CONCEPT: TRANSCRIPTIONAL REGULATORS OF GENE EXPRESSION

How Transcriptional Regulators Work

● Transcriptional regulators _____ gene expression by activating or repressing the transcription of genes

□ Transcriptional **repressors** turn genes off and therefore inhibit transcription

- Can compete with activators for binding

- Can inhibit transcription via protein-protein interactions

□ Transcriptional **activators** turn genes on, and therefore activate transcription

- Help make promoters fully functional by connecting with RNA polymerase

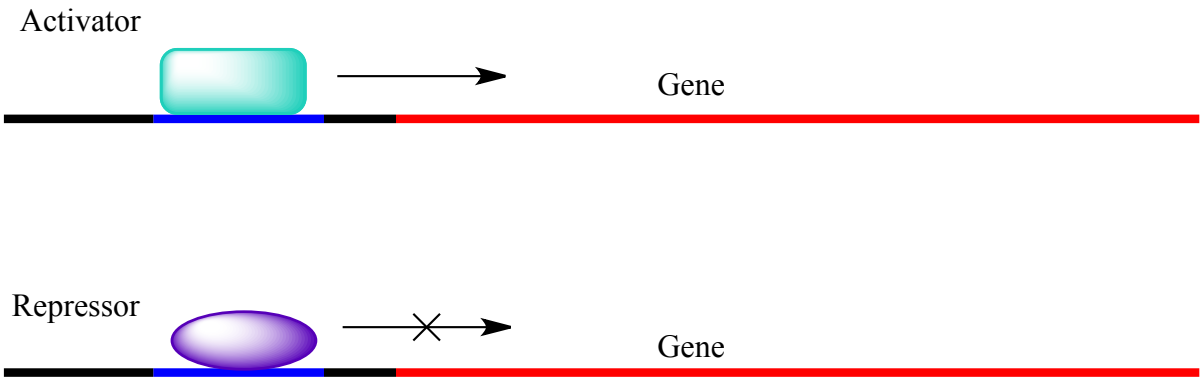
□ Can work with **coactivators** or **corepressors** which help to control transcription

- Modifying chromatin structure

- Activating the regulatory protein

□ **Mediator** is a 24 subunit complex that acts as a connector between regulatory proteins and RNA polymerase

EXAMPLE: Comparison of activators and repressors



□ Rarely do they work alone, and require other interactions and _____ to be fully functional

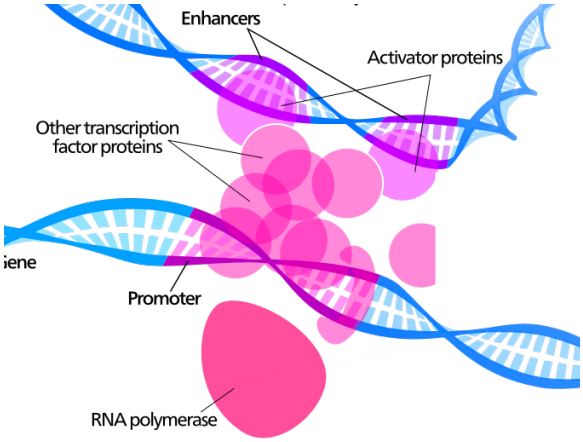
- Other **transcription factors** are recruited to regulate gene expression

- **General transcription factors**: bind to core promoter site (Ex: TFIIB, TFIIH)

- **Sequence specific factors** bind to regulatory sites to activate/repress expression

- Each gene is regulated differently

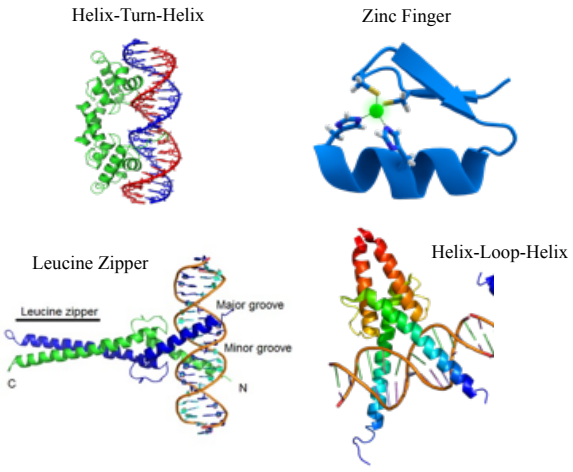
EXAMPLE: Combination of transcription factors results in gene regulation



DNA binding motifs

- There are four common DNA binding _____ that transcriptional regulators contain
  - □ **Helix-turn-Helix**: One helix makes contact with the DNA, while the other helix stabilizes the interaction
    - **Homeodomains** are found on *Hox genes* which are crucial for proper development
  - □ **Zinc Finger:** Has repeats of cysteine and histidine that bind zinc and fold into a finger-like structure to bind DNA
  - □ **Leucine Zipper**: Dimerization of alpha helices with many leucine residues can bind DNA
  - □ **Helix-loop-Helix:** Two alpha helices connected by a loop can bind DNA
  - □ Transcriptional regulators bind to regulatory DNA sequences between 10 and 10,000 nucleotides in length
    - Regulator proteins are **degenerate** meaning they don't need an exact sequence to bind
    - They don't necessarily bind to the DNA nucleotides – can recognize and noncovalently bind to the helix

EXAMPLE: DNA binding domains



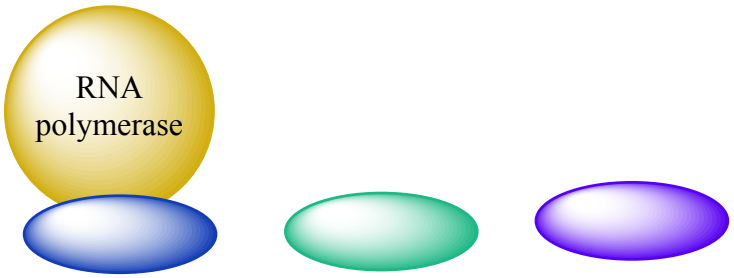
● Prokaryotes use _____ RNA polymerase subunits to control gene transcription

□ *Sigma subunit* of RNA polymerase is required to recognize a promoter

- Many sigma subunits exist – and each recognizes a different set of promoters

□ Gene expression is controlled by replacing the sigma subunits of RNA polymerase

EXAMPLE: Sigma factor replacement allows for gene regulation in prokaryotic cells



Three different sigma factors

Types of Transcriptional Regulators

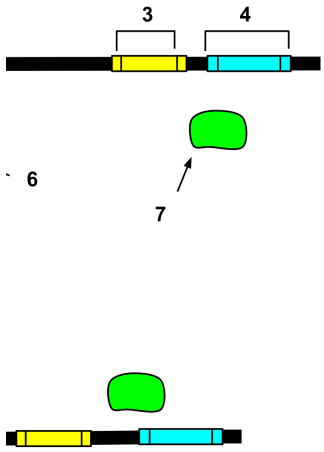
● Transcriptional regulators can _____ to sequences located near or far from the gene they're regulating

□ **Promoter-proximal** elements lie near to the promoter site

- **Promoter** binds RNA polymerase and orients it correctly so it can transcribe the gene

- Contains the initiation site where RNA synthesis begins

EXAMPLE: A promoter (yellow) recruiting RNA polymerase (green) to the gene (blue)



□ There are numerous regulators that bind to DNA sequences _____ from the gene

- **Enhancer** is a DNA site to which gene activators bind

- Can be upstream or downstream from gene, and usually 1000s nucleotides away from promoter

- DNA between enhancer and promoter loop out to allow the two regions to interact

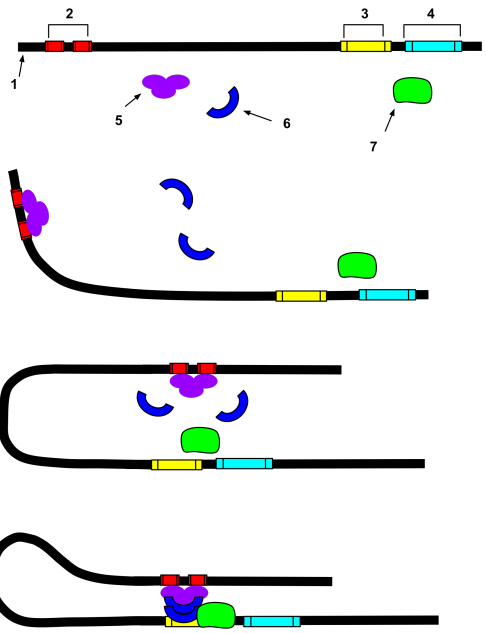
- **Silencers** is a DNA site to which gene repressors bind. Acts similarly to an enhancer

□ **Insulators** (barrier elements) divide chromosomes into independent segments

- Prevents distant elements (enhancers) from acting on promoters in a different segment

□ **Gene control region:** entire DNA sequence involved in regulating and initiating transcription of a gene

EXAMPLE: Example of enhancer activation



Tryptophan Repressor and Lac Operon

● The amino acid _____ is a major regulator of gene expression in prokaryotes

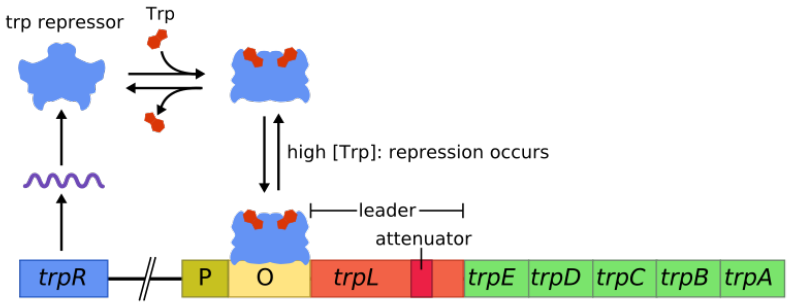
□ Can bind to **operons** (stretches of many related genes) and inhibit transcription

- Tryptophan binds to a transcriptional repressor to activate it

- The activated repressors binds to regulatory sequences to inhibit genes involved in tryptophan creation

□ Allows gene expression to be controlled by environmental levels of tryptophan

EXAMPLE: Control of the *trp* operon



● The *lac* operon controls the _____ of lactose in *E. coli*

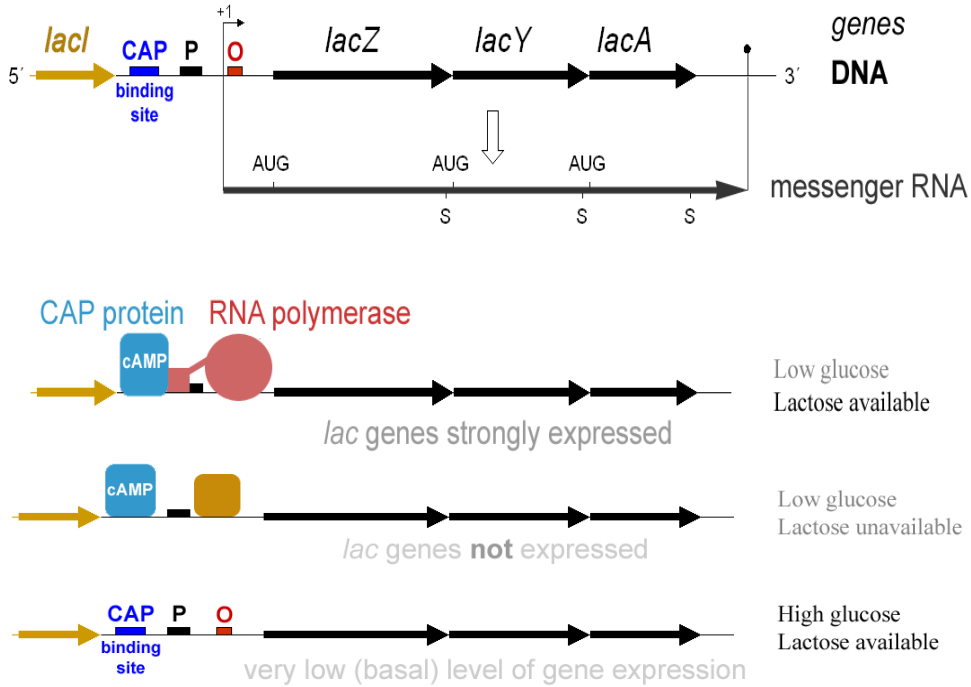
□ No lactose available: The lac repressor binds and halts transcription of lac operon

□ Glucose available: the activator **Catobolie activator protein (CAP)** remains inactive, but no direct repression

□ Lactose available: the activator **Catobolie activator protein (CAP)** binds upstream of promoter and activates

EXAMPLE: Control of the *lac* operon

<u>The *lac* Operon and its Control Elements</u>



PRACTICE

1. Which of the following is not a DNA binding motif?
    a. Zinc Finger
    b. Leucine Zipper
    c. Helix-loop-Helix
    d. Helix-zipper-Helix

2. What is the purpose of a transcriptional mediator?
    a. To mediate regulation between transcription and translation
    b. To mediate the process of transcription
    c. To mediate between regulatory proteins and RNA polymerase
    d. To mediate between RNA polymerase and DNA

3. True or False: Enhancers can reside downstream of the gene they regulate.
    a. True
    b. False

4. If lactose is present, what happens to the *lac* operon?
    a. It is activated
    b. It is repressed

5.