بسم الله الرحمن الرحيم

MOLECULAR BIOLOGY 2

Very important

Extra explanation

"STAY FOCUSED TO STAY ALIVE"

هذا العمل لا يغني عن المذاكرة من المصدر الأساسي

OBJECTIVES:

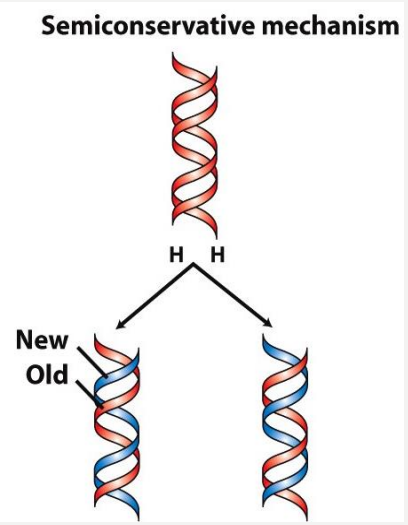
- To understand DNA replication
- To know the transcription of genetic material into messenger RNA
- To get an idea about the translation of mRNA into a functional protein.

FEATURES OF EUKARYOTIC DNA & DNA REPLICATION

- **DNA is the genetic material, therefore it must :**

1- Replicate faithfully

2- Have the coding ability to produce proteins for all cellular functions



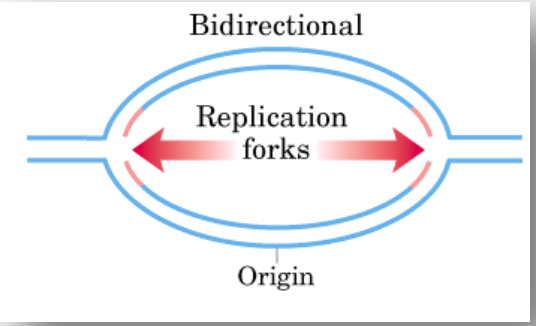
- **DNA replication**

1- Semiconservative with respect to parental strand.

Daughter DNA molecules contain one parental stand

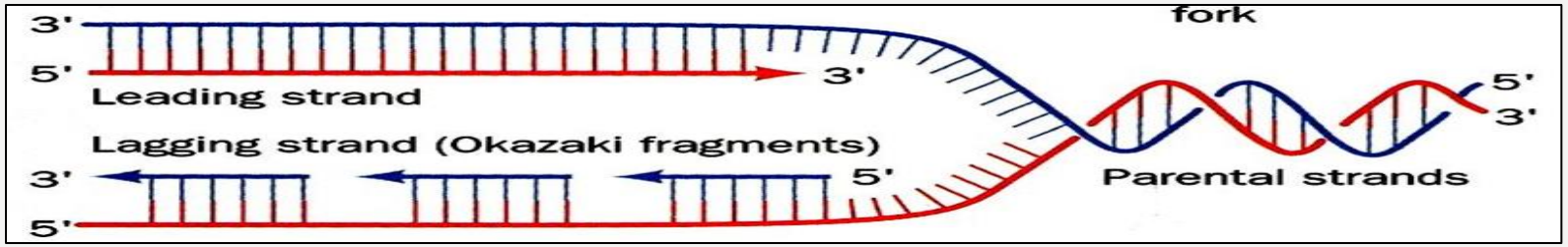
and one newly strand.

2- Bidirectional with multiple origins of replication (in two direction) .

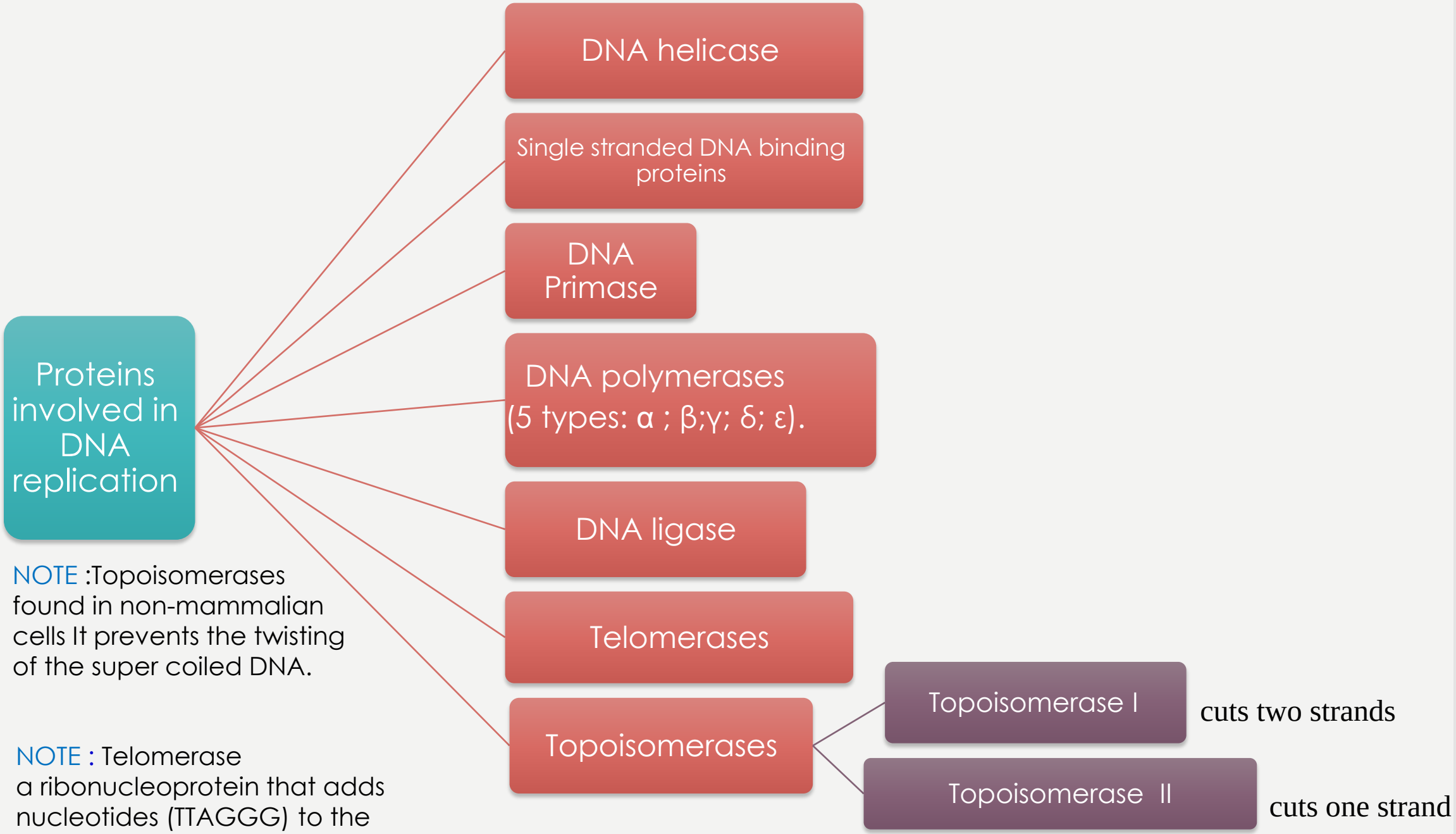


3-Primed by short stretches of RNA.

4- Semi-discontinuous:

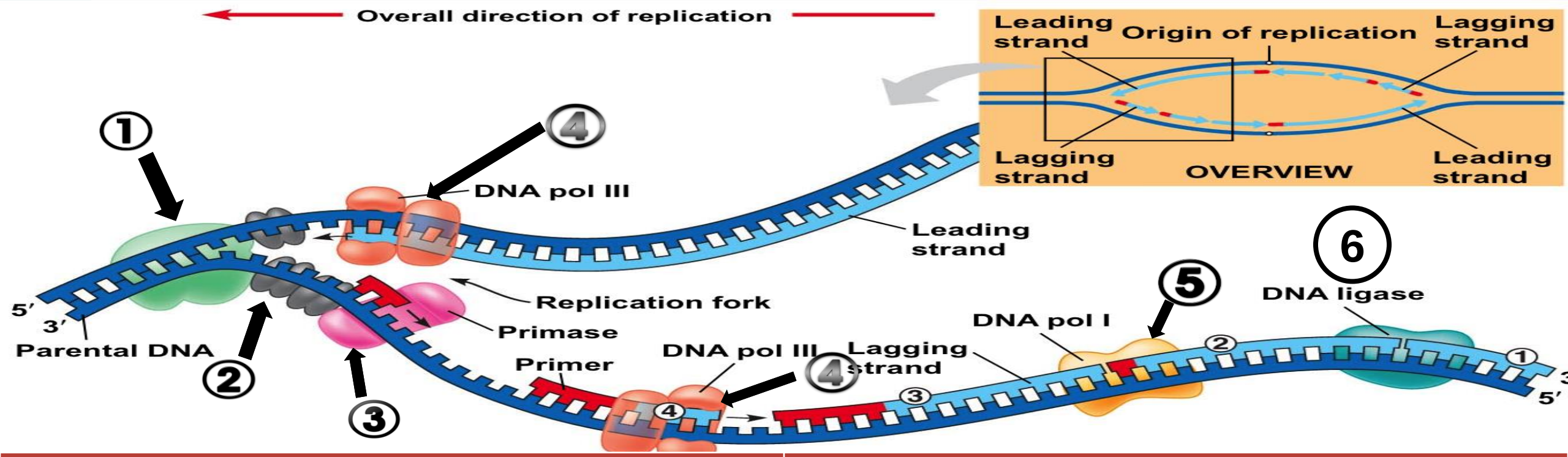


*(Leading strand *Red* lagging strand *Blue*) are synthesized in their 5'→3' direction



NOTE :Topoisomerases found in non-mammalian cells It prevents the twisting of the super coiled DNA.

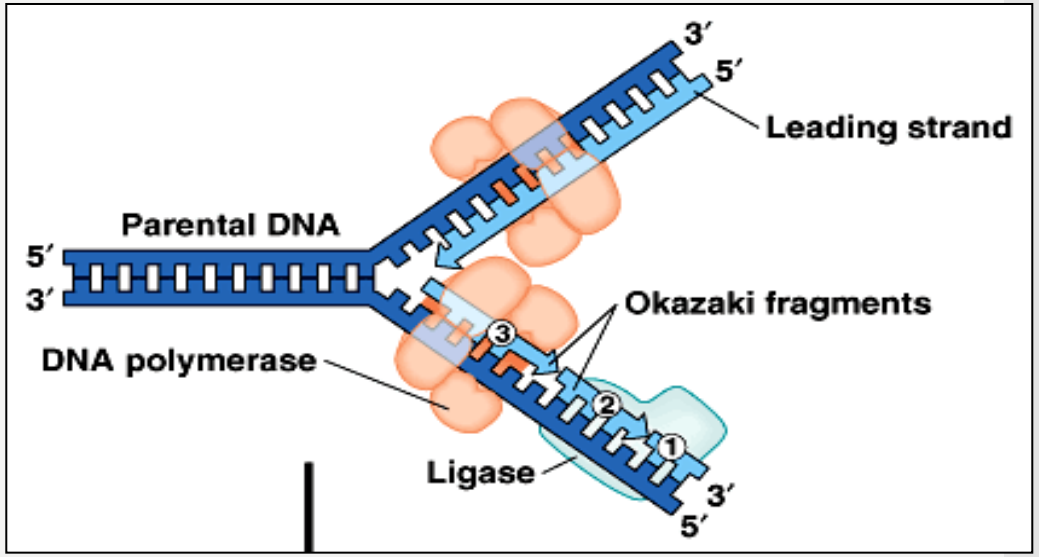
NOTE : Telomerase a ribonucleoprotein that adds nucleotides (TTAGGG) to the chromosome end (telomeres).

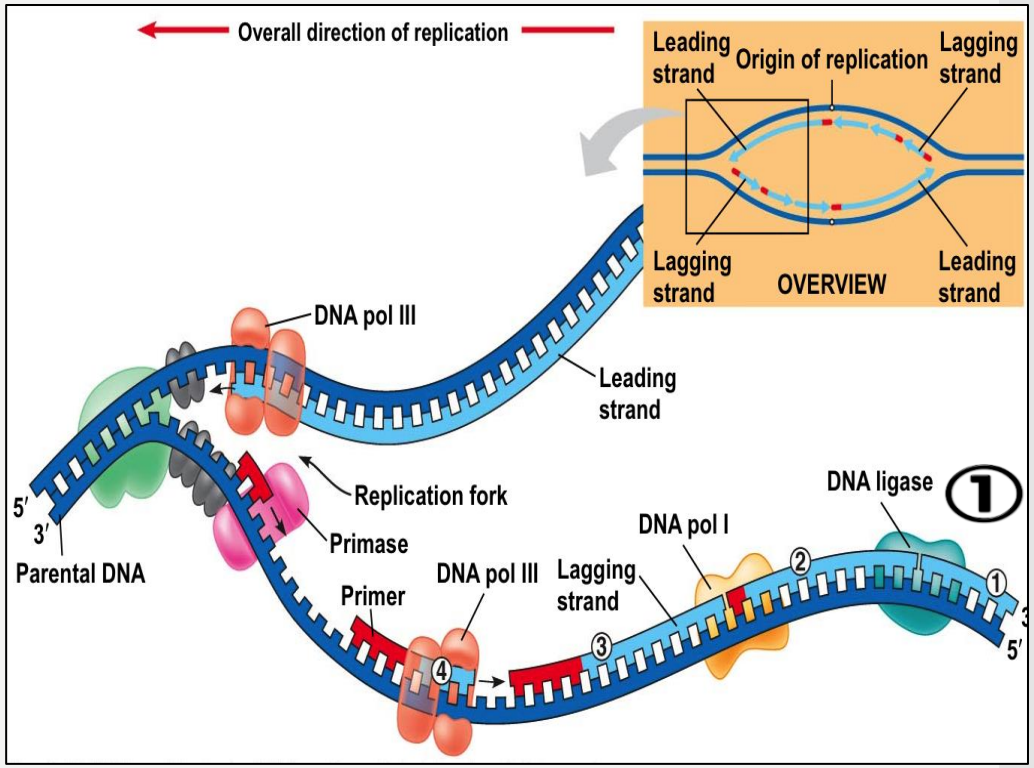


Enzyme name	Function
1- Helicase	Untwists and separates parental double helix.
2- Single-Stranded binding proteins	prevent single strands from rewinding.
3- Primase	Adds a short segment of RNA, 10 nucleotides long.
4- DNA polymerase	▪ Adds new DNA nucleotides to RNA primer. ▪ Proofreads bases added and replaces incorrect nucleotides.
5- DNA polymerase	▪ First: Exonuclease activity of DNA polymerase removes RNA primers. ▪ Then: DNA polymerase fills the gaps by DNA nucleotides.
6- DNA Ligase	forms bonds between sugar phosphate backbone

DNA REPLICATION

- **DNA polymerases** can only add nucleotides to **5→3** of a growing DNA strand.
- At the replication fork, one parental strand the **Leading Strand** (synthesis continues in a 5' to 3' direction)
- The other parental strand the **Lagging strand** (Discontinuous synthesis produces 5' to 3') , is copied away from the fork in **short segments (Okazaki fragments).**
- **So** DNA polymerase fills the gaps, and **(1-Ligase)** forms bonds between sugar phosphate backbone





STEPS IN DNA REPLICATION ☺:

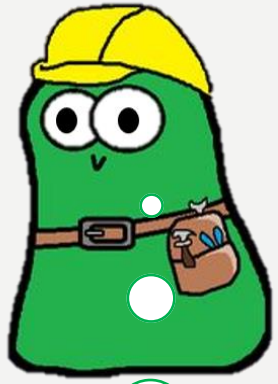
الشرائح 7,8,9,10 هي شرائح إضافية مفصلة لتعميق فهم DNA replication

قبل لا نبدأ القصة لازم نتعرف على الشخصيات الأساسيه ☺ :

HELICASE

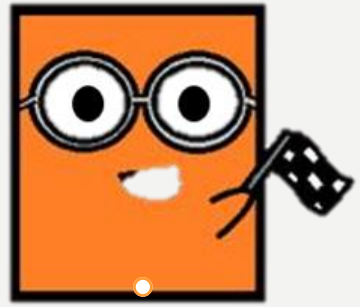
I am the unzipper enzyme .. I unzip the two strands DNA ☺

DNA POLYMERASE



I am a master builder! ... I build the complementary strands ☺ .. I add nucleotides only to the 3' end of the growing DNA strand

PRIMASE



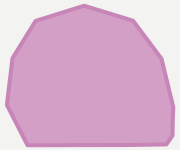
This way Master builder!

LIGASE

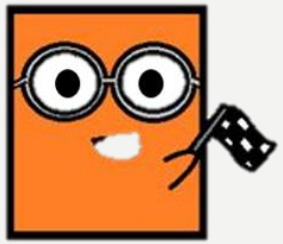
I am the Gluer!

#STEPS IN DNA REPLICATION ☺:

1-DNA Helicase comes and binds to DNA sequences called origins and unwinds (unzips :P) the DNA strands.



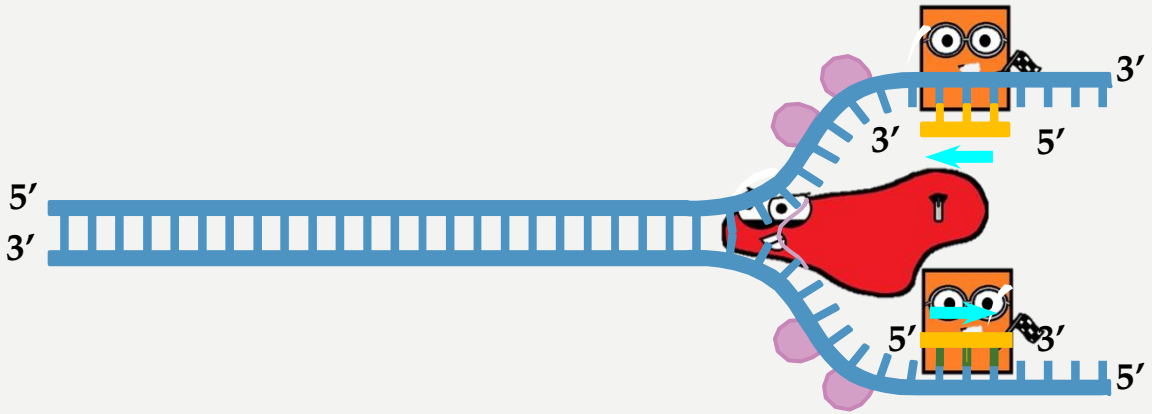
2-Single-Stranded binding proteins binds to the DNA strands to keep them separated (prevent the strands from rewinding).



3-Primase comes in and then makes RNA Primer on both strands.

-This Is really important because otherwise when DNA polymerase comes in it won't know where to start!☺

- primer: is a short segment of RNA that is complementary to DNA.



#STEPS IN DNA REPLICATION ☺:

4-DNA polymerase:

- DNA polymerase comes in but …!

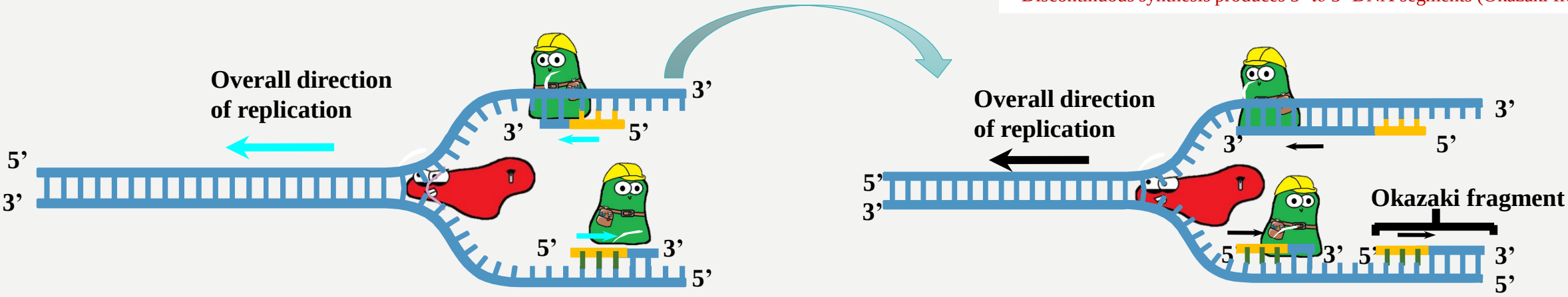
1- We have two strands and these two strands are not identical they complement each other + they are antiparallel! *one goes from 5'→3' and the other goes from 3'→5'*

2- It can only add nucleotides to 3' end of the growing DNA strand!

- it's okay with 5'→3' strand which is called **Leading Strand**.
- The other 3'→5' strand which is called **lagging strand** will make a little tricky!

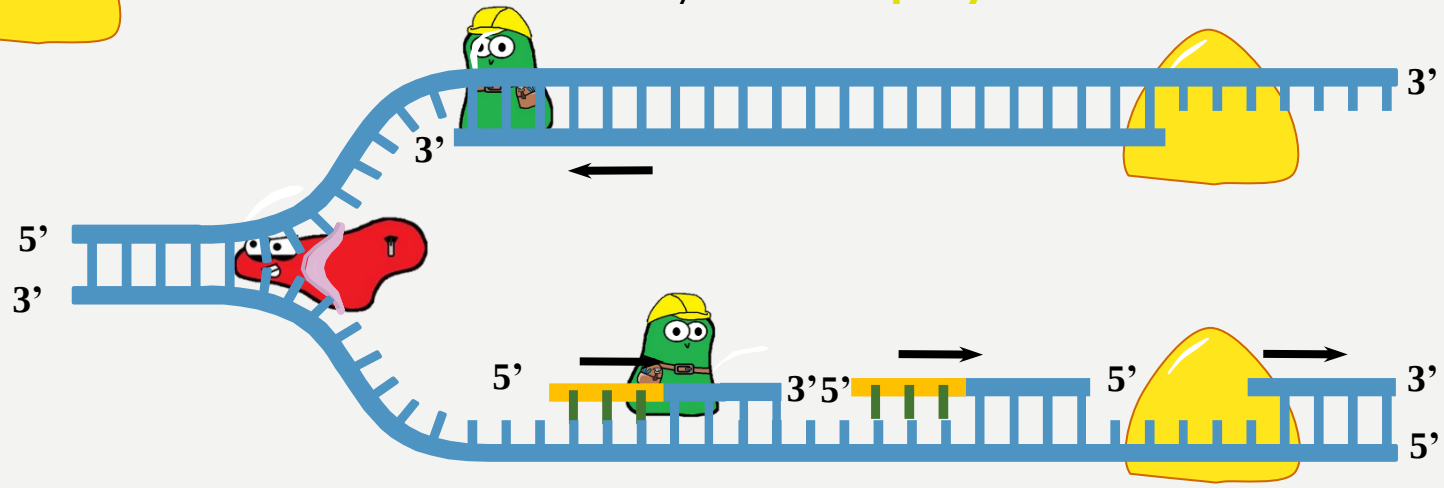
So DNA polymerase will Add DNA nucleotides and forms Okazaki fragments.

*Leading strand synthesis continues in a 5' to 3' direction.
*Discontinuous synthesis produces 5' to 3' DNA segments (Okazaki fragments).



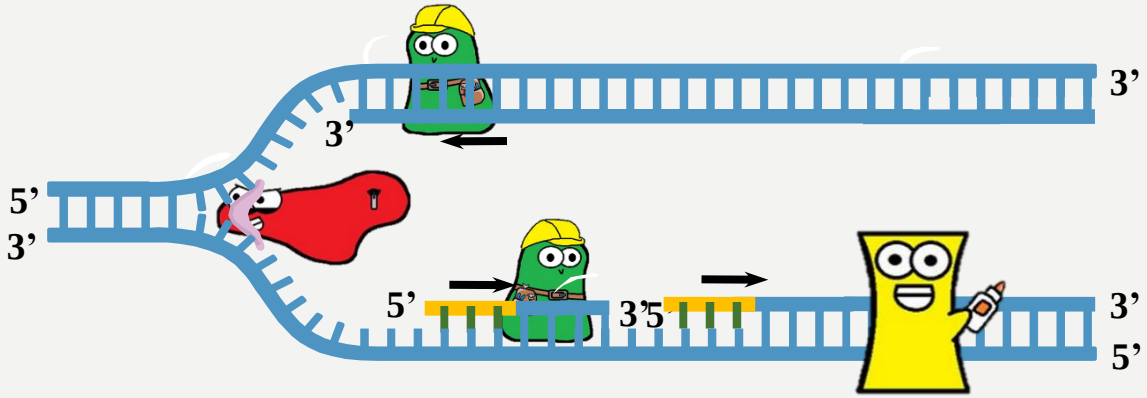
#STEPS IN DNA REPLICATION ☺:

5-Exonuclease activity of **DNA polymerase** removes RNA primers



6-DNA polymerase fills the gaps.

7-Ligase forms bonds between sugar-phosphate backbone



435 Biochemistry Team

Biochemistry Team 435

DIFFERENCES BETWEEN LEADING STRAND AND LAGGING STRAND

هذي مقارنة خارجيه قد تساعدكم في فهم العملية وفي فهم الفرق بين الليدنق ستراند واللاقنق سترند :

No	Leading Strand	Lagging strand
1	It is a replicated strand of DNA which grows continuously without any gap.	It is a replicated strand of DNA which is formed in short segments called: okazaki fragments. Its growth is discontinues.
2	It does not require DNA ligase.	DNA ligase is required for joining okazaki fragments.
3	The direction of growth of the leading strand is 5'→3'	The direction of growth of the lagging strand is 3'→5' through in each okazaki fragment it is 5'→3'
4	Only a single RNA Primer is required.	Starting of each okazaki fragment requires a new RNA primer.
5	Formation of leading strand is quite rapid.	Formation of lagging strand is slower.
6	Its template open in 3'→5' direction.	Its template open in 5'→3' direction.

Transcription

A portion of **DNA** (a **gene**) is transcribed into messenger RNA (**mRNA**).

Direction of transcription

5`→ 3` direction.

The transcribed strand in transcription

Only one of the DNA ***antisense*** strand(3→5) strands is transcribed.

Responsible enzyme

RNA polymerase II

*NOTE: The transcription of mRNA is done in one DNA strand only(antisense) , the one with 3 to 5 end, but the transcription it's self done in 5 to 3 direction.

TRANSCRPITION

1- Chain initiation:

RNA polymerase II binds to **promoter region** of DNA to start transcription.

2- Chain elongation:

a) Starts when portion of DNA **unwinds** (at the point of RNA synthesis).

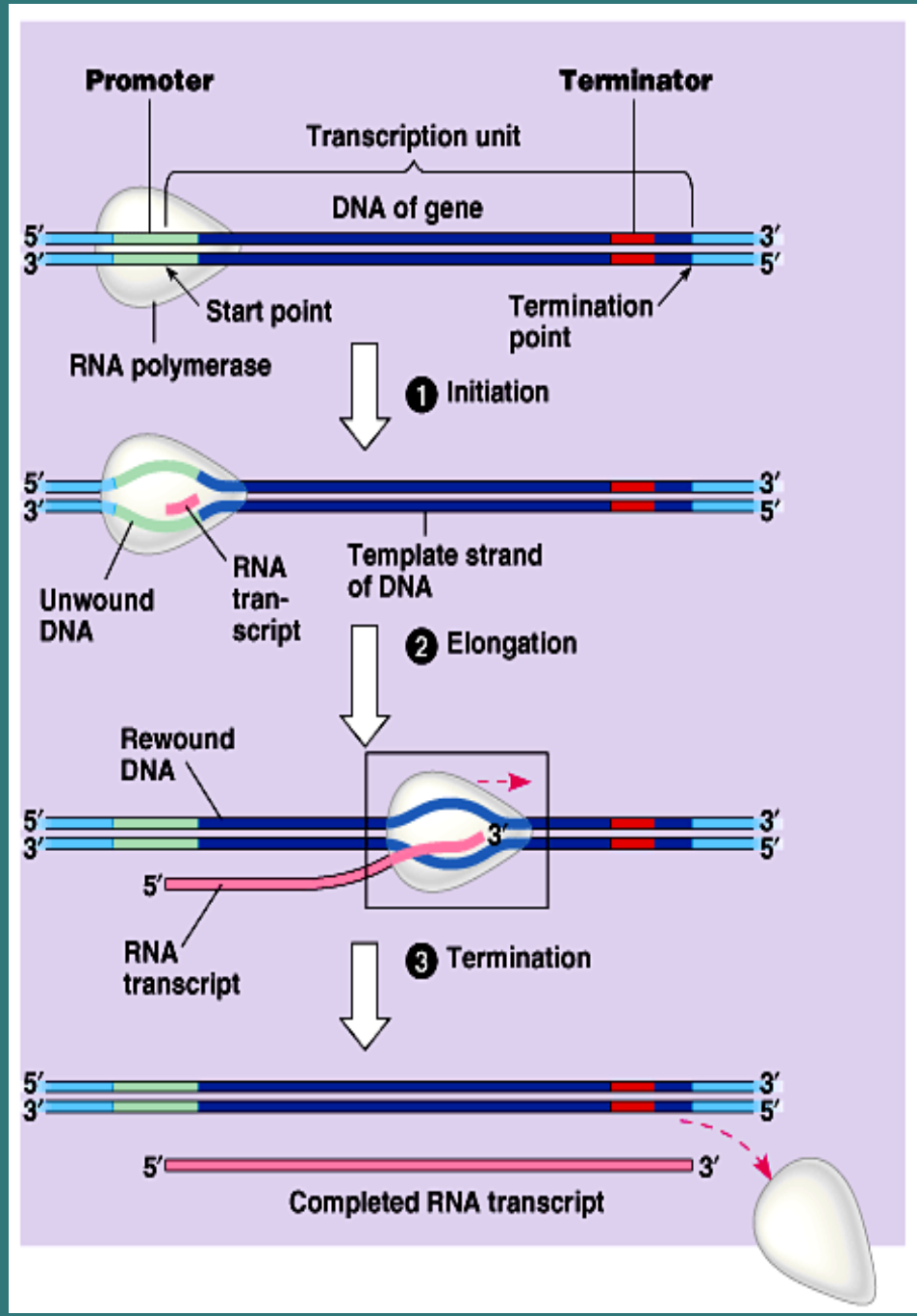
b) RNA polymerase II moves along the template strand of the DNA Synthesizing the complementary single stranded mRNA molecules.
the direction of transcription is from 5'→3'

c) as the RNA polymerase II moves the double helix rewinds.

d) This forms a short length of RNA-DNA hybrid

3- Chain Termination:

Transcription stops proceeding when it reaches a specific sequence on the DNA (at a sequence of 4-10 AT base pairs).



POST-TRANSCRIPTIONAL MODIFICATION

Before mRNA leaves the nucleus it is modified to be protected and mature .

Modifications of mRNA

Capping

Addition of methylated guanine nucleotide at 5' end of mRNA

Function:

1- To prevent mRNA degradation by exonucleases.

2- It helps the transcript bind to the ribosome during protein synthesis.

polyadenylation

Addition of a poly(A) tail (a highly conserved AAUAA sequence) at 3' end of mRNA.

Functions:

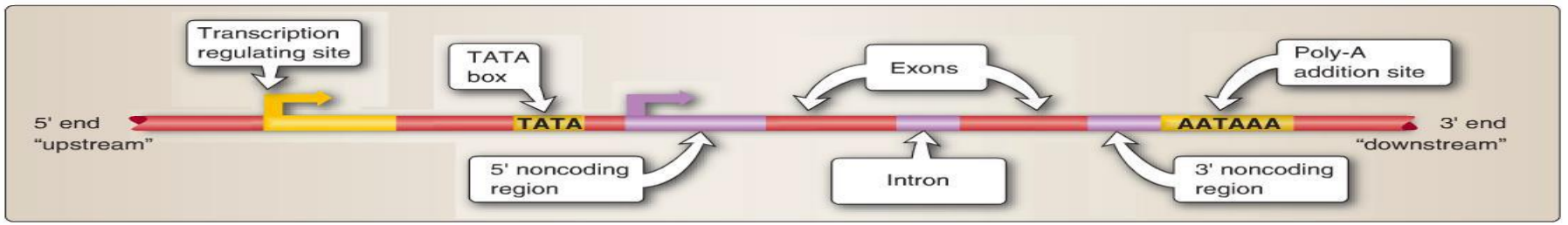
1- To protect the mRNA from degradation.

2- For ribosomal RNA recognition

Intron removal

for releasing mature mRNA from nucleus.

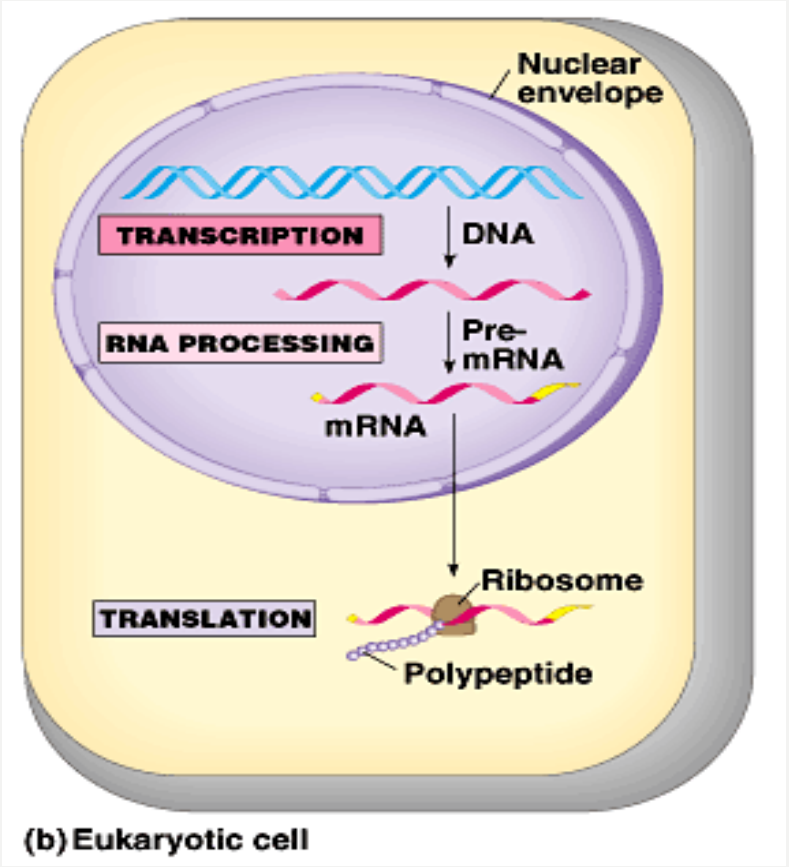
NOTE: function of intron is regulation of mRNA transcription.

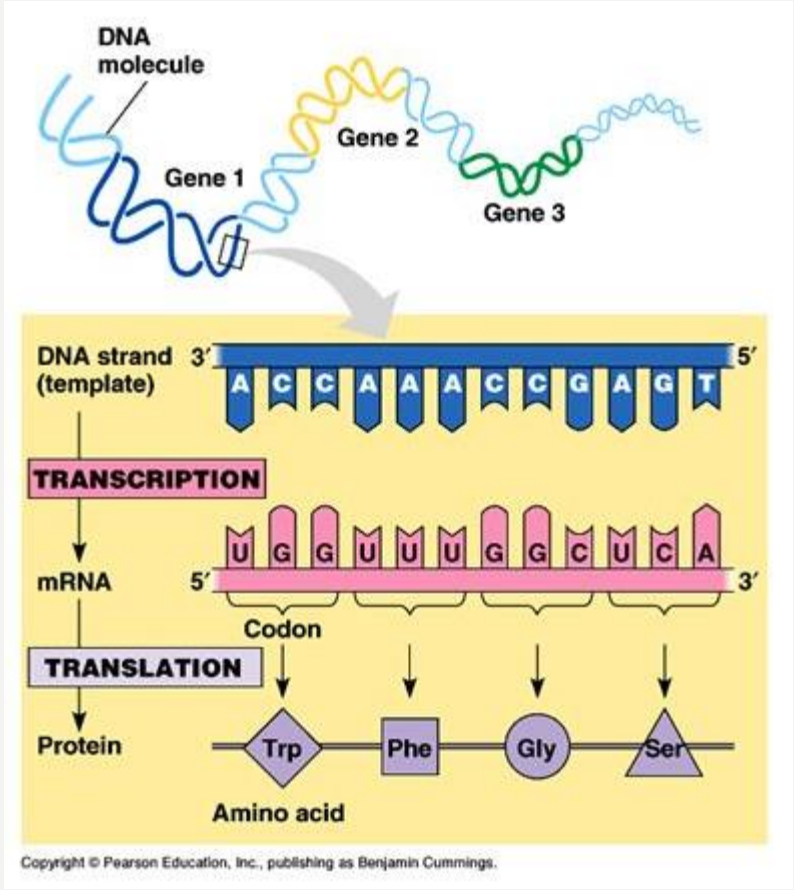


CENTRAL DOGMA OF MOLECULAR BIOLOGY

Central dogma of molecular biology :

The flow of information from DNA to RNA to Protein.





- A portion of DNA called gene is transcribed to mRNA

DNA → *Transcription* → **mRNA** → *Translation* → **Protein**

Translation (protein synthesis) & possible codons

What is translation?

A process of protein synthesis from mRNA

- mRNA has genetic codes for amino acids present in proteins.
- The **genetic code** is a dictionary that identifies the correspondence between a sequence of nucleotide bases and a sequence of amino acids.

- Each individual word in the code is composed of three nucleotide bases (**codons**).

64 possible codons

- 61 codons specify 20 amino acids
- 1 start codon:
  - AUG (Methionine)
- 3 stop codons:
  - UAA
  - UAG
  - UGA

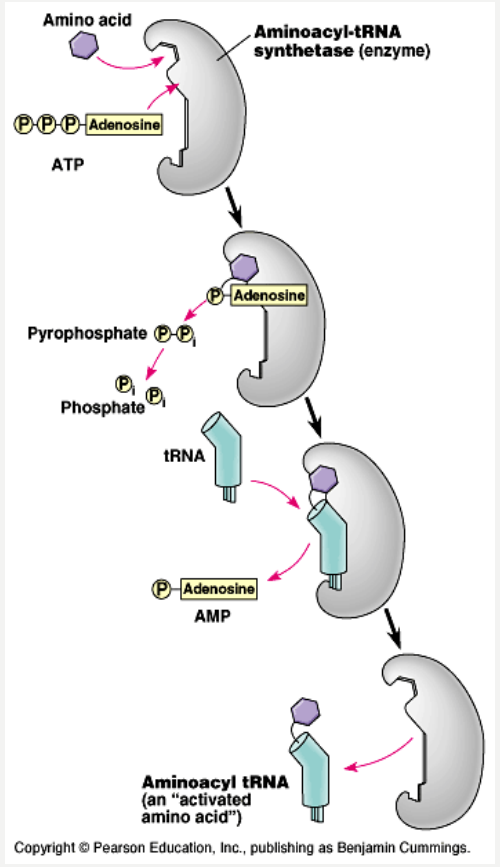
First base (5′ end)	Second base: U	Second base: C	Second base: A	Second base: G	Third base (3′ end)
U	UUU Phe	UCU Ser	UAU Tyr	UGU Cys	U
	UUC Phe	UCC Ser	UAC Tyr	UGC Cys	C
	UUA Leu	UCA Ser	UAA Stop	UGA Stop	A
	UUG Leu	UCG Ser	UAG Stop	UGG Trp	G
C	CUU Leu	CCU Pro	CAU His	CGU Arg	U
	CUC Leu	CCC Pro	CAC His	CGC Arg	C
	CUA Leu	CCA Pro	CAA Gln	CGA Arg	A
	CUG Leu	CCG Pro	CAG Gln	CGG Arg	G
A	AUU Ile	ACU Thr	AAU Asn	AGU Ser	U
	AUC Ile	ACC Thr	AAC Asn	AGC Ser	C
	AUA Ile	ACA Thr	AAA Lys	AGA Arg	A
	AUG Met or start	ACG Thr	AAG Lys	AGG Arg	G
G	GUU Val	GCU Ala	GAU Asp	GGU Gly	U
	GUC Val	GCC Ala	GAC Asp	GGC Gly	C
	GUA Val	GCA Ala	GAA Glu	GGA Gly	A
	GUG Val	GCG Ala	GAG Glu	GGG Gly	G

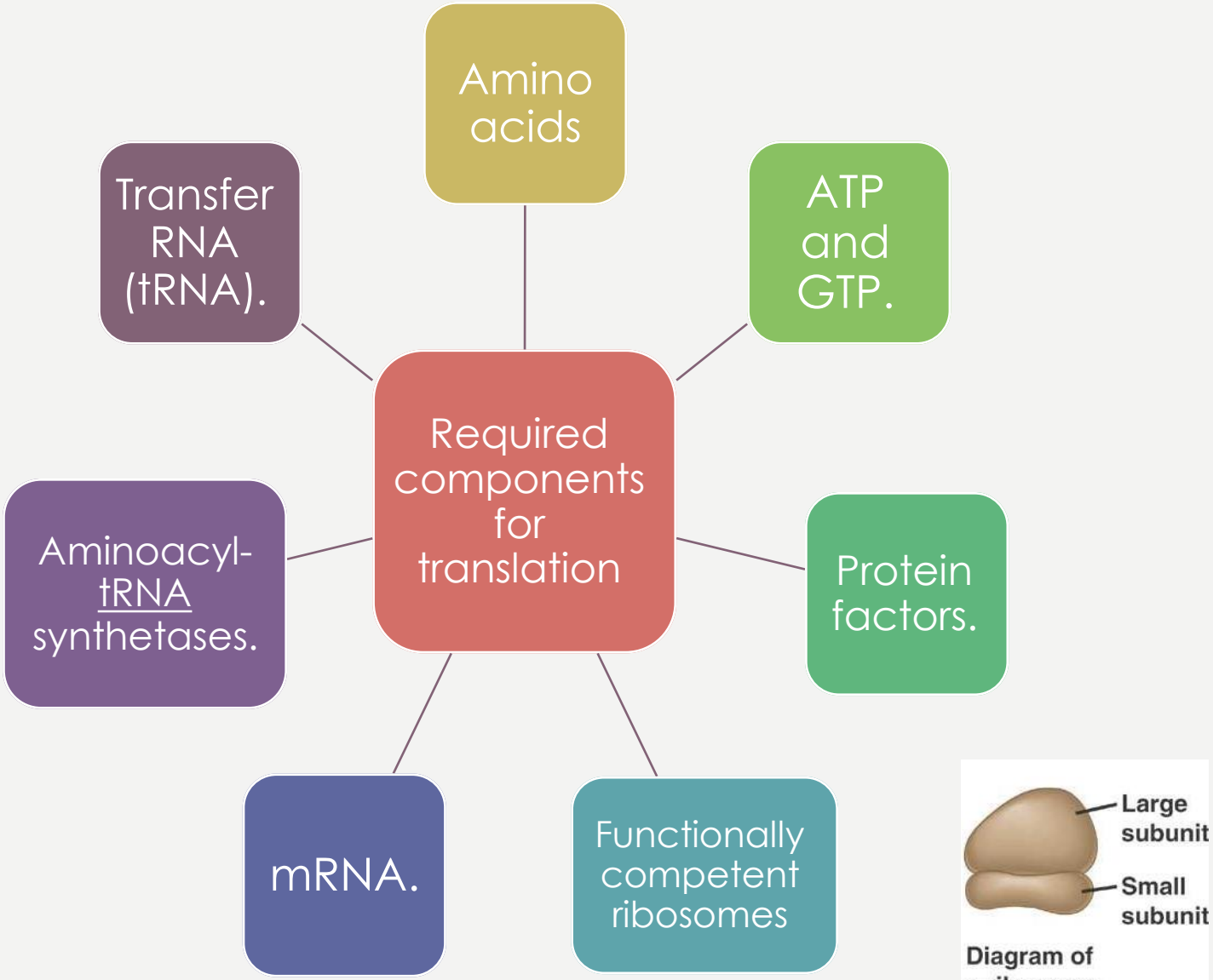
- الكودون هو عبارة عن ثلاثة نيوكليوتيدات تكون موجودة على شريط mRNAوكل كودون يشفر حمضاً أمينياً واحداً ، يمكن لعدة كودونات مختلفة تشفير نفس الحمض الأميني.
- من المهم جداً معرفة أسماء كودونات البداية و الإيقاف.

*To memorize stop codons :
UAA (u are away) – UAG (u are gone) – UGA (u go away)

Biochemistry Team 435

Required components for translation



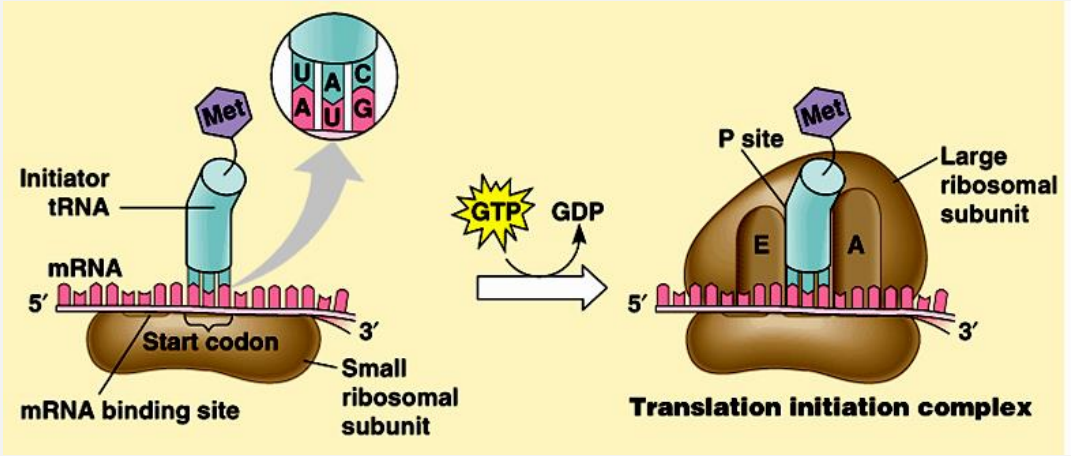


- Aminoacyl-tRNA synthesae : is an enzyme that attaches the appropriate amino acid onto its tRNA.

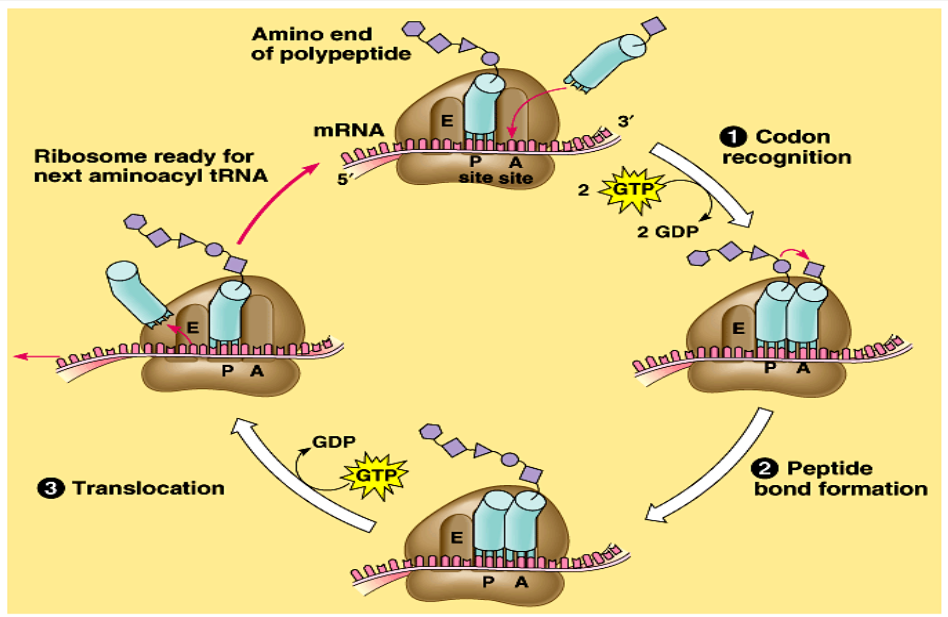
Summary of translation stages

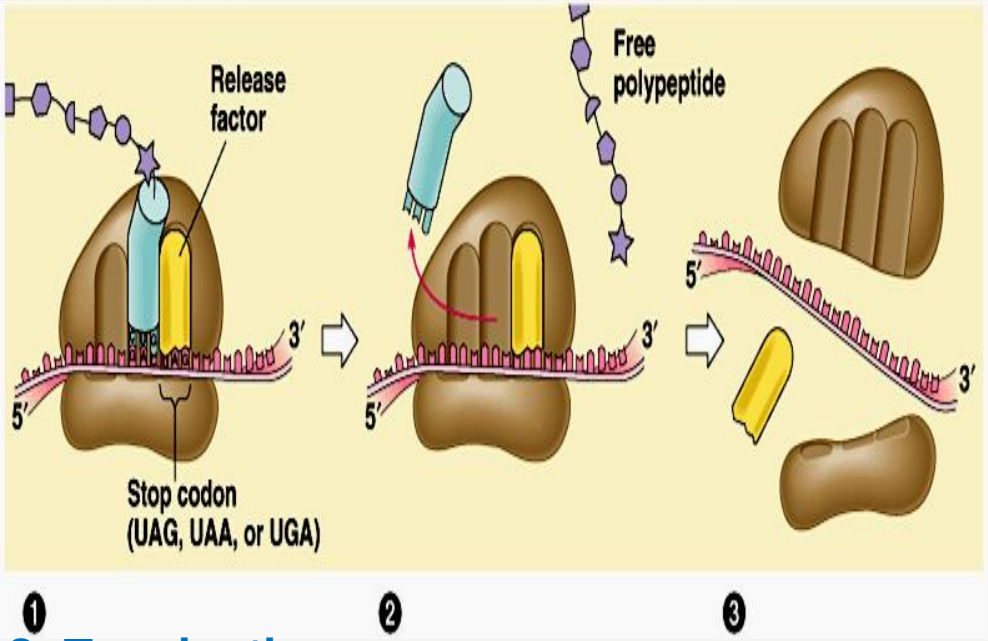
1- Initiation

brings together mRNA, tRNA (with the first amino acid) and the two ribosomal subunits (large & small).



2- Elongation





3- Termination

Occurs when one of the three stop codons reaches the A site.

- DNA REPLICATION
  HTTPS://WWW.YOUTUBE.COM/WATCH?V=VNXFK_D6Y80

  https://www.youtube.com/watch?v=5qSrmeiWsuc ← أنصح بهذا الفيديو لأن اقتبسنا القصة منه

TRANSCRIPTION

- https://www.youtube.com/watch?v=ztPkv7wc3yU

Translation:

- https://www.youtube.com/watch?v=KZBljAM6B1s

Boys Team:

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- علا النهير.
- أفنان المالكي.
- أمجاد الدهيش.
- دلال الحزيمي.
- فاطمه الدين.
- جواهر الحربي.
- جوهره المالكي.
- خوله العريني.
- لجين السواط.
- منيال باوزير.
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