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The Hashemite University

# MOLECULAR BIOLOGY – GENE EXPRESSION AND REGULATION

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هاي المواضيع هي basics بتلزمنا حتى نفهم ال biotechnology ablication

هل كل الخلايا اللي بجسم الشخص الواحد بتحمل نفس المادة الوراثية ؟

الجواب الصح أنه كل الخلايا بكل جسمنا تحتوي نفس ال genetic material
الاختلاف بكون بال gene expression
مش كل الجينات بصيرلها expression
وبنظم هاي العملية ال gene regulation وال control mechanism الموجودة بالجين

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# AUTHORS DISCLOSURE

The authors have no actual or potential financial conflicts of interest associated with this presentation.

This presentation is directed to the students registered on the 'Pharmaceutical Biotechnology' course at the School of Pharmaceutical Sciences, the Hashemite University, Jordan. Academic year 2024/2025.

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# LEARNING OBJECTIVES

➢ **By the end of this presentation, students will be able to:**

1. Define key terms related to gene expression, including transcription, translation, and regulation.
2. Explain why the control of gene expression is essential for cellular functions.
3. Identify and describe the various levels at which gene expression can be regulated in eukaryotic cells, including chromatin, transcriptional, post-transcriptional, translational, and post-translational control.
4. Evaluate how different levels of gene expression control interact and integrate to ensure proper cellular responses to environmental cues and developmental signals.
5. Explore the implications of gene expression regulation in biotechnology and medicine, including gene therapy, cancer research, and the development of therapeutic strategies.
6. Critically analyze case studies or examples where dysregulation of gene expression is linked to specific diseases, discussing potential therapeutic approaches that target these regulatory mechanisms.

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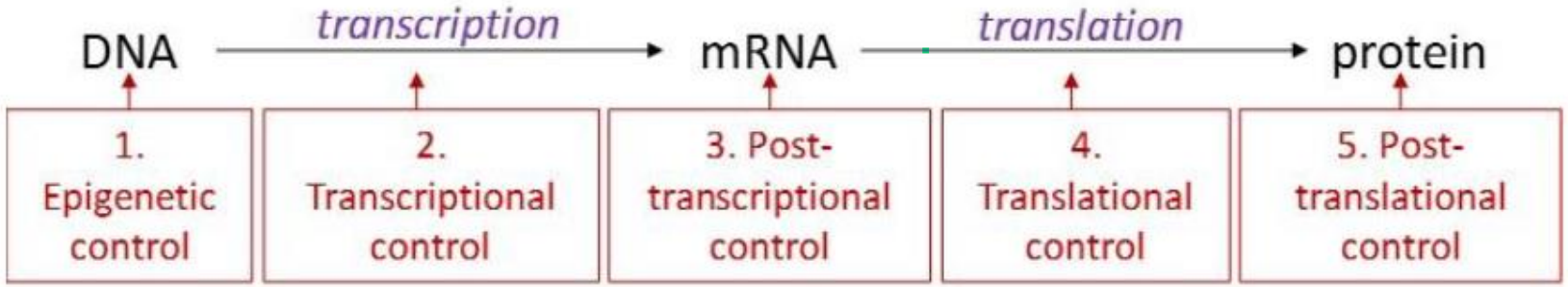
# GENE EXPRESSION AND CONTROL IN EUKARYOTES

- Each somatic cell in the body generally ***contains the same DNA***. !!
  - (A few exceptions include red blood cells, which contain no DNA in their mature state, and some immune system cells that rearrange their DNA while producing antibodies.)
- ***If each cell has the same DNA, how is it that cells differ in their structure and function? Why do cells in the eye differ so dramatically from cells in the liver?***
- In general, the genes that determine whether you have green eyes or brown hair, or how fast you metabolize food are the same in eye cells and liver cells, even though these organs function quite differently!

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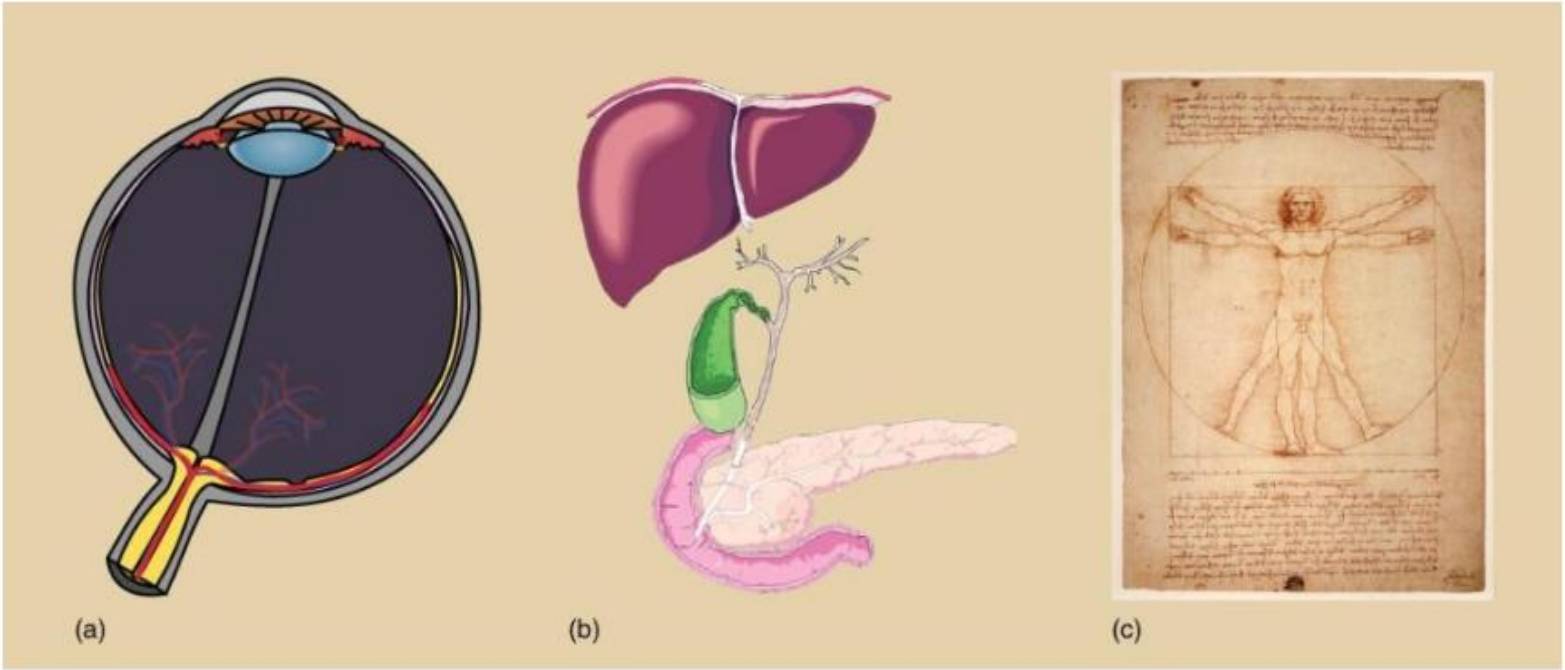
# GENE EXPRESSION AND CONTROL IN EUKARYOTES

ينتج الاختلاف من عملية ال expression

- The genetic content of each somatic cell in an organism is the same, but not all genes are expressed in every cell. The control of which genes are expressed dictates whether a cell is: **(a) an eye cell or (b) a liver cell. It is the differential gene expression patterns that arise in different cells that give rise to (c) a complete organism.**

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# GENE EXPRESSION AND CONTROL IN EUKARYOTES

## Control of Gene Expression

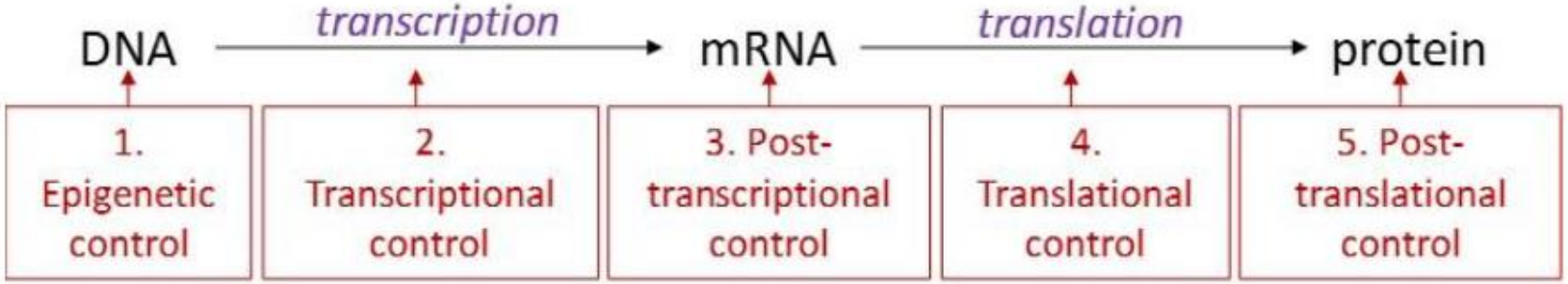
- **Why Control is Important**:
  1) Allows cells to respond to environmental changes.
  2) Regulates development, cell differentiation, and maintains homeostasis.
- **Key Mechanisms**: The control or regulation of gene expression in eukaryotic cells can take place at different levels:
  - Chromatin level
  - Transcriptional Control
  - Post-Transcriptional Control
  - Translational
  - Post-Translational Control.
  - Post-translational

لازم الخلية يكون عندها مرونة للتحكم بال expression of gene حسب حالتها وحسب ال environment اللي حواليها

لانه هون بصير تباين بأنواع الخلايا لانه ال expression كان مختلف بينهم

وين بالضبط(بأي مرحلة) الخلية بتقدر تعمل control

الطريقة التي يترتب فيها الجين داخل الخلية كتير مهم في عملية ال expression

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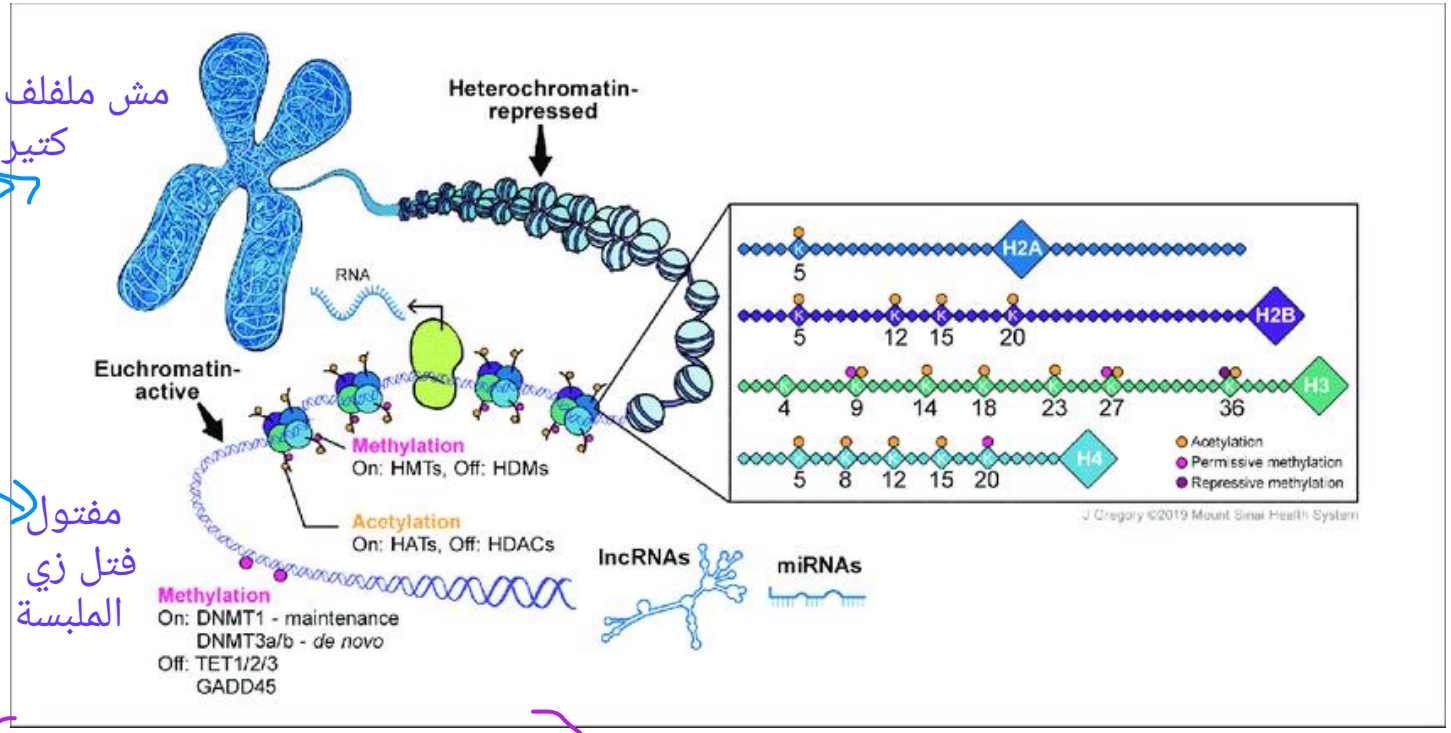
# Gene Expression And Control- Regulation At The Chromatin Level

- Gene expression is regulated at the chromatin level through three main mechanisms:

two form of chromatin

1. **Chromatin condensation**: Euchromatin, which is less compact, is associated with actively expressed genes, while heterochromatin, which is more compact, prevents gene expression. Heterochromatin can be constitutive (consistent across cells) or facultative (tissue-specific).
2. **Supercoiling**: DNA's negative supercoiling, controlled by enzymes like topoisomerases, alters access for transcription proteins.
3. **Methylation**: Methylation of cytosine bases silences genes, while unmethylated genes remain active for transcription.




add methyl group on cytosine

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# Gene Expression And Control- Epigenetics Regulation

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- **Epigenetics:** is defined as the study of heritable changes in gene expression without altering DNA sequence.
- It studies the set of mechanisms that cause the change from euchromatin to heterochromatin and vice versa.
- **Mechanisms**:
  - **DNA Methylation**: Silences genes by adding methyl groups to DNA.
  - **Histone Modification**: Alters chromatin structure to activate or repress genes.
  - **Non-coding RNAs**: miRNA and lncRNA can regulate gene expression at various stages.

- **Epigenetics is responsible for several processes such as genomic imprinting or X chromosome inactivation, as well as for the development of some cancers and other diseases.**

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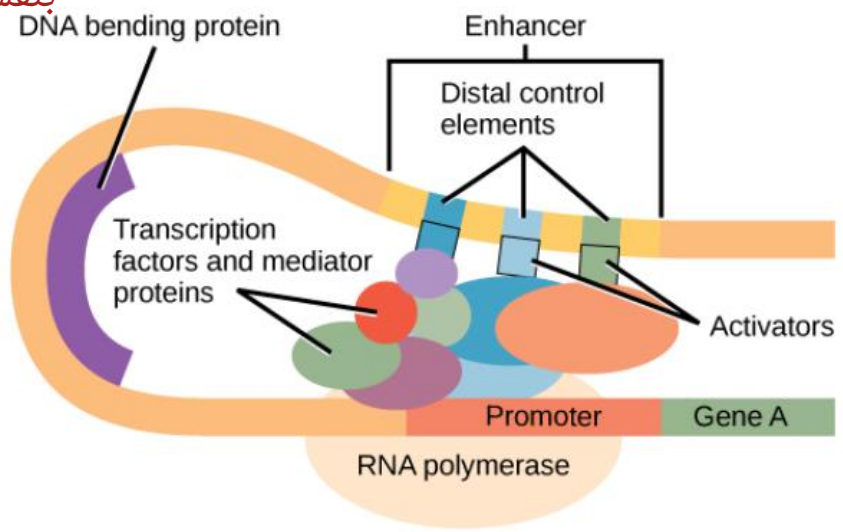
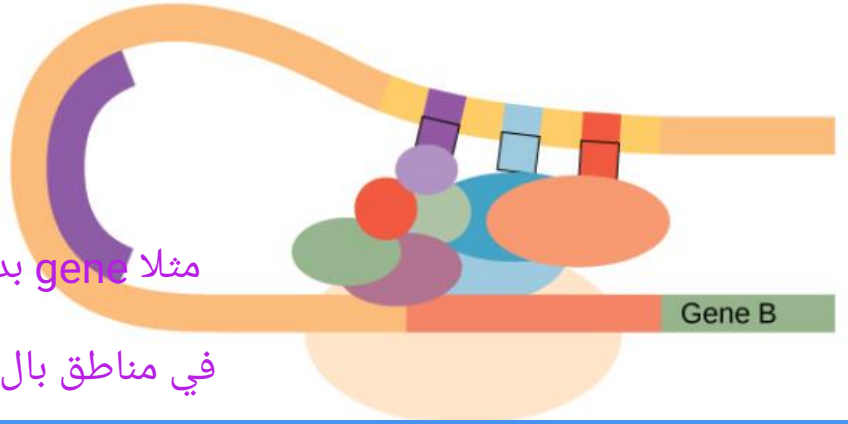
transcription : DNA is transcribed to mRNA

# Gene Expression And Control- Regulation At The Transcriptional Level

- **Cis Elements**: Regulatory sequences on the same DNA strand located near the genes they regulate, including:
  - **Promoter**: Initiates transcription, e.g., TATA box guides RNA polymerase.
  - **Enhancers**: Boost transcription by binding coactivators (can be tissue-specific or respond to external signals).
  - **Silencers**: Suppress transcription by binding transcription factors.
- **Trans Factors**: Transcription factors that bind to cis elements, classified as:
  - **General**: Form pre-initiation complexes with RNA polymerase.
  - **Sequence-specific**: Act as activators or repressors, e.g., zinc fingers, leucine zippers, helix-turn-helix motifs.




اسمهم cis لأنهم قريبين أو بنفس مكان الجين

تعزز

عكس ال Enhancers ال silencers

ال silencers هي cis element تمنع عملية ال transcription

factor mobile

مثلا gene بده يصيرله transcription ما بتبلش الانزيمات ( DNA polymerase ) مباشرة عملية ال transcription

لازم يكون في RNA primer

في مناطق بال DNA اسمها promoter تسبق الجين تسمح ل ال RNA يبني فوقها حتى تبلش عملية ال transcription

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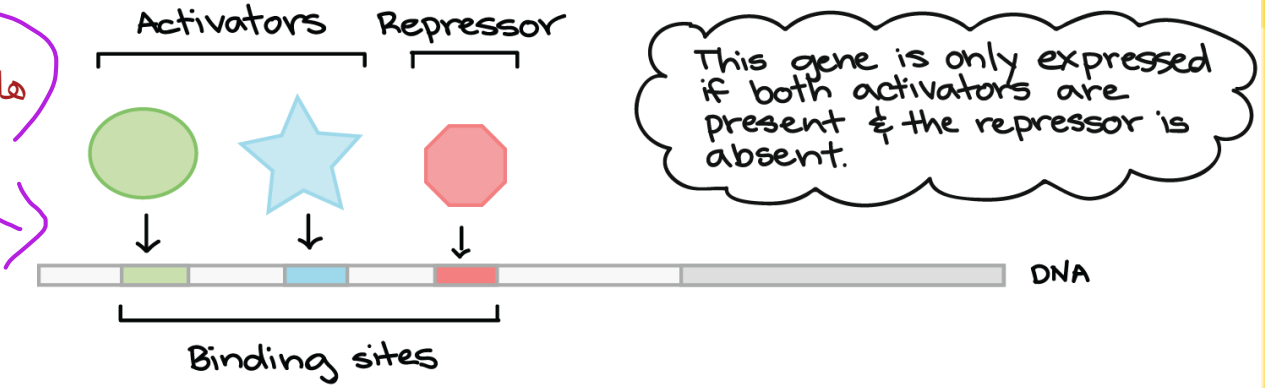
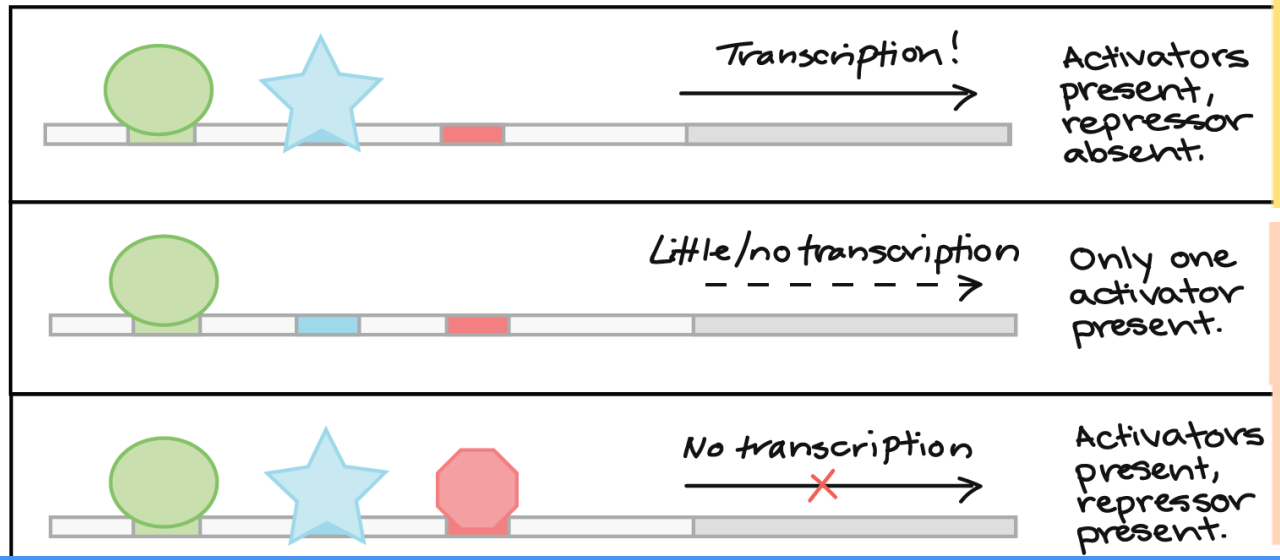
# Gene Expression And Control- Regulation At The Transcriptional Level

شرح عن السلايد اللي بعد هاد the post transcription level

هاد ال diagram ببسط الفكرة




اهم سيناريو في هاي الحالة ال alternative splicing و mRNA transport ال
حكينا أنه عشان احصل ال final mRNA لازم يصير splicing أنه ال non coding ينشالو والخلية تاخد ال exon وتتخلص من intron
بتقدر الخلية حسب حاجتها تختار شو ال exon اللي تجمعهم مع بعض بناءا عليه بكون في تصنيع اكتر من نوع من البروتين بس من جين واحد بحيث انها تتحكم بعمل splicing ال
مثال عليه ال calcitonin gene

السيناريو التاني ال mRNA transport يتكون ال mRNA في ال nucleus بس عشان يصير له translation يستخدم الرايبوزوم اللي بالسايتوبلازم فهون الخلية لازم تسهل عملية ال mRNA transport للمكان اللي لازم يصير فيه translation فالخلية ممكن تسهل هاد الموضوع او تمنعه

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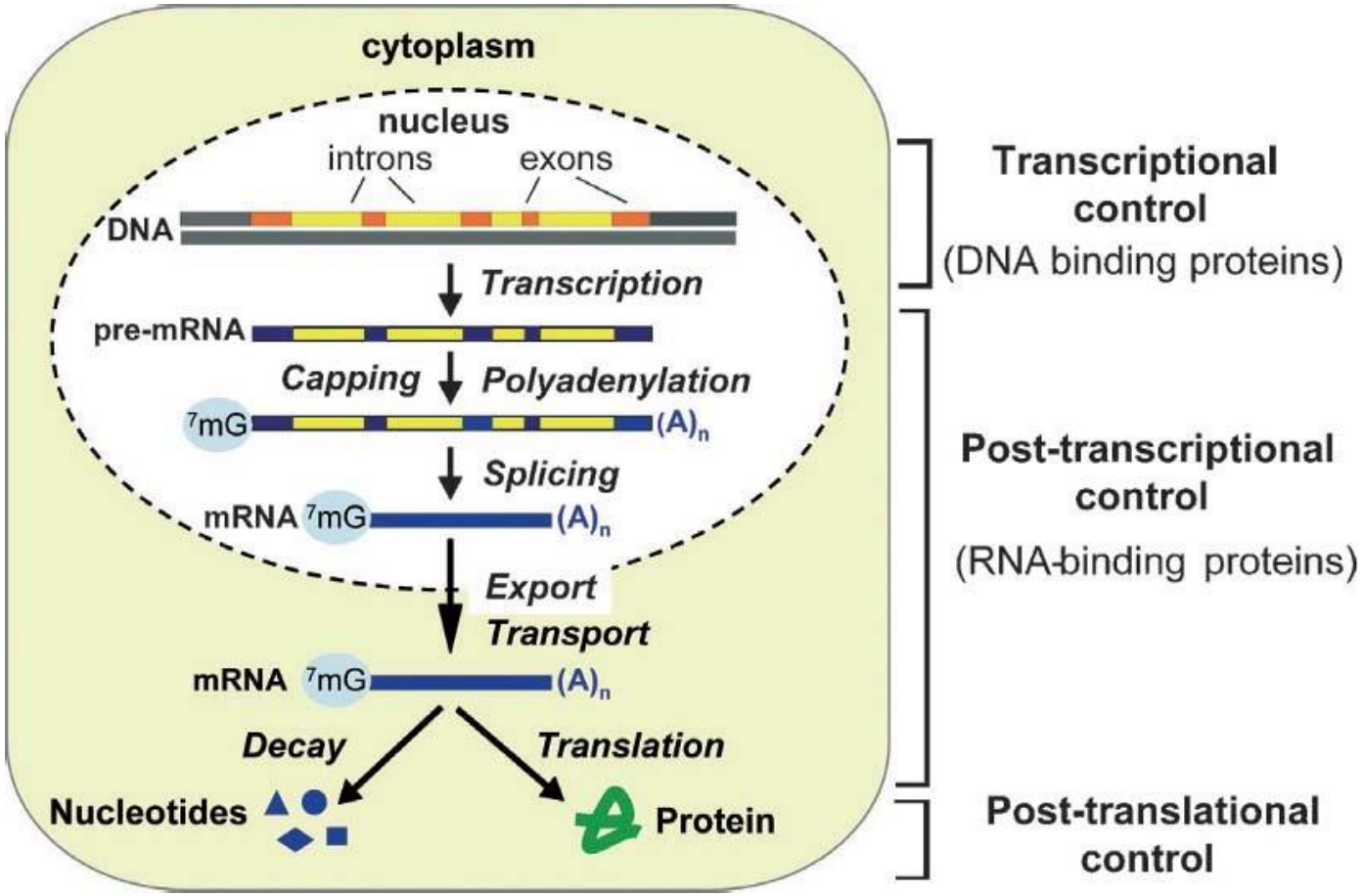
هاي العملية بتكون بين ال transcription يعني تكون ال mRNA وقبل الوصول إلى عملية ال translation

# Gene Expression And Control- Regulation At The Post-Transcriptional Level

- **Alternative Splicing**: Allows one gene to produce multiple proteins by selectively removing or retaining introns. Example: Calcitonin gene produces calcitonin in the thyroid and Calcitonin gene-related peptide (CGRP) in the hypothalamus.
- **mRNA Transport**: Only about 5% of mRNA is transported from the nucleus to the cytoplasm. Proteins like SR (Serine/Arginine-rich Proteins) promote mRNA transport, while hnRNPs (Heterogeneous Nuclear Ribonucleoproteins) inhibit it.

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# Gene Expression And Control- Regulation At Translational Level


اول ما تبدأ عملية ال translation ممكن هاي العملية تعمل degradation ل mRNA

1. **Control of mRNA Degradation**: mRNA's half-life varies widely and is influenced by the length of the poly-A tail and sequences in the 3'UTR region (e.g., AU-rich elements).
2. **Cell Tracking Control**: mRNA localization in the cytoplasm is controlled by "zip codes" in the 3'UTR, with transport facilitated by motor proteins and microtubules.

حتى يتحرك ال mRNA ويتم التعرف عليه بكون عليه زي label
وهون الخلية بتتحكم وين يروح

3. **Control of Translation Initiation**: Mechanisms include – phosphorylation of eIF2 (initiation factor 2) under stress, to inhibit translation; leading to a broad reduction in protein synthesis, conserving resources, and helping the cell cope with stress. As well as specific mRNA elements like the iron response element (IRE) in ferritin mRNA. The iron response element (IRE) in ferritin mRNA enables selective control of translation based on iron levels; IRP binding to IRE under low iron blocks translation, while iron presence releases IRP, allowing ferritin synthesis.

ممكن الخلية تمنع ال translation أو تتحكم فيه

4. **RNA Interference**: miRNAs can block translation, control mRNA stability, and prevent splicing or cytoplasmic transport by forming double-stranded RNA.

ممكن يعمله sailant بشكل مباشر

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المرحلة الأخيرة التي تسبق ال release لل active protein

# Gene Expression And Control- Regulation At The Post-Translational Level



- Proteins undergo modifications like glycosylation, phosphorylation, or acetylation, influencing their function and gene expression control.
- Different modifications on the same protein can lead to distinct functional outcomes (e.g., neuropeptides processed by various proteases).
- Polyproteins, like insulin, are processed through cleavage to produce active forms.
- Some enzymes are activated by protease cleavage (e.g., chymotrypsin).
- Protein modifications in pharmaceuticals enable controlled activation of therapeutic enzymes and improve monoclonal antibody stability and efficacy, crucial for effective treatments.
  - Therapeutic Enzymes Activation: In pharmaceuticals, enzymes like pro-drug enzymes are often modified or cleaved to activate their therapeutic form. For instance, chymotrypsin's activation by protease cleavage serves as a model for similar controlled activation in drug formulations.
  - Monoclonal Antibody Stability: Glycosylation and other modifications in monoclonal antibodies enhance stability, efficacy, and reduce degradation, making them more effective for therapeutic use in conditions like autoimmune diseases and cancer.

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البروتين قبل ما يروح على المكان اللي لازم يشتغل فيه بصيرله activation وفي طرق كتير حسب نوعه ممكن ( acetylation , phosphorylation ...)

ف ممكن ال gene expression process ل protein معين تتم كل الخطوات بشكل كامل بس يكون ال control أو dis function

أنه عنده مشكلة في الانزيمات المسؤولة عن ال activation للبروتين وال modification

عشان هيك مهم نعرف شو بصير بالخلية حتى نحدد مكان المشكلة ونحلها

# IN-CLASS GROUP ACTIVITY



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# ACTIVITY TITLE: "GENE EXPRESSION IN ACTION: REAL-WORLD APPLICATIONS IN PHARMA"

- **Duration:**
  - 15-20 minutes
- **Objective:**
- Students will explore various applications of gene expression in pharmaceutical biotechnology, specifically in drug discovery, production of therapeutic proteins, gene therapy, and diagnostic tools.
- **Instructions:**
  - **Students will be divided into small groups** of 3-4 members each.
- **Each group will be assigned to a specific application area** related to gene expression:
  - Group 1: **Drug discovery and development**
  - Group 2: **Production of therapeutic proteins (e.g., insulin, monoclonal antibodies)**
  - Group 3: **Gene therapy**
  - Group 4: **Diagnostic tools (e.g., biomarkers, PCR-based tests)**

- **Tasks for each group**:
  - **Identify** how gene expression is used in their assigned area.
  - **Discuss real-life examples** or current products in their area.
  - **Brainstorm potential challenges** (e.g., costs, scalability, regulatory concerns) and propose one solution.
- **Present findings**:
  - Each group will share a brief summary of their findings (2-3 minutes) with the class.
- **Class discussion**:
  - After presentations, a class discussion on how these applications impact healthcare and the pharmaceutical industry. Consider asking, "Which application has the most potential for future development?"

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# THE END …

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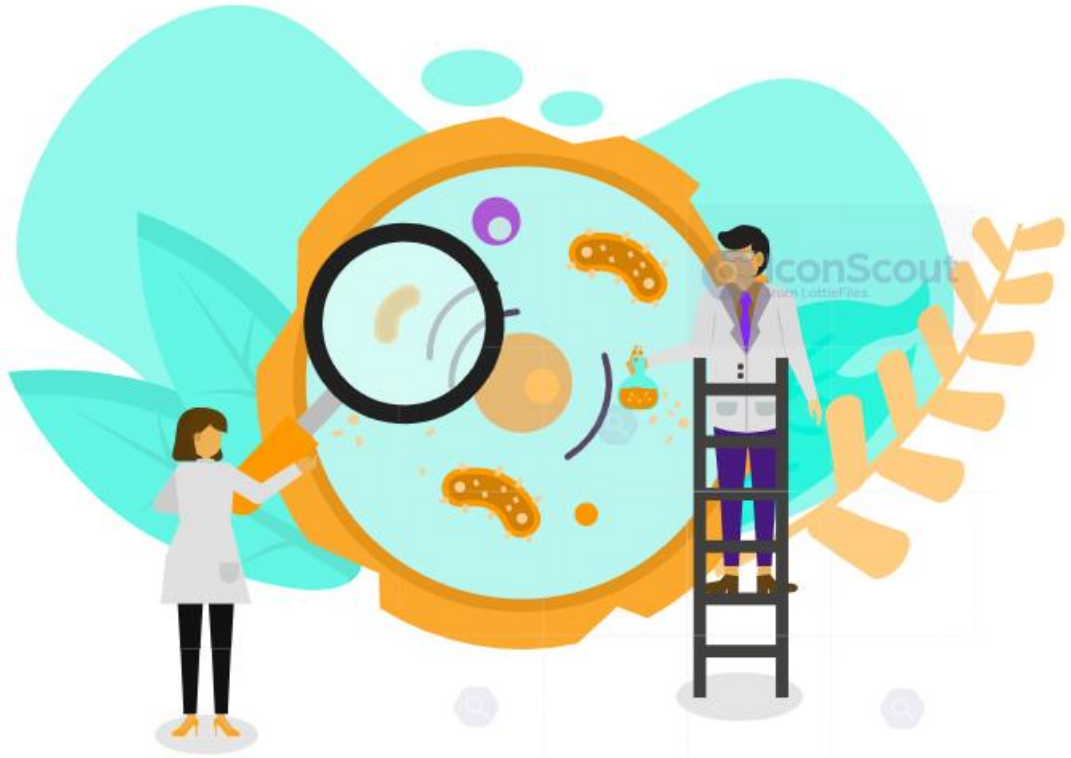
## Any questions? ☺



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