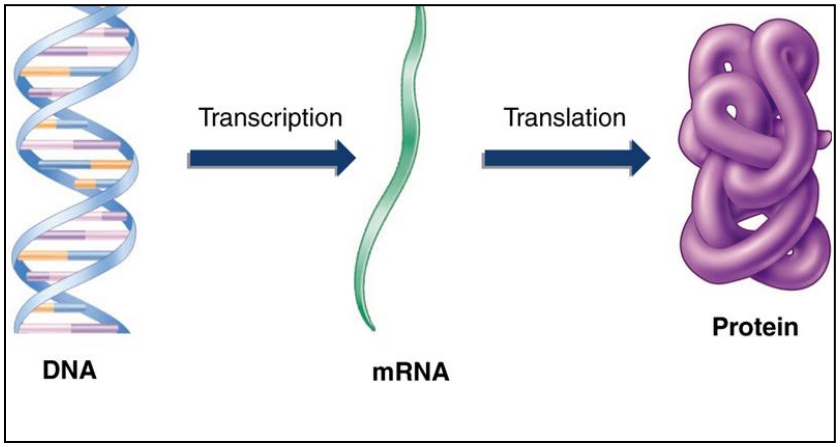
How genes are controlled?

Background:
the central dogma of molecular biology

Gene expression to form a specific polypeptide (protein) occurs in two steps:

1. ***Transcription***: **copies** information from a DNA sequence (a gene) to a complementary RNA sequence

2. ***Translation***: **converts RNA** sequence to amino acid sequence of a polypeptide



Video content: https://youtu.be/FZHs-TZtWKQ?si=YQwdaZ7lm299-vTE

What is gene expression?

The process by which the genetic information passes

from gene to protein

- **Activated gene**: an **mRNA** which will be subsequently **translate into a protein**

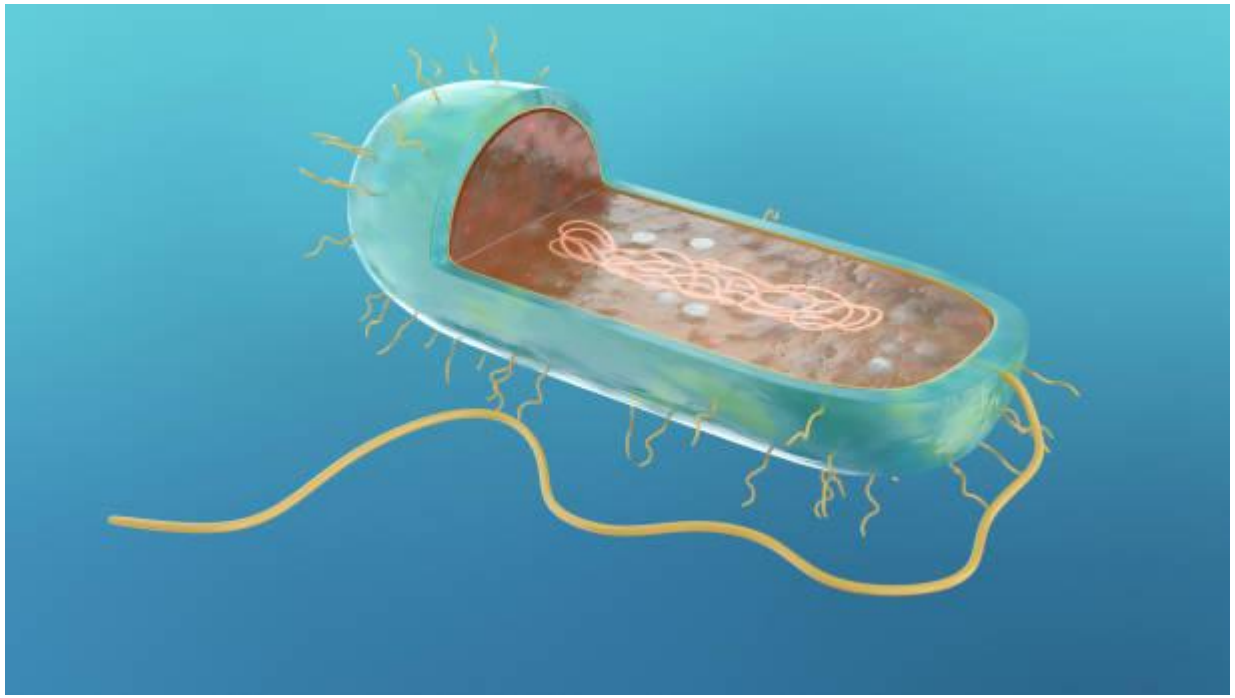
What are the main characteristics?

- is **highly regulated**;
- **may be modified** to counteract environmental changes/to alter function in cells.

Genes:

- are subjected to **positive** and **negative** regulation;
- may be always expressed **(constitutive genes)** or at certain times/in certain cells **(inducible genes).**

Gene expression in prokaryotes



The *Operon*: fine control of prokaryotic transcription

Operon: the unit of transcriptional regulation in prokaryotes

A **single transcriptional unit** is composed by **several genes** which may be inducible or repressible.

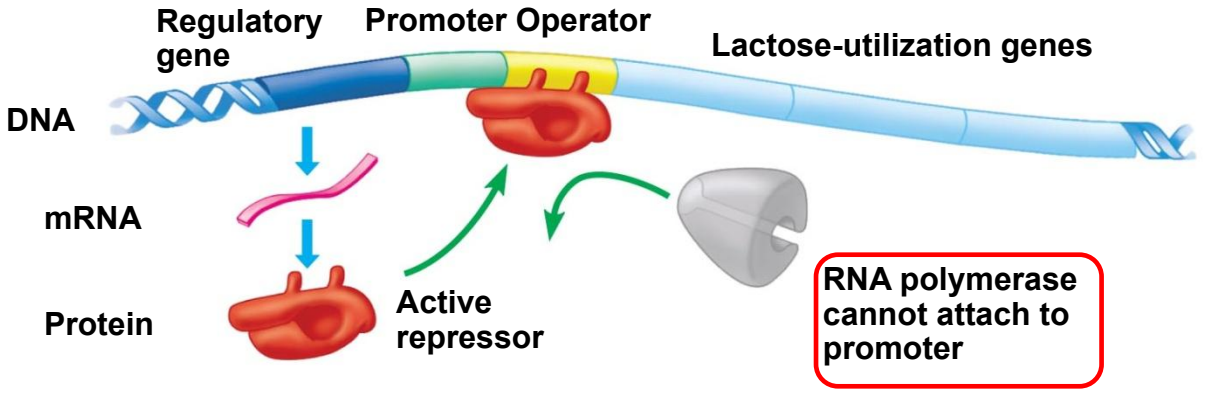
Different types of operons:

- **Inducible** operon: turned off unless needed (ex. *Lac* operon);
- **Repressible** operon: turned on unless *not* needed (ex. *Trp* operon).

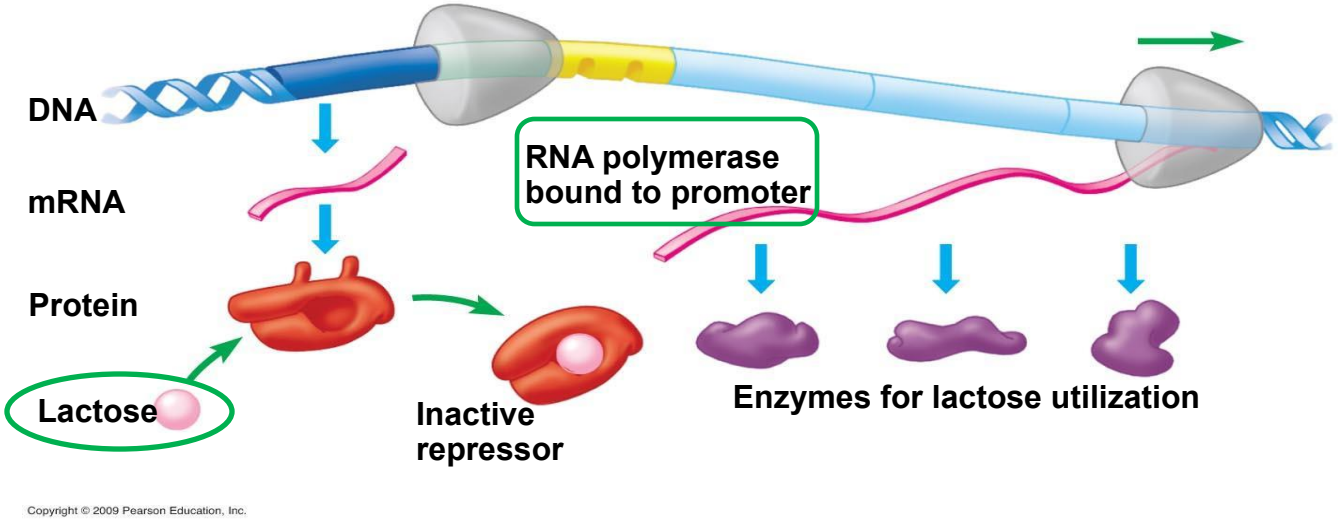
Video: https://youtu.be/Xwk6qrcqiMc?si=3884AAlhxpnZiWpV

"*Lac operon*": an inducible system in *E. coli*

Operon **OFF**
(**Lactose -**)



Operon **ON**
(**Lactose +**)



Video: https://youtu.be/CqVgXxs7hGQ?si=uyXeOUndW_WLqPHG

"*Trp operon*": a constitutive system in E.coli

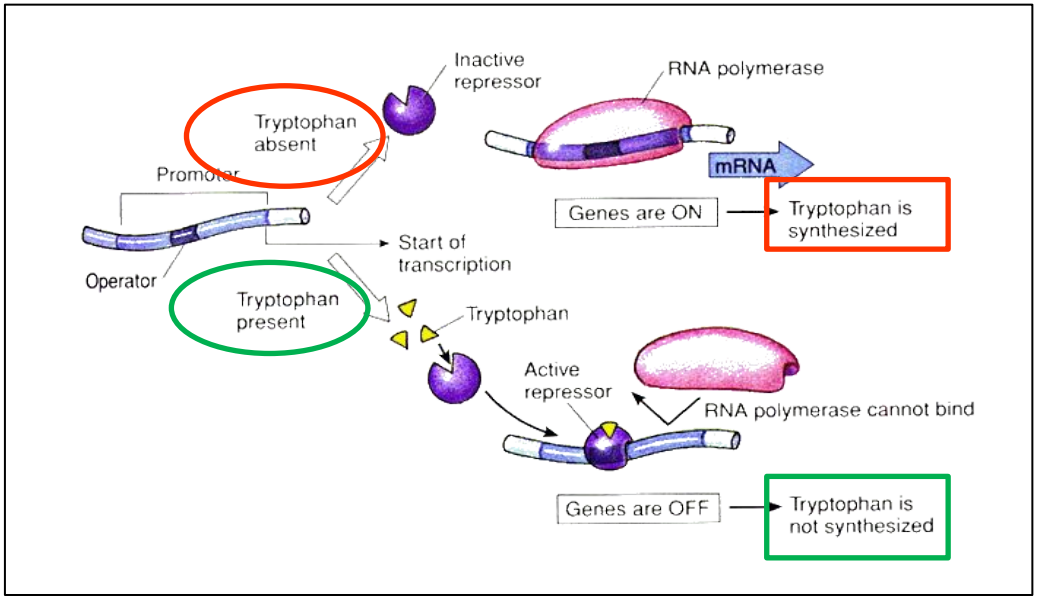
1) Tryptophan is absent

The *Trp* repressor is inactive so that it does not block transcription of the tryptophan-producing enzymes of the operon.

As a result, **tryptophan is generally produced by the cell.**

2) Tryptophan is present

It is energetically efficient for the cell to use the externally supplied amino acid. Tryptophan binds to the inactive repressor, converting it to an active repressor that blocks transcription.

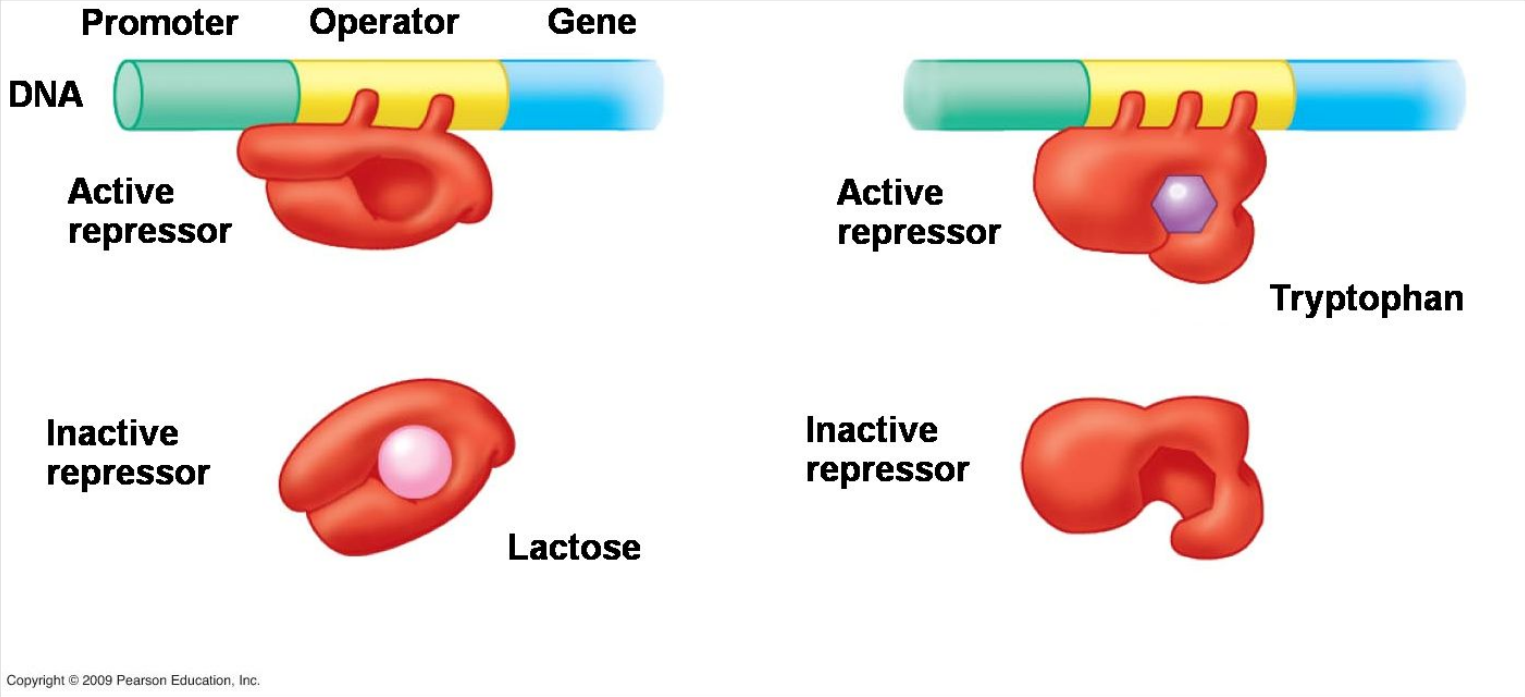


Video: https://youtu.be/tW64JOdXVLM?si=U_UUvAFuCOrm0uV6

Summarizing…

lac operon

trp operon



Inducible

Turn **on** when the **lactose is present**

Repressible

Turned **on** when the **tryptophan is absent.**

Turned **off** when the **tryptophan is present**

Gene expression in eukaryotes

Different strategies are used to control gene expression

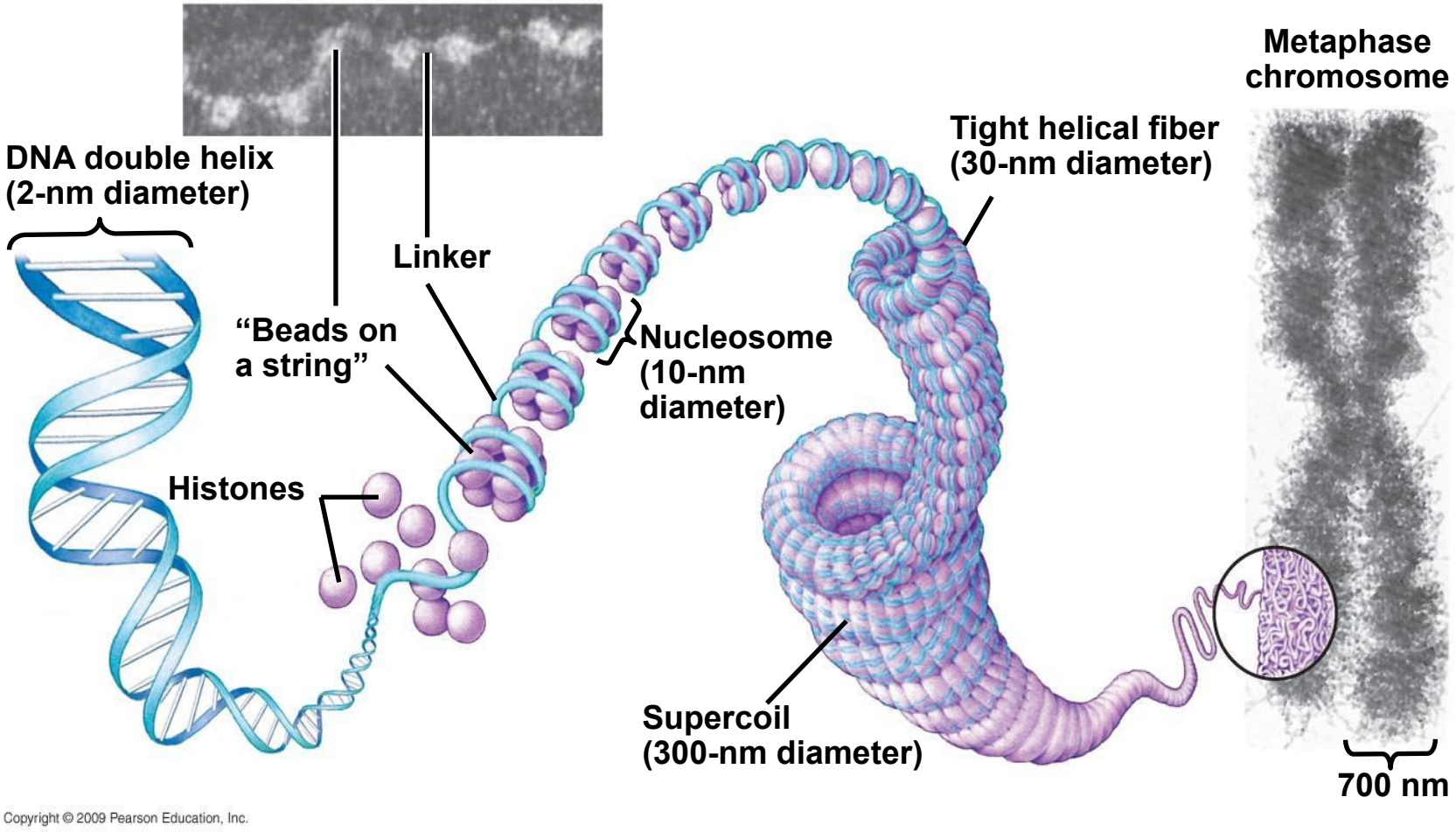
1) **Chromatin remodeling** (DNA packaging and chromosome inactivation)
2) **Transcription**
3) **RNA processing**
4) **Post-transcription**

DNA packing and gene accessibility

Chromatin packaging influences gene expression

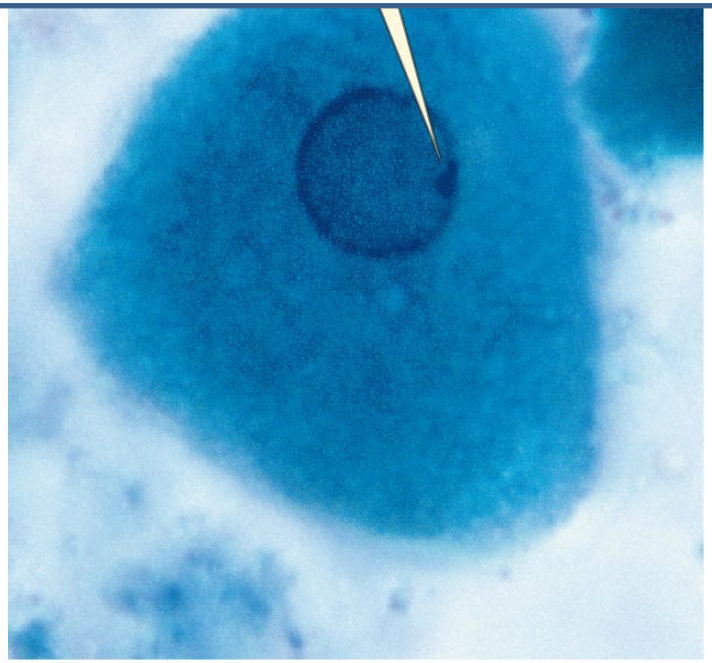
- Transcription may be:
  - **difficult** (or impossible) when chromatin is **tightly packaged**;
  - **possible** when chromatin is **loose packaged**
- DNA is associated to **proteins** (**histones**) to form a condensed chromatin
- **Nucleosomes** are complexes containing **DNA and histones** in a tight complex, inaccessible to RNA polymerase;

DNA packing in an eukaryotic chromosome

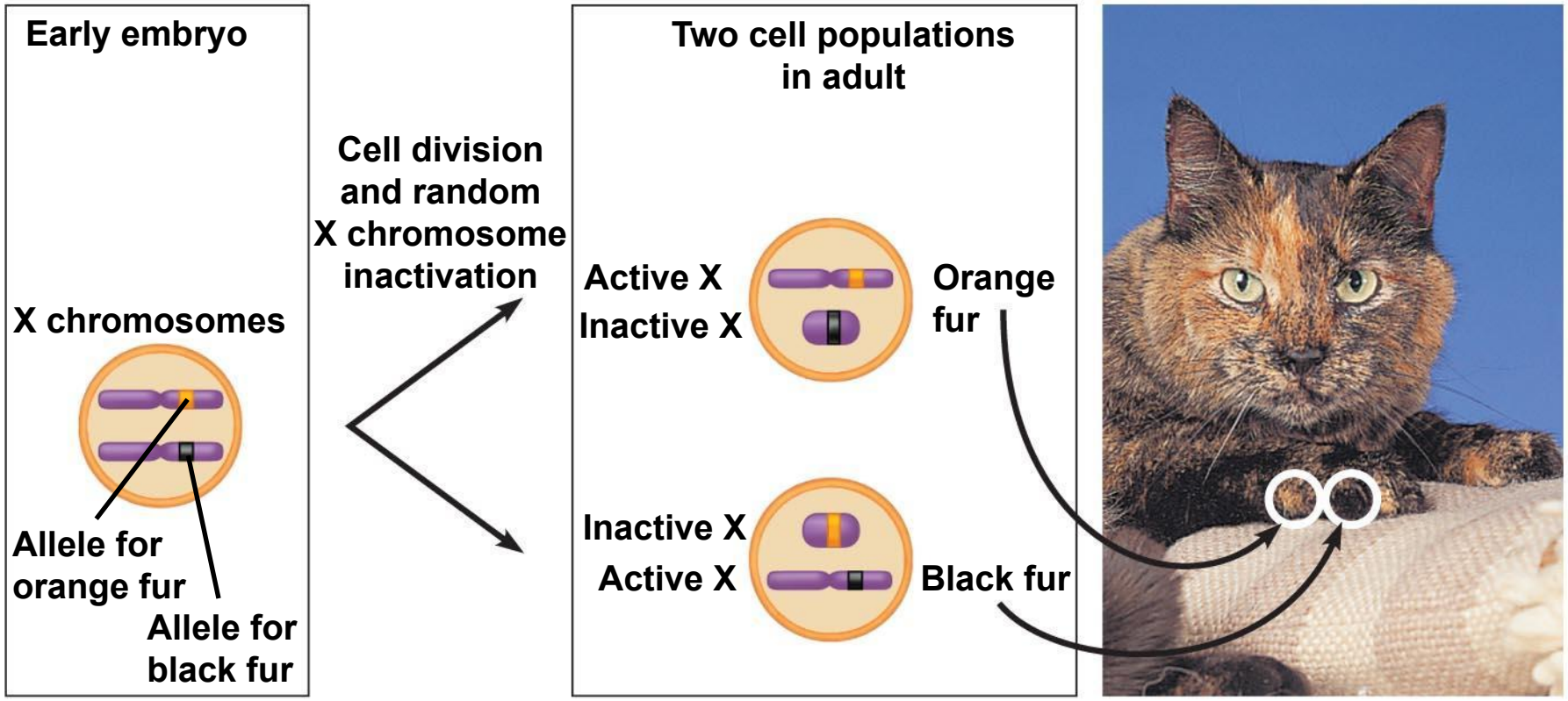


Chromosome X inactivation: the Barr body

Barr body is a chromosome X which is highly condensed and so transcriptionally inactive.
The other chromosome X is not condensed so it is transcriptionally active.



The *tortoiseshell* cat: a phenotypic consequence of chromosome X inactivation

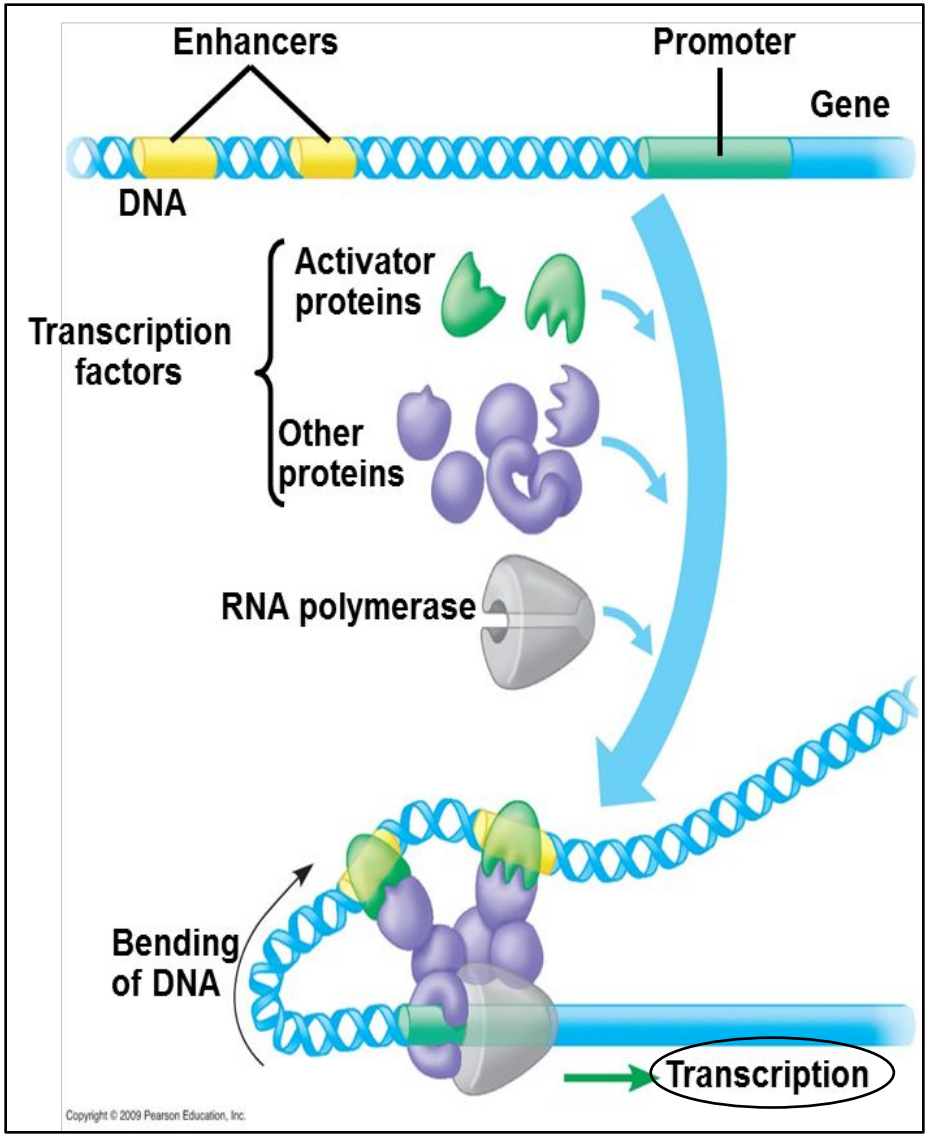


Gene regulation in eukaryotic cells: *Transcription factors*

Eukaryotic genes are regulated by **Transcription factors** and **DNA changes**

Transcription factors (TFs): regulatory proteins that bind DNA and regulate gene expression

- Activator proteins bind to an enhancer sequence.
- DNA bends to bring the enhancer sequence closer to the promoter region.
- Activators interact with other transcription factors that bind to the promoter.
- RNA polymerase is properly positioned on the promoter and transcription is initiated.



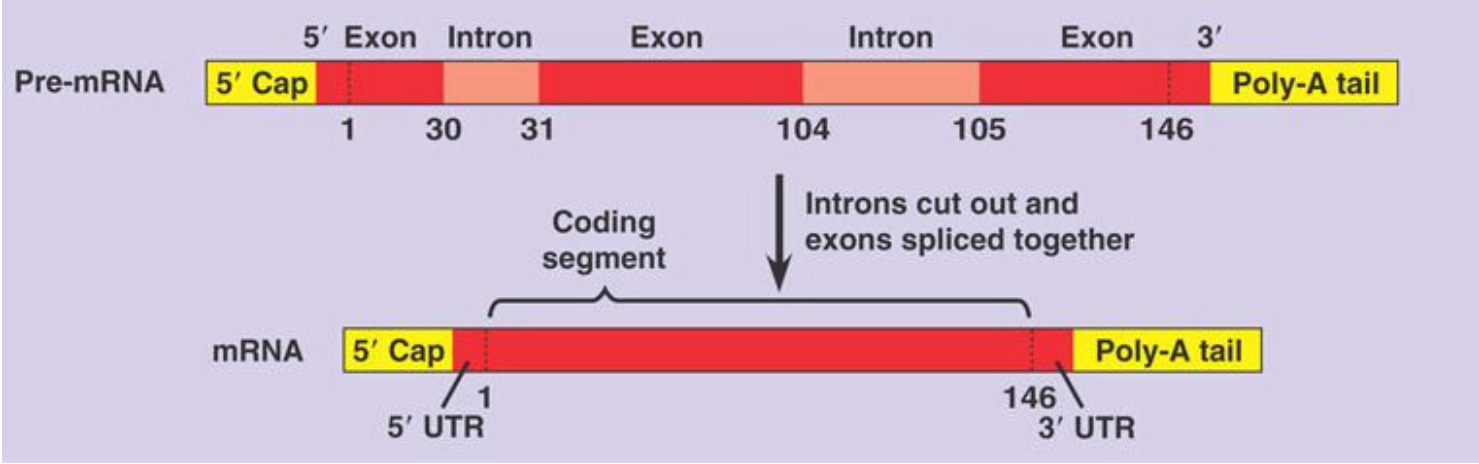
RNA processing in eukaryotic cells: *Splicing*

Coding regions : sequences of a DNA molecule that are expressed as proteins.

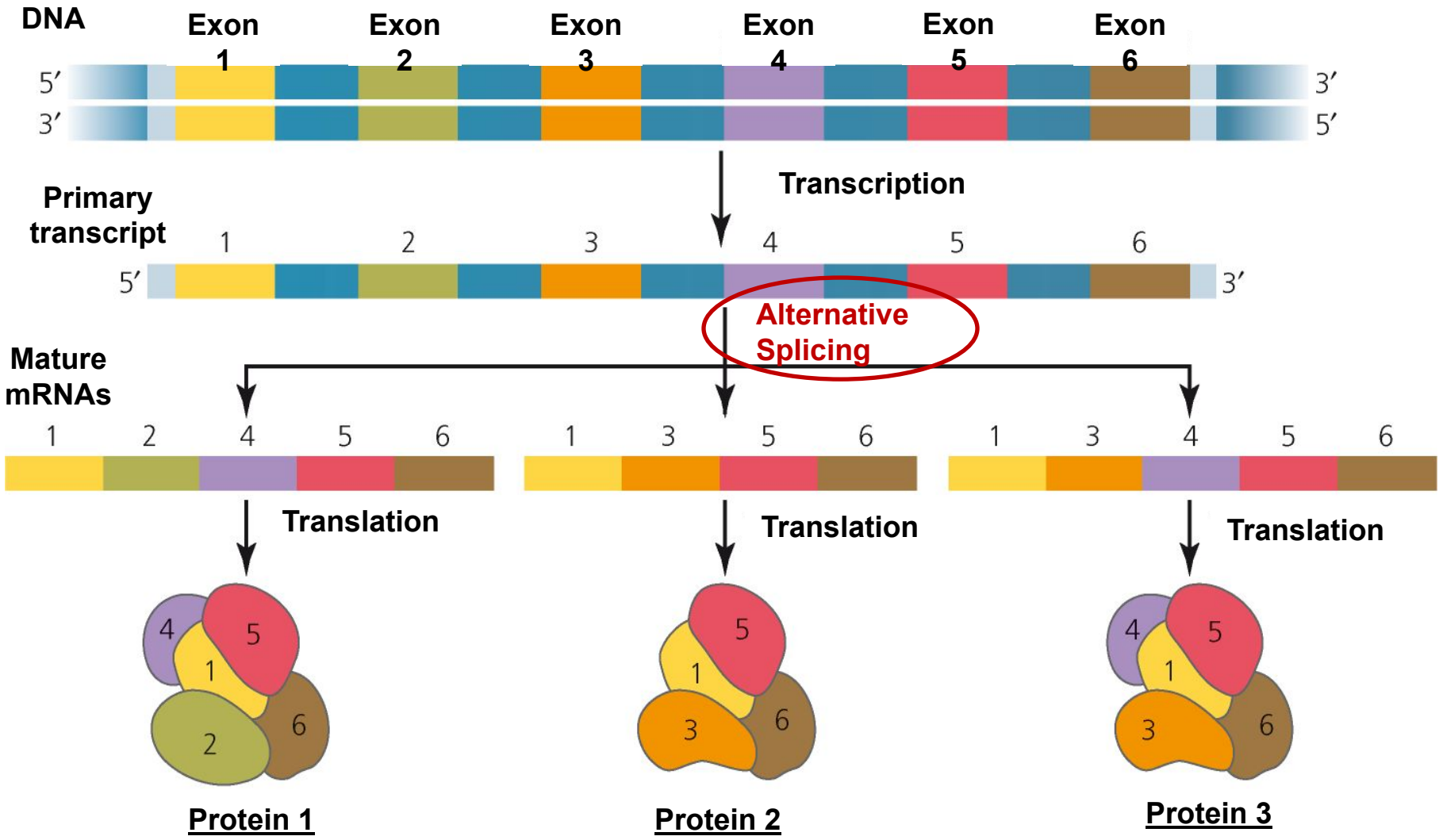
Eukaryotic genes may have non-coding sequences called **introns.**

The coding sequences are **exons**.

Introns and exons appear in the primary mRNA transcript (**pre-mRNA)**; introns are removed from the final mRNA.



RNA processing in eukaryotic cells: *Alternative splicing*

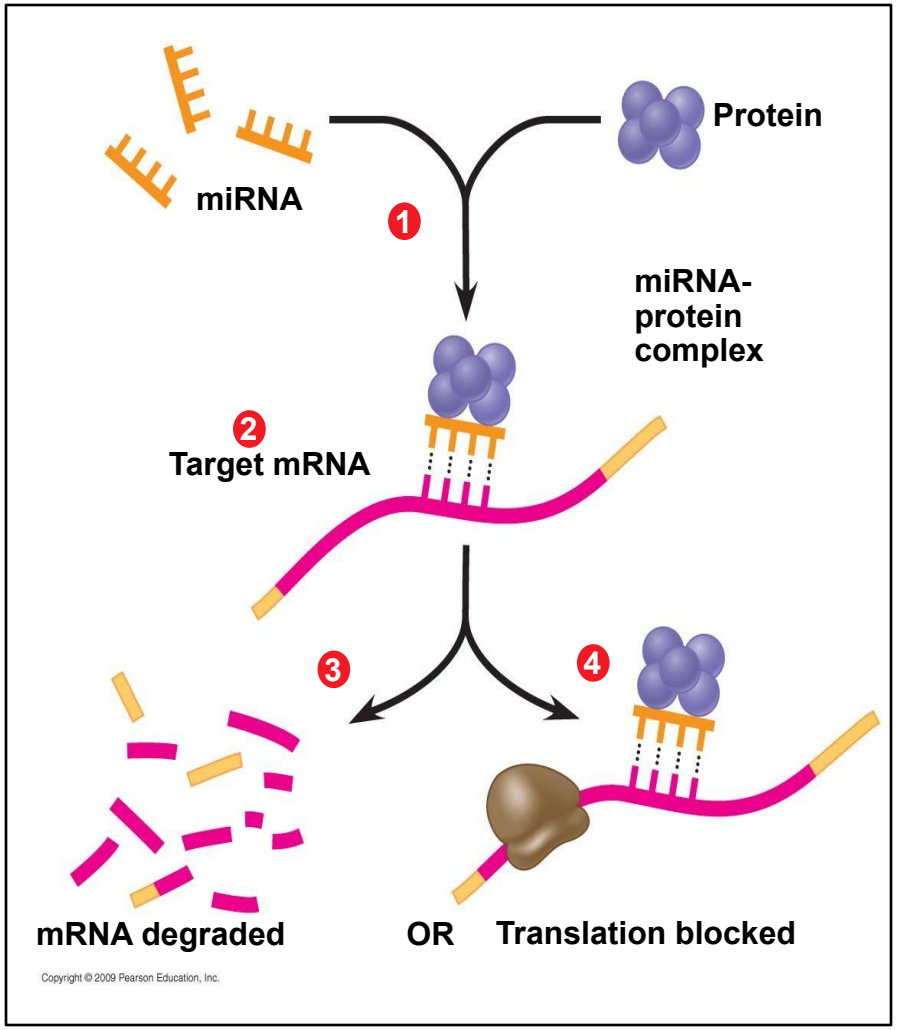


Post-transcriptional regulation in eukaryotic cells: *microRNAs*

MicroRNAs (**miRNAs**): **are small molecules of noncoding RNAs which are important regulators of gene expression**

The miRNA-protein complex binds to target mRNA

mRNA degradation or Block of translation



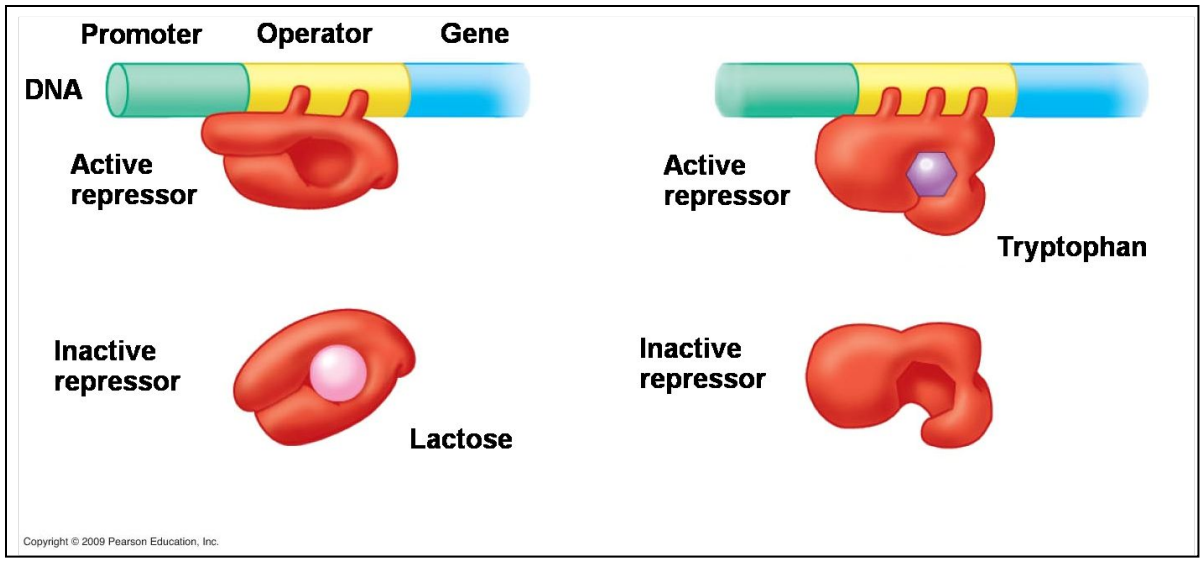
Summary:

Gene expression in prokaryotic cells…

Operon

Types of operons

***lac* operon**



***trp* operon**

Inducible

Repressible

Summary:

…while in eukaryotic cells…

- Transcription factors
- Chromatin remodeling
- RNA processing
- miRNAs