Regulation of Gene Expression in Eukaryotes

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How does a eukaryotic organism regulate the expression of gene leading to the production of correct protein?

Expression of Different Genes

- House keeping genes
- Genes required during cellular differentiation
- Genes which get triggered as a response to some external factors
- Genes which get triggered during apoptosis

Mechanism of Gene Regulation in Prokaryotes and Eukaryotes

- In prokaryotes the primary control point is the process of transcription initiation
- In eukaryotes expression of gene into proteins can be controlled at various locations.

Check Points for Gene Expression in Eukaryotes

- Synthesis of proteins is controlled right from the chromatin stage.
- Expression of gene is controlled at many steps during the process of transcription and translation.
- Description of the control points is dealt in detail in the subsequent slides.

1.Chromatin Structure

Two forms of chromatin

- Euchromatin – A lesser coiled transcriptionally active region which can be easily accessed by the RNA polymerases.

- Heterochromatin – A highly condensed transcriptionally inactive region. The genes in this region cannot be accessed by the RNA polymerases for active transcription.

1.Chromatin Structure

Mechanisms which affect the chromatin structure and hence the expression of gene are:

- **Histone modifications** – These modifications make a region of gene either transcriptionally active or inactive.
  a) **Acetylation**
  - ↑Acetylation ----↓ Condensation of DNA ----- ↑ Transcription of genes in that region

1.Chromatin Structure

Methylation

- Methylation of histone H4 on R4 (arginine residue at the 4th position) →→ opens the chromatin structure →→ leading to transcriptional activation
- Methylation of histone H3 on K4 and K79 (lysines residues at the 4th and 79th position) →→ opens the chromatin structure →→ leading to transcriptional activation
- Methylation of histone H3 on K9 and K27 (lysines residues at the 9th and 27th position) →→ condenses the chromatin structure →→ leading to transcriptional inactivation

1.Chromatin Structure

b) **Ubiquitination**
   - Ubiquitination of H2A – Transcriptional inactivation
   - Ubiquitination of H2B - Transcriptional activation

2) **Methylation of DNA**
   - Target sites of methylation are - The cytidine residues which exist as a dinucleotide, CG (written as CpG)
   - ↑ methylated cytidine -- ↓ Transcriptional activity

2.Regulation of Transcription

- **The differences in the mechanisms by which the transcription of gene is controlled in prokaryotes and eukaryotes are listed below:**

Prokaryotes	Eukaryotes
The linked genes are organized into clusters known as operons which are under the control of a single promoter.	Eukaryotic genes are not organized into operons and each of these genes requires its own promoter.
These genes are primarily regulated by repressors.	Regulation by repressors is very occasional and the primary role of regulation is played by the transcriptional activators known as transcription factors.

2.Regulation of Transcription

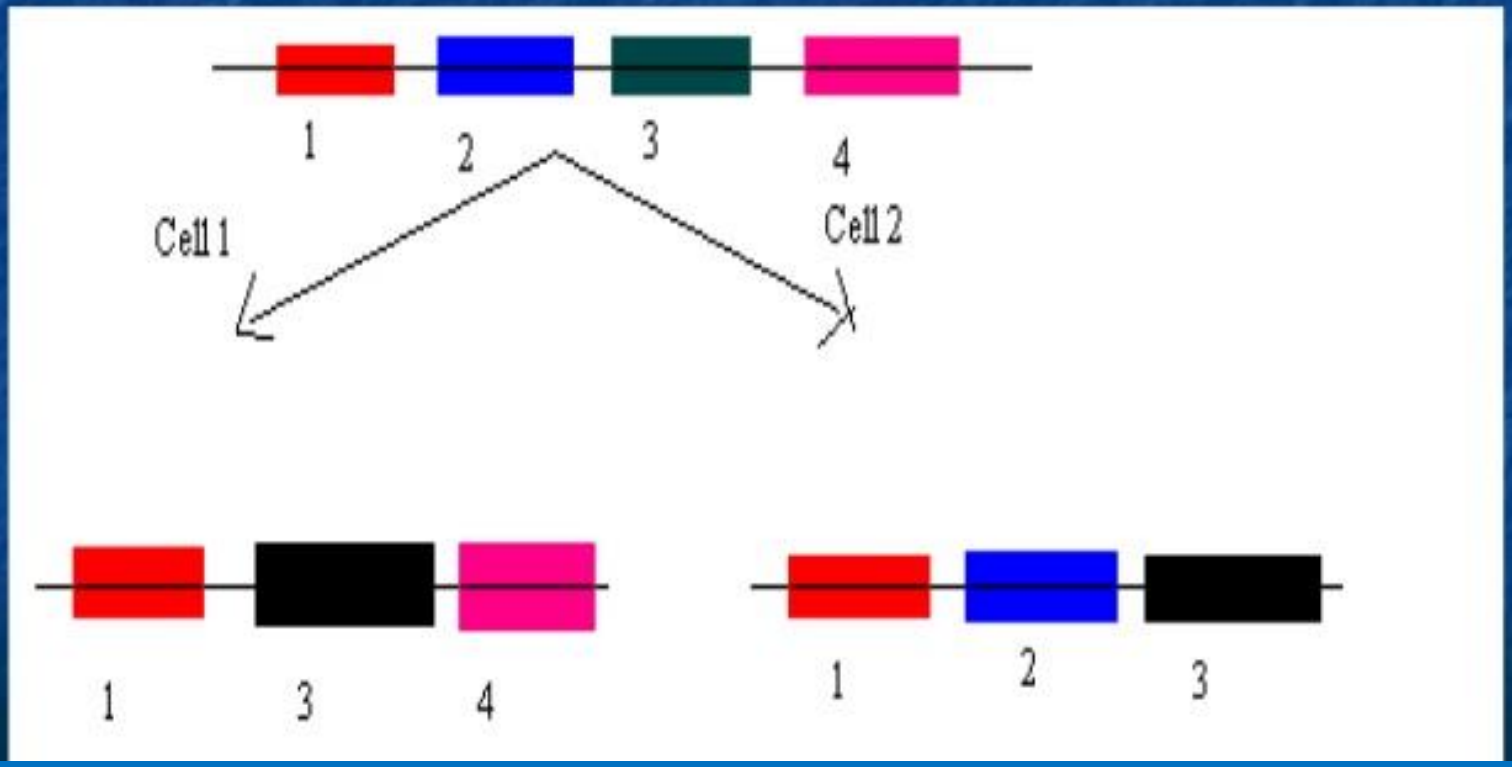
Prokaryotes	Eukaryotes
A promoter sequence which controls an operon lies upstream of the operon. Accessory or the regulatory proteins control the recognition of the transcriptional initiation sites by RNA polymerases	Those genes which code for a protein have a basic structure consisting of: ▪Exons – Gene sequences which encode for a polypeptide ▪Introns – These sequences will get removed from the mRNA before it gets translated. ▪A transcription initiation site ▪Promoter sequences.
A single operon gets transcribed into a polycistronic mRNA which can be translated into multiple proteins	Monocistronic mRNAs which can produce a single polypeptide are produced

3.Regulation of RNA Processing

- RNA processing involves
  - Addition of 5' cap
  - Addition of a 3' poly (A) tail
  - Removal of introns
- The RNAs which get translated to proteins are transported out from the nucleus to cytoplasm.
- Depending on the final combination of exons after splicing different kinds of proteins are obtained which can perform different functions in the cell.

Exon Shuffling

- The functions of two proteins synthesized from the same mRNA are different in different cells as different combination of exons exist in different cells.



4.Regulation of RNA Transport

- Only some RNAs function within the nucleus whereas all other RNAs which are meant for protein synthesis have to be transported from the nucleus to the cytoplasm via nuclear pores.

5.Regulation of RNA Longevity

- mRNAs from different genes have different life spans.
- The information of the life span of mRNA is found in the 3' UTR.
- The sequence AUUUA within 3' UTR acts as a signal for early degradation.
- More the number of times the sequence is repeated → Shorter the lifespan of mRNA

6.Regulation of Translation

- **Translational initiation**
  - The expression of a gene product also depends on the ability of the ribosome to recognize the correct AUG codon out of the multiple methionine codons present in the mRNA.
- **Control of translational process**
  - In many animals large amounts of mRNAs are produced by the eggs but all of them do not get translated until the egg is fertilized.

7.Post Translational Control Points

- **Post translational modifications**
  - Functional state of protein depends on modifications like glycosylation, acetylation, fatty acylation, disulfide bond formations.
  - Chaperons
- **Protein transport**
  - Transportation to the site of action
- **Protein stability**
  - The lifespan of a protein depends on the specific amino acid sequence present within them

Summary of the Class

- The expression of genes is controlled at various levels in eukaryotes.
- At the chromatin stage the level of condensation determines whether the genes will remain transcriptionally active or not.
- The unique combination of the promoter sites, transcription factors and enhancers regulates the transcriptional rate of a gene.
- After transcription the gene expression is controlled by RNA processing.
- The expression of gene is also controlled at the level of translation and after translation.

Video link

https://www.youtube.com/watch?v=gG7uCskUOrA

Thank you