Gene Regulation (Part-I)

(BIOT 4006: Genetics and Molecular Biology)

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Importance of Gene Regulation

- The proteins expressed by the cells govern their biological properties.
- These properties include: structural composition, enzymes, physiological properties, interaction with environment etc.
- Not all RNAs and proteins, from an encoded genome, are expressed at a particular time in a cellular lifespan.
- Depending on many inter related factors a cells requirements for its survival and growth changes with time.
- Accordingly the amounts and levels of expression of different proteins and RNAs needs to be up-regulated and down-regulated.

- Gene regulation is the control over the manufacturing of gene transcripts and its protein product.

- Regulation of gene expression can be done at many levels.

- Most of the genes finally synthesize proteins so in that case regulation of protein expression is achieved at the level of transcription or translation.

- Apart from the adjustments of transcription and translation, gene regulation can also be achieved at many other levels like varying the mRNA stability or posttranslational modifications of proteins.

- However, majority of gene regulation is done at the level of gene transcription.

- Extracellular or intracellular molecular signals cause the binding of regulatory proteins with the specific sites on DNA present near the protein coding region.
- This binding of regulatory proteins on the DNA modulates the transcription rate.
- There is a possibility of direct/indirect role of these regulatory proteins in assisting or preventing the binding of RNA polymerase at the promoter site.
- Transcriptional modulation is done by the regulatory proteins through one or more of their functional domains.

- These functional domains of regulatory proteins are involved in transcriptional modulation:

1. DNA docking site of the protein (it identifies the correct regulatory element)

2. Domain interacting with proteins of the basal transcription apparatus (RNA polymerase or an RNA-polymerase-associated protein)

3. Domain interacting with proteins bound to nearby docking sites so that they can do cooperative regulation of transcription

4. Domain that directly or indirectly influences the chromatin condensation

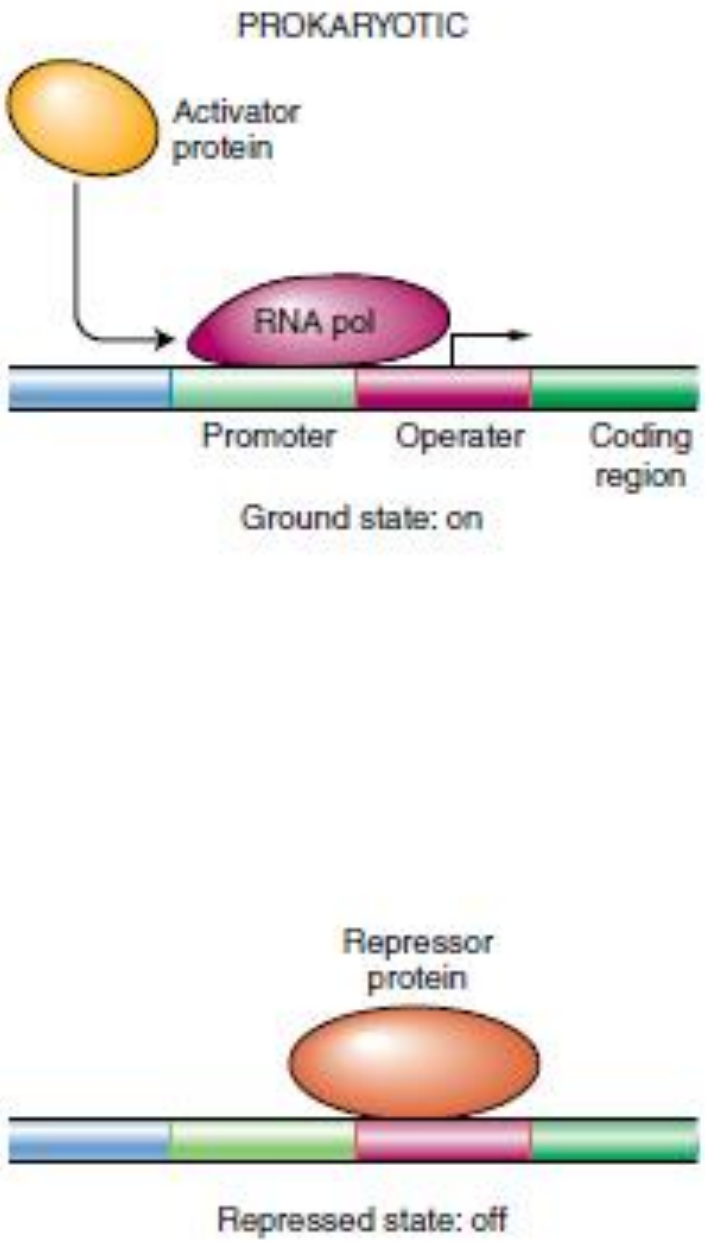
5. Sensory domain for the physiological conditions inside the cell

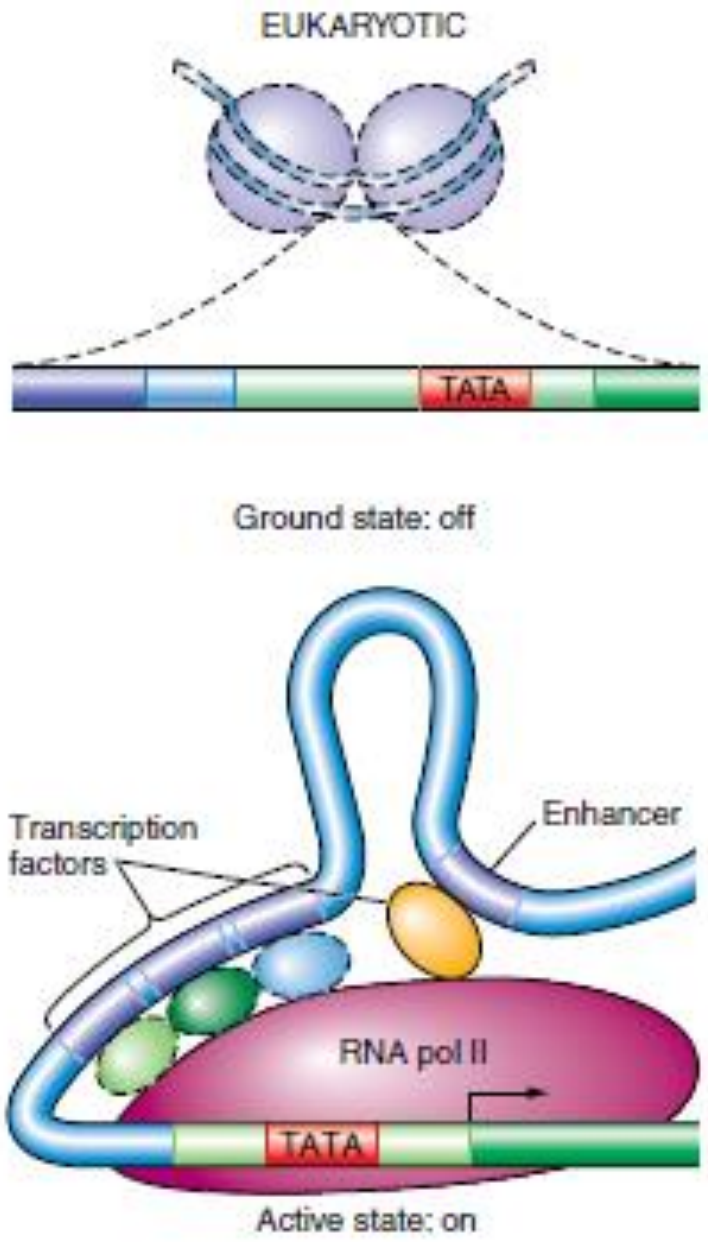
- The regulatory mechanisms has their importance in enhancing the cell's capabilities to handle with perturbing variations in the following conditions:

1. nutrient availability
2. attacking infectious agents
3. various environmental stresses
4. changing developmental stages

- The sensory domain of the regulatory protein molecule senses the cellular environment through its interaction with the varying factors present over there.

- In this way, it is ensured that the regulatory protein acts promptly in appropriate manner so that it makes the cellular machinery deliverable as per the cell's needs at a given moment.





Prokaryotic and Eukaryotic Transcriptional Regulation

- Many of the gene regulatory mechanisms are common between prokaryotes and eukaryotes except a few fundamental differences.
- In prokaryotes, a repressor protein blocks a usually transcribing RNA polymerase.
- In eukaryotes, transcription is prevented by the packaging of DNA (specifically the key binding sites on DNA). The regulatory proteins push and release the key binding sites out of nucleosome packaging.

Reference: Introduction to Genetic Analysis, Ninth Edition, Anthony Griffiths et al., Chapter 10

- Prokaryotic and eukaryotic regulatory proteins bind adjacent to the coding region to regulate the transcription rate.

- Regulation of gene expression is more complex in case of eukaryotes owing to the bigger genome size and larger range of functions.

- In comparison with prokaryotes, larger number of regulatory proteins interacting with many regulatory regions are involved in eukaryotes.

- Eukaryotes and prokaryotes differ in the packaging of their genetic material.

- Eukaryotes have their DNA packaged into nucleosomes and chromatin whereas no such packaging occurs in prokaryotes. The chromatin structure is dynamic and has an important role in gene regulation.

- The prokaryotic gene remains in an ‘always on’ state and the RNA polymerase can bind usually to a promoter site in the absence of other regulatory proteins.

- In prokaryotes, the regulation of gene expression is done by the repressor regulatory proteins when they totally prevent or reduce transcription through blocking of the binding of the RNA polymerase with the promoter site.

- In contrast, the repressor regulatory proteins, the activator regulatory proteins enhance RNA polymerase binding to promoter site thereby increasing the rate of transcription.

- Opposite to the prokaryotes, eukaryotes have a transcription machinery which remains in an ‘always off’ mode. It requires presence of other regulatory proteins for binding of the basal transcription apparatus with the promoter. Until the nucleosome is ‘opened’ by the regulatory proteins, the key binding sites on DNA are not available for the transcription apparatus.