GENE REGULATION IN EUKARYOTES

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GENE REGULATION IN EUKARYOTES

- Unlike prokaryotes, multiple gene-regulating mechanisms operate in the nucleus:

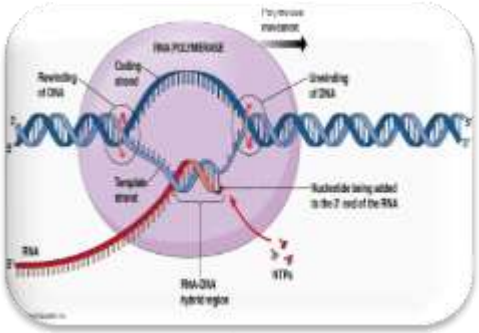
i. before and after RNA transcription, and

ii. in the cytoplasm both before and after translation in eukaryotes.

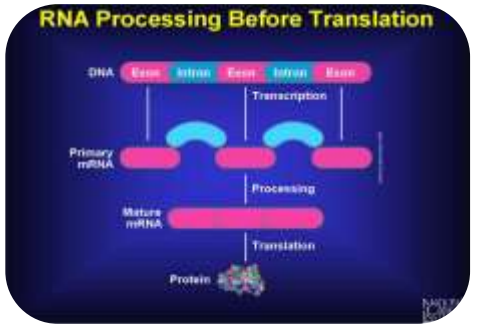
GENE REGULATION IN EUKARYOTES

- Eukaryotic gene expression is regulated at **5 main levels**:

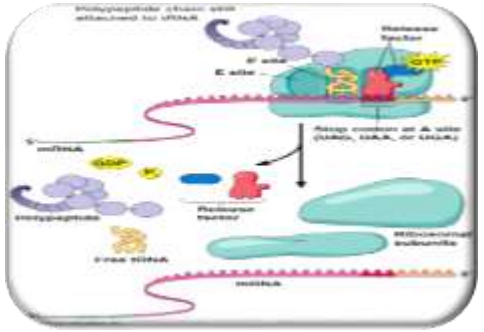
Genome



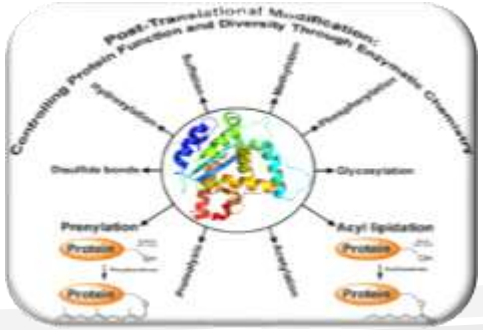
Transcription



RNA processing



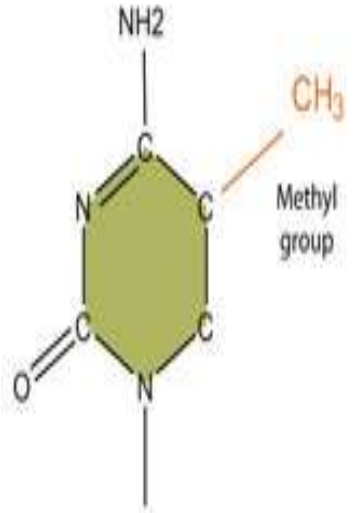
Translation

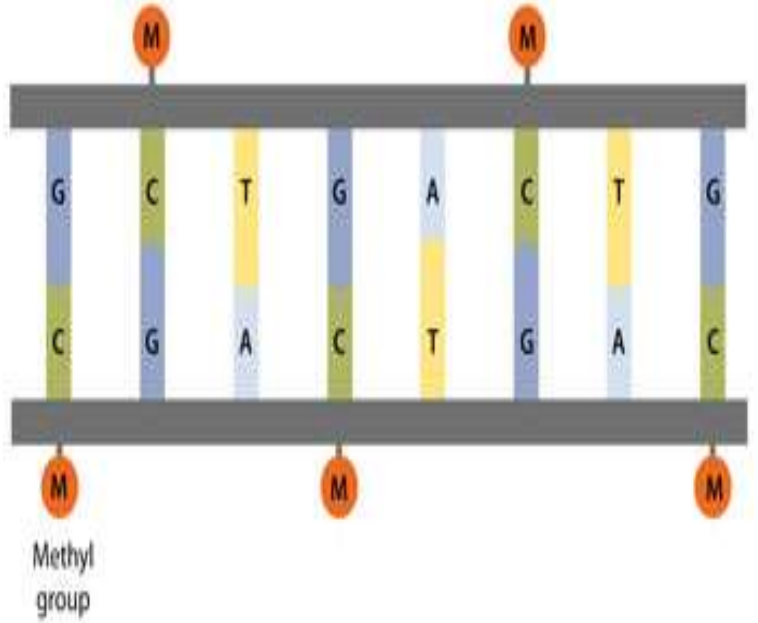


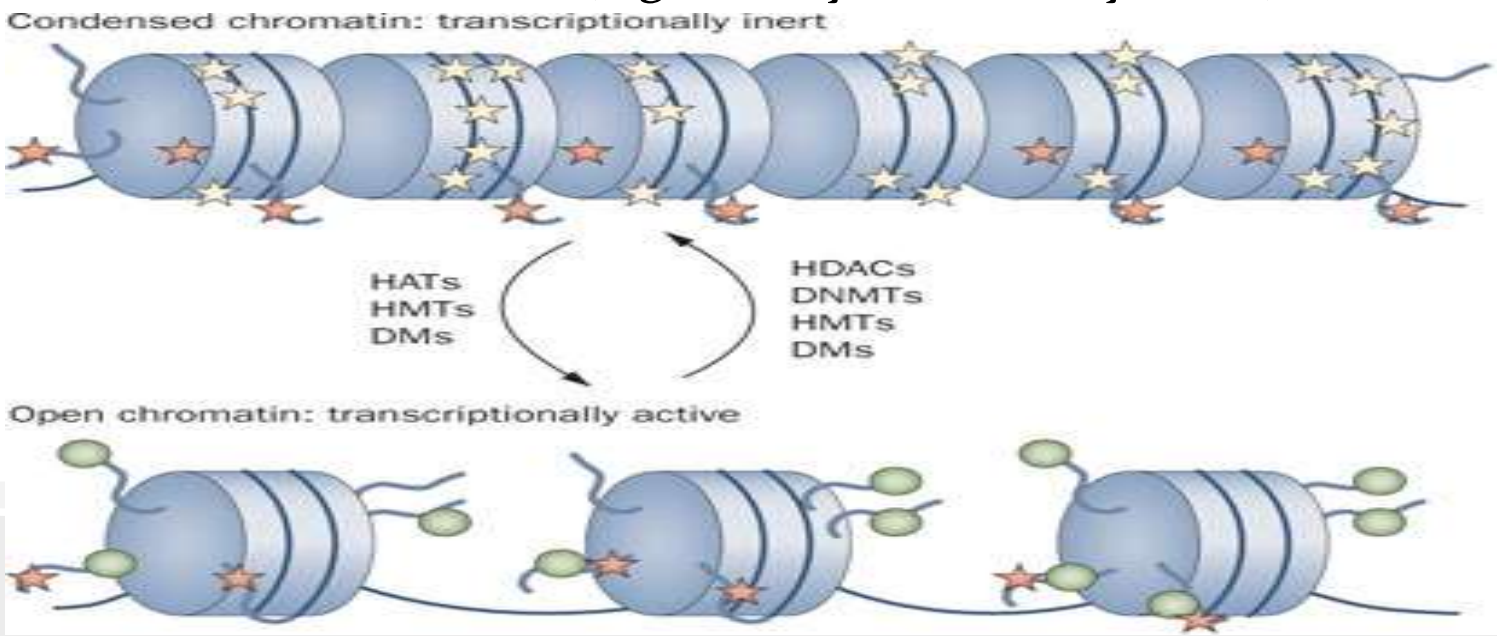
Post-translational events

GENOME LEVEL

- Gene amplification/deletion (rare),
- DNA rearrangements (rare),
- DNA methylation,
- Chromatin de condensation and condensation, &
- Histone modifications (e.g., methylation, acetylation)







Epigenetic marks:

DNA: Hypermethylation at CpG sites

Histones: Hypoacetylation
Methylation H3K9, H3K27, H4K20

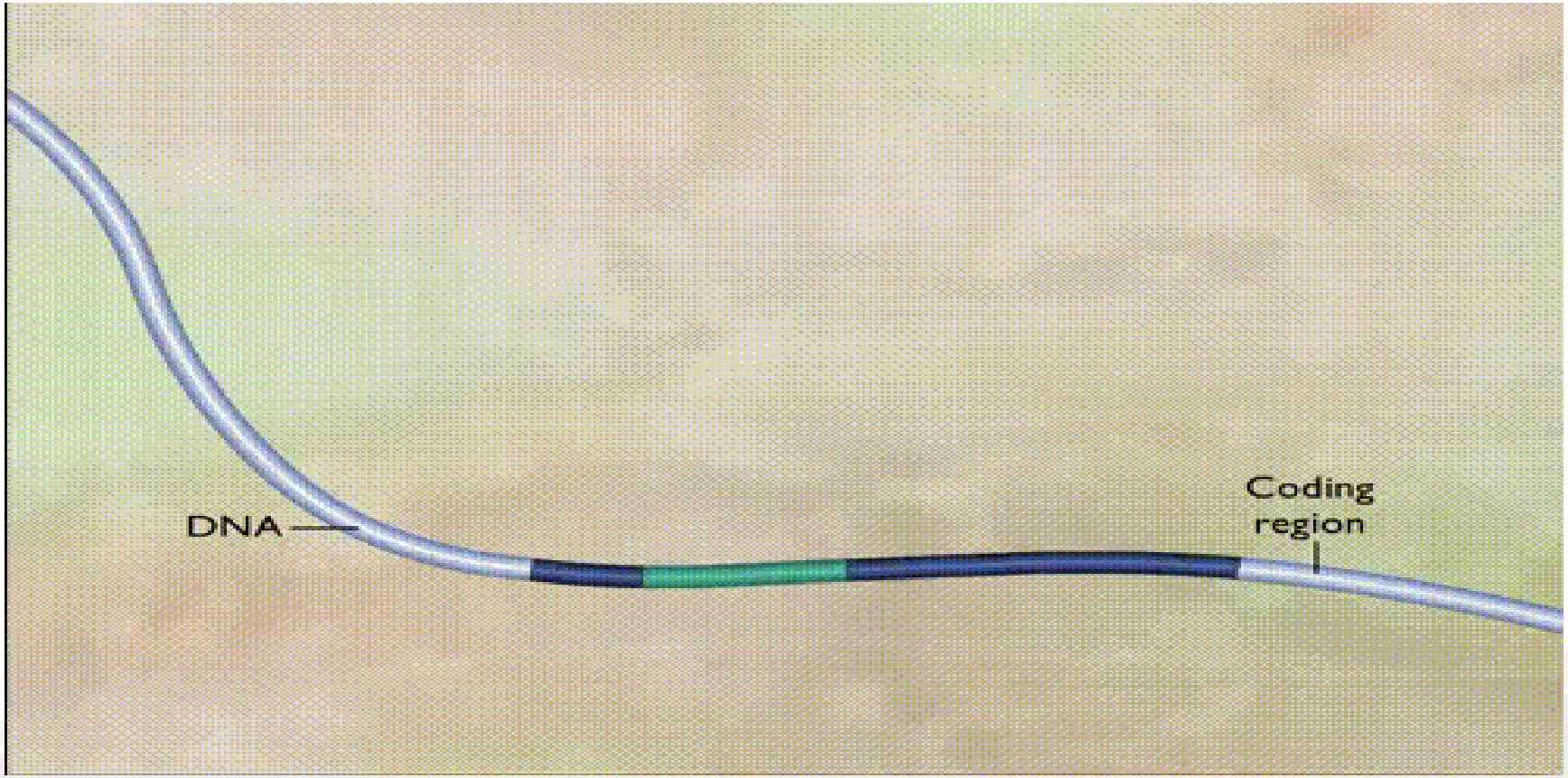
Epigenetic marks:

DNA: Hypomethylation at CpG sites

Histones: Hyperacetylation
Methylation H3K4, H3K36, H4K79

Transcriptional Level

- Transcription factors



RNA processing

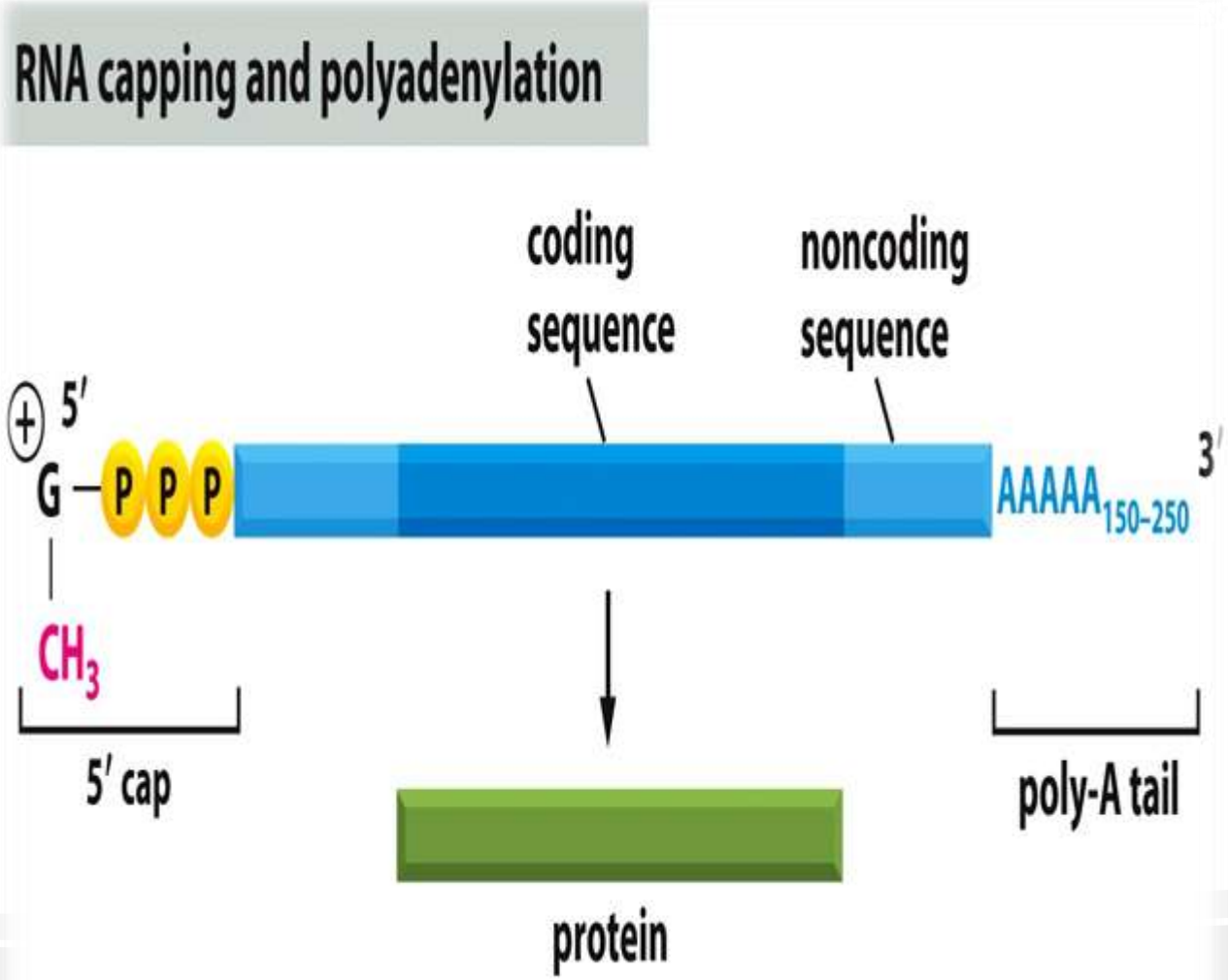
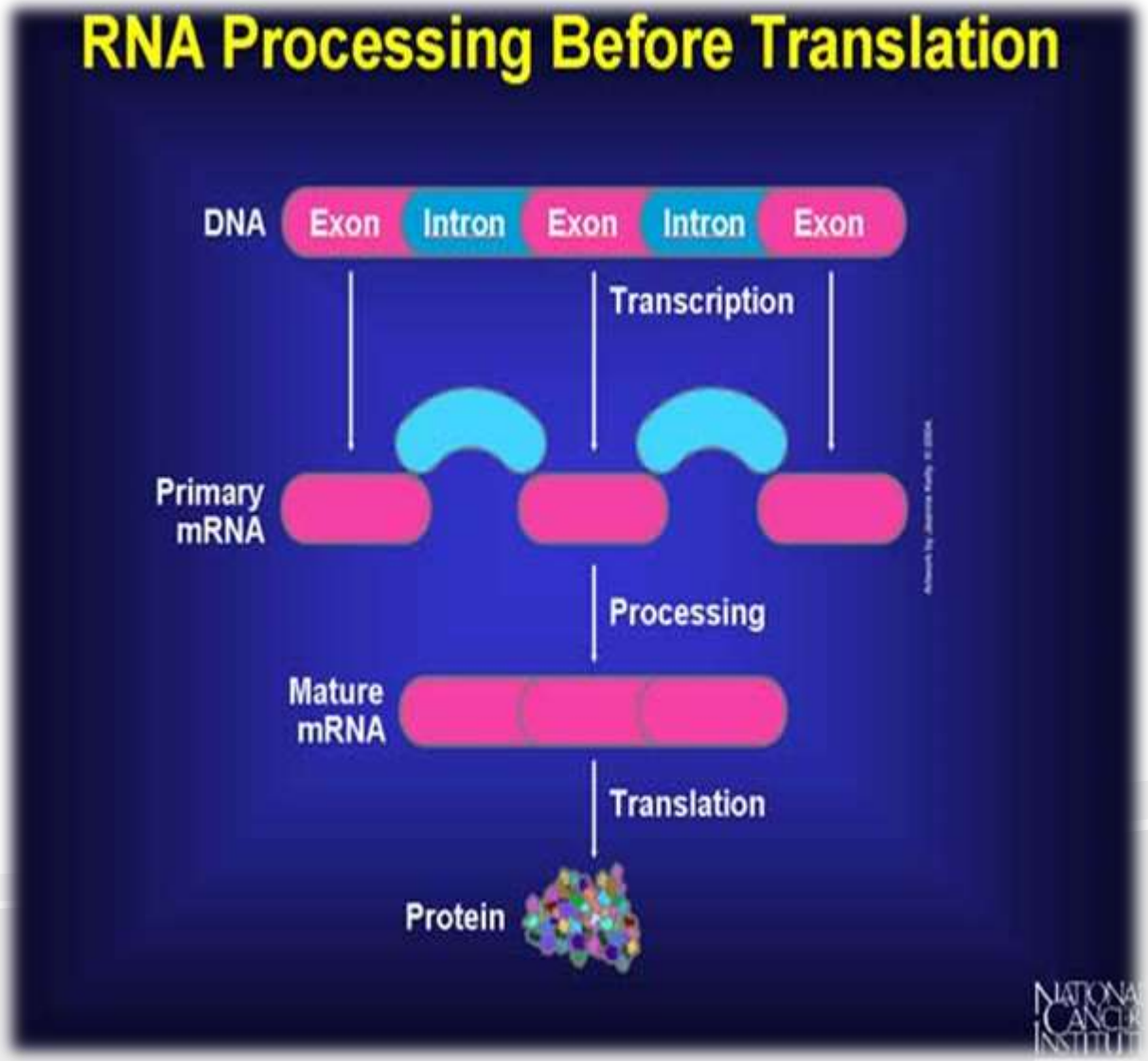
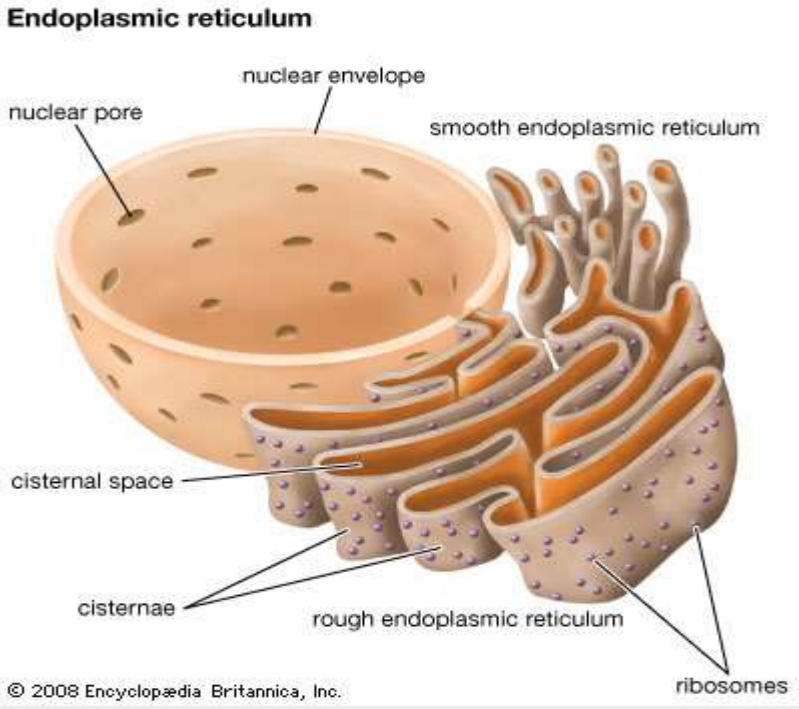


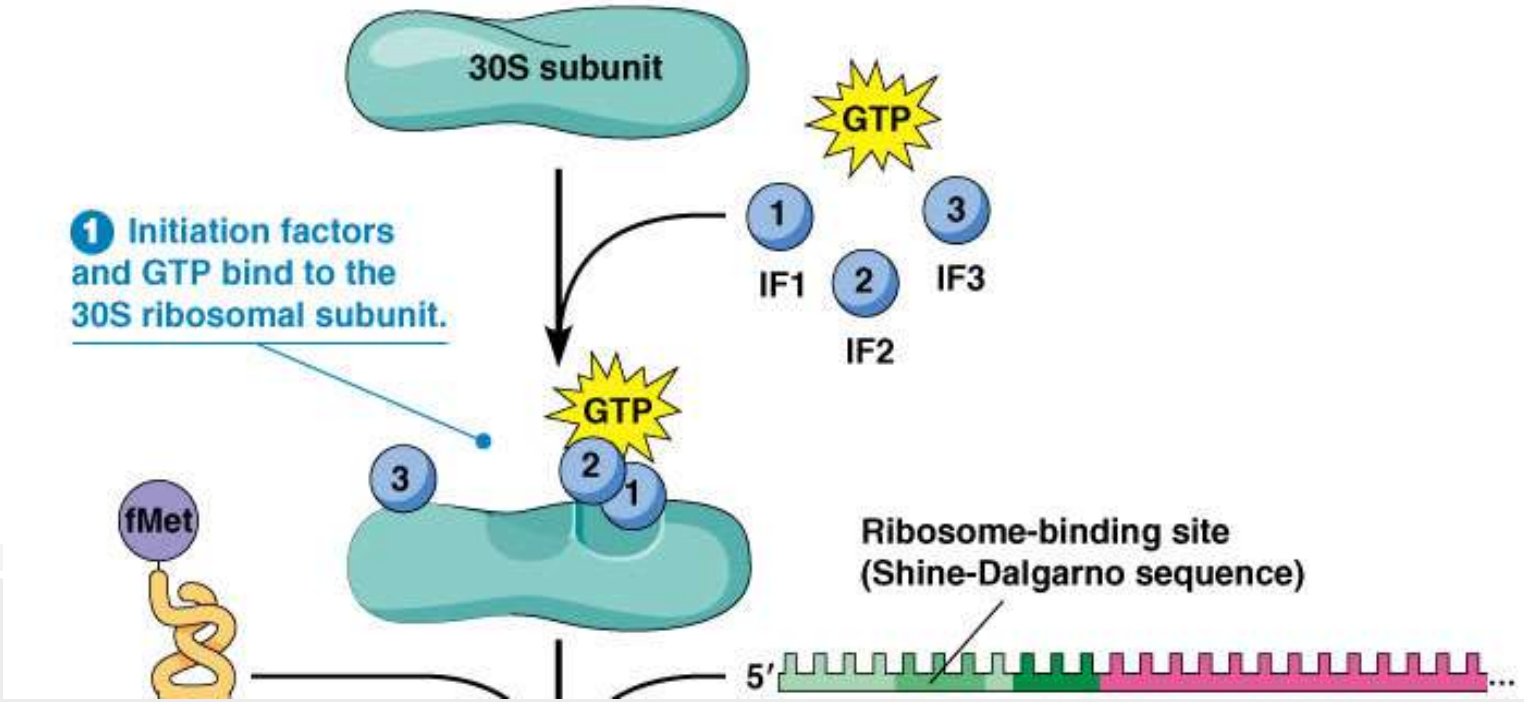
Figure 7-16a Essential Cell Biology 3/e (© Garland Science 2010)



Translational Level

- includes targeting of some newly forming polypeptides to the ER,
- plus control of translation by initiation factors
- and translational repressors, including microRNAs



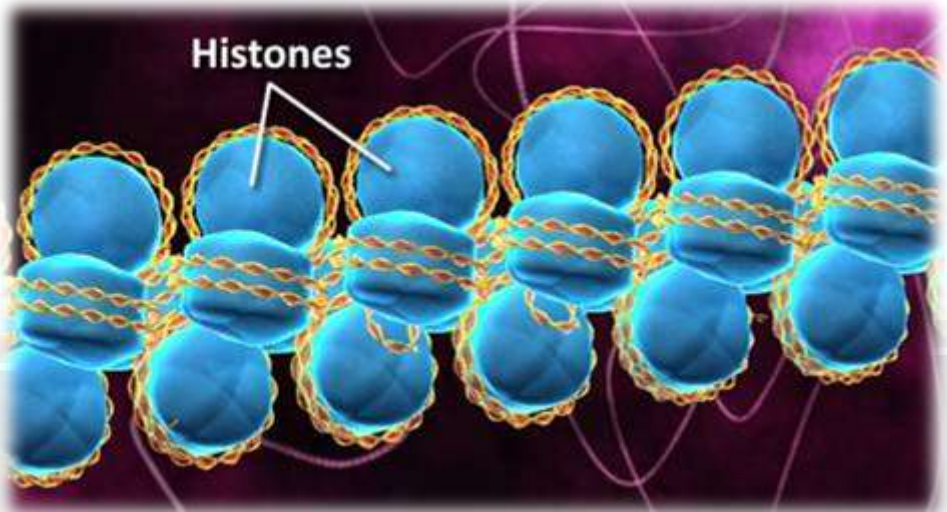


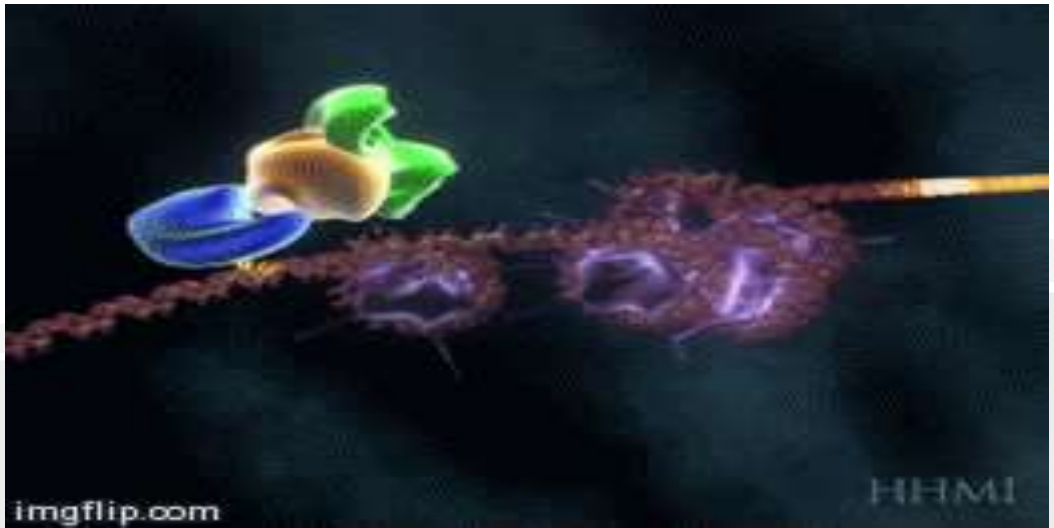
Posttranslational events

- Protein folding and assembly,
- Possible polypeptide cleavage,
- Possible modification,
- Possible import into organelles

Histone & Gene regulation

- Small proteins packed inside the molecular structure of the DNA double helix.
- Tight histone packing prevents RNA polymerase from contacting and transcribing the DNA.
- This type of overall control of protein synthesis is regulated by genes that control the packing density of histones.





Activator-Enhancer Complex

- Unique in eukaryotes because they normally have to be activated to begin protein synthesis, which requires the use of transcription factors and RNA polymerase.
- In general, the process of eukaryotic protein synthesis involves **four** steps:

1. Activators
2. Activator enhancer complex
3. Additional transcription factors
4. Silencers

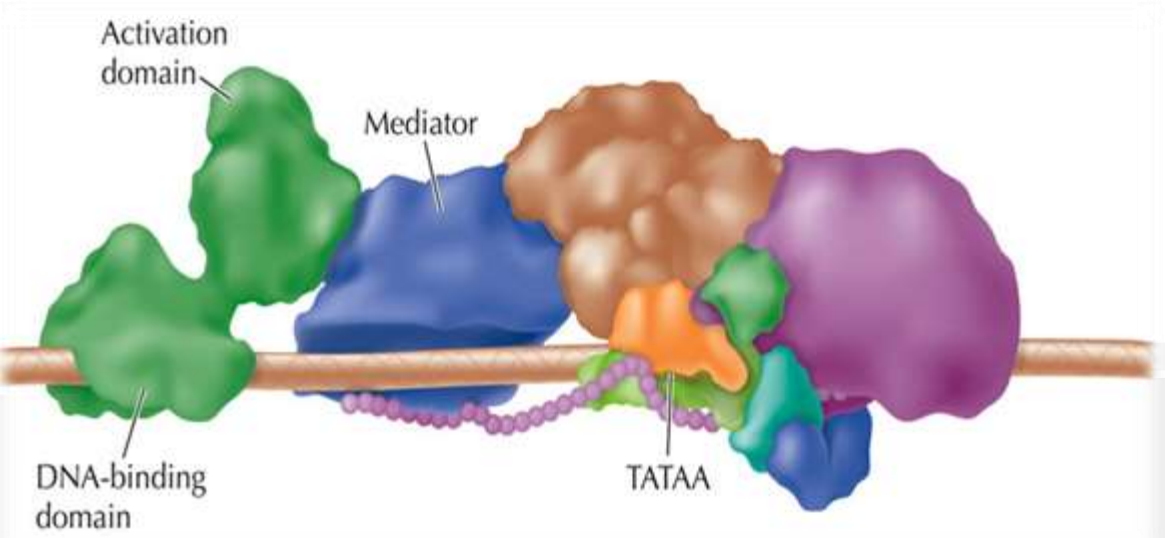
Activator-Enhancer Complex

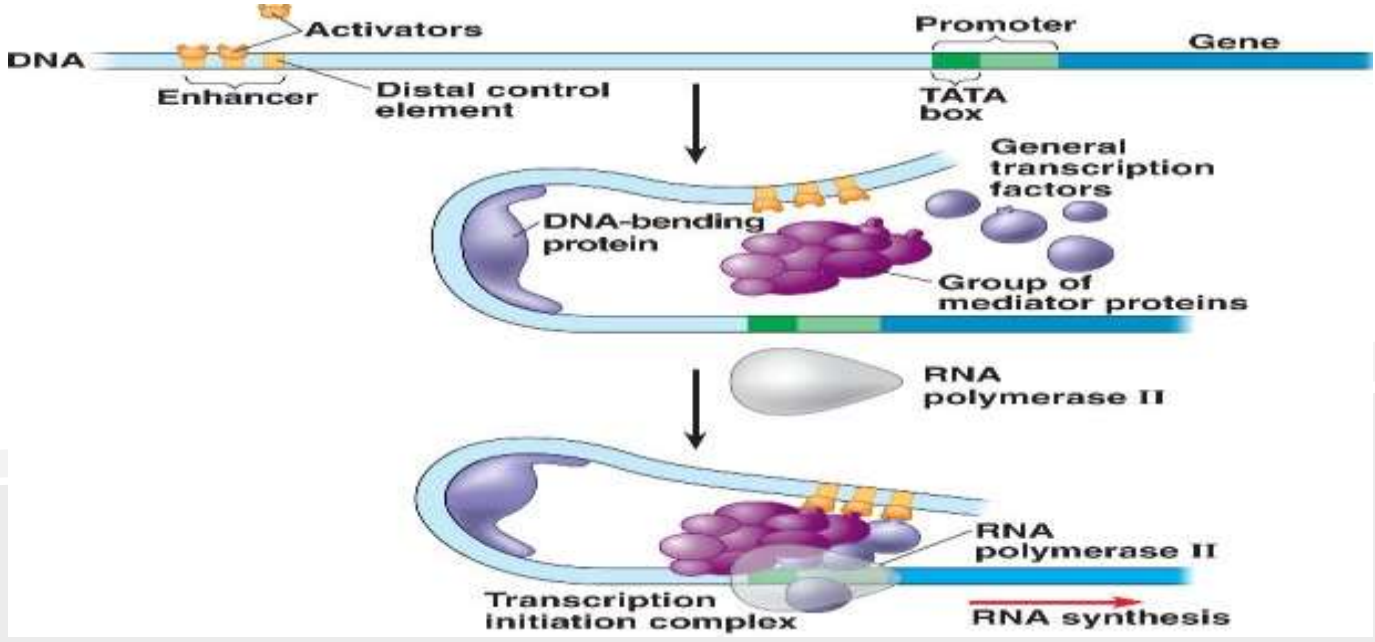
Activators:

A special type of transcription factor, bind to enhancers, which are discrete DNA units located at varying points along the chromosome.

Activator-enhancer complex:

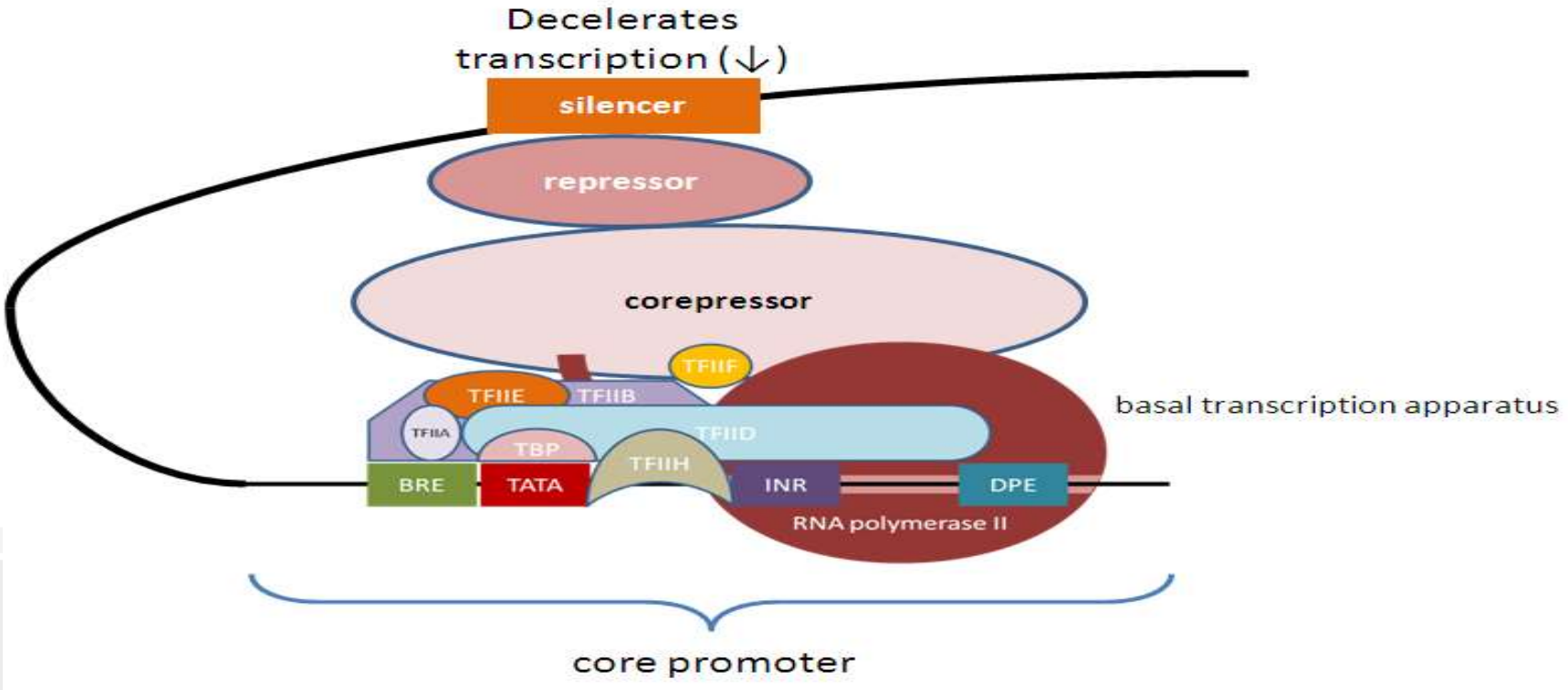
- bends the DNA molecule so that additional transcription factors have better access to bonding sites on the operator.

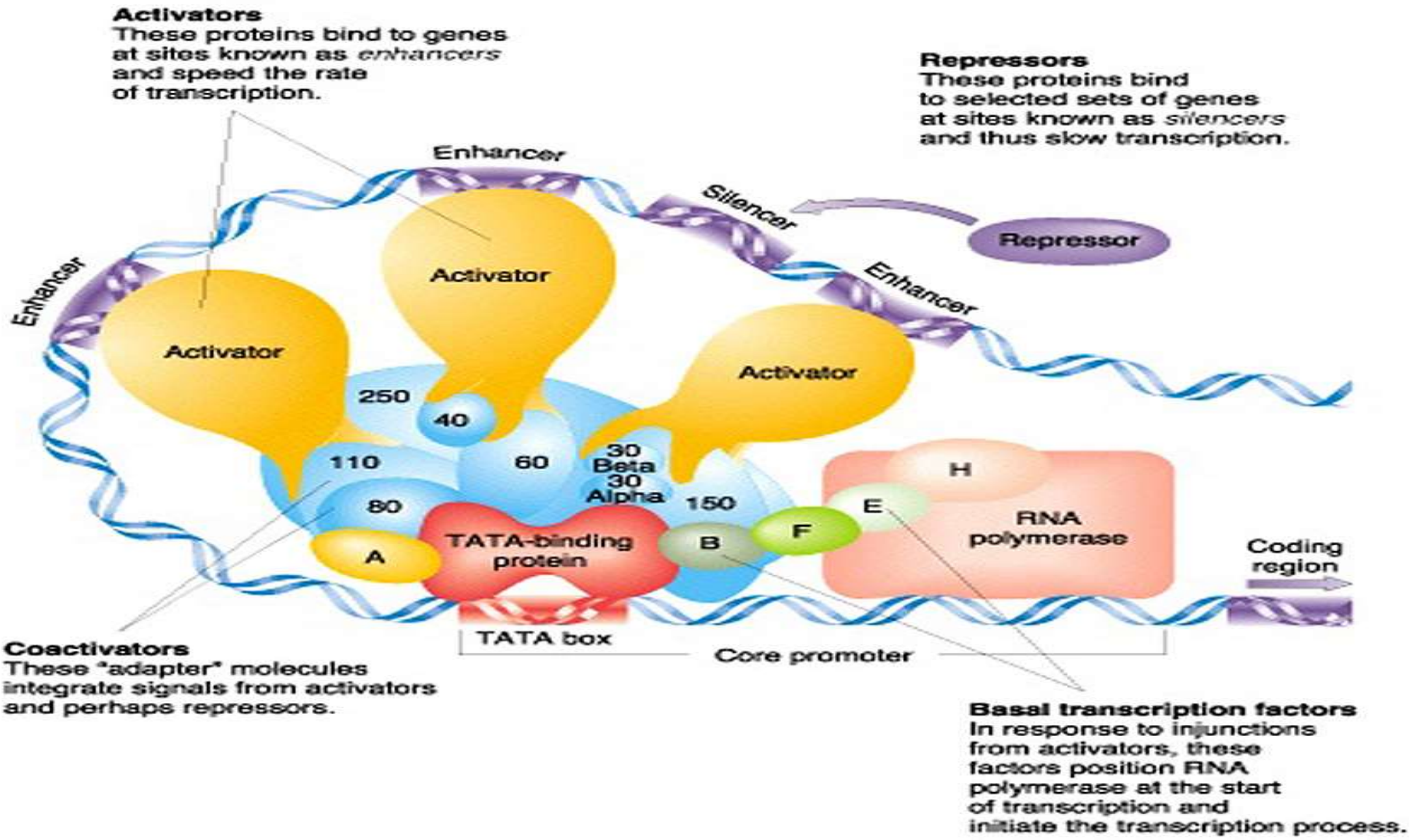




Activator-Enhancer Complex

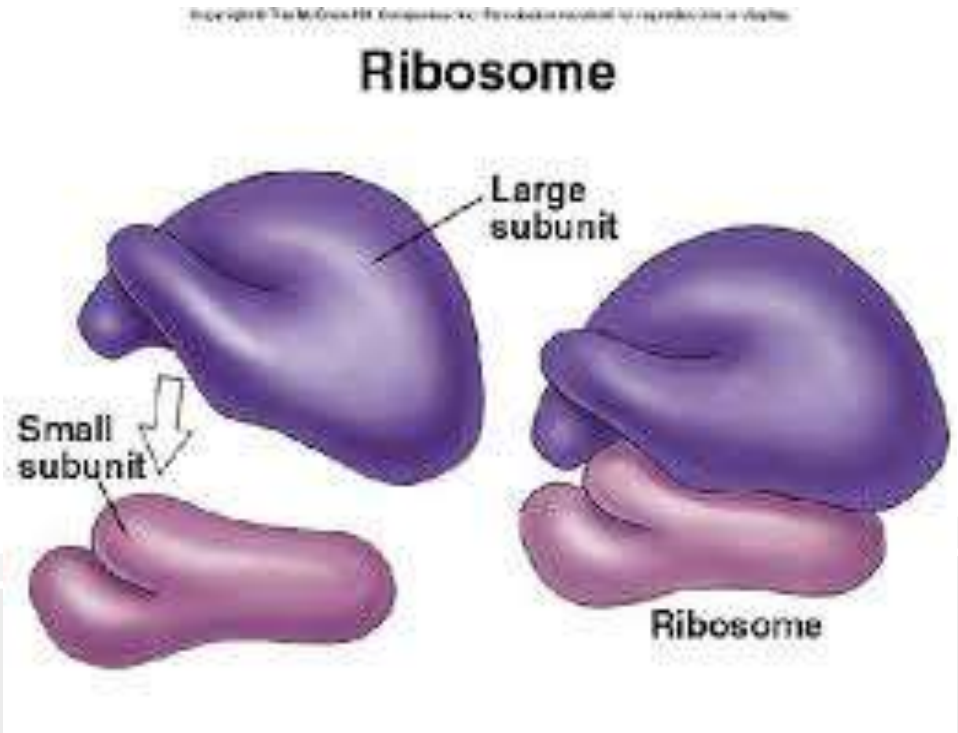
- The bonding of **additional transcription factors** to the operator allows greater access by the RNA polymerase, which then begins the process of transcription.
- **Silencer** is a DNA sequence capable of binding transcription regulation factors, called repressors. They block the transcription.




Activators
These proteins bind to genes at sites known as enhancers and speed the rate of transcription.
Repressors
These proteins bind to selected sets of genes at sites known as silencers and thus slow transcription.
Enhancer
Silencer
Repressor
Enhancer
Enhancer
Activator
Activator
Activator
250
40
110
60
30 Beta
30 Alpha
150
80
A
TATA-binding protein
B
F
E
H
RNA polymerase
Coding region
TATA box
Core promoter
Coactivators
These "adapter" molecules integrate signals from activators and perhaps repressors.
Basal transcription factors
In response to injunctions from activators, these factors position RNA polymerase at the start of transcription and initiate the transcription process.

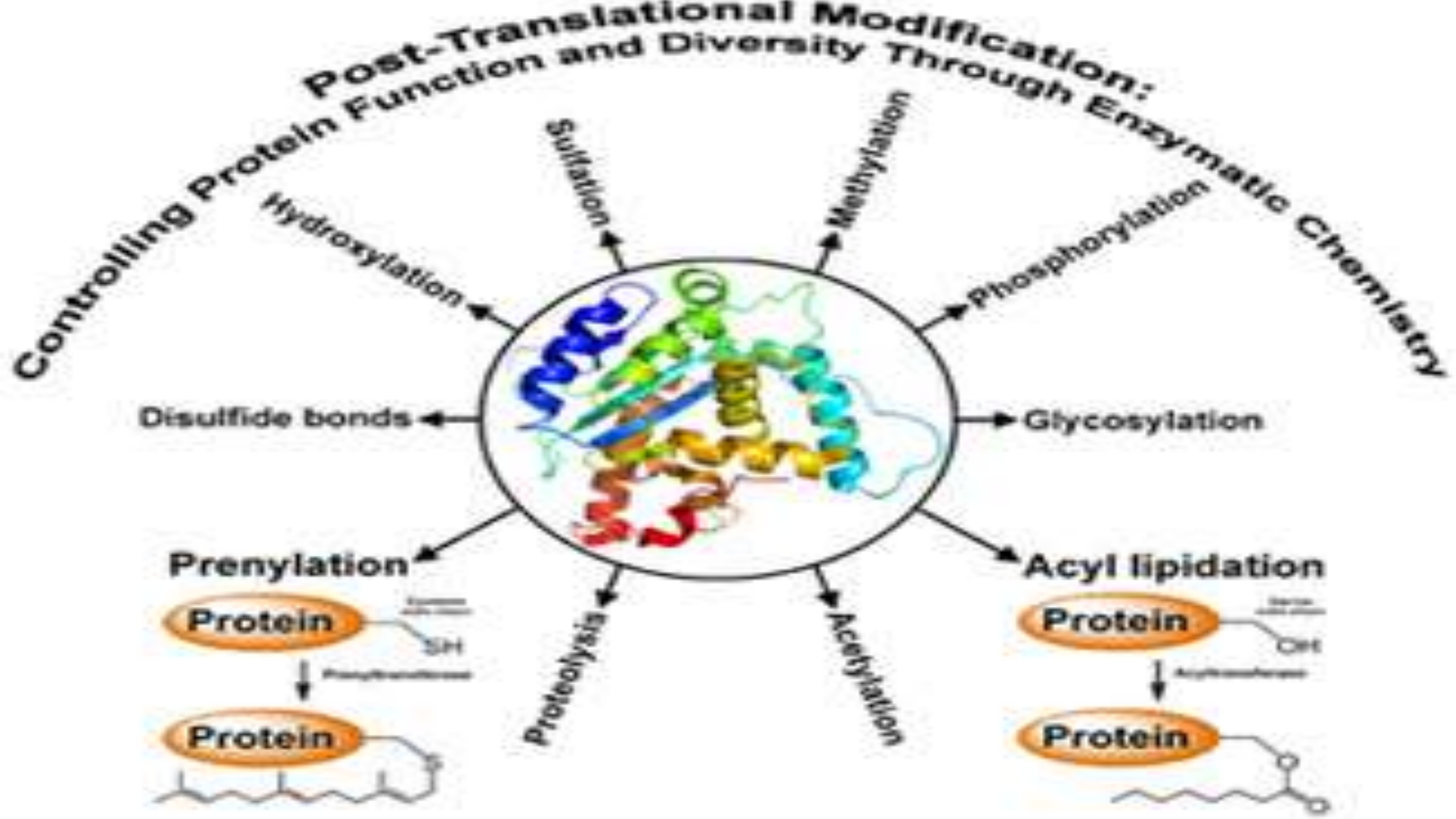
Inhibitory Protein

- **Inhibitory proteins** prevent the translation of mRNA.
- It usually refers to substances that act at the ribosome level (either the ribosome itself or the translation factor)



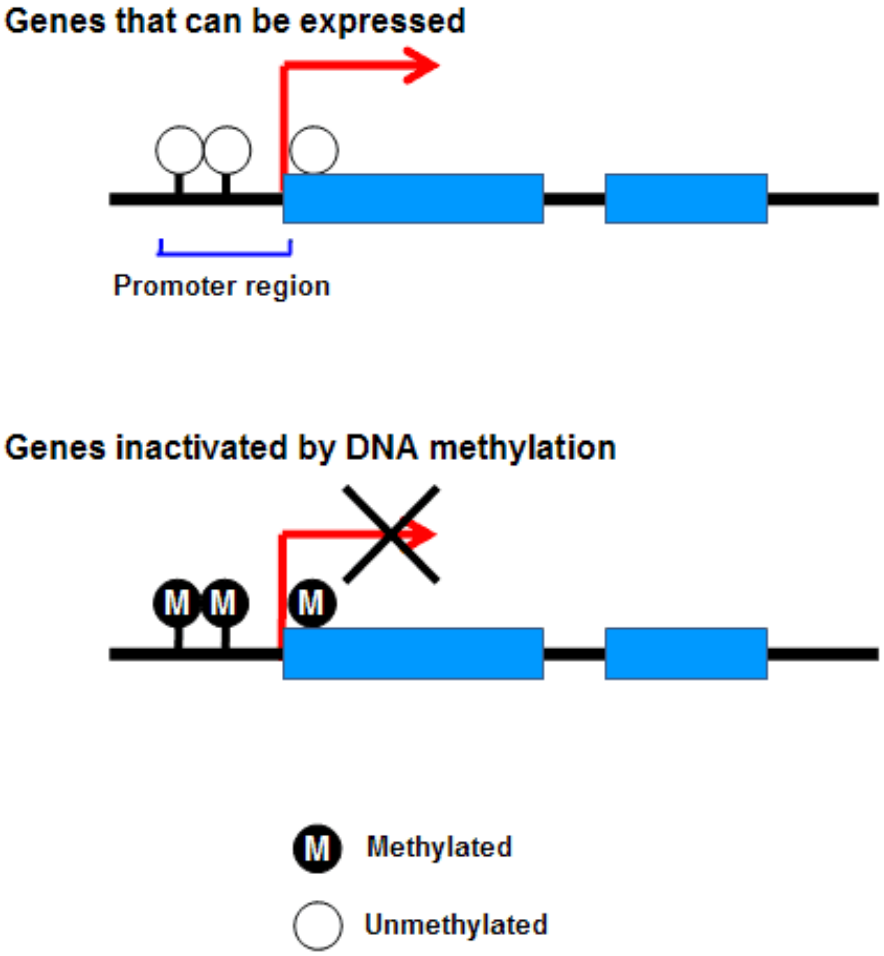
Post translational control

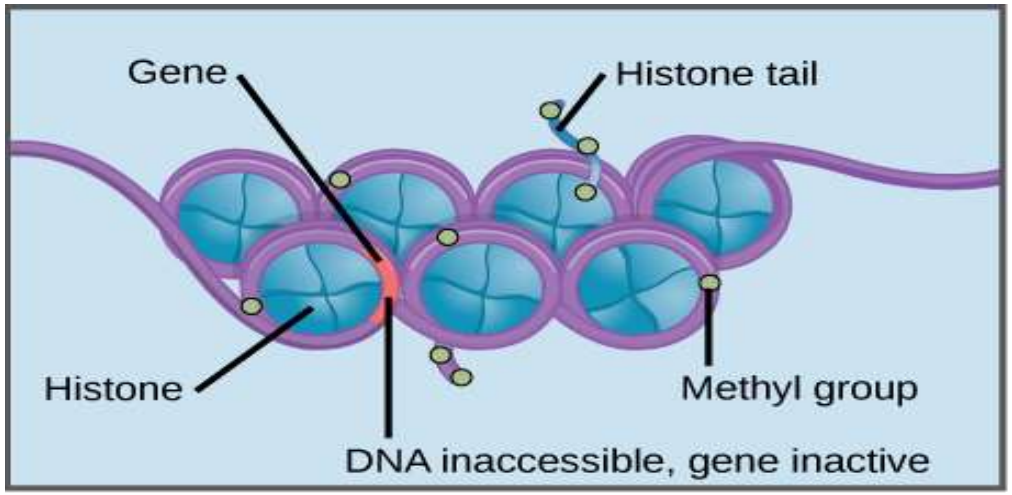
- "Posttranslational regulation" means regulation (of the level of active protein product present in the cell) that takes place AFTER the protein product is produced (by the act of translation of the mRNA).
- **Post-translational** regulation refers to the **control** of the levels of active protein.
- There are several forms.
- It is performed either by means of reversible events (**posttranslational** modifications, such as phosphorylation) or
- by means of irreversible events (proteolysis: breakdown of proteins into smaller polypeptides or amino acids)


Post-Translational Modification:
Controlling Protein Function and Diversity Through Enzymatic Chemistry
Sulfation
Methylation
Hydroxylation
Phosphorylation
Disulfide bonds
Glycosylation
Prenylation
Acyl lipidation
Proteolysis
Acetylation
Protein
SH
Protein
Protein
OH
Protein

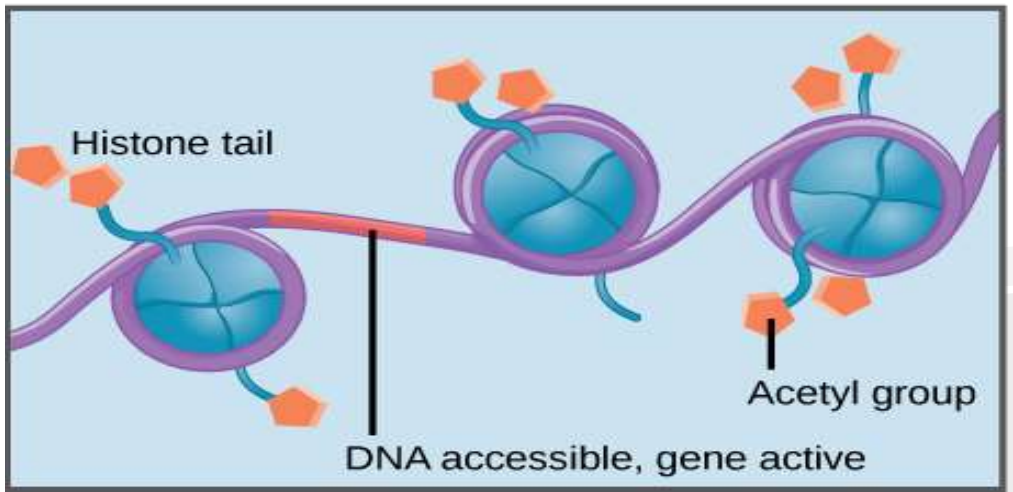
DNA METHYLATION

- Associated with Inactive Regions of the Genome





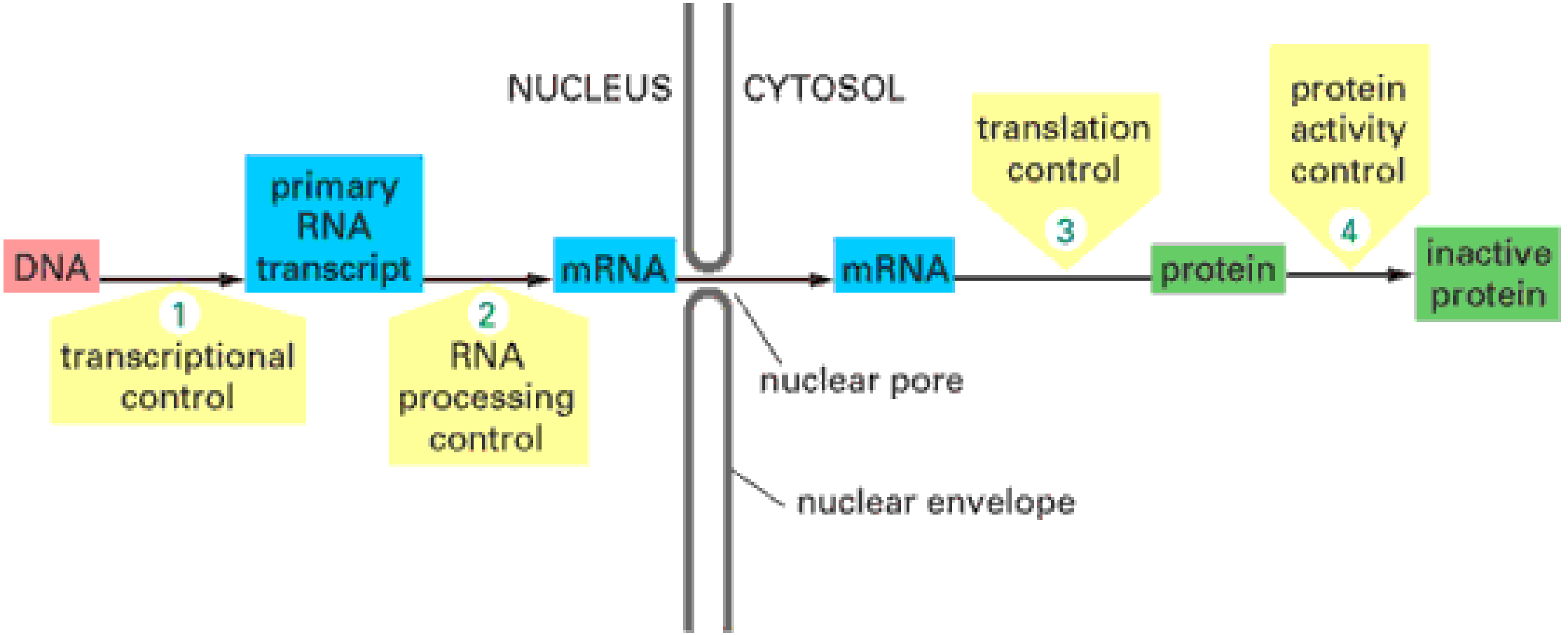
Methylation of DNA and histones causes nucleosomes to pack tightly together. Transcription factors cannot bind the DNA, and genes are not expressed.



Histone acetylation results in loose packing of nucleo-somes. Transcription factors can bind the DNA and genes are expressed.

mRNA Features Due To Gene Regulation

- The longevity of the individual mRNA molecule determines how many times it can be used and reused to create proteins.
- In eukaryotes, the mRNA tends to be stable, which means it can be used multiple times; which is efficient, but
- It prevents eukaryotes from making rapid response changes to environmental disruptions.
- The mRNA of prokaryotes is unstable, allowing for the creation of new mRNA, which has more opportunities to adjust for changing environmental conditions.


NUCLEUS
CYTOSOL
DNA
primary RNA transcript
mRNA
mRNA
protein
inactive protein
translation control
3
protein activity control
4
1
transcriptional control
2
RNA processing control
nuclear pore
nuclear envelope

YOU CAN ASK QUESTIONS!

Thank You!!!