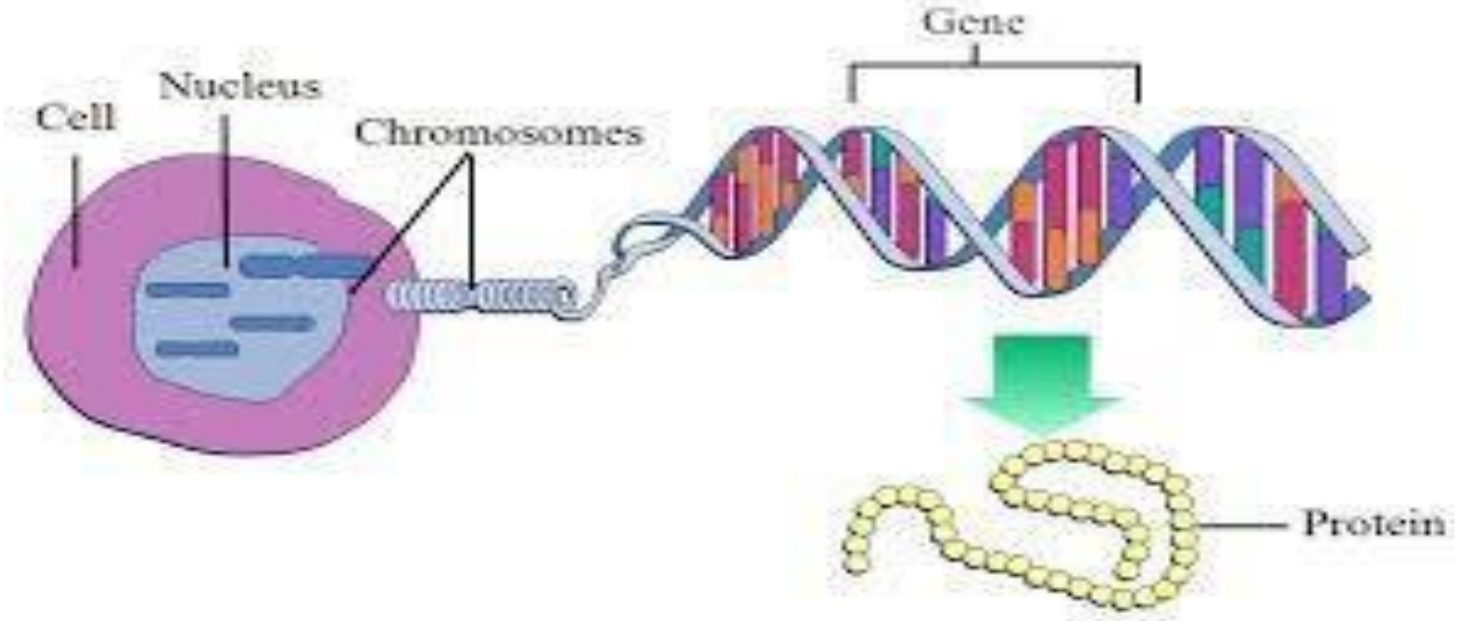
GENE CONCEPT & GENE EXPRESSION

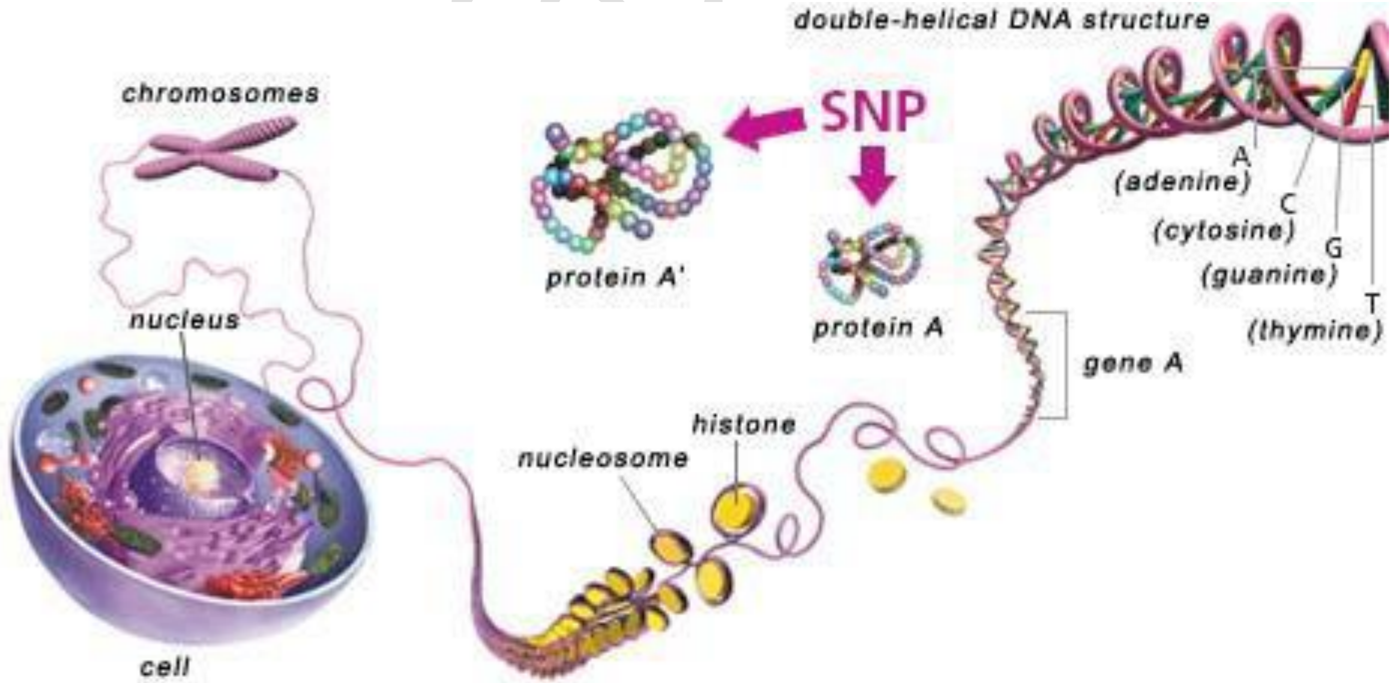
- The term gene was introduced by Johannsen (1909).
- The gene concept was introduced by Sutton.
- The basic physical unit of heredity consisting of a DNA sequence at a specific location on a chromosome.



- T.M Morgan proposed the gene theory which state that:

➢ Chromosomes are bearers of hereditary units and each chromosome carries hundreds or thousands of genes.

➢ The genes are arranged on the chromosomes in the linear order and on the special regions or locus.



Classical Vs Modern Concept of gene

- **Classical definition of gene:** Gene is the unit of Function (one gene specifies one character), Recombination, and Mutation.

- **Modern definition of gene:** Unit of Genetic Information (Unit of DNA that specifies one polypeptide) Includes coding as well as non-coding regulatory sequences.

Terms Related To Gene: S. Benzer (1957) coined different terms for different nature of gene and genetic material in relation to the chromosome on the basis of genetic phenomena to which they involve.

- **Recon:** It is the smallest unit of DNA capable of undergoing Crossing Over and Recombination.

- **Muton:** It is the smallest unit of DNA which can undergo Mutation.

- **Cistron:** It is the unit of Function. It is the Gene in real sense capable of synthesizing a Polypeptide chain of an Enzyme.

- **Complon:** It is the unit of Complementation. It has been used to replace cistron. Certain enzymes are formed of two or more polypeptide chains, whose active groups are complementary to each other.
- **Operon:** operon is the combination of operator gene and sequence of structure genes which act together as a unit. Therefore, it is composed of several genes.
- **Replicon:** It is the unit of replication. Several replicons constitute a chromosome.
- **Exons:** The coding units containing biological information.

- **Introns:** Intervening noncoding DNA segments.

ESSENTIAL FEATURES OF GENE

- Determines the physical as well as physiological characters.
- Situated in the chromosome.
- Occupies a specific position known as Locus.
- Arranged in single linear order.
- Occur in functional states called Alleles.

- Some have more than 2 alleles known as Multiple Alleles.

- Some may undergo sudden and permanent change in expression called as Mutant Gene (Mutation).

- May be transferred to its homologous (Cross-over) or non-homologous counterpart (Translocation).

- Can duplicate themselves very accurately (Replication).

- Synthesizes a particular Protein.

- Determines the sequence of amino acid in the polypeptide chain.

ESSENTIAL FEATURES OF GENE

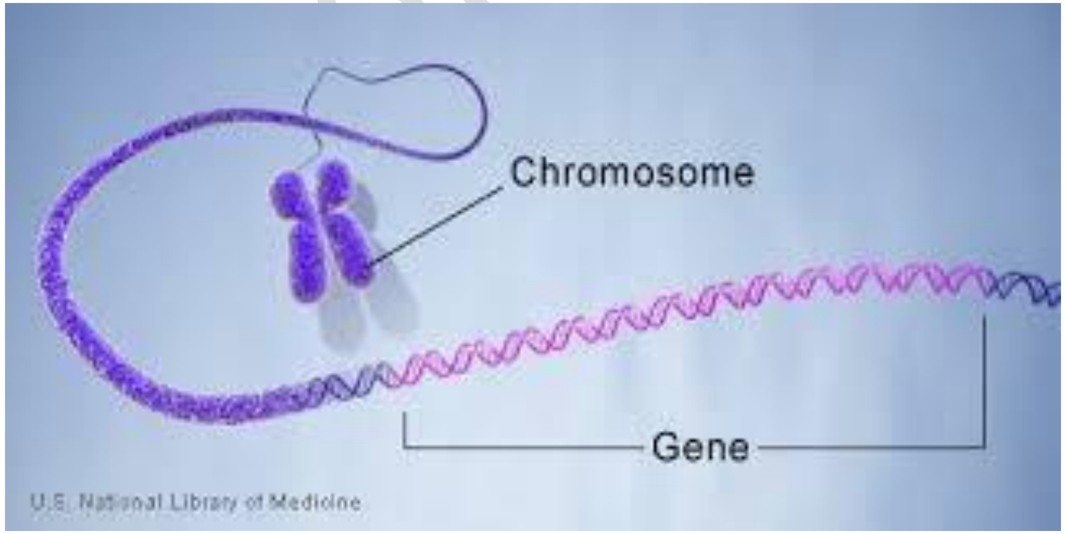
- Average size of Prokaryotic gene is 1 kbp and have little diversity
- Average size of Eukaryotic gene is 16 kbp and have great diversity

GENE TYPES

- Basic genes: These are the fundamental genes that bring about expression of particular character.
- Lethal genes: These bring about the death of their possessor.
- Multiple gene: When two or more pairs of independent genes act together to produce a single phenotypic trait.

- Cumulative gene: Some genes have additive effects on the action of other genes. These are called cumulative genes.

- Pleiotropic genes: The genes which produce changes in more than one character is called pleiotropic gene.
- Modifying gene: The gene which cannot produce a character by itself but interacts with other to produce a modified effect is called modifier gene.
- Inhibitory gene: The gene which suppresses or inhibits the expression of another gene is called inhibitory gene



- Regulator genes: These genes code for repressor proteins which regulate transcription of cistrons.

- Operator genes: These genes act as switch and turn on or off the transcription of an structural gene as and when required by the cell.

- Promoter genes: These genes provide sites for the binding of RNA polymerase enzyme for the transcription of RNAs by structure genes.

- Terminator genes: These DNA segments lie in the end of messages and stop or terminate transcription activity of structure genes.

Transposons (Jumping Genes)

- Transposable elements (TEs), also known as "jumping genes" or transposons, are sequences of DNA that move (or jump) from one location in the genome to another.

- Maize geneticist Barbara McClintock discovered TEs in the 1940s.

- Insertion of these elements may produce deletions, inversions, chromosomal fusions and even more complicated rearrangements.

- TEs can serve as switches turning genes on and off or by inverting sequences containing promoters.

- The process of insertion of transposon between two base pairs in a recipient DNA molecule is called transposition.

- Two major events during transposition:

➢ There is duplication of target sequence in the recipient DNA molecule. The target sequence consists of 3-12 base pairs.

➢ The inserted transposon is sandwiched between the repeated target sequences.

GENETIC CODE

- ❖ The genetic code is a set of rules defining how the four-letter (A, T, G, C) code of DNA is translated into the 20-letter code of amino acids, which are the building blocks of proteins.

- ❖ The genetic code is a collection of three-letter combinations of nucleotides called codons, each of which corresponds to a specific amino acid or to translational signal.

- ❖ The concept of codons was first described by

Francis Crick and his colleagues in 1961.

- Any altered codon (triplet of DNA nucleotides) that encodes an incorrect amino acid or stop signal, resulting in an altered or non-functioning peptide or protein product is known as missense codon.

Characters of genetic code:

- **The code is triplet:** Each codon consists of three bases (triplet). There are 64 codons. 61 codons code for amino acids.

- **There is one start codon (initiation codon):** AUG acts as start codon. AUG code for methionine. Protein synthesis begins with methionine (Met) in eukaryotes, and formylmethionine (fmet) in prokaryotes.

- **Some codons acts as stop codons:** These three (UAA, UGA, UAG) are stop codons (or nonsense codons) that terminate translation.

- **The code is unambiguous:** Each codon specifies no more than one amino acid.

- **The code has polarity:** They are all written in the 5' to 3' direction.

- **The code is degenerate**: More than one codon can specify a single amino acid.

➢ All amino acids, except Met and tryptophan (Trp), have more than one codon.

➢ For those amino acids having more than one codon, the first two bases in the codon are usually the same. The base in the third position often varies (Wobble hypothesis).

- **The code is almost universal:** (the same in all organisms). Some minor exceptions to this occur in mitochondria and some organisms.

- **The code is commaless (contiguous):** There are no spacers or "commas" between codons on an mRNA.

- **The code is non-overlapping:** Neighboring codons on a message are non-overlapping.

The Wobble Hypothesis: Proposed by Francis Crick in 1966

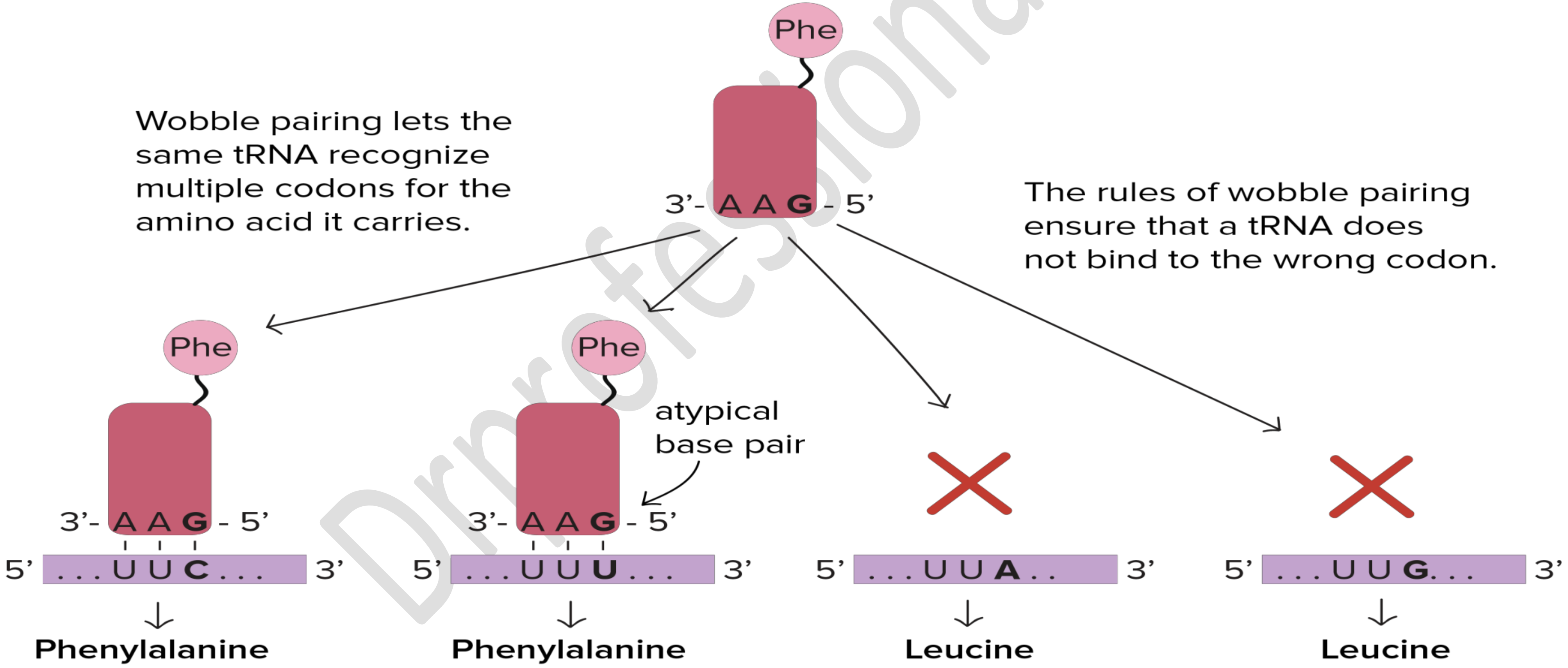
- There are more than one codon for one **amino acid**. This is called degeneracy of genetic code.

- According to this hypothesis, only the first two bases of the codon have a precise pairing with the bases of the anticodon of tRNA, while the pairing between the third bases of codon and anticodon may Wobble (wobble means to sway or move unsteadily).

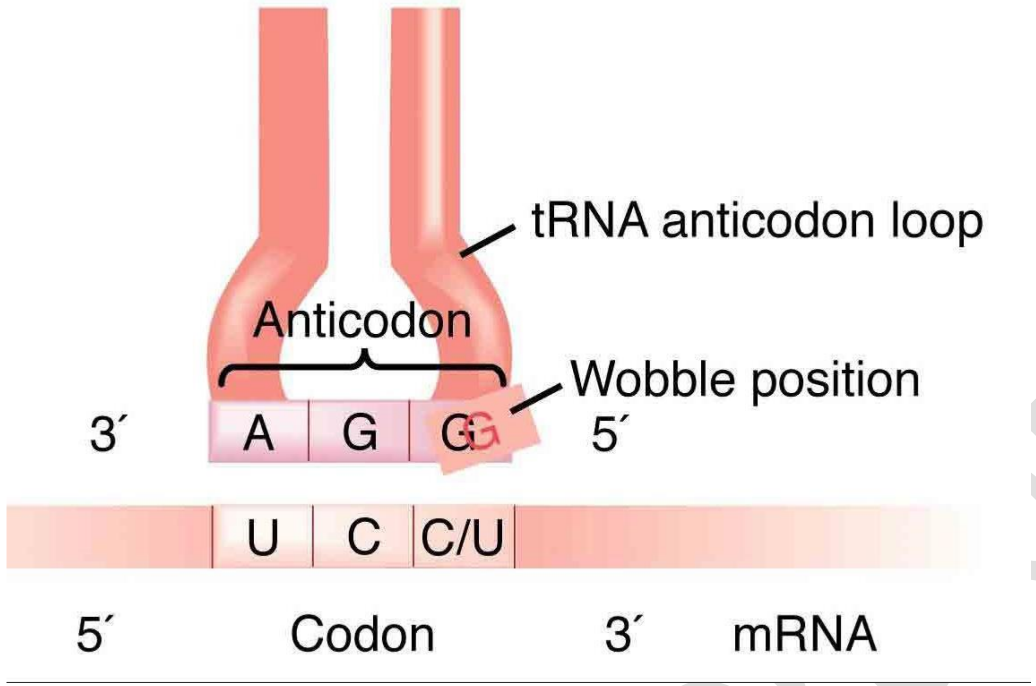
- The phenomenon permits a single tRNA to recognize more than one codon. Therefore, although there are 61 codons for amino acids, the number of tRNA is far less (around 40) which is due to wobbling.

Atypical base pairs—between nucleotides other than A-U and G-C—can form at the third position of the codon, a phenomenon known as **wobble**.

Wobble pairing doesn't follow normal rules, but it does have its own rules. For instance, a G in the anticodon can pair with a C or U (but not an A or G) in the third position of the codon, as shown below. Rules like this ensure codons are read correctly despite wobble.



Differences between “Codon” and “Anticodon”



Codon:

1. It is found in DNA and mRNA.

2. Codon is complementary to a triplet of template strand.

3. It determines the position of an amino acid in a polypeptide.

Anticodon

1. It occurs in tRNA.

2. It is complementary to a codon.

3. It helps in bringing a particular amino acid at its proper position during translation.

Gene Action

- The influence of gene resulting in the expression of a genetic character is called gene action.
- Gene expression is the process by which the information encoded in a gene is used to synthesis of a protein molecule.
- The genes are generally associated with the production of enzymes, which they synthesize from chemical substance available in the body cells.

- As a rule one gene affects one enzyme. The various actions of genes are expressed in their development of

✓ pigments

✓ Colours

✓ hormones

✓ production of proteins

✓ antigen and antibody

- Jacob and Monod proposed "Operon model" To explain the mechanism of gene action, in which protein involved in lactose metabolism are expressed by E.coli only in the presence of lactose and absence of glucose.

- Protein synthesis is regulated by three specific genes located on chromosomes.

➢ **Structural genes:** It regulates to produce specific mRNA

Determine the kind of protein to be synthesized.

➢ **Operator genes:** These genes act as switches to turn on or turn off the activities of structural genes regulating the elongation and termination of polypeptide chain.

- **Regulator genes:** These genes produce certain proteinaceous substance called repressor, which prevent the operator genes from their action.

TYPES OF REGULATION OF GENE

POSITIVE REGULATION :

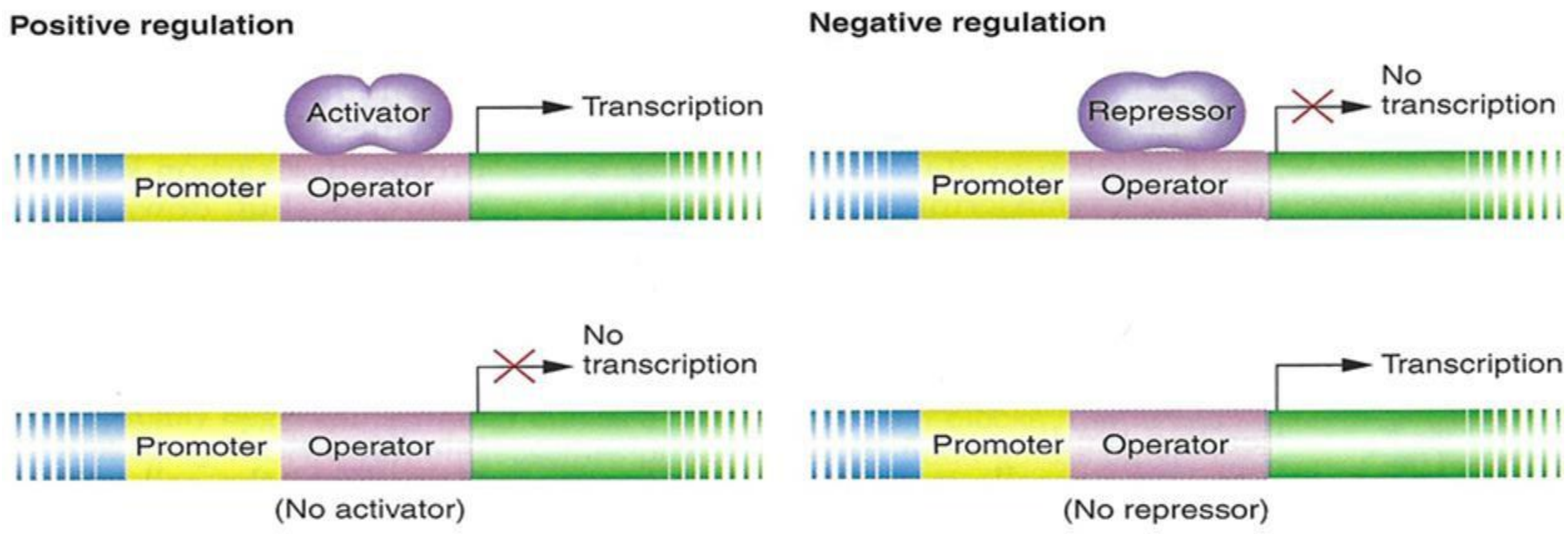
- When the expression of genetic information is quantitatively increased by the presence of specific regulatory element is known as positive regulation.
- Element modulating positive regulation is known as activator or effector or inducer.

NEGATIVE REGUATION:

- When the expression of genetic information is diminished by the presence of specific regulatory element is known as negative regulation.

- **The element or molecule mediating the negative regulation is said to be repressor.**

Positive and negative regulation



Positive Regulation

The binding of specific protein (**activator**) is required for transcription to begin.

DNA bound activators can regulate transcription by helping with ignition. To do this they sometimes tether RNA polymerase to the promoter.

Negative Regulation

The binding of a specific protein (**repressor**) inhibits transcription from occurring.

DNA bound repressors often act to prevent RNA polymerase from binding to the promoter, or by blocking the movement of RNA polymerase

STEPS INVOLVING REGULATION OF GENE EXPRESSION

Synthesis of the primary RNA transcript (transcription)

↓

Post-transcriptional modification of mRNA

↓

Messenger RNA degradation

↓

Protein synthesis (translation)

↓

Post-translational modification of proteins

↓

Protein targeting & transport

↓

Protein degradation

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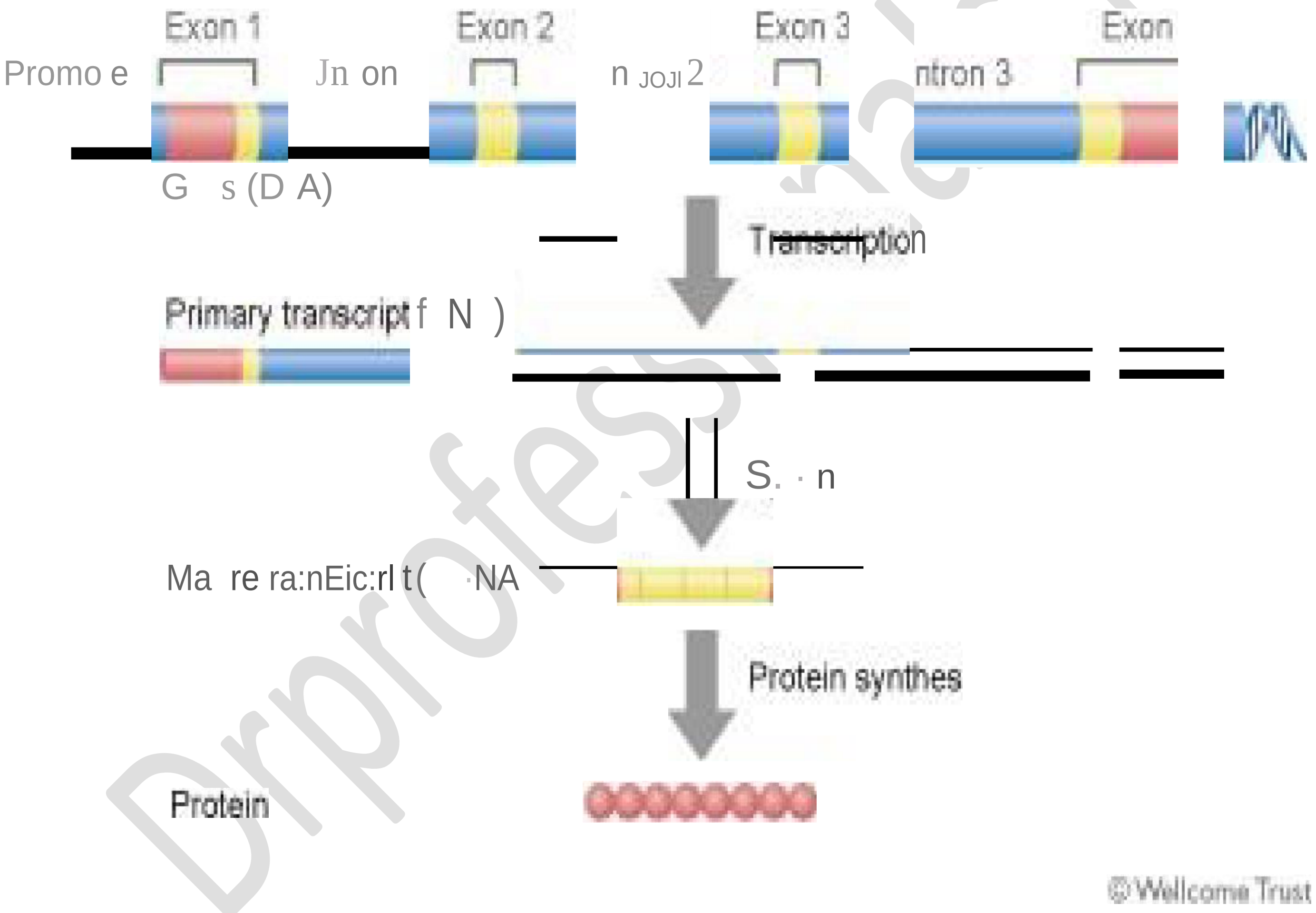
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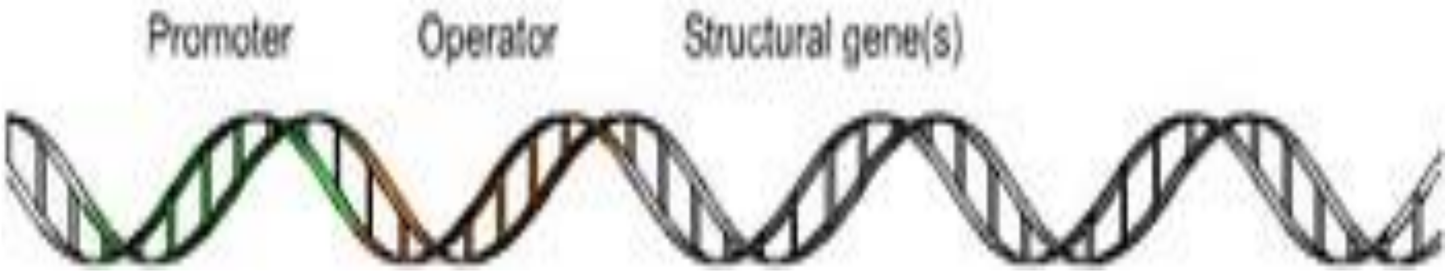
GENE REGULATION IN PROKARYOTES

- **In prokaryotes the primary control point is the process of transcription initiation .**
- **Regulation of gene expression can be done by some operon pathways such as**

1. **Lac operon**
2. **Tryptophan operon**

OPERON

- In genetics, an operon is a functioning unit of genomic DNA containing a cluster of genes under the control of a single promoter.
- Operons occur primarily in prokaryotes but also in some eukaryotes.
- An operon is made up of several structural genes arranged under a common promoter and regulated by a common operator.
- It is defined as a set of closely linked structural genes and the associated control genes (operator and promoter genes) which regulate the genetically metabolic activity..



General structure of an operon

An operon is made up of 4 basic DNA components:

Control genes

Promoter – **a nucleotide sequence that enables a gene to be transcribed. The promoter is recognized by RNA polymerase, which then initiates transcription of structural genes.**

Regulator – **These genes control the operator gene in cooperation with certain compounds called inducers and repressors present in the cytoplasm.**

Operator – **a segment of DNA that a repressor binds to. It lies close to the structural gene.**

Structural genes –**These carry those segments of DNA which carry codes for the synthesis of proteins. Determine the**

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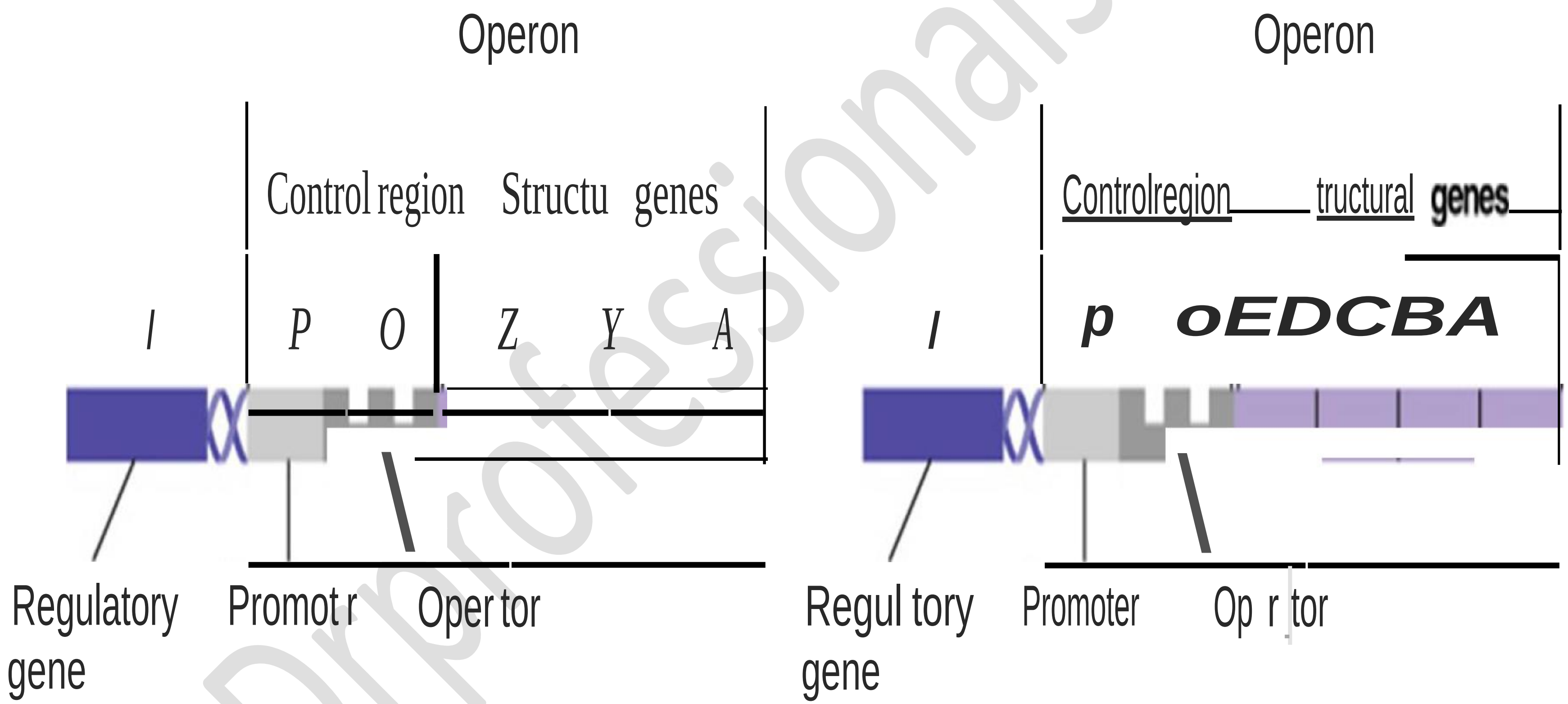
re of polypeptide chain by controlling the sequence amino acids during the synthesis.

- **Repressors** are proteins that suppress transcription of a gene in response to an external stimulus. In other words, a repressor keeps a gene “off.” eg. When tryptophan is not present in the cell, the repressor by itself does not bind to the operator; therefore, the operon is active and tryptophan is synthesized. But when a cell has plenty of tryptophan, it doesn’t need to synthesize more. So the repressor is triggered (by the presence of plenty of tryptophan), thus turning off further synthesis of tryptophan.
- **Activators** are proteins that increase the transcription of a gene in response to an external stimulus. In other words, an activator turns a gene “on.”eg. One example of an activator is the protein CAP. In the presence of cAMP, CAP binds to the promoter and increases RNA polymerase activity. In the absence of cAMP, CAP does not bind to the promoter. Transcription occurs at a low rate.
- **Inducers** are small molecules that either activate or repress transcription depending on the needs of the cell and the availability of substrate.

Inducers basically help speed up or slow down “on” or “off” by binding to a repressor or activator. In other words: they don’t work alone.

GENERAL STRUCTURE OF AN OPERON



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OPERON REGULATION

Operon regulation can be either negative or positive by induction or repression.

- Negative control involves the binding of a repressor to the operator to prevent transcription.
- In negative inducible operons, a regulatory repressor protein is normally bound to the operator, which prevents the transcription of the genes on the operon .
- If an inducer molecule is present, it binds to the repressor and changes its conformation so that it is unable to bind to the operator. This allows for expression of the operon.

The lac operon is a negatively controlled inducible operon, where the inducer molecule is allolactose.

- In negative repressible operons, transcription of the operon normally takes place.
- Repressor proteins are produced by a regulator gene, but they are unable to bind to the operator in their normal conformation. However, certain molecules called corepressors are bound by the repressor protein, causing a conformational change to the active site. The activated repressor protein binds to the operator and prevents transcription

- The trp operon, involved in the synthesis of tryptophan (which itself acts as the corepressor), is a **negatively controlled repressible operon**.

- **With positive control, an activator protein stimulates transcription by binding to DNA.**
- **In positive inducible operons, activator proteins are normally unable to bind to the pertinent DNA.**

When an inducer is bound by the activator protein, it undergoes a change in conformation so that it can bind to the DNA and activate transcription.

- **In positive repressible operons, the activator proteins are normally bound to the pertinent DNA segment.**

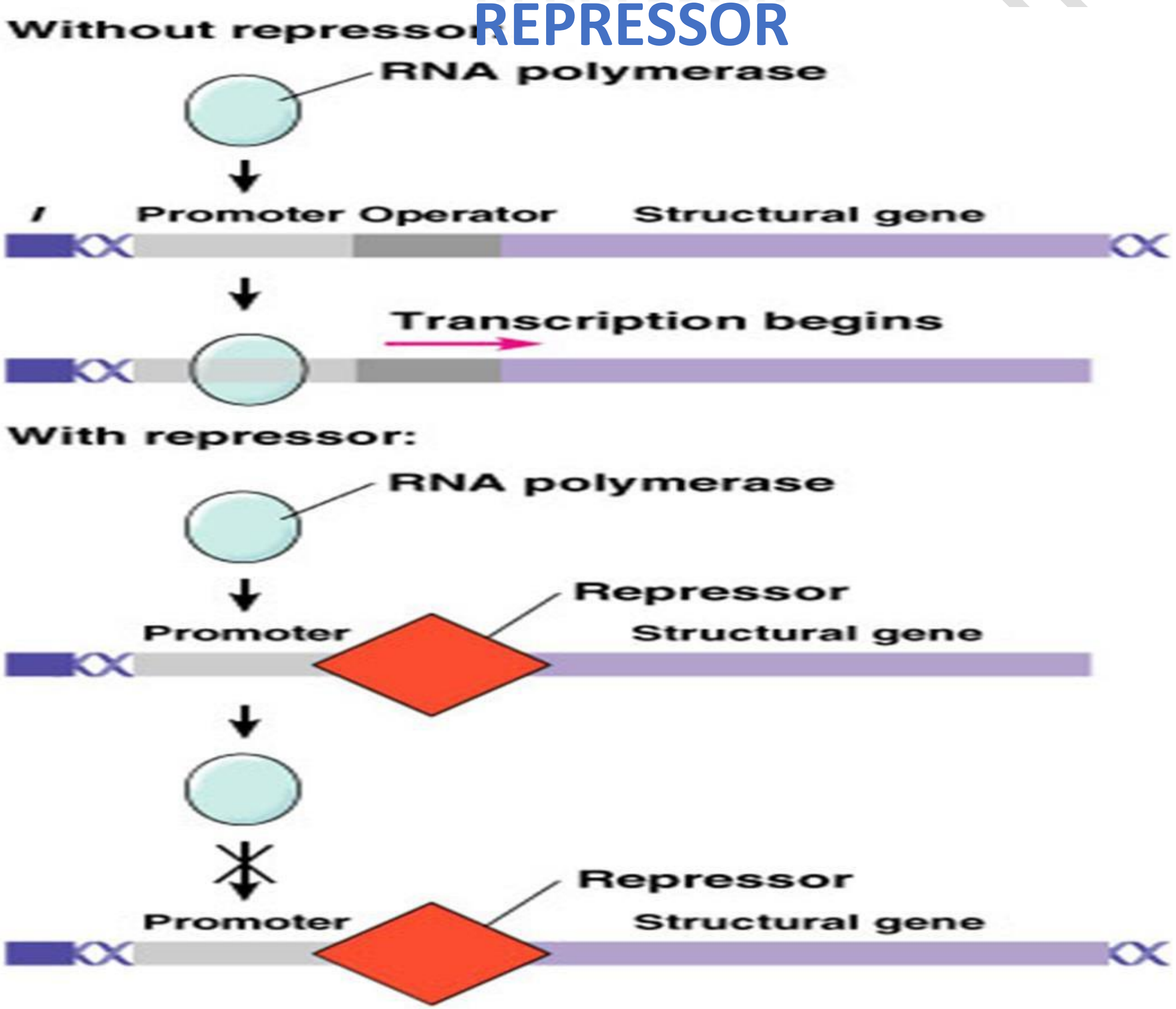
However, when an inhibitor is bound by the activator, it is prevented from binding the DNA.

This stops activation and transcription of the system.

Classification:
1 Lac-operon (catabolic pathway)
2 Try-operon (Repressible)

THE ACTIVITY OF AN OPERON IN THE PRESENCE OR THE ABSENCE OF REPRESSOR

THE ACTIVITY OF AN OPERON IN THE PRESENCE OR THE ABSENCE OF REPRESSOR



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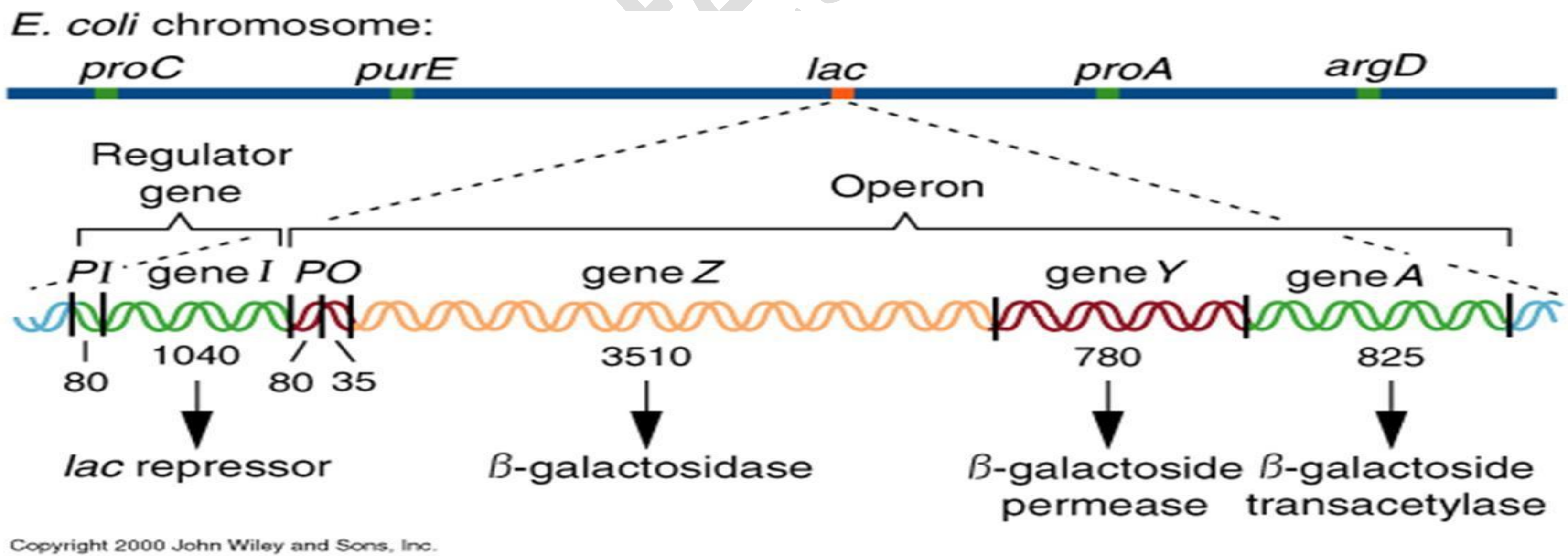
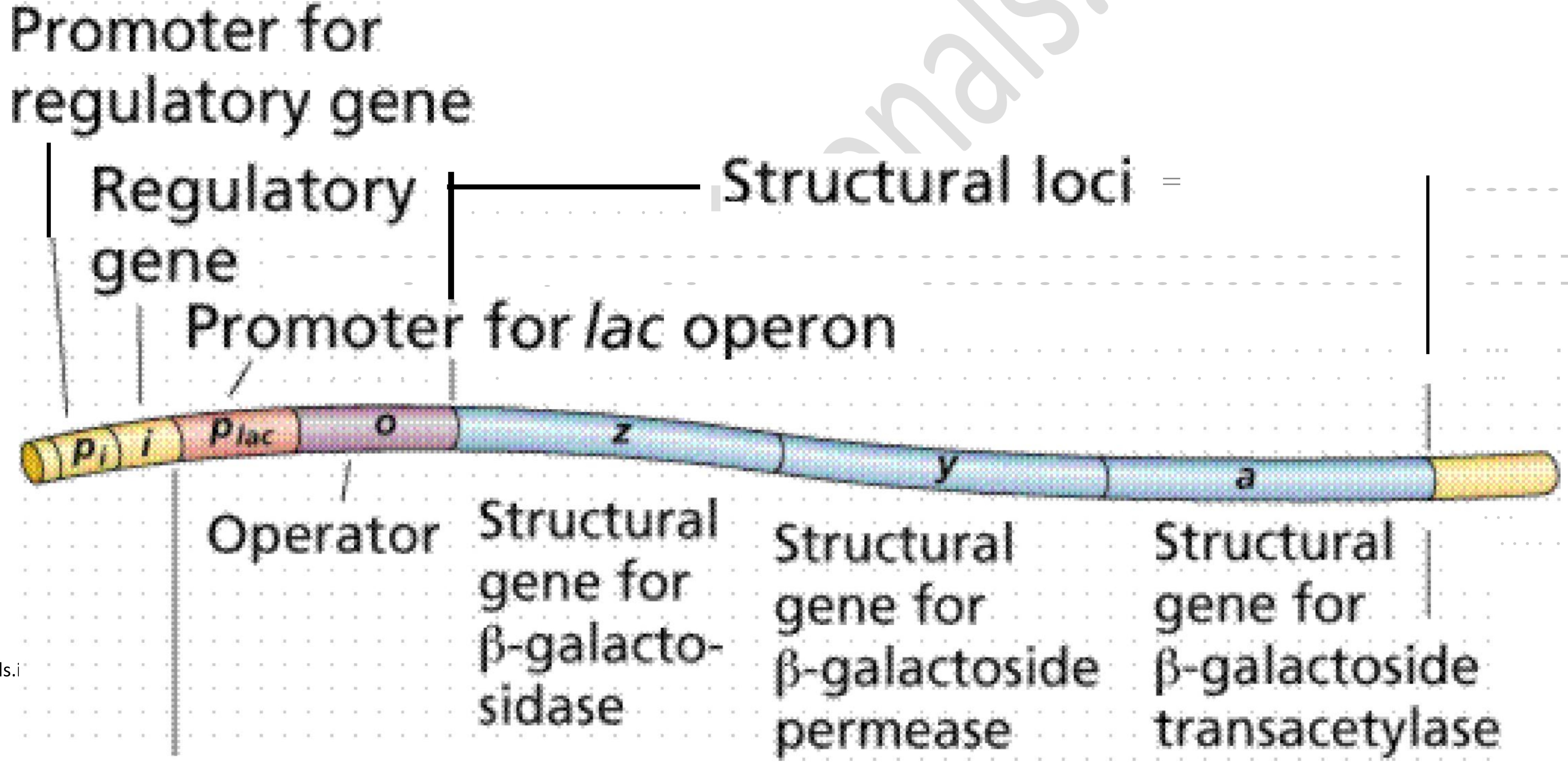
The Lac Operon

- The lac operon of the model bacterium Escherichia coli was the first operon to be discovered and provides a typical example of operon function.
- It consists of three adjacent structural genes, a promoter and an operator.
- The lac operon is regulated by several factors including the availability of glucose and lactose.



lac Operon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Structural
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transacetylase


lac Operon

Components of Lac Operon

Lac Operon Gene	Gene function
Lac I	Constitutive gene synthesizes lac repressor constantly
Lac Z	Gene for β-galactosidase subunit
Lac Y	Gene for Permease subunit
Lac A	Gene for Thiogalactoside transacetylase subunit
Promoter or P	Site for RNA polymerase binding & initiator of transcription
Operator or O	Repressor binding site

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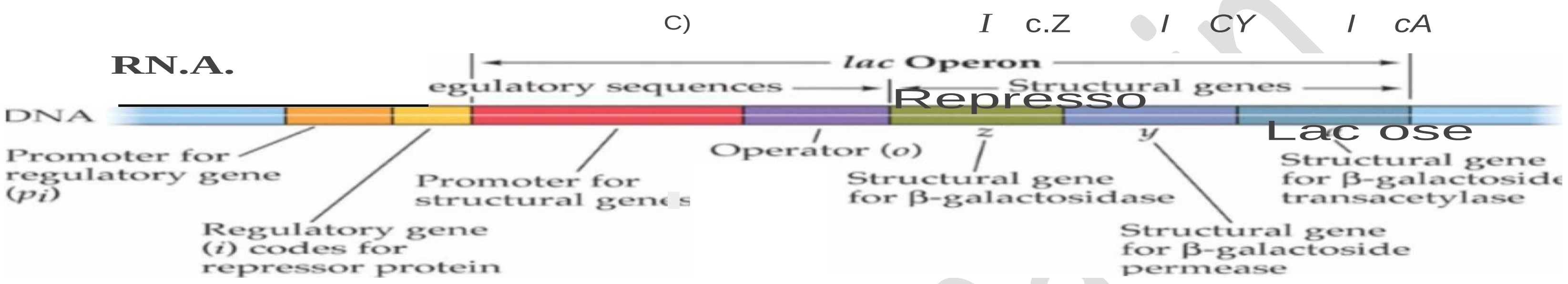
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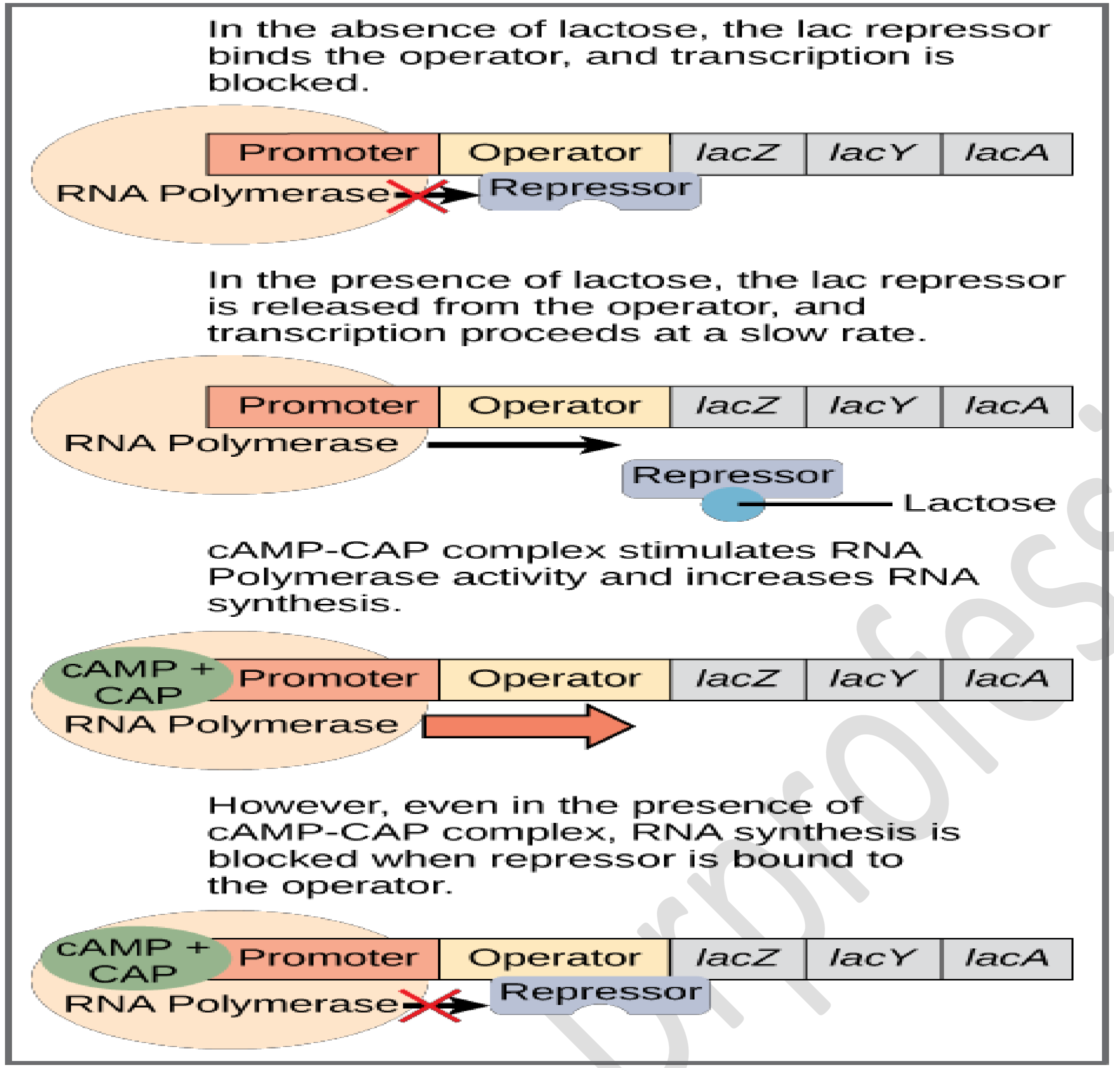
Functioning of Lac Operon:

- In the absence of an inducer- lactose, the regulator gene-I produces a repressor protein which binds strongly to the operator site and prevents its transcription. As a result, the structural genes do not synthesize mRNA and proteins are not formed
- When an inducer-lactose is introduced in the medium, it enters the cells and gets modified in such a way that it binds to the repressor. The repressor now fails to bind to the operator.

The operator is, therefore, free and induces the RNA polymerase to bind to the initiation site on promoter and to transcribe the cistrons into a polycistronic mRNA. This codes for three enzymes for lactose metabolism.

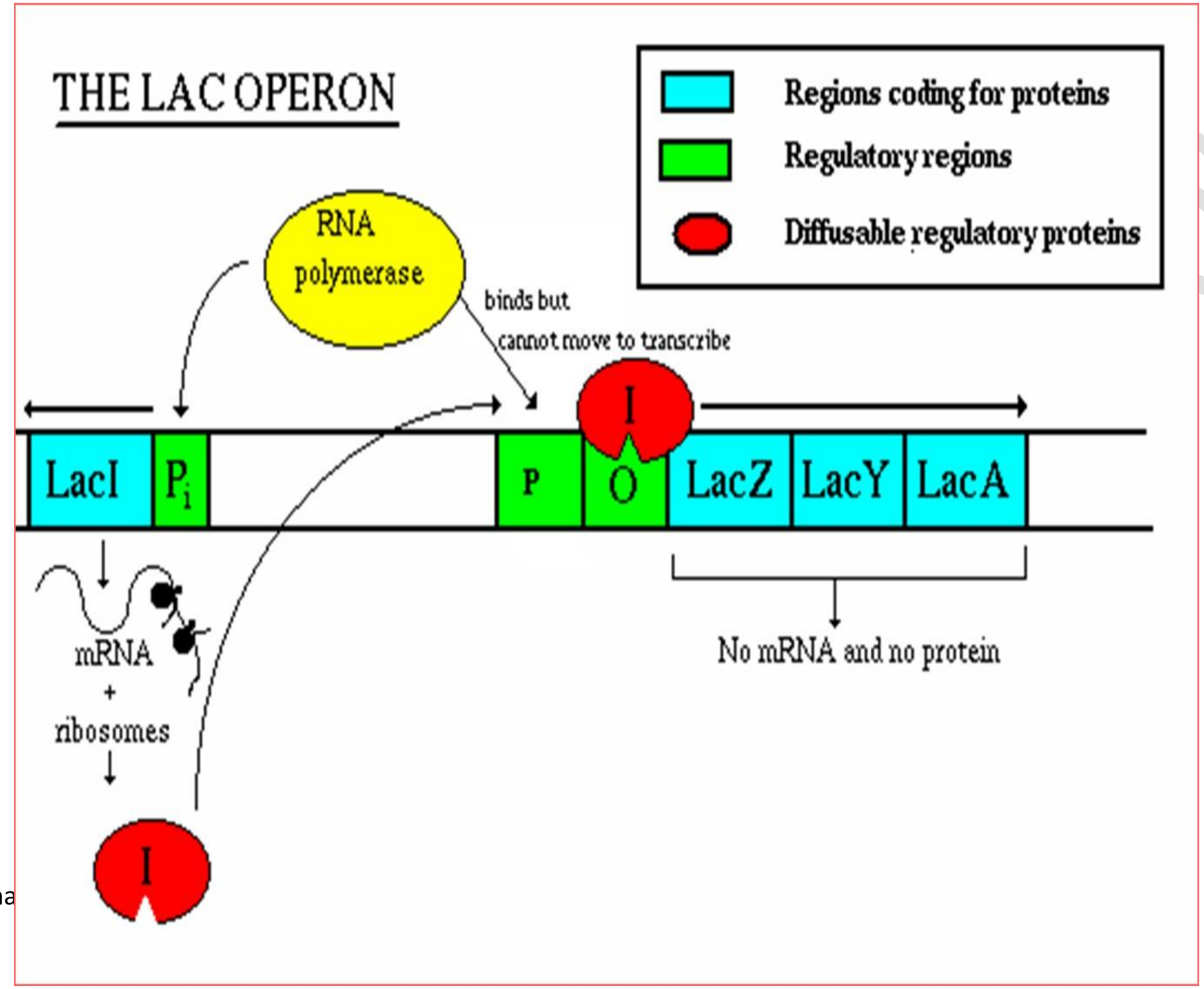
For the *lac* operon to be activated, two conditions must be met:

- First, the level of glucose must be very low or non-existent.
- Second, lactose must be present.
- In the absence of glucose, the binding of the CAP (catabolite activator protein) protein makes transcription of the *lac* operon more effective.
- When lactose is present, it binds to the *lac* repressor and changes its shape so that it cannot bind to the *lac* operator to prevent transcription.
- This combination of conditions makes sense for the cell, because it would be energetically wasteful to synthesize the enzymes to process lactose if glucose was plentiful or lactose was not available.



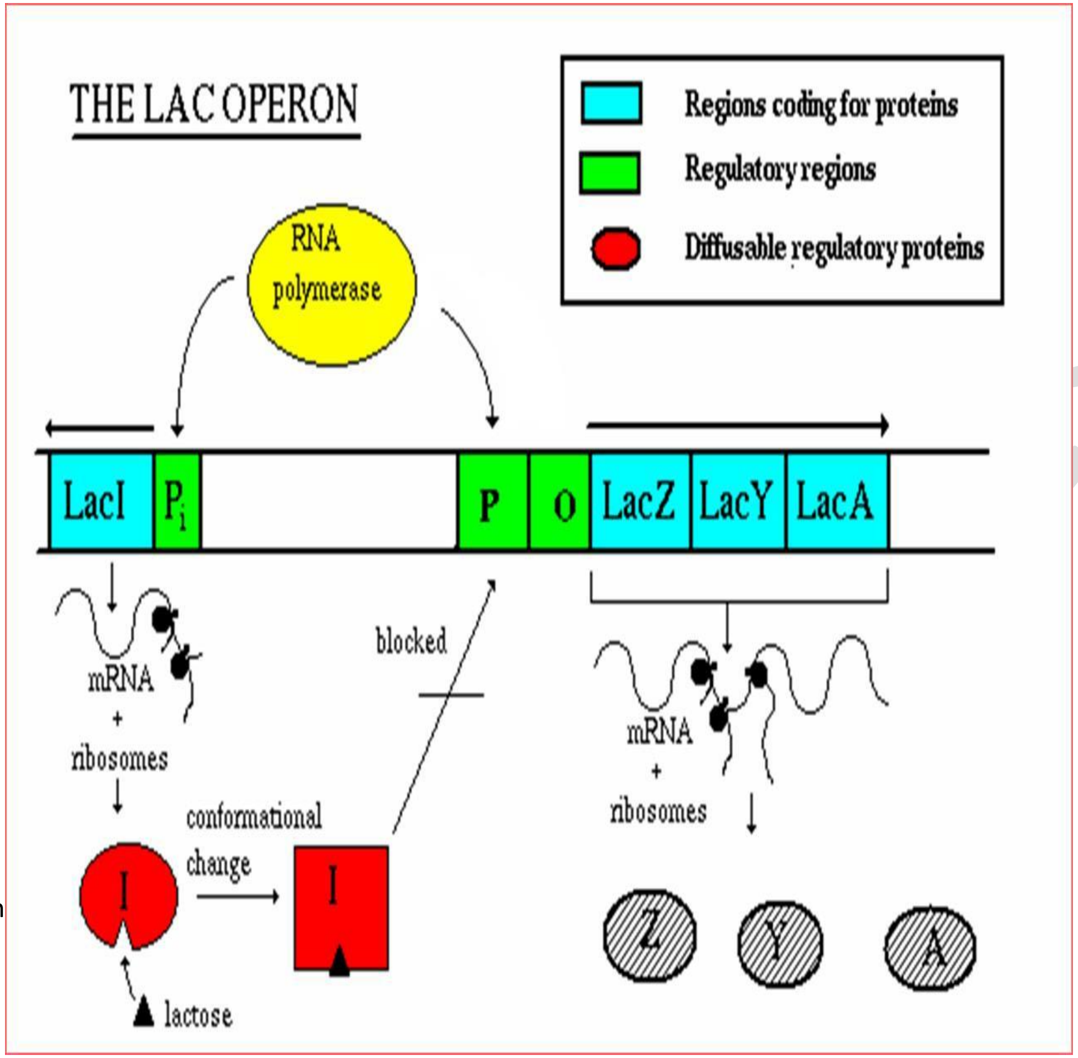
If glucose is present, then CAP fails to bind to the promoter sequence to activate transcription. If lactose is absent, then the repressor binds to the operator to prevent transcription. If either of these conditions is met, then transcription remains off. Only when glucose is absent and lactose is present is the *lac* operon transcribed

Absence of lac operon



No lactose is present in the medium, thus no enzymes will be needed to process lactose. That is why operator is blocked by the repressor

Presence of lac operon



Lactose is present in the medium and enzymes will be needed to process lactose. Thus, lactose gets modified in such a way that it binds to the repressor. The repressor now fails to bind to the operator.

The operator is, therefore, free and induces the RNA polymerase to bind to the initiation site on promoter and to transcribe the cistrons into a polycistronic mRNA. This codes for three enzymes for lactose metabolism.

Activity of an lac operon in the presence or absence of inducer

Lactose, a sugar found in milk, is not always available. It makes no sense to make the enzymes necessary to digest an energy source that is not available, so the lac operon is only turned on when lactose is present