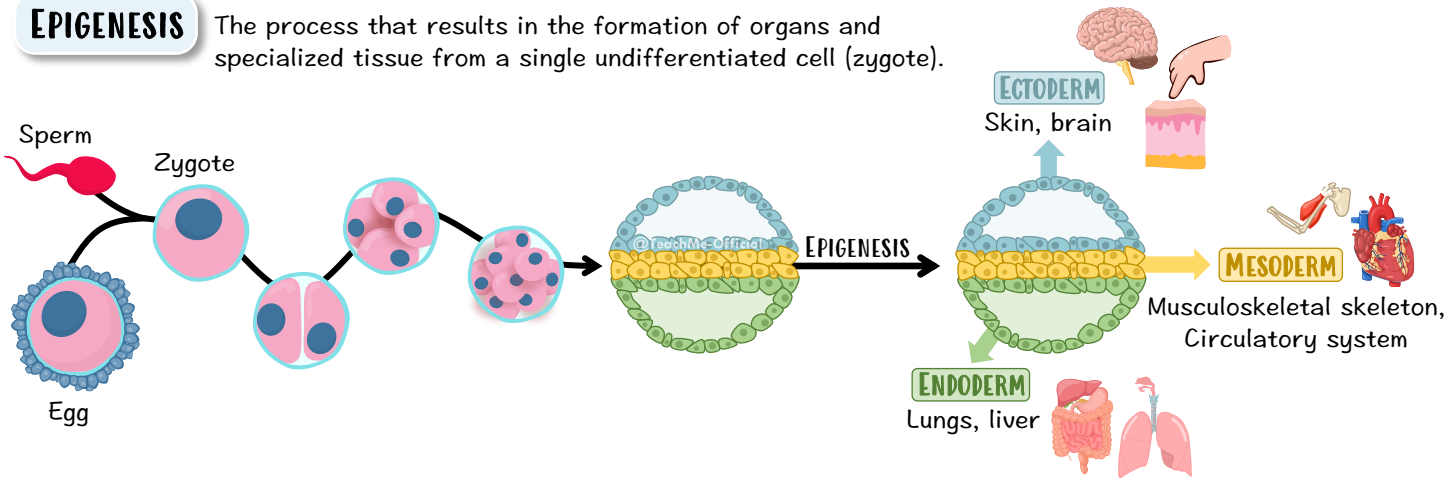
D2.2

Gene Expression (HL)

Introduction

Epigenesis

The process that results in the formation of organs and specialized tissue from a single undifferentiated cell (zygote).



Gene Expression!

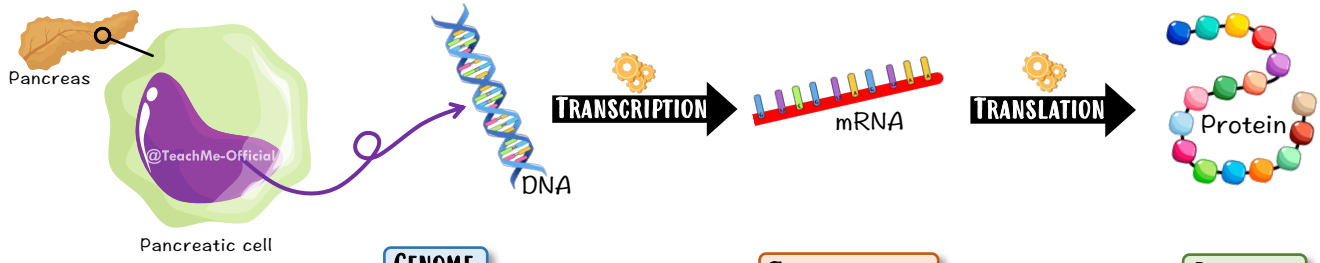
If each cell has the exact same DNA (instruction manual), then why do we have different cell types?

It is simple. Different cells will read a different segment of DNA and do what is says (GENE EXPRESSION). This way some cells read the instructions that allow them to become muscle cells, and other cells read the instruction that allow them to become nerve cells. The same concept applies to each different kind of cell.

Gene Expression

↳The process of reading a gene and building a protein that will then be used by the organism.

A pancreatic cell will read only the DNA and EXPRESS the genes related to pancreatic cells.



Important Terms

Genome
All the genetic information that an organism receives from its parents.

Transcriptome
All the RNA that a cell makes. Pancreatic cells transcriptome differs from muscle cells.

Proteome
All proteins that a cell, a tissue or an organism can produce.

This process can be controlled (⚙) at various stages of the process.
[See page 2]

Key Concepts

- Each cell in the body possess a FULL COPY of the persons GENOME.
- NO CELL expresses ALL the genes in its genome. They only express those needed to perform their special function.
- Different cell types will have different TRANSCRIPTOMES and different PROTEOMES but will have the same GENOME.
- Different organisms have different GENOTYPES and therefor gene expression may result in different proteins (and hence PHENOTYPES).

Genotype
The genetic information for a characteristic/trait.

GENE EXPRESSION

Phenotype
Set of observable traits or characteristics of an organism.

D2.2

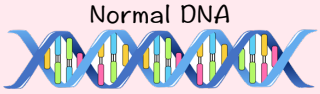
Gene Expression (HL)

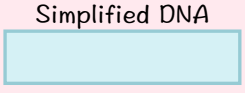
1. Regulation of Gene Expression [In Eukaryotes]

A. Regulation of Transcription

Big Brain FYI!

For simplicity:

Normal DNA 

Simplified DNA 

To promote transcription:

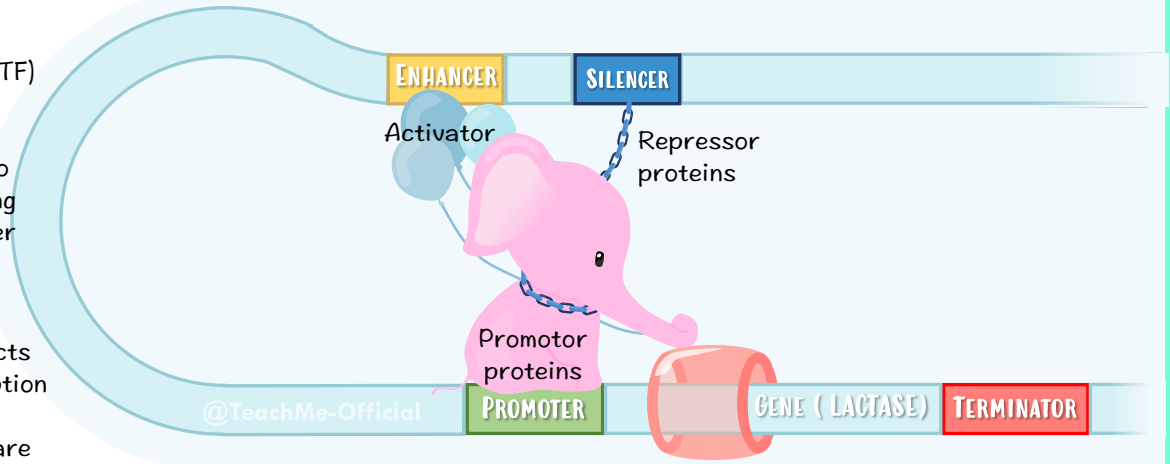
1. A **promoter region** is found upstream the target gene (we want to transcribe).
(In front of)

2. Transcriptions factors (TF) bind to the **promoter region** . These TF are called promoter proteins.

3. These attract RNA polymerase to the promoter region. This is where RNA polymerase will start transcription of the target gene. Without these promotor proteins, RNA polymerase would't know where to go.

4. Activators (kind of TF) binds to the enhancer region (upstream). This causes the DNA to fold over itself, bringing the **enhacer region** closer to the **promoter region**

5. The enhancer region acts by "allowing" transcription to occur, so when transcription factors are bound to BOTH the enhancer region AND the promoter region - then transcription starts.



Transcription Factors

Proteins that bind to specific segments (enhancer, silencer, promotor) of DNA to to control transcription.

- Promotor proteins
- Activator proteins
- Repressor proteins

Promoter Region upstream of DNA where RNA polymerase and promotor proteins binds to begin transcription.

Enhancer Sequences that promote transcription when bound to a transcription factor (ON).

Silencer Sequences that inhibit transcription when bound to a transcription factor (OFF).

To Prevent transcription:

1. Repressor proteins bind to the **silencer region** (upstream).

2. When bound, these repressor proteins represses or prevent transcription from occuring.

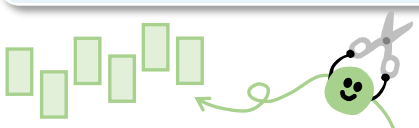
NOTE!

Transcription begins when transcription factors are connected to both the **enhancer region** and the **promotor region.**

Successful transcription results in the synthesis of an mRNA molecule that will undergo translation.

Gene Expression (HL)

B. mRNA Degradation Regulation



Exonuclease

Enzyme that chops up mRNA by removing its nucleotides one by one from their extremities.

mRNA

5' [Not resistant to exonuclease] 3'

(1) Decapping complex
Group of enzymes that remove the cap.

(2) Deadynelase complex
Group of enzymes that can remove the poly A tail.

Cap (5') + poly A tail (3') are added to the mRNA.

Cap

mRNA

5' [Resistant to exonuclease] 3'

Poly A tail

Cap is made of modified guanine nucleotide with three phosphates.

Poly A tail is made of around 150-250 adenine.

(1)Protecting mRNA from degradation
(2) Nuclear export role
(3) Enhance translation (ribosomes)

Key Takeaways

mRNA may persist for minutes up to days before being broken down by **exonucleases**.

When an mRNA is needed, it is protected by a cap and poly A tail so it can be translated over and over again into a protein.

When a protein is no longer needed, transcription will cease, and the existing mRNA will be destroyed by exonucleases.

Before mRNA can be destroyed by exonucleases, the cap and poly A tail needs to be removed by a Decapping complex and a Deadenylase complex.

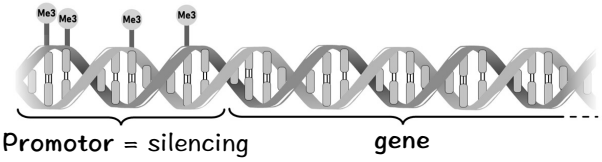
C. Epigenetic Modifications

What: Study of changes in gene activity that are NOT caused by changes in the DNA base sequences. Changes occur in phenotype but not genotype.

How: Methylation (adding CH_3) to **DNA** OR **Histone Tails**, to influence gene expression.

DNA Methylation

The methylation of cytosine bases at promotor regions causes silencing of the gene: this gene does NOT get transcribed.



Histone Tail Methylation

Two positions on histone tails can be methylated: K4 and K27. Gene expression is affected differently depending on which is methylated: K4 methylation causes activation and K27 causes silencing.

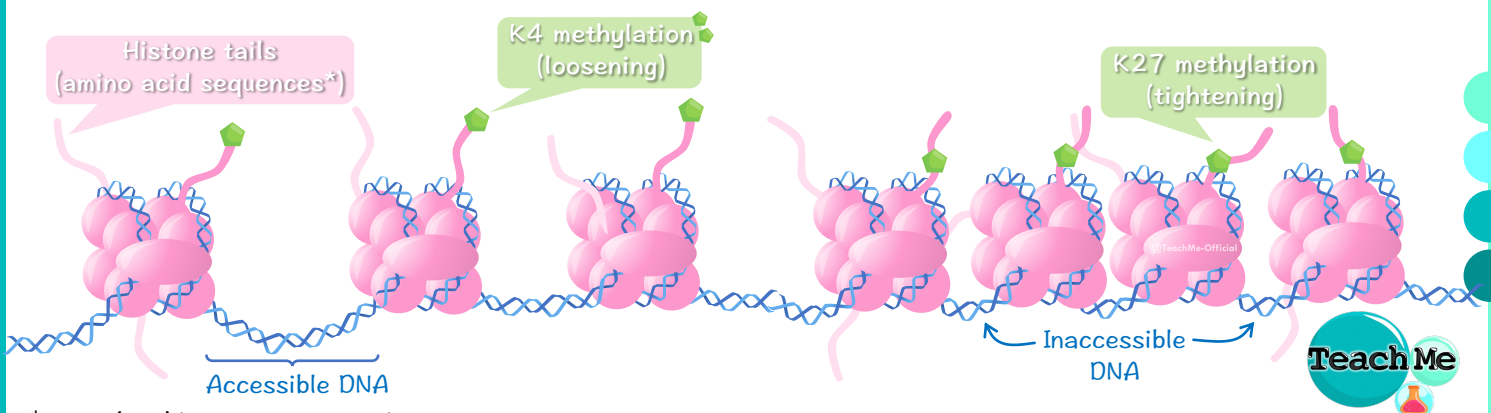
Methyl group

Lysine (K) has multiple positions:

K4 = activation K27 = silencing

Activating (with methylation): Loosening (uncoil) the loops of DNA from histones, making the DNA accessible to RNA polymerase.

Silencing (with methylation): Tightening (coiling) the loops of DNA around histones, making DNA inaccessible to RNA polymerase.



*remember histones are proteins!

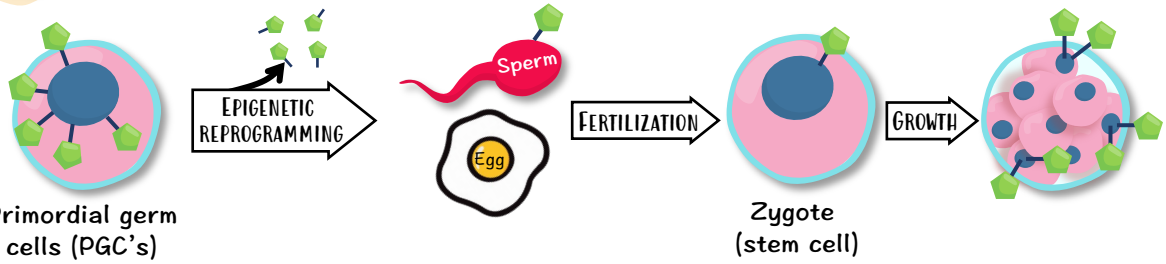
Gene Expression (HL)

II. Epigenetic Inheritance

DNA or **histone methylation** is an example of an **epigenetic tag**.

Chemical modifications that cause some genes to be activated and others to be silenced.

Are these EPIGENETIC TAGS inherited (passed on to offspring)?



They are lost (MOSTLY) when sperm and egg cells are produced → EPIGENETIC REPROGRAMMING.

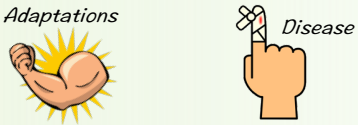
(Embryonic) Stems cells → TOTIPOTENT. They are not methylated, during development, methylation becomes widespread (but is unique to the cell type).

With time, methylation becomes widespread. Methylation patterns are unique to cell type.

Ex. In muscle cells, appropriate genes for muscles will remain free from epigenetic silencing tags. Hence, they can be expressed. Other genes are silenced with tags.

However, SOME epigenetic tags are passed on to the next generation.

Implication: *Adaptations* *Disease*



Experiences your ancestors had may influencing which genes are being activated or silenced in genome. Not only GOOD, can also be BAD.

BIG BRAIN TIP!

Key facts about epigenetic modifications:

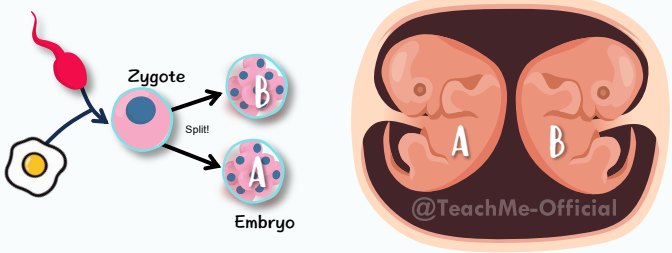
- Are reversible*.
- Mostly get erased but may be passed on genetically.
- Do not alter the DNA code itself.

Twins

Monozygotic (identical) twins

Both twins originate from the same zygote. Same sperm & egg. Instead of forming a single embryo, two embryos form. They have the same genetic code.

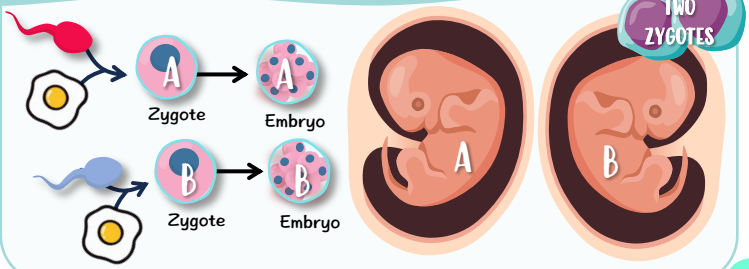
ONE ZYGOTE



Heterozygotic twins (fraternal)

When **two separate eggs** are fertilized at the same time by **different sperm** cells. These twins do not look any more alike than other sibling might. They have a different genetic code.

TWO ZYGOTES



Why same genotype, but different phenotype?

Monozygotic twins have the exact same DNA, but sometimes one twin will develop cancer and the other be completely healthy. Sometimes one has a slightly different phenotype (trait) than the other. This is because the phenotype is controlled by the genome, but the environment also plays a role in affecting which genes are expressed and which are silenced. Throughout life the twins will have different environments and experiences leading to different DNA methylation patterns. DIFFERENTIALLY METHYLATED REGIONS (DMRs) – regions with different methylation statuses among different people.

Very few differences in DMRs in newborn monozygotic twins, but the differences in methylation patterns increase with age. The difference is bigger in twins that grew up in different environments compared to those that grew up in the same environment.

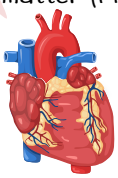
Gene Expression (HL)

III. Environmental Effects

Environmental factors can affect gene expression, sometimes leading to disease.

What:

- **Air pollution** (O_3, nitrogen oxides, particulate matter (PM) and polycyclic aromatic hydrocarbons (PAHs))
- Nutrition
- Toxins & chemicals,
- Stress & psychological factors
- Physical activity, etc...



Diseases (caused by air pollution) :

Asthma, heart disease, lung cancer, placenta formation issues, lower body mass babies.

[Pregnant females should be careful about: eat and drink (alcohol, nicotine and caffeine).]

How:

DNA methylation increased in - white blood cells, brain cells and certain genes related to inflammation.

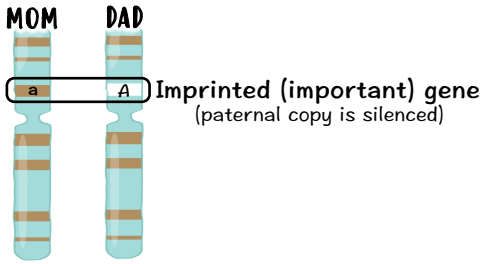
IV. Imprinted Genes

Imprinted genes are those that have been silenced in only one of the two copies, either the paternal copy or the maternal copy of the gene. These genes bypass the **epigenetic reprogramming** process.

Genes in the egg and sperm are imprinted differently.

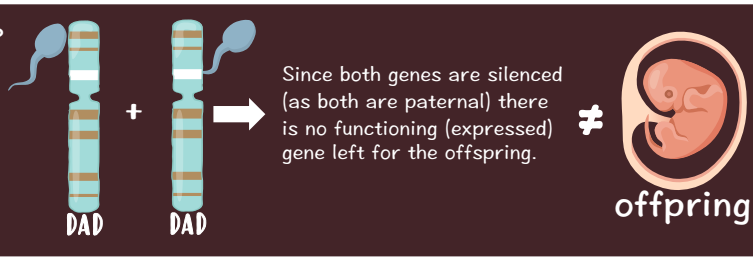
With imprinted genes, one parent's copy is silenced using **methylation**. The remaining copy alone will determine the phenotypic outcome.

Think about this: A dominant allele can be silenced!



How was the phenomenon discovered?

Researchers combined the nuclei from two mouse eggs (or sperm) to form a zygote··· No cells developed into mice embryos. Despite sufficient genetic material.



Example

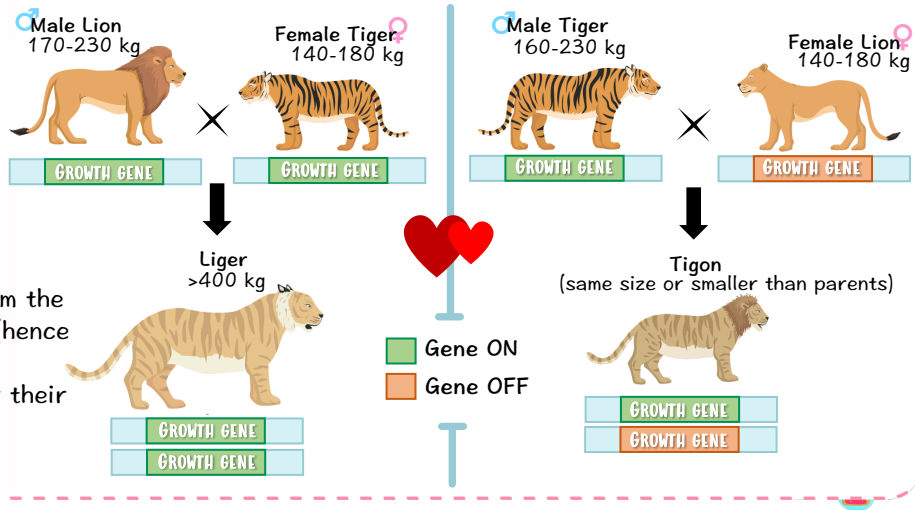
Lions

Female lions mate with multiple male lions. From the male lion's perspective, only his baby matters (hence his growth gene is ON). From the female perspective, they have no preference between their babies (hence her growth gene is OFF).

Tigers

Female tigers mate with one male tiger. From the male tiger's perspective, his baby matters (hence his growth gene is ON). From the female perspective, they require optimal genes for their babies. (hence her growth gene is ON).

Tigers and lions are similar enough species that they can produce hybrids:



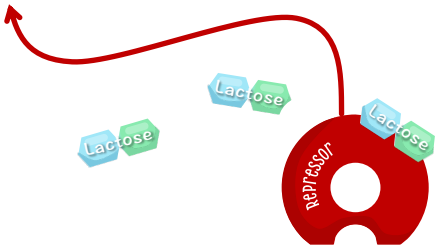
Gene Expression (HL)

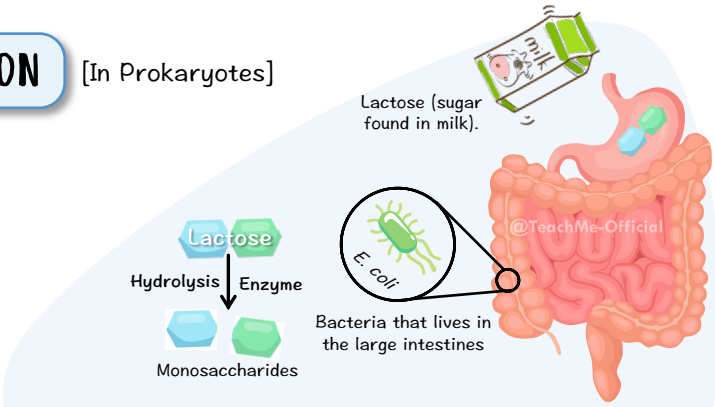
V. Regulation of Gene Expression [In Prokaryotes]

Example 1 – The Lac Operon*

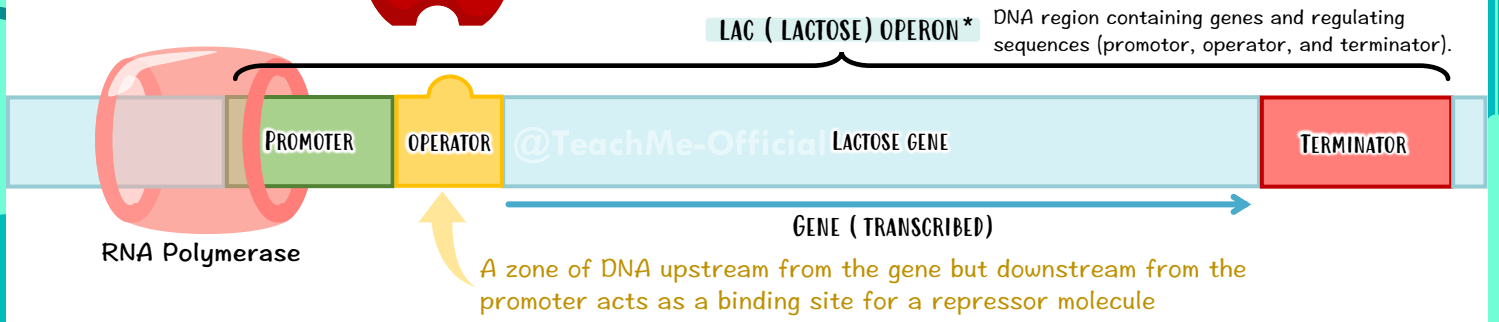
This is an example of an INDUCIBLE OPERON. Meaning it is usually turned **OFF**, but it can be induced (turned ON).

Repressor: Binds to the operator to prevent transcription.





E. coli have an enzyme (lactase) which allows them to breakdown lactose into monosaccharides. The transcription of lactase is regulated by lactose.



Presence of Lactose

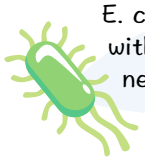
- LACTOSE arrives and combines with lac REPRESSOR.
- This causes its DEACTIVATION and detachment from the operator.
- This ALLOWS the RNA polymerase to transcribe the genetic code.

Absence of Lactose

- Lactose is used up, leading to an empty lac REPRESSOR.
- This causes its activation and attachment to the operator.
- This PREVENTS the RNA polymerase to latch and transcribe the genetic code.

Example 2 – The TRP Operon

This is an example of a REPRESSIBLE OPERON. meaning it is usually turned **ON**, but it can be repressed (turned OFF).



E. coli synthesizes tryptophan (amino acid) with specific enzymes. When amino acid is needed all the enzymes in the metabolic pathway are synthesized at once.

Presence of Tryptophan

- TRYPTOPHAN (co-repressor) binds to TRP REPRESSOR.
- This causes repressors change to active form that can bind operator.
- Upon binding transcription is INHIBITED.

Absence of Tryptophan

- NO TRYPTOPHAN to bind repressor
- This returns repressor shape change to INACTIVE form. cannot bind operator.
- When there is no binding, transcription is ALLOWED.

notes