**Operons**

An operon is a group of genes transcribed at the same time.  It is **only** found in prokaryotes.  They regulate biochemical process.   Each operon consists of a promoter, an operator and a regulator whose products function in a common pathway.

The lactose operon or the lac operon is one of the many operons that operates in bacteria.  The lac operon encodes a set of genes that are involved in the metabolism of a simple sugar, lactose.

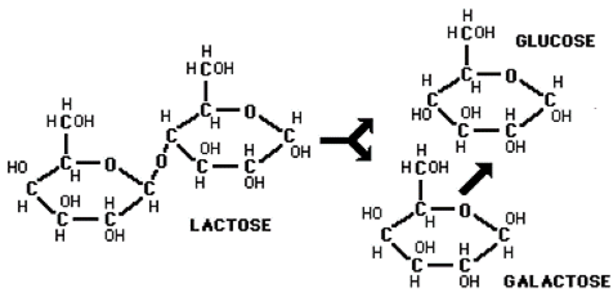



*Figure 1- Lactose is a disaccharide composed of two sugars (galactose and glucose) with a βlinkage between carbon 1 of galactose and carbon 4 of glucose*

The lac operon encodes three proteins (i) **β-galactosidase** - the product of the **lacZ** gene (ii) **lactose permease** - the product of the **lacY** gene and (iii) **lactose transacetylase** -the product of the **lacA** gene.  All these genes are transcribed from a common promoter site.

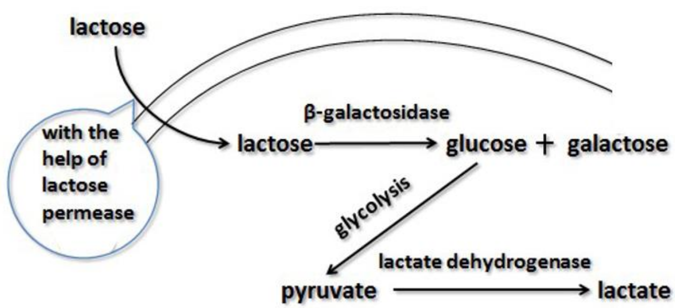



*Figure 2- Activity of β galactosidase and lactose permease in the metabolism of lactose*

Escherichia coli use either glucose or lactose.  There can be four options like:

1. When glucose is present and lactose is absent the E. coli does not produce β galactosidase.

2. When glucose is present and lactose is present the E. coli does not produce β galactosidase.

3. When glucose is absent and lactose is absent the E. coli does not produce β galactosidase.

4. When glucose is absent and lactose is present the E. coli does produce β galactosidase

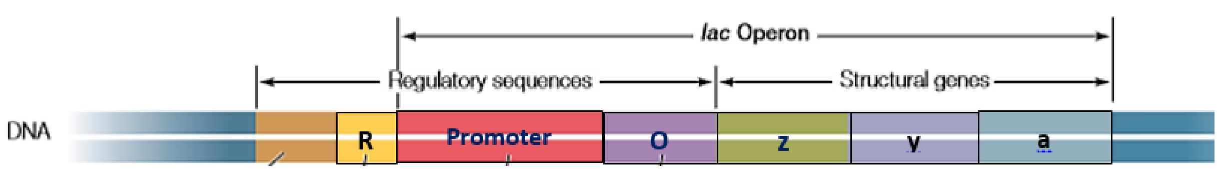
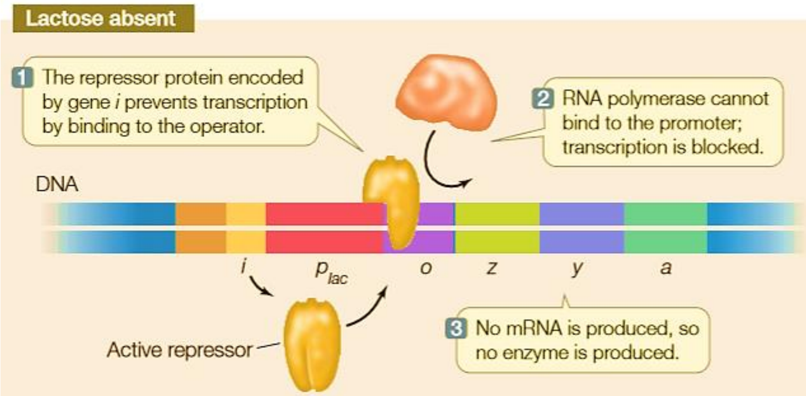


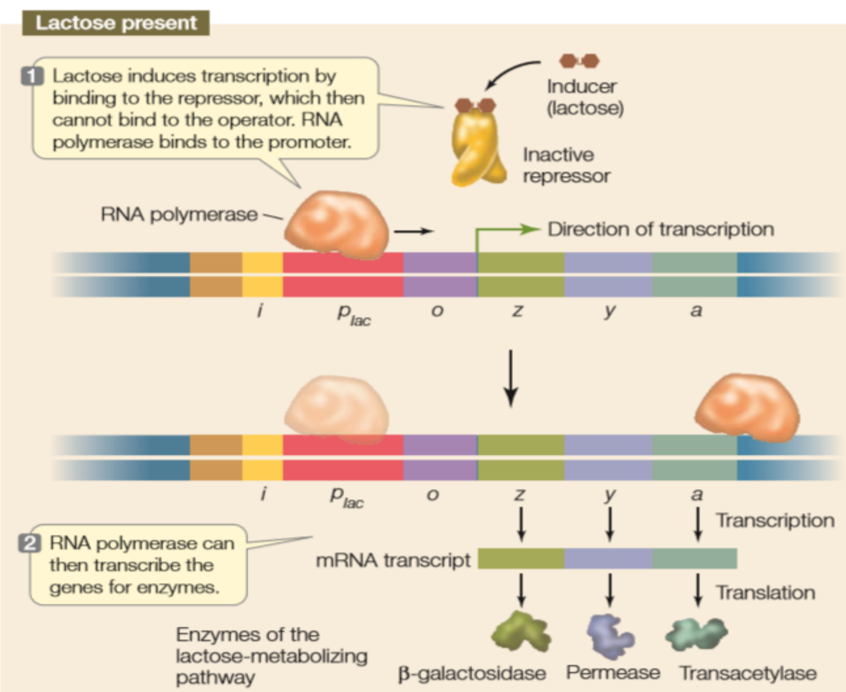

*Figure 3- Lac operon (R- Regulatory gene (i) codes for repressor protein; O- operator)*

## The regulation of lac operon




When lactose is absent, a repressor protein is continuously synthesized. It binds to the operator site of the lac operon. The operator site is located just in front of the three genes of the operon. As a result of repressor binding the RNA polymerase is not able to move forward to the three genes. Therefore the transcription of the genes are blocked. The repressor protein is synthesized from regulator genes

*Figure 4- Repression of lac operon expression in absence of lactose*




When lactose is present, a small amount of a sugar allolactose is formed within the bacterial cell. This fits onto the repressor protein at another active site (allosteric site). This causes the repressor protein to change its shape (a conformational change). It can no longer sit on the operator site. RNA polymerase can now reach its promoter site and transcribes the gene lac Z, lac Y and lac A. As a result, the lactose can be metabolized.

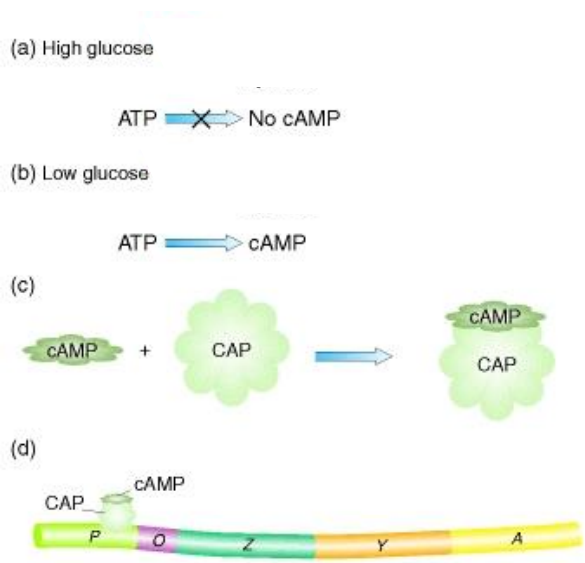
*Figure 5- Activation of lac operon in presence of lactose*

When glucose and lactose are present RNA polymerase can sit on the promoter site but it is unstable and it keeps falling off. For stabilizing RNA polymerase another protein is needed known as the activator protein. The activator protein only works when glucose is absent. In this way E. coli only makes enzymes to metabolize other sugars in the absence of glucose.

| Carbohydrates | Activator protein | Repressor protein | RNA polymerase | *lac* Operon |
|---|---|---|---|---|
| + GLUCOSE + LACTOSE | Not bound to DNA | **Lifted off operator site** | Keeps falling off promoter site | **No transcription** |
| + GLUCOSE - LACTOSE | Not bound to DNA | Bound to operator site | Blocked by the repressor | **No transcription** |
| - GLUCOSE - LACTOSE | **Bound to DNA** | Bound to operator site | Blocked by the repressor | **No transcription** |
| - GLUCOSE + LACTOSE | **Bound to DNA** | **Lifted off operator site** | **Sits on the promoter site** | **Transcription** |

**Catabolite Repression of the lac Operon: Choosing the Best Sugar to Metabolize:**

An additional control system is superimposed on the repressor–operator system. This control system is thought to have evolved because the cell can capture more energy from the breakdown of glucose than it can from the breakdown of other sugars. If both lactose and glucose are present, the synthesis of β-galactosidase is not induced until all the glucose has been utilized. Thus, the cell conserves its energy pool used, for example, to synthesize the Lac enzymes by utilizing any existing glucose before going through the energy-expensive process of creating new machinery to metabolize lactose.




The glucose breakdown product modulates the level of an important cellular constituent—cyclic adenosine monophosphate (cAMP). When glucose is present in high concentrations, the cell's cAMP concentration is low; as the glucose concentration decreases, the cellular concentration of cAMP increases correspondingly. The high concentration of cAMP is necessary for activation of the lac operon. cAMP binds with CAP (catabolite activator protein) to form the cAMP-CAP complex. This complex then binds to the CAP binding site on the lac operon and increases the affinity of RNA polymerase for the lac promoter. In this way, the catabolite repression system contributes to the selective activation of the lac operon.

*Figure 6- The operon is inducible by lactose to the maximal levels when cAMP and CAP form a complex. (a) Under conditions of high glucose, a glucose breakdown product inhibits an enzyme, preventing the conversion of ATP into cAMP. (b) Under conditions of low glucose, there is no breakdown product, and therefore the enzyme is active and cAMP is formed. (c) When cAMP is present, it complexes with CAP. (d) The cAMP–CAP complex acts as an activator of lac operon transcription by binding to a region within the lac promoter.*