Chapter 18

Regulation of Gene Expression

PowerPoint® Lecture Presentations for

Biology

Eighth Edition

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Overview: Conducting the Genetic Orchestra

- Prokaryotes and eukaryotes alter gene expression in response to their changing environment.
- In multicellular eukaryotes, gene expression regulates development and is responsible for differences in cell types.
- RNA molecules play many roles in regulating gene expression in eukaryotes.
Concept 18.1: Bacteria often respond to environmental change by regulating transcription

- Natural selection has favored bacteria that produce only the products needed by that cell
- A cell can regulate the production of enzymes by feedback inhibition or by gene regulation
- Gene expression in bacteria is controlled by the operon model
Fig. 18-2

(a) Regulation of enzyme activity

(b) Regulation of enzyme production

Regulation of gene expression

Feedback inhibition

Precursor

Enzyme 1

Enzyme 2

Enzyme 3

Tryptophan

trpE gene

trpD gene

trpC gene

trpB gene

trpA gene

Tryosol

Pred of enzyme production
Operons: The Basic Concept

• A cluster of functionally related genes can be under coordinated control by a single on-off “switch”

• The regulatory “switch” is a segment of DNA called an operator usually positioned within the promoter

• An operon is the entire stretch of DNA that includes the operator, the promoter, and the genes that they control
• The operon can be switched off by a protein repressor
• The repressor prevents gene transcription by binding to the operator and blocking RNA polymerase
• The repressor is the product of a separate regulatory gene
• The repressor can be in an active or inactive form, depending on the presence of other molecules

• A **corepressor** is a molecule that cooperates with a repressor protein to switch an operon off

• For example, *E. coli* can synthesize the amino acid tryptophan
• By default the trp operon is on and the genes for tryptophan synthesis are transcribed

• When tryptophan is present, it binds to the trp repressor protein, which turns the operon off

• The repressor is active only in the presence of its corepressor tryptophan; thus the trp operon is turned off (repressed) if tryptophan levels are high
Polypeptide subunits that make up enzymes for tryptophan synthesis

(a) Tryptophan absent, repressor inactive, operon on

(b) Tryptophan present, repressor active, operon off
Polypeptide subunits that make up enzymes for tryptophan synthesis

(a) Tryptophan absent, repressor inactive, operon on
(b) Tryptophan present, repressor active, operon off

DNA → mRNA → Protein

Active repressor

No RNA made

Tryptophan (corepressor)
(b) Tryptophan present, repressor active, operon off
Repressible and Inducible Operons: Two Types of Negative Gene Regulation

• A repressible operon is one that is usually on; binding of a repressor to the operator shuts off transcription

• The trp operon is a repressible operon

• An inducible operon is one that is usually off; a molecule called an inducer inactivates the repressor and turns on transcription
The *lac* operon is an inducible operon and contains genes that code for enzymes used in the hydrolysis and metabolism of lactose.

By itself, the *lac* repressor is active and switches the *lac* operon off.

A molecule called an *inducer* inactivates the repressor to turn the *lac* operon on.
(a) Lactose absent, repressor active, operon off

(b) Lactose present, repressor inactive, operon on
(a) Lactose absent, repressor active, operon off
(b) Lactose present, repressor inactive, operon on
• Inducible enzymes usually function in catabolic pathways; their synthesis is induced by a chemical signal

• Repressible enzymes usually function in anabolic pathways; their synthesis is repressed by high levels of the end product

• Regulation of the trp and lac operons involves negative control of genes because operons are switched off by the active form of the repressor
Positive Gene Regulation

• Some operons are also subject to positive control through a stimulatory protein, such as catabolite activator protein (CAP), an activator of transcription

• When glucose (a preferred food source of *E. coli*) is scarce, CAP is activated by binding with cyclic AMP

• Activated CAP attaches to the promoter of the *lac* operon and increases the affinity of RNA polymerase, thus accelerating transcription
• When glucose levels increase, CAP detaches from the lac operon, and transcription returns to a normal rate

• CAP helps regulate other operons that encode enzymes used in catabolic pathways
(a) Lactose present, glucose scarce (cAMP level high): abundant \( lac \) mRNA synthesized

(b) Lactose present, glucose present (cAMP level low): little \( lac \) mRNA synthesized
Concept 18.2: Eukaryotic gene expression can be regulated at any stage

- All organisms must regulate which genes are expressed at any given time
- In multicellular organisms gene expression is essential for cell specialization
Differential Gene Expression

- Almost all the cells in an organism are genetically identical
- Differences between cell types result from **differential gene expression**, the expression of different genes by cells with the same genome
- Errors in gene expression can lead to diseases including cancer
- Gene expression is regulated at many stages
**Fig. 18-6a**

Signal

**Gene available for transcription**

DNA → Chromatin modification

**Gene**

DNA → RNA → Exon

**Primary transcript**

RNA → Intron

**RNA processing**

Cap → mRNA in nucleus

**Transport to cytoplasm**

**NUCLEUS**

**Chromatin**

**CYTOPLASM**
mRNA in cytoplasm

Translation

Polypeptide

Protein processing

Active protein

Transport to cellular destination

Cellular function

Degradation of mRNA

Degradation of protein
Regulation of Chromatin Structure

- Genes within highly packed heterochromatin are usually not expressed
- Chemical modifications to histones and DNA of chromatin influence both chromatin structure and gene expression
Histone Modifications

• In **histone acetylation**, acetyl groups are attached to positively charged lysines in histone tails.

• This process loosens chromatin structure, thereby promoting the initiation of transcription.

• The addition of methyl groups (methylation) can condense chromatin; the addition of phosphate groups (phosphorylation) next to a methylated amino acid can loosen chromatin.
Fig. 18-7

(a) Histone tails protrude outward from a nucleosome

(b) Acetylation of histone tails promotes loose chromatin structure that permits transcription
The histone code hypothesis proposes that specific combinations of modifications help determine chromatin configuration and influence transcription
DNA Methylation

- DNA methylation, the addition of methyl groups to certain bases in DNA, is associated with reduced transcription in some species.

- DNA methylation can cause long-term inactivation of genes in cellular differentiation.

- In **genomic imprinting**, methylation regulates expression of either the maternal or paternal alleles of certain genes at the start of development.
**Epigenetic Inheritance**

- Although the chromatin modifications just discussed do not alter DNA sequence, they may be passed to future generations of cells.

- The inheritance of traits transmitted by mechanisms not directly involving the nucleotide sequence is called **epigenetic inheritance**.
Regulation of Transcription Initiation

• Chromatin-modifying enzymes provide initial control of gene expression by making a region of DNA either more or less able to bind the transcription machinery
Organization of a Typical Eukaryotic Gene

- Associated with most eukaryotic genes are **control elements**, segments of noncoding DNA that help regulate transcription by binding certain proteins.

- Control elements and the proteins they bind are critical to the precise regulation of gene expression in different cell types.
Fig. 18-8-1

Enhancer (distal control elements) - Proximal control elements - Promoter - DNA

Upstream - Promoter - Downstream

Exon - Intron - Exon - Intron - Exon

Poly-A signal sequence - Termination region
Fig. 18-8-2

Enhancer (distal control elements)
Proximal control elements
Promoter
Upstream
Downstream
DNA
Exon
Intron
Exon
Intron
Exon
Exon
Poly-A signal sequence
Termination region
Primary RNA transcript
5′ end of primary transcript
Poly-A signal
Cleaved 3′ end of primary transcript
Fig. 18-8-3

Enhancer (distal control elements)
Proximal control elements
Promoter

DNA

Upstream

Exon
Intron
Exon
Intron
Exon

Termination region

Downstream

Primary RNA transcript

Transcription

RNA processing

Intron RNA

Coding segment

mRNA

5’ Cap
5’ UTR
Start codon
Stop codon
3’ UTR
Poly-A tail

Cleaved 3’ end of primary transcript

Poly-A signal

Sequence

5’ - 3’

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The Roles of Transcription Factors

• To initiate transcription, eukaryotic RNA polymerase requires the assistance of proteins called transcription factors.

• General transcription factors are essential for the transcription of all protein-coding genes.

• In eukaryotes, high levels of transcription of particular genes depend on control elements interacting with specific transcription factors.
Enhancers and Specific Transcription Factors

• Proximal control elements are located close to the promoter

• Distal control elements, groups of which are called **enhancers**, may be far away from a gene or even located in an intron
• An activator is a protein that binds to an enhancer and stimulates transcription of a gene

• Bound activators cause mediator proteins to interact with proteins at the promoter
Fig. 18-9-1

Enhancer

Activators

Distal control element

Promoter

TATA box

Gene

DNA
Enhancer

Distal control element

Activators

Promoter

TATA box

Gene

DNA

General transcription factors

DNA-bending protein

Group of mediator proteins

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Fig. 18-9-3

Activation of transcription involves the interaction of several components:

1. **Enhancer** - Enhancers are regulatory DNA elements that increase the transcription rate of genes.
2. **Distal control element** - These elements are located far upstream of the gene they regulate.
3. **Activators** - These are proteins that bind to enhancers and enhance transcription.
4. **Promoter** - The promoter is a specific DNA sequence that binds RNA polymerase and initiates transcription.
5. **TATA box** - A conserved sequence within the promoter that helps in the recognition and binding of RNA polymerase.
6. **DNA-bending protein** - Enzymes that bend DNA to facilitate access of transcription factors.
7. **Group of mediator proteins** - These proteins help in the recruitment of RNA polymerase to the promoter.
8. **General transcription factors** - These are essential for the binding of RNA polymerase to the promoter.
9. **RNA polymerase II** - The enzyme that synthesizes RNA.
10. **Transcription initiation complex** - A complex of proteins that includes RNA polymerase, transcription factors, and other proteins.
11. **RNA synthesis** - The process by which RNA polymerase II synthesizes RNA from the DNA template.
• Some transcription factors function as repressors, inhibiting expression of a particular gene.

• Some activators and repressors act indirectly by influencing chromatin structure to promote or silence transcription.
Fig. 18-10

(a) Liver cell
- Albumin gene expressed
- Crystallin gene not expressed

(b) Lens cell
- Albumin gene not expressed
- Crystallin gene expressed
Coordinately Controlled Genes in Eukaryotes

• Unlike the genes of a prokaryotic operon, each of the coordinately controlled eukaryotic genes has a promoter and control elements.

• These genes can be scattered over different chromosomes, but each has the same combination of control elements.

• Copies of the activators recognize specific control elements and promote simultaneous transcription of the genes.
Mechanisms of Post-Transcriptional Regulation

- Transcription alone does not account for gene expression
- Regulatory mechanisms can operate at various stages after transcription
- Such mechanisms allow a cell to fine-tune gene expression rapidly in response to environmental changes
RNA Processing

- In **alternative RNA splicing**, different mRNA molecules are produced from the same primary transcript, depending on which RNA segments are treated as exons and which as introns.
mRNA Degradation

- The life span of mRNA molecules in the cytoplasm is a key to determining protein synthesis
- Eukaryotic mRNA is more long lived than prokaryotic mRNA
- The mRNA life span is determined in part by sequences in the leader and trailer regions
Initiation of Translation

- The initiation of translation of selected mRNAs can be blocked by regulatory proteins that bind to sequences or structures of the mRNA.

- Alternatively, translation of all mRNAs in a cell may be regulated simultaneously.

- For example, translation initiation factors are simultaneously activated in an egg following fertilization.
Protein Processing and Degradation

• After translation, various types of protein processing, including cleavage and the addition of chemical groups, are subject to control.

• **Proteasomes** are giant protein complexes that bind protein molecules and degrade them.
Proteasome and ubiquitin to be recycled

Protein fragments (peptides)

Protein entering a proteasome

Ubiquitinated protein

Protein to be degraded

Ubiquitin
Concept 18.3: Noncoding RNAs play multiple roles in controlling gene expression

- Only a small fraction of DNA codes for proteins, rRNA, and tRNA
- A significant amount of the genome may be transcribed into noncoding RNAs
- Noncoding RNAs regulate gene expression at two points: mRNA translation and chromatin configuration
Effects on mRNAs by MicroRNAs and Small Interfering RNAs

- **MicroRNAs** (miRNAs) are small single-stranded RNA molecules that can bind to mRNA

- These can degrade mRNA or block its translation
Fig. 18-13

(a) Primary miRNA transcript

(b) Generation and function of miRNAs

Hairpin

miRNA

Hydrogen bond

Dicer

miRNA

miRNA-protein complex

mRNA degraded

Translation blocked

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• The phenomenon of inhibition of gene expression by RNA molecules is called RNA interference (RNAi)

• RNAi is caused by small interfering RNAs (siRNAs)

• siRNAs and miRNAs are similar but form from different RNA precursors
Chromatin Remodeling and Silencing of Transcription by Small RNAs

- siRNAs play a role in heterochromatin formation and can block large regions of the chromosome
- Small RNAs may also block transcription of specific genes
Concept 18.4: A program of differential gene expression leads to the different cell types in a multicellular organism

- During embryonic development, a fertilized egg gives rise to many different cell types
- Cell types are organized successively into tissues, organs, organ systems, and the whole organism
- Gene expression orchestrates the developmental programs of animals
A Genetic Program for Embryonic Development

- The transformation from zygote to adult results from cell division, cell differentiation, and morphogenesis
(a) Fertilized eggs of a frog
(b) Newly hatched tadpole
(a) Fertilized eggs of a frog
Fig. 18-14b

(b) Newly hatched tadpole
• **Cell differentiation** is the process by which cells become specialized in structure and function.

• The physical processes that give an organism its shape constitute **morphogenesis**.

• Differential gene expression results from genes being regulated differently in each cell type.

• Materials in the egg can set up gene regulation that is carried out as cells divide.
Cytoplasmic Determinants and Inductive Signals

- An egg’s cytoplasm contains RNA, proteins, and other substances that are distributed unevenly in the unfertilized egg.

- **Cytoplasmic determinants** are maternal substances in the egg that influence early development.

- As the zygote divides by mitosis, cells contain different cytoplasmic determinants, which lead to different gene expression.
Fig. 18-15

(a) Cytoplasmic determinants in the egg

(b) Induction by nearby cells

Unfertilized egg cell

Sperm

Fertilization

Zygote

Mitotic cell division

Two-celled embryo

Two different cytoplasmic determinants

Signal molecule (inducer)

Signal transduction pathway

Signal receptor

NUCLEUS

(a) Cytoplasmic determinants in the egg

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Two different cytoplasmic determinants

Unfertilized egg cell

Sperm

Fertilization

Nucleus

Two-celled embryo

Zygote

Mitotic cell division

(a) Cytoplasmic determinants in the egg
(b) Induction by nearby cells

Early embryo (32 cells)

Signal transduction pathway

Signal receptor

Signal molecule (inducer)

NUCLEUS
• The other important source of developmental information is the environment around the cell, especially signals from nearby embryonic cells.

• In the process called induction, signal molecules from embryonic cells cause transcriptional changes in nearby target cells.

• Thus, interactions between cells induce differentiation of specialized cell types.
Sequential Regulation of Gene Expression During Cellular Differentiation

• **Determination** commits a cell to its final fate

• Determination precedes differentiation

• Cell differentiation is marked by the production of tissue-specific proteins
• Myoblasts produce muscle-specific proteins and form skeletal muscle cells

• *MyoD* is one of several “master regulatory genes” that produce proteins that commit the cell to becoming skeletal muscle

• The MyoD protein is a transcription factor that binds to enhancers of various target genes
Embryonic precursor cell

Nucleus

Master regulatory gene *myoD*

OFF

Other muscle-specific genes

OFF
Embryonic precursor cell

- Master regulatory gene myoD
  - DNA: OFF

- Other muscle-specific genes
  - mRNA: OFF
  - MyoD protein (transcription factor)

Myoblast (determined)
Embryonic precursor cell

Nucleus

Master regulatory gene *myoD*

OFF

Other muscle-specific genes

OFF

OFF

mRNA

MyoD protein (transcription factor)

mRNA

Myoblast (determined)

mRNA

MyoD

Another transcription factor

mRNA

Myosin, other muscle proteins, and cell cycle–blocking proteins

Part of a muscle fiber (fully differentiated cell)
Pattern formation is the development of a spatial organization of tissues and organs.

In animals, pattern formation begins with the establishment of the major axes.

Positional information, the molecular cues that control pattern formation, tells a cell its location relative to the body axes and to neighboring cells.
Pattern formation has been extensively studied in the fruit fly *Drosophila melanogaster*.

Combining anatomical, genetic, and biochemical approaches, researchers have discovered developmental principles common to many other species, including humans.
The Life Cycle of Drosophila

- In *Drosophila*, cytoplasmic determinants in the unfertilized egg determine the axes before fertilization.
- After fertilization, the embryo develops into a segmented larva with three larval stages.
(a) Adult

1. Egg cell developing within ovarian follicle

2. Unfertilized egg

3. Fertilized egg

4. Segmented embryo

5. Larval stage

(b) Development from egg to larva
Fig. 18-17a

BODY AXES

Dorsal
Right
Posterior

Ventral
Left
Anterior

0.5 mm

Head
Thorax
Abdomen

(a) Adult
(b) Development from egg to larva

1. Egg cell developing within ovarian follicle
2. Unfertilized egg
3. Fertilized egg
4. Segmented embryo
5. Larval stage
Edward B. Lewis, Christiane Nüsslein-Volhard, and Eric Wieschaus won a Nobel 1995 Prize for decoding pattern formation in *Drosophila*

Lewis demonstrated that genes direct the developmental process
Antenna

Eye

Wild type

Mutant

Leg
Fig. 18-18a

Antenna

Eye

Wild type
• Nüsslein-Volhard and Wieschaus studied segment formation

• They created mutants, conducted breeding experiments, and looked for corresponding genes

• Breeding experiments were complicated by embryonic lethals, embryos with lethal mutations

• They found 120 genes essential for normal segmentation
Axis Establishment

- **Maternal effect genes** encode for cytoplasmic determinants that initially establish the axes of the body of *Drosophila*

- These maternal effect genes are also called **egg-polarity genes** because they control orientation of the egg and consequently the fly
Bicoid: A Morphogen Determining Head Structures

- One maternal effect gene, the *bicoid* gene, affects the front half of the body.
- An embryo whose mother has a mutant *bicoid* gene lacks the front half of its body and has duplicate posterior structures at both ends.
EXPERIMENT

Wild-type larva

Mutant larva (bicoid)

RESULTS

Fertilization, translation of bicoid mRNA

Anterior end Bicoid protein in early embryo

CONCLUSION

Nurse cells

Developing egg Bicoid mRNA in mature unfertilized egg Bicoid protein in early embryo
Wild-type larva

Mutant larva (*bicoid*)

EXPERIMENT
RESULTS

*Fig. 18-19b*

**Bicoid mRNA in mature unfertilized egg**

**Fertilization, translation of *bicoid* mRNA**

**Anterior end Bicoid protein in early embryo**

*Bicoid mRNA in mature unfertilized egg*
CONCLUSION

Developing egg

*bicoid* mRNA

Egg

*Bicoid* mRNA in mature unfertilized egg

Bicoid protein in early embryo
• This phenotype suggests that the product of the mother’s *bicoid* gene is concentrated at the future anterior end.

• This hypothesis is an example of the gradient hypothesis, in which gradients of substances called **morphogens** establish an embryo’s axes and other features.
• The *bicoid* research is important for three reasons:
  
  – It identified a specific protein required for some early steps in pattern formation
  
  – It increased understanding of the mother’s role in embryo development
  
  – It demonstrated a key developmental principle that a gradient of molecules can determine polarity and position in the embryo
Concept 18.5: Cancer results from genetic changes that affect cell cycle control

- The gene regulation systems that go wrong during cancer are the very same systems involved in embryonic development.
Types of Genes Associated with Cancer

• Cancer can be caused by mutations to genes that regulate cell growth and division

• Tumor viruses can cause cancer in animals including humans
Oncogenes and Proto-Oncogenes

• **Oncogenes** are cancer-causing genes

• **Proto-oncogenes** are the corresponding normal cellular genes that are responsible for normal cell growth and division

• Conversion of a proto-oncogene to an oncogene can lead to abnormal stimulation of the cell cycle
Fig. 18-20

**Proto-oncogene**

DNA

Translocation or transposition:
- New promoter
- Normal growth-stimulating protein in excess

Gene amplification:
- Normal growth-stimulating protein in excess

Point mutation:
- Oncogene within a control element
- Oncogene within the gene
- Hyperactive or degradation-resistant protein

Gene amplification:
- Normal growth-stimulating protein in excess

Point mutation:
- Normal growth-stimulating protein in excess

Point mutation:
- Hyperactive or degradation-resistant protein
• Proto-oncogenes can be converted to oncogenes by
  – Movement of DNA within the genome: if it ends up near an active promoter, transcription may increase
  – Amplification of a proto-oncogene: increases the number of copies of the gene
  – Point mutations in the proto-oncogene or its control elements: causes an increase in gene expression
Tumor-Suppressor Genes

• **Tumor-suppressor genes** help prevent uncontrolled cell growth

• Mutations that decrease protein products of tumor-suppressor genes may contribute to cancer onset

• Tumor-suppressor proteins
  – Repair damaged DNA
  – Control cell adhesion
  – Inhibit the cell cycle in the cell-signaling pathway
Interference with Normal Cell-Signaling Pathways

• Mutations in the \textit{ras} proto-oncogene and \textit{p53} tumor-suppressor gene are common in human cancers

• Mutations in the \textit{ras gene} can lead to production of a hyperactive Ras protein and increased cell division
Receptor
Growth factor

Protein kinases (phosphorylation cascade)
Ras
GTP
Hyperactive Ras protein (product of oncogene) issues signals on its own

Figure 18-21
(a) Cell cycle–stimulating pathway

MUTATION
Defective or missing transcription factor, such as p53, cannot activate transcription

Protein that inhibits the cell cycle

(b) Cell cycle–inhibiting pathway

(c) Effects of mutations

Protein overexpressed → Cell cycle overstimulated
Increased cell division
Protein absent → Cell cycle not inhibited
Fig. 18-21a

1. Growth factor

2. Receptor

3. G protein

4. Protein kinases (phosphorylation cascade)

5. Transcription factor (activator)

NUCLEUS

DNA

Gene expression

Protein that stimulates the cell cycle

(a) Cell cycle—stimulating pathway

MUTATION

Hyperactive Ras protein (product of oncogene) issues signals on its own

Hyperactive Ras protein

Issues signals on its own

MUTATION

Gene expression

Protein that stimulates the cell cycle

(a) Cell cycle—stimulating pathway
Defective or missing transcription factor, such as p53, cannot activate transcription.
(c) Effects of mutations

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• Suppression of the cell cycle can be important in the case of damage to a cell’s DNA; \( p53 \) prevents a cell from passing on mutations due to DNA damage

• Mutations in the \( p53 \) gene prevent suppression of the cell cycle
The Multistep Model of Cancer Development

- Multiple mutations are generally needed for full-fledged cancer; thus the incidence increases with age
- At the DNA level, a cancerous cell is usually characterized by at least one active oncogene and the mutation of several tumor-suppressor genes
EFFECTS OF MUTATIONS

Malignant tumor (carcinoma)

Colon

Colon wall

Loss of tumor-suppressor gene
APC (or other)

Activation of ras oncogene

Loss of tumor-suppressor gene
DCC

Loss of tumor-suppressor gene
p53

Additional mutations

Larger benign growth (adenoma)

Small benign growth (polyp)

Normal colon epithelial cells

Malignant tumor (carcinoma)
Colon

Colon wall

Normal colon epithelial cells
1. Loss of tumor-suppressor gene APC (or other)

Small benign growth (polyp)
2 Activation of *ras* oncogene

3 Loss of tumor-suppressor gene *DCC*

Larger benign growth (adenoma)
4. Loss of tumor-suppressor gene *p53*

5. Additional mutations

Malignant tumor (carcinoma)
Inherited Predisposition and Other Factors Contributing to Cancer

- Individuals can inherit oncogenes or mutant alleles of tumor-suppressor genes.
- Inherited mutations in the tumor-suppressor gene *adenomatous polyposis coli* are common in individuals with colorectal cancer.
- Mutations in the BRCA1 or BRCA2 gene are found in at least half of inherited breast cancers.
Fig. 18-UN1

Operon

Promoter

Operator

RNA polymerase

Genes

A B C

Polypeptides

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Fig. 18-UN2

Genes expressed

Promoter

Genes

Operator

Inactive repressor:
no corepressor present

Genes not expressed

Active repressor:
corepressor bound

Corepressor

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Fig. 18-UN3

Promoter

Operator

Genes

Active repressor: no inducer present

Genes not expressed

Genes expressed

Inactive repressor: inducer bound
**Chromatin modification**
- Genes in highly compacted chromatin are generally not transcribed.
- Histone acetylation seems to loosen chromatin structure, enhancing transcription.
- DNA methylation generally reduces transcription.

**Transcription**
- Regulation of transcription initiation: DNA control elements bind specific transcription factors.
  - Bending of the DNA enables activators to contact proteins at the promoter, initiating transcription.
- Coordinate regulation:
  - Enhancer for liver-specific genes
  - Enhancer for lens-specific genes

**RNA processing**
- Alternative RNA splicing:
  - Primary RNA transcript
  - mRNA

**Translation**
- Initiation of translation can be controlled via regulation of initiation factors.

**mRNA degradation**
- Each mRNA has a characteristic life span, determined in part by sequences in the 5' and 3' UTRs.

**Protein processing and degradation**
- Protein processing and degradation by proteasomes are subject to regulation.
miRNA or siRNA can target specific mRNAs for destruction.

- miRNA or siRNA can block the translation of specific mRNAs.

- Small RNAs can promote the formation of heterochromatin in certain regions, blocking transcription.
Fig. 18-UN8

Diagram showing the relationship between Enhancer and Promoter regions adjacent to genes labeled Gene 1 to Gene 5.
You should now be able to:

1. Explain the concept of an operon and the function of the operator, repressor, and corepressor

2. Explain the adaptive advantage of grouping bacterial genes into an operon

3. Explain how repressible and inducible operons differ and how those differences reflect differences in the pathways they control
4. Explain how DNA methylation and histone acetylation affect chromatin structure and the regulation of transcription

5. Define control elements and explain how they influence transcription

6. Explain the role of promoters, enhancers, activators, and repressors in transcription control
7. Explain how eukaryotic genes can be coordinately expressed

8. Describe the roles played by small RNAs on gene expression

9. Explain why determination precedes differentiation

10. Describe two sources of information that instruct a cell to express genes at the appropriate time
11. Explain how maternal effect genes affect polarity and development in *Drosophila* embryos

12. Explain how mutations in tumor-suppressor genes can contribute to cancer

13. Describe the effects of mutations to the *p53* and *ras* genes