10.1 What Is Gene Control?

- A typical cell in your body uses only about 10 percent of its genes at one time
  - Some genes affect structural features and metabolic pathways and are expressed in many cell types
  - Others genes are expressed only by certain subsets of cells (e.g., globin in RBCs)
  - Control over gene expression allows cells to respond to changes in their environment
Gene Expression Control

• The “switches” that turn a gene on or off are molecules or processes that trigger or inhibit the individual steps of its expression
Transcription

- Transcription factors: bind directly to DNA and affect whether and how fast a gene is transcribed
  - Repressors: bind to promoters or silencers to shut off or slow down transcription
    - Operators: prokaryotic silencers
  - Activators: recruit RNA polymerase to a promoter region to enhance transcription
    - Enhancer: distant DNA binding site for eukaryotic activators

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Transcription (cont’d.)
Transcription (cont’d.)

• Chromatin structure affects transcription
  – Only DNA regions that are unwound from histones are accessible to RNA polymerase
  – Adding acetyl groups (—COCH$_3$) to a histone loosens the DNA
    • Promotes transcription
  – Adding methyl groups (—CH$_3$) to a histone tightens the DNA
    • Inhibits transcription
mRNA Processing and Transport

• Delaying the post-transcriptional modifications of mRNA delays translation by preventing mRNA from reaching the nucleus
  – mRNA must first be spliced, capped, and finished with a poly-A tail before leaving the nucleus
mRNA Processing and Transport (cont’d.)

- Control over post-transcriptional modification can affect the form of a protein
  - Example: alternative splicing of mRNA by different cell types
- mRNAs are delivered to organelles or specific regions of cytoplasm via zip codes
  - This allows translation of an mRNA close to where its protein product is being used
Translation

• An mRNA’s sequence affects translation
  – A cap on an mRNA zip code sequence prevents translation until mRNA has reached its final destination
  – mRNA stability alters translation rates and is affected by base sequence, the length of its poly-A tail, and bound proteins
In eukaryotes, translation of a particular mRNA can be shut down by tiny bits of noncoding RNA called microRNAs:
- microRNA: complementary in sequence to part of an mRNA
- Expression of a microRNA results in the destruction of all mRNA complementary to it via the process of RNA interference
Double-stranded RNA is also a factor in control over translation in prokaryotes

- Bacteria can shut off translation of a particular mRNA by expressing an antisense (complementary) RNA strand

- With double-stranded RNA, ribosomes cannot initiate translation
Post-Translational Modification

• Many newly synthesized polypeptide chains must be modified before they become functional
  – Example: some enzymes become active only after they have been phosphorylated

• Post-translational modifications inhibit, activate, or stabilize many molecules
10.2 How Do Genes Control Development in Animals?

• As an animal embryo develops, its cells differentiate and form tissues, organs, and body parts
  – Driven by cascades of master gene expression

• The products of *master genes* affect the expression of many other genes
  – Final outcome is the completion of an intricate task such as the formation of an eye
How Do Genes Control Development in Animals? (cont’d.)

• Orchestration of gene expression during development:
  – Maternal mRNAs are delivered to opposite ends of an unfertilized egg as it forms
  – These mRNAs are translated only after the egg is fertilized
  – Protein products diffuse away, forming gradients that span the entire developing embryo
How Do Genes Control Development in Animals? (cont’d.)

• Orchestration of gene expression during development (cont’d.):
  – The nucleus turns on master genes based on its position relative to the gradient proteins
  – Master gene products also form gradients, further influencing which additional master genes the nucleus will turn on
  – Eventually, the products of master genes cause undifferentiated cells to differentiate, and specialized structures to form
How Do Genes Control Development in Animals? (cont’d.)

A

90 minutes

100 minutes

B

120 minutes

140 minutes

165 minutes

C

13 hours
Homeotic Genes

- A **homeotic gene** is a master gene that governs the formation of a body part - such as an eye, leg, or wing
- Animal homeotic genes encode transcription factors with a homeodomain
  - Region of about sixty amino acids that bind directly to a promoter
Homeotic Genes (cont’d.)
• Homeotic genes are often named for what happens when a mutation alters their function
  – Examples in the fruit fly:
    • Antennapedia gene
    • Groucho gene
    • Eyeless gene
Homeotic Genes (cont’d.)
• Homeotic genes evolved in the most ancient eukaryotic cells
  – Homeodomains often differ among species only in conservative substitutions
  – Example: the *eyeless* gene in fruit flies is very similar in DNA sequence (and function) to the animal gene *PAX6*
Homeotic Genes (cont’d.)
10.3 What Are Some Outcomes of Gene Control in Eukaryotes?

• X marks the spot
  – In humans and other mammals, a female’s cells contain two X chromosomes
  – In each cell, one X chromosome is always tightly condensed, termed *Barr bodies*
ANIMATION: X-chromosome inactivation

To play movie you must be in Slide Show Mode
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X Marks the Spot

• Most of the genes on a Barr body are not expressed
  – X chromosome inactivation ensures that only one of the two X chromosomes in a female’s cells is active
• Dosage compensation: mechanism in which X chromosome inactivation equalizes gene expression between males and females

• There is random inactivation of maternal and paternal X chromosomes in each cell
  – An adult female mammal is a “mosaic” for the expression of X chromosome genes
How does just one of two X chromosomes get inactivated?

- An X chromosome gene called *XIST* is transcribed on only one of the two X chromosomes.
- The gene’s product, a long noncoding RNA, sticks to the chromosome that expresses the gene, causing it to condense into a Barr body.
Male Sex Determination in Humans

• The human Y chromosome contains the master gene for male sex determination in mammals, $SRY$
  – $SRY$ expression in XY embryos triggers the formation of testes
  – Mutations in the $SRY$ gene cause XY individuals to develop external genitalia that appear female
Flower Formation

• In flowering plants, populations of cells in a shoot tip may give rise to a flower instead of leaves
  – Transcription factors produced by three sets of floral identity genes (called A, B, and C) guide the process
• When a flower forms at the tip of a shoot, differentiating cells form whorls of tissue
  – Each whorl produces one type of floral structure: sepals, petals, stamens, or carpels
• This pattern is dictated by sequential, overlapping expression of the ABC genes
ANIMATION: Flower formation

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• Prokaryotes do not undergo development, so these cells have no need for master genes

• Prokaryotes do respond to environmental fluctuations by adjusting gene expression
  – Example: bacteria transcribe certain genes only when a specific nutrient is available
  – The cell does not waste energy producing gene products that are not needed
What Are Some Outcomes of Gene Control in Prokaryotes? (cont’d.)

• Bacteria control gene expression mainly by adjusting the rate of transcription
• Genes that are used together often occur together on the chromosome, one after the other
• A single promoter precedes the genes, so all are transcribed together into a single RNA strand
What Are Some Outcomes of Gene Control in Prokaryotes? (cont’d.)

• Operon: group of genes together with a promoter–operator DNA sequence that controls their transcription
  – Although first discovered in bacteria, operons also occur in archaea and eukaryotes
The *lac* Operon

- An operon called *lac* allows *E. coli* cells to metabolize lactose
- The *lac* operon includes three genes and a promoter flanked by two operators
The *lac* Operon (cont’d.)

- Three genes of the *lac* operon:
  - One gene encodes a transport protein that brings lactose across the plasma membrane.
  - Another gene encodes an enzyme that breaks the bond between lactose’s two monosaccharide monomers, glucose, and galactose.
  - A third gene encodes an enzyme whose function is still being investigated.
The *lac* Operon (cont’d.)

- When lactose is not present, a repressor binds to the two operators and twists the region of DNA with the promoter into a loop
  - RNA polymerase cannot bind to the twisted-up promoter, so the *lac* operon’s genes cannot be transcribed
When lactose is present, some of it is converted to another sugar that binds to the repressor and changes its shape:

- The altered repressor releases the operators and the looped DNA unwinds.
- The promoter is now accessible to RNA polymerase, and transcription of lactose-metabolizing genes begins.
ANIMATON: Negative control of lactose operon

To play movie you must be in Slide Show Mode
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Lactose Intolerance

• An individual’s ability to digest lactose declines at a species-specific age
  – In the majority of human worldwide, the switch occurs at about age five, when expression of the gene for lactase shuts off
  – Results in the condition lactose intolerance
Lactose Intolerance (cont’d.)

• When lactase production slows, lactose passes undigested through the small intestine
  – The lactose ends up in the large intestine, which hosts huge numbers of *E. coli* etc.
  – The *E. coli* switch on their *lac* operons, resulting in the production of gaseous products – causing distention and pain
  – Other metabolic products lead to diarrhea
Lactose Intolerance (cont’d.)

• Not everybody is lactose intolerant
  – About one-third of human adults carry a mutation that allows them to digest milk
  – This mutation is more common in some populations than in others
Lactose Intolerance (cont’d.)

got lactase?

South Tyrol Museum of Archaeology/A. Ochsenreiter, as altered by Lisa Starr.
10.5 Can Gene Expression Patterns Be Inherited?

• Direct methylation of DNA suppresses gene expression

• Once a DNA nucleotide becomes methylated, it will usually stay methylated in all of a cell’s descendants

• Methylation is an *epigenetic* modification
  – Epigenetic: heritable changes in gene expression that are not the result of changes in DNA sequence
Can Gene Expression Patterns Be Inherited? (cont’d.)

• In eukaryotes, methyl groups are usually added to a cytosine followed by a guanine
  – The particular cytosines that end up being methylated varies by the individual
Can Gene Expression Patterns Be Inherited? (cont’d.)

[Diagram of DNA structure with highlighted nucleotides: cytosine and guanine]
Methylation is influenced by environmental factors

- Example: humans conceived during a famine have an unusually low number of methyl groups in certain genes
  - Leads to the expression of hormones that foster prenatal growth and development
  - May offer a survival advantage in a poor nutritional environment
• Inheritance of epigenetic modifications can adapt offspring to an environmental challenge much more quickly than evolution
  – Such modifications are not considered to be evolutionary because the underlying DNA sequence does not change
  – Even so, these changes may persist for generations
• Grandsons of boys who endured a winter of famine tend to outlive—by far—grandsons of boys who overate at the same age
  – The effect is presumed to be due to epigenetic modification because these results were corrected for socioeconomic and genetic factors
Can Gene Expression Patterns Be Inherited? (cont’d.)
• A mutated version of *BRCA1* and/or *BRCA2* genes is often found in breast and ovarian cancer cells

• The RNA product of the *XIST* gene does not properly coat one of the two X chromosomes in breast cancer cells
• Why does the RNA product of an unmutated \( XIST \) gene not properly coat an X chromosome in cancer cells?
  – The BRAC1 protein physically associates with the RNA product of the \( XIST \) gene
  – Researchers restored proper \( XIST \) RNA coating—and proper X chromosome inactivation—by restoring the function of the BRCA1 protein in breast cancer cells
Application: Between You and Eternity (cont’d.)