

Gene Regulation in Eukaryotes

Gene regulation is complex for a reason: the complexity ensures that the correct gene is expressed in the correct cell at the correct time. Cells rely on information encoded in their DNA to regulate protein synthesis. In eukaryotes, there is a mechanism that controls when a gene is expressed, one that controls the amount of protein made, and still another that controls when synthesis of that protein stops. A gene may also include other nucleotide sequences that act to control its expression. These sequences include promoters and operators, which control the start of transcription.

Controlling Gene Expression

Because DNA and ribosomes are located in the cytoplasm of prokaryotic cells, both transcription and translation occur at the same time. As a result, the regulation of gene expression in prokaryotes is limited to a few steps during transcription. However, the cellular and chromosomal organization in eukaryotes is much more complex. This makes it possible for eukaryotes to regulate gene expression at many different points during protein synthesis.

Pre-Transcriptional Regulation

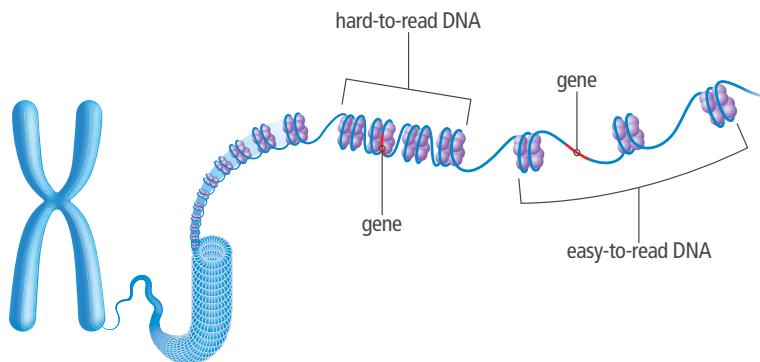
Language Arts Connection

Use Internet resources to research some of the recent discoveries in the field of epigenetics. Write a blog post to explain how a person's environment and their ancestors' environments can affect gene expression.

Recall that in eukaryotes, the DNA in chromosomes is bound tightly around proteins called histones. Chemical compounds are also added to the DNA to help regulate gene expression. All of these added chemical compounds are referred to collectively as the epigenome. The epigenome determines how easily the enzymes of transcription can access regions of the chromosome to turn genes on or off. When histones or DNA are changed chemically, the result may change the accessibility of the DNA for transcription.

Epigenetic changes can be caused by factors such as the age of the organism, inputs from the environment, and disease-causing organisms. Chemical changes to histones or DNA nucleotides may cause transcription of a DNA region either to begin or to stop. Epigenetic changes are heritable, even though they do not change the genome itself.

FIGURE 6: Epigenetic changes to chromosomes occur in a variety of ways. In one type of histone modification, the DNA molecule tightens, making it hard to read.



 **Predict** What would happen to a multicellular organism if every gene were expressed in every cell all the time?

 **Explain** How is gene expression related to how tightly DNA is wound around histones?

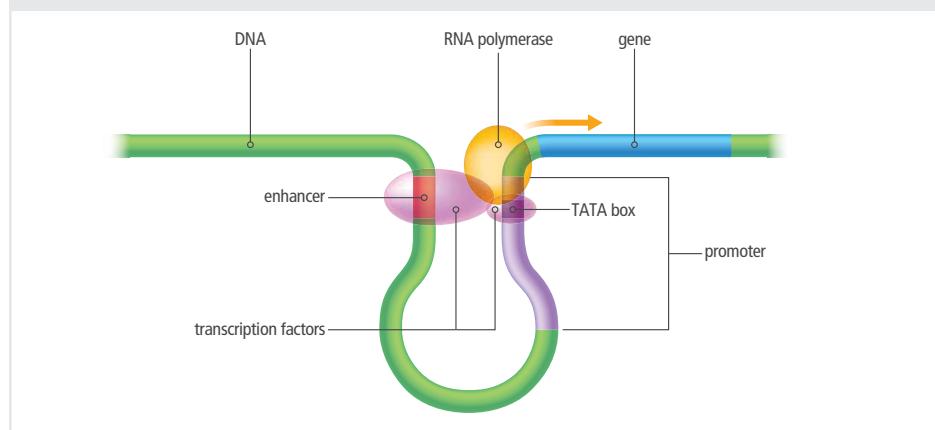
Transcriptional Regulation

Recall that a promoter is a segment of DNA that helps RNA polymerase recognize the start site of a gene. In eukaryotic cells each gene is controlled by a unique combination of promoters and other regulatory sequences. Most promoter sequences are unique to the gene, but some are repeated among many genes in many organisms. For example, most eukaryotic cells use a seven-nucleotide promoter with the sequence TATAAAA, called the TATA box.

Eukaryotic cells also have other types of promoters that are more specific to an individual gene. DNA sequences called enhancers speed up the transcription of a gene, while sequences called silencers act to slow down transcription. **Transcription factors** are proteins that bind to DNA sequences and control gene expression.

Transcription factors may bind to a promoter, an enhancer, or other sections of DNA near a gene. When the correct transcription factors are present, RNA polymerase recognizes the start site of the gene, and transcription begins.

FIGURE 7: In eukaryotes, transcription factors bind to promoters and other DNA sequences to help RNA polymerase recognize the start of a gene.



Explain Transcription factors occur in different combinations in different types of cells. How does this allow for variety in cell types?



Engineering

Using RNA Interference to Fight Disease

In the early 1990s, scientists working with the manipulation of color intensity in petunia plants saw something that was hard to explain. In an effort to increase the intensity of flower color, the scientists genetically modified petunia plants to overexpress the flower pigmentation gene for chalcone synthase (CHS). Some of the resulting flowers did indeed have the desired intense purple petals—but not all of them. Some flowers had purple and white petals, while others had completely white petals. Further investigation led to the discovery that both the introduced and naturally occurring forms of CHS had been turned off, or silenced, in some of these plants.

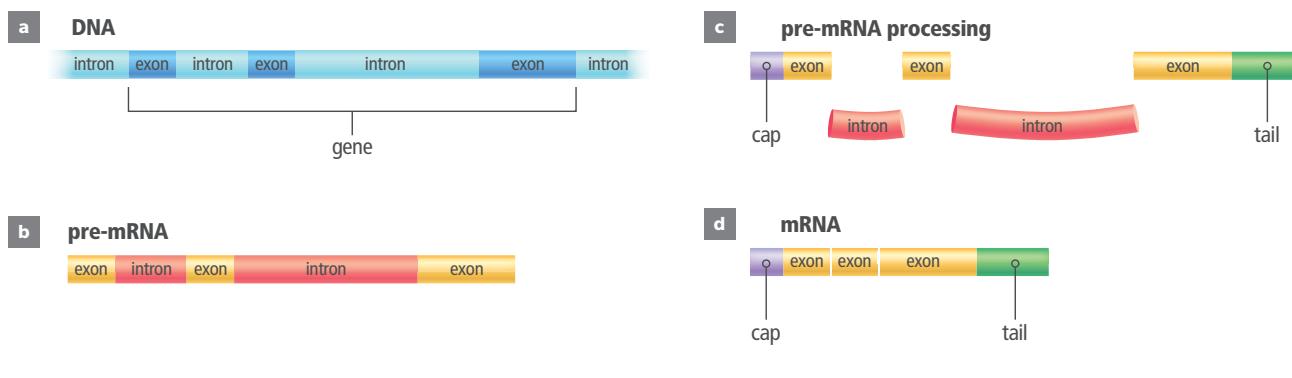
When the gene for the intense color was introduced to the plant, the cells used RNA interference (RNAi) to deactivate the gene. Small segments of double-stranded RNA began a series of reactions that degraded the mRNA molecules. RNAi does not normally occur in healthy cells, but cells may use it to fight off infections or the effects of tissue damage. The study of RNAi may lead to new treatments for a variety of diseases caused by harmful genes.

Analyze Huntington's disease is an inherited disorder that affects the nervous system, resulting in loss of coordination and declining brain function. This disease has been linked to a mutation in the HTT gene. Imagine you want to design an RNAi technology to silence this gene. Make a list of questions you would need to ask to define and delimit the problem.

Post-Transcriptional Regulation

The cell has a variety of mechanisms it can use at any stage after transcription to regulate gene expression. One method is mRNA processing, which edits the mRNA similar to the way a film editor cuts and splices the scenes of a movie.

FIGURE 8: An mRNA molecule typically undergoes processing during or immediately after DNA transcription.



The cell makes many changes to mRNA after transcription. A specialized nucleotide is added to the beginning of each mRNA molecule, forming a cap. This cap helps the mRNA strand bind to a ribosome and prevents the strand from being broken down too fast. The end of the mRNA molecule gets a string of nucleotides called the tail that improves stability and helps the mRNA molecule exit the nucleus. The “extra footage” in the mRNA molecule takes the form of nucleotide segments, called **introns**, that are not included in the final protein. The nucleotide segments that code for parts of the protein are called **exons**. Introns occur between exons. They are removed from an mRNA molecule before it leaves the nucleus. The cut ends of the exons are then joined together by a variety of molecular mechanisms.

Introns are an example of what is called noncoding DNA, which are regions of DNA that do not code for proteins. Scientists are still determining the role of noncoding regions of the human genome. It is thought that noncoding regions may play a role in regulating gene expression and in chromosome pairing and condensation.



Collaborate Why would you want to edit a rough cut of film? With a partner, discuss how this analogy relates to the transcription and translation of a gene.

Translational Regulation

Translation takes place after mRNA is moved into the cytoplasm, and it is the process that makes a protein from amino acids. In eukaryotes, gene expression may also be regulated by changes to the translation process. These changes depend mostly on the stability of the RNA molecule. For example, specific proteins help initiate the translation process. Changes in these proteins can prevent ribosomes from binding to mRNA, which slows or stops protein synthesis. These mechanisms allow eukaryotic cells to control protein production when conditions in the cell change rapidly.



Analyze Make a graphic organizer to summarize the mechanisms that allow eukaryotic cells to control gene expression at each stage of protein synthesis. How do these mechanisms compare to those in prokaryotes in terms of structure and function?