Biology

Concepts and Applications | 9e
Starr | Evers | Starr

Chapter 10

Control of Gene Expression

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

ANIMATION: Controls of eukaryotic gene expression

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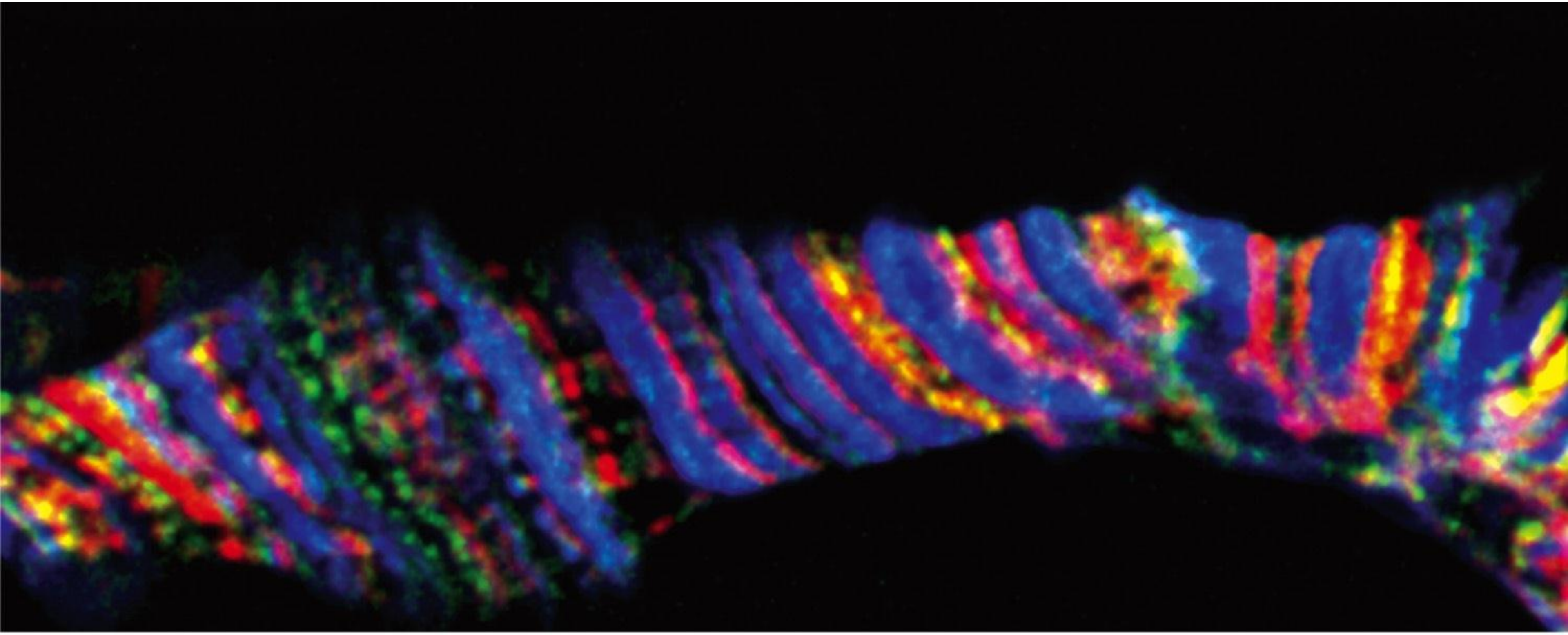
Transcription

- 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

Transcription (cont'd.)



Journal of Biosciences, Volume 36, Number 3, August 2011, Indian Academy of Sciences, Springer.

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 (—CH3) 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

Translation (cont'd.)

- 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

Translation (cont'd.)

- 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

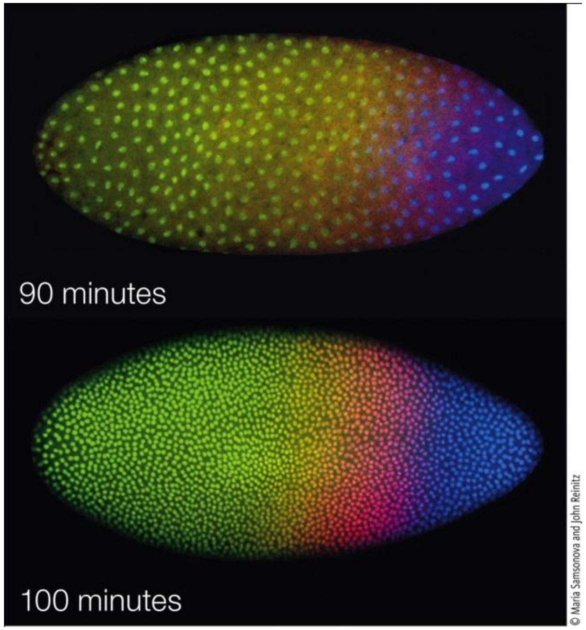
How Do Genes Control Development in Animals? (cont'd.)

- 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.)



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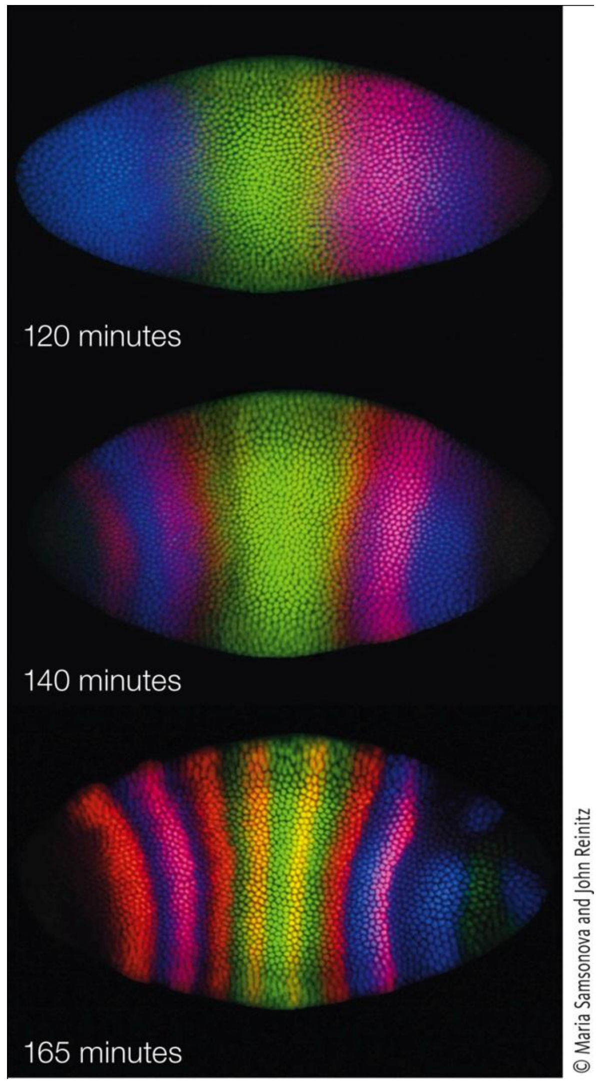

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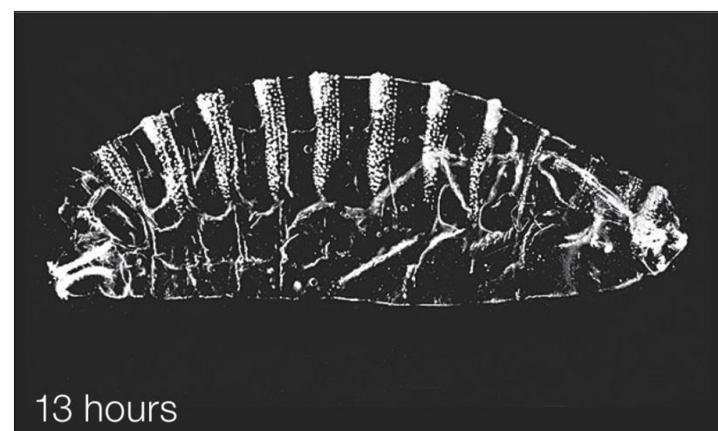

Homeotic Genes

- 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.)

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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.)

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Courtesy of Dr. Barbara Jennings, UCL Cancer Institute, www.ucl.ac.uk

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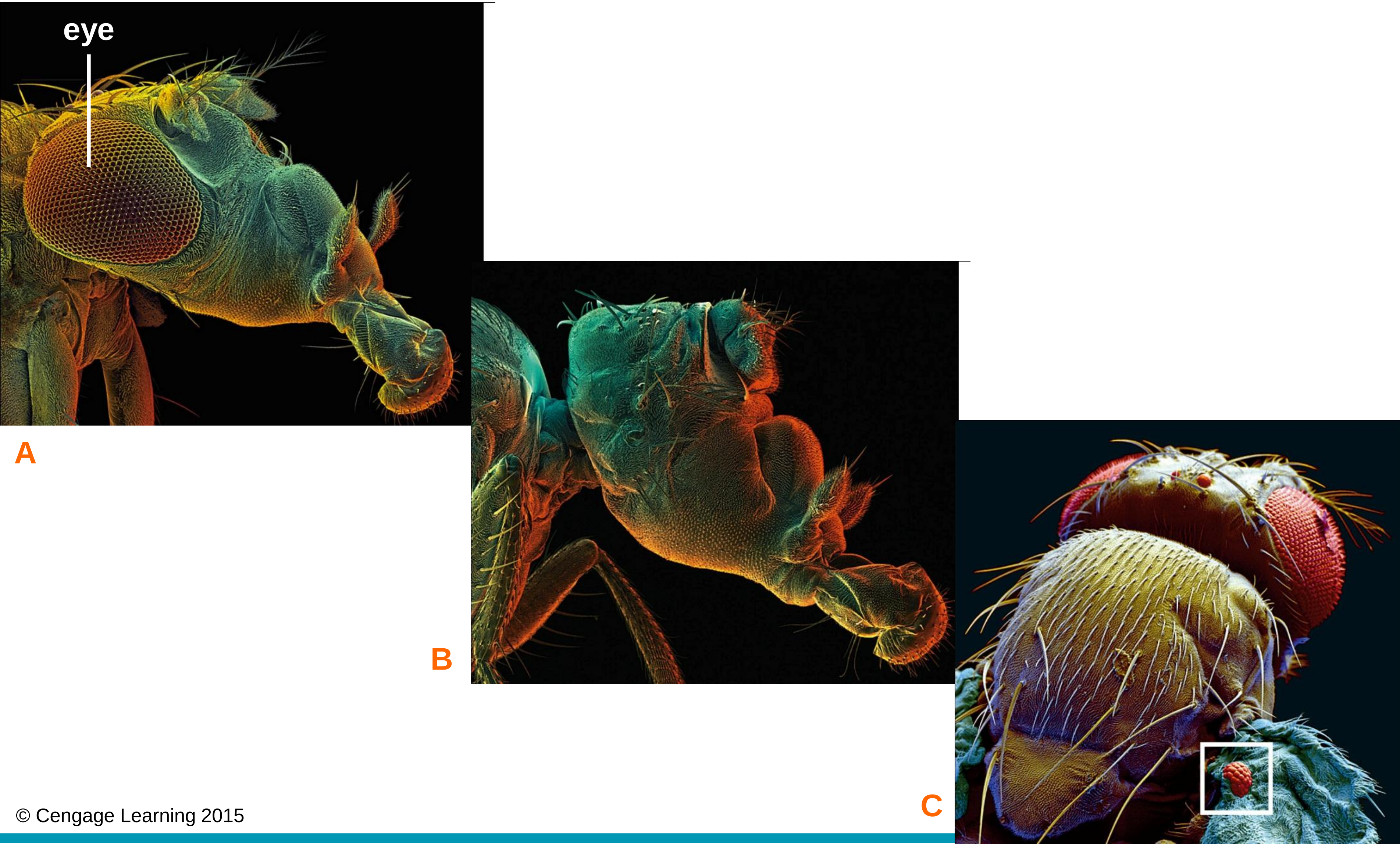
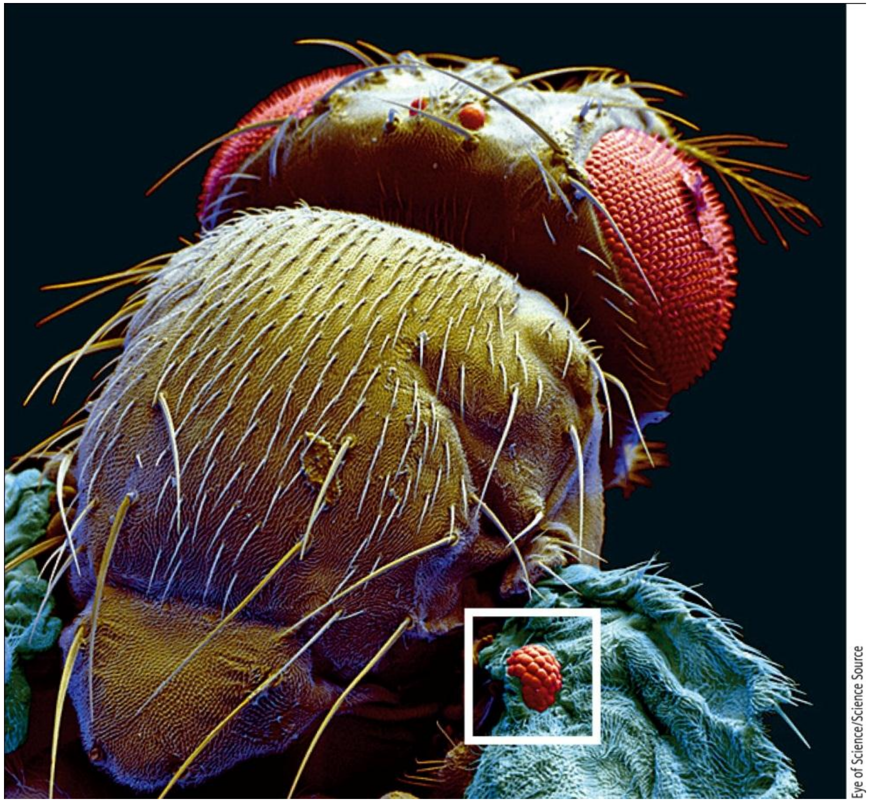
Homeotic Genes (cont'd.)



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.)



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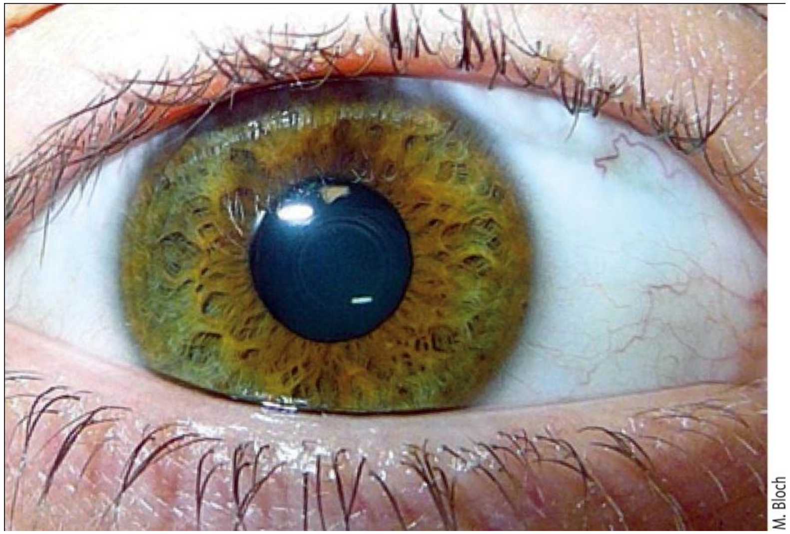

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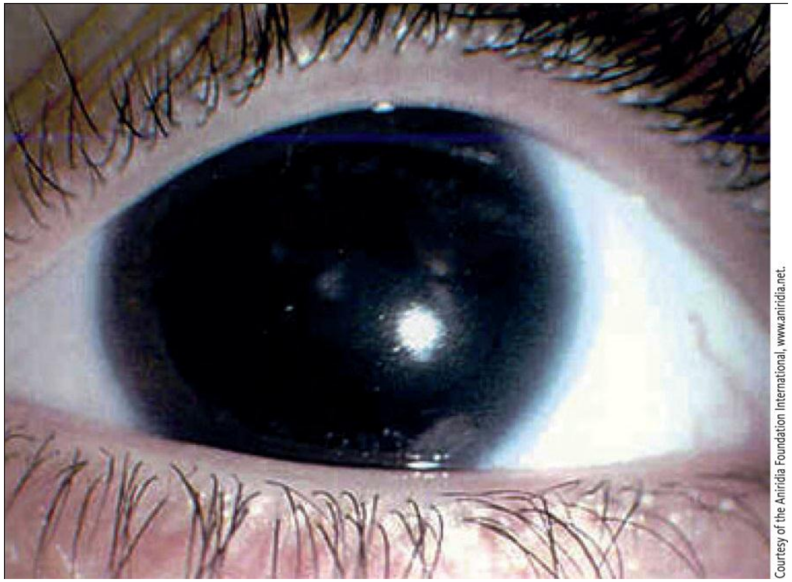

10.3 What Are Some Outcomes of Gene Control in Eukaryotes?

- 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

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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

X Marks the Spot (cont'd.)

- 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

X Marks the Spot (cont'd.)

- 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

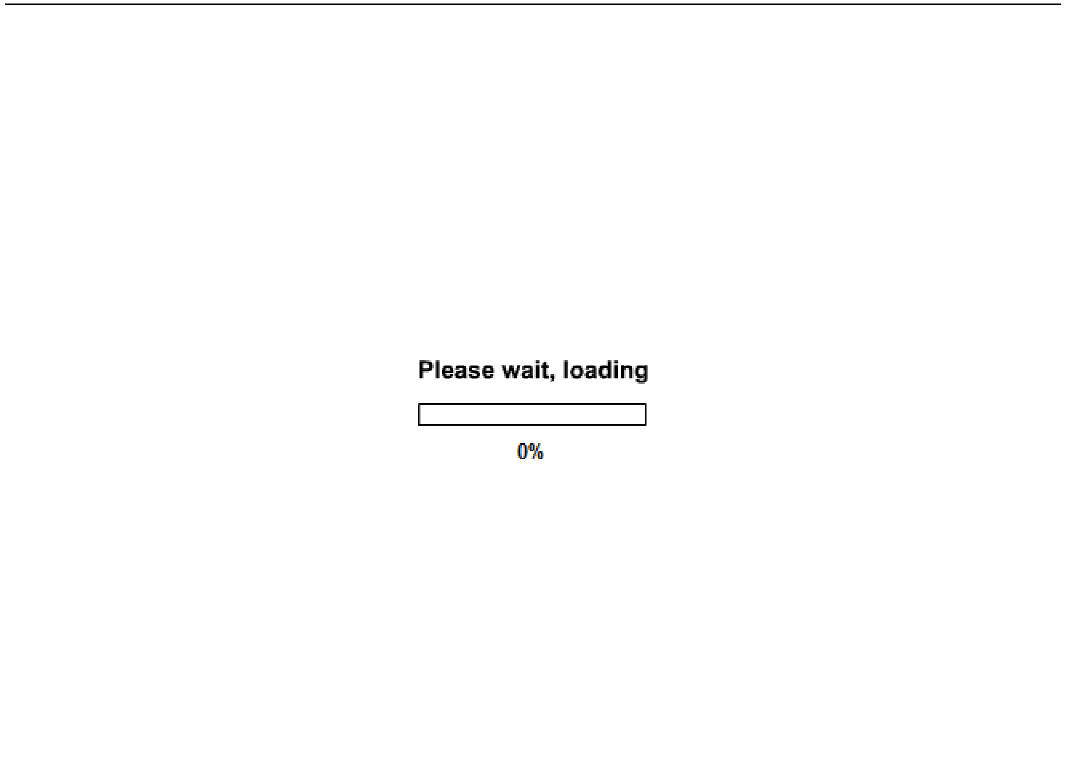
Flower Formation

- 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

Flower Formation (cont'd.)

- 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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10.4 What Are Some Outcomes of Gene Control in Prokaryotes?

- 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

The *lac* Operon (cont'd.)

- 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

ANIMATION: Negative control of lactose operon

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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

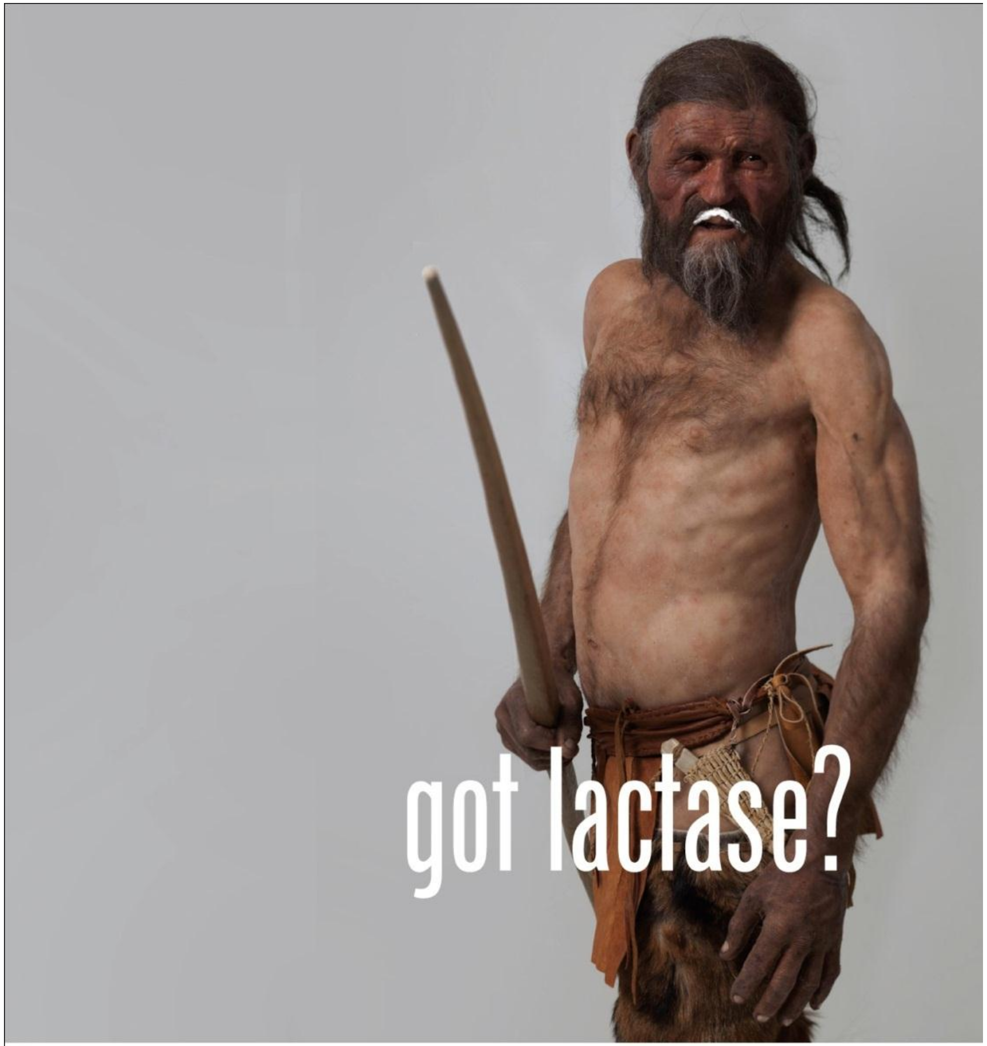
Lactose Intolerance (cont'd.)

- 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.)



South Tyrol Museum of Archaeology/A. Ochsenreiter, as altered by Lisa Starr.

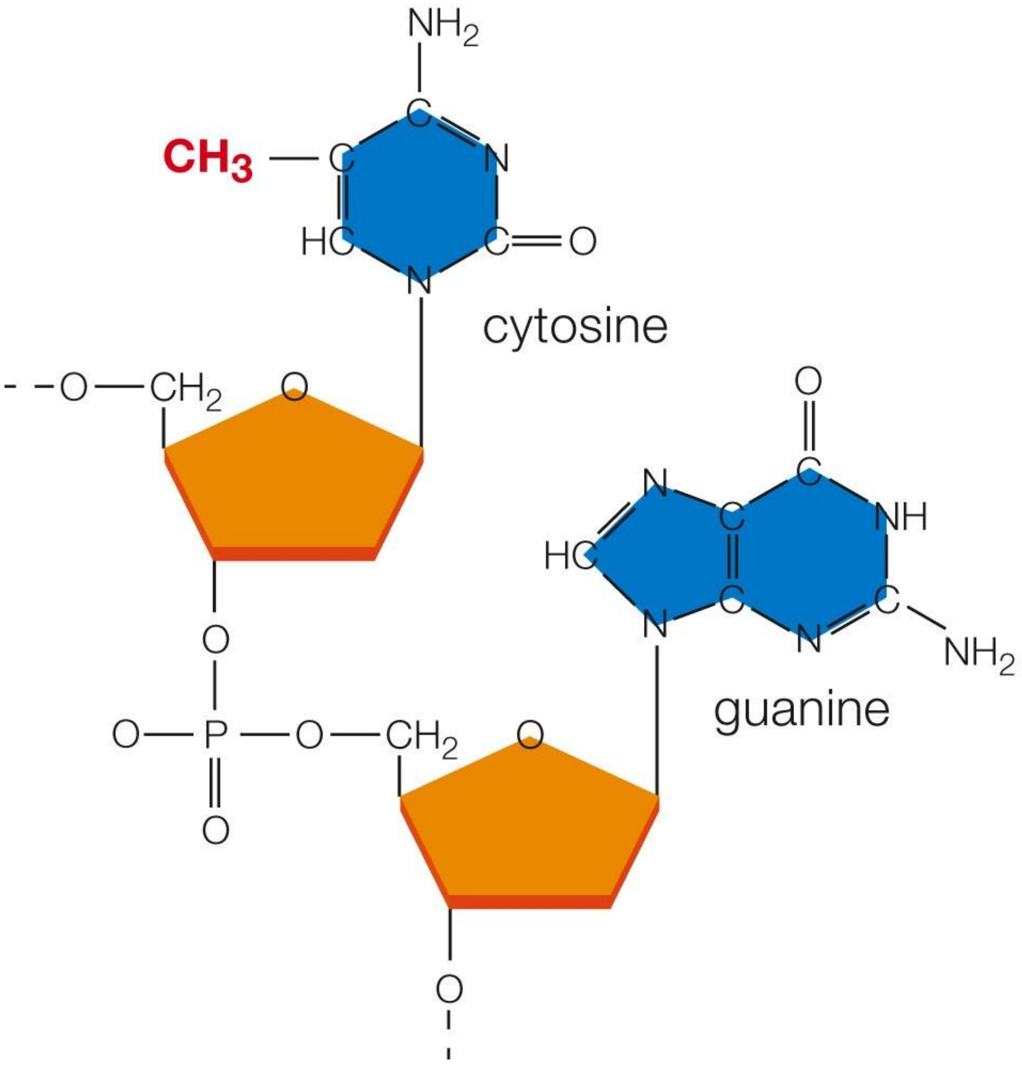
10.5 Can Gene Expression Patterns Be Inherited?

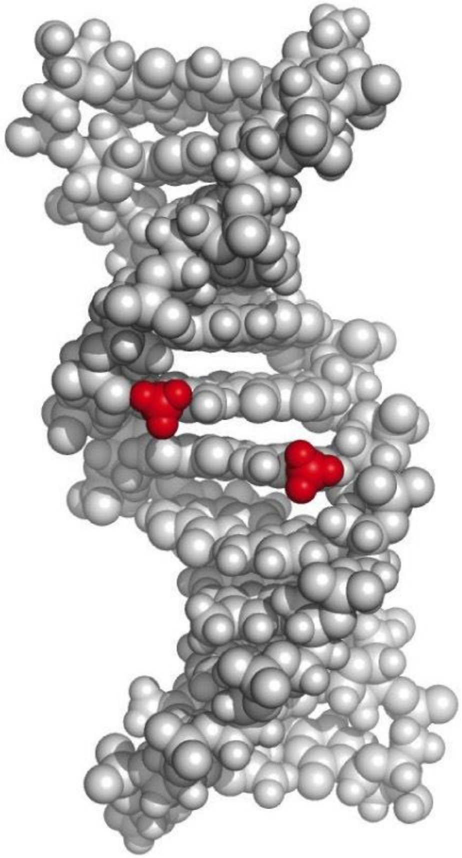
- Direct methylation of DNA suppresses gene expression
- Once a DNA nucleotide becomes methylated, it will usually stay methylated in all of a cell's descendants
- Methylation is an *epigenetic* modification
  - Epigenetic: heritable changes in gene expression that are not the result of changes in DNA 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.)





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Can Gene Expression Patterns Be Inherited? (cont'd.)

- 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

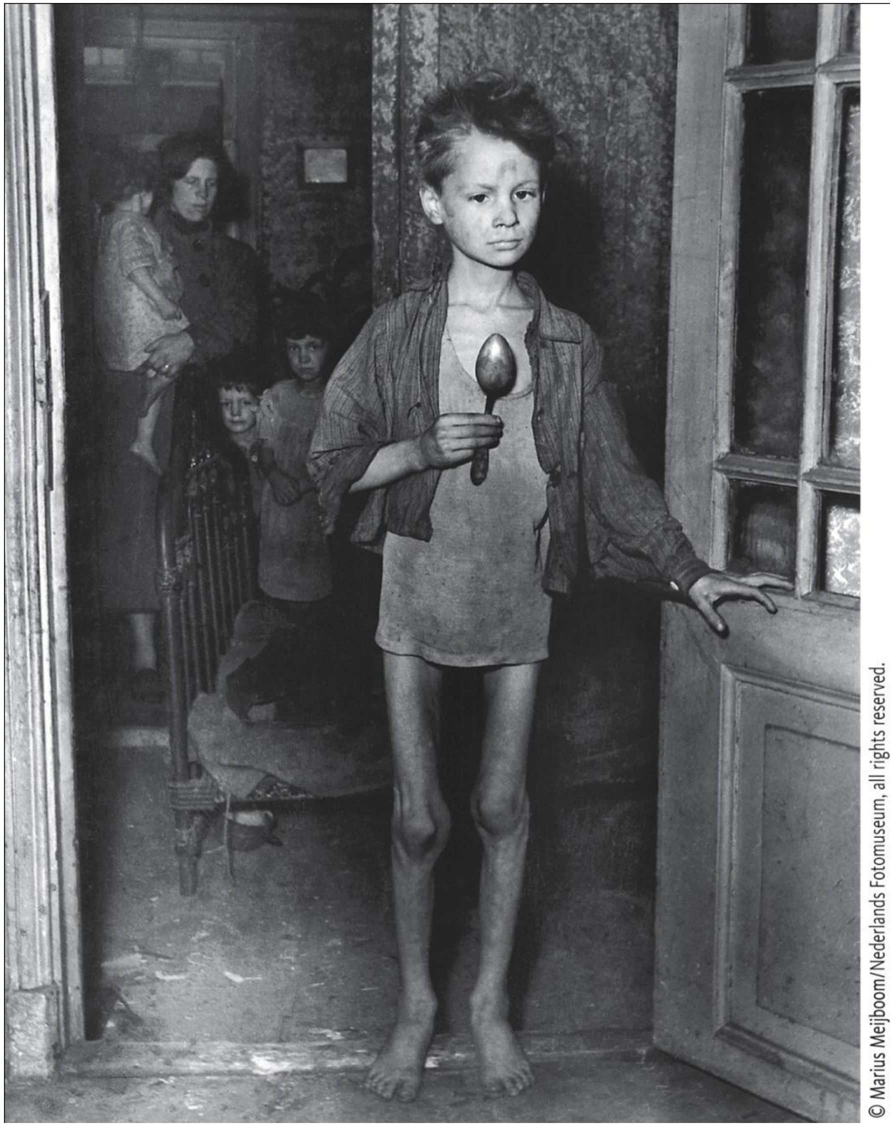
Can Gene Expression Patterns Be Inherited? (cont'd.)

- 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

Can Gene Expression Patterns Be Inherited? (cont'd.)

- 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.)



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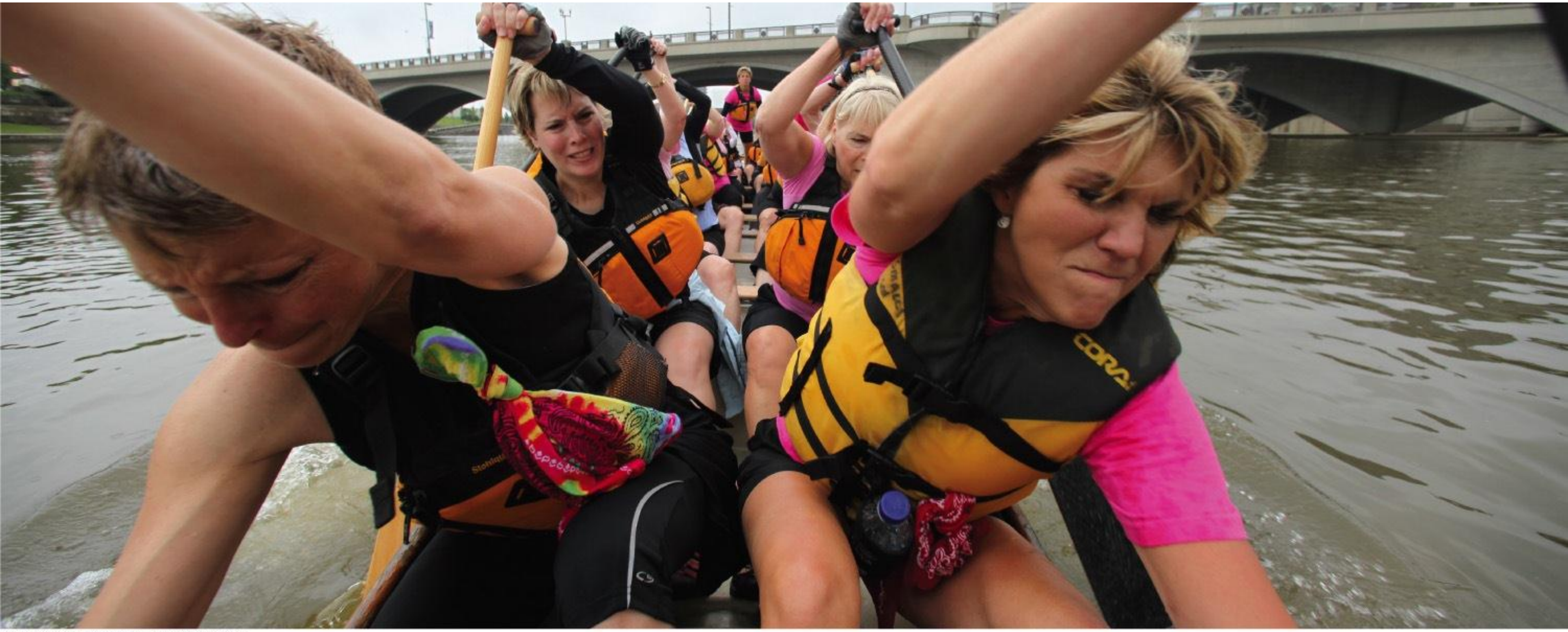
10.6 Application: Between You and Eternity

- 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

Application: Between You and Eternity (cont'd.)

- 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.)



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