Lecture for Monday

Dr. Prince

Chapter 11

How Genes Are Controlled

Lecture by Dr. Prince

CONTROL OF GENE EXPRESSION

- Remember, our genetic inheritance is all of life's history from the beginning of life to the present state of humans. It is millions of years of trial and success!
- Within this written history there are many historical genes that can still code for proteins but that we no longer use. This is like my definition of **philosophy;**
- **Philosophy - The sum total of what you know and what you chose to do with it.**
- Like you, your cells (and body) know how to do many things that are not appropriate or even compatible with our current form and function.
- You do not do everything you know how to do.

What should I wear?

What genes to use and what proteins to make?

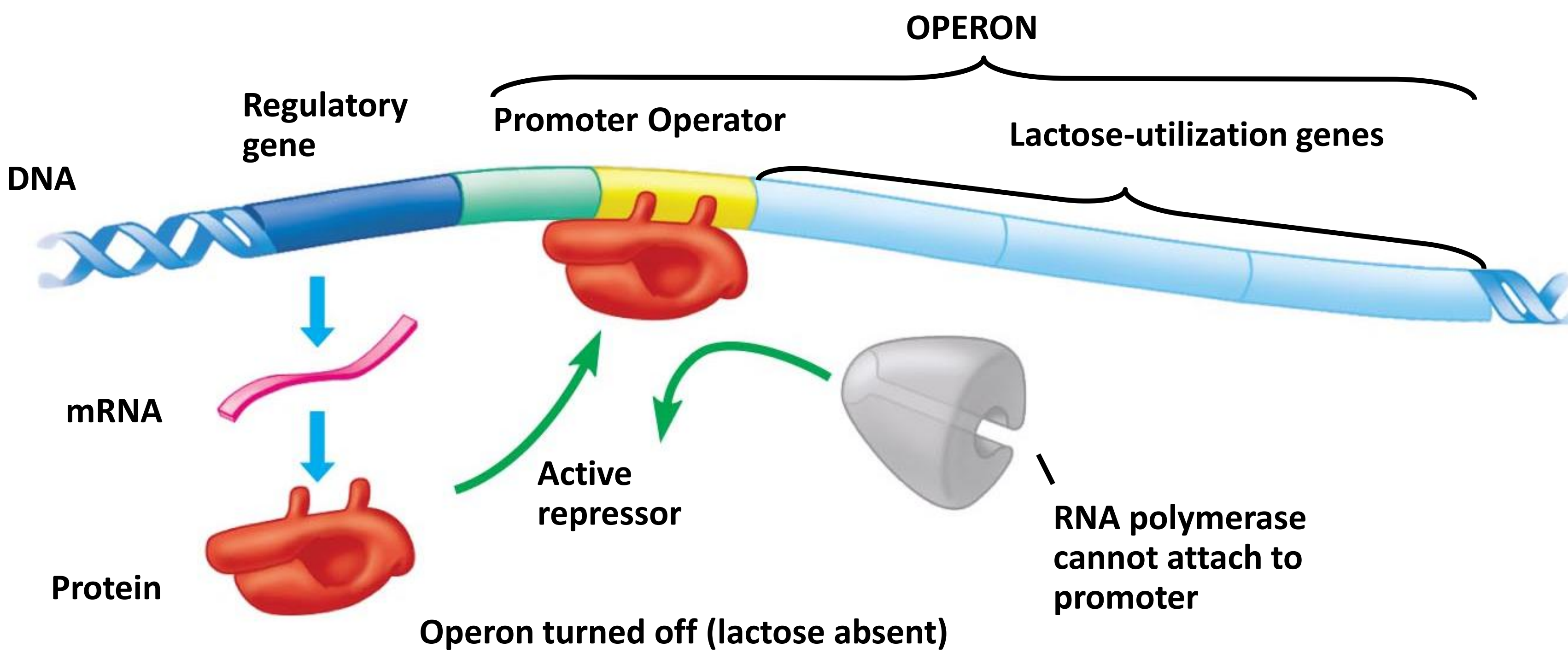
- **As living things, if we are to stay that way, we must respond to our environment.**
- **The environment is what provides the "natural selection" for evolution and is also what dictates cellular needs. If the cell is to survive, it must satisfy those needs.**
- **Gene expression** is protein synthesis. (what we covered last Wednesday in class and what we will review in lab today)
    - Only the instructions that leave the nucleus are translated by the ribosomes into proteins.
    - It is the creation of mRNA the messenger that controls gene expression.
    - Only genes that are "turned on" by the needs of the cell are being transcribed and ultimately translated into proteins.
    - In this way organisms respond to the environment, by controlling gene expression (protein synthesis).

What should I wear?

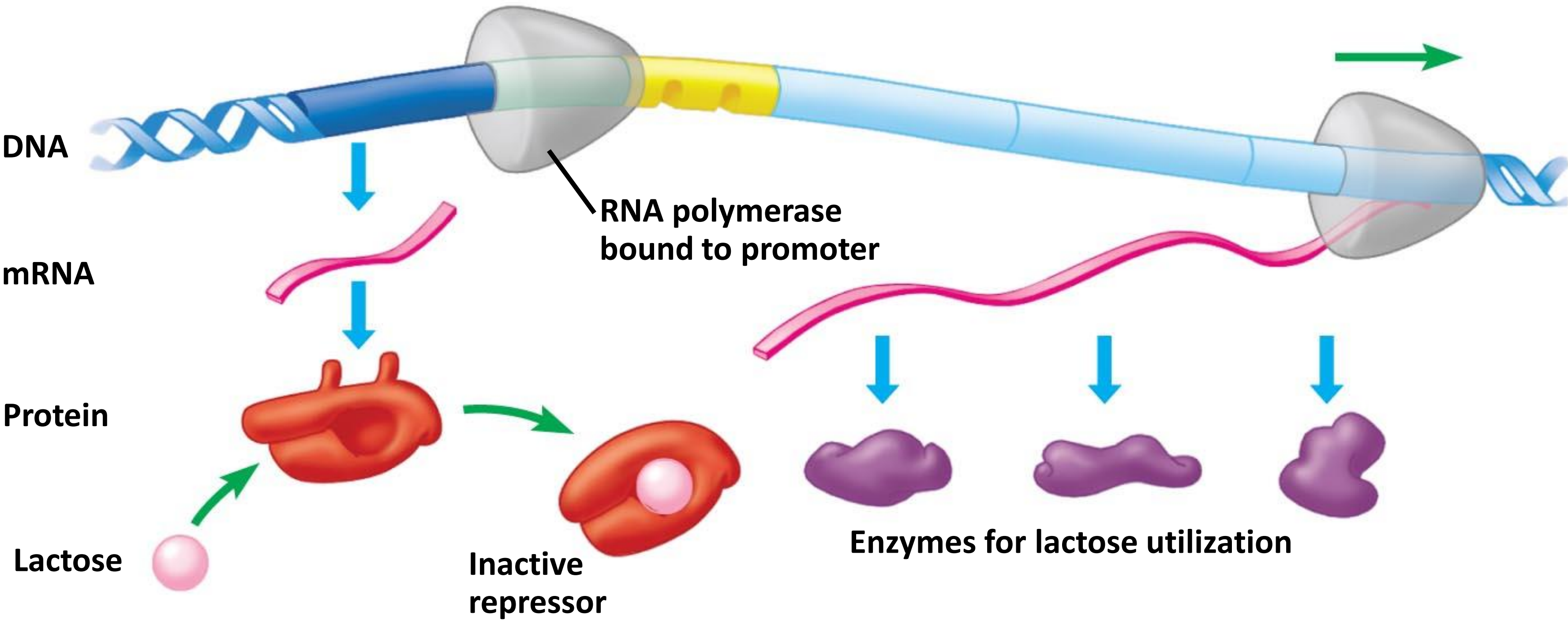
What genes to use and what proteins to make?

- An **operon** is a group of genes under coordinated control in bacteria
- The lactose (*lac*) operon includes
  - Three adjacent genes for lactose-utilization enzymes
  - **Promoter** sequence where RNA polymerase binds
  - Operator sequence is where a **repressor** can bind and block RNA polymerase action

- Regulation of the *lac* operon
  - **Regulatory gene** codes for a repressor protein
  - In the absence of lactose, the repressor binds to the operator and prevents RNA polymerase action

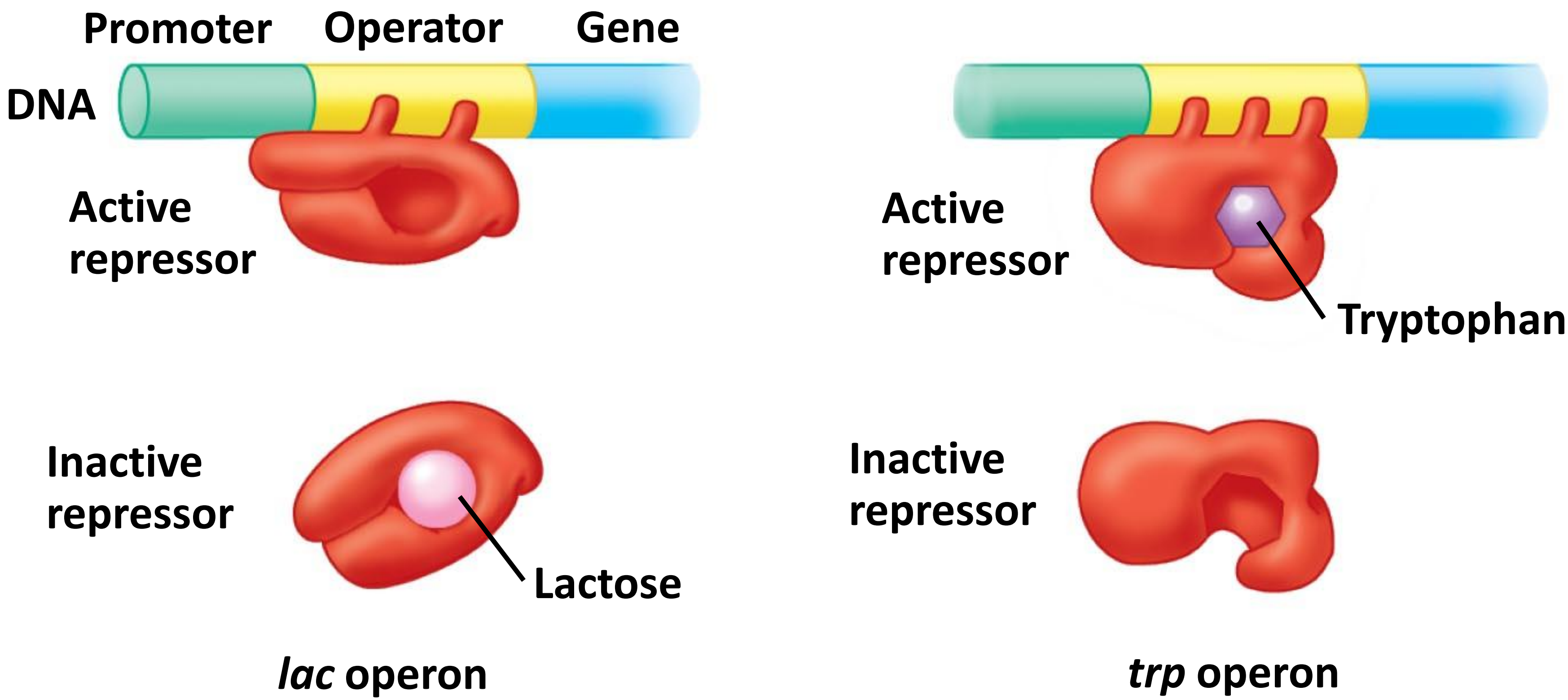


– Lactose inactivates the repressor, so the operator is unblocked



Operon turned on (lactose inactivates repressor)

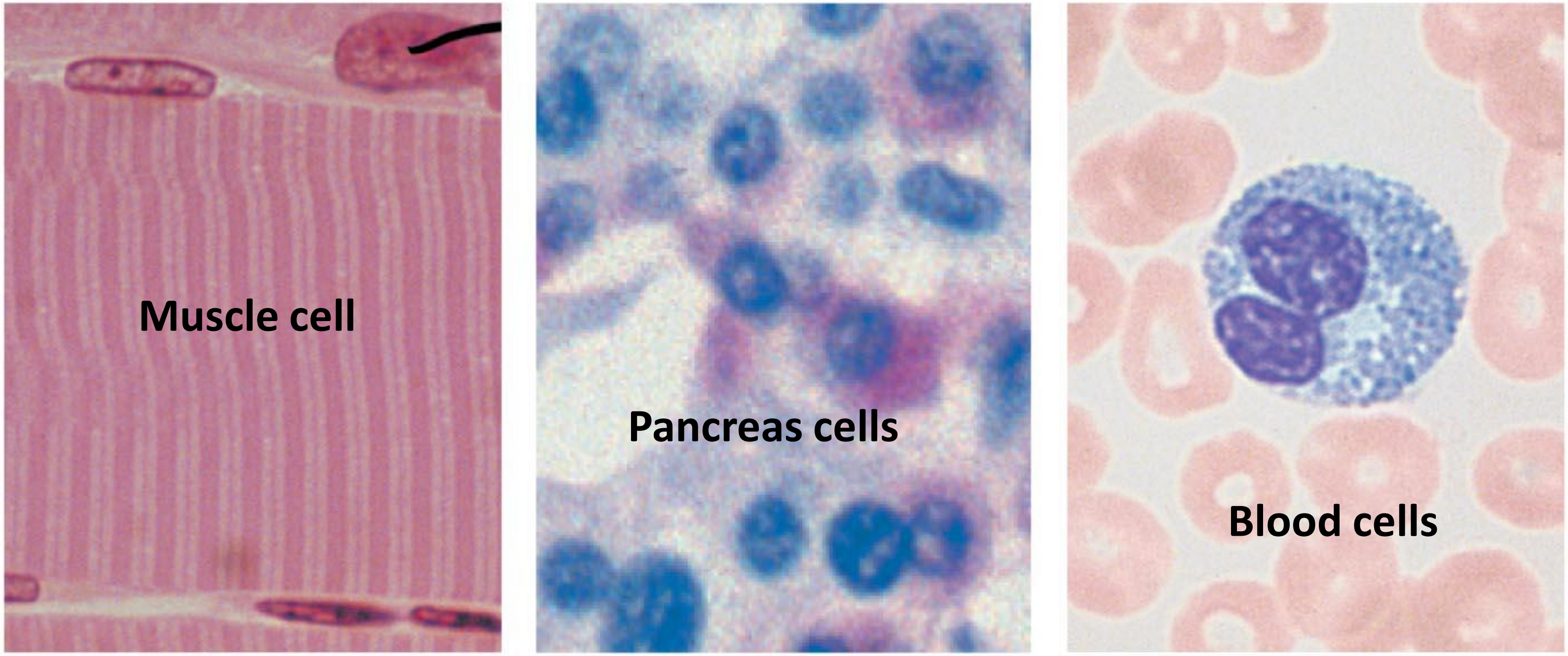
- **Inducible operon (*lac* operon)**
  - Active repressor binds to the operator
  - Inducer (lactose) binds to and inactivates the repressor



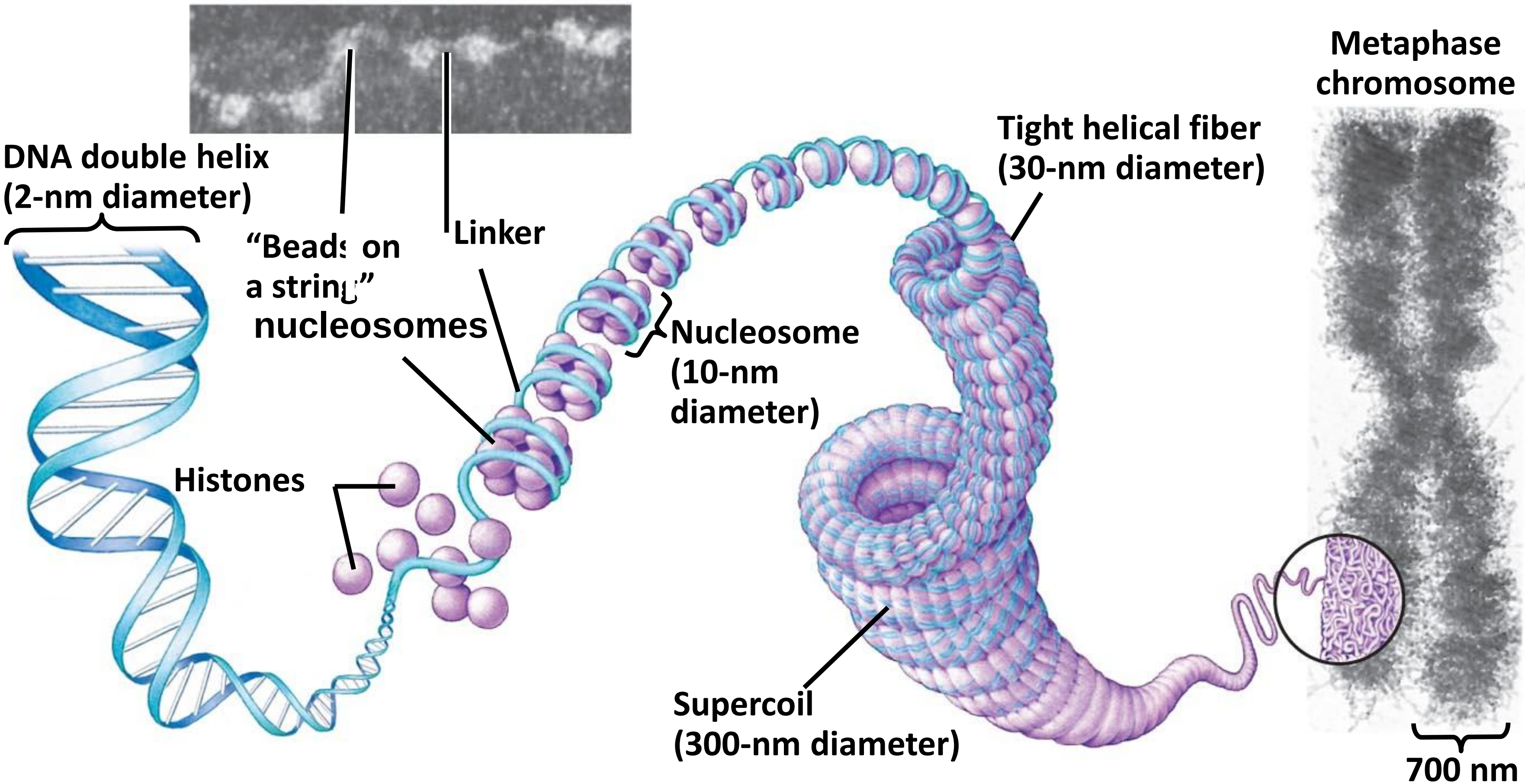
- **Repressible operon (*trp* operon)**
  - Repressor is initially inactive
  - Corepressor (tryptophan) binds to the repressor and makes it active

Different Genes Result in Different Types of Cells

- **Differentiation** involves cell specialization, in both structure and function
- Differentiation is controlled by turning specific sets of genes on or off



DNA packing into chromosomes not only helps protect the information it helps regulate gene expression

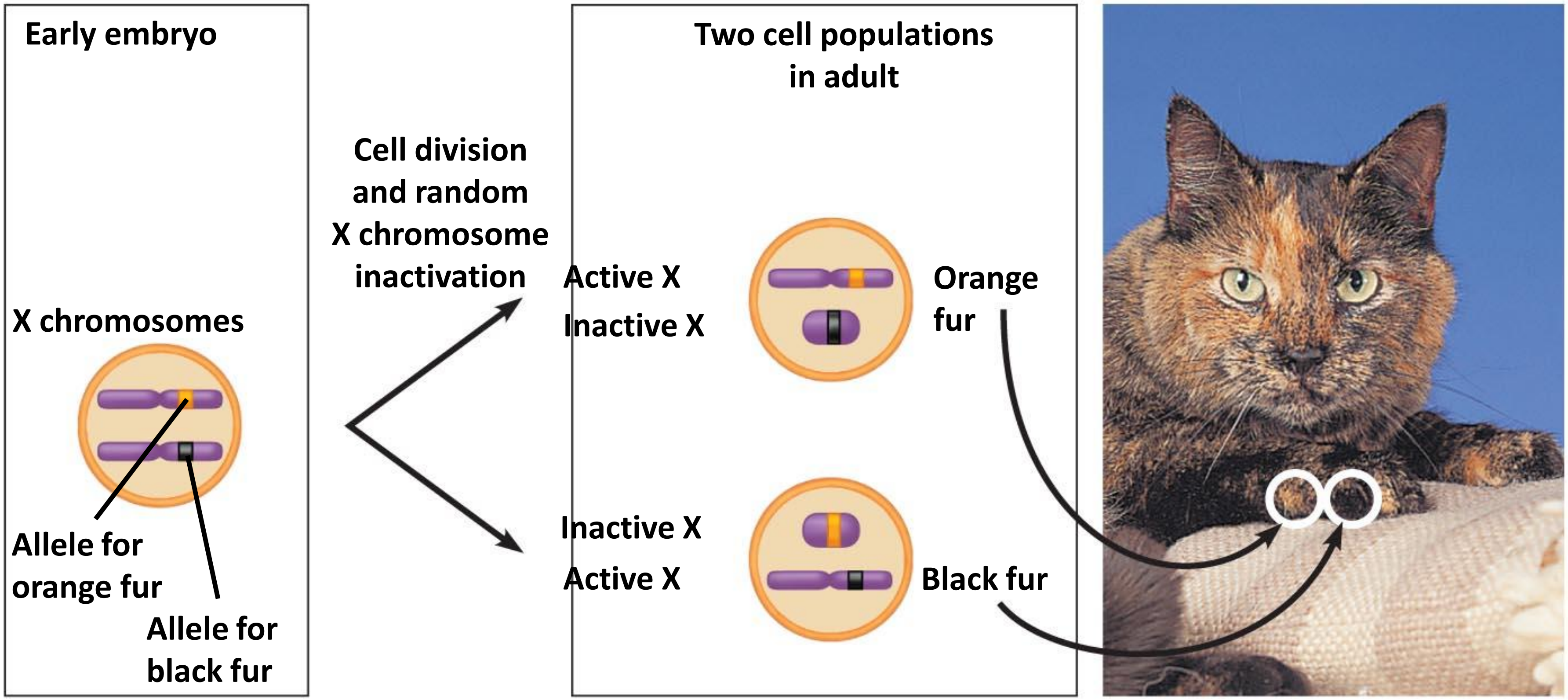


DNA packing can prevent transcription

Because females have two X chromosomes one is inactive in each somatic cell

- **X-chromosome inactivation (Barr body)**
  - Random inactivation of either the maternal or paternal chromosome
  - Occurs early in embryonic development and all cellular descendants have the same inactivated chromosome

Tortoiseshell fur coloration is due to inactivation of X chromosomes in heterozygous female cats

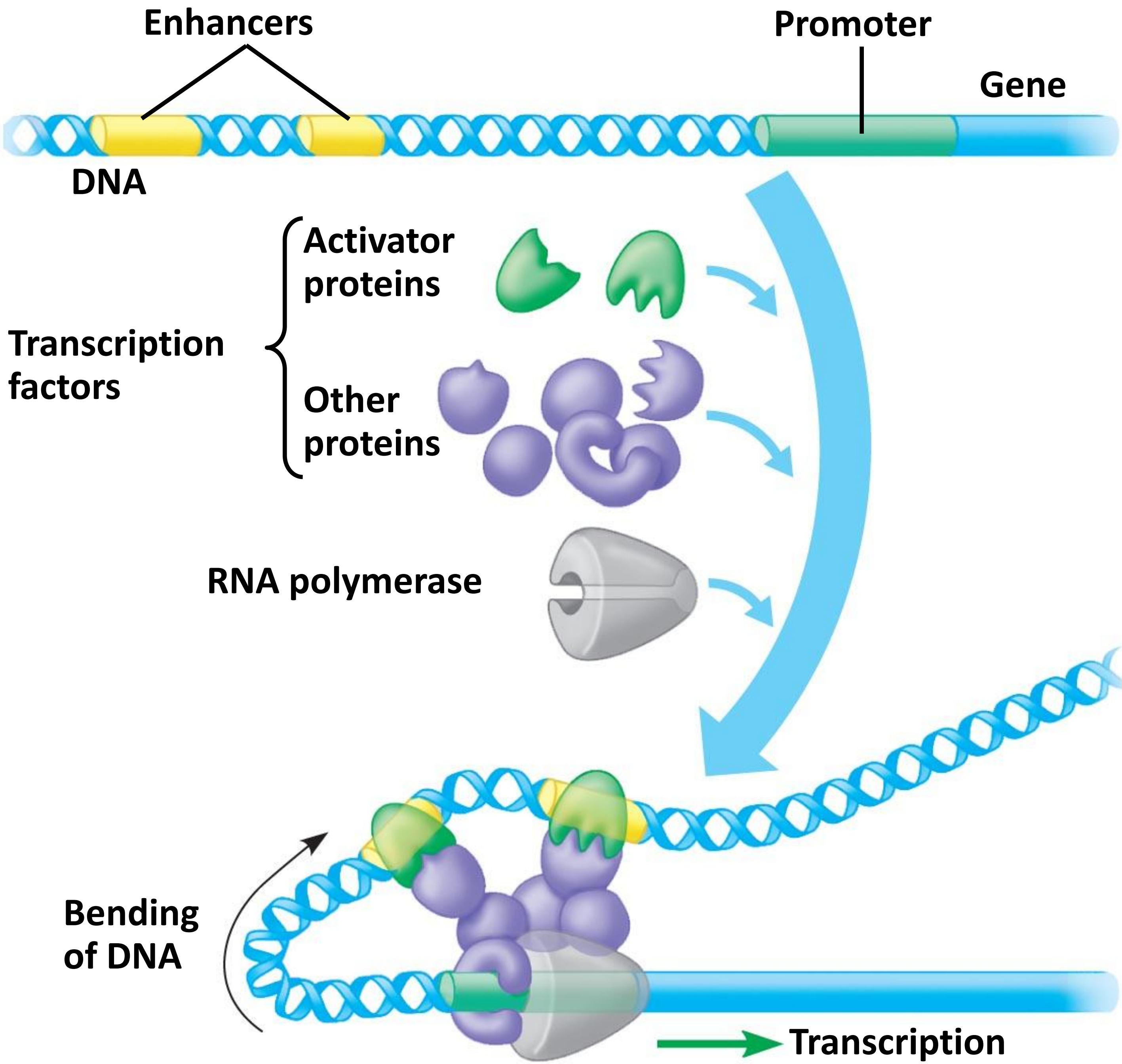


11.5 Complex assemblies of proteins control eukaryotic transcription

– Eukaryotic genes
    – Each gene has its own promoter and terminator
    – Are usually switched off and require activators to be turned on
    – Are controlled by interactions between numerous regulatory proteins and control sequences

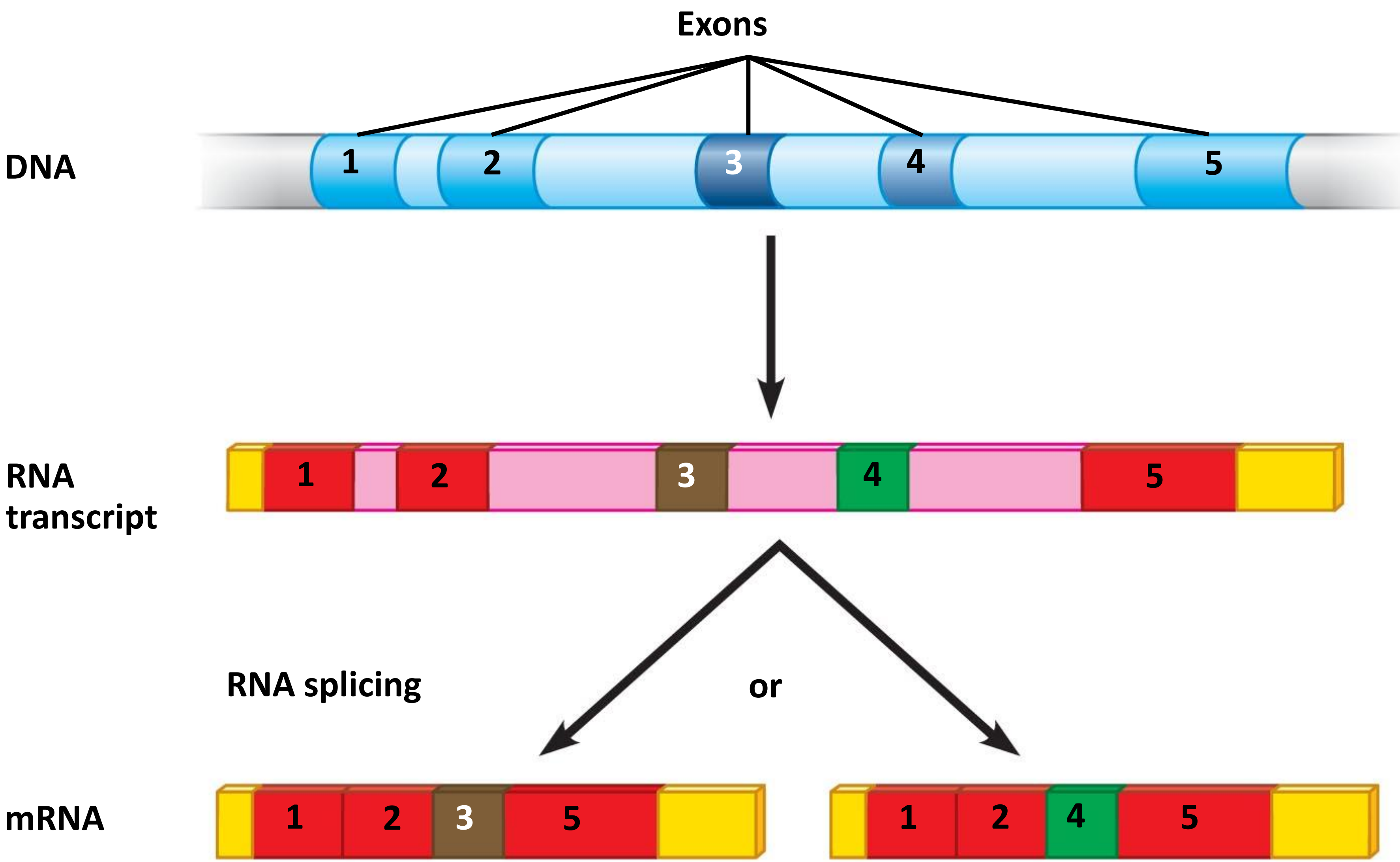
11.5 Complex assemblies of proteins control eukaryotic transcription

- Regulatory proteins that bind to control sequences
  - **Transcription factors** promote RNA polymerase binding to the promoter
  - Activator proteins bind to DNA **enhancers** and interact with other transcription factors
  - **Silencers** are repressors that inhibit transcription
- Control sequences
  - Promoter
  - Enhancer
    - Related genes located on different chromosomes can be controlled by similar enhancer sequences


Enhancers
Promoter
Gene
DNA
Activator proteins
Transcription factors
Other proteins
RNA polymerase
Bending of DNA
Transcription

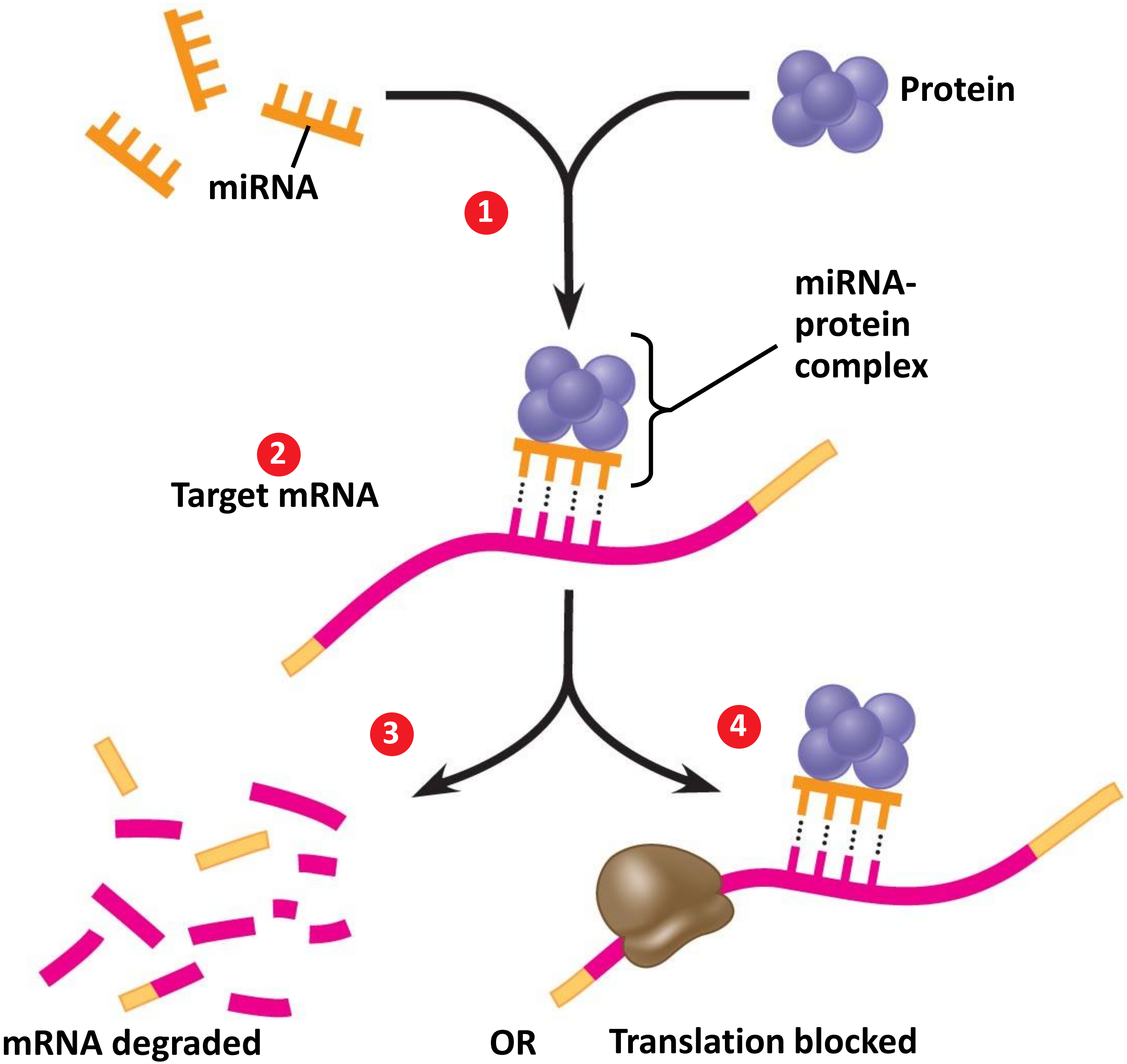
11.6 Eukaryotic RNA may be spliced in more than one way

- **Alternative RNA splicing**
  - Production of different mRNAs from the same transcript
  - Results in production of more than one polypeptide from the same gene
  - Can involve removal of an exon with the introns on either side


Exons
DNA
1
2
3
4
5
RNA transcript
1
2
3
4
5
RNA splicing
or
mRNA
1
2
3
5
1
2
4
5

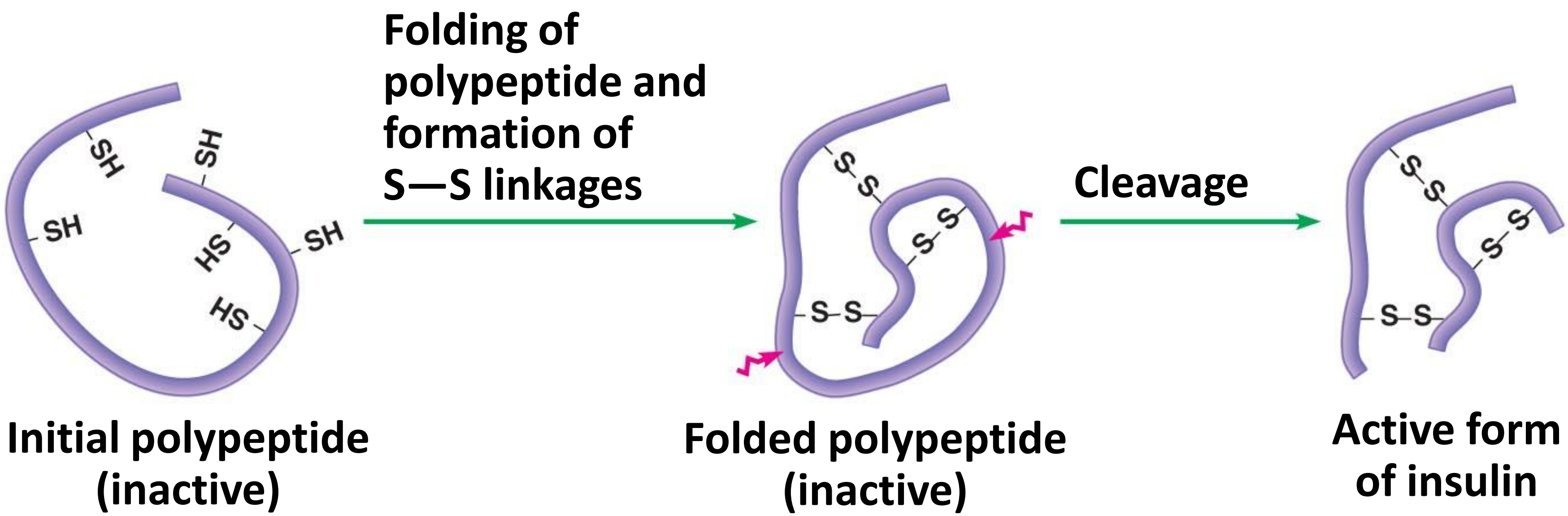
11.7 Small RNAs play multiple roles in controlling gene expression

- **RNA interference** (**RNAi**)
  - Prevents expression of a gene by interfering with translation of its RNA product
  - Involves binding of small, complementary RNAs to mRNA molecules
  - Leads to degradation of mRNA or inhibition of translation
- MicroRNA
  - Single-stranded chain about 20 nucleotides long
  - Binds to protein complex
  - MicroRNA + protein complex binds to complementary mRNA to interfere with protein production


miRNA
Protein
1
miRNA-
protein
complex
2
Target mRNA
3
4
mRNA degraded
OR
Translation blocked

11.8 Translation and later stages of gene expression are also subject to regulation

- Control of gene expression also occurs with
  - Breakdown of mRNA
  - Initiation of translation
  - Protein activation
  - Protein breakdown


Folding of
polypeptide and
formation of
S—S linkages
Cleavage
SH
SH
SH
HS
SH
HS
S-S
S-S
S-S
S-S
S-S
S-S
Initial polypeptide
(inactive)
Folded polypeptide
(inactive)
Active form
of insulin

11.9 Review: Multiple mechanisms regulate gene expression in eukaryotes

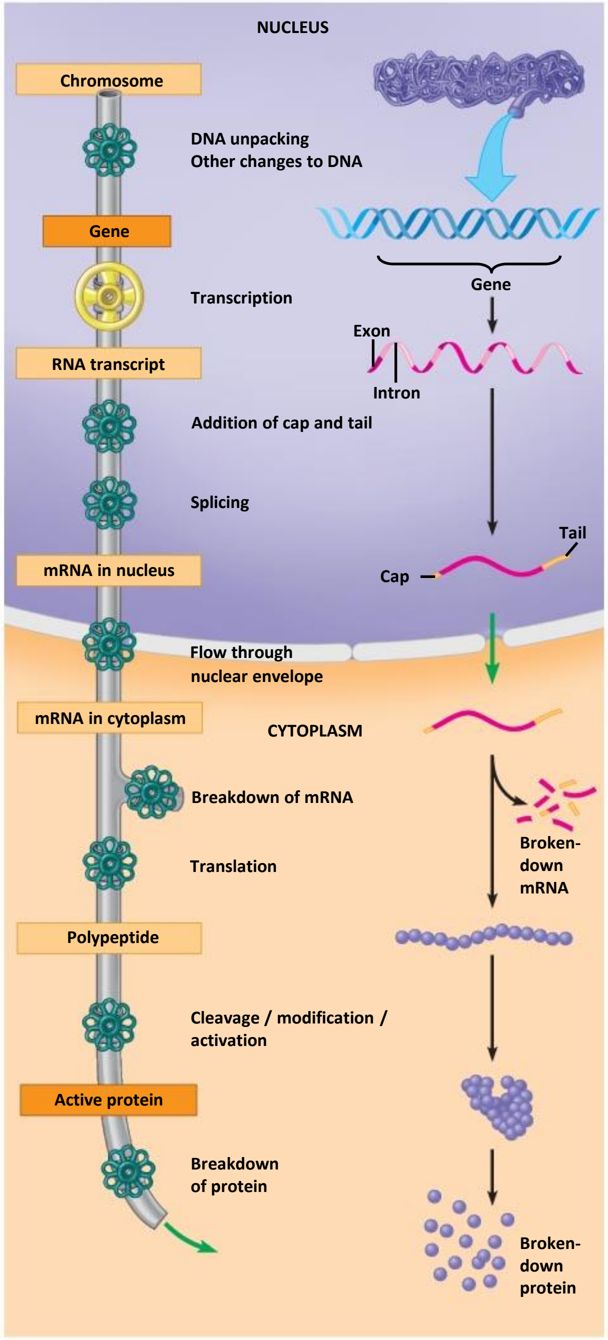
- Many possible control points exist; a given gene may be subject to only a few of these
  - Chromosome changes (1)
    - DNA unpacking
  - Control of transcription (2)
    - Regulatory proteins and control sequences
  - Control of RNA processing
    - Addition of 5’ cap and 3’ poly-A tail (3)
    - Splicing (4)
  - Flow through nuclear envelope (5)

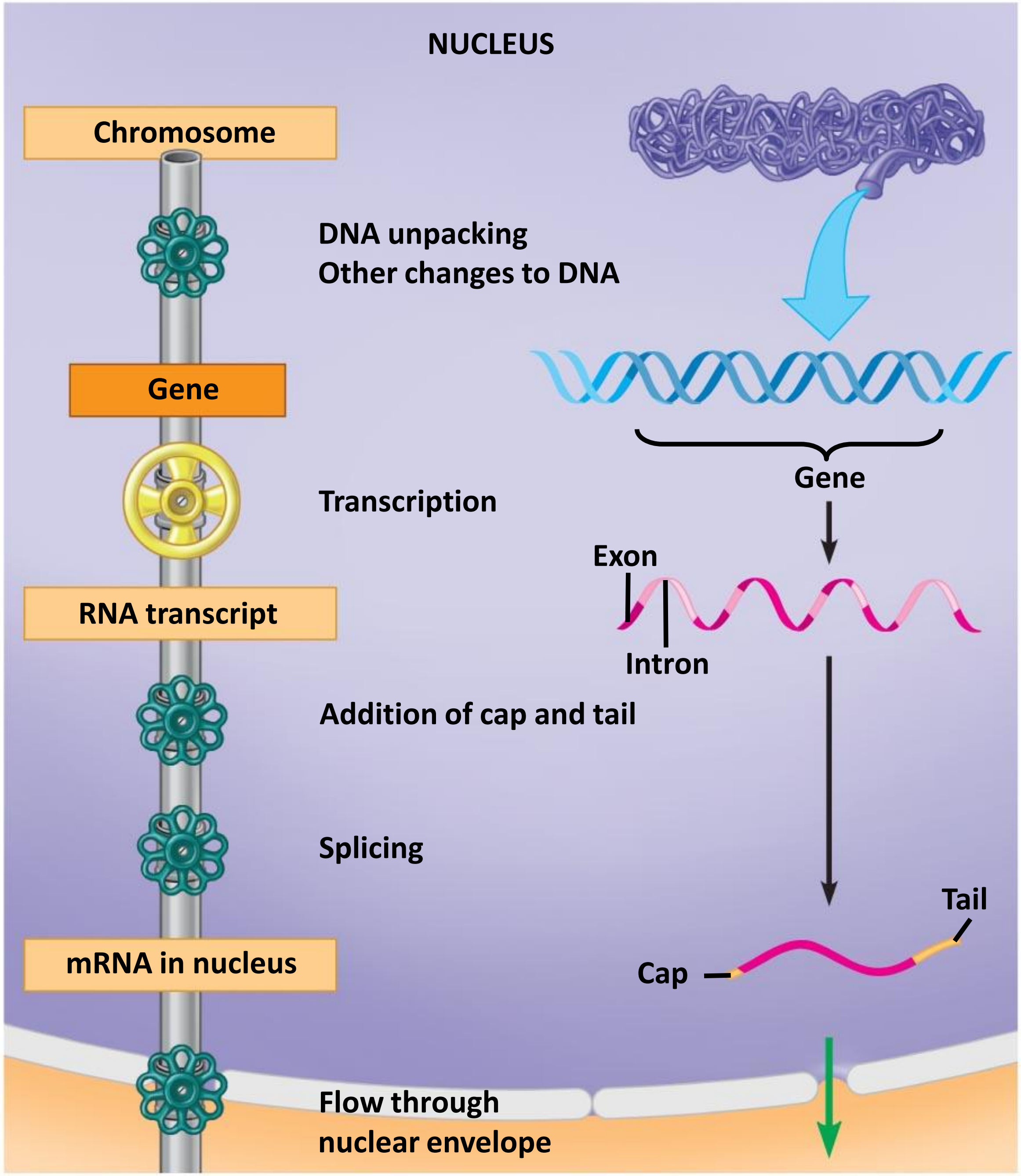
11.9 Review: Multiple mechanisms regulate gene expression in eukaryotes

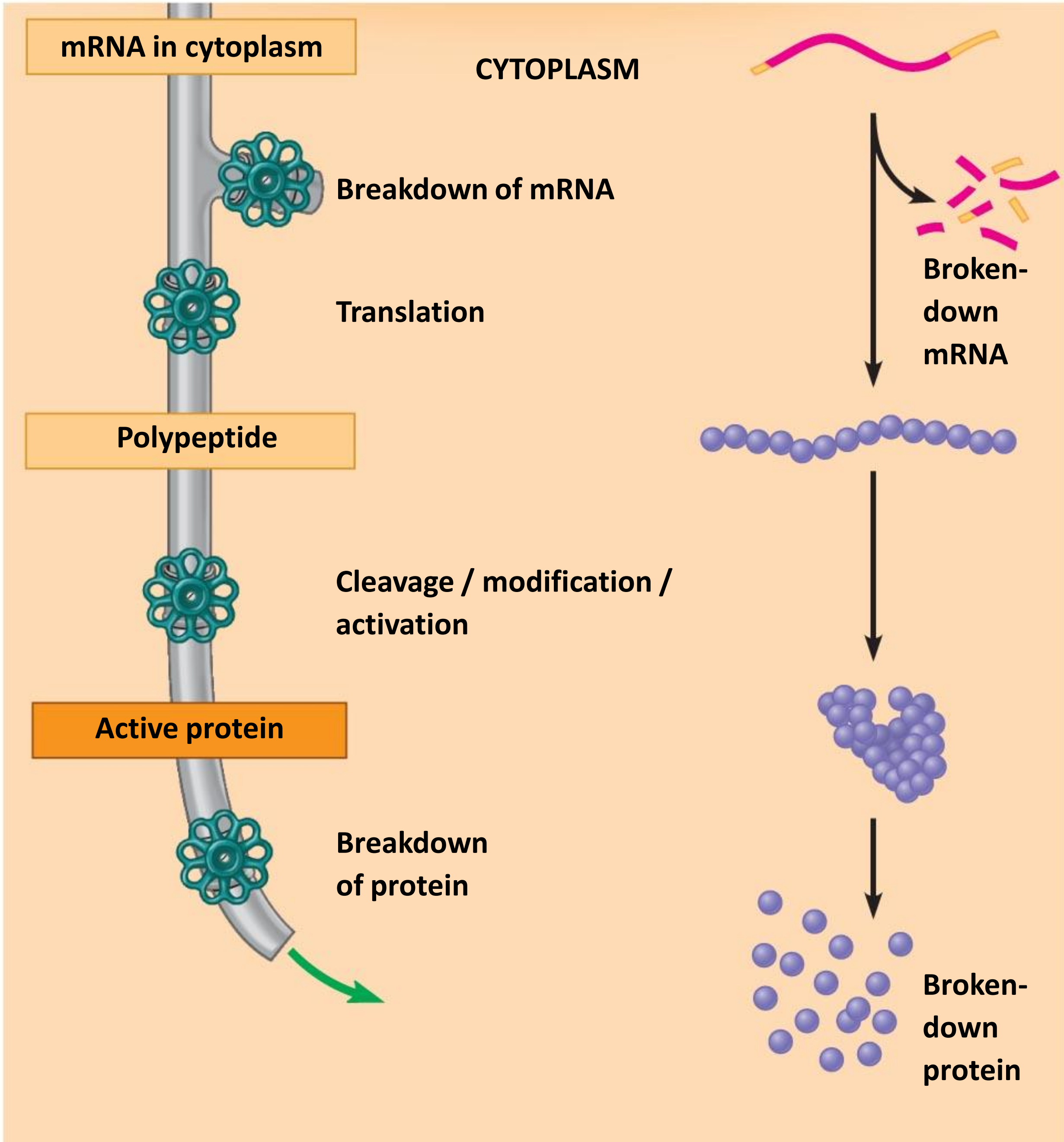
- Many possible control points exist; a given gene may be subject to only a few of these
  - Breakdown of mRNA (6)
  - Control of translation (7)
  - Control after translation
    - Cleavage/modification/activation of proteins (8)
    - Breakdown of protein (9)

11.9 Review: Multiple mechanisms regulate gene expression in eukaryotes

- Applying Your Knowledge
  For each of the following, determine whether an increase or decrease in the amount of gene product is expected
  - The mRNA fails to receive a poly-A tail during processing in the nucleus
  - The mRNA becomes more stable and lasts twice as long in the cell cytoplasm
  - The region of the chromatin containing the gene becomes tightly compacted
  - An enzyme required to cleave and activate the protein product is missing

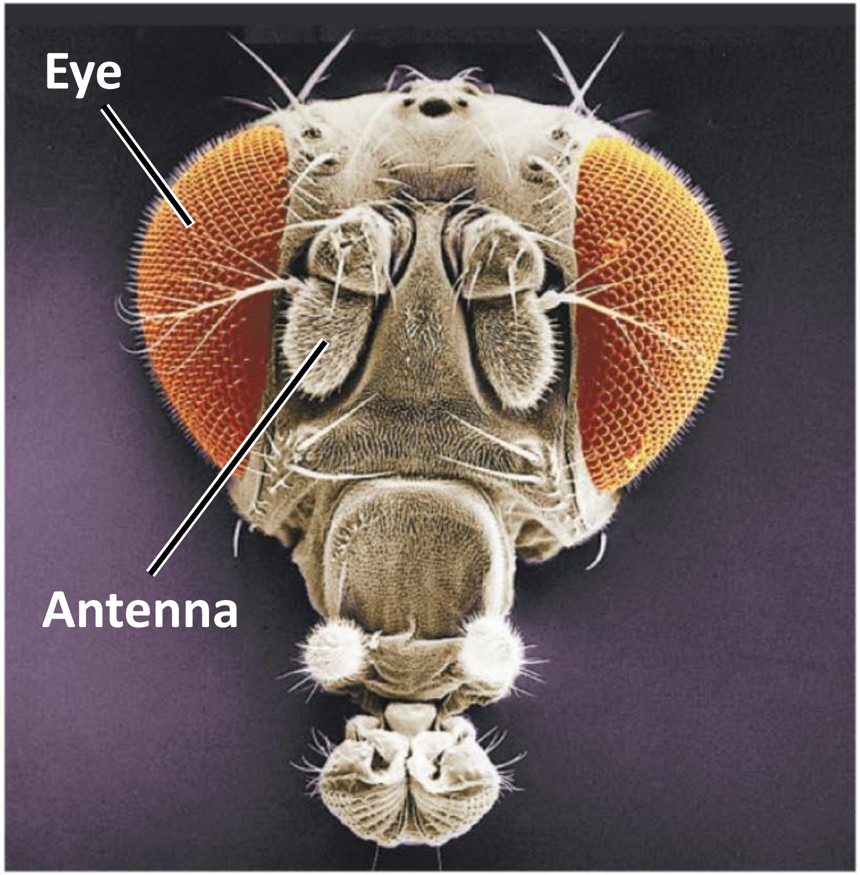

NUCLEUS
Chromosome
DNA unpacking
Other changes to DNA
Gene
Gene
Transcription
Exon
RNA transcript
Intron
Addition of cap and tail
Splicing
Tail
mRNA in nucleus
Cap
Flow through
nuclear envelope
mRNA in cytoplasm
CYTOPLASM
Breakdown of mRNA
Broken-
down
mRNA
Translation
Polypeptide
Cleavage / modification /
activation
Active protein
Breakdown
of protein
Broken-
down
protein


NUCLEUS
Chromosome
DNA unpacking
Other changes to DNA
Gene
Gene
Transcription
Exon
RNA transcript
Intron
Addition of cap and tail
Splicing
Tail
mRNA in nucleus
Cap
Flow through
nuclear envelope


mRNA in cytoplasm
CYTOPLASM
Breakdown of mRNA
Broken-
down
mRNA
Translation
Polypeptide
Cleavage / modification /
activation
Active protein
Breakdown
of protein
Broken-
down
protein

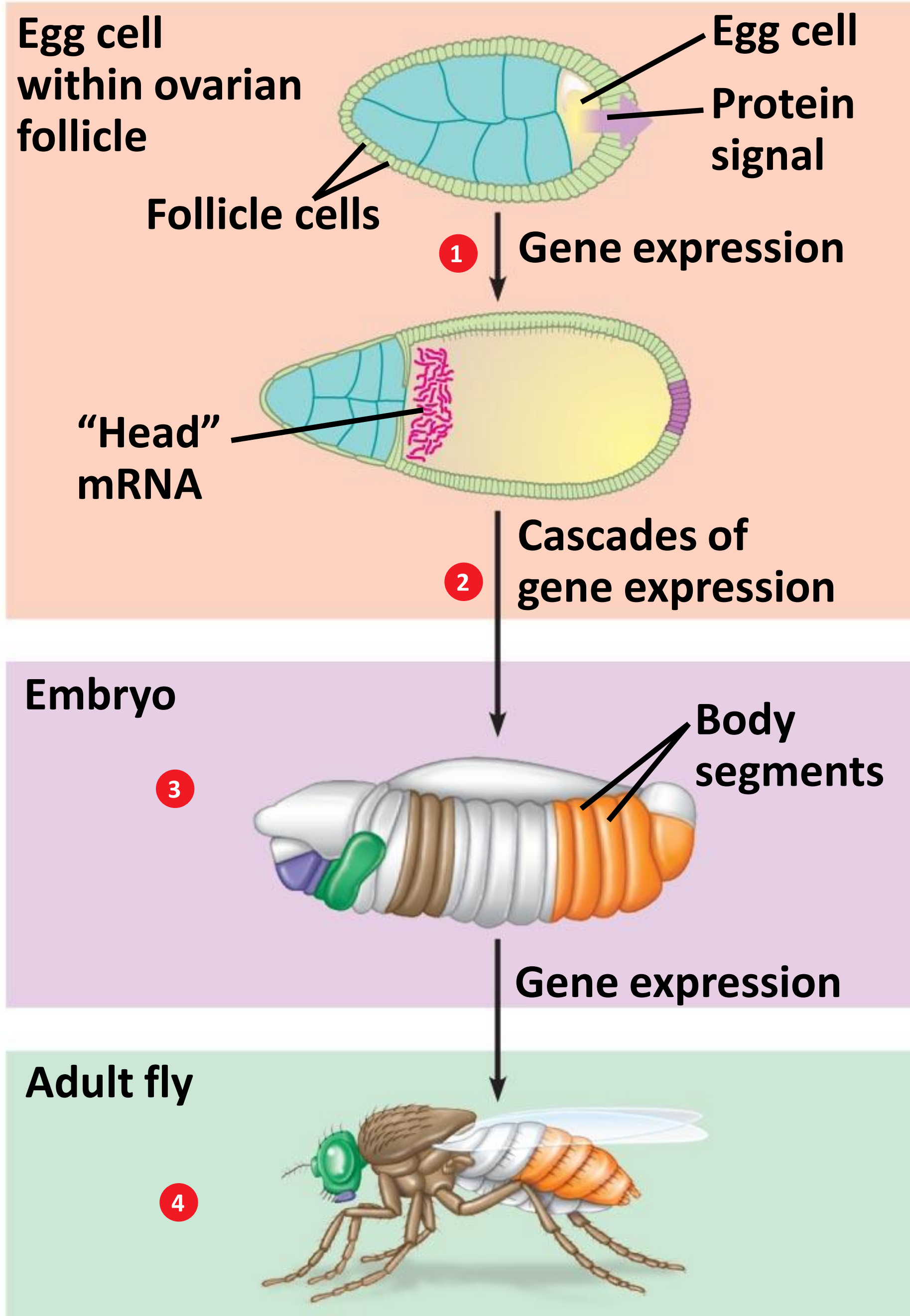
11.10 Cascades of gene expression direct the development of an animal

- Role of gene expression in fruit fly development
  - Orientation from head to tail
    - Maternal mRNAs present in the egg are translated and influence formation of head to tail axis
  - Segmentation of the body
    - Protein products from one set of genes activate other sets of genes to divide the body into segments
  - Production of adult features
    - **Homeotic genes** are master control genes that determine the anatomy of the body, specifying structures that will develop in each segment



Head of a normal fruit fly

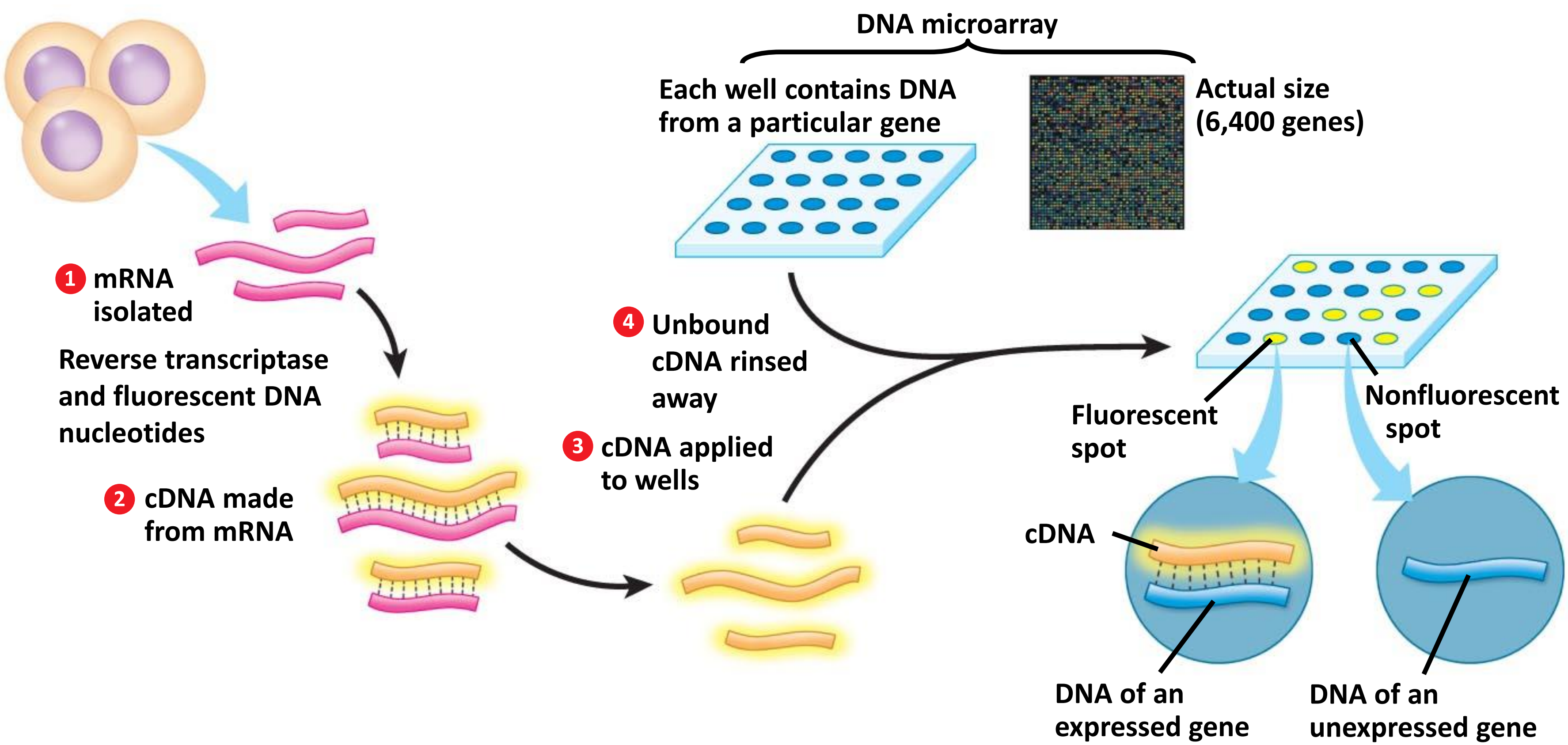
Head of a developmental mutant



Egg cell within ovarian follicle
Egg cell
Protein signal
Follicle cells
1
Gene expression
"Head" mRNA
2
Cascades of gene expression
Embryo
3
Body segments
Gene expression
Adult fly
4

11.11 CONNECTION: DNA microarrays test for the transcription of many genes at once

- **DNA microarray**
  - Contains DNA sequences arranged on a grid
  - Used to test for transcription
    - mRNA from a specific cell type is isolated
    - Fluorescent cDNA is produced from the mRNA
    - cDNA is applied to the microarray
    - Unbound cDNA is washed off
    - Complementary cDNA is detected by fluorescence



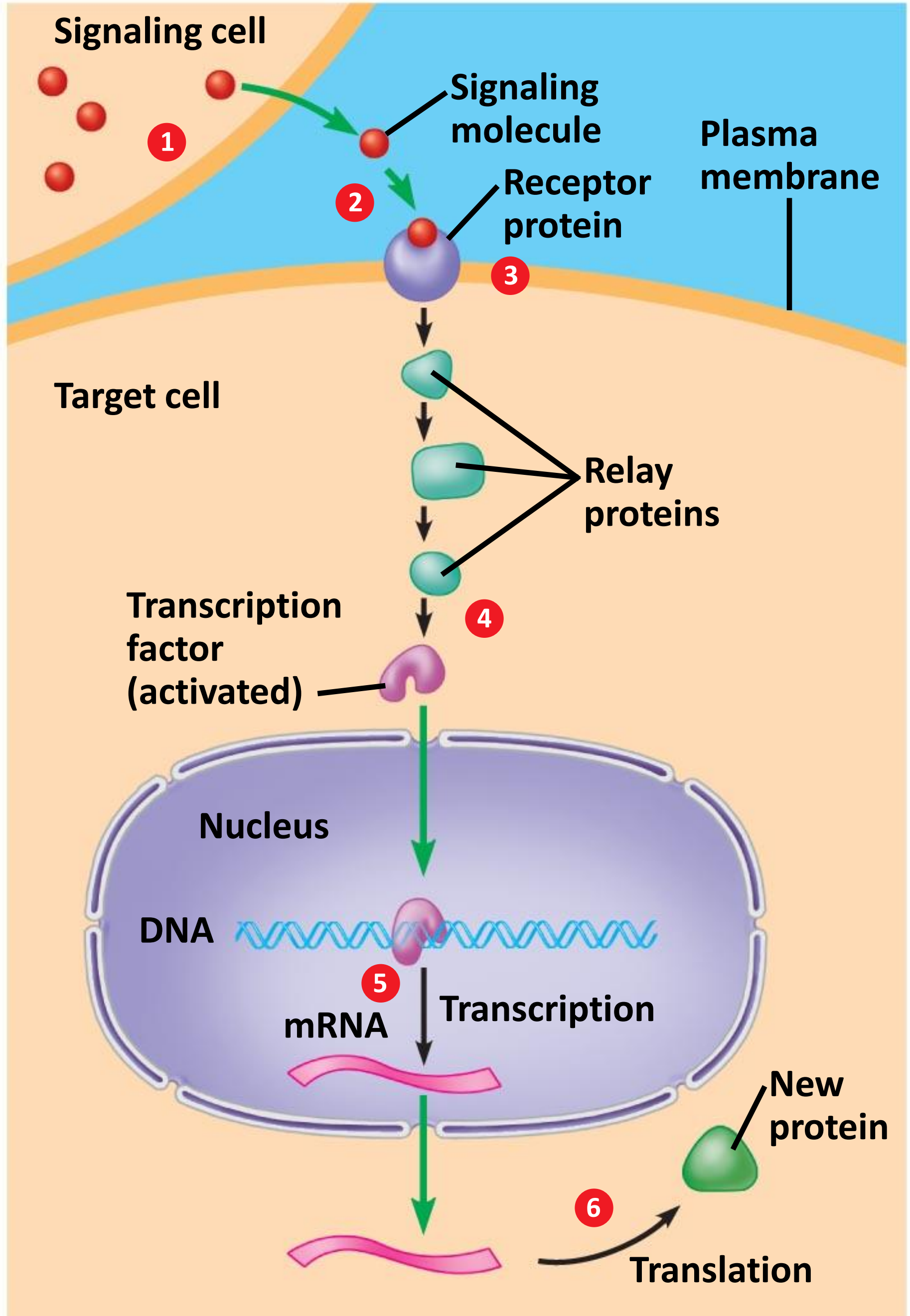
DNA microarray
Each well contains DNA from a particular gene
Actual size (6,400 genes)
1 mRNA isolated
Reverse transcriptase and fluorescent DNA nucleotides
2 cDNA made from mRNA
3 cDNA applied to wells
4 Unbound cDNA rinsed away
Fluorescent spot
Nonfluorescent spot
cDNA
DNA of an expressed gene
DNA of an unexpressed gene

11.12 Signal transduction pathways convert messages received at the cell surface to responses within the cell

- **Signal transduction pathway** is a series of molecular changes that converts a signal at the cell's surface to a response within the cell
  - Signal molecule is released by a signaling cell
  - Signal molecule binds to a receptor on the surface of a target cell

11.12 Signal transduction pathways convert messages received at the cell surface to responses within the cell

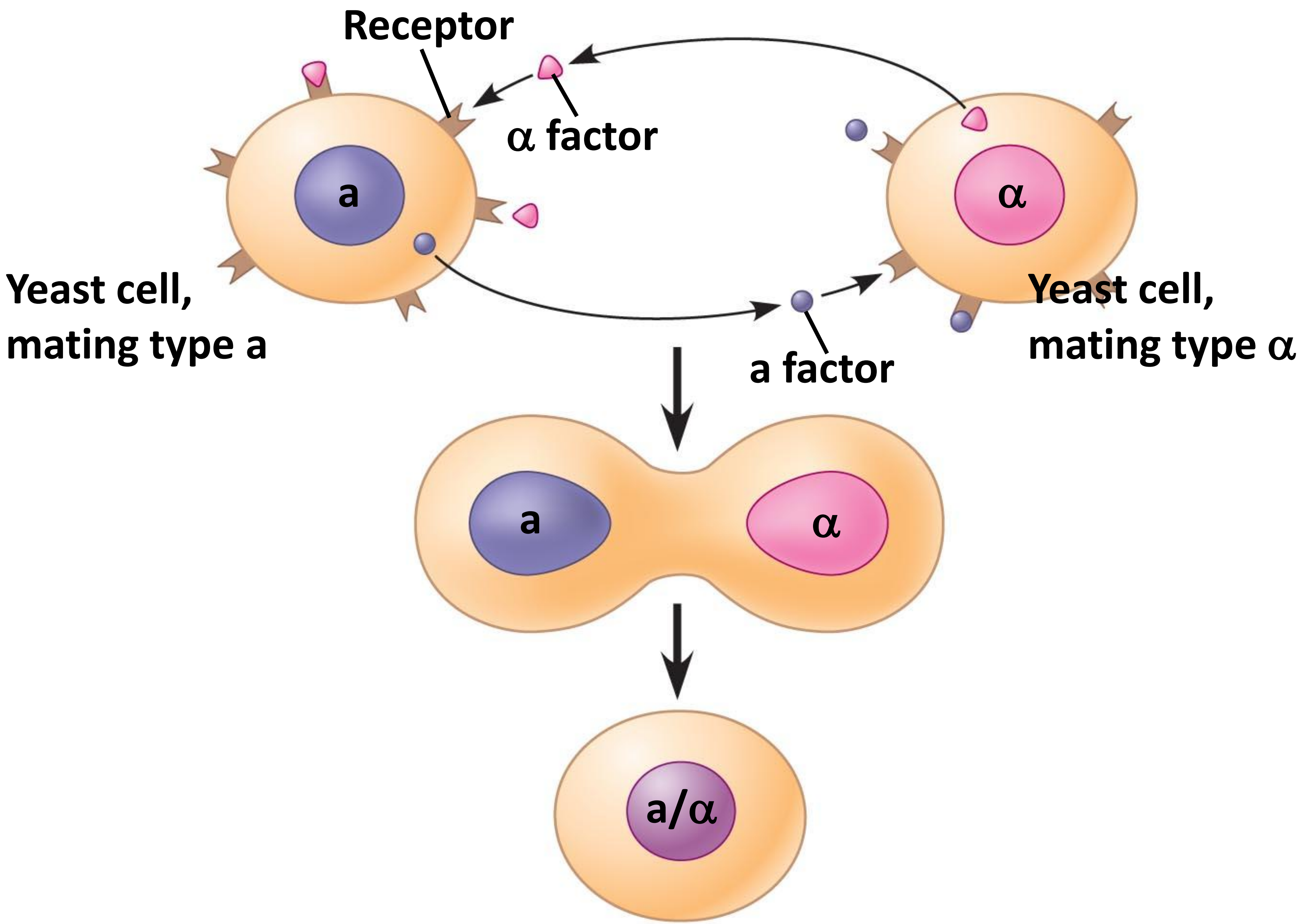
- Relay proteins are activated in a series of reactions
- A transcription factor is activated and enters the nucleus
- Specific genes are transcribed to initiate a cellular response



Signaling cell
1
Signaling molecule
2
Receptor protein
3
Plasma membrane
Target cell
Relay proteins
4
Transcription factor (activated)
Nucleus
DNA
5
Transcription
mRNA
New protein
6
Translation

11.13 EVOLUTION CONNECTION: Cell-signaling systems appeared early in the evolution of life

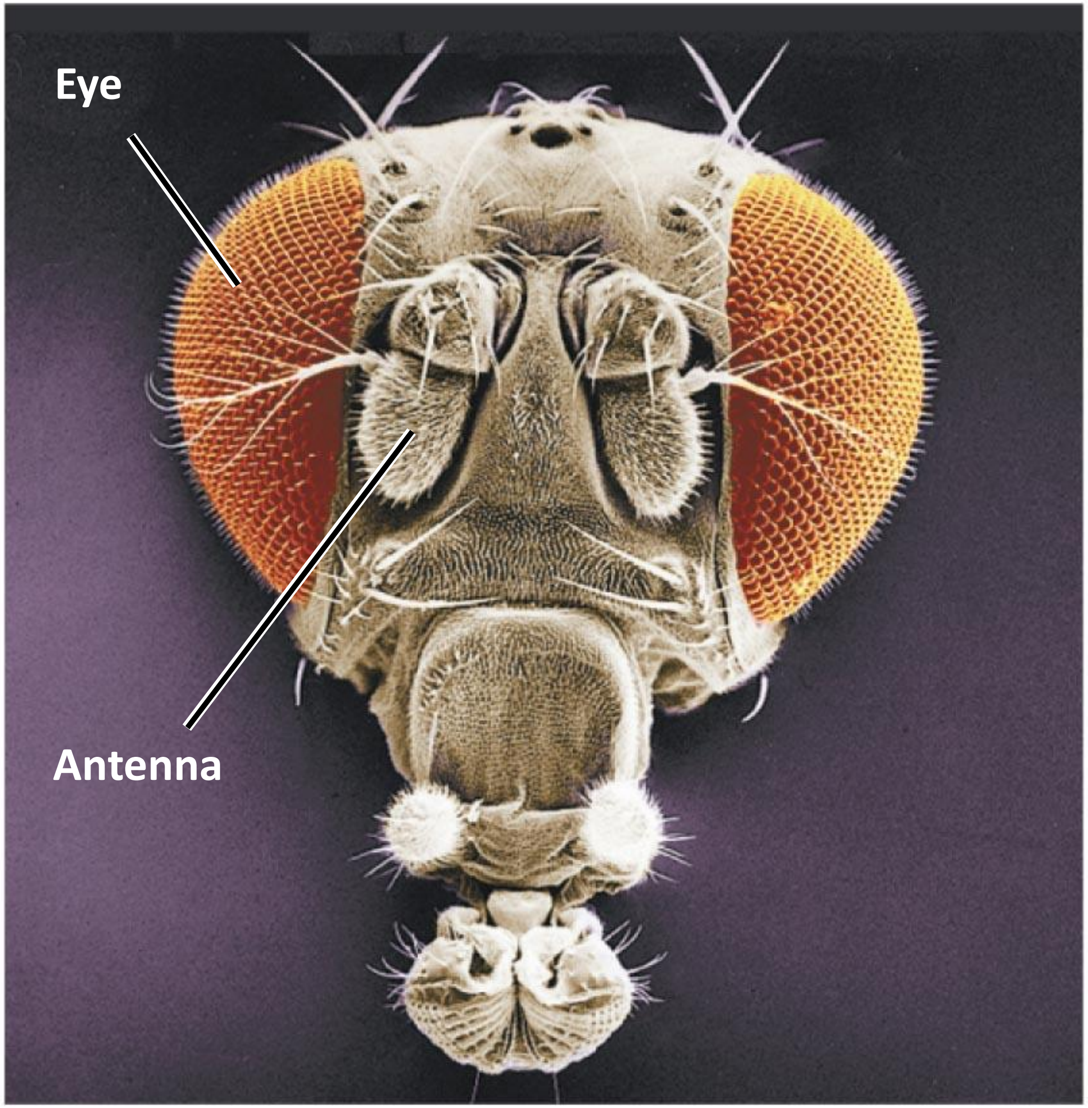
- Yeast mating is controlled by a signal transduction pathway
  - Yeast have two mating types: **a** and α
  - Each produces a chemical factor that binds to receptors on cells of the opposite mating type
  - Binding to receptors triggers growth toward the other cell and fusion
- Cell signaling processes in multicellular organisms are adaptations of those in unicellular organisms such as bacteria and yeast



Receptor
α factor
a
α
Yeast cell,
mating type a
a factor
Yeast cell,
mating type α
a
α
a/α

Introduction: *Cloning to the Rescue?*

- Cloning has been attempted to save endangered species
  - A clone is produced by asexual reproduction and is genetically identical to its parent
  - Dolly the sheep was the first cloned mammal
  - Endangered animals that were cloned include cows, oxen, sheep, wildcats, and wolves
- Disadvantages of cloning
  - Does not increase genetic diversity
  - Cloned animals may have health problems related to abnormal gene regulation



Head of a normal fruit fly

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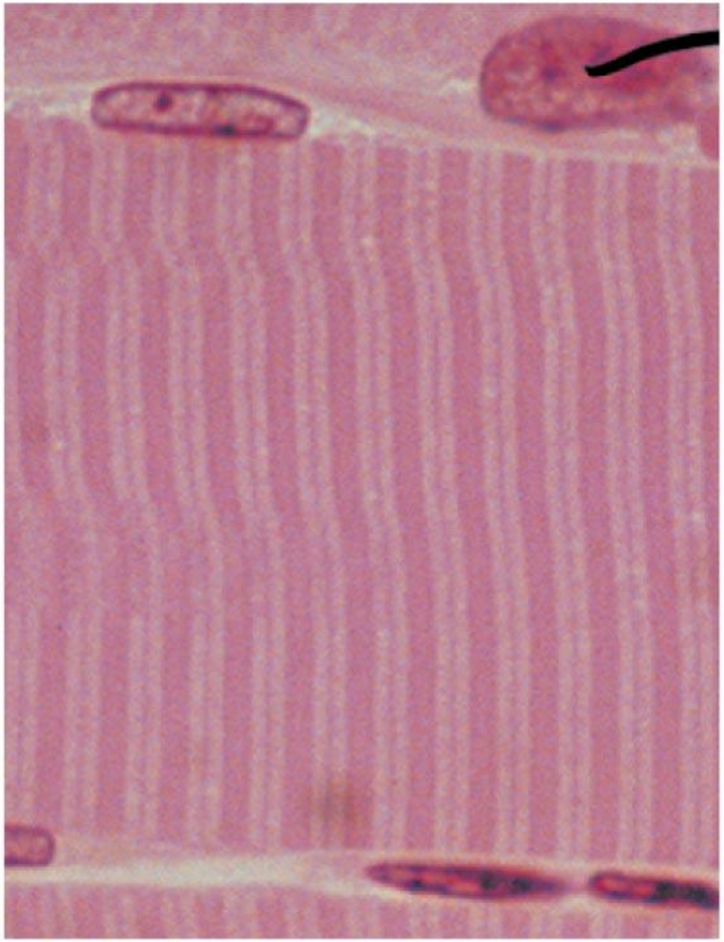
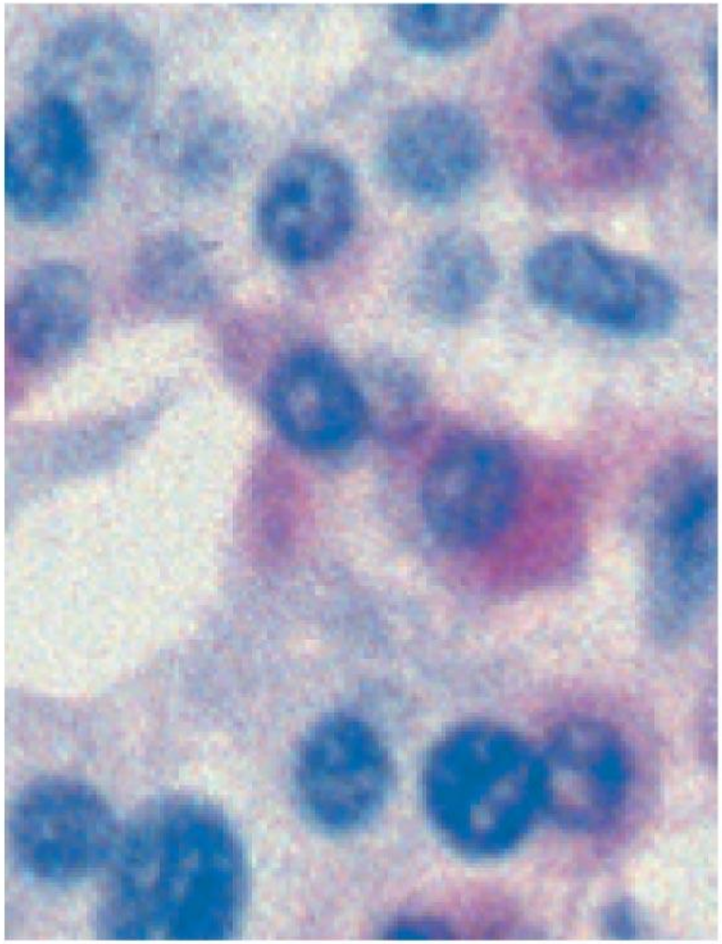
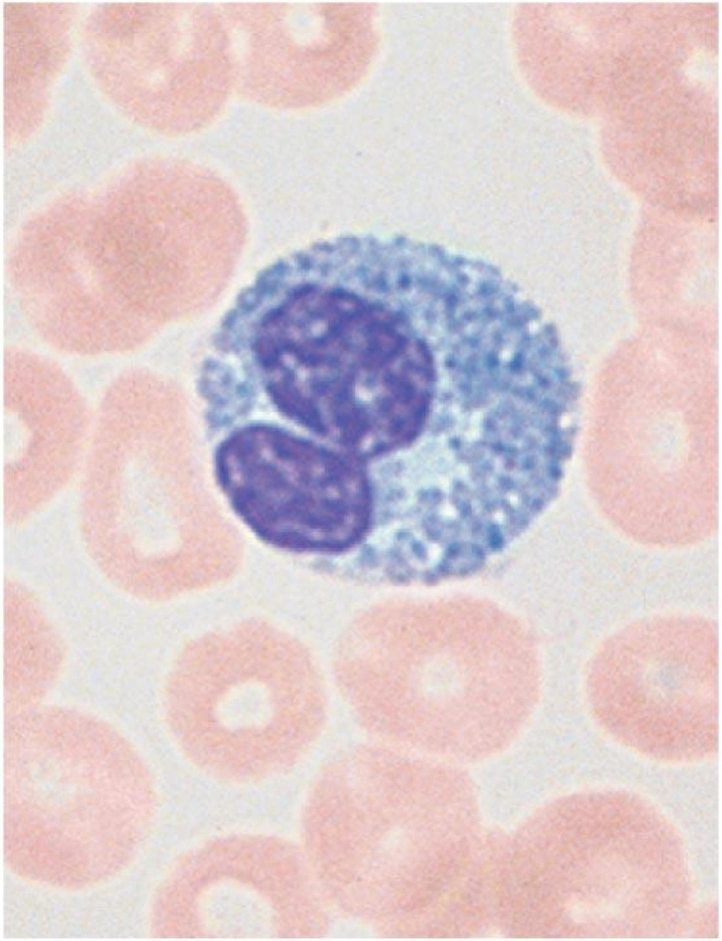


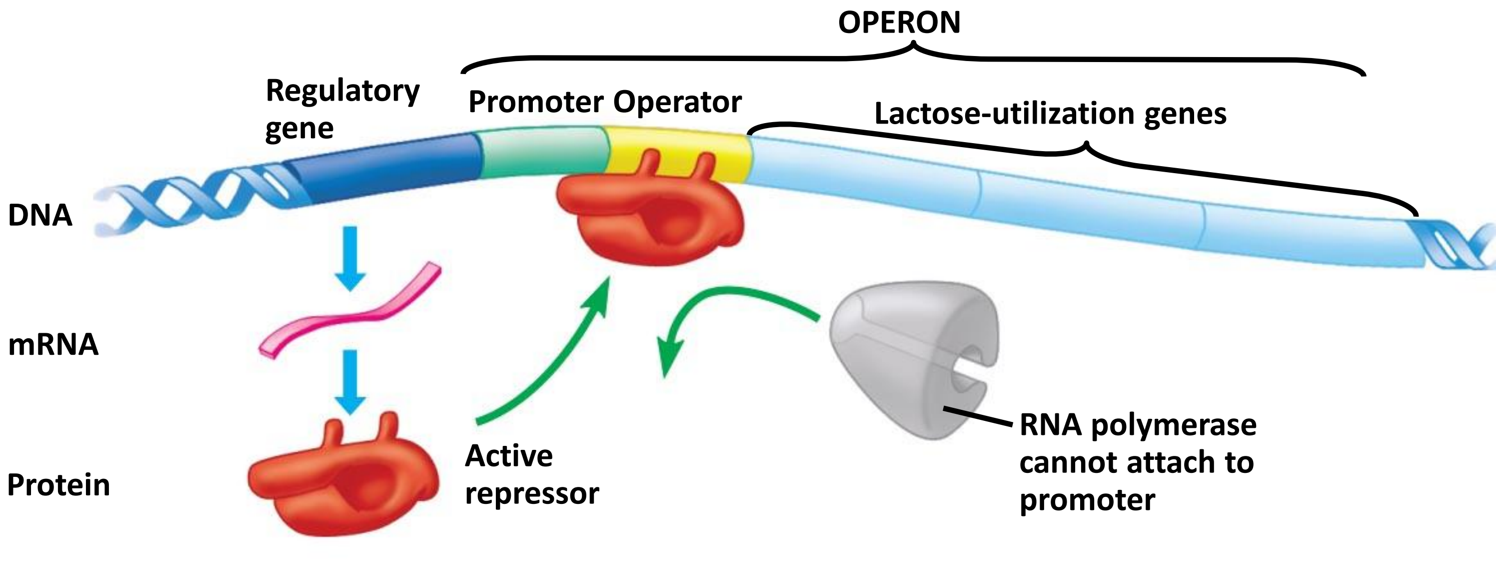
Muscle cell



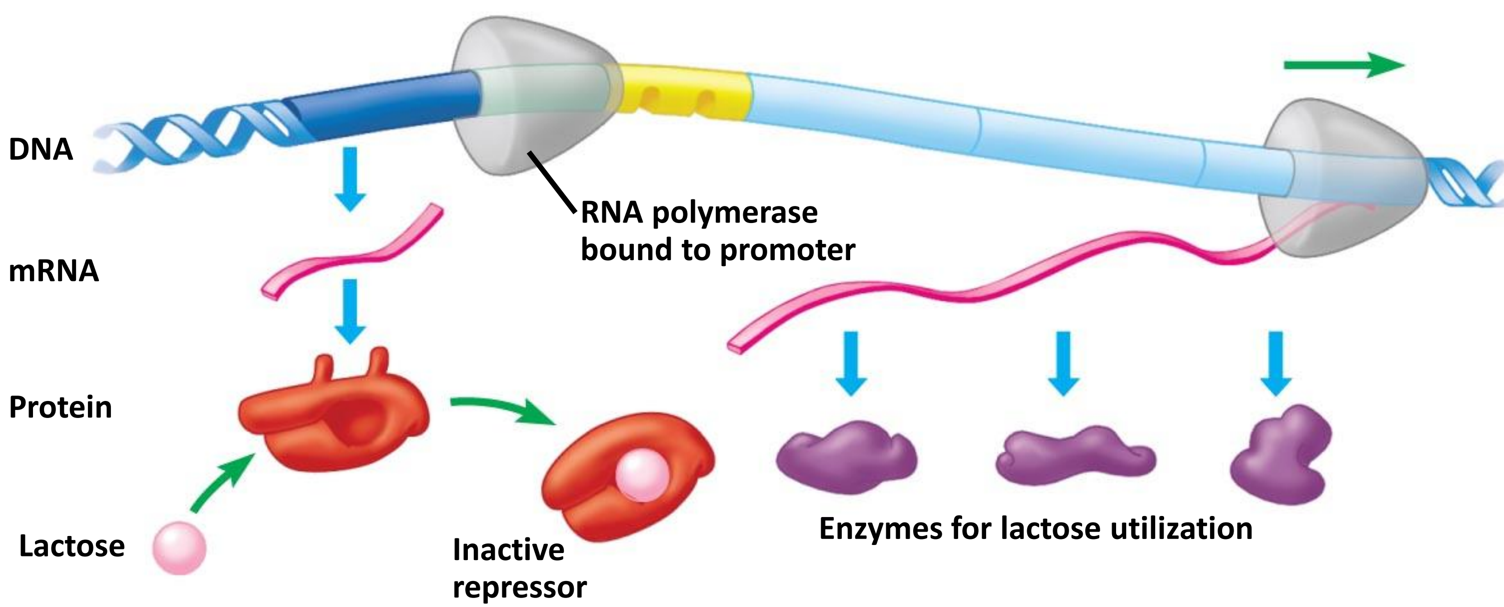
Pancreas cells



Blood cells



Operon turned off (lactose absent)



Operon turned on (lactose inactivates repressor)