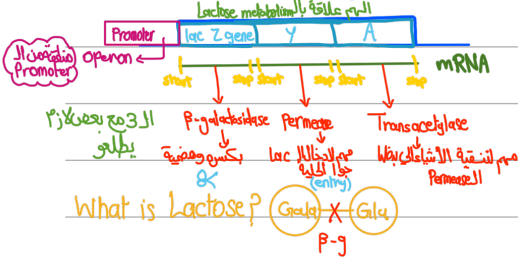


→ in bacteria *E. coli*

Lactose operon

Transcr. unit 3 قطع



normally ↓ lactose ∴ normally there is a repressor attached with the promoter



((Positive regulation)) off

little transcription ∴ ↓ β-galactosidase

↓ Permease ↓ Transacetylase

رجع يدل على لوي Permease قابل بفتح lac ↑ فربط بالرب

Inducer = activator

تقبل بها ال lac by β-galactosidase → Allolactose

فتلك وعلى المنطقة active وينتج lac وينتج بالباراني

Positive regulation / Inducible gene

like we want to induce it (make it active)

* consensus TATA box → 25-30 bp upstream of transcription start site

(TATA X X X) where x: (A or T)

* 10,000 Known human core promoters

& Inr is present in about half

& DPE & BRE present in about quarter

& TATA box present in about one-eighth

→ general Transcription factor

TFIIA, TFIIB, TFIID, TFIIF, TFIIF

لمتروفيهاي بتتم protein fractionation scheme

Factor	No. of Subunits	Functions
TFIIA	2	Stabilizes TBP and TFIID binding. Blocks the inhibitory effects of TAF1 and other proteins.
TFIIB	1	Stabilizes TFIID-promoter binding. Contributes to transcription start site selection. Helps recruit RNA polymerase II • TFIIF complex to the core promoter.
TFIID (TBP and TAFs)	14	Binds to the TATA box, Inr, and DPE. It can deform promoter DNA and serve as a platform for the assembly of TFIIB.
TFIIE	2	Helps to recruit TFIIF to the core promoter and is required for promoter melting.
TFIIF	3	Binds RNA polymerase II and is involved in recruiting the polymerase to the pre-initiation complex. Required to recruit EFlIE and EFlIH to the pre-initiation complex.
TFIIH	10	Functions in transcription and DNA repair. It has kinase and helicase activities and is essential for open complex formation.

* أول التي يرتبط بها TFIID أو TBP على ال TATA Promoter

(TAFs) bind to elements in TATA less promoter

يفضل هون ترفع للثبات او السلايات عنان لهم الخوض بالتحليل أكثر

بعدين بساعده A & B & F عشان يفتح ال RNA polymerase

بعدين بصر ال C-terminus ال RNA polymerase - فسوق على 5 متنازل اعان

امنية التي على والفندق مهمة جدًا لل elongation لان هون

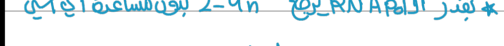
realizing ال B, E, H ثم بصر ال elongation بعدا

2) Elongation

* backtracking → pause ال رجوع

* بقدر ال RNA polymerase بفتح 2-4 ن بفتح مساعدة أي كتي

* بقدر بفتح ال 7-14 بواسطة TFIIIS



* Enhancers in SV40

72 bp repeat → Transcription

ممكن بيعطي اثر حتى لو كان على بعد 1000 bp up/down stream

* silencers → repress transcription

Epigenetic Modifications

(مافوق الجينان بدون ما تغير الجين بتغير الجين وبتحكم بال

expression الجيننا ايه

e.g. on ATP-dependent chromatin remodeling complexes:

- Reposition nucleosomes
- Eject nucleosomes
- Unwrap nucleosomes
- Exchange or eject histone dimers

Active genes have acetylated histones

Histone Acetyltransferase (HAT) منفتح ال active الجين

وبصر ال specific lysine acetylation

- Chromatin remodeling complexes respond to advancing transcription by:
 - 1) displacing histones from DNA onto chaperones
 - Reassemble after the DNA region has been transcribed
 - 2) Only one H2A·H2B heterodimer needs to be removed

بفضل ال methylation for DNA

core promoters ال vertebrate على ال CpG island

بنسبة الجين وان يكون كالميثيل

so methyl transferase add methyl groups to specific lysine and arginine

Ch 13 Eukaryotic Transcription

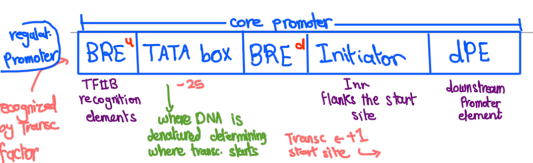
Parameter	prokaryotic	eukaryotic
RNA Polymerase	1 for all types	3; each for every type I, II, III
Binding to promoter	Direct	indirect
Transcription factors	few	numerous
amanitin	not sensitive	Sensitive (II, I)
Transcript processing	no	yes
promoter	simple	complicated
nucleosomes	absent	present

Enzyme	Location	RNA Products	Sensitivity to α-amanitin	Sensitivity to actinomycin D
RNA polymerase I	Nucleolus	Pre-rRNA (leading to 5.8S, 18S, and 28S rRNAs)	Resistant	Very sensitive
RNA polymerase II	Nucleoplasm	mRNA and some small nuclear RNAs (snRNAs)	50% inhibition at 0.02 µg/mL	Slightly sensitive
RNA polymerase III	Nucleoplasm	tRNA, 5S rRNA, U6 snRNA, and 7SL RNA	50% inhibition at 20 µg/mL	Slightly sensitive

1) Initiation

Initiation الجين Transcriptional عوامل

* core promoter (40 bp قبل ال start site و 40 bp بعد ال start site)



Ch 14. mRNA Processing

happens only in Eukaryotes

CO & Post

تعدلات ال Transcr



Pre mRNA Processing

Processing ال mRNA ال 5' UTR و ال 3' UTR

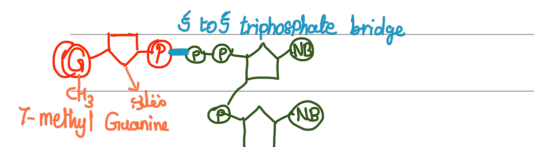
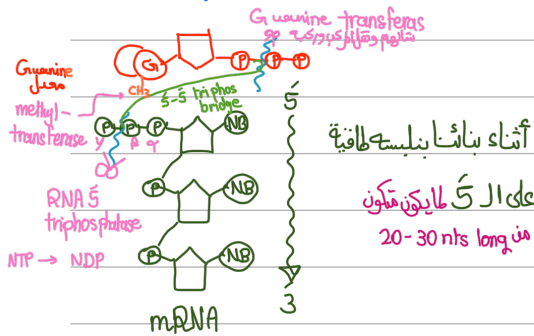
exonucleasom ال cap و ال 3' UTR

∴ processing (capping/splicing/poly A tail)

* ما نغزل ال exons مع ال cistron البكتريا، ما الم دخل

للتصون يكون عبارة عن جين واحد وبطنين 1 protein

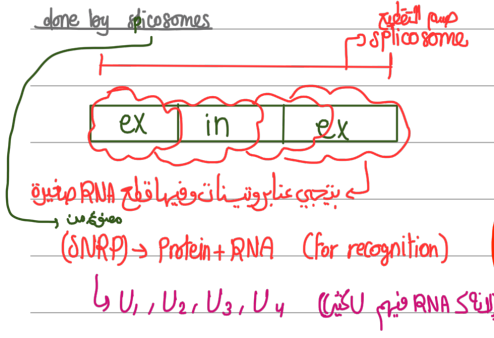
5' cap



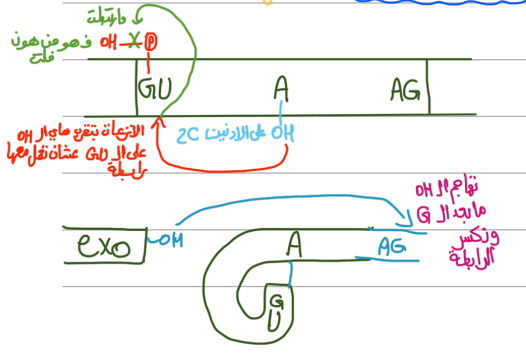
- 1) so it's resistant to exonuclease → so we protect mRNA
- 2) it leads to translation



splicing removal of introns



snRNP = small nuclear RNA proteins

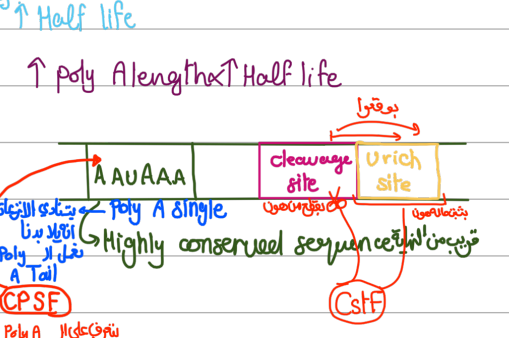


والإنترن يتكسر ويرجع
 الحثلانية lupus
 Auto Immune disease

Anti bodies - snRPs
 • Alternative splicing وجودنا في طرق مختلفة لل splicing مثلاً لو كان عندي 10 exons ممكن اضمهم 8 او ازيد 10 او ازيد 10 بغير ترتيب وهكذا.
 وهو ما يفسر ان ال mRNA الواحد ممكن يعطى بروتينات Different by Eukaryotes
 • every exon domain

مثلاً لو كان عندي 10 exons ممكن اضمهم 8 او ازيد 10 او ازيد 10 بغير ترتيب وهكذا.
 لما صيرنا بروتين كذا بغير Folding كمال

3' poly A Tail
 Termination AA...AAA
 protects from exonucleases
 coding sites in mRNA



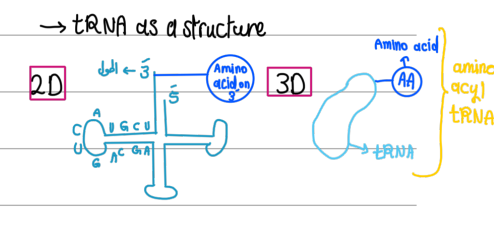
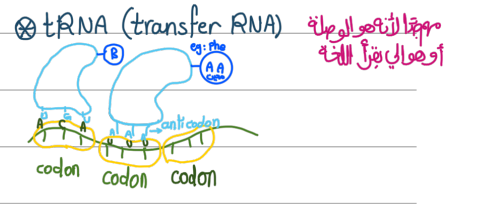
then by → Poly (A) polymerase ... AAA
 وجودنا في 85 بروتين بل بغير جوارها!

Spliceosomes

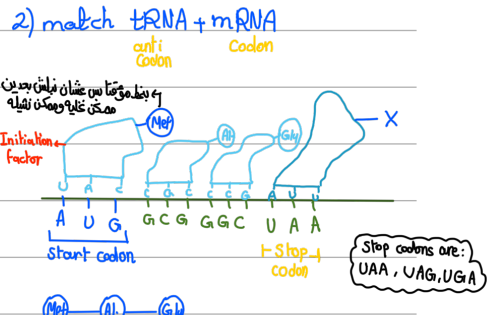
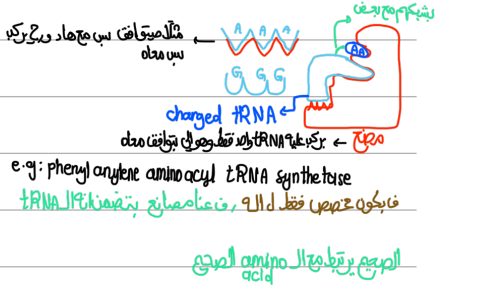
- RNA and protein may both contribute to the spliceosome's catalytic site
- Splicing factor 1 (SF1) also called branchpoint binding protein binds to the branchpoint sequence
 - U2AF⁶⁵ binds to the polypyrimidine tract
 - U2AF³⁵ binds to the AG dinucleotide at the 3' splice site
 - U1 snRNP binds to the 5' splice site
 - Creates the E (early) complex

ch 16. Translation → in cytosol !!

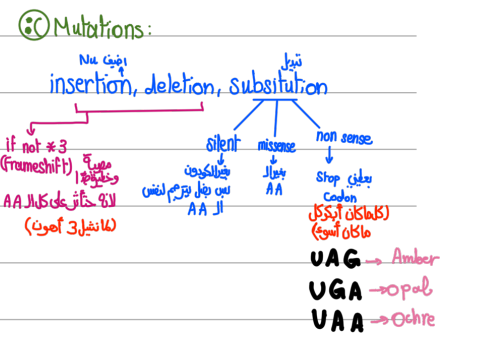
= Protein synthesis
 amino acid (tRNA) → mRNA → Poly peptide



→ tRNA as a structure
 match tRNA + Amino acid
 Done by → Amino acyl tRNA Synthetase
 ATP → Amino acid + tRNA



• يمكن جيب سوال ويحطين نسال mRNA ونسال ان كم مينس
 بل عندي؟؟ بلين ترجمه من ال AUG وبعد كمال STOP CODON



← شوية خصائص عن عملية ال Translation

● non overlapping ما بي تداخل

AAAUUUU من AAAUUUU

أقبل ما قبل ما يرتبط يلي بعده وهكذا

● commaless (دون فراغات)

AAAUUUA X

● Universal

((الكل عنده نفس الكودونات))

● Unambiguous

غير مبهم، واضح وثابت دائماً

● degenerate/redundant

مكرر، بمعنى أكثر من كودون ممكن يعطو ال amino acid

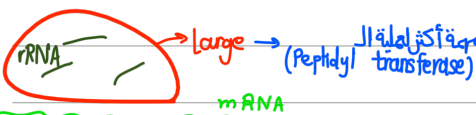
3rd base is usually flexible (wobble)

GCA CGU
GCA CGC

عادي لل base ال 3rd is usually flexible

ف عادي ممكن يكون anti codon شغال على 4 كودونات

⊗ Ribosomes = rRNA + Protein



● it translates 10-20 codons/s

Bacteria (small subunit 30S) + (large subunit 50S) = 70S

Eukaryotes 40S + 60S = 80S



القراءة من 5' → 3' وال poly peptide الي عم بنينج يكون

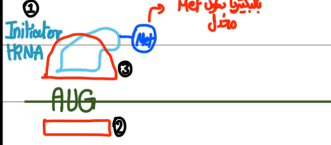
● ننبتة انه ال E & P & A موجودين على ال large and small subunits

● لا بناغكي عن الحماية بالتفصيل

⊗ Process in details

1) Initiation 2) Elongation 3) Termination
4) Recycling

⊗ Initiation (factors + energy (GTP))



* Bacteria: may be polycistronic

* أولاً، كيتي بناتوق أي AUG نبنا عن عناصرها أكتر كيتي

* before initiation

Upstream Untranslated region
Start codon (5-7n)
Shine-dalgarno sequence (Purine rich)
Ribosome ال 28S شو بي نياش العالم

Small subunit ال 16S rRNA وهو موجود على ال AUG
يكون على ال anti-shine-Dalgarno sequence بطبقة

لتوقع ال AUG والارتباط فيها

* Initiation
Initiator tRNA + Met
Initiation factors
Met-tRNA
Initiator tRNA ال 30S
Met-tRNA ال 50S
F removed later by (deformylase)

* ال 70S ال 30S ال 50S ال 30S complex

ال 70S ال 30S ال 50S ال 70S complex

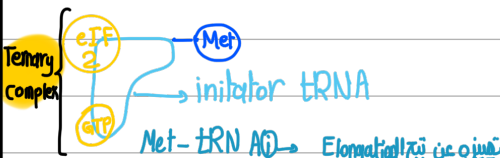
* factors: IF 3 → binds 30S

IF 1 → binds A site of 30S

IF 2 → binds Fmet-tRNA

* Eukaryotes (shine-dalgarno)

Stage 1 → mRNA ال 5' cap
Stage 2 → AUG ال 5' cap
((scanning model))

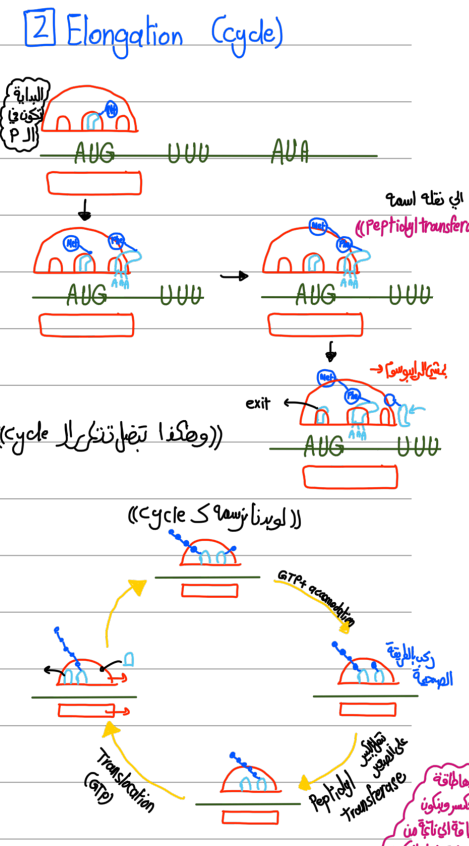


e → Eukaryote
E → Elongation
eIF → Eukaryote Initiation factor
eEF → Eukaryote Elongation factor

والا ال AUG ال 50S ال AUG ال 60S ال AUG ال 80S

Pre-initiating complex ← AUG ال 50S ال AUG ال 60S ال AUG ال 80S

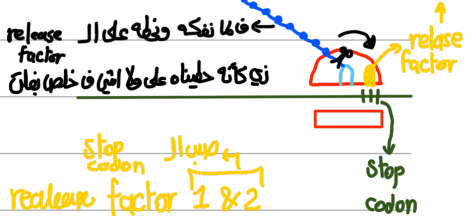
⊗ Elongation (cycle)



Factors

* Bac → EF-Tu (Thermolabile)
EF-Ts (Thermolabile)
EF-G (binds to GTP)
* Euk → eEF1A
eEF1B
eEF2

⊗ Termination (stop codon)



⊗ Recycling (Bacteria)

disassembly
GTP
Elongation, small & large subunits, TRNA already attached

* end of ch. 16