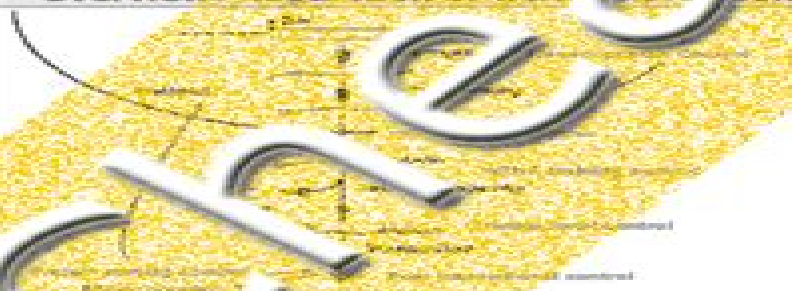


14: Regulation of Gene Expression in Eukaryotes

Key Terms

- Promoter:** A DNA sequence having a regulatory function over the transcription of an adjacent gene, and to which RNA polymerase binds prior to transcription.
- Enhancer:** a short region of DNA that can be bound with proteins to promote expression of a distal or proximal gene
- TATA Box:** Binds to transcription factor for regulating gene expression, usually within 30bp of the transcription start site
- Basal Transcription Factor:** Transcription factors that are required for all transcriptions, they unwind DNA and assist RNA polymerase to bind to transcription initiation sites.
- Modulatory Transcription Factor:** Transcription factors that regulate time/space expression, may bind to enhancers or to promoter regions to enhance or suppress gene expression under certain conditions.
- DNA binding domain:** A domain found in all transcription factors, used to bind DNA, including three types: Zinc-finger, HLH and leucine zipper.
- Zinc-Finger:** A structure found in a number of transcription factors, has repetitive two-cystein and two histidine to bind a Zn²⁺ and form a "finger" structure.
- Leucine-zipper:** A structure found in a number of transcription factors, characterized by leucine residue at every other turn of helix, 7 amino acid apart.
- HLH: Helix-loop-Helix, homeodomain,** contain many basic amino acid, also called basic HLH (bHLH). Another DNA-binding domain found in transcription factors.
- Activator:** Transcription factors that binds to DNA and activate gene expression.
- Co-activator:** do not bind DNA but bind to active or co-enhance activator function.
- Repressor:** Transcription factors that binds to DNA and repress gene expression.
- Co-repressor:** Factors that coordinate with a repressor to inhibit gene expression.
- Alternative splicing:** Introns can be spliced at different sites, generating different polypeptides isoforms.
- IRES: internal ribosome binding site, independent cap-independent translation initiation.**
- uORF: Short upstream ORF (open reading frame, start from AUG),** inhibit translation of the main ORF.
- Untranslated region:** Can be located at 5' UTR, 3' UTR, at 3' end (3' UTR), playing important roles in mRNA stability and translation regulation.
- Post-translational Control:** A series of modification, sorting and transport after protein is synthesized.

Overview: Regulation of Gene Expression



Transcriptional Control

Different levels:

• Transcriptional Initiation: controlled by transcription factors

- Basal factors: binds to promoter, required for all transcription.
- Modulatory factors: binds to enhancer, regulate gene expression.
- Major control is at transcription initiation.



• Post-transcriptional Control

- mRNA processing:
 - 5' capping
 - 3' polyadenylation
 - intron splicing
- mRNA export: nuclear pore
- mRNA stability: 5' cap, 3' polyA tail, 5' UTR, 3' UTR



• Translational Initiation: controlled by translation factors

- Cap-dependent: requires cap for translation initiation
- Cap-independent: binds to poly A binding protein which then binds to translation initiation factors and promote translation initiation
- Secondary structure: locate at 5' end and inhibit translation by acting as an obstacle for ribosome movement
- uORF: upstream short ORF (open reading frame, start from AUG), inhibit translation initiation. Usually located at 5' UTR
- IRES: internal ribosome binding site, promote cap-independent translation initiation.
- uORF: upstream short ORF (open reading frame, start from AUG), inhibit translation by competing ribosomes.

Mechanism of translation initiation:

- Cap-dependent: ribosome binds to cap and scan for AUG
- Cap-independent: Do not require cap, at least two different mechanisms:
 - Leaky Scanning:** Once the 40S subunit binds to cap, it starts to scan for AUG. Sometimes it may skip an AUG, this is called leaky scanning. It enable the translation starts from different AUG, therefore one mRNA may produce two or more polypeptides.
 - IRES Initiation:** IRES sequence form a special secondary structure which can recruit translation initiation factors independent of 5' cap.



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