

Think about the following exercises and discuss them in pairs

RNA polymerase II commonly terminates transcription of the HIV (the human AIDS virus) genome a few hundred nucleotides after it begins, unless helped along by a virus-encoded protein called Tat, which binds to a specific hairpin structure in the nascent viral RNA. Tat then recruits a collection of proteins, including the protein kinase Cdk9, which phosphorylates RNA polymerase, enhancing its ability to continue transcription. Flavopiridol is the most potent inhibitor of Cdk9 yet discovered; it blocks Cdk9-mediated phosphorylation. Would you expect flavopiridol to interfere with HIV transcription? Why or why not?

The yeast Gal4 transcription activator comprises two domains: a DNA-binding domain and an activation domain. The DNA-binding domain allows Gal4 to bind to appropriate DNA sequences located near genes that are required for metabolism of the sugar galactose. The activation domain binds to components of the transcriptional machinery (including RNA polymerase), attracting them to the promoter, so the regulated genes can be turned on. In the absence of Gal4, the galactose genes cannot be turned on. When Gal4 is expressed normally, the genes can be maximally activated. When Gal4 is massively overexpressed, however, the galactose genes are turned off. Why do you suppose that too much Gal4 squelches expression of the galactose genes?

How are histone modification enzymes and chromatin remodeling complexes recruited to unmodified chromatin, and how are they thought to aid in the activation of transcription from previously silent genes?

How is it that protein–protein interactions that are too weak to cause proteins to assemble in solution can nevertheless allow the same proteins to assemble into complexes on DNA?

Multiple Choice Questions

1. Which of the following statements are INCORRECT for transcription regulators:
 - a. Transcription regulators bind to very long DNA sequences called cis-regulatory sequences
 - b. Transcription regulators control the time and place of transcription by switching genes on and off
 - c. Dimer formation increases specificity of DNA recognition
 - d. Transcription regulators can only form homodimers (complex of 2 identical proteins)

2. DNA binding proteins recognize their target sequence by
 - a. a complementary DNA sequence
 - b. protein surfaces matching the shape of DNA
 - c. a complementary RNA sequence
 - d. a protein surface establishing interactions with a specific portion of DNA

3. Which statements are CORRECT about eukaryotic transcription control?
 - a. The transcription control is identical to the processes in prokaryotes
 - b. Cis-regulatory sequences are distributed over a large DNA stretch
 - c. The gene control region is just the promoter
 - d. Eukaryotic transcription regulators recruit the same RNA polymerase as in prokaryotes

4. Activator proteins...
 - a. ...are transcription regulators
 - b. ...block gene transcription
 - c. ...are required to make DNA more accessible for transcription
 - d. ...are the same as enhancers

5. How can repressors prevent transcription?
 - a. Competitive binding to regulatory DNA sequences
 - b. Interacting with general transcription factors
 - c. Masking activation domains of activators
 - d. Remodeling chromatin

6. Which statements are CORRECT for the Gal4-UAS system?
 - a. Gal4 gene encodes a transcription activator
 - b. It can be used to study gene expression only in *Drosophila*
 - c. UAS is an enhancer sequence
 - d. It requires a reporter gene

7. How can the activity of transcription regulators be modulated?
 - a. Transcription regulators are not modulated. They modulate transcription
 - b. By binding of ligands or proteins
 - c. By covalent modifications such as phosphorylation
 - d. By binding to inhibitory proteins

8. Which statements are CORRECT about the araBAD-operon?
 - a. It controls expression of genes required for metabolism of L-arabinose
 - b. It is an operon from *Arabidopsis thaliana*
 - c. It can be used to control the expression of a recombinant protein
 - d. araC controls the whole araBAD operon and its own expression

9. What are evolutionary advantages of transcriptional control?

- a. It allows organisms to adapt their set of expressed genes to environmental stimuli
- b. Researchers can use the systems for their experiments
- c. It has no evolutionary advantage
- d. It enables development of complex multi-cellular organisms based on the same genome

True and False

1. Any cell in an organism expresses the exact same set of genes because they all have an identical genome.
2. Transcriptional control refers to the modulation of protein synthesis from mRNA to regulate the expression profile of a cell.
3. Activator proteins block the binding of additional regulators
4. Activator proteins recruit RNA polymerase to the gene which is supposed to be transcribed and release it to begin transcription
5. Absence of insulator DNA sequences can lead to activation of inappropriate genes
6. The tryptophane operon uses transcriptional activators to activate gene expression if the tryptophane concentration is low.
7. There is a single activator or repressor for each cell type in the organism
8. Transcription factors determine the cell type and can even be used to reprogram differentiated cells into pluripotent stem cells.