CAMPBELL BIOLOGY IN FOCUS

URRY • CAIN • WASSERMAN • MINORSKY • REECE

15

Regulation of Gene Expression

Lecture Presentations by
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SECOND EDITION

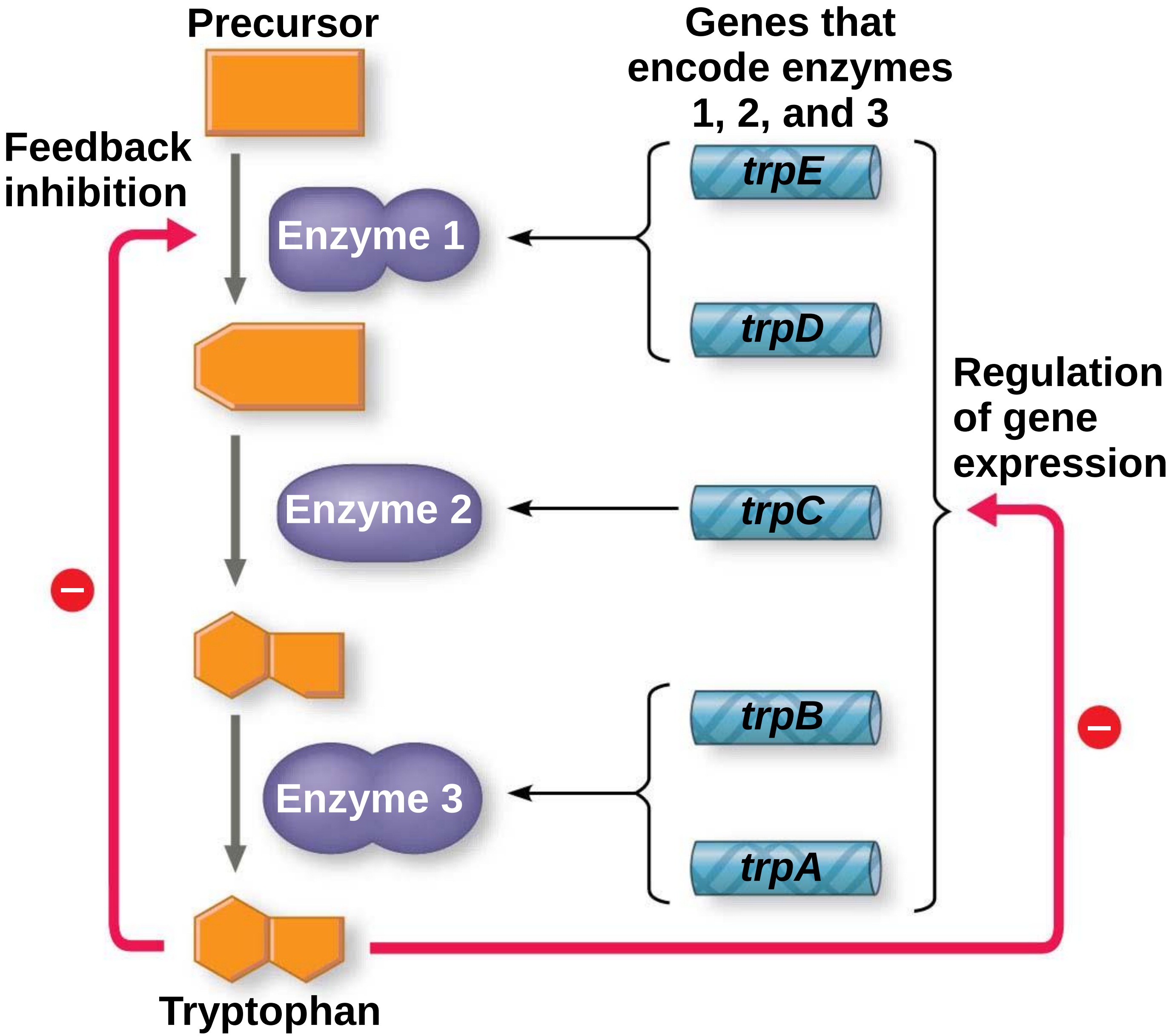
Overview: Beauty in the Eye of the Beholder

- Prokaryotes and eukaryotes alter gene expression in response to their changing environment
- Multicellular eukaryotes also develop and maintain multiple cell types

Concept 15.1: Bacteria often respond to environmental change by regulating transcription

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

Figure 15.2



(a) Regulation of enzyme activity

(b) Regulation of enzyme production

Operons: The Basic Concept

- A group of functionally related genes can be coordinately controlled 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
- The *trp* (tryptophan) operon is an example of such an operon

- 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 then 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

Figure 15.3

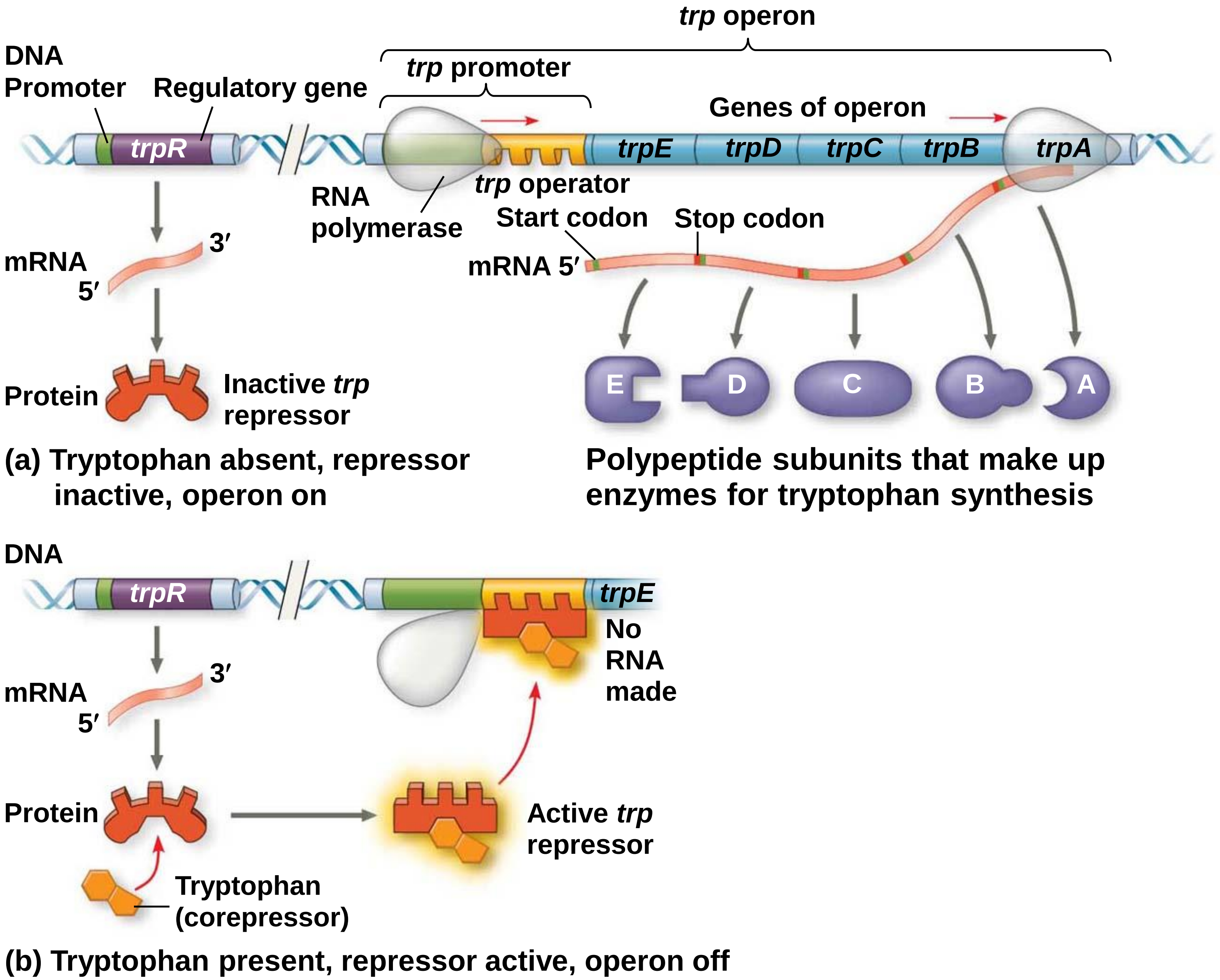
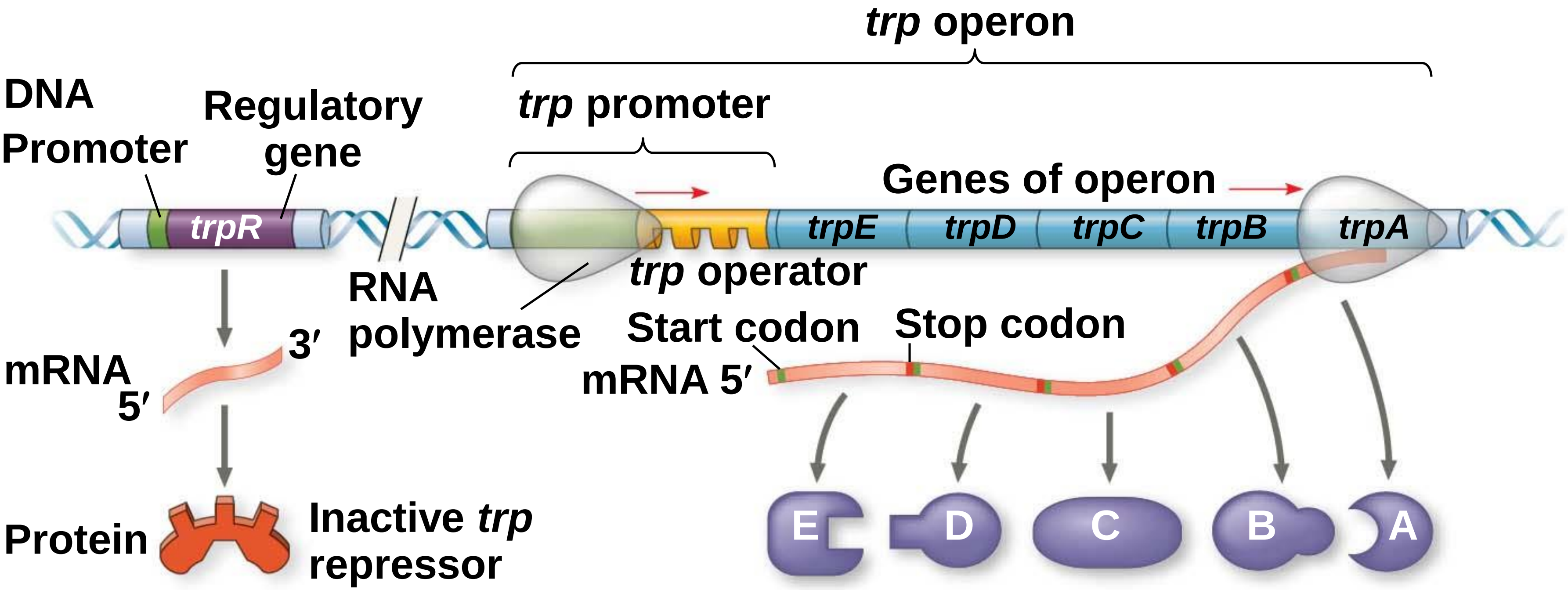

trp operon
DNA
Promoter
Regulatory gene
trp promoter
Genes of operon
trpR
trpE
trpD
trpC
trpB
trpA
RNA polymerase
trp operator
Start codon
Stop codon
mRNA 5′
mRNA
3′
5′
Protein
Inactive *trp* repressor
E
D
C
B
A
(a) Tryptophan absent, repressor inactive, operon on
Polypeptide subunits that make up enzymes for tryptophan synthesis
DNA
trpR
trpE
No RNA made
mRNA
3′
5′
Protein
Active *trp* repressor
Tryptophan (corepressor)
(b) Tryptophan present, repressor active, operon off

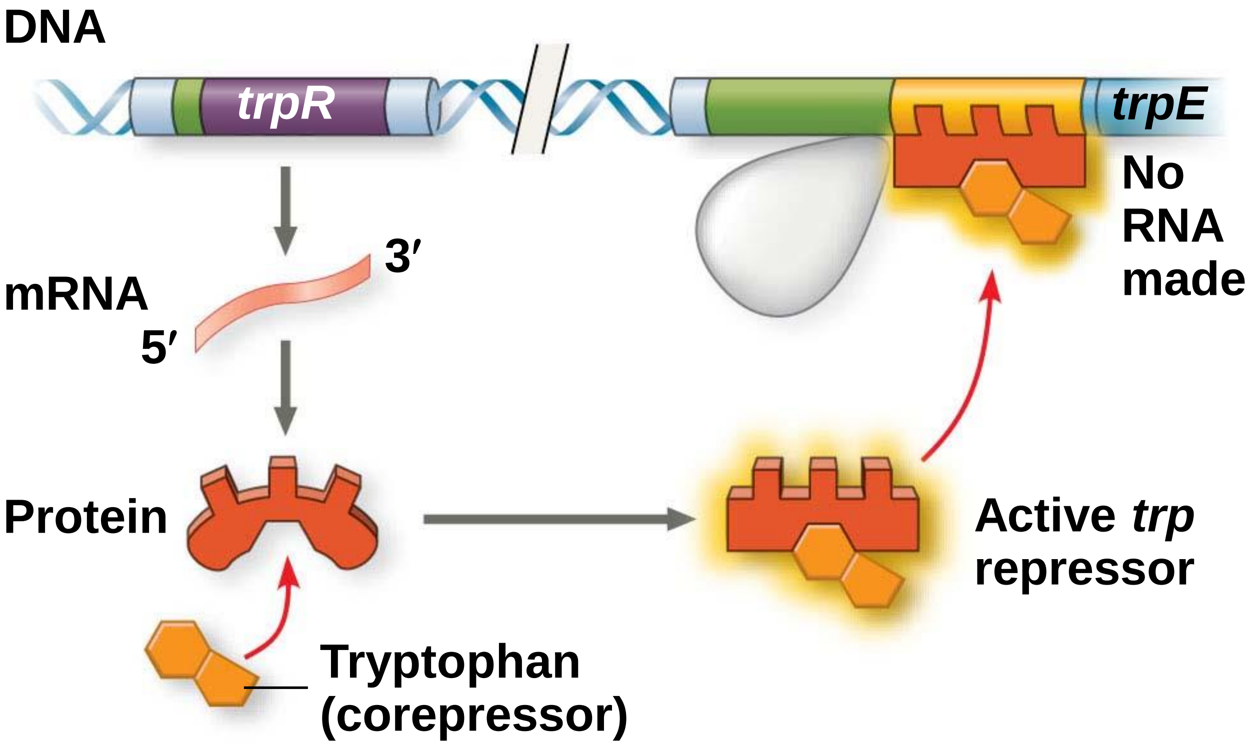
Figure 15.3-1



(a) Tryptophan absent, repressor inactive, operon on

Polypeptide subunits that make up enzymes for tryptophan synthesis

Figure 15.3-2



(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 that function in the use 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

- For the *lac* operon, the inducer is allolactose, formed from lactose that enters the cell
- Enzymes of the lactose pathway are called inducible enzymes
- Analogously, the enzymes for tryptophan synthesis are said to be repressible enzymes

Figure 15.4

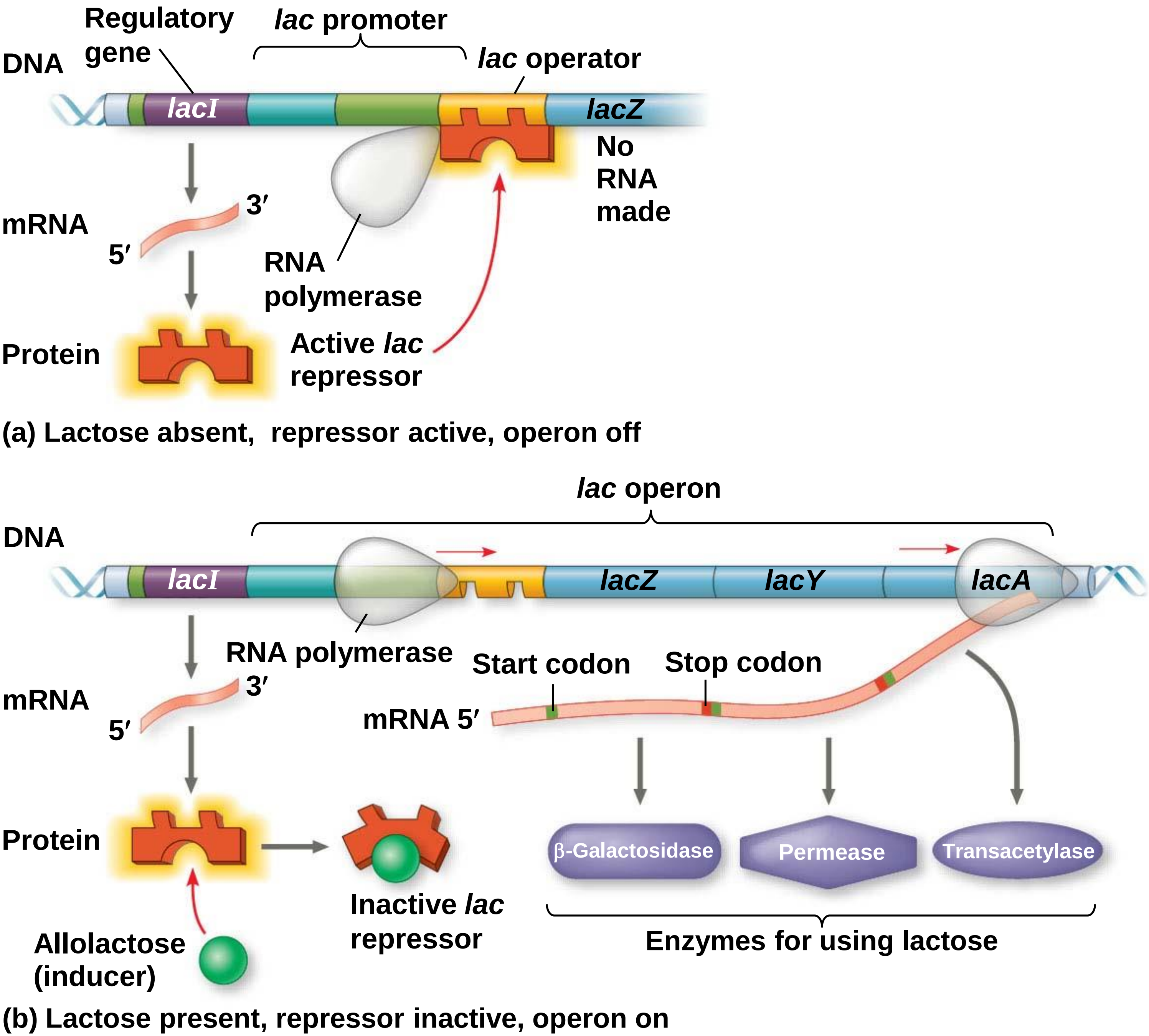
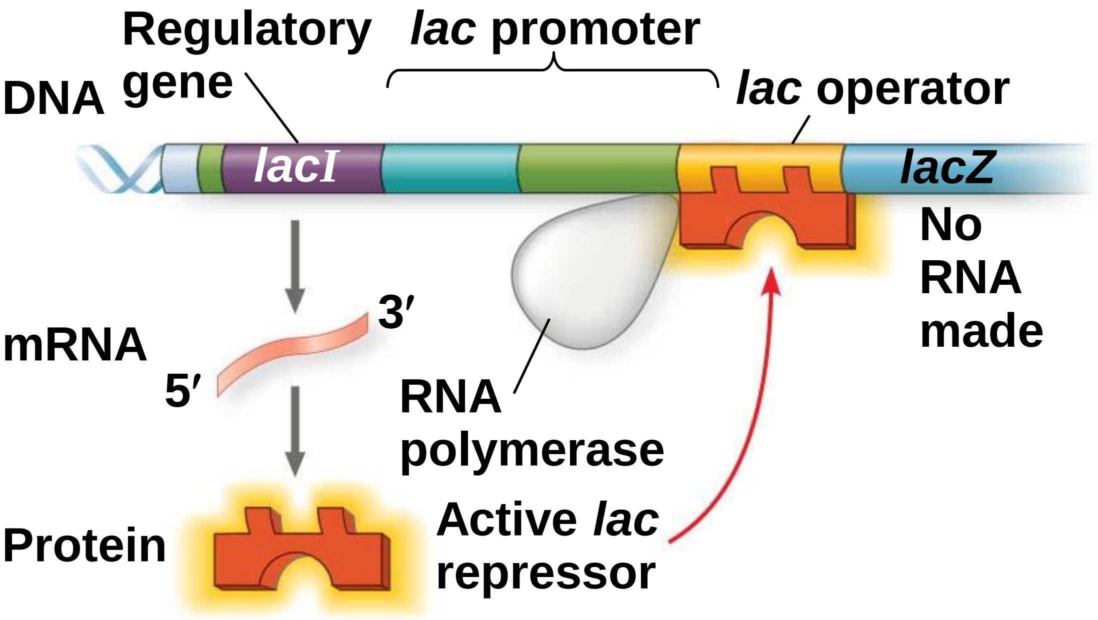
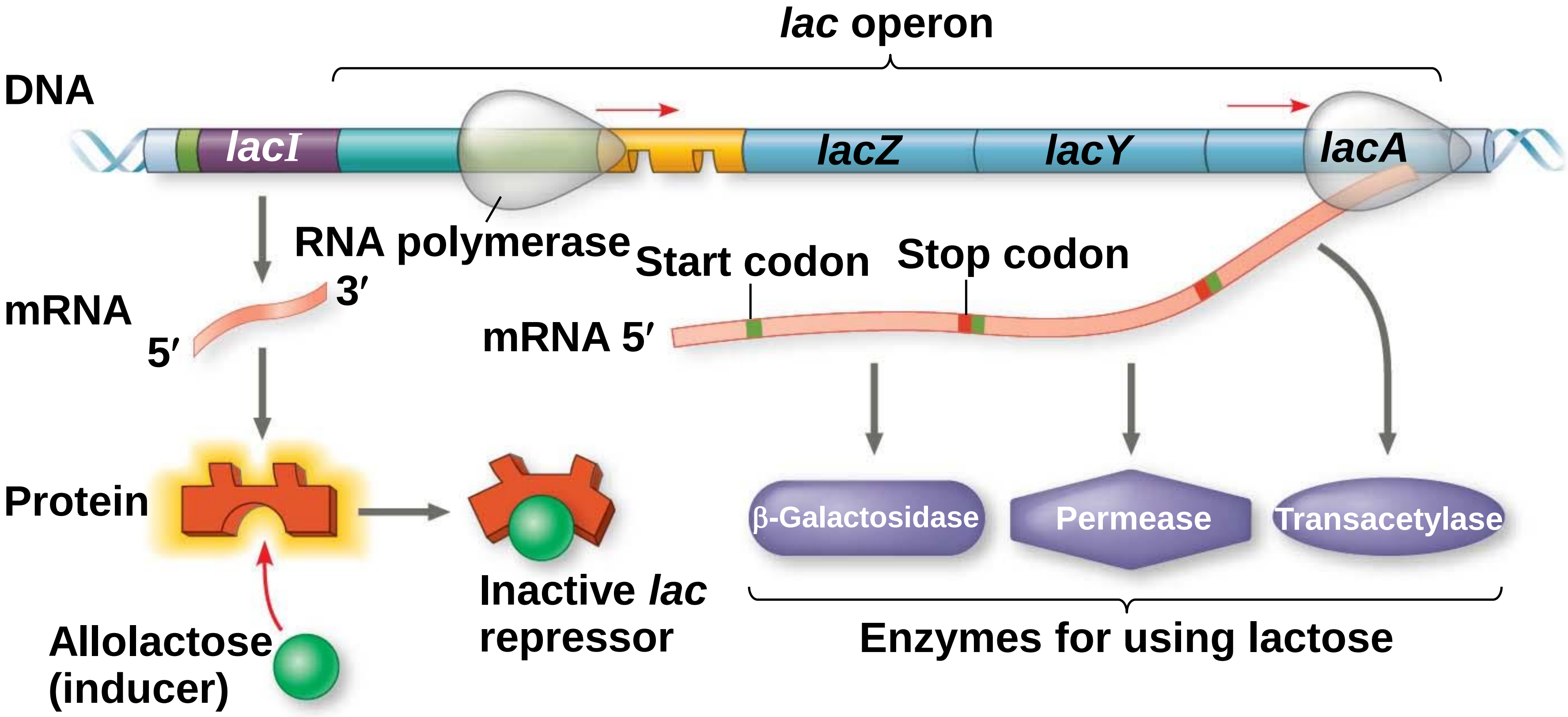

DNA
Regulatory gene
lac promoter
lac operator
lacI
lacZ
No RNA made
mRNA
3′
5′
RNA polymerase
Protein
Active *lac* repressor
(a) Lactose absent, repressor active, operon off
lac operon
DNA
lacI
lacZ
lacY
lacA
RNA polymerase
Start codon
Stop codon
mRNA
3′
5′
mRNA 5′
Protein
Inactive *lac* repressor
β-Galactosidase
Permease
Transacetylase
Enzymes for using lactose
Allolactose (inducer)
(b) Lactose present, repressor inactive, operon on

Figure 15.4-1



(a) Lactose absent, repressor active, operon off

Figure 15.4-2



(b) Lactose present, repressor inactive, operon on

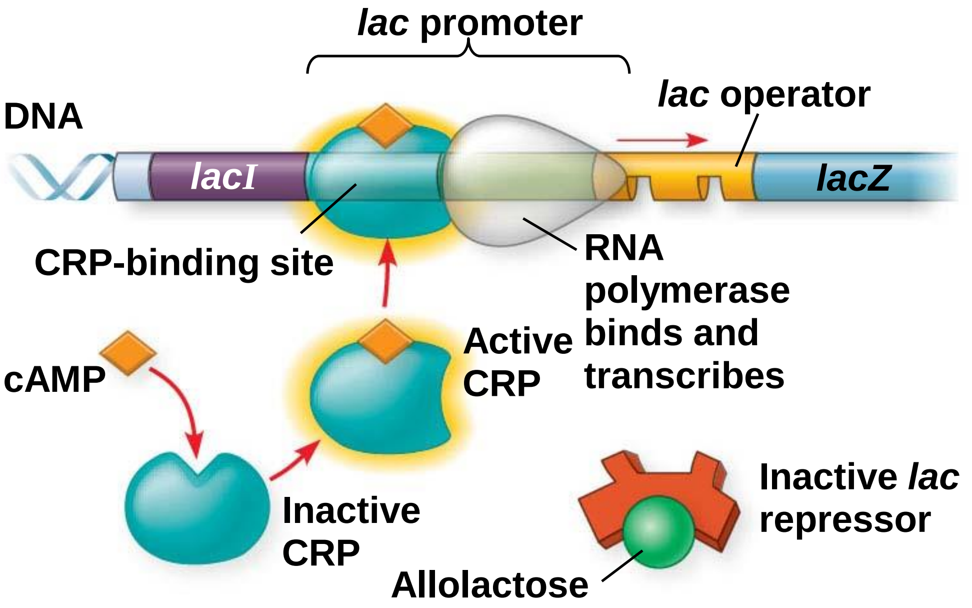
- Inducible enzymes usually function in catabolic pathways; their synthesis is induced by a chemical signal
- Repressible enzymes usually function in anabolic pathways; their synthesis is repressed by high levels of the end product
- Regulation of the *trp* and *lac* operons involves negative control of genes because operons are switched off by the active form of the repressor

Positive Gene Regulation

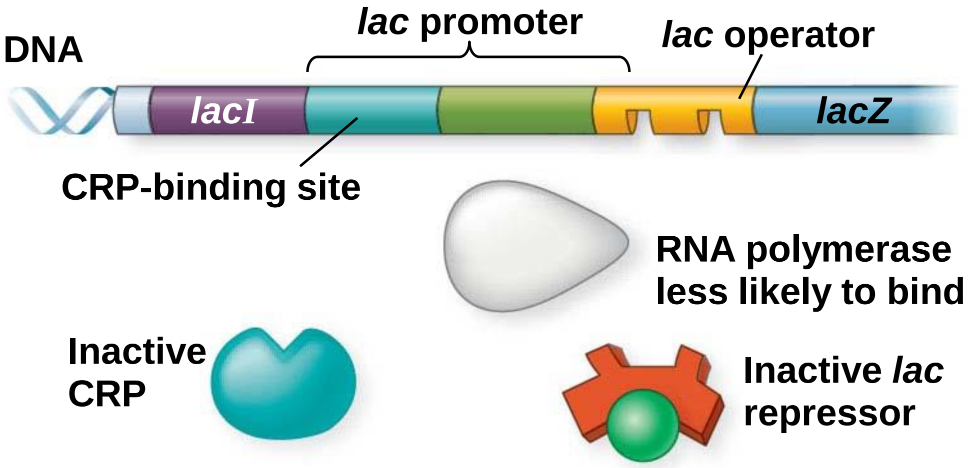
- *E. coli* will preferentially use glucose when it is present in the environment
- When glucose is scarce, CRP (cAMP receptor protein) acts as an **activator** of transcription
- CRP is activated by binding with **cyclic AMP** (**cAMP**)
- Activated CRP attaches to the promoter of the *lac* operon and increases the affinity of RNA polymerase, thus accelerating transcription

- When glucose levels increase, CRP detaches from the *lac* operon, and transcription proceeds at a very low rate, even if lactose is present
- CRP helps regulate other operons that encode enzymes used in catabolic pathways

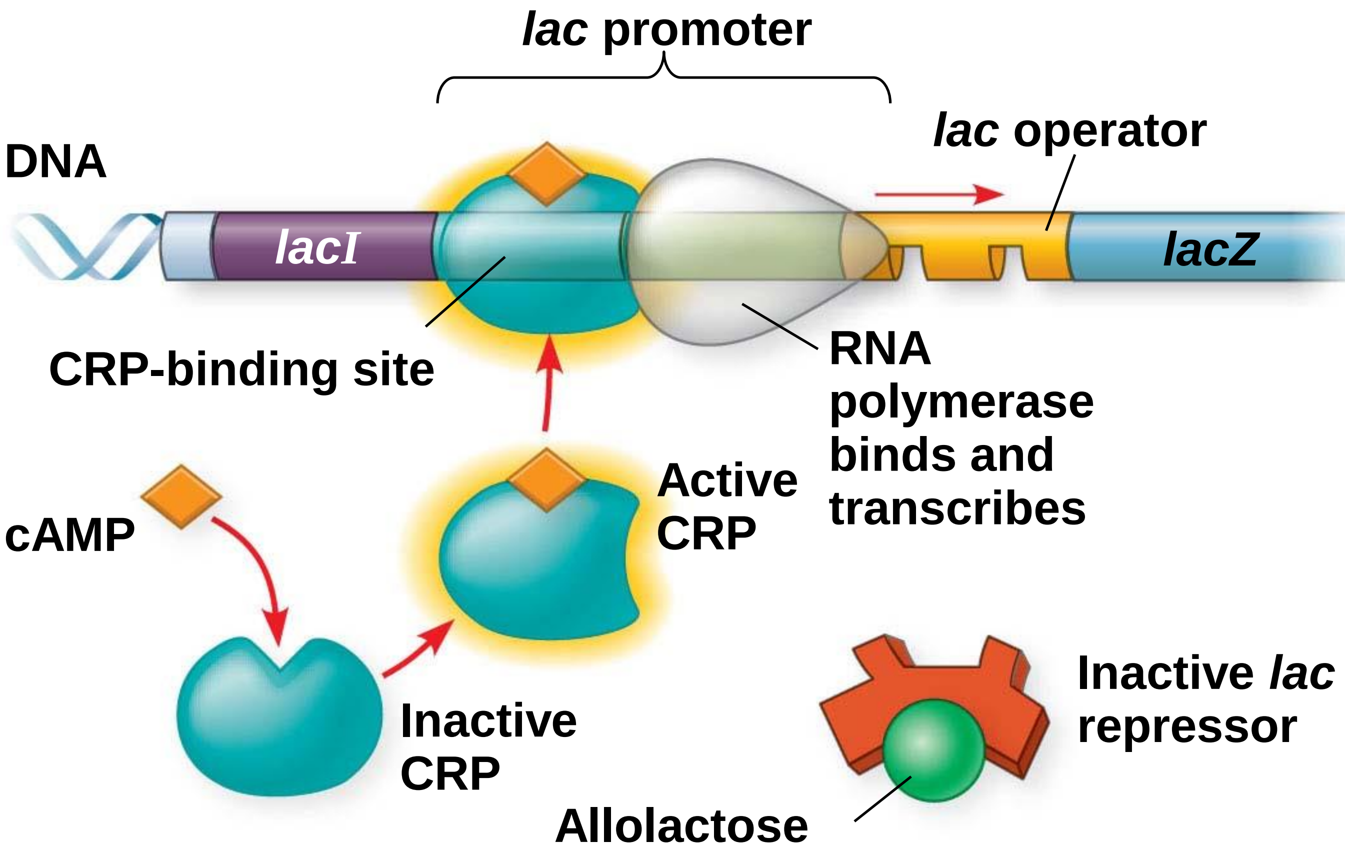
Figure 15.5



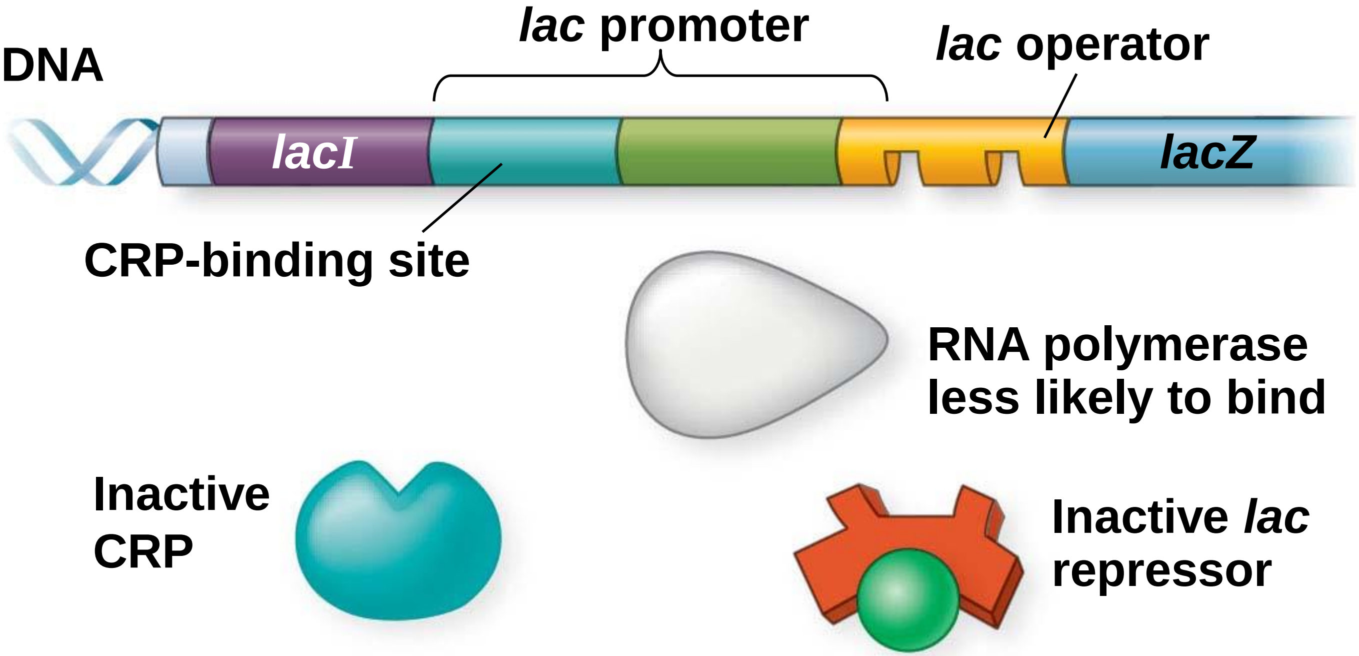
(a) Lactose present, glucose scarce (cAMP level high): abundant *lac* mRNA synthesized



(b) Lactose present, glucose present (cAMP level low): little *lac* mRNA synthesized



(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 15.2: Eukaryotic gene expression is regulated at many stages

- All organisms must regulate which genes are expressed at any given time
- In multicellular organisms, regulation of gene expression is essential for cell specialization

Differential Gene Expression

- Almost all the cells in an organism contain an identical organism
- Differences between cell types result from **differential gene expression**, the expression of different genes by cells with the same genome
- Abnormalities in gene expression can lead to imbalances and diseases, including cancer
- Gene expression is regulated at many stages

Figure 15.6

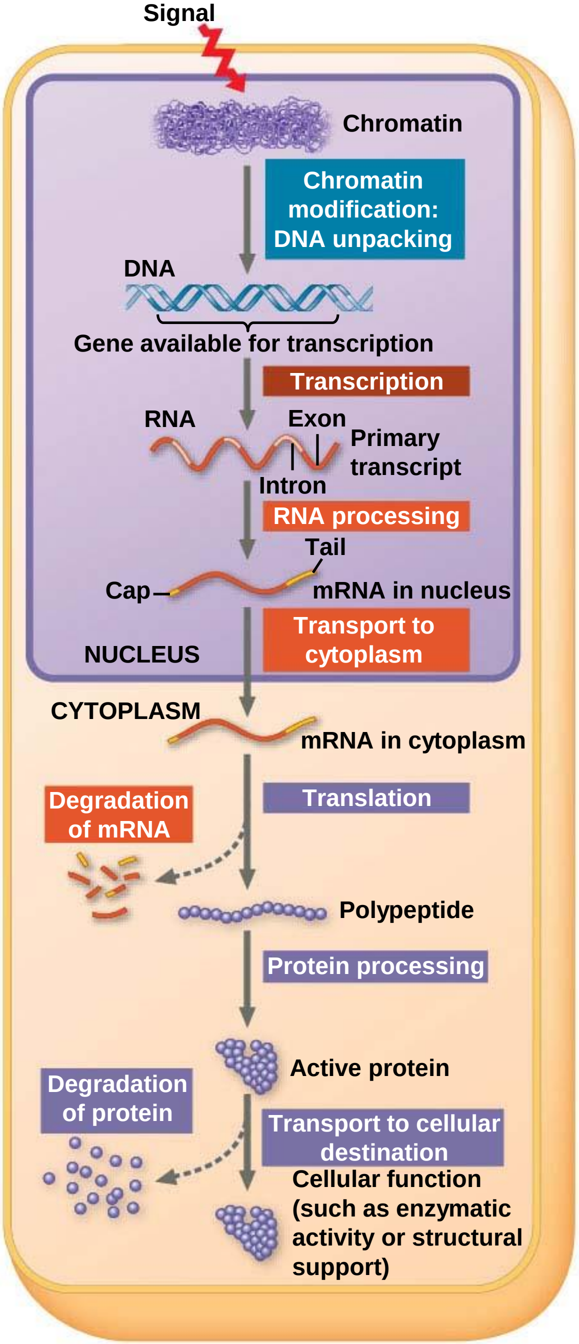

Signal
Chromatin
Chromatin modification: DNA unpacking
DNA
Gene available for transcription
Transcription
RNA
Exon
Primary transcript
Intron
RNA processing
Tail
Cap
mRNA in nucleus
Transport to cytoplasm
NUCLEUS
CYTOPLASM
mRNA in cytoplasm
Degradation of mRNA
Translation
Polypeptide
Protein processing
Active protein
Degradation of protein
Transport to cellular destination
Cellular function (such as enzymatic activity or structural support)

Figure 15.6-1

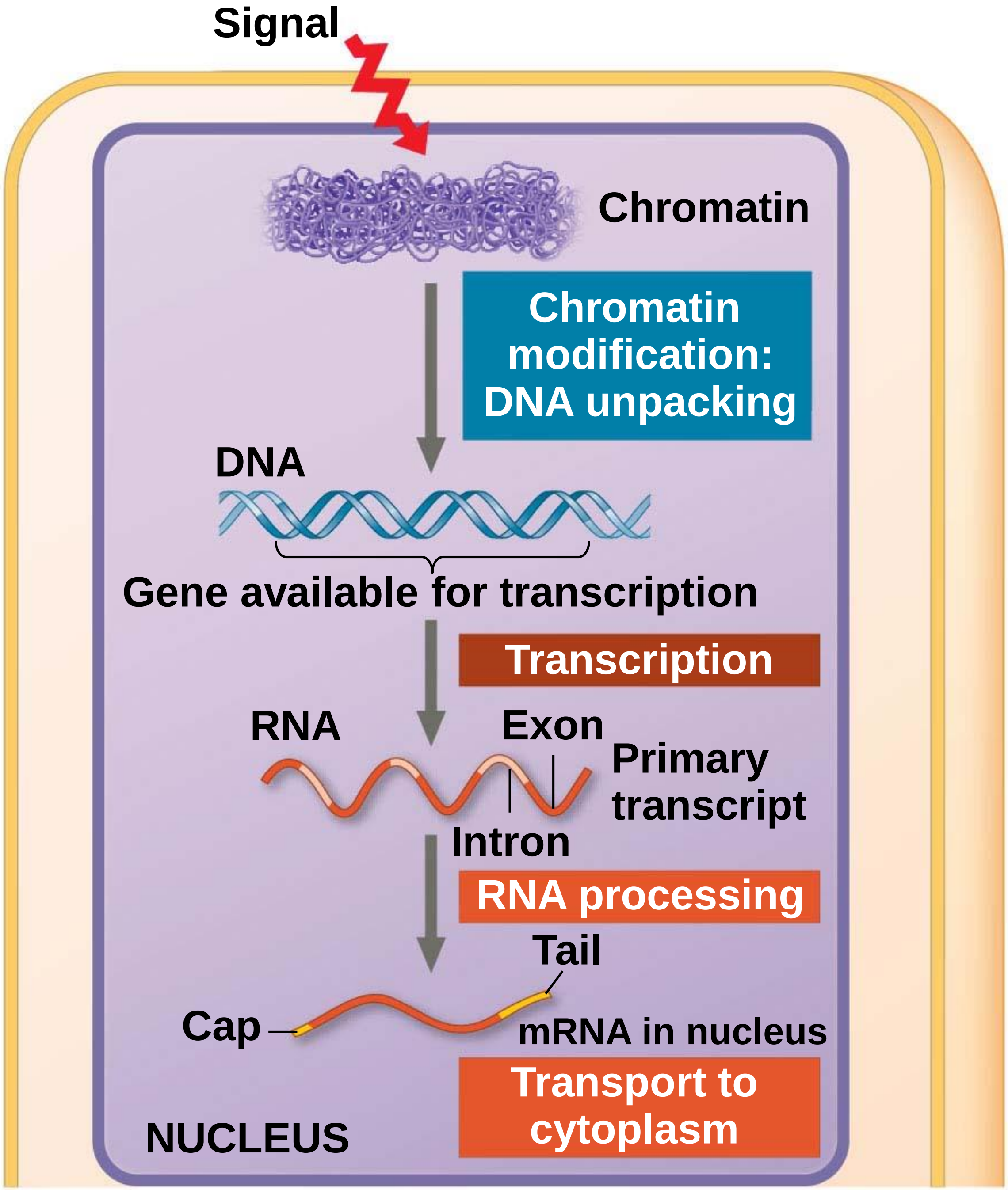
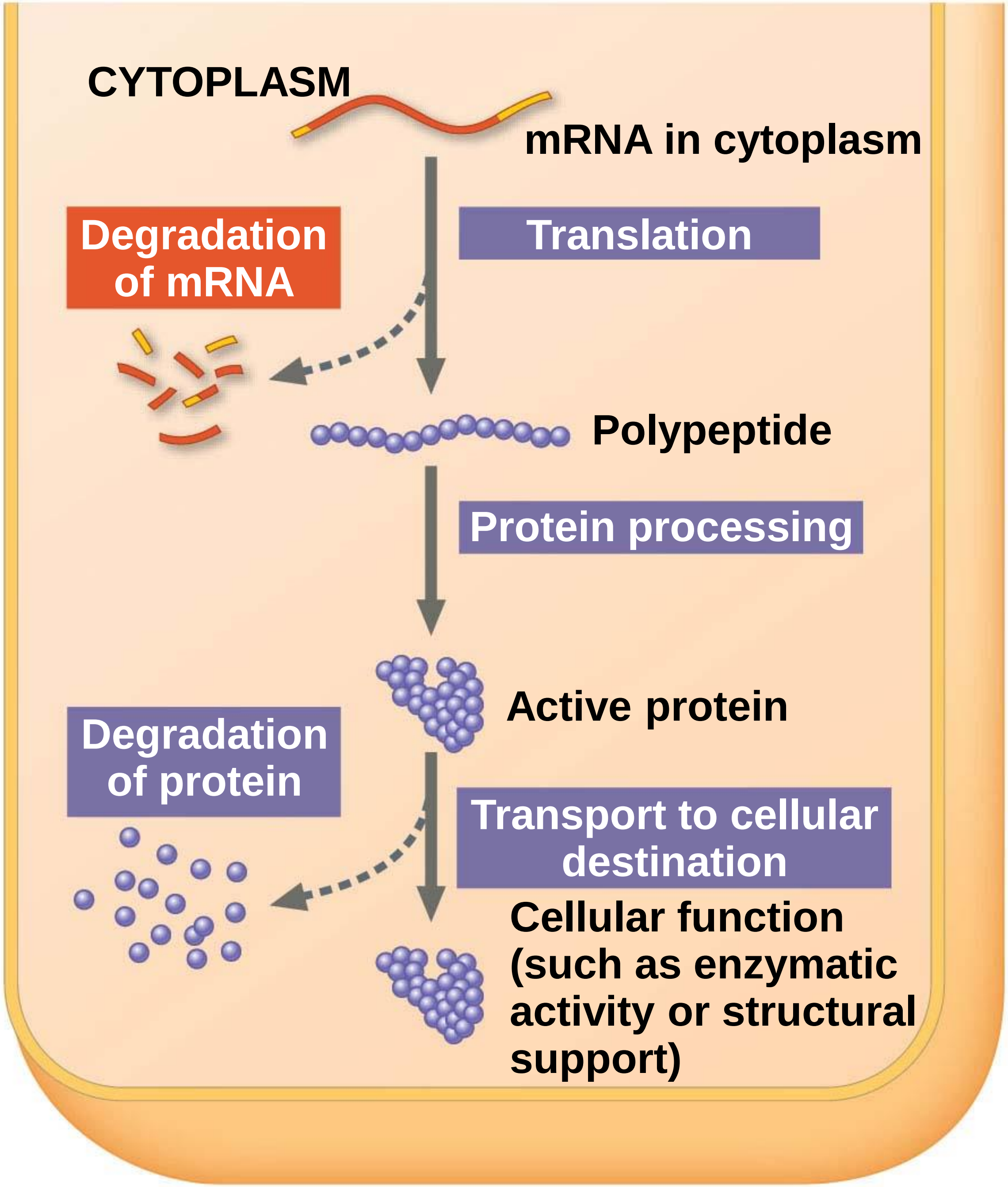

Signal
Chromatin
Chromatin modification: DNA unpacking
DNA
Gene available for transcription
Transcription
RNA
Exon
Primary transcript
Intron
RNA processing
Tail
Cap
mRNA in nucleus
Transport to cytoplasm
NUCLEUS

Figure 15.6-2



CYTOPLASM

mRNA in cytoplasm

Degradation of mRNA

Translation

Polypeptide

Protein processing

Active protein

Degradation of protein

Transport to cellular destination

Cellular function (such as enzymatic activity or structural support)

- In all organisms, gene expression is commonly controlled at transcription
- The greater complexity of eukaryotic cell structure and function provides opportunities for regulating gene expression at many additional stages

Regulation of Chromatin Structure

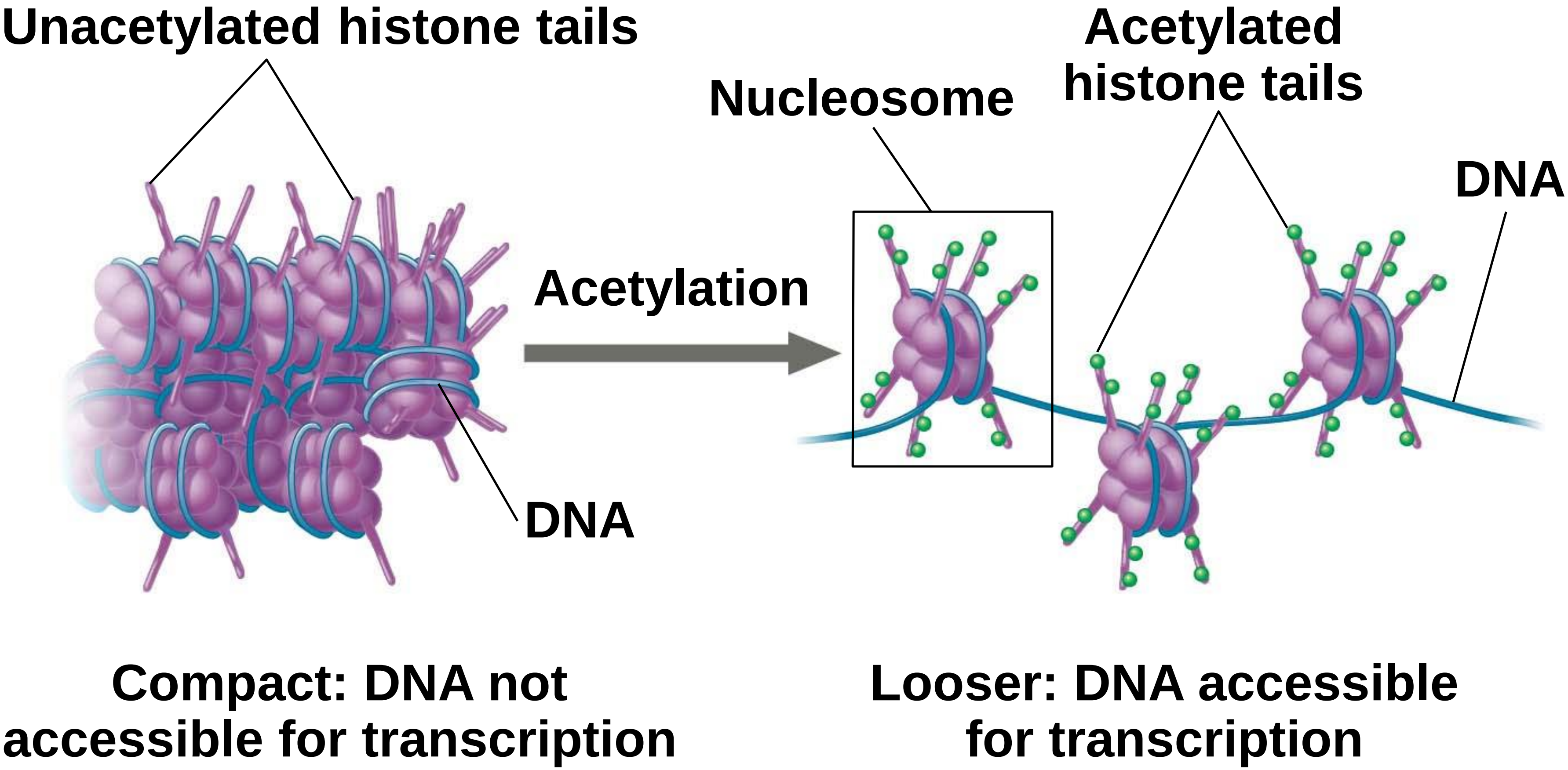
- The structural organization of chromatin packs DNA into a compact form and helps regulate gene expression in several ways
- The location of a gene promoter relative to nucleosomes and scaffold attachment sites can influence gene transcription

- Genes within highly condensed heterochromatin are usually not expressed
- Chemical modifications to histone proteins and DNA can influence chromatin structure and gene expression

Histone Modifications and DNA Methylation

- In **histone acetylation**, acetyl groups are attached to positively charged lysines in histone tails
- This generally loosens chromatin structure, promoting the initiation of transcription
- The addition of methyl groups (methylation) can condense chromatin and lead to reduced transcription

Figure 15.7


Unacetylated histone tails
Acetylated histone tails
Nucleosome
DNA
Acetylation
DNA
Compact: DNA not accessible for transcription
Looser: DNA accessible for transcription

- **DNA methylation** is the addition of methyl groups to certain bases in DNA, usually cytosine
- Individual genes are usually more heavily methylated in cells where they are not expressed
- Once methylated, genes usually remain so through successive cell divisions
- After replication, enzymes methylate the correct daughter strand so that the methylation pattern is inherited

Epigenetic Inheritance

- Though chromatin modifications 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**
- Epigenetic modifications can be reversed, unlike mutations in DNA sequence

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 multiple **control elements**, segments of noncoding DNA that serve as binding sites for transcription factors that help regulate transcription
- Control elements and the transcription factors they bind are critical for precise regulation of gene expression in different cell types

Figure 15.8

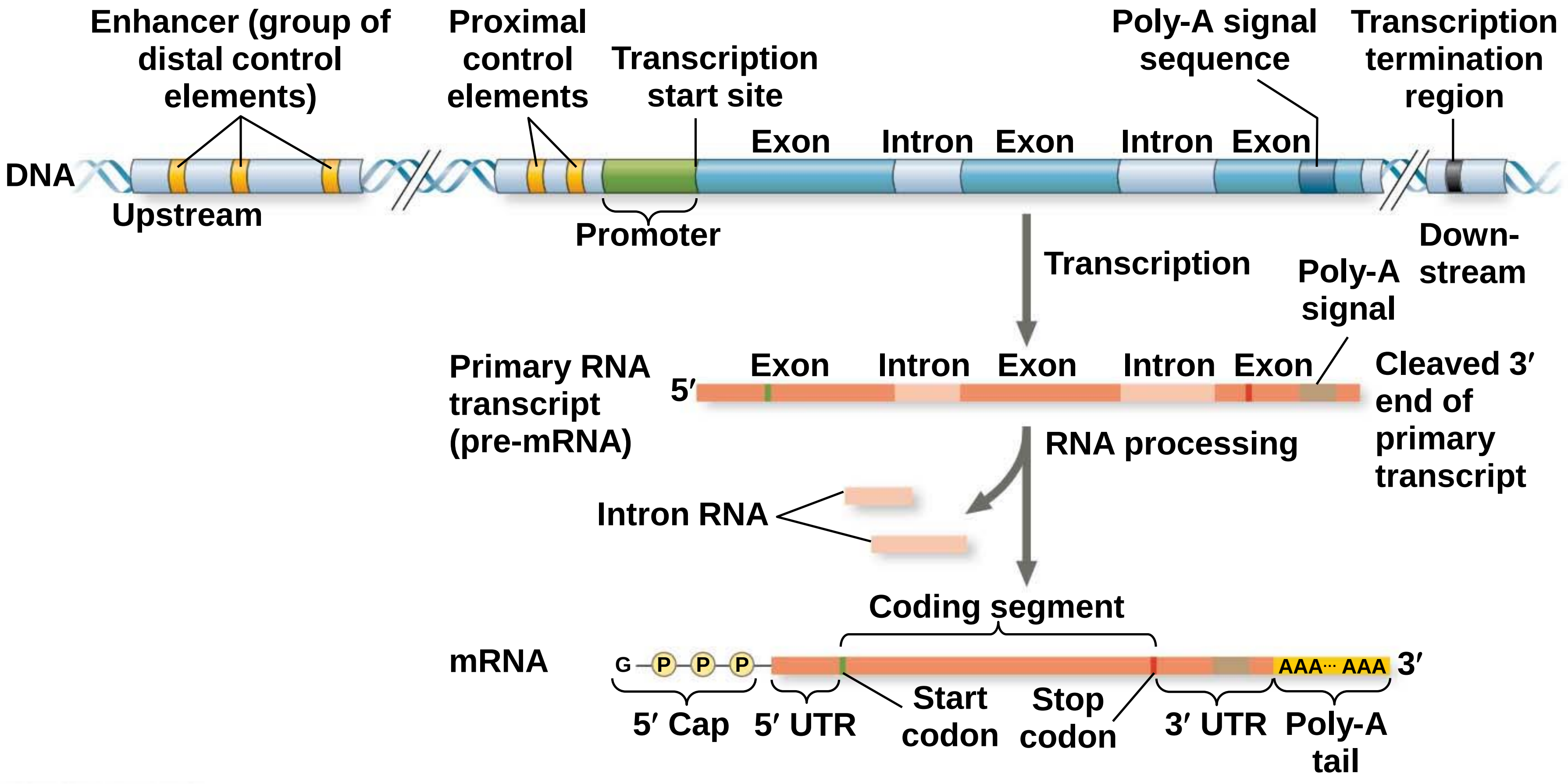

Enhancer (group of distal control elements)
Proximal control elements
Transcription start site
Poly-A signal sequence
Transcription termination region
DNA
Exon
Intron
Exon
Intron
Exon
Upstream
Promoter
Down-stream
Transcription
Poly-A signal
Primary RNA transcript (pre-mRNA)
5′
Exon
Intron
Exon
Intron
Exon
Cleaved 3′ end of primary transcript
RNA processing
Intron RNA
Coding segment
mRNA
G
P
P
P
AAA··· AAA
3′
5′ Cap
5′ UTR
Start codon
Stop codon
3′ UTR
Poly-A tail

Figure 15.8-1

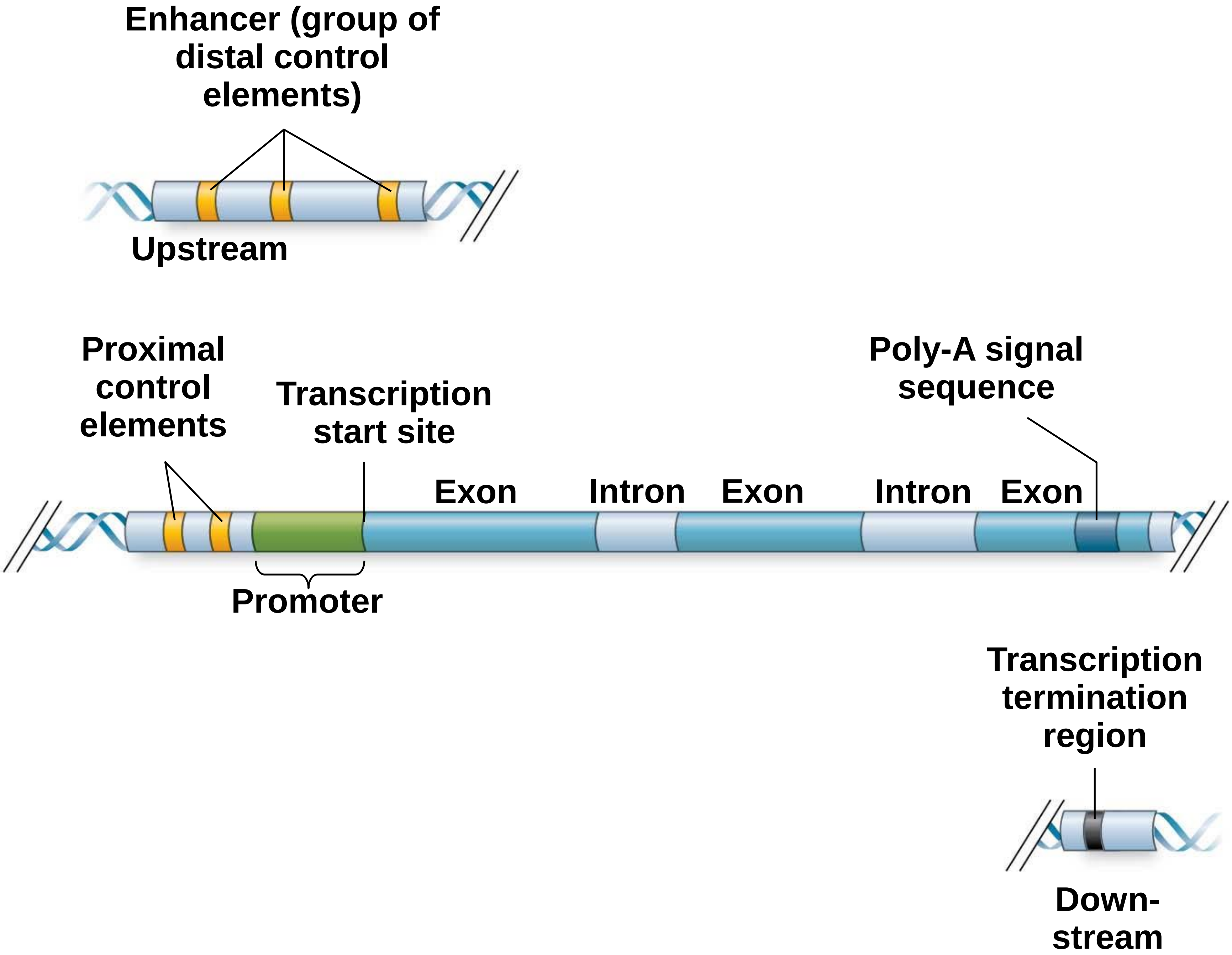

Enhancer (group of distal control elements)
Upstream
Proximal control elements
Transcription start site
Exon
Intron
Exon
Intron
Exon
Poly-A signal sequence
Promoter
Transcription termination region
Down-stream

Figure 15.8-2-s1

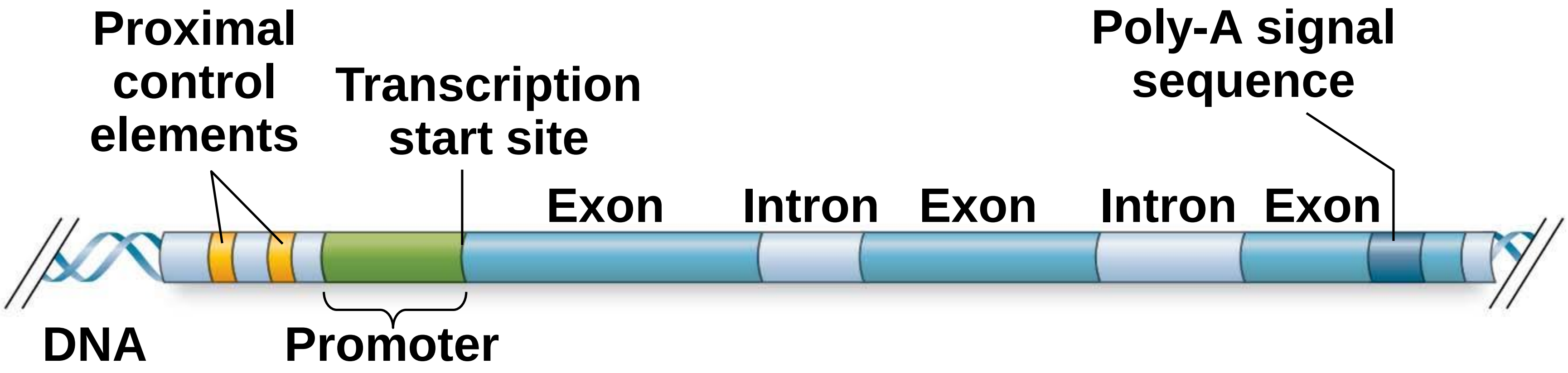
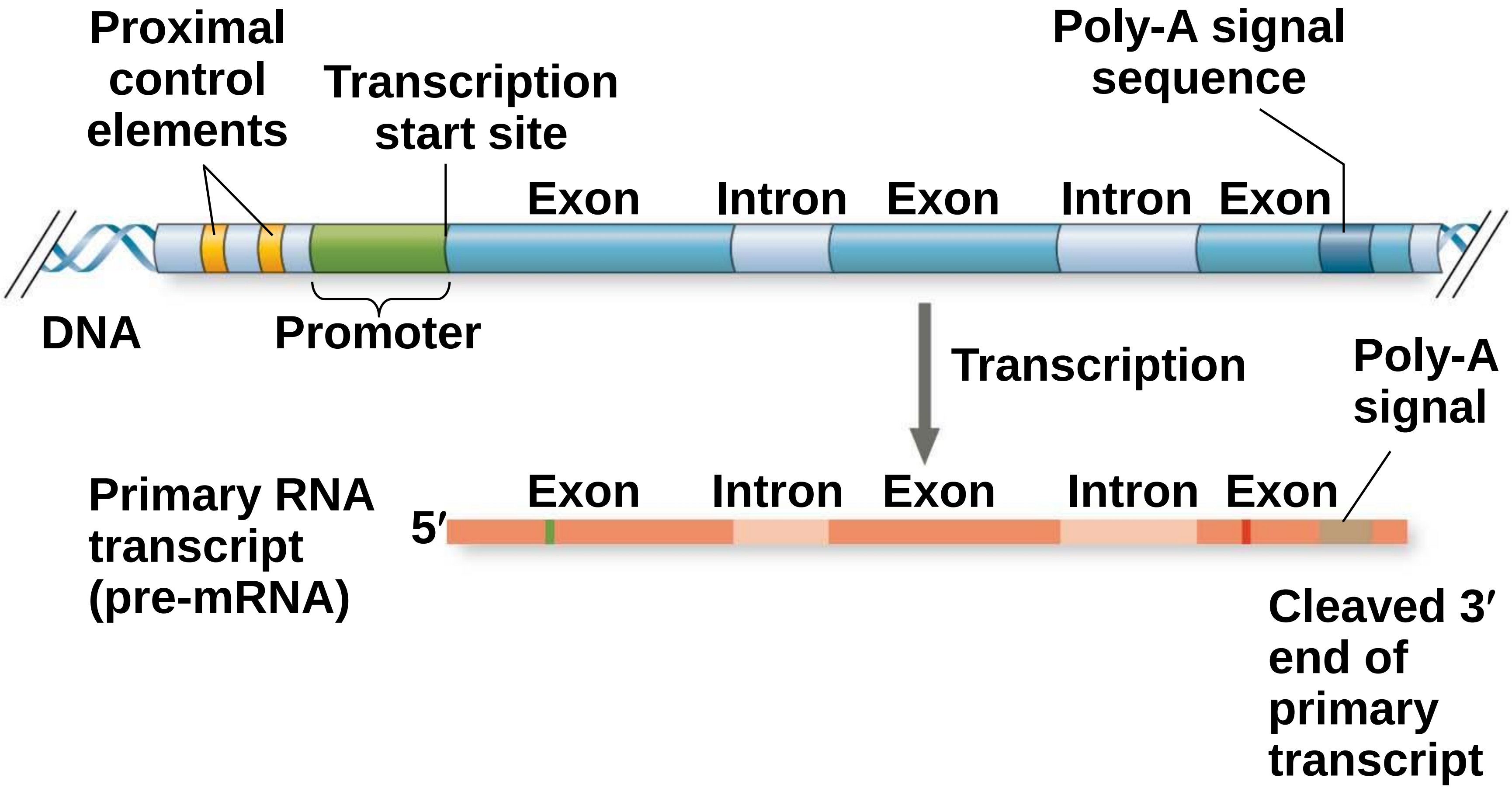
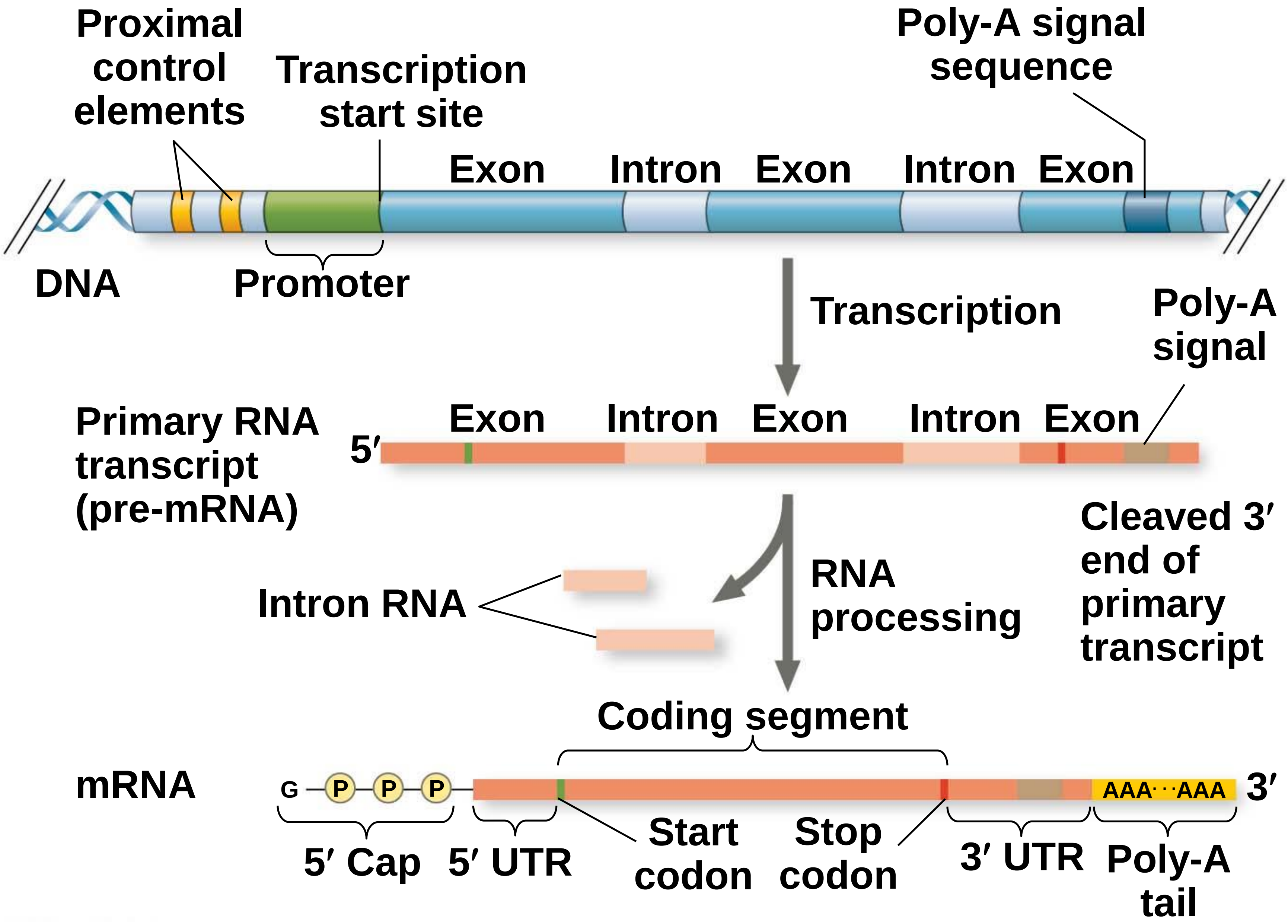


Figure 15.8-2-s2




Proximal control elements
Transcription start site
Poly-A signal sequence
Exon
Intron
Exon
Intron
Exon
DNA
Promoter
Transcription
Poly-A signal
Primary RNA transcript (pre-mRNA)
5′
Exon
Intron
Exon
Intron
Exon
Cleaved 3′ end of primary transcript
Intron RNA
RNA processing
Coding segment
mRNA
G
P
P
P
AAA···AAA
3′
5′ Cap
5′ UTR
Start codon
Stop codon
3′ UTR
Poly-A tail

The Roles of General and Specific Transcription Factors

- General transcription factors act at the promoter of all genes
- Some genes require specific transcription factors that bind to control elements close to or farther away from the promoter

General Transcription Factors at the Promoter

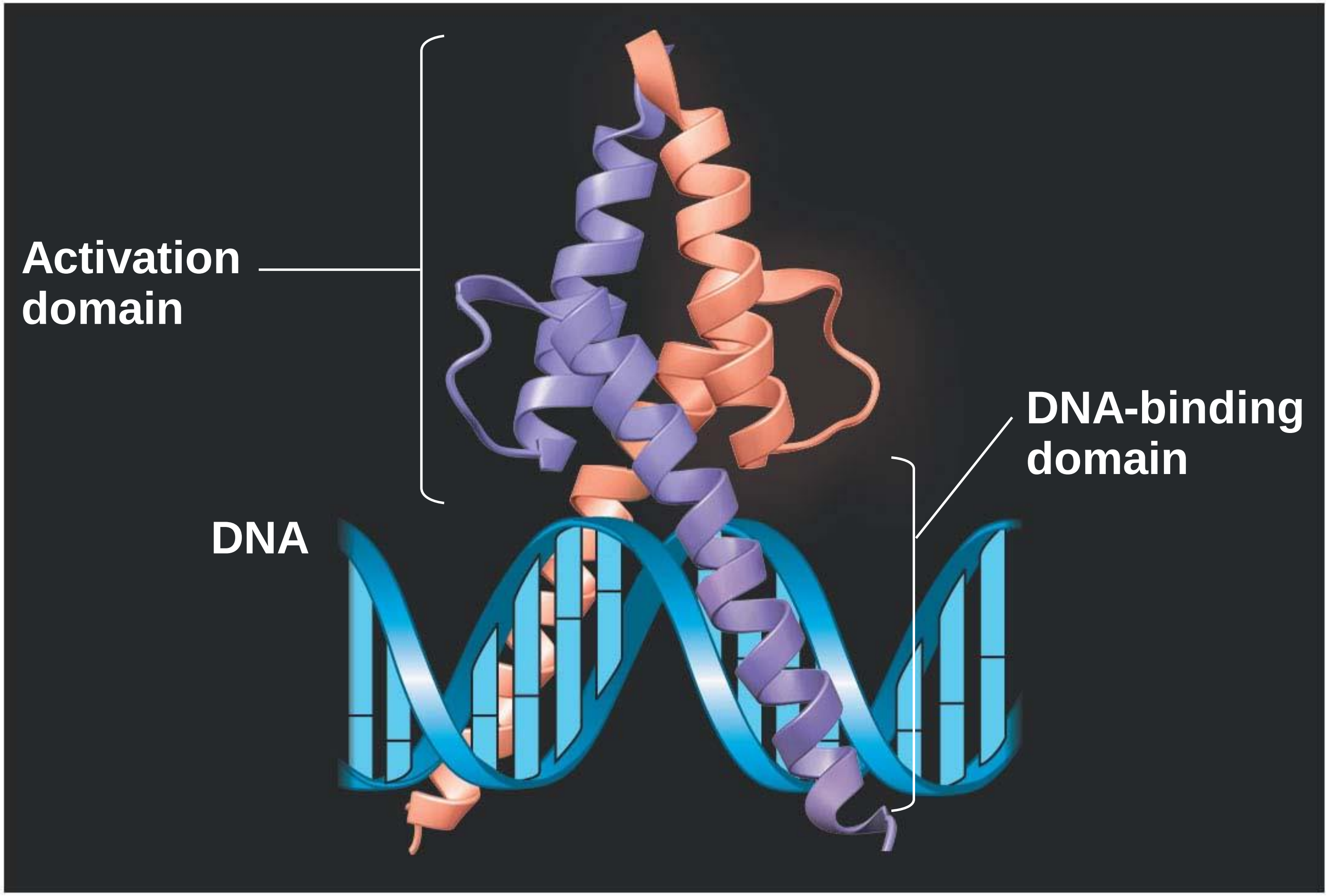
- To initiate transcription, eukaryotic RNA polymerase requires the assistance of transcription factors
- A few transcription factors bind to a DNA sequence, but many bind to proteins
- The interaction of general transcription factors and RNA polymerase II with a promoter usually leads to only a low rate of initiation

Enhancers and Specific Transcription Factors

- Proximal control elements are located close to the promoter
- Distal control elements, groupings 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
- Activators have two domains, one that binds DNA and a second that activates transcription
- Bound activators facilitate a sequence of protein-protein interactions that result in transcription of a given gene

Figure 15.9



- Bound activators are brought into contact with a group of mediator proteins through DNA bending
- The mediator proteins in turn interact with proteins at the promoter
- These protein-protein interactions help to assemble and position the initiation complex on the promoter

Figure 15.10-s1

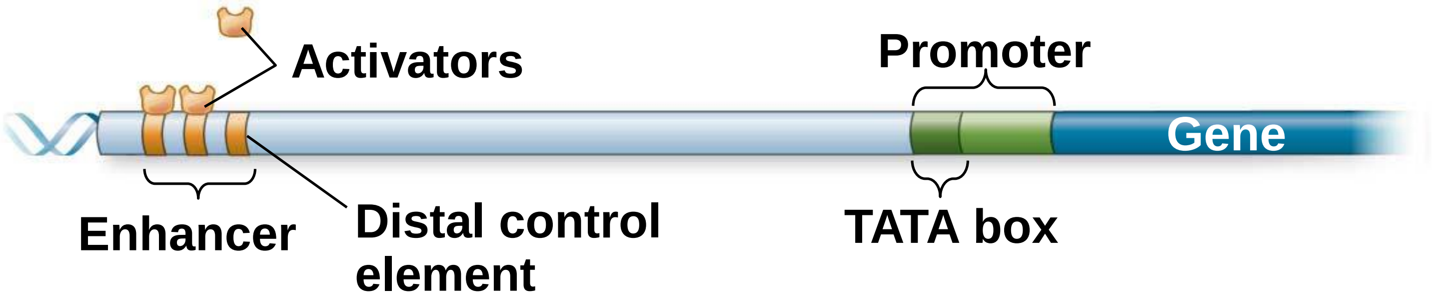


Figure 15.10-s2

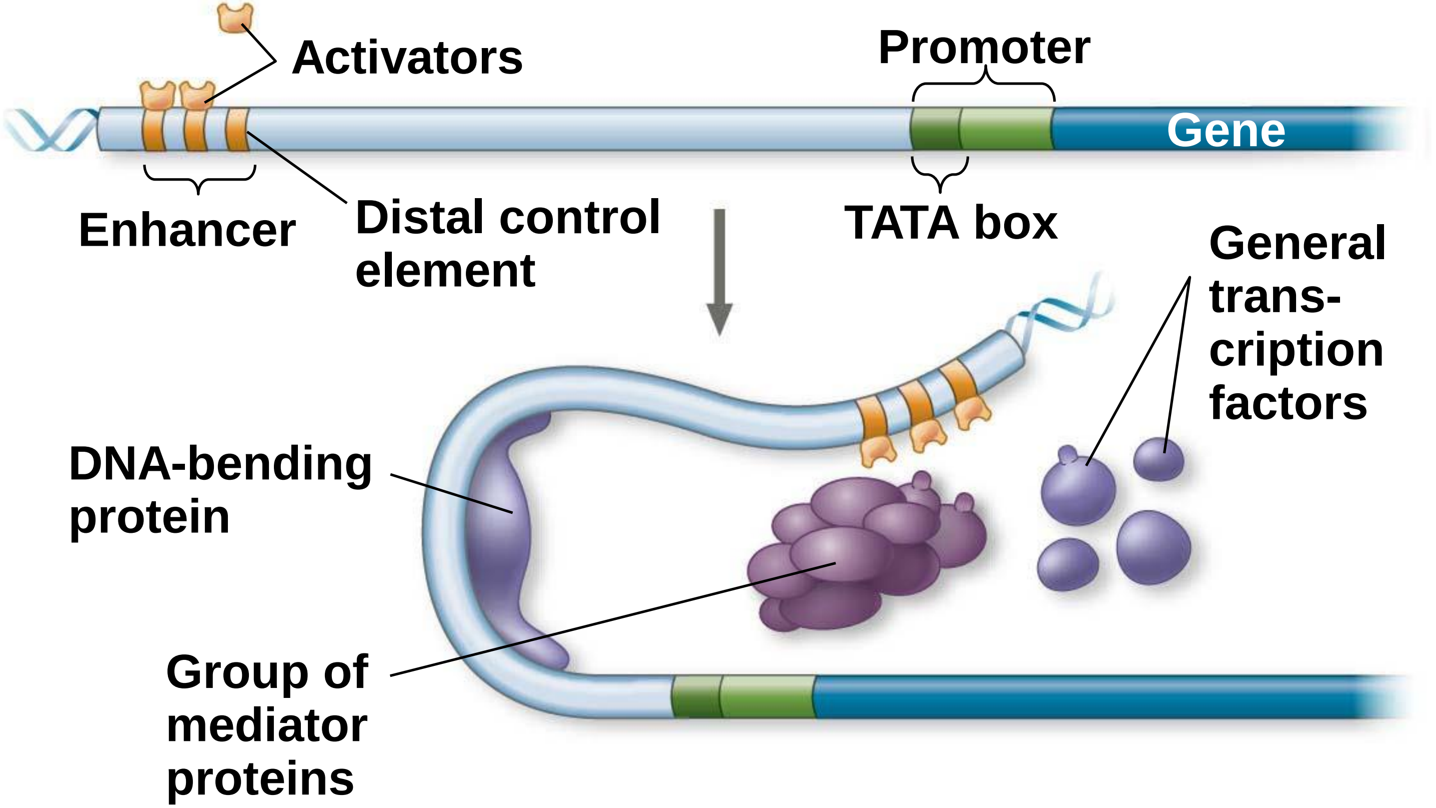
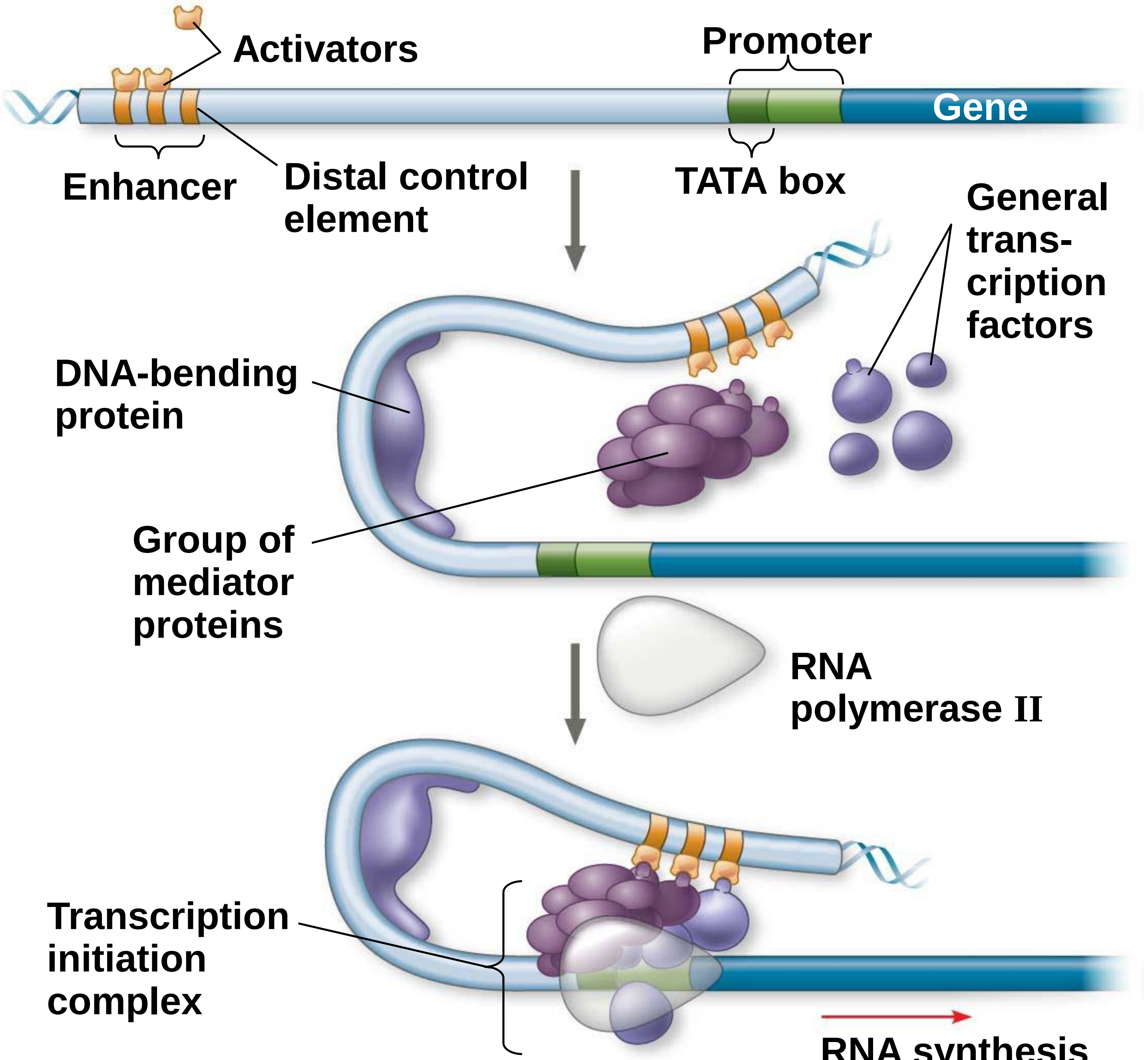


Figure 15.10-s3

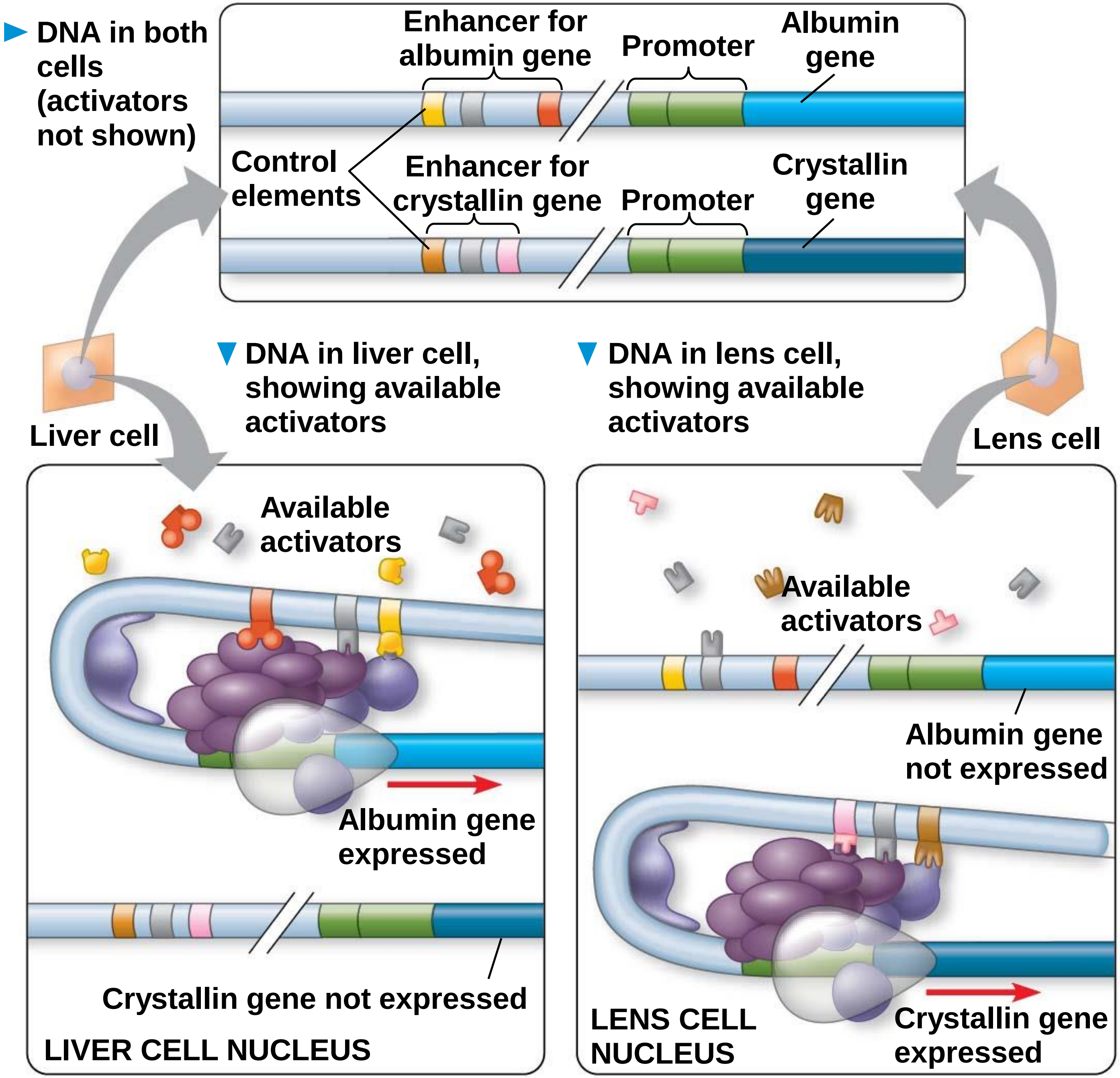


- Some transcription factors function as repressors, inhibiting expression of a particular gene by a variety of methods
- Some activators and repressors act indirectly by influencing chromatin structure to promote or silence transcription

Combinatorial Control of Gene Activation

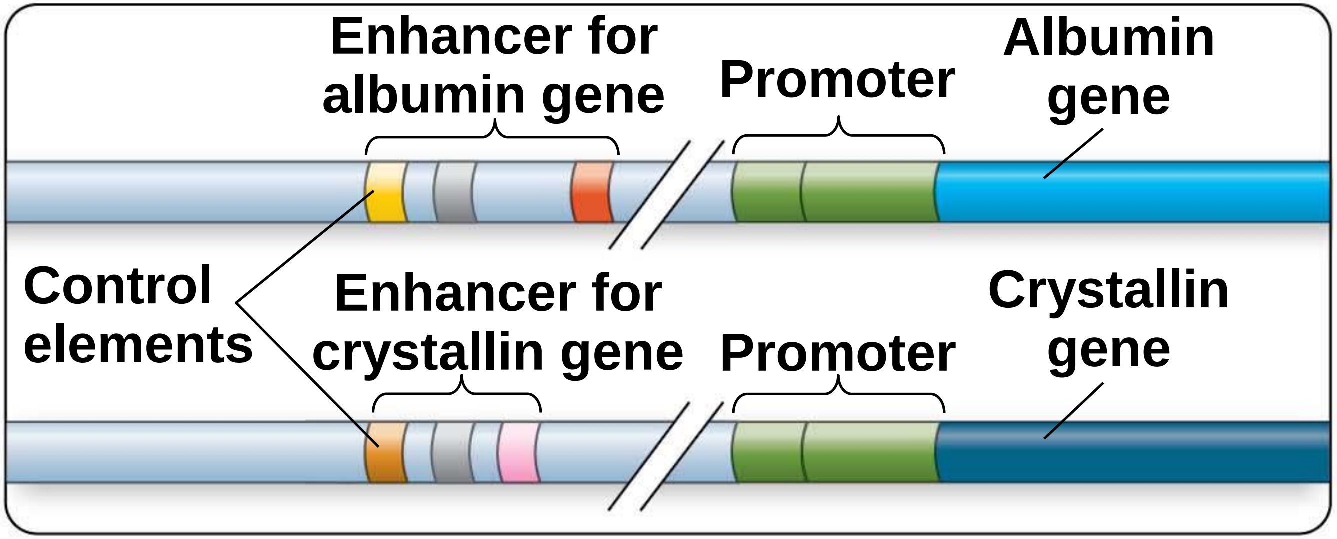
- A particular combination of control elements can activate transcription only when the appropriate activator proteins are present

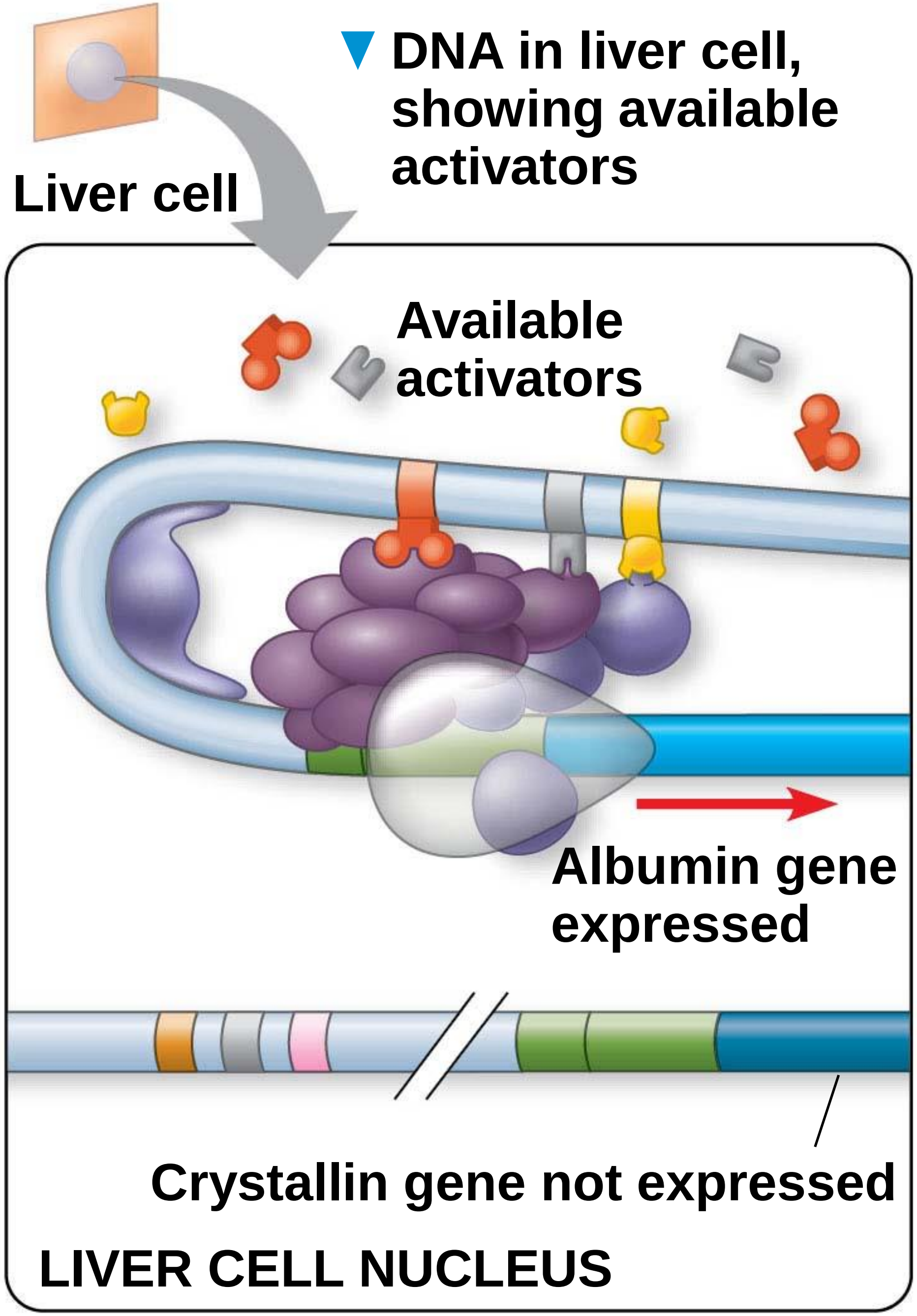
Figure 15.11

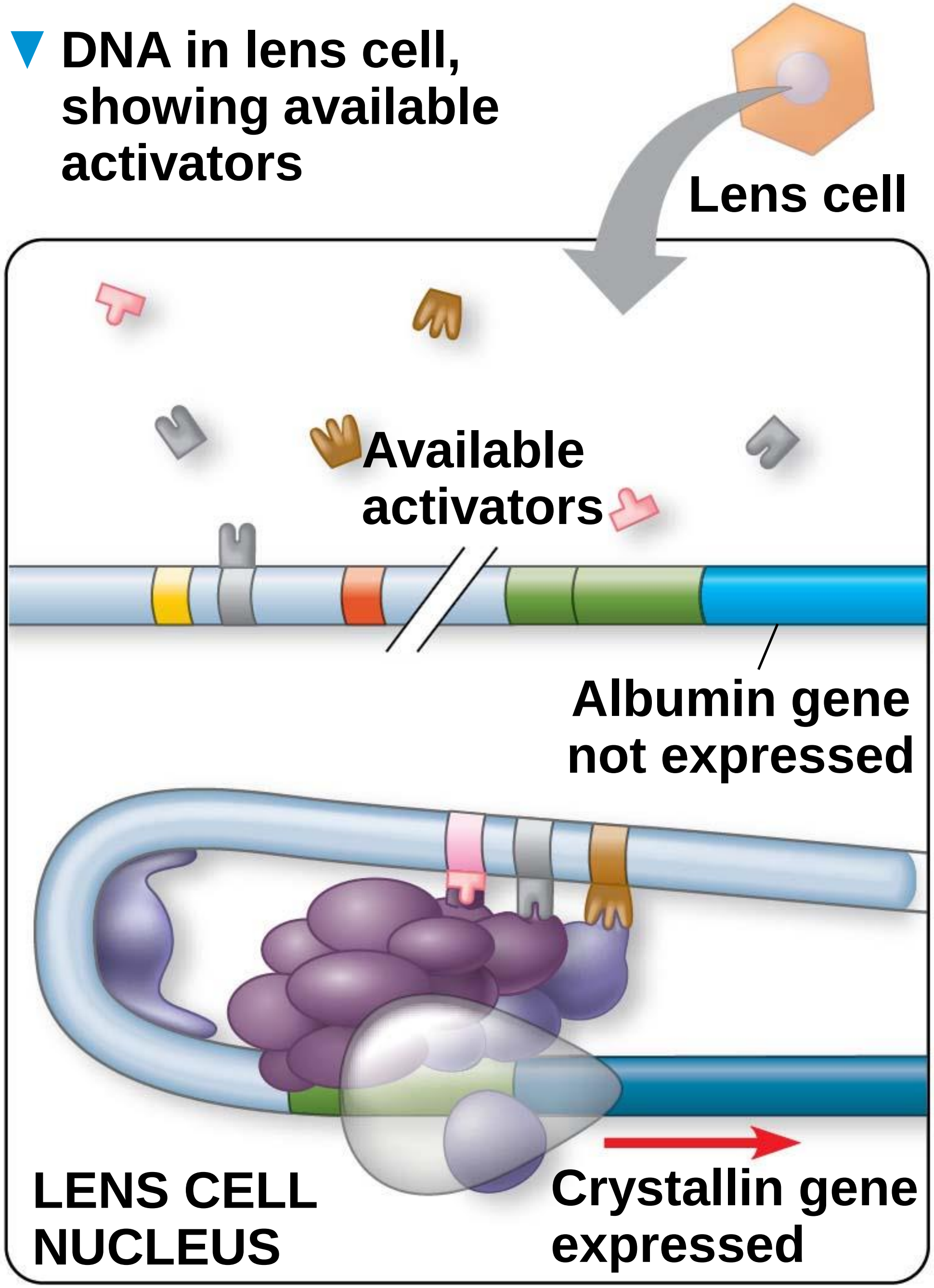


DNA in both cells (activators not shown)
Enhancer for albumin gene
Promoter
Albumin gene
Control elements
Enhancer for crystallin gene
Promoter
Crystallin gene
Liver cell
DNA in liver cell, showing available activators
DNA in lens cell, showing available activators
Lens cell
Available activators
Albumin gene expressed
Crystallin gene not expressed
LIVER CELL NUCLEUS
Available activators
Albumin gene not expressed
LENS CELL NUCLEUS
Crystallin gene expressed

- DNA in both cells (activators not shown)




▼ DNA in liver cell, showing available activators
Liver cell
Available activators
Albumin gene expressed
Crystallin gene not expressed
LIVER CELL NUCLEUS



▼ **DNA in lens cell, showing available activators**

Lens cell

Available activators

Albumin gene not expressed

LENS CELL NUCLEUS

Crystallin gene expressed

Coordinately Controlled Genes in Eukaryotes

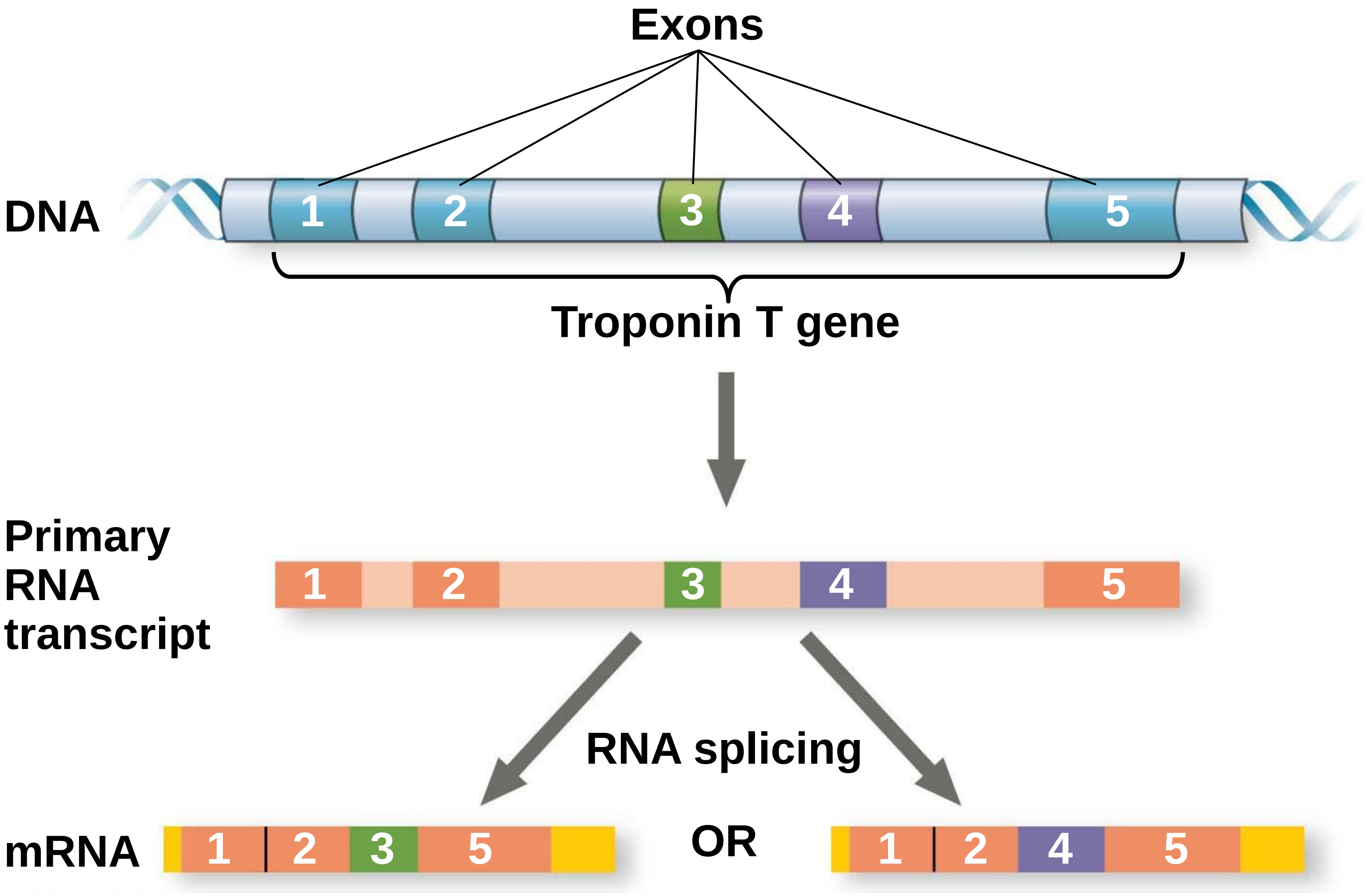
- Eukaryotic genes that are co-expressed are, for the most part, not organized into operons
- These genes can be scattered over different chromosomes, but each has the same combination of control elements
- Copies of the activators recognize specific control elements and promote simultaneous transcription 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
- Alternative splicing can significantly expand the repertoire of a eukaryotic genome


Exons
DNA
1
2
3
4
5
Troponin T gene
Primary RNA transcript
1
2
3
4
5
RNA splicing
mRNA
1
2
3
5
OR
1
2
4
5

Initiation of Translation and mRNA Degradation

- 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

- The life span of mRNA molecules in the cytoplasm is important in determining the pattern of protein synthesis in a cell
- Eukaryotic mRNA generally survives longer than prokaryotic mRNA
- Nucleotide sequences that influence the life span of mRNA in eukaryotes reside in the untranslated region (UTR) at the 3′ end of the molecule

Protein Processing and Degradation

- After translation, various types of protein processing, including cleavage and chemical modification, are subject to control
- The length of time each protein functions in a cell is regulated by means of selective degradation
- To mark a particular protein for destruction, the cell commonly attaches molecules of ubiquitin to the protein, which triggers its destruction

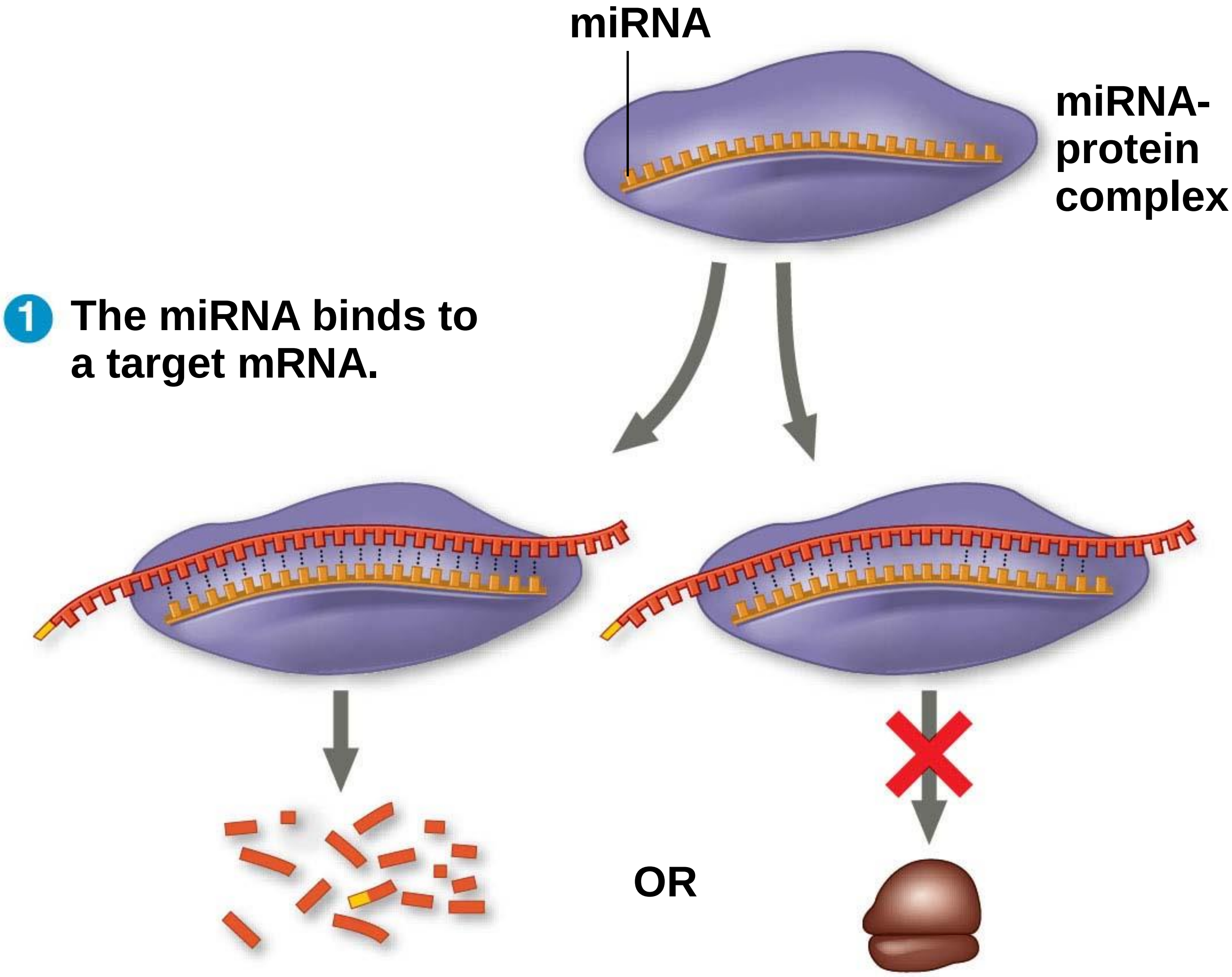
Concept 15.3: Noncoding RNAs play multiple roles in controlling gene expression

- Only a small fraction of DNA encodes proteins, and a very small fraction of the non-protein-coding DNA consists of genes for RNAs such as rRNA and tRNA
- A significant amount of the genome may be transcribed into noncoding RNAs (ncRNAs)
- A large and diverse population of RNA molecules in the cell play crucial roles in regulating gene expression

Effects on mRNAs by MicroRNAs and Small Interfering RNAs

- **MicroRNAs** (**miRNAs**) are small, single-stranded RNA molecules that can bind to complementary mRNA sequences
- These can degrade the mRNA or block its translation

Figure 15.13



① The miRNA binds to a target mRNA.

mRNA degraded

Translation blocked

② If bases are completely complementary, mRNA is degraded. If match is less complete, translation is blocked.

- Another class of small RNAs are called **small interfering RNAs** (**siRNAs**)
- siRNAs and miRNAs are similar but form from different RNA precursors
- The phenomenon of inhibition of gene expression by siRNAs is called **RNA interference** (**RNAi**)

Chromatin Remodeling and Effects on Transcription by ncRNAs

- In some yeasts, siRNAs are required for the formation of heterochromatin at the centromeres of chromosomes
- The siRNA system interacts with other noncoding RNAs and with chromatin-modifying enzymes
- This leads to condensation of centromere chromatin into heterochromatin

- A class of small ncRNAs called piwi-associated RNAs (piRNAs) also induces formation of heterochromatin
- They block expression of transposons, parasitic DNA elements in the genome
- The role of ncRNAs adds to the complexity of the processes involved in regulation of gene expression

Concept 15.4: Researchers Can Monitor Expression of Specific Genes

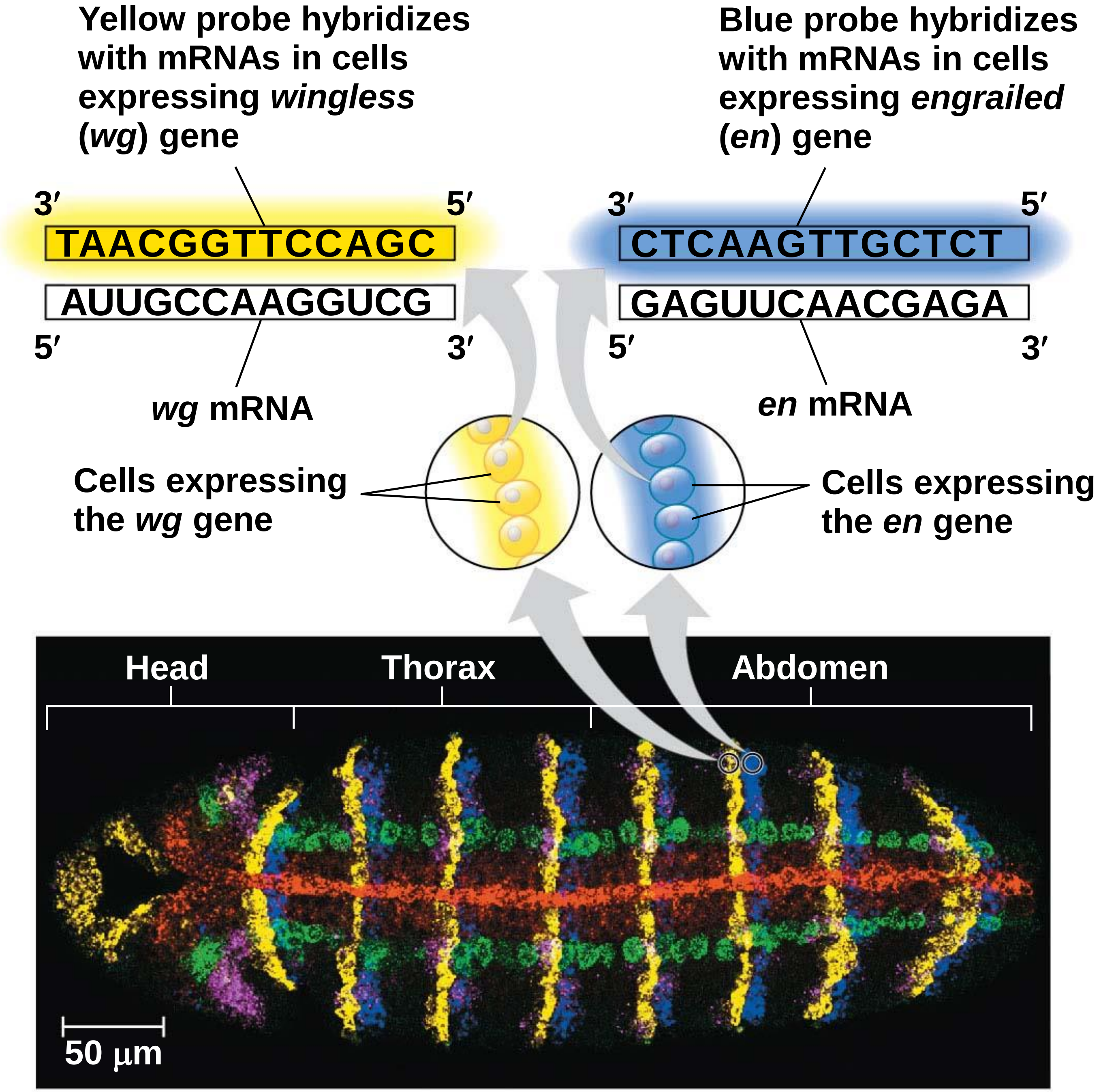
- Cells of a given multicellular organism differ from each other because they express different genes from an identical genome
- The most straightforward way to discover which genes are expressed by cells of interest is to identify the mRNAs being made

Studying the Expression of Single Genes

- We can detect mRNA in a cell using **nucleic acid hybridization**, the base pairing of a strand of nucleic acid to its complementary sequence
- The complementary molecule in this case is a short, single-stranded DNA or RNA called a **nucleic acid probe**
- Each probe is labeled with a fluorescent tag to allow visualization

- The technique allows us to see the mRNA in place (*in situ*) in the intact organism and is thus called ***in situ* hybridization**

Figure 15.14



Yellow probe hybridizes with mRNAs in cells expressing *wingless* (*wg*) gene

3′ TAACGGTTCCAGC 5′

5′ AUUGCCAAGGUCG 3′

***wg* mRNA**

Blue probe hybridizes with mRNAs in cells expressing *engrailed* (*en*) gene

3′ CTCAAGTTGCTCT 5′

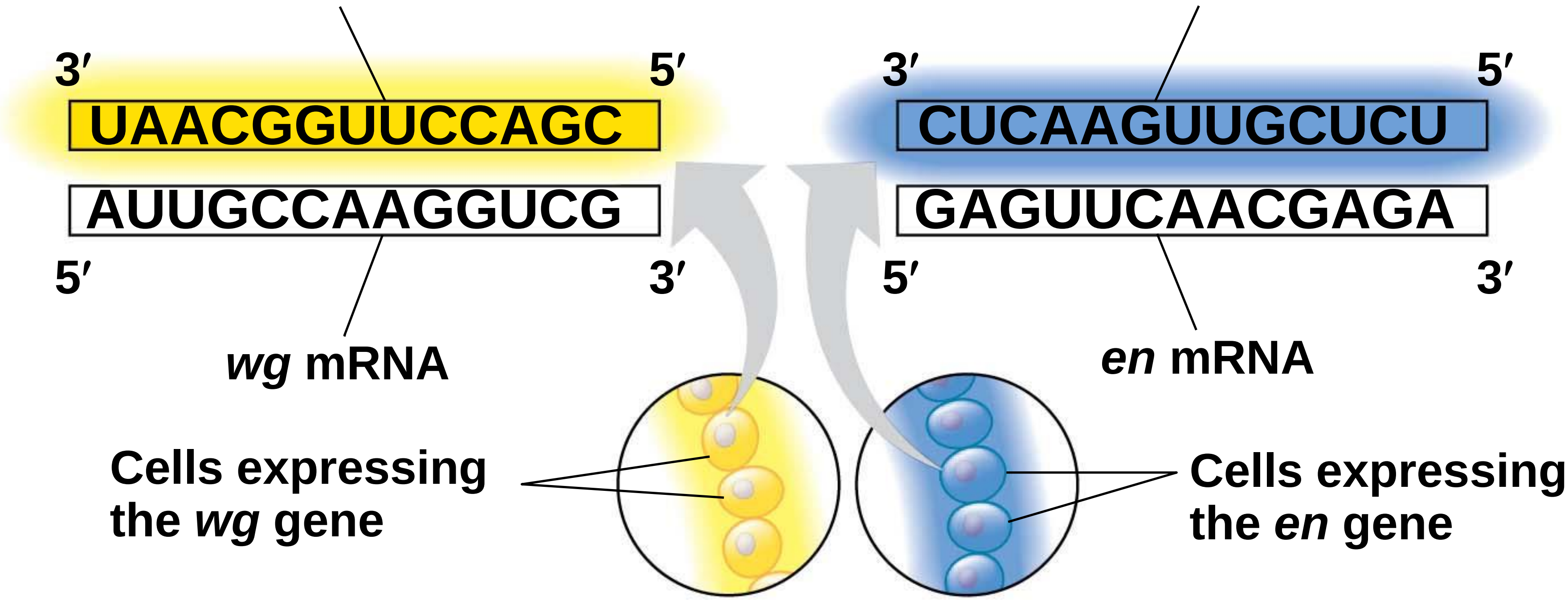
5′ GAGUUCAACGAGA 3′

***en* mRNA**

Cells expressing the *wg* gene

Cells expressing the *en* gene

Figure 15.14-1



Yellow probe hybridizes with mRNAs in cells expressing *wingless* (*wg*) gene

Blue probe hybridizes with mRNAs in cells expressing *engrailed* (*en*) gene

3′ UAACGGUUCCAGC 5′

5′ AUUGCCAAGGUCG 3′

***wg* mRNA**

3′ CUCAAGUUGCUCU 5′

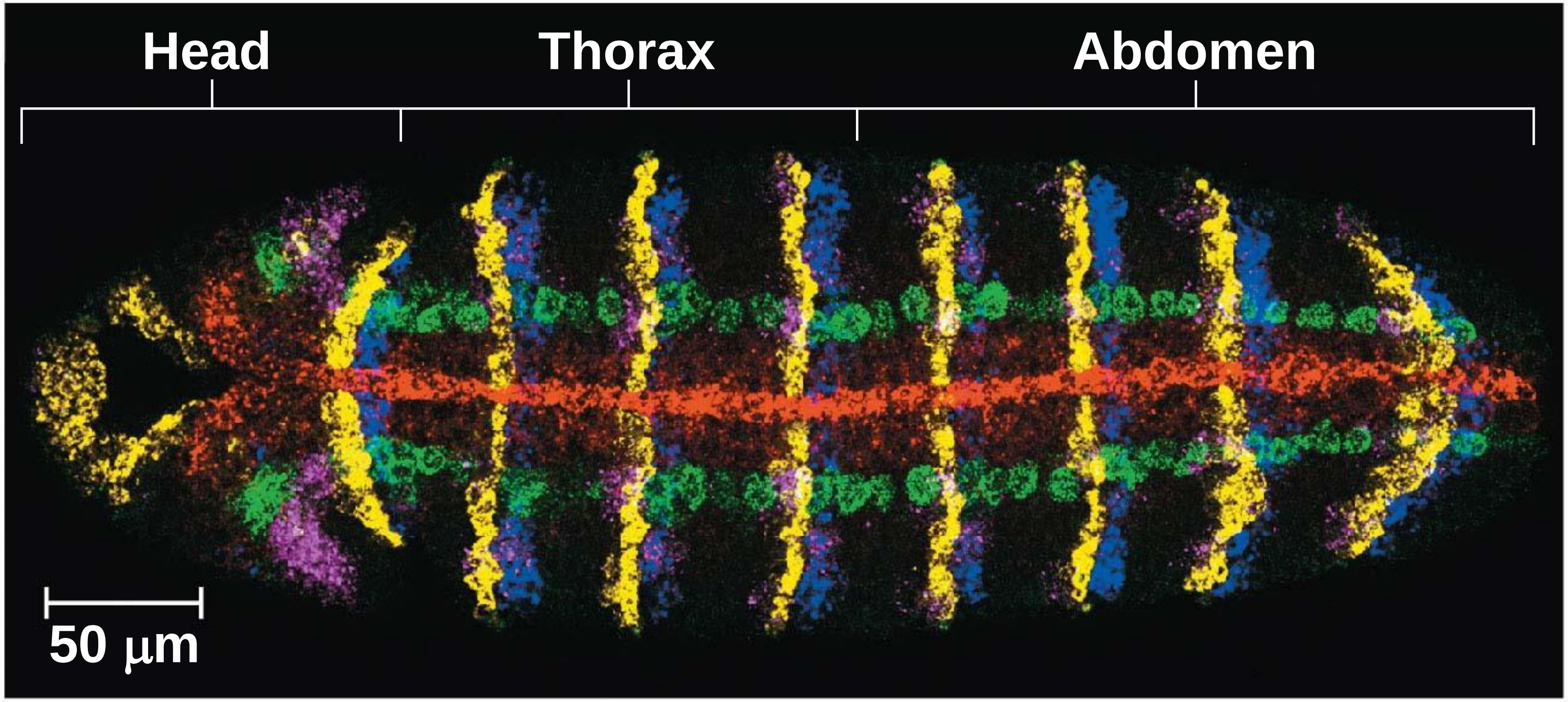
5′ GAGUUCAACGAGA 3′

***en* mRNA**

Cells expressing the *wg* gene

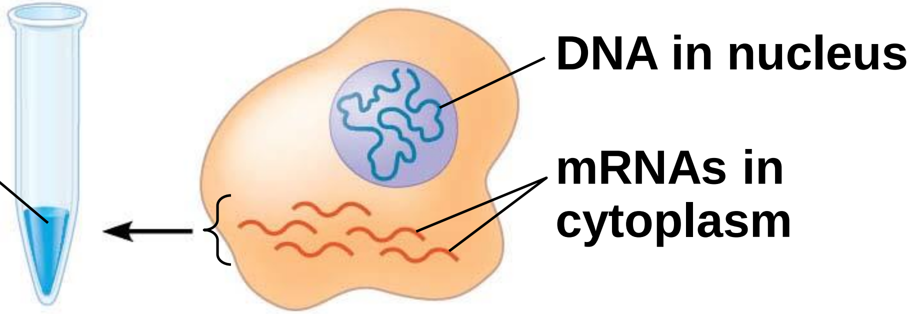
Cells expressing the *en* gene

Figure 15.14-2



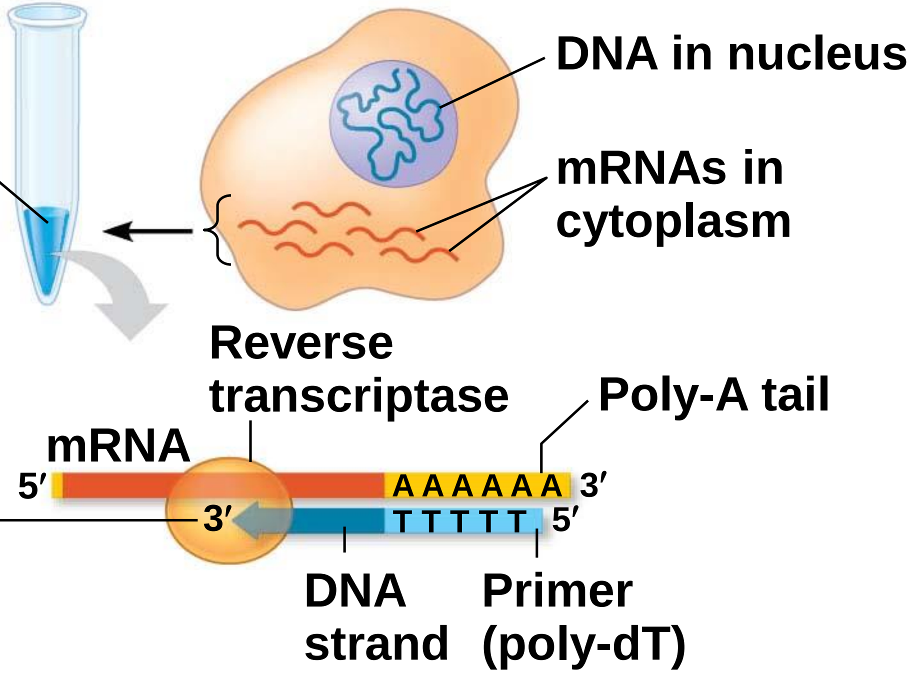
- Another widely used method for comparing the amounts of specific mRNAs in several different samples is **reverse transcriptase–polymerase chain reaction** (**RT-PCR**)
- RT-PCR turns sample sets of mRNAs into double-stranded DNAs with the corresponding sequences

Figure 15.15-s1



① **Test tube containing reverse transcriptase and mRNA**

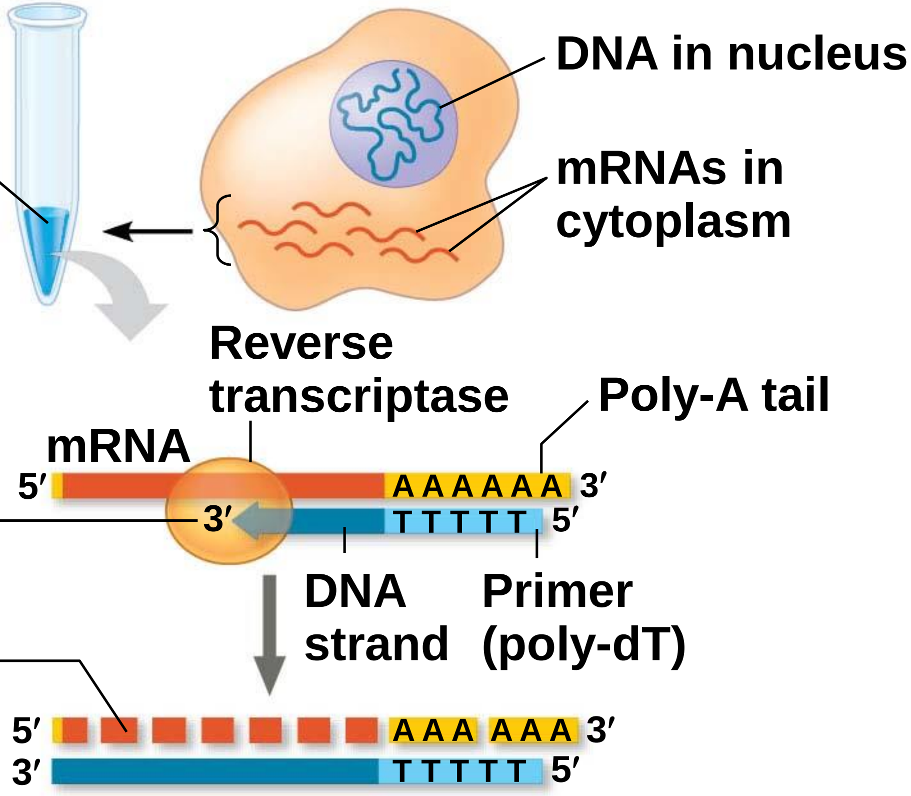
Figure 15.15-s2



① **Test tube containing reverse transcriptase and mRNA**

② **Reverse transcriptase makes the first DNA strand.**

Figure 15.15-s3

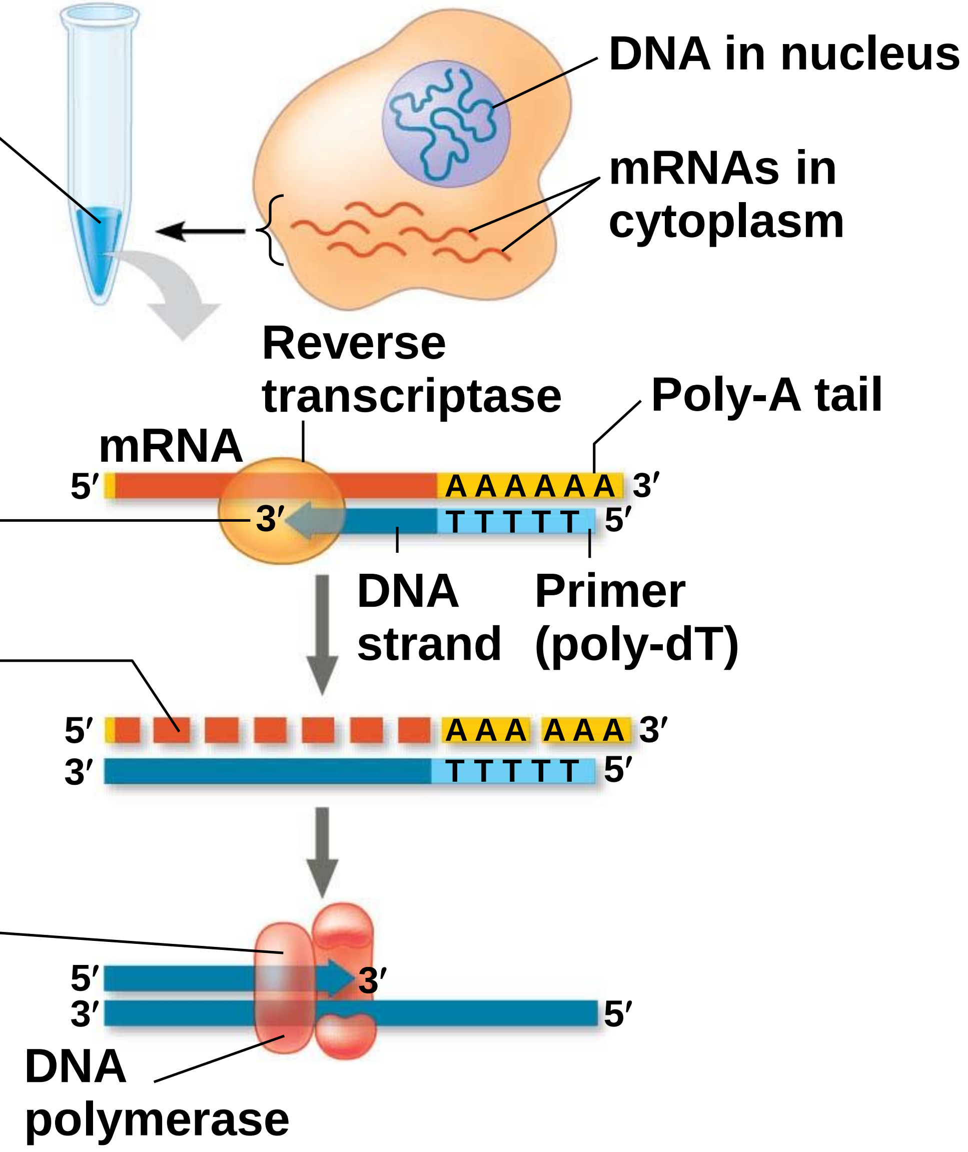


① Test tube containing reverse transcriptase and mRNA

② Reverse transcriptase makes the first DNA strand.

③ mRNA is degraded.

Figure 15.15-s4



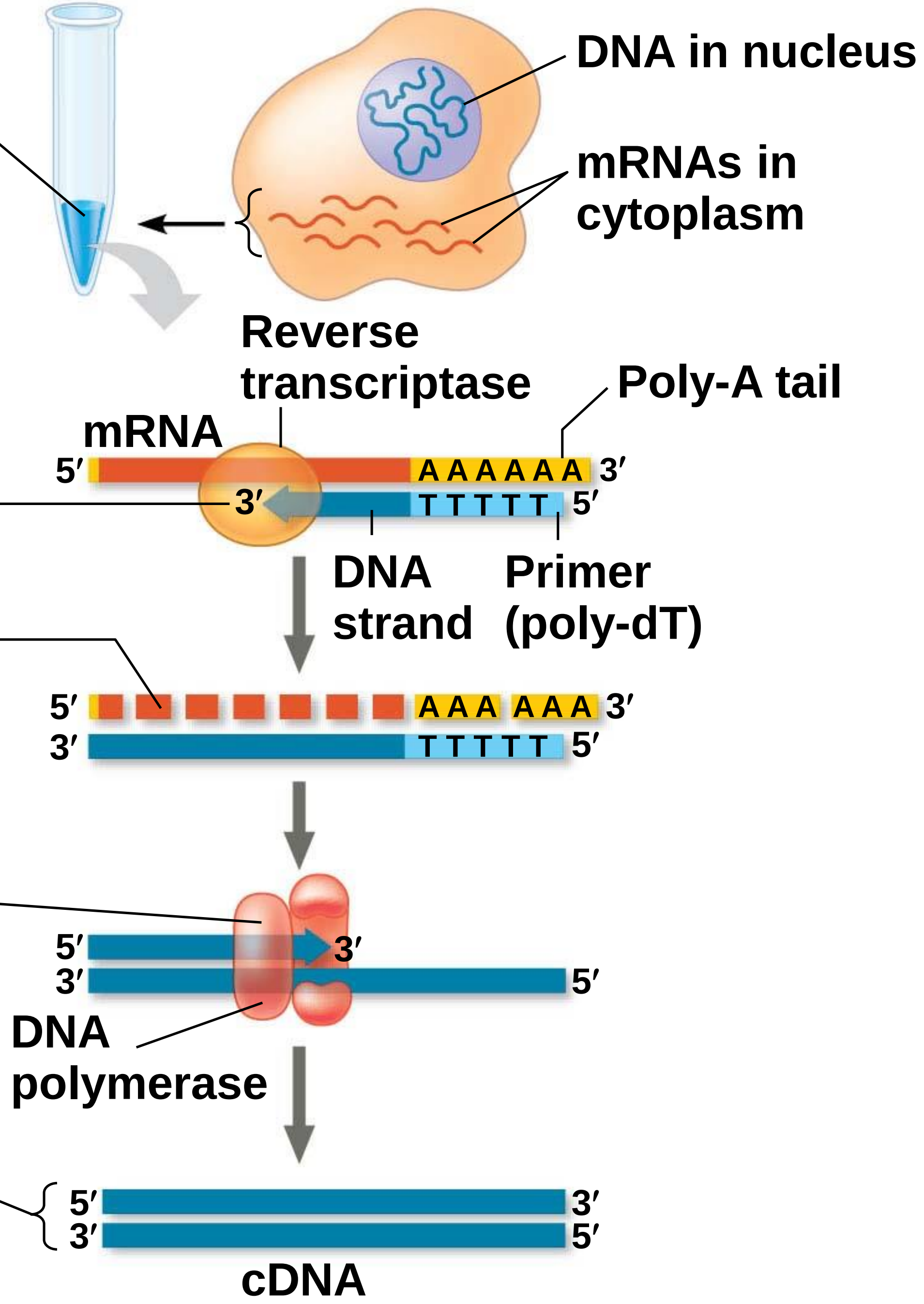
① **Test tube containing reverse transcriptase and mRNA**

② **Reverse transcriptase makes the first DNA strand.**

③ **mRNA is degraded.**

④ **DNA polymerase synthesizes the second strand.**

Figure 15.15-s5



① **Test tube containing reverse transcriptase and mRNA**

② **Reverse transcriptase makes the first DNA strand.**

③ **mRNA is degraded.**

④ **DNA polymerase synthesizes the second strand.**

⑤ **cDNA carries complete coding sequence without introns.**

- RT-PCR relies on the activity of reverse transcriptase, which can synthesize a DNA copy of an mRNA, called a **complementary DNA** (**cDNA**)
- Once the cDNA is produced, PCR is used to make many copies of the sequence of interest, using primers specific to that sequence

Figure 15.16

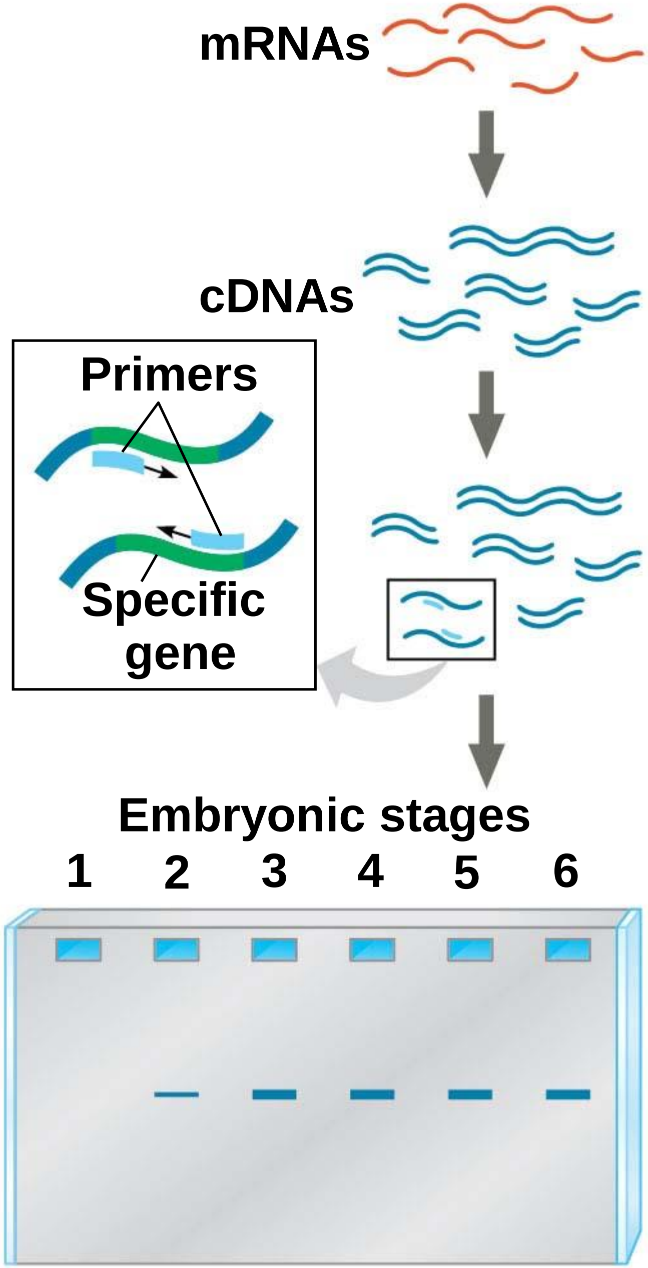
Technique

① **cDNA synthesis**

② **PCR amplification**

Results

③ **Gel electrophoresis**

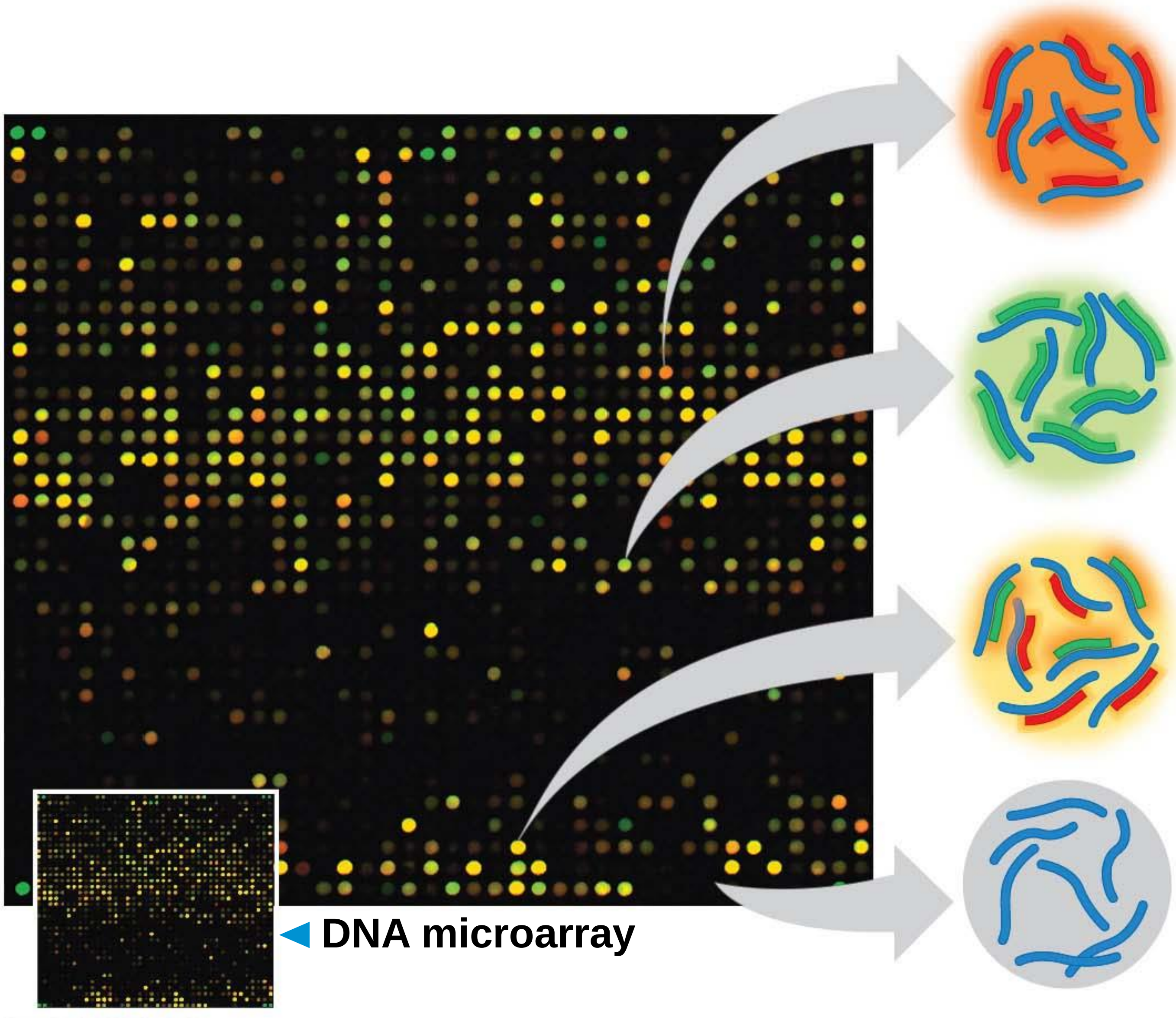


Studying the Expression of Groups of Genes

- A major goal of biologists is to learn how genes act together to produce and maintain a functioning organism
- Large groups of genes are studied by a systems approach
- The aim is to identify networks of gene expression across an entire genome

- Genome-wide expression studies can be carried out using **DNA microarray assays**
- A microarray—also called a DNA chip—contains tiny amounts of many single-stranded DNA fragments affixed to the slide in a grid
- mRNAs from cells of interest are isolated and made into cDNAs labeled with fluorescent molecules

- Usually, cDNAs from two different samples are labeled with different fluorescent tags and tested on the same microarray
- The experiment can identify subsets of genes that are being expressed differently in one sample compared to another



Genes in red wells expressed in first tissue.

Genes in green wells expressed in second tissue.

Genes in yellow wells expressed in both tissues.

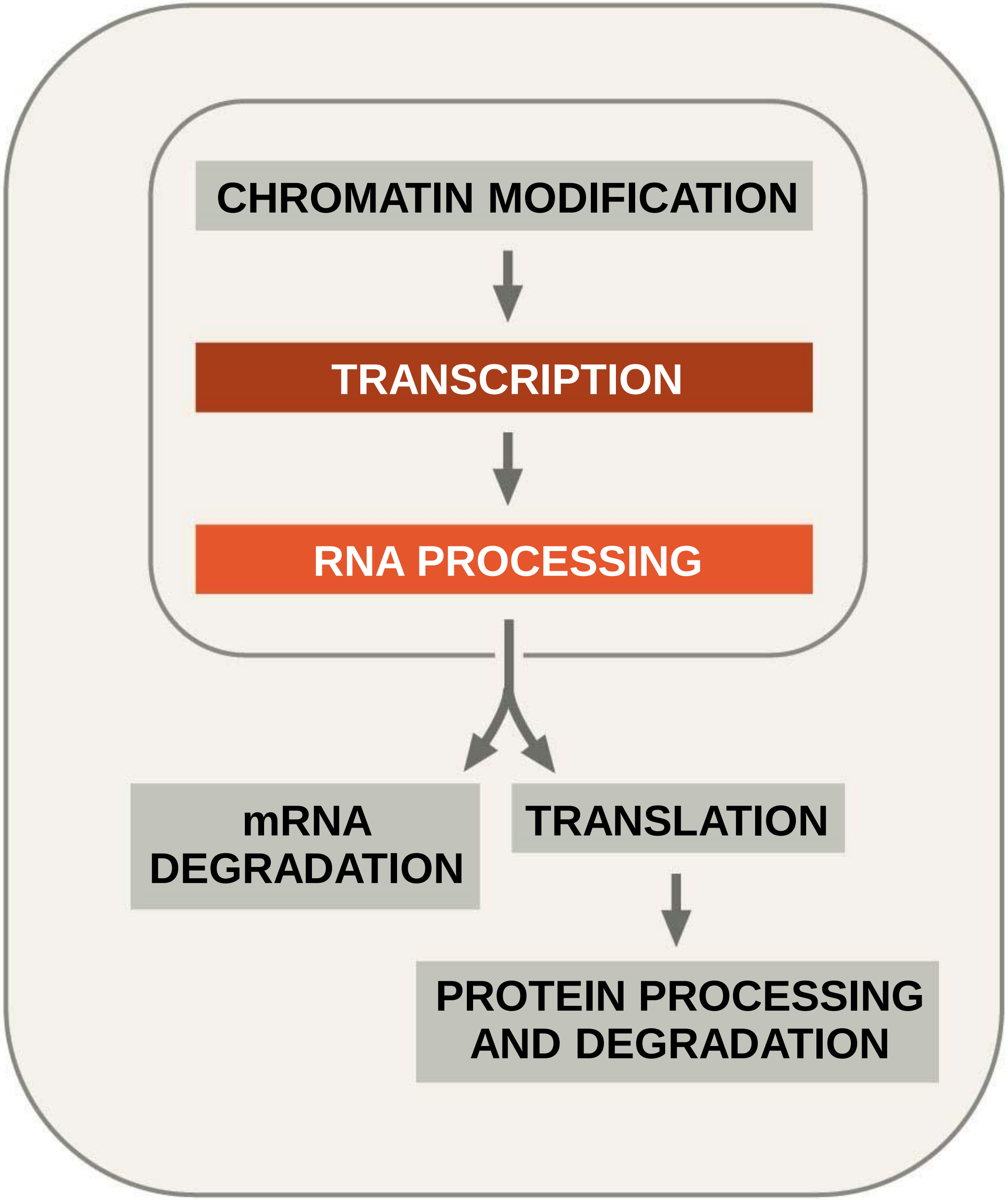
Genes in black wells not expressed in either tissue.

◄ DNA microarray

- An alternative to microarray analysis is simply to sequence cDNA samples from different tissues or stages to discover which genes are expressed
- This is called RNA sequencing, or RNA-seq
- This method is becoming more widespread as the cost of sequencing decreases

- Studies of genes that are expressed together in some tissues but not others may contribute to a better understanding of diseases and suggest new diagnostic tests or therapies

Figure 15.UN01



CHROMATIN MODIFICATION

TRANSCRIPTION

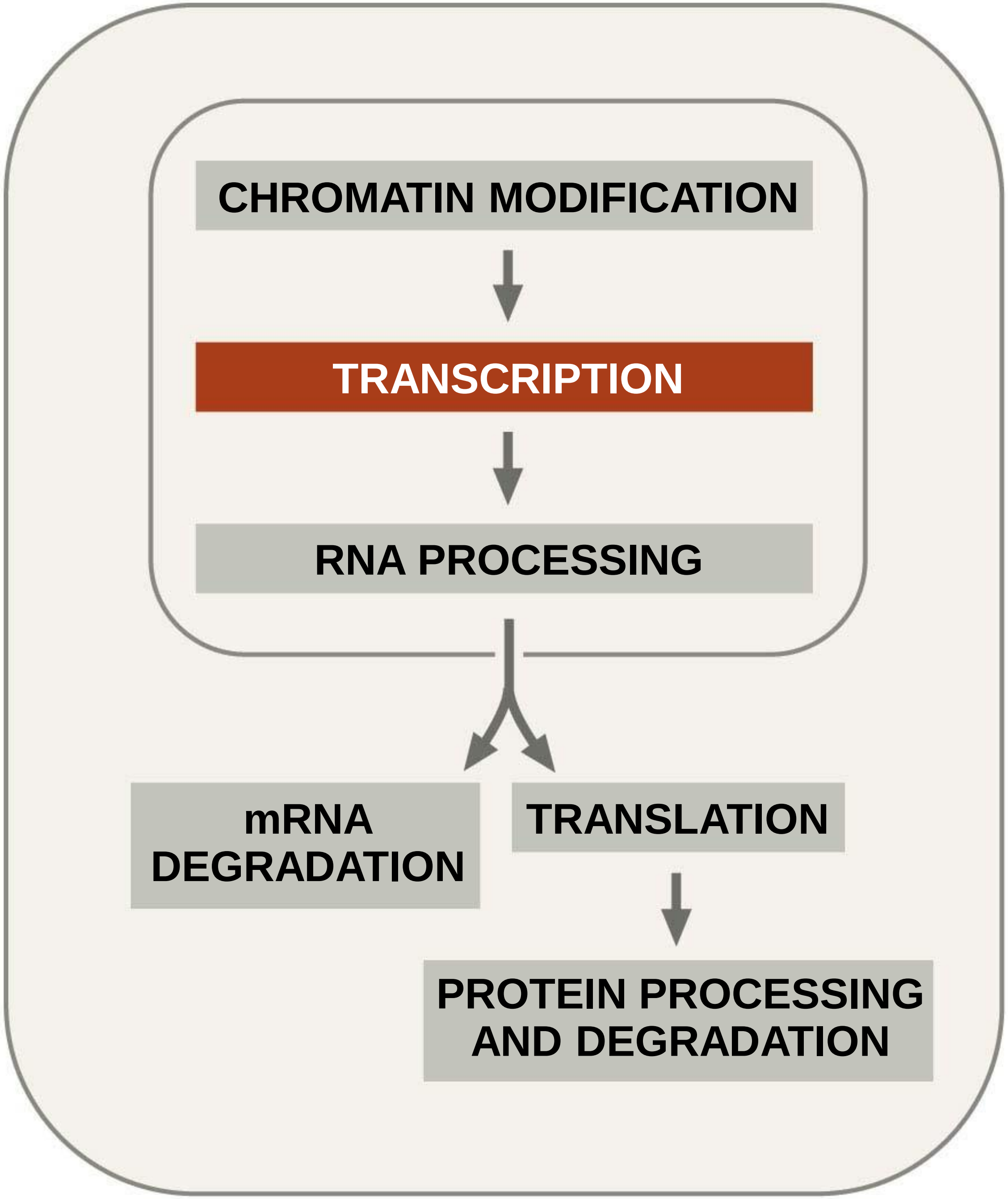
RNA PROCESSING

mRNA DEGRADATION

TRANSLATION

PROTEIN PROCESSING AND DEGRADATION

Figure 15.UN02



CHROMATIN MODIFICATION

TRANSCRIPTION

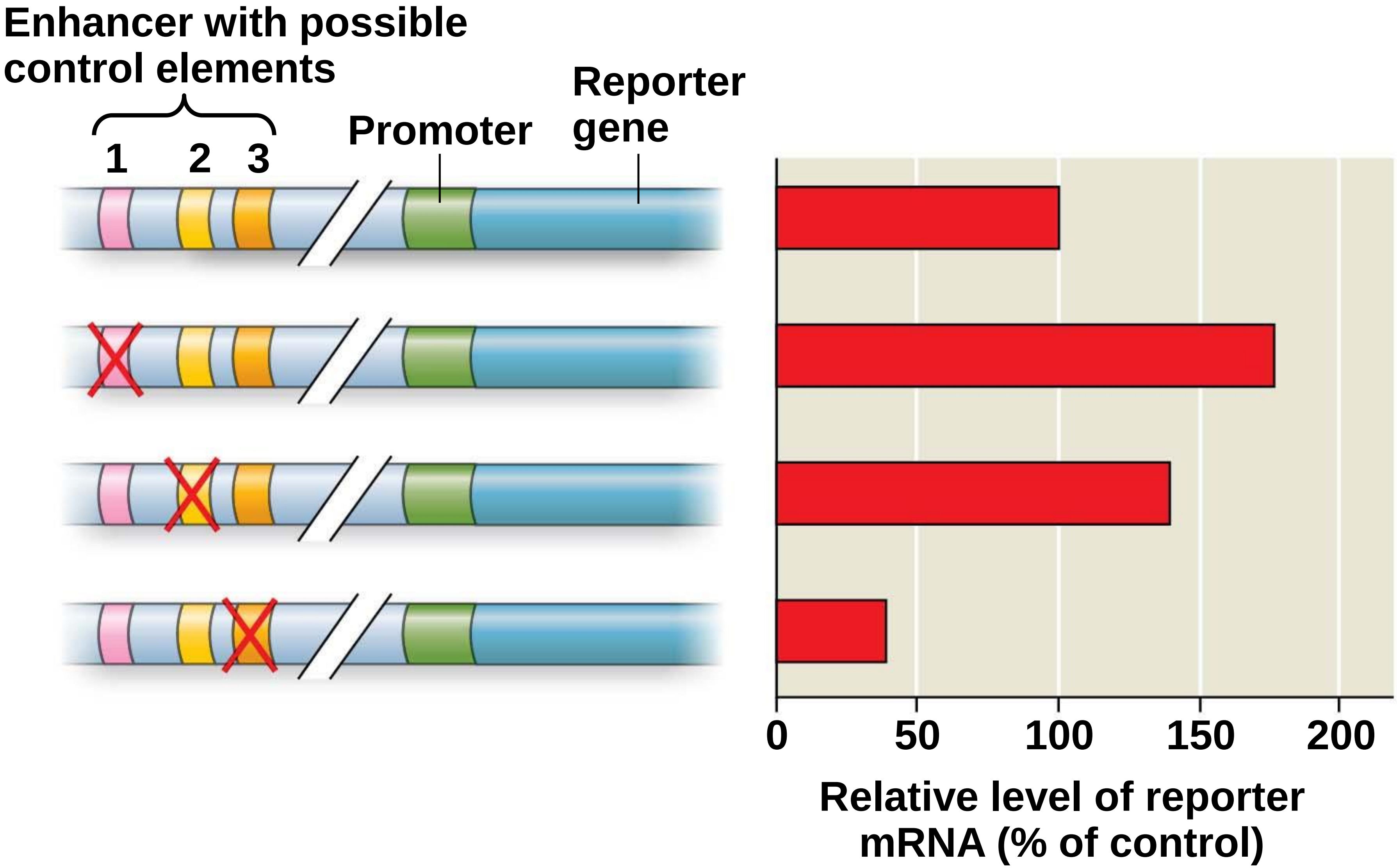
RNA PROCESSING

mRNA DEGRADATION

TRANSLATION

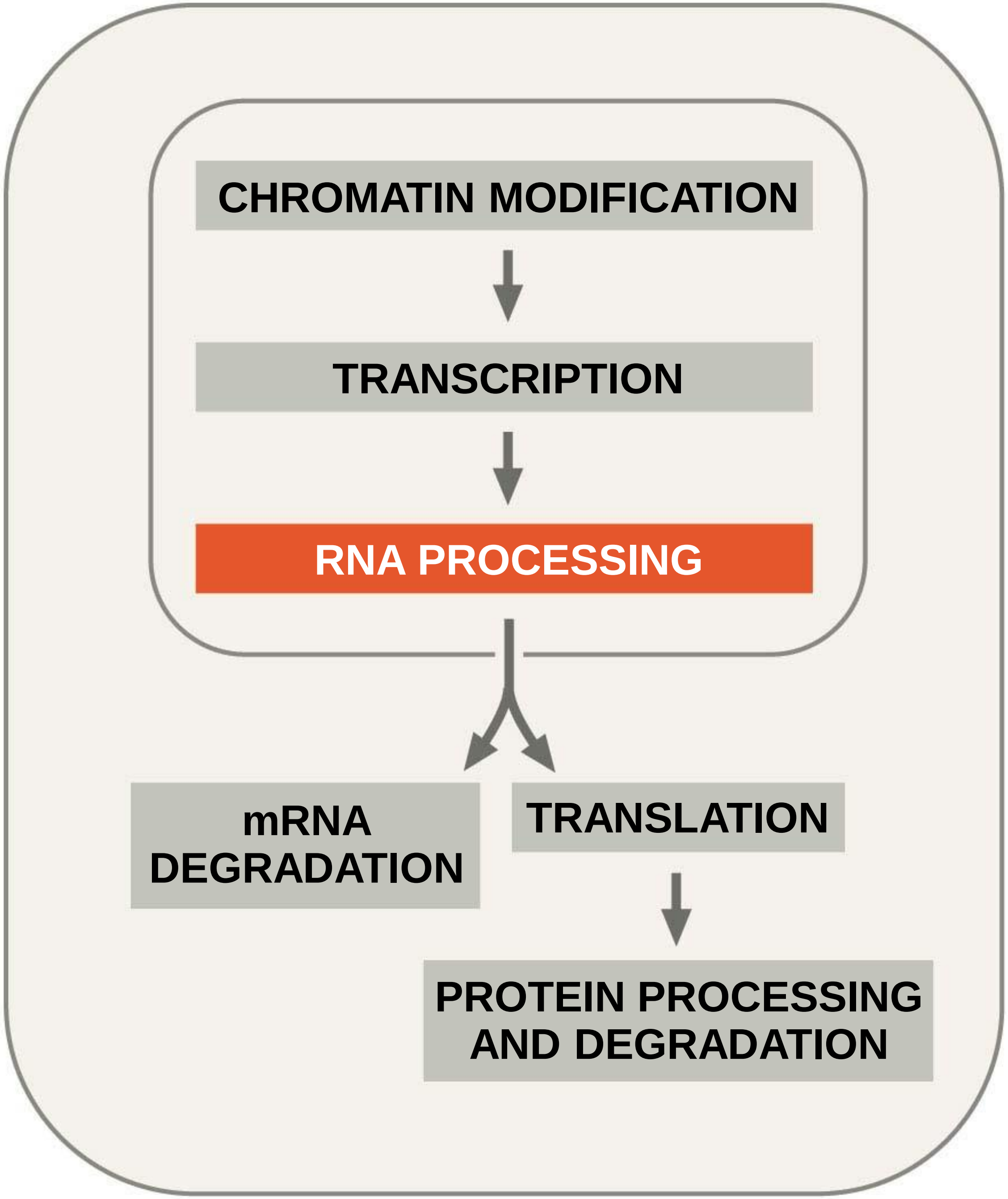
PROTEIN PROCESSING AND DEGRADATION

Figure 15.UN03-1



Data from J. N. Walters et al., Regulation of human microsomal prostaglandin E synthase-1 by IL-1β requires a distal enhancer element with a unique role for C/EBPβ, *Biochemical Journal* 443:561–571 (2012).

Figure 15.UN04



CHROMATIN MODIFICATION

TRANSCRIPTION

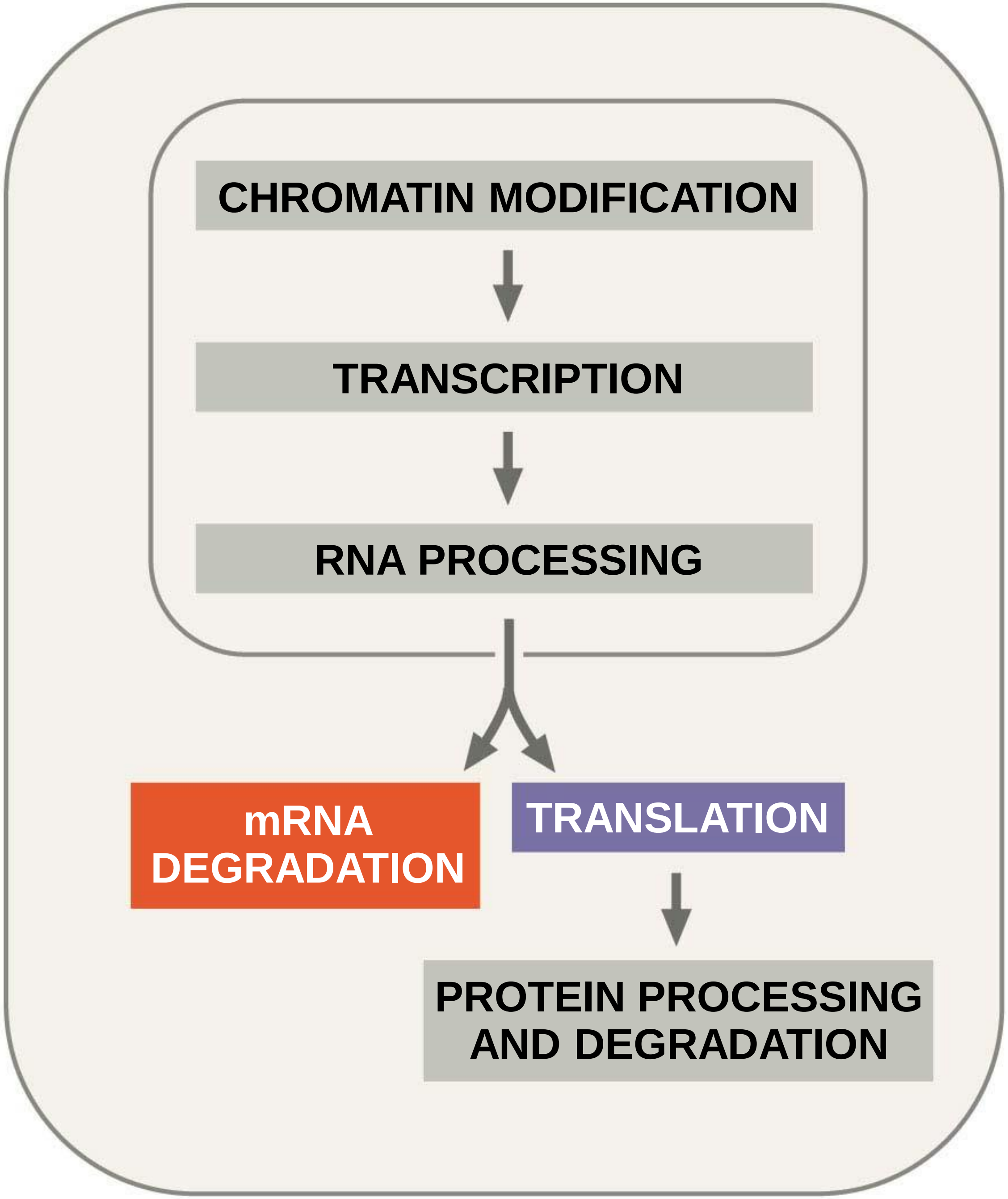
RNA PROCESSING

mRNA DEGRADATION

TRANSLATION

PROTEIN PROCESSING AND DEGRADATION

Figure 15.UN05



CHROMATIN MODIFICATION

TRANSCRIPTION

RNA PROCESSING

mRNA DEGRADATION

TRANSLATION

PROTEIN PROCESSING AND DEGRADATION

Figure 15.UN06

5′ ···CUCAUCACCGGC··· 3′

3′ GAGTAGTGGCCG 5′

Figure 15.UN07

Repressible operon:

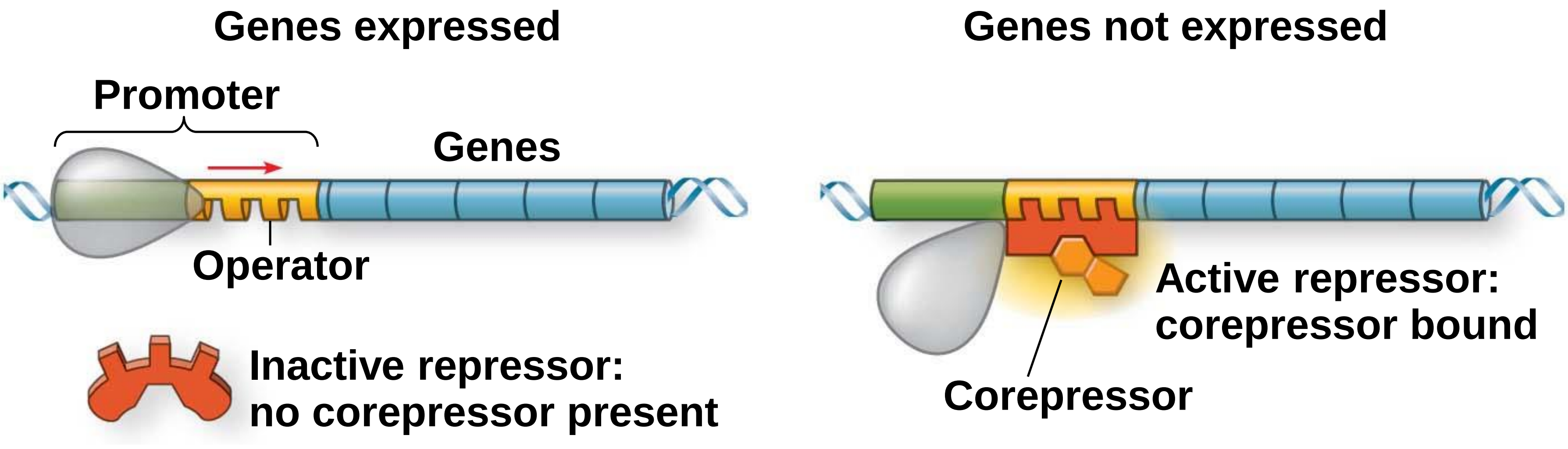
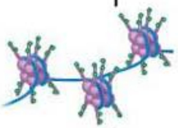


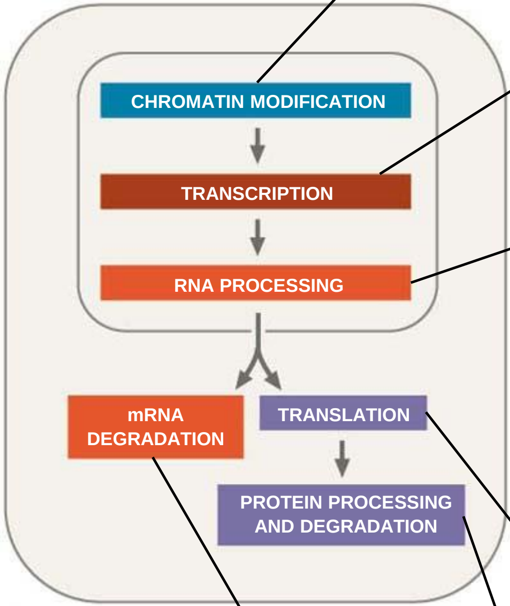
Figure 15.UN08

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.



CHROMATIN MODIFICATION

TRANSCRIPTION

RNA PROCESSING

mRNA DEGRADATION

TRANSLATION

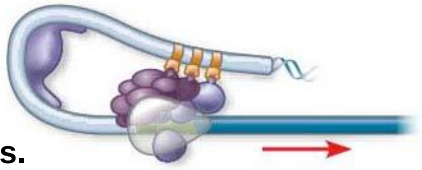
PROTEIN PROCESSING AND DEGRADATION

mRNA degradation

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

Transcription

- Regulation of transcription initiation: DNA control elements in enhancers 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

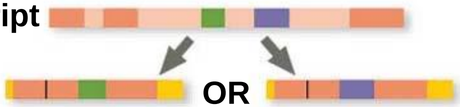
RNA processing

- Alternative RNA splicing:

Primary RNA transcript

mRNA

OR



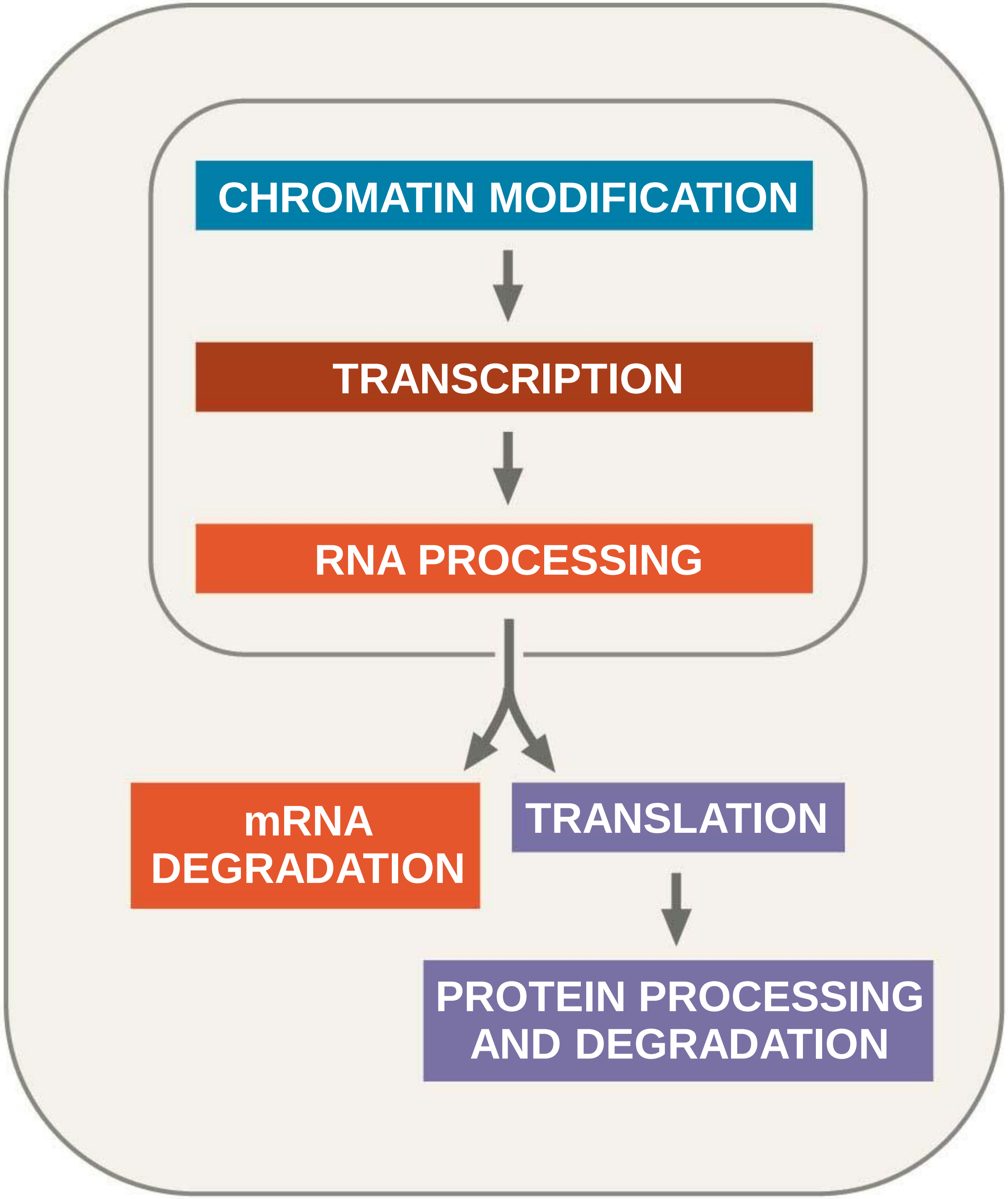
Translation

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

Protein processing and degradation

- Protein processing and degradation are subject to regulation.

Figure 15.UN08-1



CHROMATIN MODIFICATION

TRANSCRIPTION

RNA PROCESSING

mRNA DEGRADATION

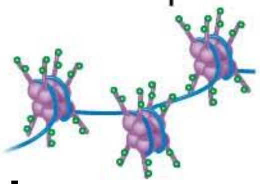
TRANSLATION

PROTEIN PROCESSING AND DEGRADATION

Figure 15.UN08-2

Chromatin modification

- Genes in highly compacted chromatin are generally not transcribed.
- Histone acetylation seems to loosen chromatin structure, enhancing transcription.



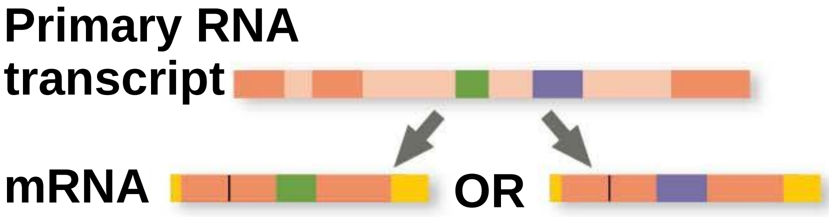
- DNA methylation generally reduces transcription.

mRNA degradation

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

RNA processing

- Alternative RNA splicing:



Translation

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

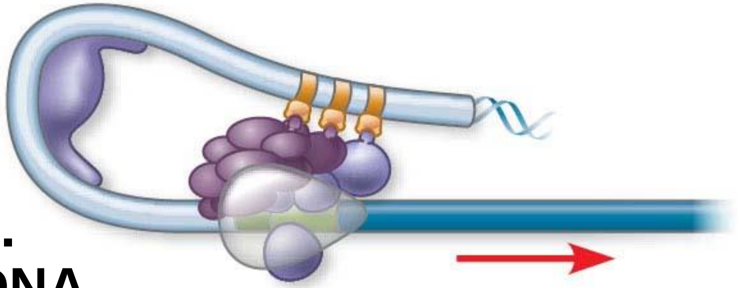
Protein processing and degradation

- Protein processing and degradation are subject to regulation.

Figure 15.UN08-3

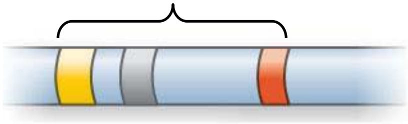
Transcription

- **Regulation of transcription initiation: DNA control elements in enhancers 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

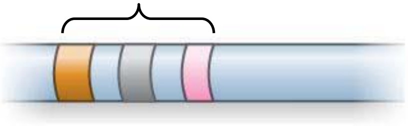


Figure 15.UN09