



# Genetics

**Subject** :

- synthesis & processing of rRNA
- synthesis & processing of tRNA
- regulation of eukaryotic gene expression

**Lec no** : 12

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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



# Synthesis & Processing of ribosomal RNA (rRNA)

- The primary transcripts of the mammalian rRNA include a **45S rRNA (pre-rRNA)** & a **5S rRNA**.  
*هو الي بنطلع منه انواع ال polymerase*
- The 45S rRNA is **synthesized by RNA polymerase I** then undergoes RNA processing in the nucleus which cleaves the precursor to release the mature 18S, 5.8S, 28S rRNA ↘

*ما بيجو من جينات مختلفة ، جين واحد بس الي بنتجهم و الي هو 45s*

شفنا زيها بال telomere كان تسلسل TTAGGG ورا بعض

- The 45S genes for 18S, 5.8S and 28S rRNA are typically **clustered together and tandemly repeated** (one copy each of 18S, 5.8S and 28S occur, followed by untranscribed spacer DNA, then another set occur and so on).  
متجمعين مع بعض بمكان واحد (زي بالصورة تحت)

- **5S RNA gene** is transcribed by **RNA polymerase**

**III**

- Hundreds of copies of these genes are present in every cell. This large number of genes is required to **synthesize sufficient copies of each type of rRNA to form the  $10^7$  ribosomes required for each cell replication.**

ليش في نسخ كثير من ال 45s بال genome ؟  
لانه بنحتاجها عشان نصنع ال ribosomes

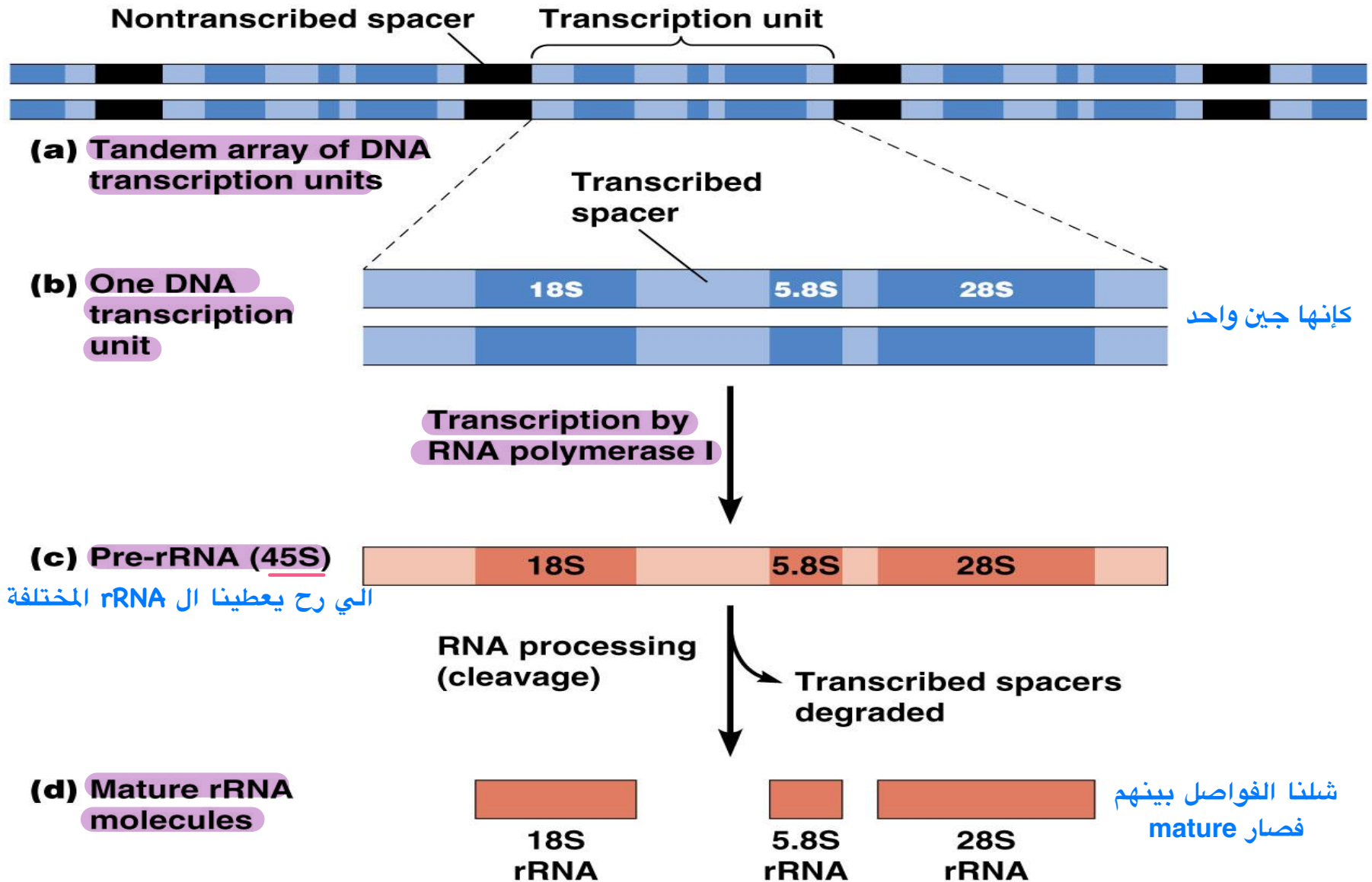
الباقى ( 28s , 5.8s , 18s ) تصنعو بال nucleolus

Unlike pre-rRNA genes, 5S-rRNA genes are transcribed by RNA polymerase III in the nucleoplasm outside of the nucleolus. **Without further processing**, 5S RNA diffuses to the nucleolus, where it assembles with the 28S and 5.8S rRNAs and proteins into large ribosomal subunits. When assembly of ribosomal subunits in the nucleolus is complete, they are transported through nuclear pore complexes to the cytoplasm, where they appear first as free subunits.

ال 5s اول  
ما ينصنع  
بكون جاهز

بعدين ال 5s لازم يدخل جوا ال nucleolus عشان يتحد مع  
الباقى و يكون large ribosomal subunits

يفصل بين ال Transcription unit قطع ال spacer ، عاملين زي القطار و يكونو مرصوصين جنب بعض

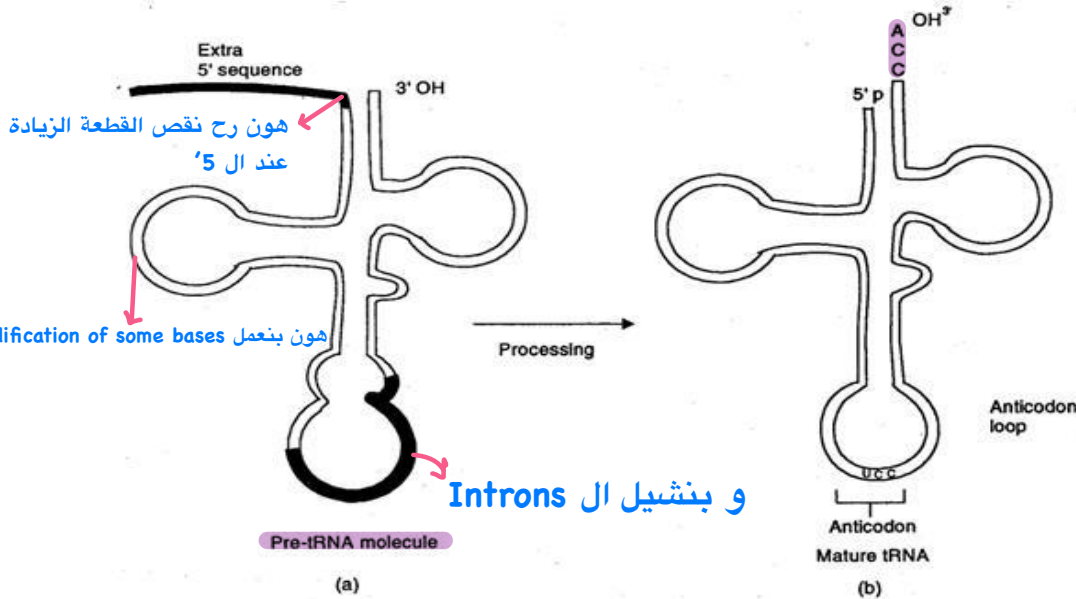


# Synthesis & Processing of tRNA

- Eukaryotic tRNA genes are all transcribed by RNA polymerase III.
- The primary transcript (pre-tRNA molecules) requires up to 4 different types of RNA processing steps as follows:
  - 1- Addition of the CCA sequence at the 3' end by the nucleotidyl transferase.
  - 2- Excision of the nucleotide extension at the 5' end.
  - 3- Excision of introns present in the anticodon loop.
  - 4- Modification of some bases by methylation of uracil into thymine or reduction of uracil into dihydrouracil and formation of pseudouracil

بنغير بال attachment عشان يصير هيك

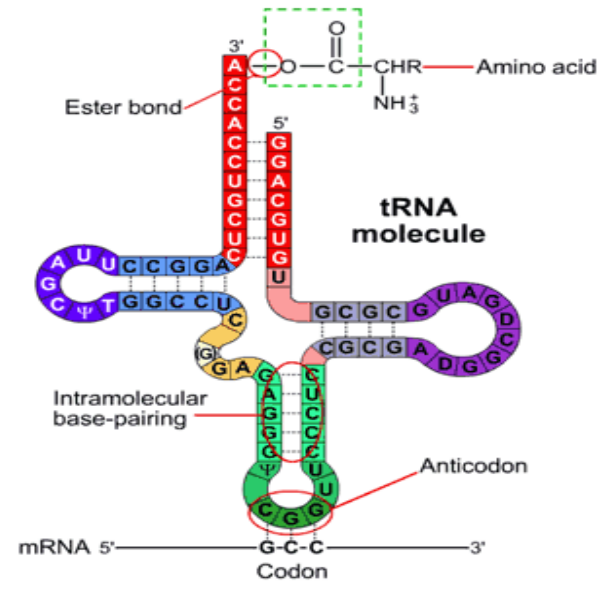
\* لما نضيف ميثيل على ال Uracil بصير Thymine / و حكينا انه ال tRNA هو ال RNA الوحيد الي عنده Thymine



Primary transcript

و هاد الشكل ال mature

هاد شكل ال tRNA اول ما ينزل





# Regulation of eukaryotic gene expression

- The levels of eukaryotic gene regulation include the following:

**1- Alteration of gene content.** كيف بتتأثر الجينات بشكل ال DNA

**2- Transcriptional regulation.** During transcription

**3- Post-transcriptional regulation.**

# 1-Alteration of gene content

## (regulation through modification to DNA)

- The eukaryotic genome may be changed by the following mechanisms:

■ **Gene amplification:** بنزید عدد الجينات عشان يزيد عدد البروتينات الناتجة مثل الهستون  
التي بلف حوالين ال DNA

- It is the increase of a gene product by increasing the number of genes coding for that product e.g. histone & rRNA genes.
- More than 20 genes are known to be amplifiable e.g. dihydrofolate reductase genes. هاد مثال على الجينات التي بنزید عددهم

- Dihydrofolate (FH<sub>2</sub> is a derivative of folic acid) is reduced to tetrahydrofolate (FH<sub>4</sub>) by dihydrofolate reductase.
- Methylene-FH<sub>4</sub> is required for conversion of dUMP to dTMP which is utilized for DNA synthesis.
- It has been demonstrated in patients receiving methotrexate ( an inhibitor of FH<sub>2</sub>-reductase) as a treatment for cancer that malignant cells can develop drug resistance by increasing the number of genes for dihydrofolate reductase.
- *For cancer, methotrexate competitively inhibits dihydrofolate reductase (DHFR) (methotrexate is structurally similar to folate). The affinity of methotrexate for DHFR is about 1000-fold that of folate.*

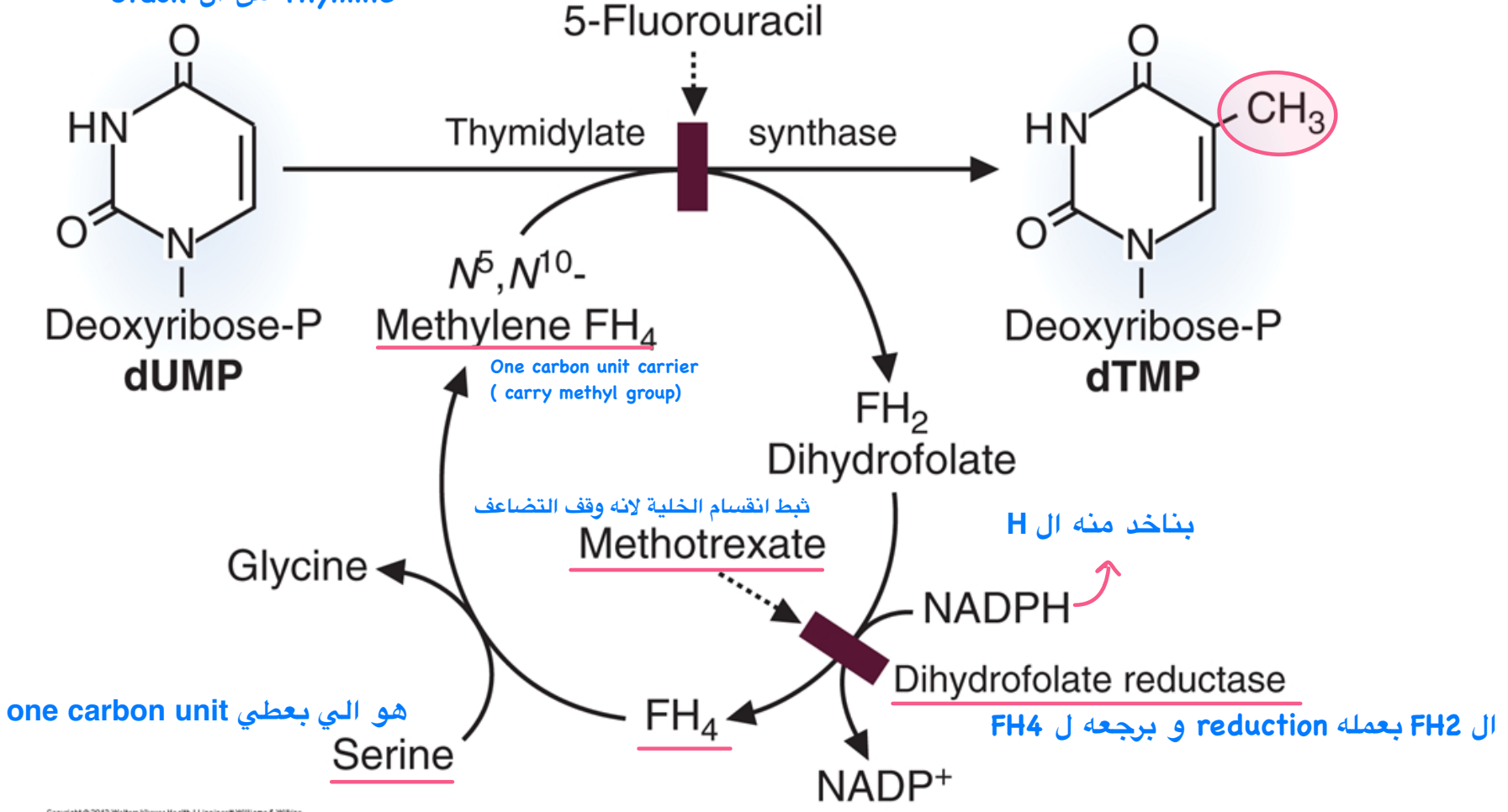
ال methotrexate يشبه ال folic acid و لكن ال affinity تاعته

اعلى ب 1000 مرة من ال Dihydrofolate

بروح يعمل amplification لل dihydrofolate reductase و

بخرب ال methotrexate يعني يبطل اله تأثير

عشان نصنع ال DNA لازم يكون عندي ال 4 قواعد  
 نيتروجينية و منهم ال Thymine و بنجيب ال  
 Uracil من ال Thymine



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\* في كمان مركب اخدناه كان one carbon carrier الي هو SAM شاييل CH3

## **Gene diminution:** عكس ال gene amplification

- It is a rare form of regulation by removing a gene or genes from the genome e.g. complete loss of all genes in red blood cells during development. ال RBC's كانت جاية من ال bone marrow فيها نواة و جينات و لكن عند ال development فقدنا كل شي
- *A gene whose expression is only needed at a particular developmental point or in a particular tissue may be shut off by gene diminution. As reticulocytes mature into red blood cells all of their genes are lost as the nucleus is degraded.*

ففي بعض الجينات بنحتاجهم بفترة معينة من ال development و بعد هيك بتروح

## 2- Transcriptional regulation.

**Chromatin remodeling**

```
graph LR; A[Chromatin remodeling] --> B[Cytosine methylation]; A --> C[Histone acetylation];
```

**Cytosine methylation**

**Histone acetylation**

**DNA regulatory regions**

```
graph LR; A[DNA regulatory regions] --> B[Basal expression elements]; A --> C[Regulated expression elements];
```

**Basal expression  
elements**

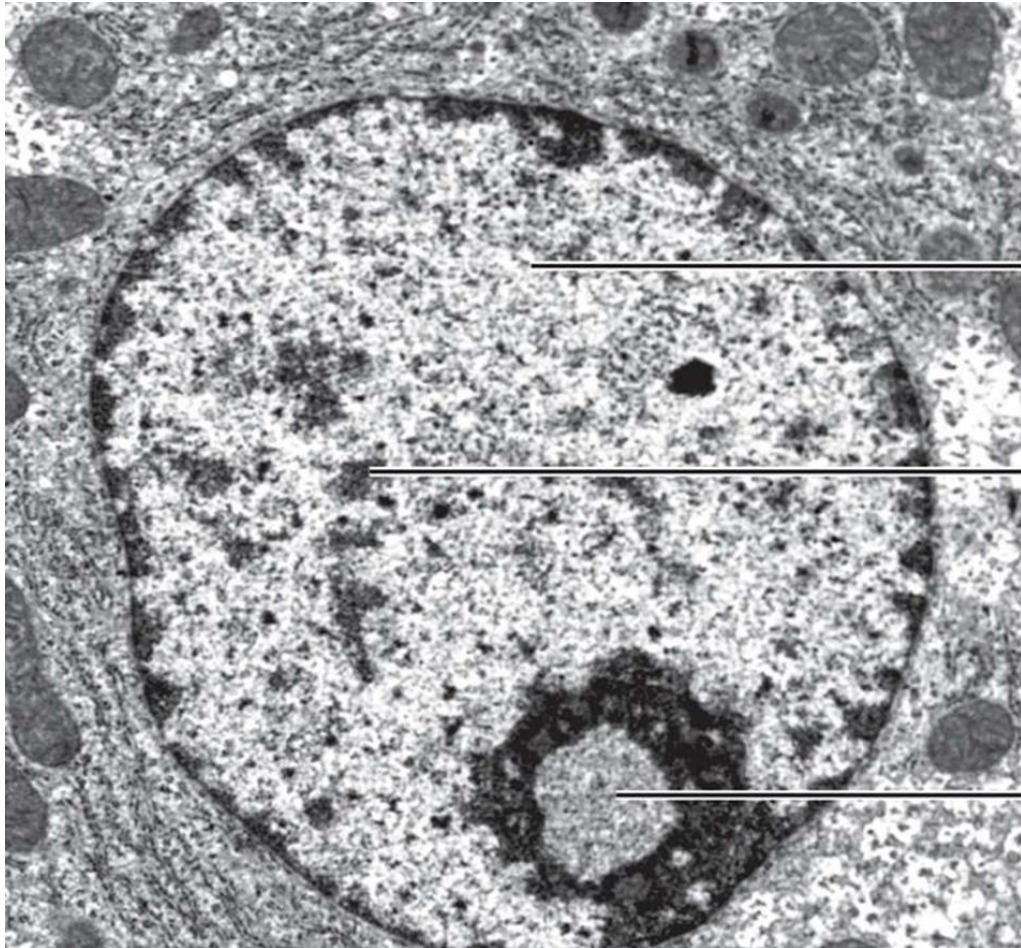
**Regulated expression  
elements**

# Cytosine methylation

- Many mammalian genes have CG- rich regions upstream of the coding region, that provide multiple sites for methylation.
- The methyl group is added by DNA methylase on both strands of DNA in 5`-CG-3` dinucleotides.

- Heavy methylation is associated with genes for which the rate of transcription is low. عمل turn off للجينات
- Transcriptionally inactive chromatin is densely packed (a highly coiled and compact structure) during interphase as observed by electron microscopic studies and is referred to as heterochromatin; transcriptionally active chromatin stains less densely and is referred to as euchromatin. مناطق غامقة مناطق فاتحة
- methylation converts the active euchromatin into inactive heterochromatin and it may result in transcriptional silencing. Reactivation occurs by demethylation. اذا بدنا نعكس بينهم بنشيل ال methyl عن ال heterochromatin و بنخليه active و العكس للثاني بنضيف methyl لل euchromatin و بصير inactive





Transcriptionally active  
methyl group و ما فيها  
euchromatin

heterochromatin  
Transcriptionally inactive  
methylated و

nucleolus

- **Heavy methylation is one of epigenetic mechanisms that marks a gene for silencing.**
- The Greek prefix *epi-* (ἐπι- "over, outside of, around") in *epigenetics* implies features that are "on top of" or "in addition to" the traditional genetic basis for inheritance. *Therefore epigenetic refers to heritable changes in gene expression that are not due to changes in the DNA sequence itself.*

# Histone acetylation

\* ال histone موجب ، اذا حظيت acetyl group عند ال N terminal رح تقل الموجبية تاعته و ما رح يمسك بال DNA و بالتالي ما رح اقدر اضغط الكروماتين و بصير ال DNA مكشوف

- **Acetylation at the N-terminal (lysine) reduces the histone positive charges & decreases the binding affinity of histones for the negative charged DNA, which allows the access of the different transcription factors to act.**

هون بنسهل عملية ال gene expression لانه بنفك ال DNA و بصير مكشوف

- **Deacetylation reverses the process.**

# DNA regulatory regions

- Each gene can be divided into coding & regulatory regions, as defined by the transcription start site.
  - In case of class II gene (transcribed by polymerase II), the coding region contains the DNA sequence that is transcribed into mRNA, which is translated into protein.
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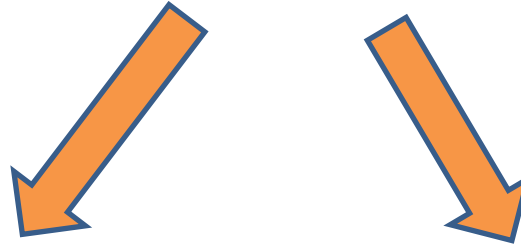
**The regulatory region consists of two classes of elements as follows:**

**A- Basal expression  
elements**

على طول لازم تكون موجودة

**B- Regulated expression  
elements  
(cis-acting elements)**

- Basal expression elements: it contains



لأنها قريبة من ال +1  
proximal element or  
تعتبر من المناطق المنظمة  
TATA box that  
directs the RNA  
polymerase II to the  
correct start site  
(+1)

The upstream element  
e.g. CAAT box or GC  
box that specify the  
frequency of initiation  
يعني رح نعمل initiation كم مرة

- **Regulated expression elements (cis-acting elements):** they are specific DNA sequences that are present on the same gene, so termed cis-elements, and are responsible for regulation of expression & include the following elements:

زي ال promoter

## Enhancers

بتزيد ال gene expression

they interact with gene regulatory proteins or trans-factors (so termed because they are produced by other genes) and increase the rate of expression (they facilitate initiation of transcription)

جاية من جينات اخرى

## Silencers

بتقلل ال gene expression

they interact with gene regulatory proteins or trans-factors and decrease the rate of expression (they inhibit initiation of transcription)

## Other regulatory elements

هاي مناطق بتتأثر بهرمون معين و بنظم عمل الجين من خلالها

They mediate response to various signals including chemicals, metals and hormones. In the latter case, it is termed the hormone response elements (HRE)