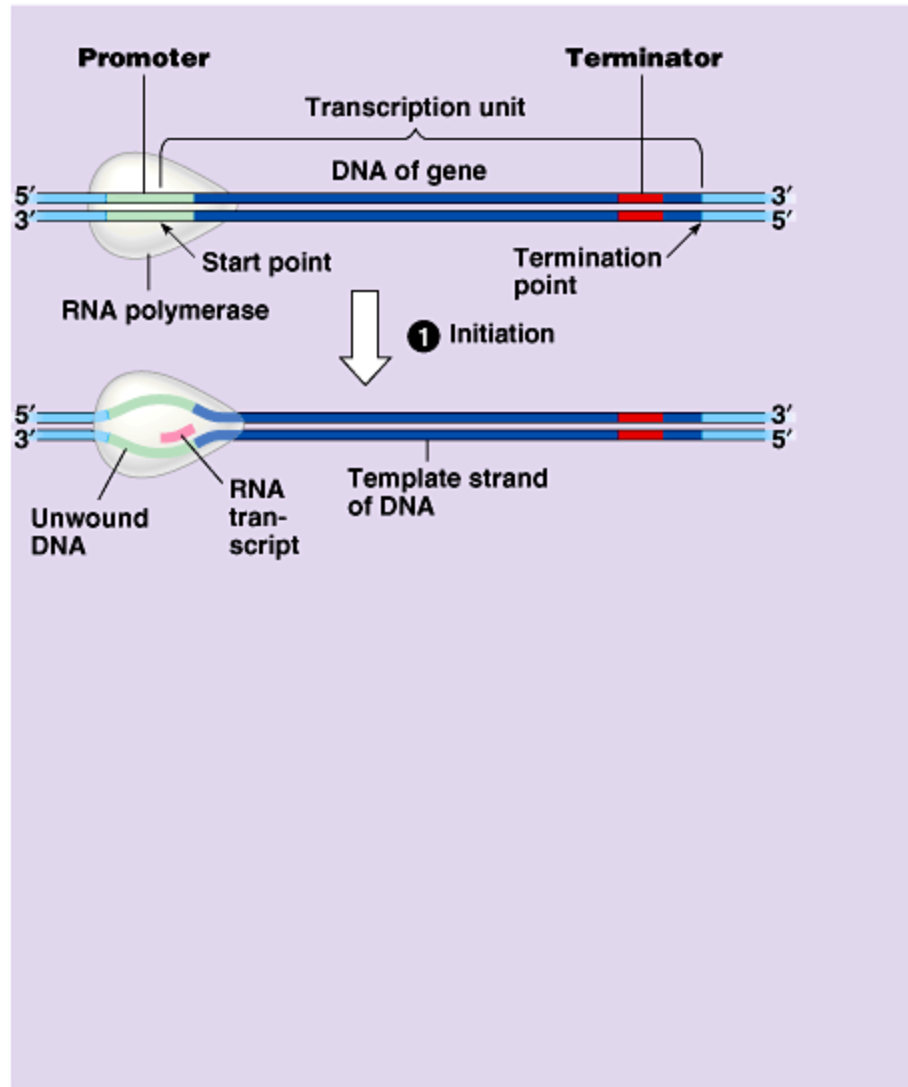
RNA polymerase I is responsible for the synthesis of pre-ribosomal RNA.

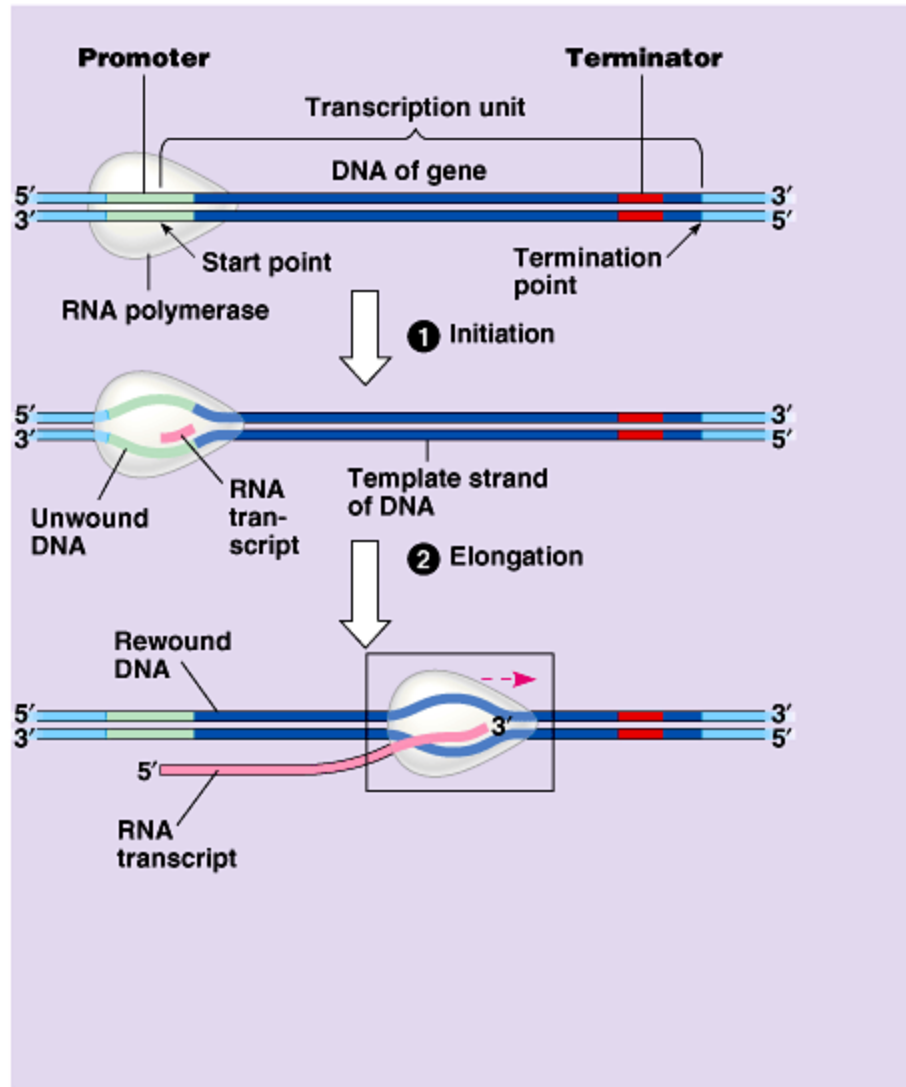
The principal function of RNA polymerase II is synthesis of mRNAs and some specialized RNAs

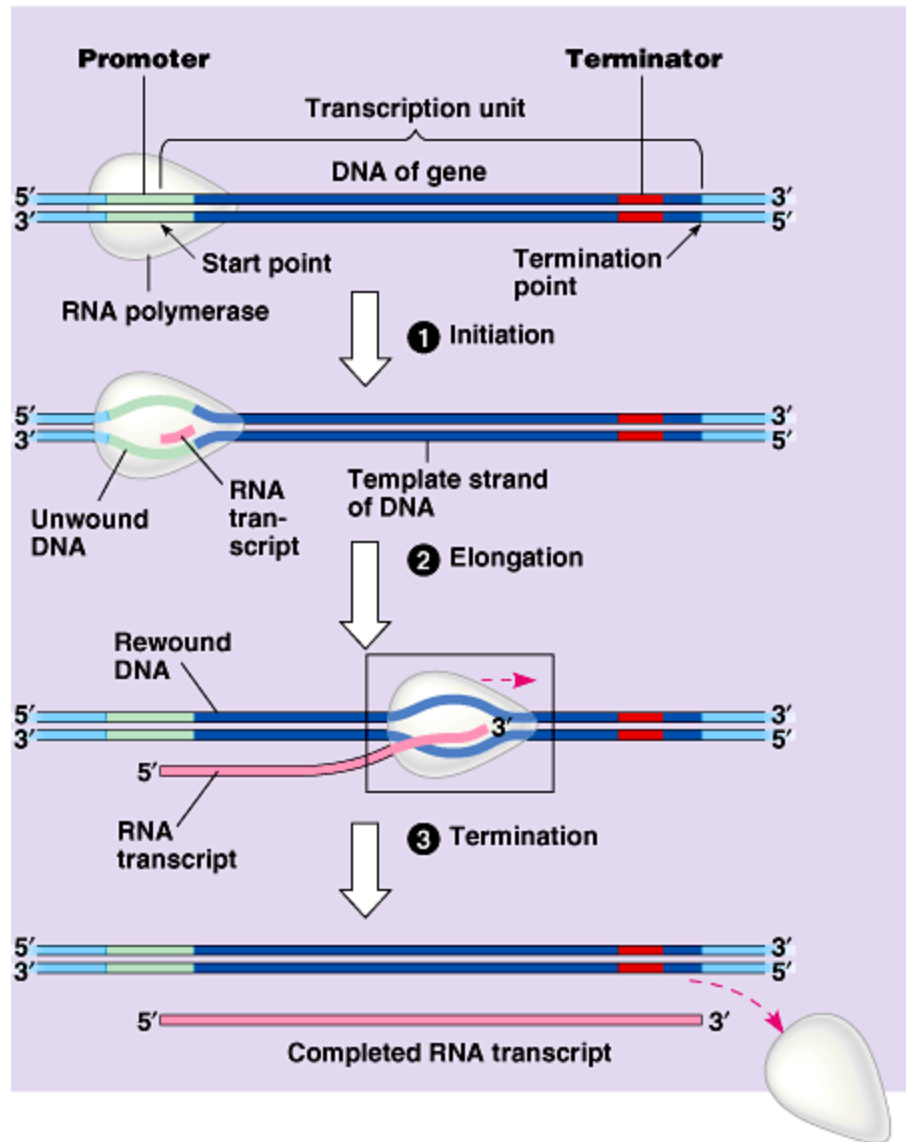
RNA polymerase III makes tRNAs, and some other small specialized RNAs.







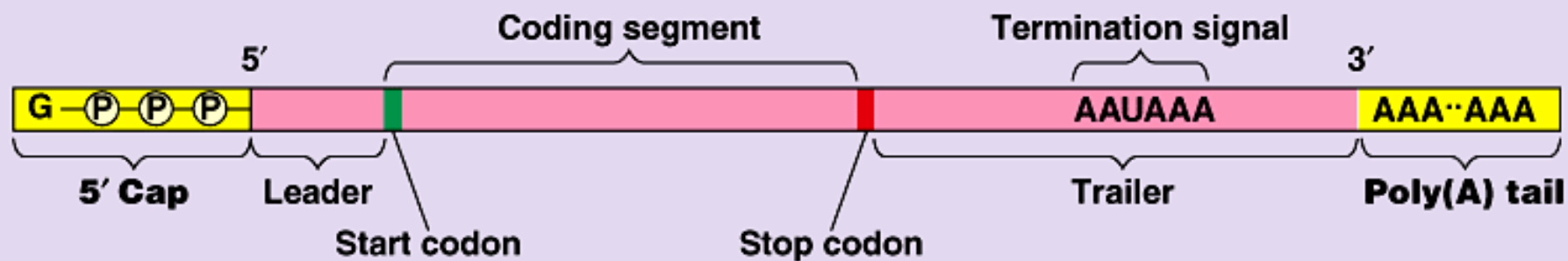




A newly synthesized RNA molecule is called **primary transcript**.

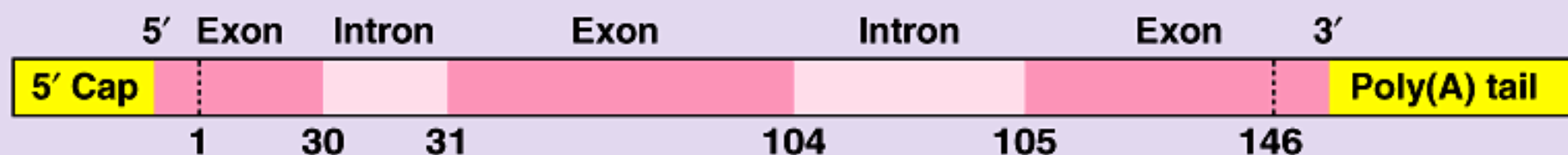
The primary transcript for a eukaryotic mRNA typically contains two types of sequences: **noncoding segments** that break up the coding region are called **introns**, and the **coding segments** are called **exons**.

In a process called **splicing**, the introns are removed from the primary transcript and the exons are joined to form a continuous sequence that defines a functional polypeptide



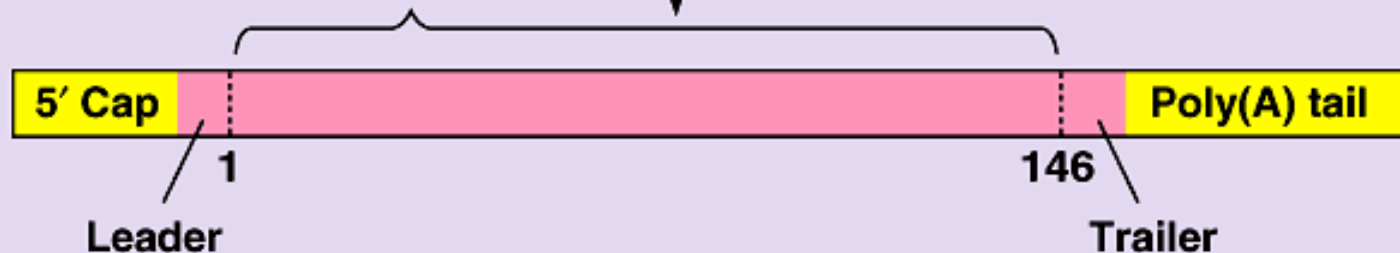
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Pre-mRNA



Introns excised and exons spliced together

mRNA



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