12–5 Gene Regulation

Only a fraction of the genes in a cell are expressed at any given time. An expressed gene is a gene that is transcribed into RNA. How does the cell determine which genes will be expressed and which will remain “silent”? A close look at the structure of a gene provides some important clues.

At first glance, the DNA sequence of a gene is nothing more than a confusing jumble of the four letters that represent the bases in DNA. However, if we take the time to analyze those letters, patterns emerge. Molecular biologists have found that certain DNA sequences serve as promoters, binding sites for RNA polymerase. Others serve as start and stop signals for transcription. In fact, cells are filled with DNA-binding proteins that attach to specific DNA sequences and help to regulate gene expression. A typical gene might look something like Figure 12–22.

As we’ve seen, there is a promoter just to one side of the gene. But what are the “regulatory sites” next to the promoter? These are places where other proteins, binding directly to the DNA sequences at those sites, can regulate transcription. The actions of these proteins help to determine whether a gene is turned on or turned off.

Gene Regulation: An Example

How does an organism “know” whether to turn a gene on or off? The common bacterium E. coli provides us with a perfect example of how gene expression can be regulated. The 4288 protein-encoding genes in this bacterium include a cluster of three genes that are turned on or off together: a group of genes that operate together is known as an operon. Because these genes must be expressed in order for the bacterium to be able to use the sugar lactose as a food, they are called the lac operon.

Figure 12–22

A typical gene includes start and stop signals, with the nucleotides to be translated in between. The DNA sequence shown is only a very small part of an actual gene. Interpreting Graphics

What is the function of the promoters?

- Figure 12–22

DNA and RNA
**Use Visuals**

**Figure 12–23** Reinforce the operation of the lac operon by diagramming the illustration on the board while students follow along in their textbooks. Ask: **When is the repressor protein bound to the operator? (When lactose is not present)** Can transcription occur when the repressor is bound to the operator? (No) **Why not? (The repressor protein blocks RNA polymerase from binding to the promoter.)** How does the presence of lactose help start transcription of the lac genes? (Lactose binds to the repressor protein, causing it to release from the operator site, and RNA polymerase can bind to the promoter.) You may wish to discuss what inactivates a lac operon once it has become active. The enzymes produced by the active lac operon eventually digest the lactose, including the molecules that had bound up the repressor protein. Once this happens, the repressors again bind the operator, and the operon closes down.  

**Build Science Skills**

**Inferring** Help students realize how efficiently the cell is able to control its production of proteins involved in the utilization of lactose. Challenge students to make inferences about why the cell has evolved such an elaborate method of gene regulation. Have them consider why regulating the production of proteins that utilize lactose is advantageous to the cell. They can also consider why it is not advantageous to produce the lac proteins continuously.

**Why must E. coli turn on the lac genes in order to use lactose for food? Lactose is a compound made up of two simple sugars, galactose and glucose. To use lactose for food, the bacterium must take lactose across its cell membrane and then break the bond between glucose and galactose. These tasks are performed by proteins coded for by the genes of the lac operon. This means, of course, that if the bacterium is grown in a medium where lactose is the only food source, it must transcribe the genes and produce these proteins. If grown on another food source, such as glucose, it would have no need for these proteins.**

Remarkably, the bacterium almost seems to “know” when the products of these genes are needed. The lac genes are turned off by repressors and turned on by the presence of lactose. This process tells us a great deal about how genes are regulated.

On one side of the operon’s three genes are two regulatory regions. In the promoter (P), RNA polymerase binds and then begins transcription. The other region is the (O). E. coli cells contain several copies of a DNA-binding protein known as the lac repressor, which can bind to the O region. As **Figure 12–23** shows, when the lac repressor binds to the O region, RNA polymerase is prevented from beginning the process of transcription. In effect, the binding of the repressor protein turns the operon “off” by preventing the transcription of its genes.

If the repressor protein is always present, how are the lac genes turned on in the presence of lactose? Besides its DNA binding site, the lac repressor protein has a binding site for lactose itself. When lactose is added to the medium in which E. coli is growing, sugar molecules diffuse into the cell and bind to the repressor proteins. This causes the repressor protein to change shape in a way that causes the repressor to fall off the operator. Now, with the repressor no longer bound to the O site, RNA polymerase can bind to the promoter and transcribe the genes of the operon.

The lac operon shows one way in which prokaryotic genes are regulated. Many genes are regulated by repressor proteins, while others use proteins that speed transcription. Sometimes regulation occurs at the level of protein synthesis. Regardless of the system, the result is the same: Cells turn their genes on and off as needed.

**Checkpoint** What is the operator?
Eukaryotic Gene Regulation

The general principles of gene regulation in prokaryotes also apply to eukaryotic cells, although there are some important differences. Operons are generally not found in eukaryotes. Most eukaryotic genes are controlled individually and have regulatory sequences that are much more complex than those of the lac operon.

Figure 12–24 shows some of the features of a typical eukaryotic gene. One of the most interesting is a short region of DNA about 30 base pairs long, containing a sequence of TATATA or TATAAA, before the start of transcription. This region is found before so many eukaryotic genes that it even has a name: the “TATA box.” The TATA box seems to help position RNA polymerase by marking a point just before the point at which transcription begins. Eukaryotic promoters are usually found just before the TATA box, and they consist of a series of short DNA sequences.

Genes are regulated in a variety of ways by enhancer sequences located before the point at which transcription begins. An enormous number of proteins can bind to different enhancer sequences, which is why eukaryotic gene regulation is so complex. Some of these DNA-binding proteins enhance transcription by opening up tightly packed chromatin. Others help to attract RNA polymerase. Still other proteins block access to genes, much like prokaryotic repressor proteins.

Why is gene regulation in eukaryotes more complex than in prokaryotes? Think for a moment about the way in which genes are expressed in a multicellular organism. The genes that code for liver enzymes, for example, are not expressed in nerve cells. Keratin, an important protein in skin cells, is not produced in blood cells. Cell specialization requires genetic specialization, but all of the cells in a multicellular organism carry the complete genetic code in their nucleus. Therefore, for proper overall function, only a tiny fraction of the available genes needs to be expressed in the appropriate cells of different tissues throughout the body. The complexity of gene regulation in eukaryotes makes this specificity possible.

Address Misconceptions

Many students might think that all genes are expressed in all cells of an eukaryotic organism. Help students understand that not every gene is expressed in every body cell. Explain that the pancreas secretes many digestive enzymes, such as amylase, which help break down starches. Expression of the amylase-coding gene in the pancreas enables it to perform one of its main functions—secreting this starch-digesting enzyme. However, the same gene in bone marrow cells and in most other body cells has never been activated, so those cells do not secrete amylase. The activated genes in bone marrow and other cells respond to different conditions, and each produces its own appropriate proteins.

Answer to . . .

The operator is a region to which a repressor can bind, preventing transcription of the genes.

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Development and Differentiation

Regulation of gene expression is especially important in shaping the way a complex organism develops. Each of the specialized cell types found in the adult develops from the same fertilized egg cell. This means that cells don’t just grow and divide during embryonic development; they also undergo differentiation, meaning they become specialized in structure and function. The study of genes that control development and differentiation is one of the most exciting areas in biology today.

A series of genes, known as the hox genes, control the differentiation of cells and tissues in the embryo. A mutation in one of these “master control genes” can completely change the organs that develop in specific parts of the body. Mutations affecting the hox genes in the fruit fly, Drosophila, for example, can replace the fly’s antennae with legs growing on its head!

In flies, the hox genes are located side-by-side in a single cluster, as shown in Figure 12–25. Remarkably, similar clusters exist in the DNA of other animals, including humans. The function of the hox genes in humans seems to be almost the same—to tell the cells of the body how they should differentiate as the body grows. Careful control of expression in these genes is essential for normal development.

The striking similarity of genes that control development has a simple scientific explanation: Common patterns of genetic control exist because all these genes have descended from the genes of common ancestors. One such gene, called Pax 6, controls eye growth in Drosophila. A similar gene was found to guide eye growth in mice and other mammals. When a copy of the mouse gene was inserted into the “knee” of a Drosophila embryo, the resulting fruit fly grew an eye on its leg! The fly gene and the mouse gene are similar enough to trade places and still function—even though they come from animals that have not shared a common ancestor in at least 600 million years.

In fruit flies, a series of hox genes along a chromosome determines the basic structure of the fly’s body. Mice have very similar genes on four different chromosomes. The color bars along the mouse’s back show the approximate body area affected by genes of the corresponding colors. Interpreting Graphics What section of the bodies of flies and mice is coded by the genes shown in blue?

12–5 Section Assessment

1. **Key Concept** How is the lac operon regulated?
2. **Key Concept** Describe how most eukaryotic genes are controlled.
3. What genes control cell differentiation during development?
4. What is a promoter?
5. **Critical Thinking** Comparing and Contrasting How is the way hox genes are expressed in mice similar to the way they are expressed in fruit flies? How is it different?

Making an Analogy

Make an analogy to demonstrate the different components of the lac operon. Then, explain in a short paragraph—using your analogy—how the lac operon works.