



Genetics

Subject :  Termination in eukaryotes
 Processing of mRNA

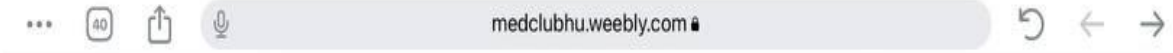
Lec no : 11

Done By : Esra'a Khaled

وَقُلْ رَبِّ زِدْنِي عِلْمًا

تجدون في guidance مادة الجينتكس على موقع النادي :

للوصول الى guidance الجينتكس و تفاريغ
المادة كاملة :



GUIDANCE

SLIDES

NOTES

RECORDS

تجدون هنا شرح المادة كاملة

GENITICS ALAA AL-GAZZAR

تجدون هنا شرح الفريق العلمي للمادة كاملة

شرح قديم (الاسلايدات مختلفة) ، يمكن الاستفادة منها لفهم المواضيع

OLD GENETICS

يمكن الاستفادة من تفاريغ الدفع السابقة

ATHAR BATCH

YAQEEN BATCH

VEIN BATCH

شرح الدكتورة ولاء الجزار للمادة



كل اعمال الفريق العلمي تنشر على قناة
التيليجرام



Termination in eukaryotes:

- Leads to the dissociation^① of the complete transcript and the release^② of RNA polymerase from the template DNA. The process differs for each of the three RNA polymerases. هاي العملية مختلفة بين انواع ال RNA polymerase الثلاثة
- As Pol II reaches the end of a gene, two protein complexes carried by the CTD (carboxy terminal domain), CPSF (cleavage and polyadenylation specificity factor) and CSTF (cleavage stimulation factor), recognize the poly-A signal (polyadenylation signal sequence AAUAAA) in the transcribed RNA.
رح يساعدني
عمل Cleavage
لل Transcript
- The sequences that, once transcribed into RNA, trigger transfer of these factors to the RNA are called poly-A signals

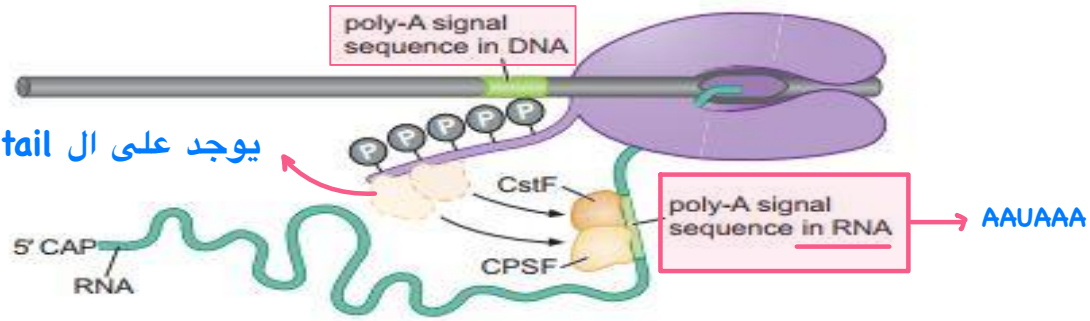
- Poly-A-bound CPSF and CSTF recruit other proteins to carry out RNA cleavage and then polyadenylation. **Poly-A polymerase** adds approximately 200 adenines to the cleaved 3' end of the RNA without a template. The long poly-A tail is unique to transcripts made by Pol II.
- The RNA molecule made by RNA pol II is called a primary transcript, which needs extensive RNA processing in order to produce a ^{Or functional} mature mRNA for translation & protein synthesis.

اول شبي ال polymerase عمل transcription ل DNA عشان يعطينا mRNA

بساعدنا بالفصل

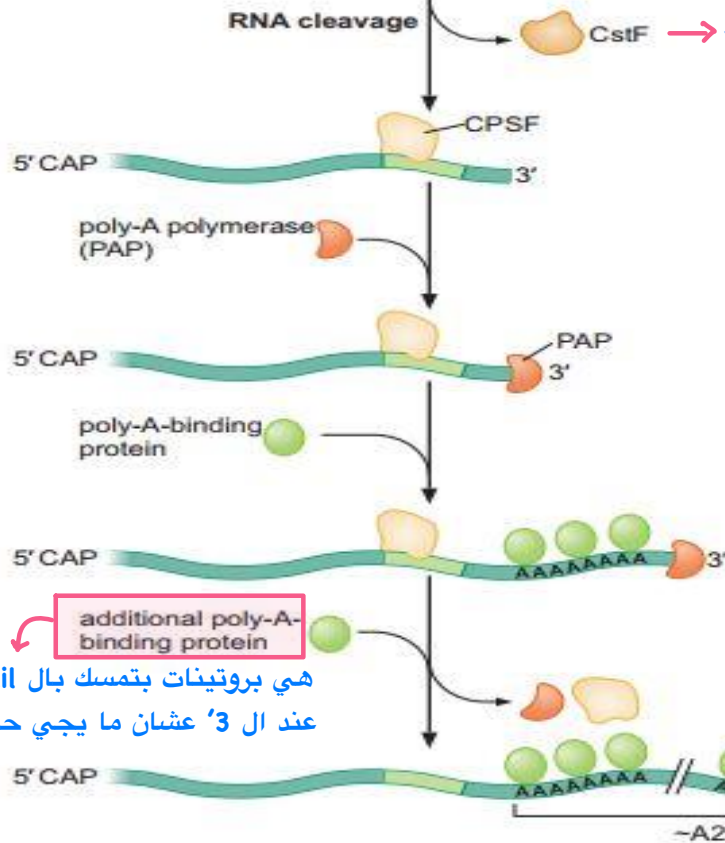
يوجد على ال tail بروتينات **CSTF** , **CPSF**

هاد بعمل cleavage للسلسلة الناتجة عن الانزيم و بعمل tail لل polyadenylation



RNA cleavage

بعد ما ساعدنا بال cleavage رح يغادر



additional poly-A-binding protein

بعملو masking

هي بروتينات بتمسك بال poly A tail و هي بتخفي ال tail عند ال 3' عشان ما يجي حدا يكسره زي ال 3' exonucleases

- **Processing of mRNA**
- **Synthesis & Processing of ribosomal RNA (rRNA)**
 - **Synthesis & Processing of tRNA**

By
Dr. Walaa El Gazzar

A) 5' - capping

B) Addition of poly (A) tail

C) Removal of introns and
splicing of exons

عشان نكون mature RNA لازم نعمله modification ب 3 خطوات :

Processing of mRNA

(Post transcription modifications)

A. 5'-Capping :

متى بنحطه ال Cap ؟

- ❑ The RNA is capped as soon as it emerges from the RNA-exit channel of polymerase. This happens when the transcription cycle has progressed only as far as the transition from the initiation to elongation phases.
- ❑ The cap is a 7- methylguanosine triphosphate attached to the 5' terminal end of the mRNA (which terminates at a triphosphate group).
- ❑ One of the terminal phosphate groups is removed by RNA triphosphatase, leaving a bisphosphate group
بروح بشيل وحدة phosphate الي هي الغاما

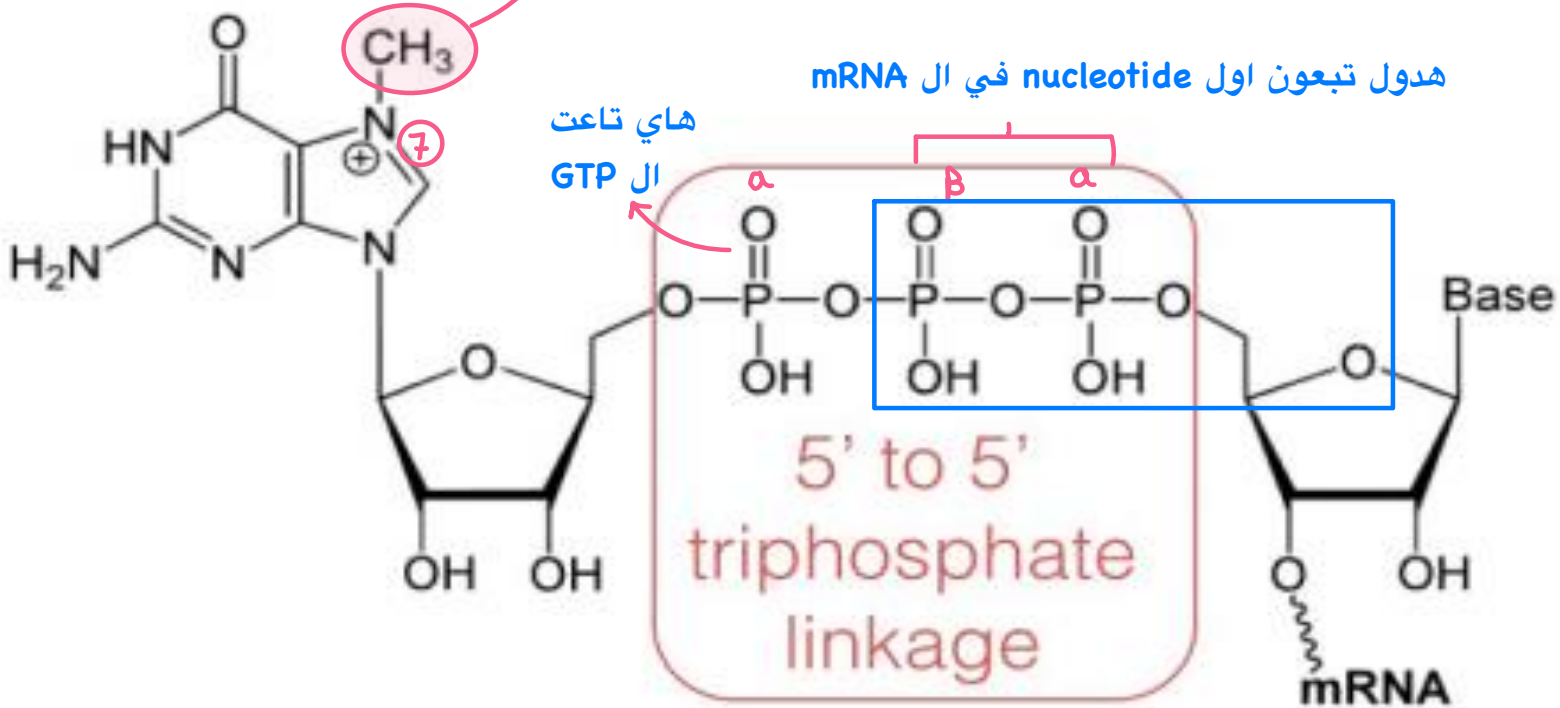
* اول nucleotide بتكون triphosphate لانه قبلها ما في شي اما الباقي (الجداد) يكونو monophosphate

رح تطلع pyrophosphate و تصير GMP

- GTP is added to the terminal bisphosphate by mRNA guanylyltransferase, losing a pyrophosphate from the GTP substrate in the process. This results in the unusual 5\' to 5\' triphosphate linkage.

ال CH3 بنجيبها بعملية ال methylation عن طريق انزيم
Guanine-7-methyltransferase

7-meG cap



5' end of mRNA

➤ Methylation of this terminal guanine is catalyzed by guanine-7-methyltransferase.

➤ S adenosylmethionine, SAM, (active methionine) is the source of methyl group.

Methylation of N-7 of guanine of the GTP cap occurs in the nucleus.

➤ In the cytoplasm, methylation may occur at 2' OH of ribose of some nucleotides, and at N-6 of adenine of some nucleotides

(secondary methylations)

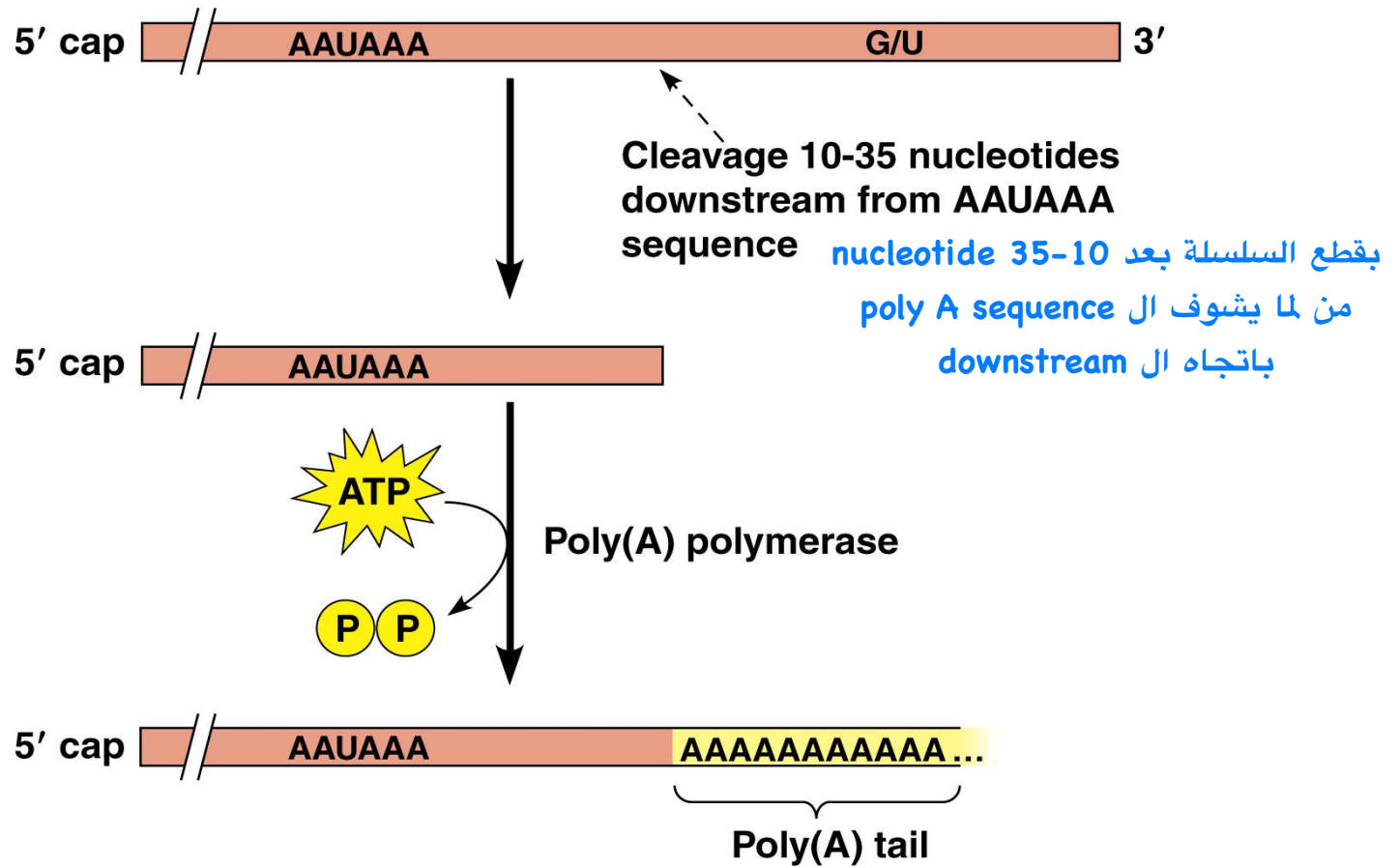
بس تطلع عالسييتوبلازم ممكن يصير لها methylation بأماكن مختلفة

❖ Importance of capping:

- It protects the 5' end of the mRNA from 5' **exonuclease** enzyme.
- It helps its recognition by the ribosome.
- It helps the initiation of protein synthesis.
- Eukaryotic mRNA lacking the cap are not efficiently translated.
- Helps transport of mRNA to the cytoplasm.

B. Addition of poly(A) tail:

- ✓ The final RNA processing event, polyadenylation of the 3' end of the mRNA, is intimately linked with the termination of transcription
- ✓ It is the addition of poly- A tail at the 3' end of mRNA (100-200 A bases).
- ✓ This poly-A tail is not transcribed from DNA but added after transcription by the enzyme polyadenylate polymerase using ATP as a substrate. ما بمشي على قاعدة ال base pairing بحط Adenine لحاله
- ✓ This occurs after the mRNA is cleaved 15-20 nucleotides downstream from the AAUAAA recognition sequence.
- ✓ The poly-A tail immediately binds several copies of a poly (A) binding proteins that protect mRNA against 3' exonuclease.



❖ Importance of poly-A tail:

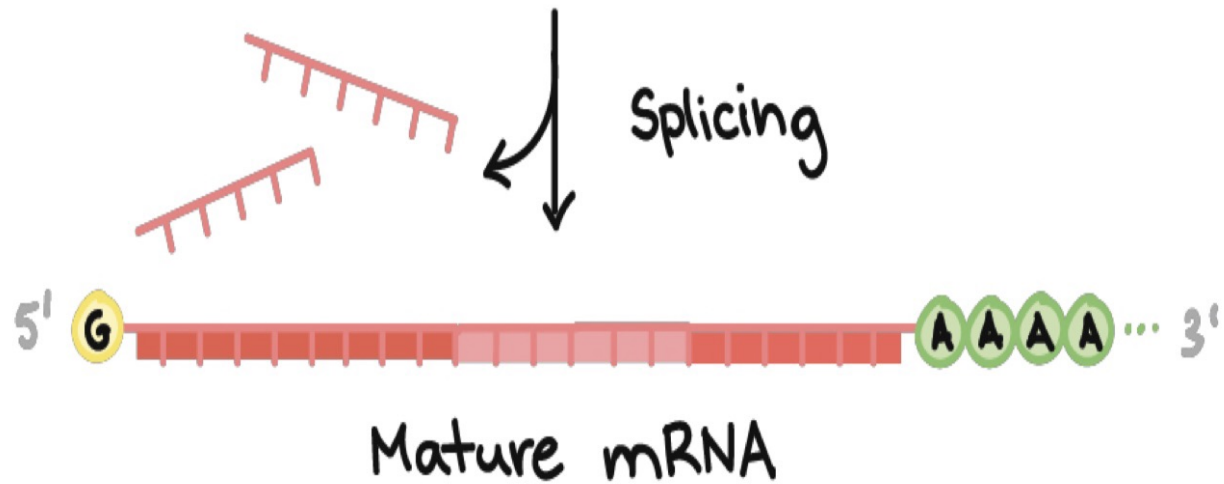
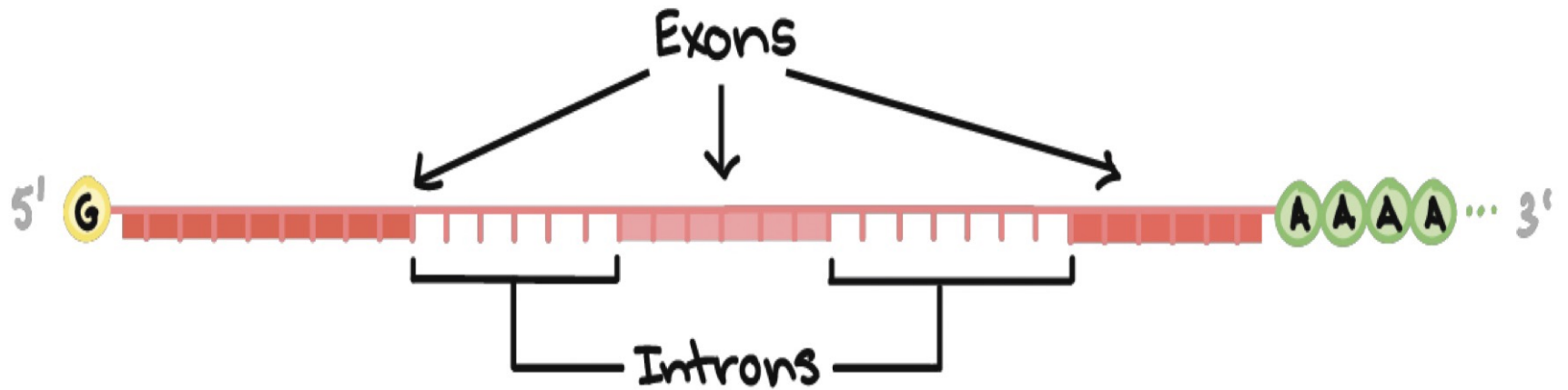
- It stabilizes the mRNA & protects it from exonucleases enzymes. The length of poly (A) tail determines the half life time of mRNA.
- Increases the efficiency of translation.
- It facilitate their exit from the nucleus .After the mRNA enters the cytosol, the poly-A tail is gradually shortened. * كل ما قعدنا بال cytoplasm اكثر بنلاقي ال tail بقصر

C. Removal of introns and splicing of exons :

- It means excision of introns and joining the ends of exons to leave only the functional mRNA molecule.
- This process occurs in the nucleus by the help of ^{polymerase II and polymerase III} البي بطلعهم the small nuclear ribonucleoproteins (snRNP, or snurps) which are composed of small nuclear RNA (snRNA) and proteins.

- Snurps acting on mRNA are called **spliceosomes**. This is an example of catalytic RNAs or RNA enzymes, which are termed **ribozymes**. عبارة عن enzymes داخل في تركيبها RNA
- The sequence of bases at the exon-intron junction determines the site of splicing.

* ال sequence بين ال introns و ال exons هو الي بحدد لل snurps وين يقطع



- One type of β thalassemia appears to result from nucleotide change at the exon-intron junction leading to failure to remove introns, reducing the synthesis of the β globin chain.

مرض الذئبة الحمراء

- Patients with systemic lupus erythematosus (SLE) produce antibodies against snRNP.

خطوة ال splicing ما رح تصير

- Histone mRNAs (replication-dependent histones that are expressed during the S-phase of the cell cycle) do not contain introns.

و هاد اشني منيح لانه اذا ما في introns يعني ما رح يصير splicing و بالتالي ما رح يآثر عليها لو صار مشكلة بال snRNA

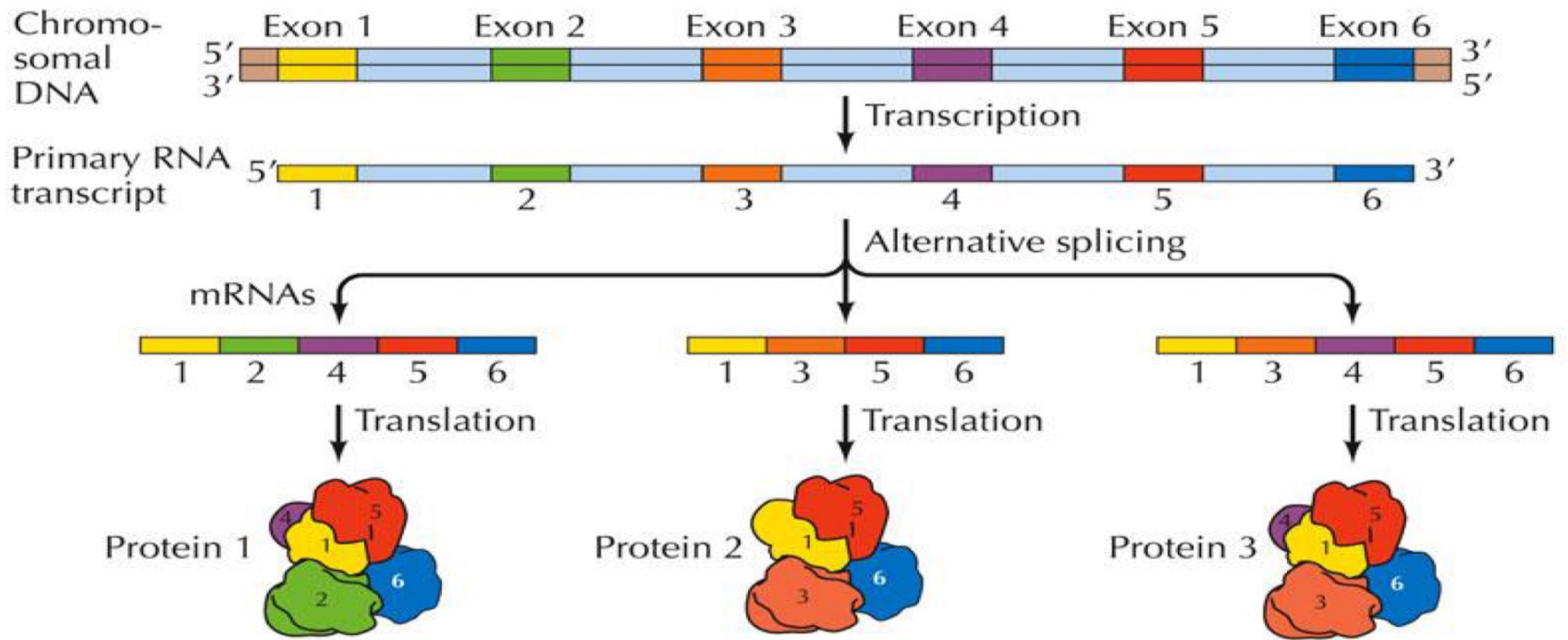
بكون عالي جداً بال S-phase لانه ال DNA replication بصير هناك

Two advantages are suggested for having protein-coding genes organized as exons & introns:

يعني نطلع انواع كثير من ال mRNA

- 1- **Alternative splicing** may lead to the formation of different types or new types of mRNA molecules or proteins.
- 2- Also this will **decreases the possibility of effective mutations** , (that result in protein abnormalities or disease), if it occurs at the regions of introns.

* وجود ال introns يقلل من حدوث الطفرات لانه عددها كبير فالطفرات بتصيبها هي بدل ال exons



- **Alternative splicing, or differential splicing, is a regulated process during gene expression that results in a single gene coding for multiple proteins.**
- In this process, particular exons of a gene may be included within or excluded from the final, processed messenger RNA (mRNA) produced from that gene.
- Notably, alternative splicing allows the human genome to direct the synthesis of many more proteins than would be expected from its 20,000 protein-coding genes. عدد البروتينات يفوق عدد الجينات