



Genetics

Subject : Genetics

Lec no : 15

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وَقُلْ رَبِّ زِدْنِي عِلْمًا

mRNA يتكون داخل ribosome (تامة مثل البروتين) التي تسمى عبارة عن subunits والخطرة التي بداخلها هي mRNA
 In initiation, the ribosome assembles around the mRNA to be read and the first tRNA (carrying the amino acid methionine, which matches the start codon, AUG). This setup, called the initiation complex, is needed in order for translation to get started.

mRNA BINDS TO THE RIBOSOME

هذا يحدث في initiation
 methionin-tRNA يرتبط بـ P site وليس A site
 mRNA يكون داخل ribosome

Initiation ("beginning"): in this stage, the ribosome gets together with the mRNA and the first tRNA so translation can begin.

II. Elongation

- The ribosome moves along the mRNA in the 5` to 3` direction, translating the successive codons. It adds amino acids one by one to the **carboxyl end** of the growing peptide chain.
- **Elongation requires:**
 - The 80S initiation complex
 - Aminoacyl-tRNAs, as sources of amino acids
 - GTP, as source of energy
 - Elongation factors

from initiation
(48S + 60S)

←



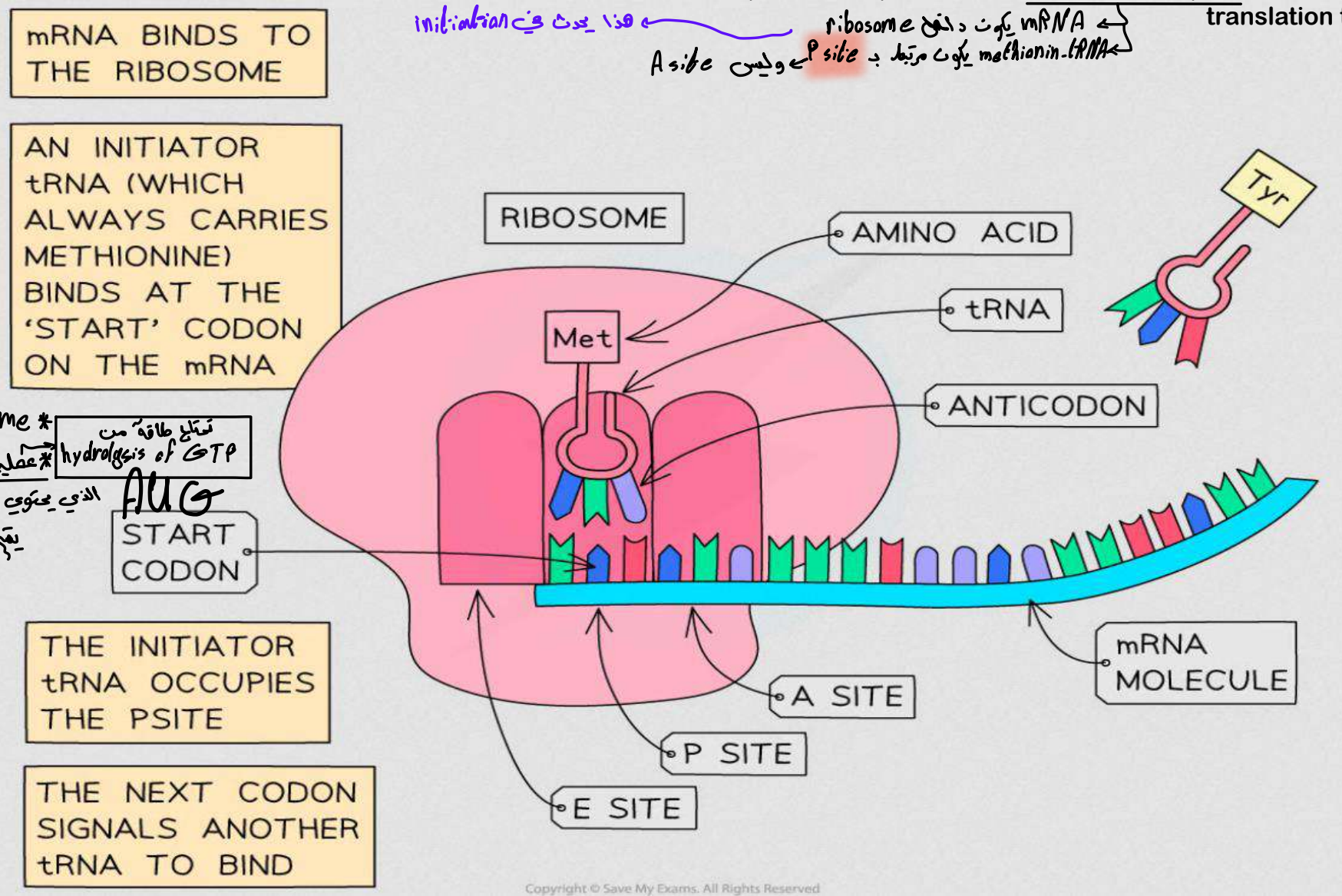
1. Binding of aminoacyl-tRNA to the A site of the ribosome

- Initiation ends in the formation of 80S ribosome with the P site containing the initiation codon and occupied by met-tRNA.
- The **A site** contains the codon for the second amino acid and is waiting to be occupied by the aminoacyl-tRNA with a complementary anticodon.
- eEF-1 binds GTP & forms a complex with aminoacyl-tRNA. This complex delivers aminoacyl-tRNA to the A site, with the release of eEF-1 & hydrolysis of GTP to GDP and Pi.

Our first, methionine-carrying tRNA starts out in the middle slot of the ribosome, called the P site. Next to it, a fresh codon is exposed in another slot, called the A site. The A site will be the "landing site" for the next tRNA, one whose anticodon is a perfect (complementary) match for the exposed codon.

موقع التثبيت و بداية الارتباط
amino acyl-tRNA

(mRNA يكون داخل ribosome (تعاماً مثل البروتين) التي تم تجميعها من subunits والخطيرة التي بداخلها هي mRNA)
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 methionin-tRNA يكون مرتبط ب P site وليس A site

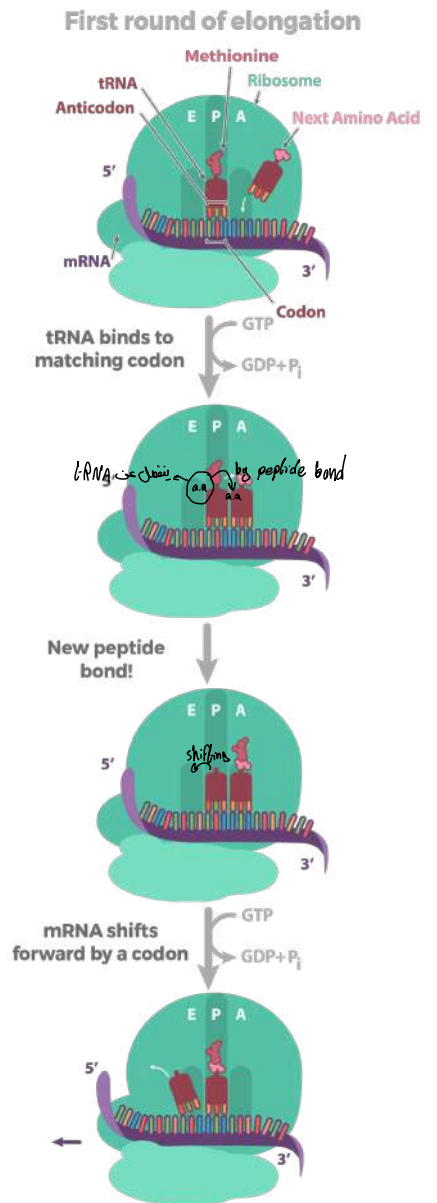
الوجود في P site
 AUG start codon
 * ribosome يتعرف على start codon
 hydrolysis of GTP
 aminoacyl-tRNA
 الذي يحتوي على anticodon العاكس لـ codon
 يتم عن طريق Elongation factor 1
 عندما يتم ربط aminoacyl-tRNA
 يحدث release لـ EF-1
 وينتج aminoacyl-tRNA آخر
 عملية الإحضار تكون في A site
 methionin-tRNA يكون مرتبطاً في P site في initiation
 قبل الانتقال إلى elongation

Elongation

I like to remember what happens in this "middle" stage of translation by its handy name: **elongation** is when the polypeptide chain gets **longer**.

But how does the chain actually grow? To find out, let's take a look at the first round of elongation—after the initiation complex has formed, but before any amino acids have been linked to make a chain.

Our first, methionine-carrying tRNA starts out in the middle slot of the ribosome, called the P site. Next to it, a fresh codon is exposed in another slot, called the A site. The A site will be the "landing site" for the next tRNA, one whose anticodon is a perfect (complementary) match for the exposed codon.



Extending the chain: Elongation

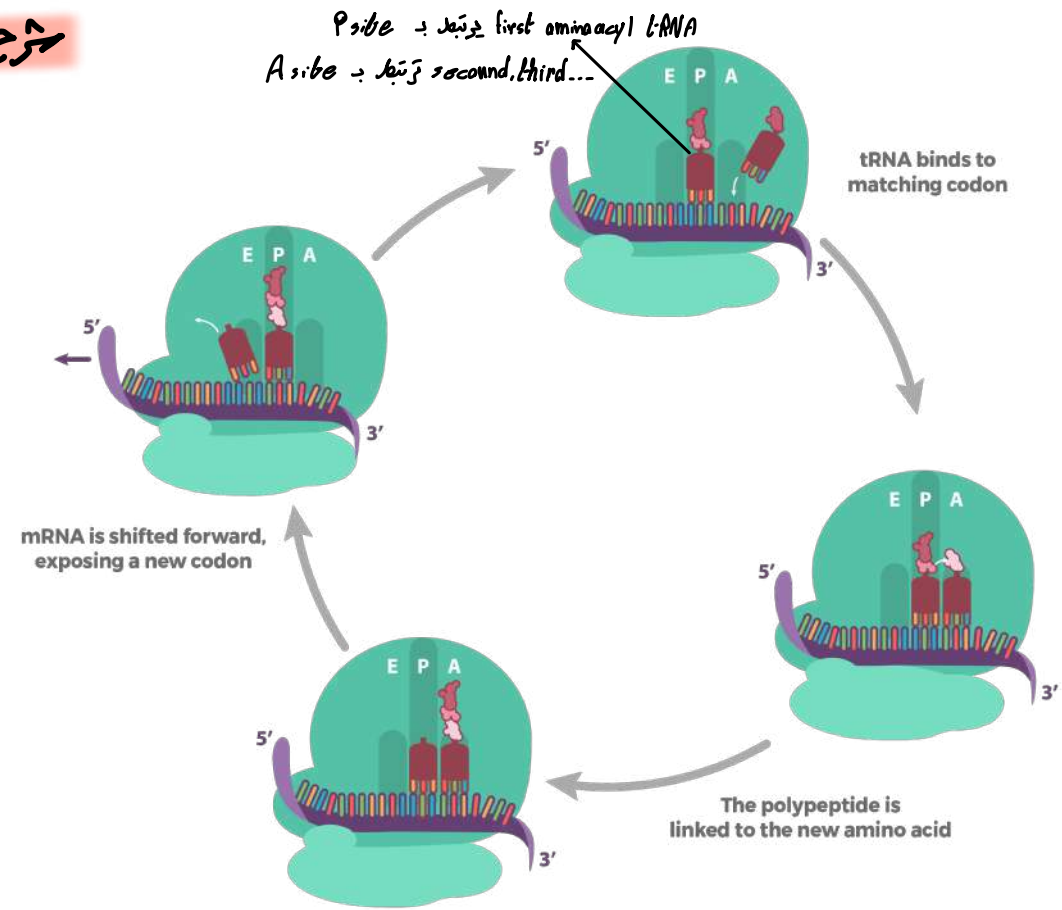
شرح خارجيہ

Elongation is the stage where the amino acid chain gets longer. In elongation, the mRNA is read one codon at a time, and the amino acid matching each codon is added to a growing protein chain.

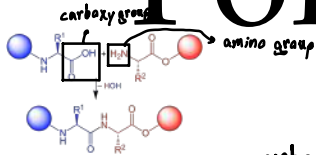
Each time a new codon is exposed:

- A matching tRNA binds to the codon
- The existing amino acid chain (polypeptide) is linked onto the amino acid of the tRNA via a chemical reaction
- The mRNA is shifted one codon over in the ribosome, exposing a new codon for reading

During elongation, tRNAs move through the A, P, and E sites of the ribosome, as shown above. This process repeats many times as new codons are read and new amino acids are added to the chain.



Formation of peptide bond



Amino group of the second a.a. ← carboxyl group of the first a.a. (first a.a and second a.a) amino acids peptide bonds.

- The 60S ribosomal subunit contains the enzyme peptidyltransferase (an RNA enzyme or ribozyme).
- It connects the carboxyl group of the 1st amino acid to the amino group of the 2nd amino acid, forming the 1st peptide bond in the peptide chain
- This enzyme transfers the 1st amino acid from its tRNA to the 2nd amino acid.
- Now a dipeptide is connected to the 2nd tRNA in the A site. The 1st tRNA is now free & vacates the P site.

P site ← first a.a. ← RNA ← (P site) ← first a.a. ← انتقال ← ا.a مع a.a ← A site ← second a.a

A tRNA (ATTACHED TO AN AMINO ACID) BINDS TO THE NEXT CODON AND OCCUPIES THE A SITE

عملية الربط بين a.a's يرتبطها انفعال
 a.a عن tRNA الخاص به الموجود في P site
 تنتقل هذه الخطوة الميثيونين من الحمض النووي الريبوزي الأول إلى
 الأحماض الأمينية من الحمض النووي الريبوزي الثاني في الموقع A.

PEPTIDE BOND

لما حدث في
 في الدورة في
 باليد القادم ويرافق
 هذا عملية shifting

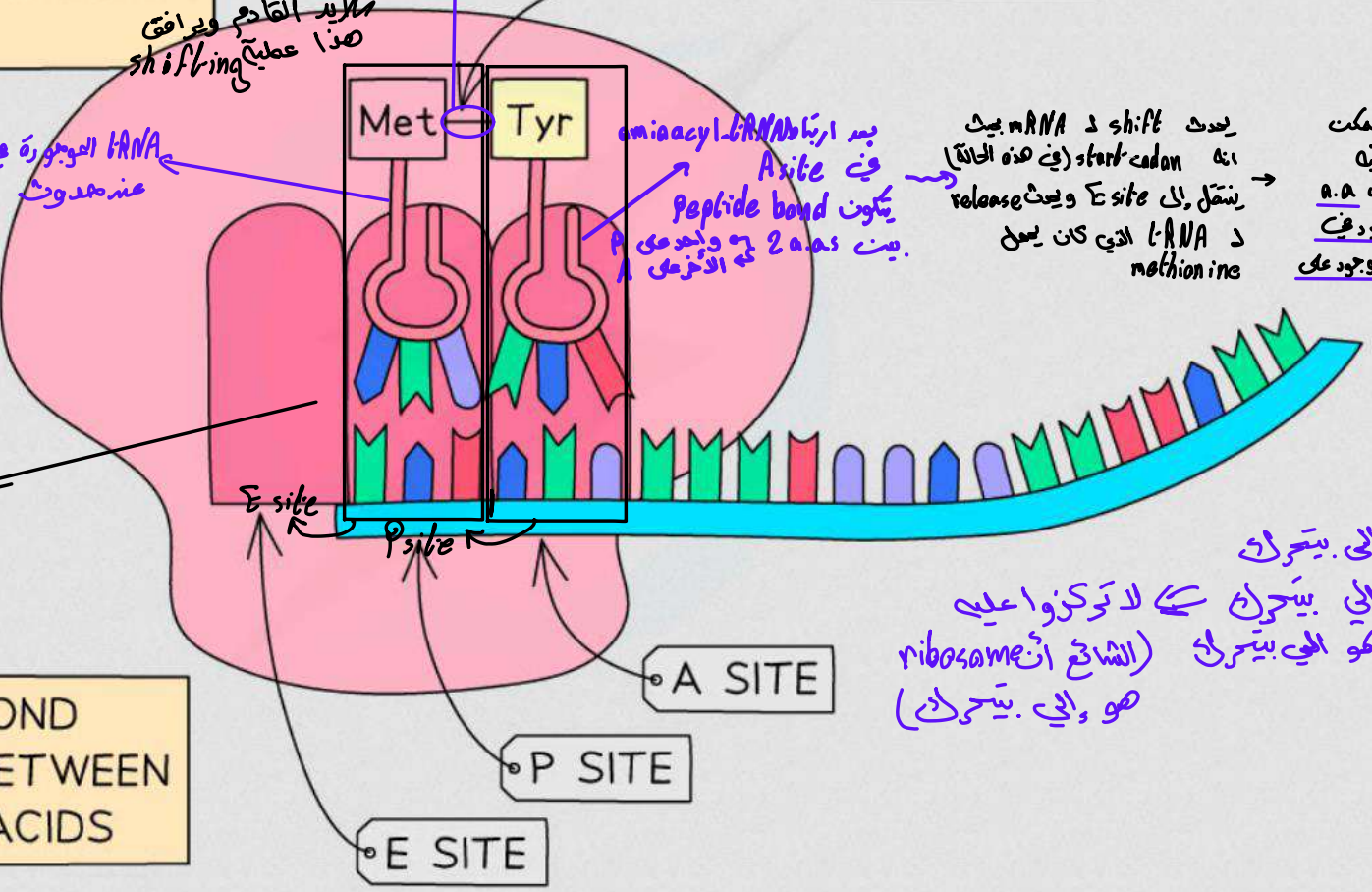
tRNA الموجودة في P site تفصل عن mRNA
 عند حدوث shift ل start codon إلى E site

* مع عملية انفعال tRNAs وتكون polypeptide chain
 هذه chain تكون free

عملية الانتقال تكون ل (codon مع tRNA التي يرتبط بها)

من A ← P
 من P ← E

A PEPTIDE BOND IS FORMED BETWEEN THE AMINO ACIDS



بعد ارتباط aminoacyl-tRNA في A site
 يكون peptide bond بين 2 a.a's في الأخرى
 يحدث shift ل mRNA إلى start codon (في هذه الحالة) وينتقل إلى E site ويحدث release ل tRNA الذي كان يعمل methionine

يصبح A site فارغ بحيث يمكن ارتباط aminoacyl-tRNA في peptide bond بين a.a الموجود على tRNA الموجود في P site وبين a.a الموجود على tRNA الموجود في A site

* موضع مين والي يتحرك
 هي ribosome هو والي يتحرك لا تركزوا عليه
 أو أن mRNA هو والي يتحرك (الشائع أن ribosome هو والي يتحرك)

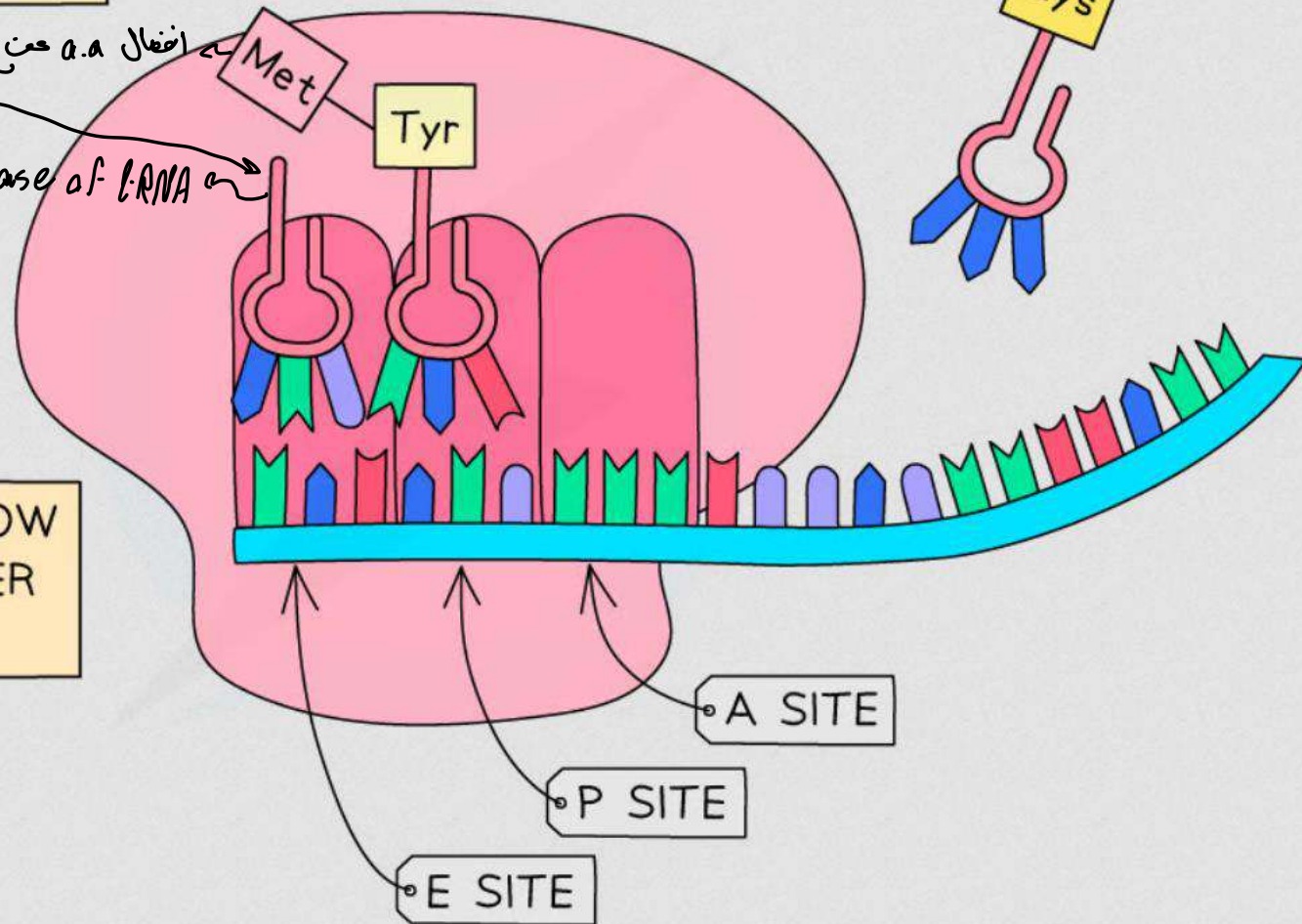
THE RIBOSOME MOVES
THREE BASES ALONG
THE mRNA

THE INITIATOR
tRNA NOW
OCCUPIES THE
E SITE AND
RELEASED THE
AMINO ACID

THE A SITE IS NOW
FREE FOR ANOTHER
tRNA

التحرير a.a من tRNA

التحرير a.tRNA



Translocation of the peptidyl-tRNA from the A site to the P site

- The newly formed peptidyl-tRNA is translocated, together with its codon , from the A site to the P site.

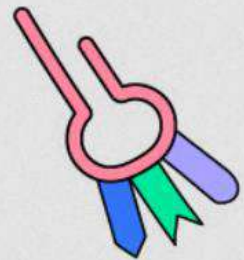
هه یربط second a.a (الوجودیة P site) مع third

للوجودیة A site • This requires eEF-2 & **GTP**, which is hydrolyzed to GDP and Pi.

- Now the A site contains the codon for the 3rd amino acid & can accept the aminoacyl-tRNA with the proper anticodon & a new cycle of elongation occurs.
-

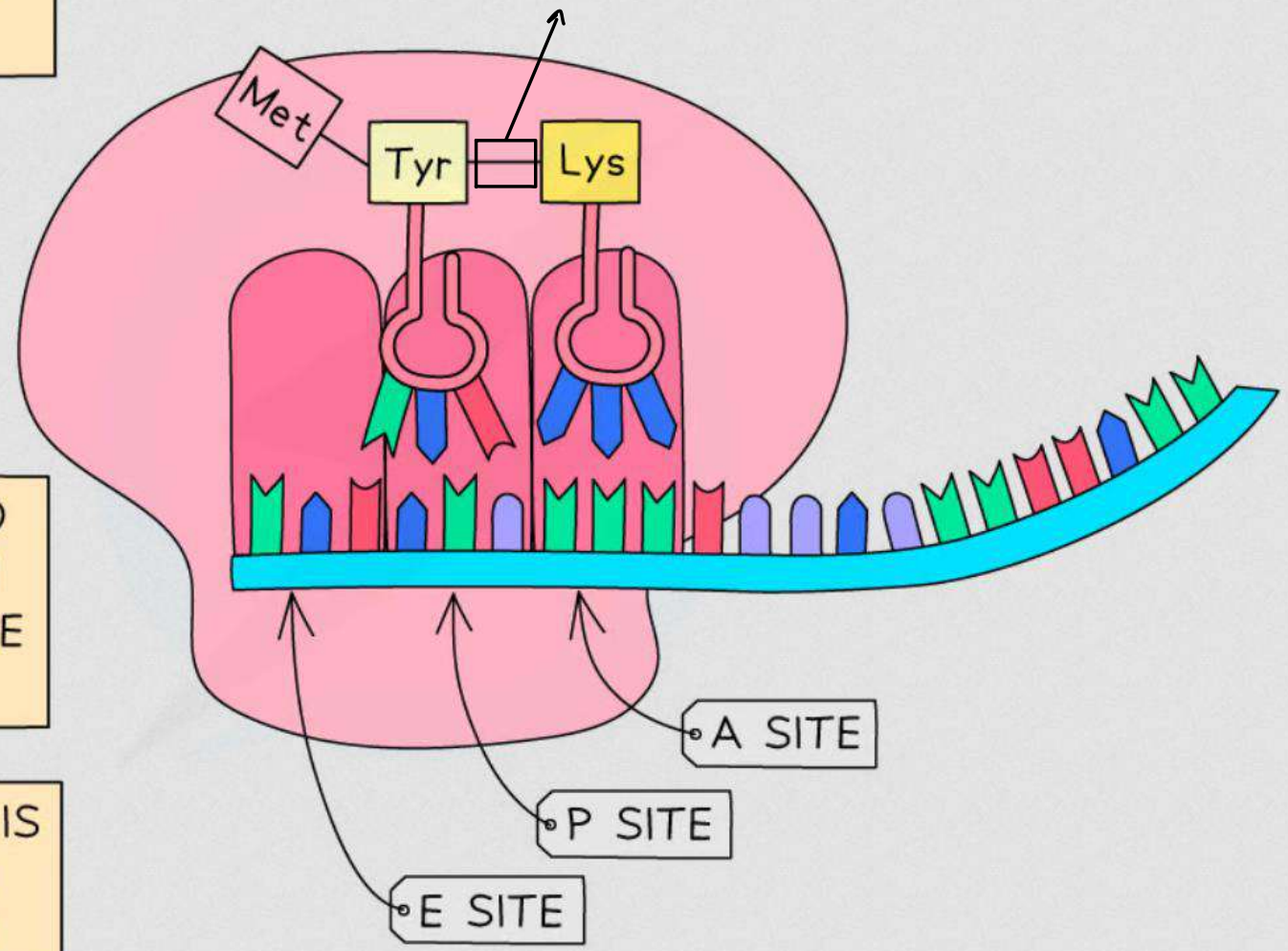
THE INITIATOR tRNA IS RELEASED FROM THE E SITE

علاوة بناء peptide bond تكونت بيت α . α التريبول \rightarrow tRNA الموجود في A site مع α . α التريبول \rightarrow tRNA الموجود في E site



A tRNA BINDS TO THE NEXT CODON AND OCCUPIES THE A SITE

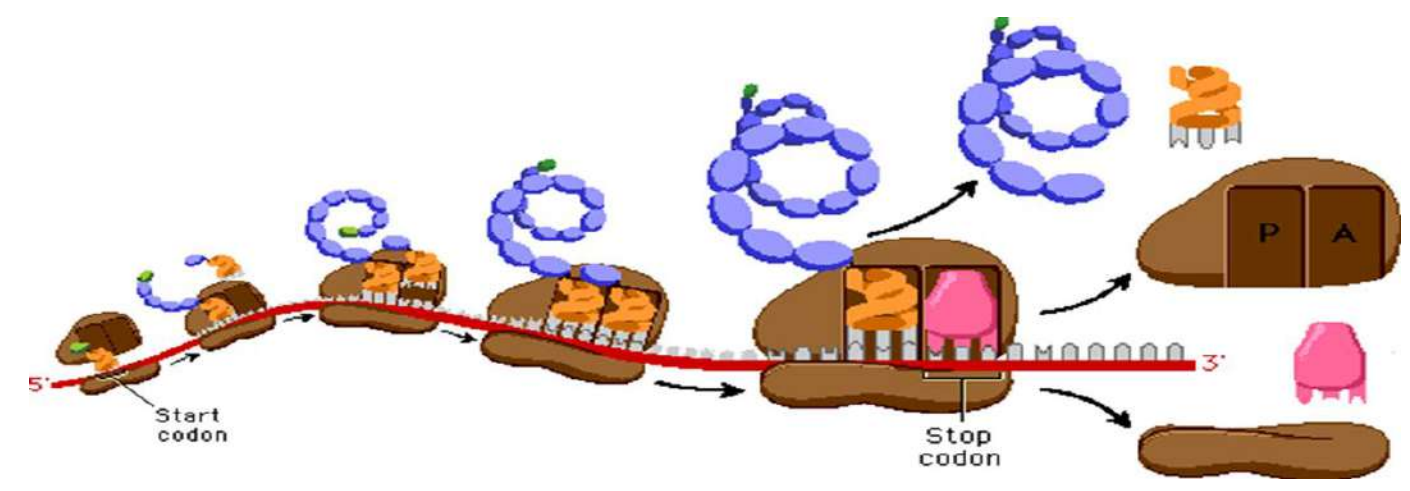
A PEPTIDE BOND IS FORMED BETWEEN THE AMINO ACIDS



- Multiple ribosomes can translate the same mRNA. → يقوم 80 nucleotides بترجمة ribosome أخرى .
 وفي نفس الوقت يقوم بترجمة 80 nucleotides أخرى

ribosomes تعمل على نفس mRNA
 كل ribosome يبدأ عند start-codon وينتهي عند stop-codon وبالتالي يتم إنتاج العديد من poly peptides المتماثلة
 عدد ribosomes = عدد poly peptide chains

- As the ribosome moves along the mRNA, a new ribosome can attach to the initiating codon (with a distance of 80 nucleotides in between), starting the synthesis of a new peptide chain .
- Thus, several ribosomes may translate the same mRNA simultaneously. They form together a polyribosome or polysome.

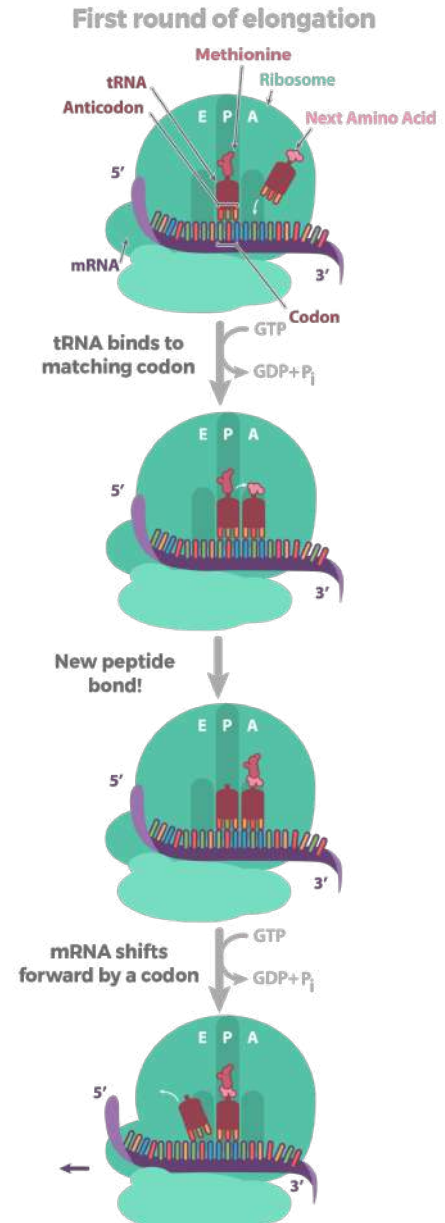


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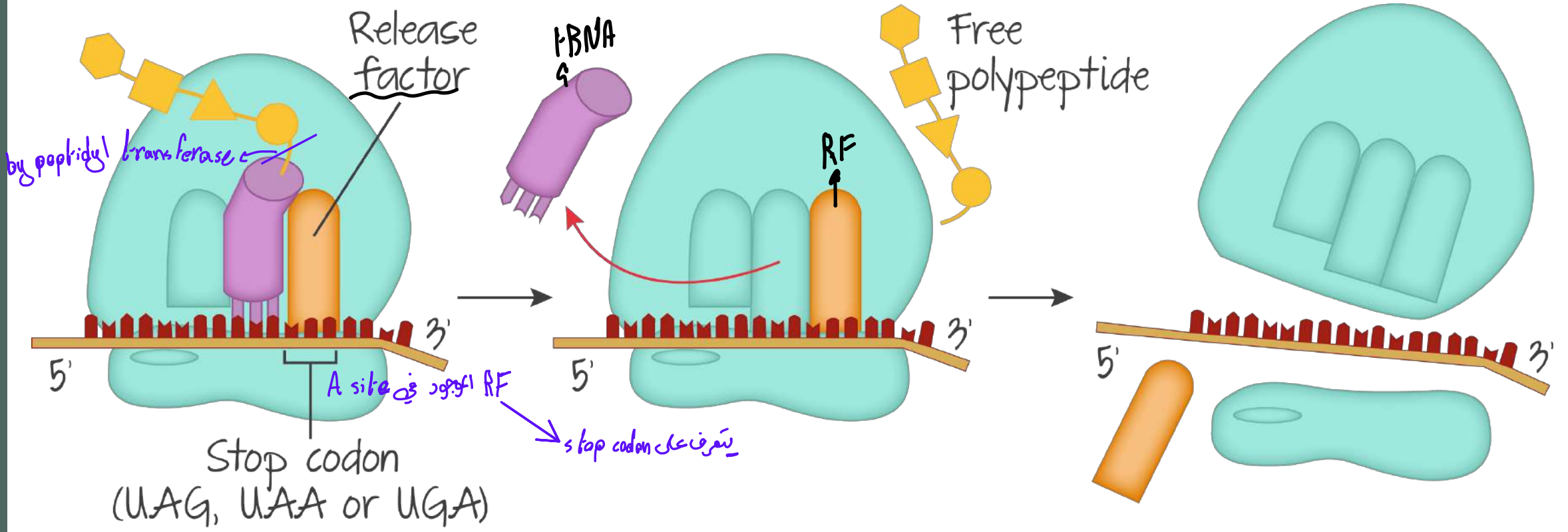
Termination happens when a stop codon in the mRNA (UAA, UAG, or UGA) enters the A site.

III. Termination

* عند وجود stop codon في A site هذا يعني أن translation انتهى
هو يرتبط (RF) في A site

عملية hydrolysis bond الموجودة بين a.a و tRNA موجودة في P site
التي هي إعادة استخدام في عملية translation أخرى.
التي تحصل له dissociation
ribosome ←
tRNA ←
mRNA ←
polypeptide chain ←
RF ←

- Termination occurs when one of the three termination stop codons appears into the **A site**.
- These codons are recognized by releasing factors (**eRF**). It also requires **GTP**.
- The binding of these release factors induces peptidyl transferase to hydrolyze the bond linking the peptide to the tRNA at the P site, causing the nascent protein to be released from the ribosome.
- The ribosomal subunits, mRNA, tRNA and protein factors are dissociated and can be recycled and used to synthesize another polypeptide.



Inhibitors of translation → apoptosis des.

E, P, A sites موجود فيها

- **Tetracycline**: an antibiotic that combines with the 30S ribosomal subunit of bacteria, preventing access of aminoacyl-tRNA (block A site).

لـ يمنع ارتباط tRNA

in 60S of eukaryotes
in 50S of prokaryotes ← peptidyl transferase

- **Chloramphenicol**: an antibiotic that inhibits peptidyltransferase in bacterial 50S ribosomal subunit.

- **Clindamycin and erythromycin**: two antibiotics bind to the 50S ribosomal subunit of bacteria, inhibiting translocation of peptidyl-tRNA (inhibits the movement of ribosome along the mRNA).