

# Gene expression in eukaryotes

## Lecture 17

SLE254 Genetics and Genomics  
Concepts of Genetics (11<sup>th</sup> edition)

Chapter 17 pages 451-478

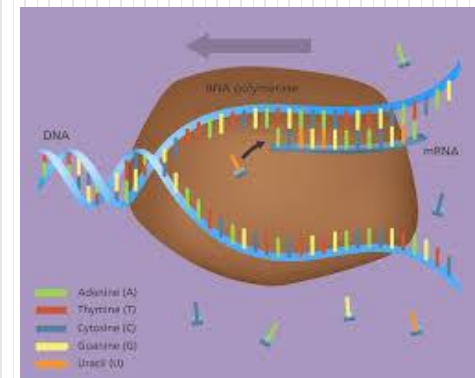
Concepts in Genetics (12<sup>th</sup> ed)

Chapter 17 pages 432-449

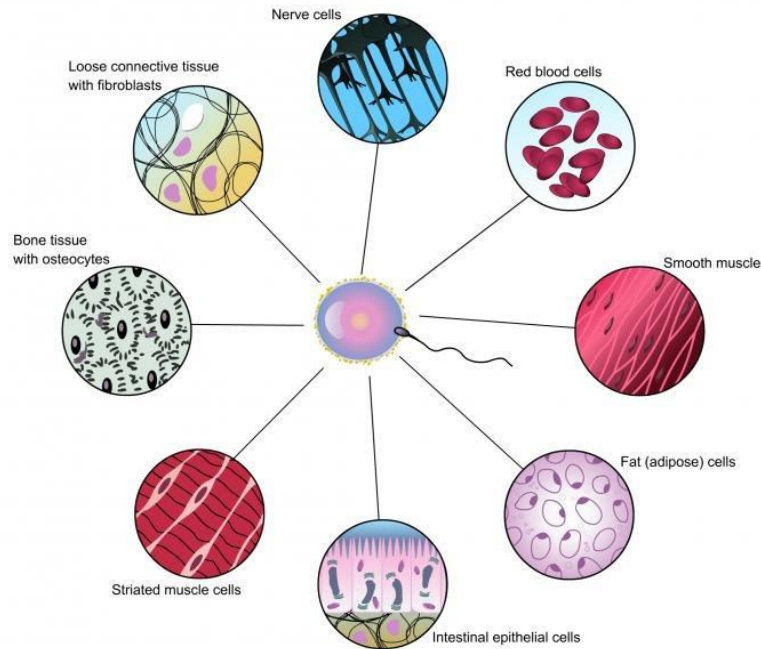
He's differentiating from us Rita.



**GENE EXPRESSION**  
PARENTS WON'T ALWAYS UNDERSTAND



# Multicellular = Stringent Gene Expression Regulation

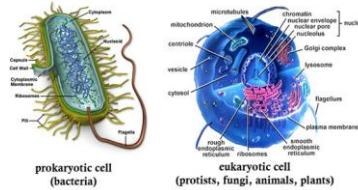


Eukaryotic gene expression is highly controlled to express required levels of gene products:

- At specific times
- In specific cell types
- And in response to changes in the environment.

## Prokaryotic gene expression

- Many genes controlled by a single promoter (Operon)
- Transcription initiation control (Activators, repressors)
- Transcription progression control (Attenuation or Riboswitches)
- Less DNA = less packaging
- No nucleus = no transport
- No mRNA splicing



## Eukaryotic gene expression

Single genes controlled by a single promoter

- Transcription initiation control (Activators, repressors)
- Lots of DNA = complex packaging = added gene regulation
- Has nucleus = transport control
- Post transcriptional modifications (mRNA splicing, cap and poly A tail)
- Post translational modifications (digestion, glycosylation, phosphorylation)

# Eukaryotic Gene 'Regulation'

Initiation: On  
Termination: Off

And every level in  
between – think of it as  
adjusting the biological  
'volume' depending on  
the cells requirements

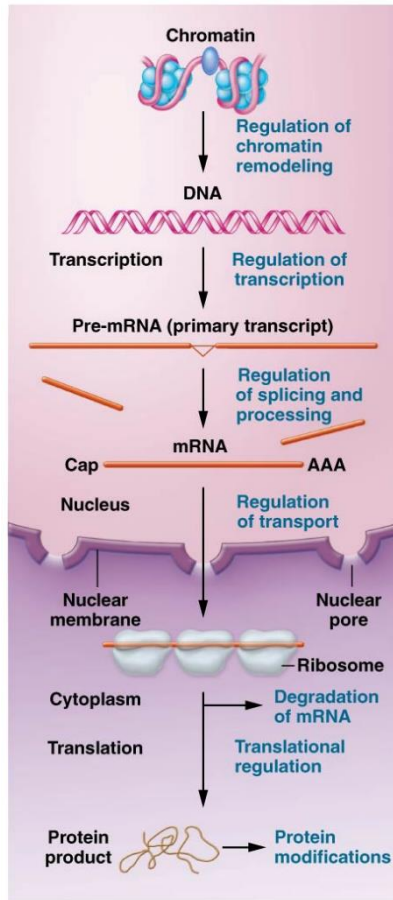
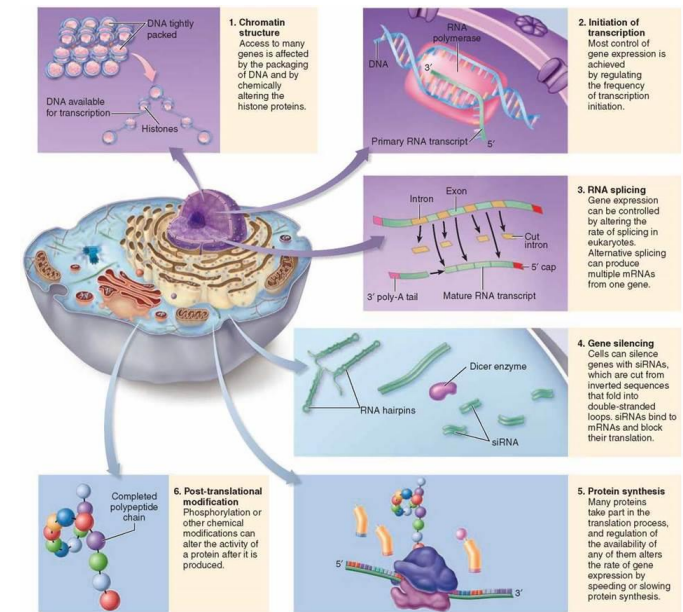


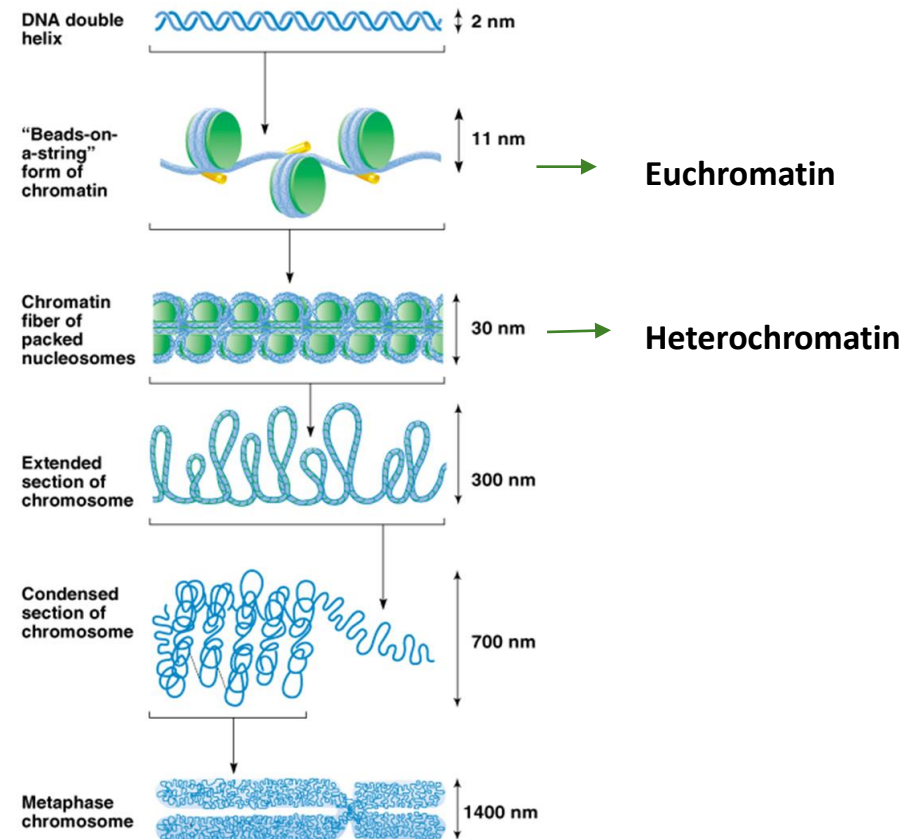
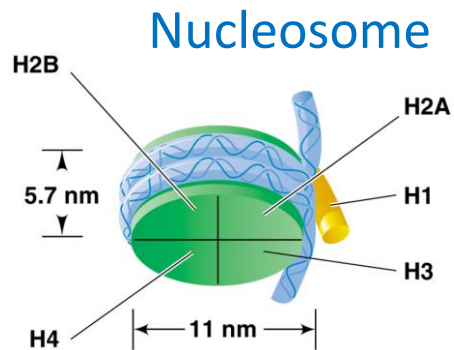
Figure 17-1



<https://schoolbag.info/biology/living/92.html>

# DNA Structure can regulate gene expression

- Chromatin remodelling
- Histone remodelling
- DNA modifications

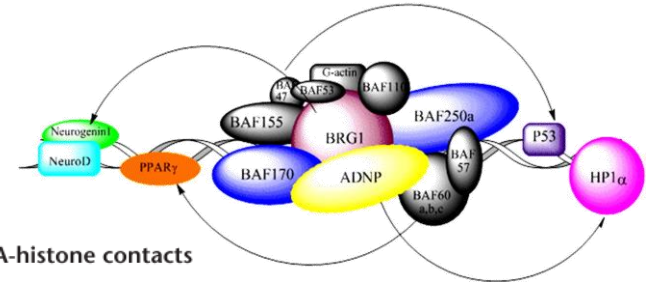


# 1. Chromatin remodelling

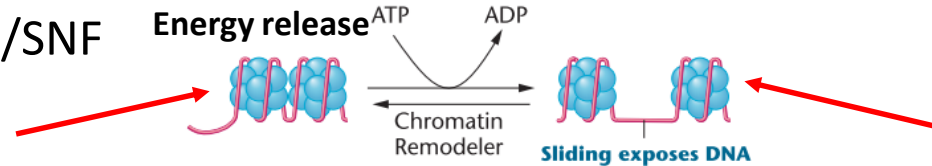
Opens up regions of the chromatin for association with transcription machinery

- Involves the action of **chromatin remodelling** complexes e.g. SWI/SNF
- Complexes use **ATP** to:
  - Loosen the attachment between histones
  - Loosen the DNA strand from the nucleosome core
  - Disrupt the nucleosome core

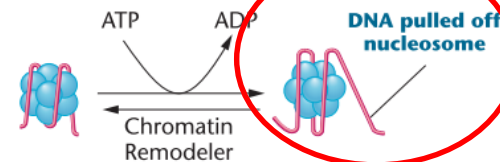
The SWI/SNF chromatin remodeling complex



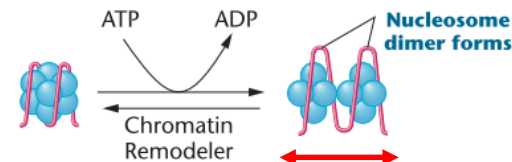
(a) Alteration of DNA-histone contacts



(b) Alteration of the DNA path

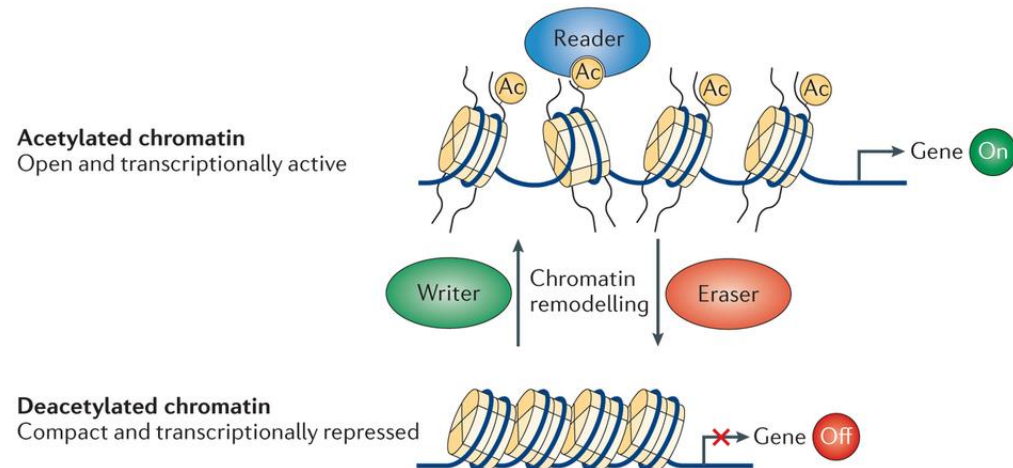
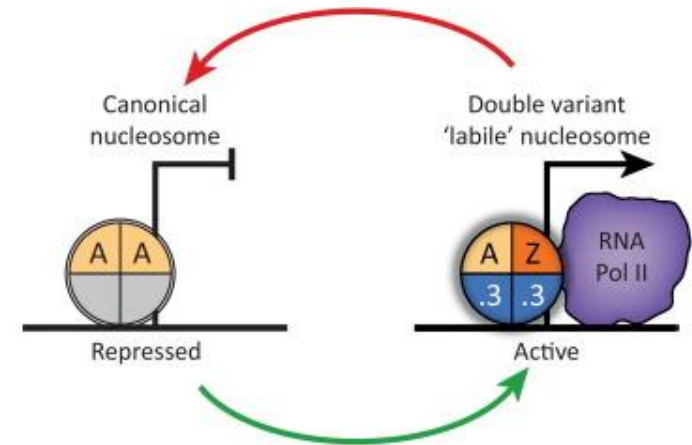


(c) Remodeling of nucleosome core particle



## 2. Histone remodelling

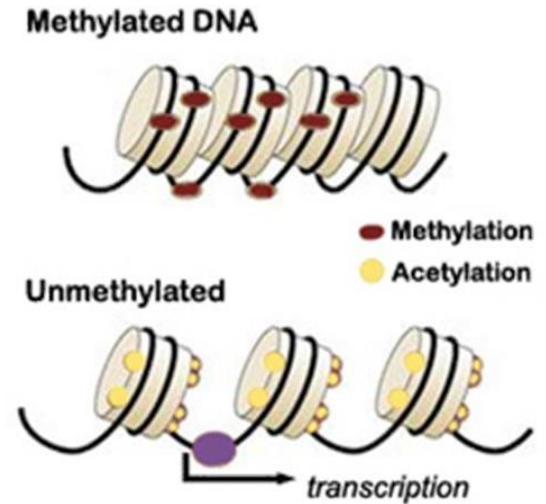
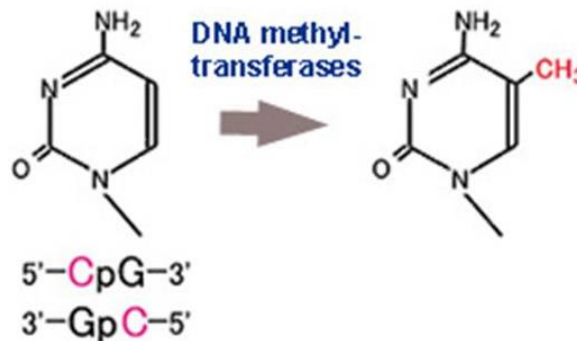
- Nucleosome composition
  - H2A is considered a core histone, along with H2B, H3 and H4.
  - **H2AZ is a variant that exchanges with conventional H2A core protein**
  - Important for gene activation/silencing
- Histone modification
  - Addition of acetyl, methyl or phosphate groups
  - **Acetylation**: allows proteins to interact with exposed DNA to activate gene transcription





### 3. DNA modification: note: Direct DNA modification not protein modification

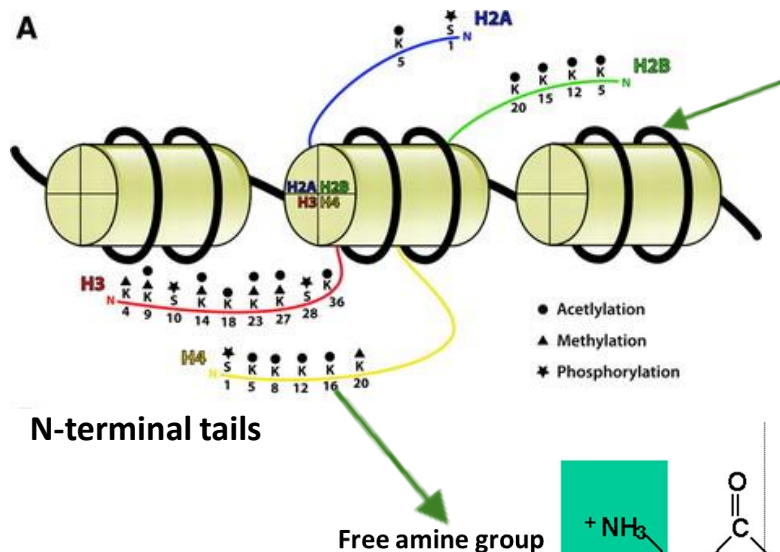
- Addition or removal of methyl groups to **nucleotide bases**
- Methylation is abundant on inactivated X-chromosomes.
- These changes can be heritable
  - Epigenetic effects





# Summary DNA structure and gene expression

Nucleosome: 147 base pairs of DNA that encircle an octameric core of histone proteins



**Bound DNA**

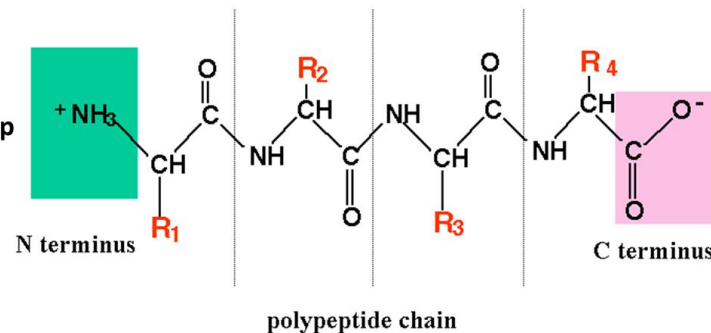
The N-terminal tails of these histone proteins are subject to a variety of covalent modifications:

**-acetylation**

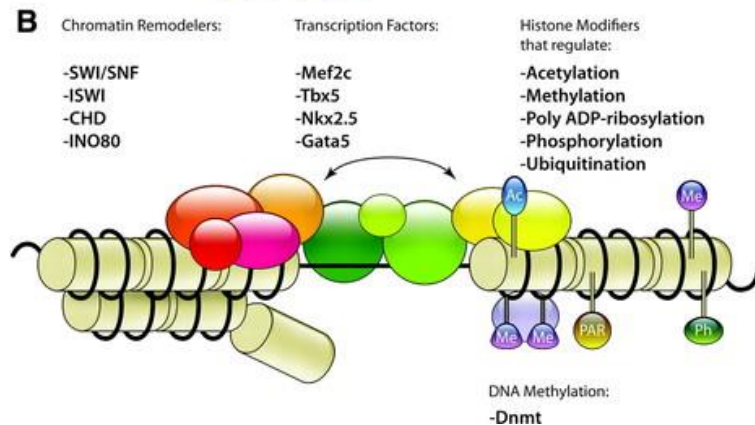
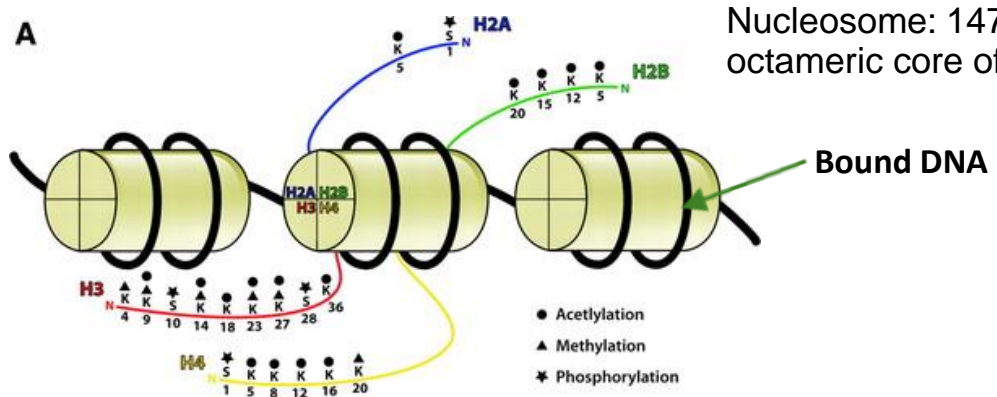
**-methylation**

**-phosphorylation**

-numbers indicate position of modified amino acids



# Summary DNA structure and gene expression



The N-terminal tails of these histone proteins are subject to a variety of covalent modifications:

**-acetylation**

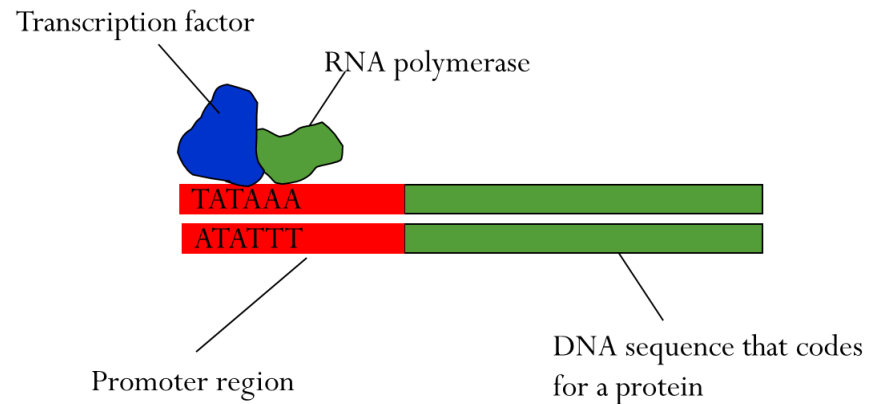
**-methylation**

**-phosphorylation**

-numbers indicate position of modified amino acids

# Eukaryotic transcription *initiation*

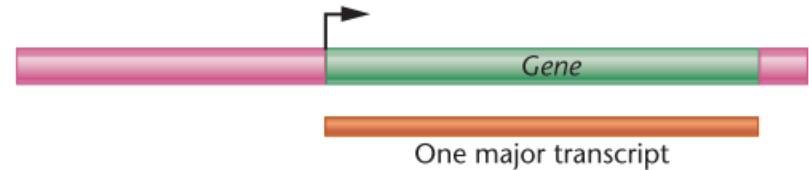
- **Promoters**
  - Focused or dispersed
- **Enhancers/Silencers**
  - *trans*- and *cis*- acting sites.
- **Transcription factors**
  - Helix-turn helix, Zinc-fingers, bZIPs
- **Activation/Repression**
  - Enhanceosome



# Promoters

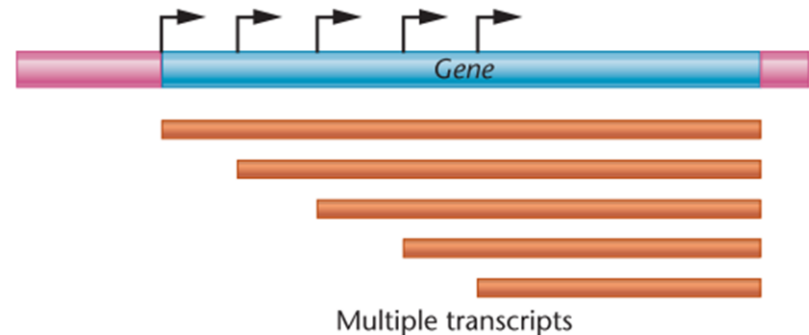
- 5' Region which binds the transcription machinery
  - **TATA box**
- Contains many other important binding sites that enhance transcription
- They can be either **focused** or **dispersed**

(a) Focused promoter



A **focused promoter** contains either a single transcription start site or a distinct cluster of start sites over several nucleotides

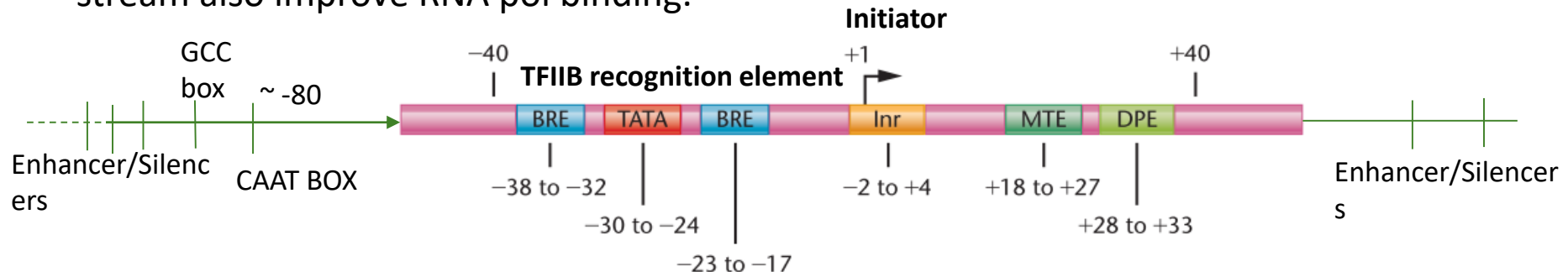
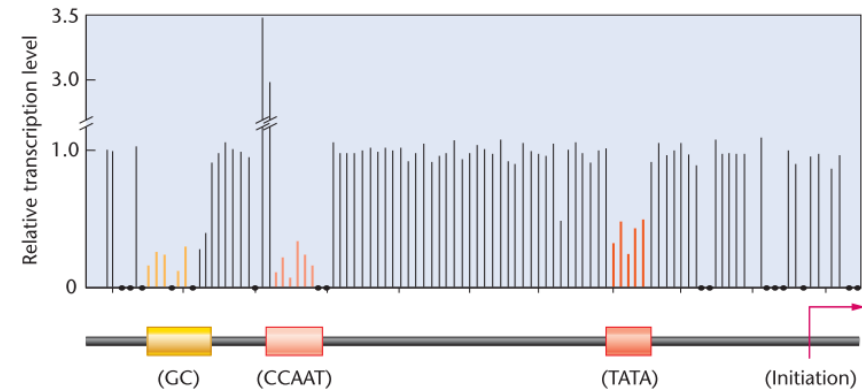
(b) Dispersed promoter



A **dispersed promoter** is a region of DNA that facilitates the transcription of a particular gene, where this promoter region contains several transcription start sites over 50-100 nucleotides

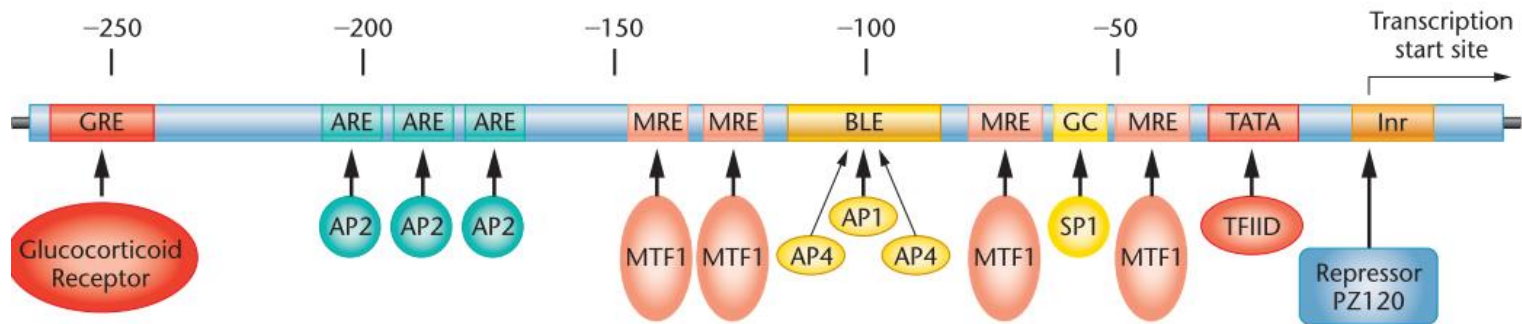
# Core promoter

- Contains many conserved DNA sequence elements that are required for proper binding and positioning of RNA polymerase
  - Almost always have TATA box, BRE, Inr domains.
  - Many have MTE, DPE, GCC-box and CAAT box domains.
- Enhancer and Silencer regions up and down stream also improve RNA pol binding.



# Enhancer and Silencer regions

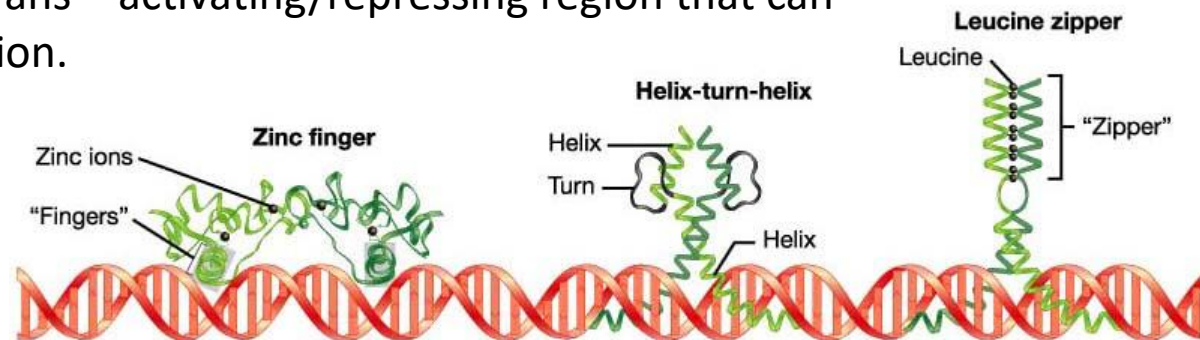
- *cis*-acting sites that are bound by specific *trans*-acting factors called transcription factors (TFs, often called response elements).
- TFs that activate transcription = activators- recruit RNAPol.
- TFs that reduce transcription = repressors- block recruitment of RNAPol II.



Promoter and enhancer regions of the Human Metallothionein IIA gene

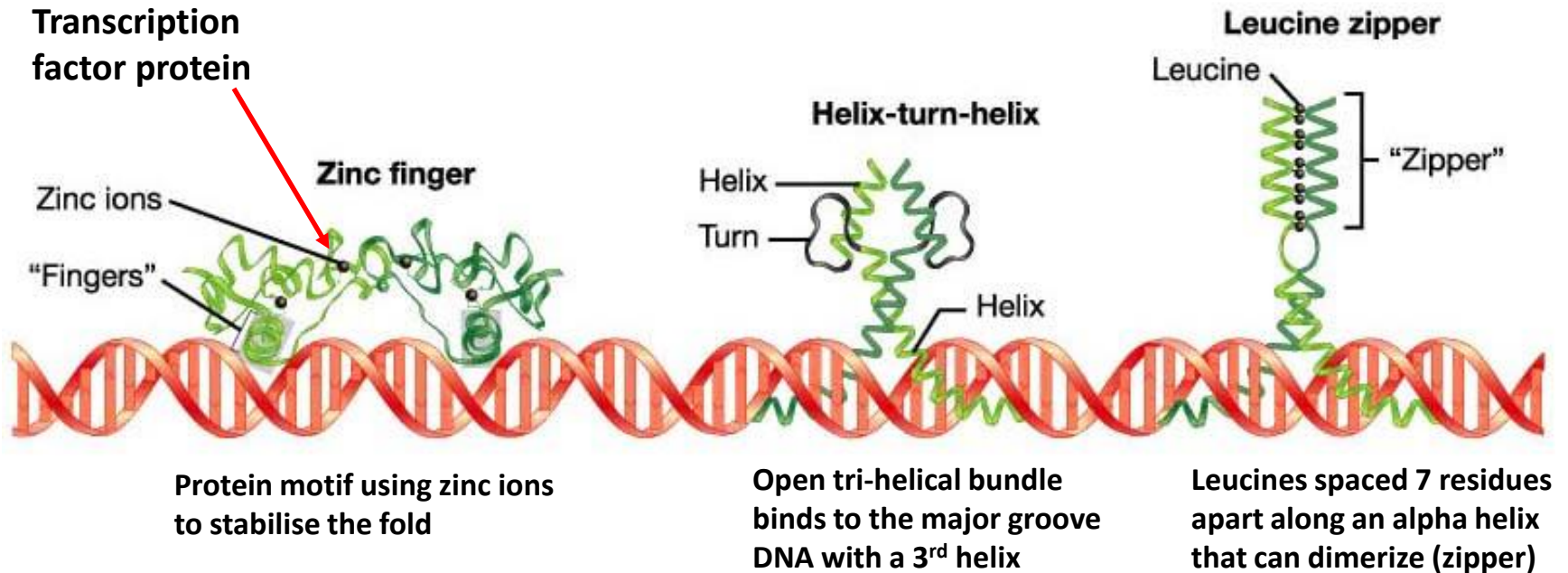
# Binding domains of transcription factors

- There are three main types of **DNA binding domains**
  - Zinc finger
  - Helix-turn-Helix
  - Leucine zipper (bZIP)
- These domain regions of the TFs bind to the *cis*-acting sites present within promoters and enhancer/silencer regions.
- The other domain acts as a trans – activating/repressing region that can activate or repress transcription.



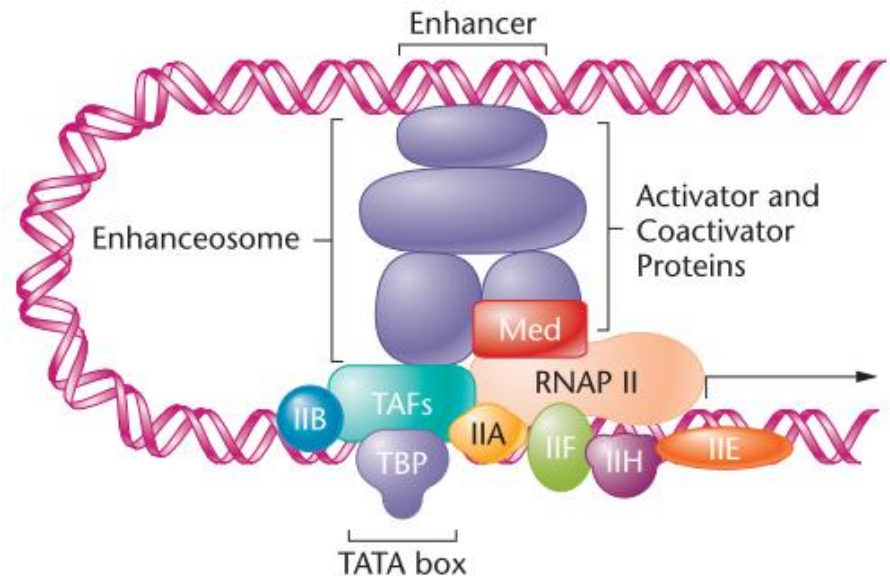


# Binding domains of transcription factors- sequence recognition and basic structure



# Enhanceosomes

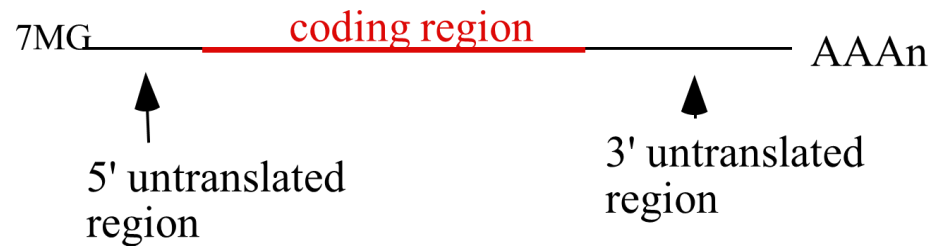
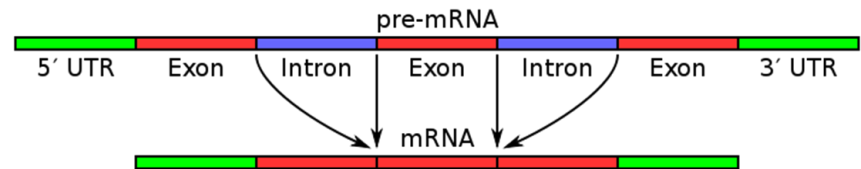
- *Trans*-acting sites on TFs can bind to co-activators
- Can cause DNA to bend and form an Enhanceosome.
- Can increase the efficiency of RNA polymerase binding and transcription initiation.



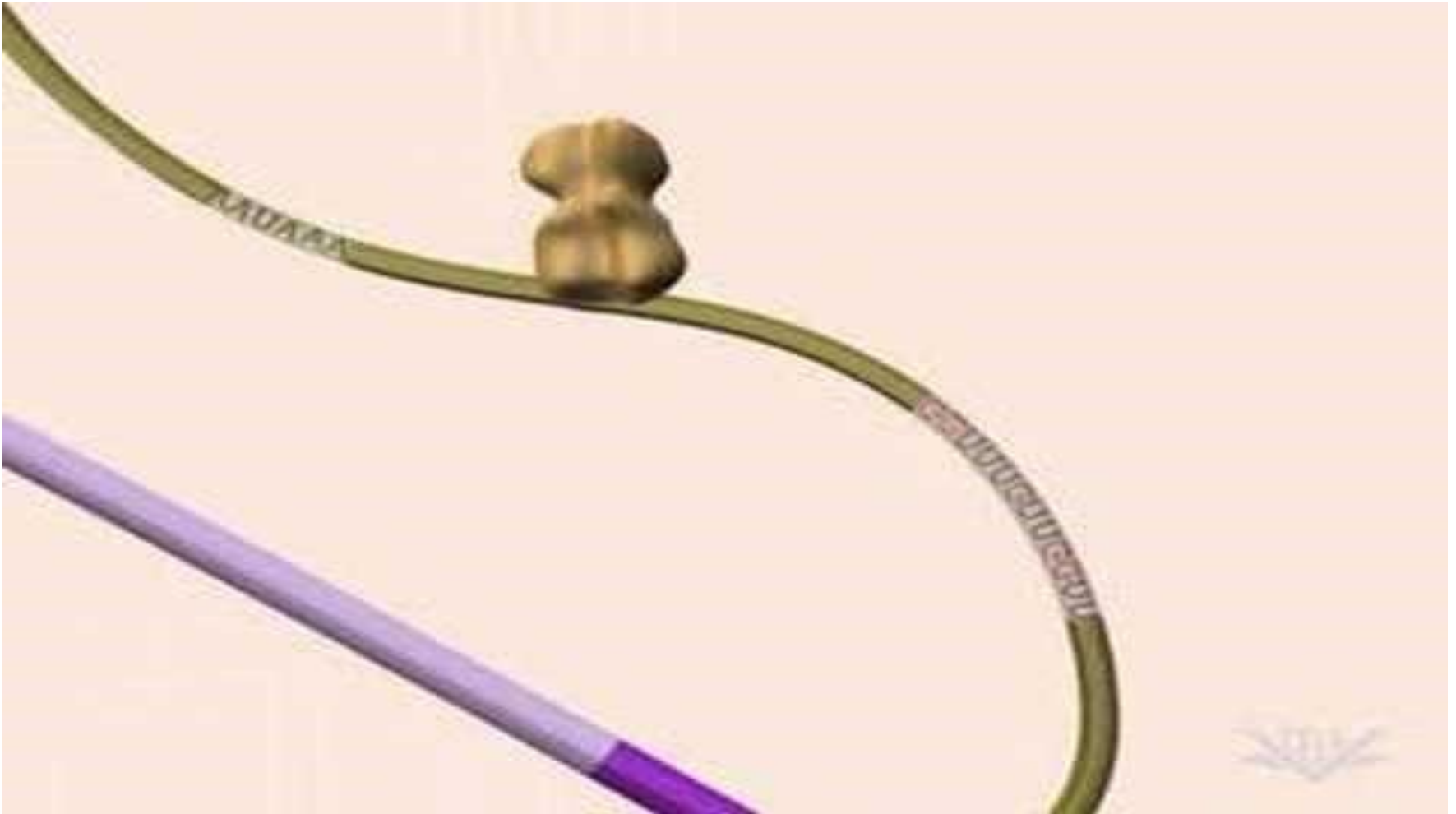
The **enhanceosome** is a higher-order protein complex assembled at the enhancer and regulates expression of a target gene.

# Post-transcriptional gene regulation

- RNA stability
  - Transport, 5'Cap, polyA tail.
- RNA splicing
  - Splicosomes
- RNA silencing

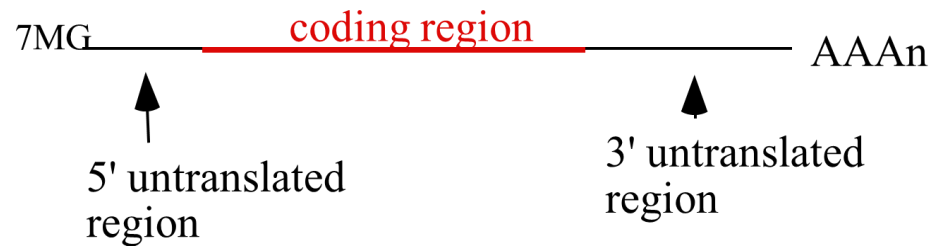
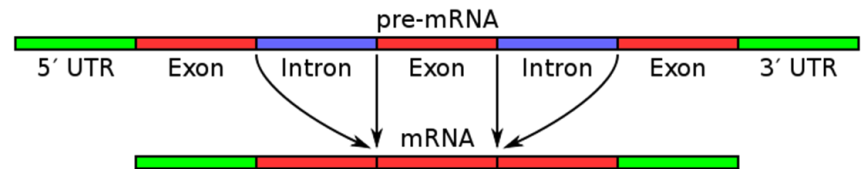


<https://youtu.be/YjWuVrzvZYA>

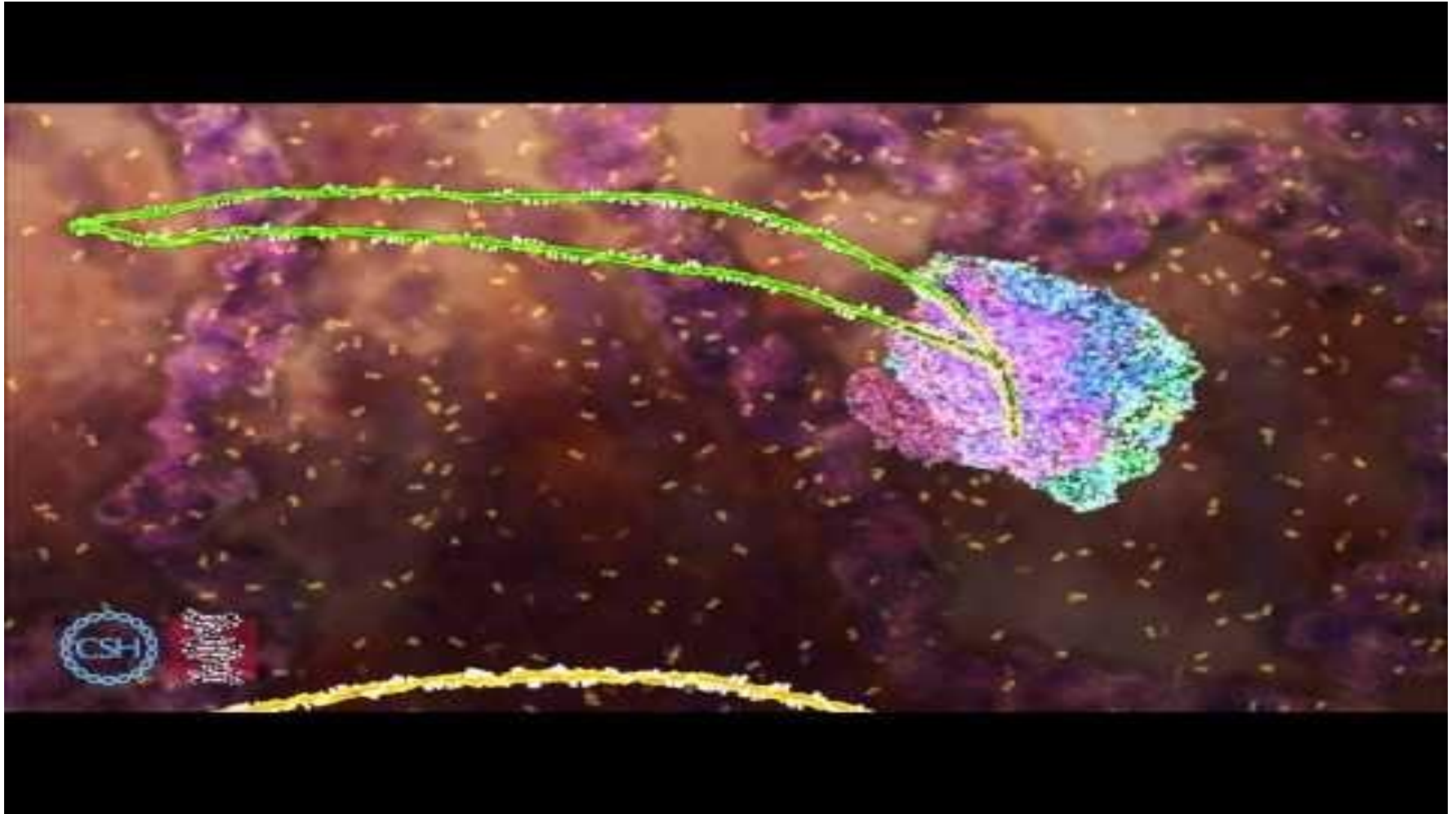


# Post-transcriptional gene regulation

- RNA stability
  - Transport, 5'Cap, polyA tail.
- RNA splicing
  - Splicosomes
- RNA silencing

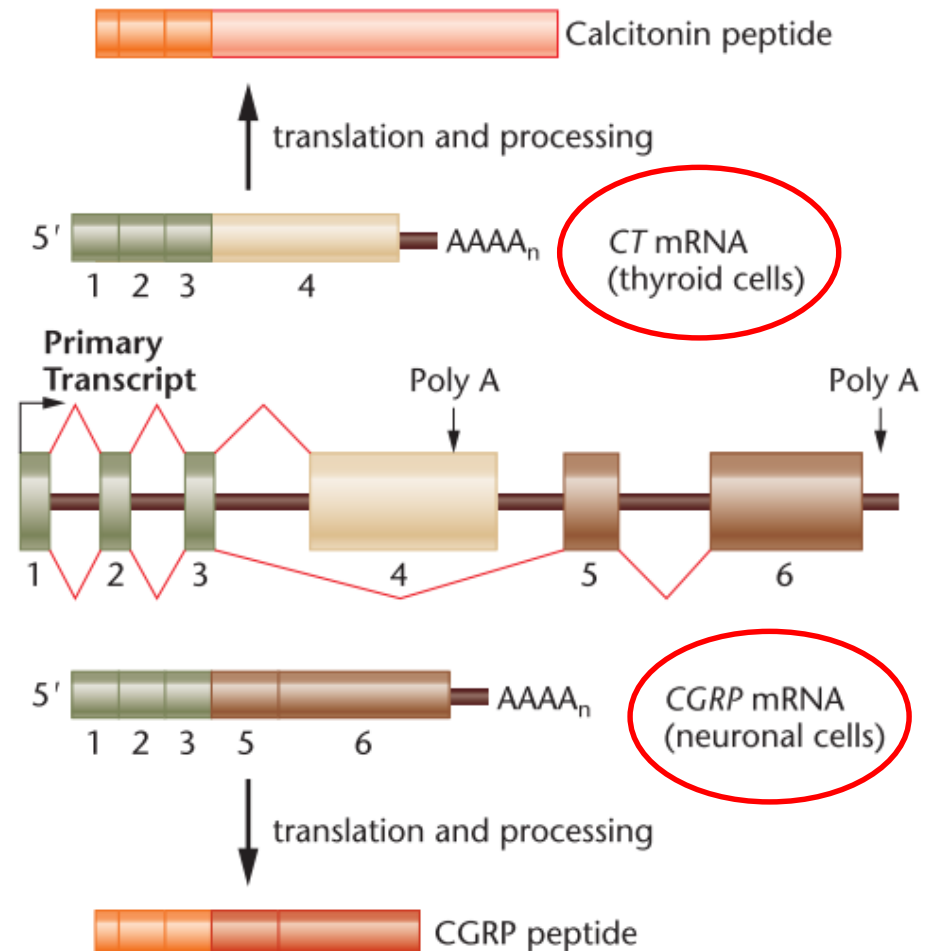


<https://youtu.be/aVgwr0QpYNE>



# Alternative splicing

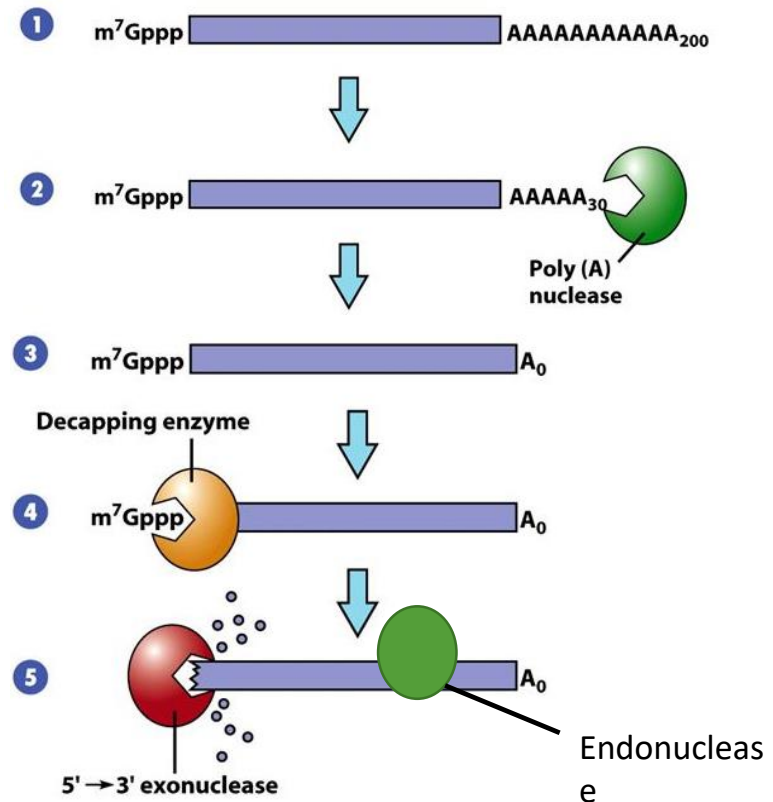
- Immature RNA (pre-mRNA) contains introns and exons.
- Introns are spliced out in spliceosomes and exons are ligated together.
- Different combinations of exons can result in different proteins.
- This causes the number of possible proteins that can be produced (proteome) in a cell exceed the number of genes in the genome.





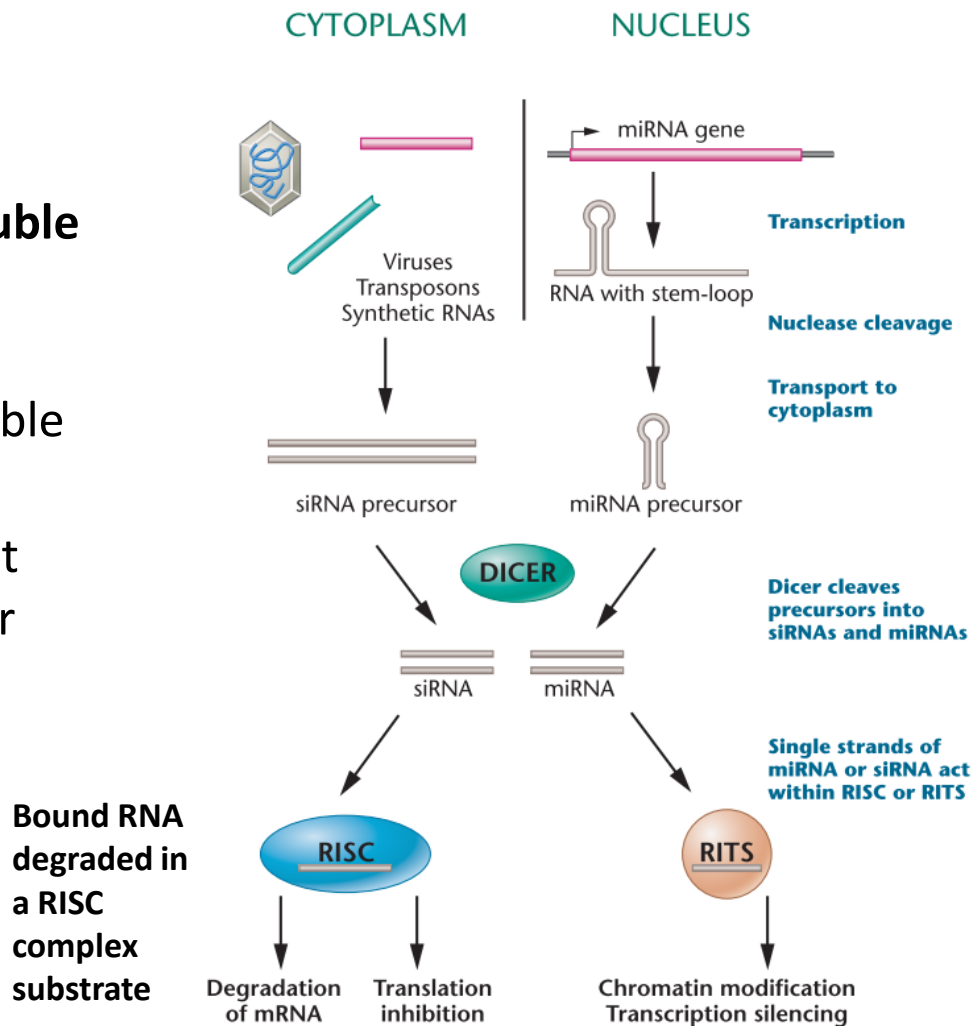
# RNA stability affects regulation

- mRNA has a half life ( $t_{1/2}$ )
- Poly A tail degradation
- 5'Cap degradation
- Endonuclease activity
- This degradation can be facilitated by RNA degradation elements

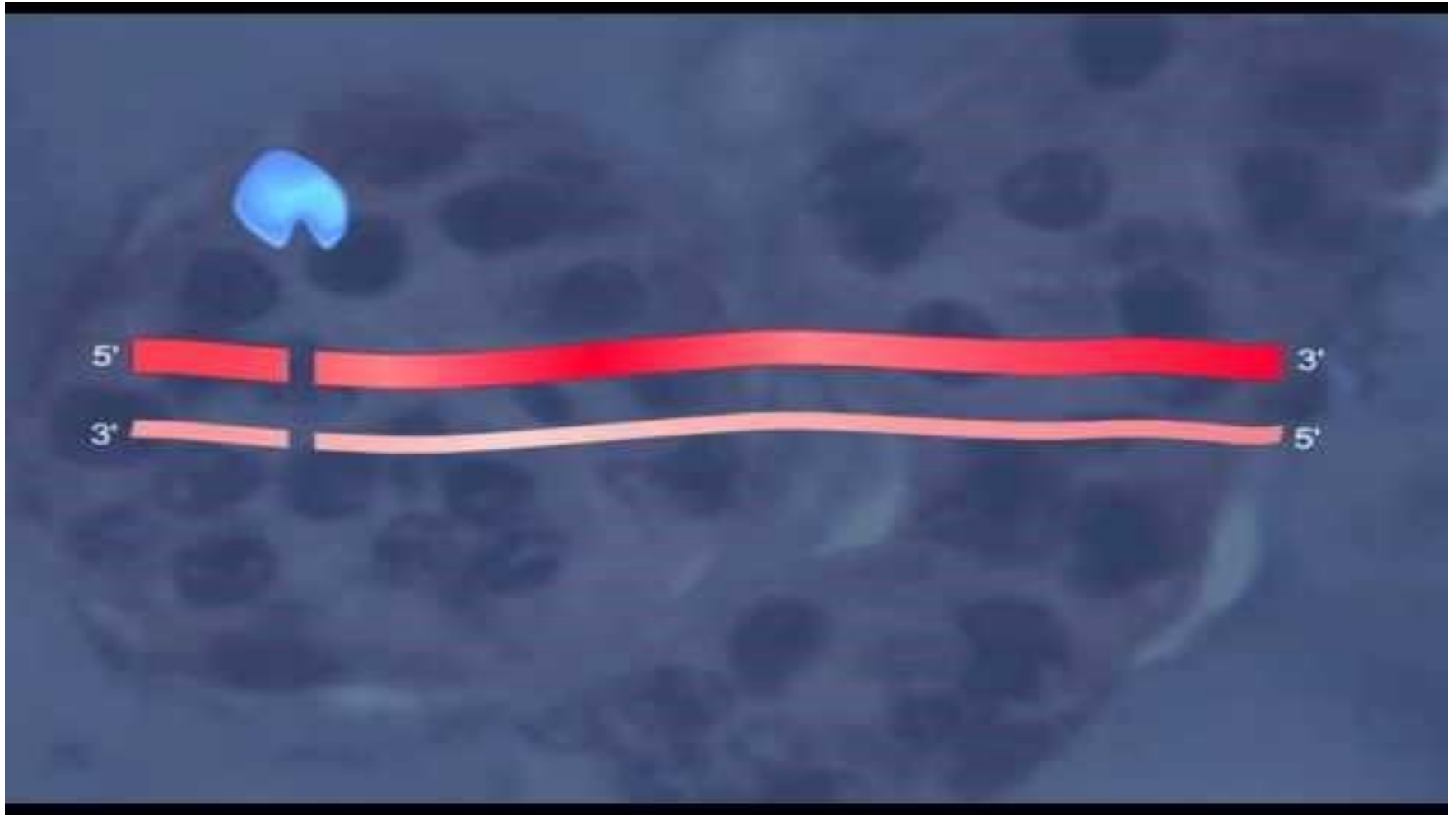


# RNA silencing

- Certain sequences can form **double stranded DNA/hairpin loops**.
- Enzyme complex called **DICER** cleaves these to form small double stranded siRNA or miRNAs
- These can then be used to direct degradation complexes to either silence transcription or degrade specific mRNAs.



<https://youtu.be/J4b0oRdFeF4>



# Translational and Post-translational regulation

- Immature proteins require peptide processing to be active
- Differences in processing can result in different protein functions and/or activities.

