Hello Friends and welcome to this presentation on Gene Expression and Regulation. In this module we will be talking about: Gene Expression and Regulation, Induction and Repression and Catabolite Repression. At the end of the presentation you will be able to define terms like gene expression, transcriptional level gene regulation, translational gene regulation. You will be able to compare and contrast between induction and repression. And you will be able to explain catabolite repression. So let's begin with the Central Dogma. According to the Central Dogma, DNA makes RNA and RNA makes protein. So this happens by the process of transcription and translation respectively. This formation of protein from DNA is actually what is gene expression. Expression of the gene can be controlled. It can be controlled by controlling m RNA synthesis. Or it can be controlled by controlling the protein

synthesis.

If control of gene expression is through mRNA synthesis control it is referred to as transcriptional level of control. And if the control is with respect to protein synthesis, then the control is said to be at the translational level. Such a control of gene expression through transcription and translation is referred to as regulation of gene expression. Though transcription and translation are similar in all domains, Bacteria, Archaea and Eukarya, Regulation of gene expression differs in each of these. Today we will be concentrating only on the bacterial regulatory processes and in particular regulation at the transcriptional level. So this regulation happens by induction of enzyme synthesis and repression of enzyme synthesis. In a cell or in a system, there are enzymes which catalyze reactions that are needed by the cell all the time. So these enzymes are functional all the time and they are referred to as housekeeping

enzymes. For example, the enzymes of the glycolytic pathway. And the genes that code for such enzymes are continuously expressed. They have to be continuously expressed so such genes are called as constitutive genes. On the other hand, there are enzymes which are made only when needed. So the expression of these genes, the genes for these enzymes, is regulated. Their expression is regulated. Such enzymes could be inducible enzymes, or they could be repressible enzymes and the genes in turn are called as inducible genes and repressible genes. Let us take a look at inducible enzymes. A very good example of an inducible enzyme is beta galactosidase. The levels of betagalactosidase are found to rise in the presence of effector molecules like lactose or allolactose. Now betagalactosidase is an enzyme which breaks down lactose to give you glucose and galactose. This enzyme is not produced until and unless the substrate that is lactose is present in the medium. When lactose is present in the medium, it is converted into its isomer allolactose. And this allolactose binds to the repressor, inactivates it, and thus induces the gene responsible for the production of betagalactosidase.

Therefore, allolactose is called the inducer and the gene which gets triggered is called the inducible gene. This is the process of induction. So in induction the enzymes are produced only when the substrate is present. And the production of the enzyme requires the presence of inducers. Repressible enzymes, on the other hand. A good example to study repressible enzymes is biosynthesis of amino acids. The enzymes responsible for the biosynthesis of amino acids are said to be under repressible control. Amino acids present in the surroundings inhibit the enzyme responsible for its own biosynthesis. If you look at this illustration, suppose you have a system where there is no amino acid in the medium, then the genes for production of the enzyme for the biosynthesis of the amino acid is expressed, as, the repressor is inactive. Once the enzyme is produced, the amino acid is produced.

So the levels of amino acid in the system increase.

The minute high levels of amino acid are present in the environment, the amino acid acts on the repressor and activates the repressor. Once the repressor is active it inhibits the transcription of those genes responsible for producing the enzyme. Thus, the amino acid itself inhibits the enzyme for its own biosynthesis. It acts as a corepressor, along with the repressor. And the genes which are affected by such a repressor corepressor interaction are called repressible genes. And the phenomena is referred to as repression. If you compare the two that is inducible enzymes and repressible enzymes, We notice that inducible enzymes are required only when the substrate is available. If you recall, we spoke about beta galactosidase which is made only when lactose is present in the medium. Again, it is made only when the inducer allolactose is present in the

medium. And such enzymes are usually seen in catabolic

pathways. On the other hand, repressible enzymes are known to be involved in biosynthetic pathways, and they are not needed if the substance is already present in the medium. as we said earlier, as in the case of amino acids. Thus induction and repression both act to regulate gene expression. Besides these two, let us look at another condition. Another phenomena that happens in E. coli. When E. coli are grown in a medium containing glucose and lactose, it is observed that glucose is utilized first. The enzymes for lactose breakdown are not produced at all, until all the glucose is exhausted. Which means that the expression of the genes coding for the enzymes of lactose breakdown is repressed because of the presence of glucose. This phenomena was referred to as glucose effect because it was felt that it was glucose in the medium that was bringing about repression or inhibition of enzymes of lactose. But later on it was found that there is another protein which regulates enzymes of lactose

breakdown. This protein is the Catabolite Activator Protein which is also called as the cyclic AMP Receptor Protein. And this kind of a regulation is called as catabolite repression. To understand catabolite repression, let us take a look at the catabolite activator protein. So catabolite activator protein or CAP, as it is commonly called or CRP, that is the cyclic AMP receptor protein, exists in two states. An inactive state and the active state. In the inactive form, CAP is unable to bind to the DNA, to the CAP binding site. It has to be activated to bind. And to activate it, we require high levels of cyclic AMP in the system. When cyclic AMP is present in high levels, it is able to bind to CAP and activate it. Active CAP, that is the cyclic AMPCAP complex is now able to bind to the CAP binding site on the Lac operon. It bends the DNA by almost 90 degrees and stimulates transcription of beta galactosidase gene by triggering the binding of RNA polymerase. Now since CAP requires cyclic AMP in high levels.

We notice that cyclic AMP itself is dependent on the levels of adenylate cyclase. And adenylate cyclase is said to be active in the system only when the levels of glucose are low. So when levels of glucose are low adenylate cyclase is active; and brings about the production of cyclic AMP. So cyclic AMP levels rise. And when cyclic AMP levels rise, it can activate CAP. Therefore, the levels of glucose is inversely proportional to the levels of cyclic AMP in a system. Thus, presence or absence of glucose in the system regulates CAP and finally the metabolism of lactose through regulation of the gene for beta galactosidase. If you talk about the presence of the sugar, glucose and lactose. And the absence of the sugar glucose and the absence of the sugar lactose, we have four different combinations possible. Let us take a look at only two. When glucose is present and lactose is absent: Now, since the glucose is present Cyclic AMP levels will be low. We said when glucose is in high concentration, cyclic AMP is low, therefore CAP is not

activated and you will not have transcription of the structural genes. At the same time we said there is no lactose in the medium, so, no transcription. On the other hand when glucose is absent in the medium and lactose is present. So the absence of glucose results in high levels of cyclic AMP, which in turn activates CAP and results in stimulating the structural genes and expression of the operon. At the same time, presence of lactose in the medium acts as an inducer and triggers the gene to produce the enzyme beta galactosidase, again resulting in high levels of gene expression. Thus the Lac operon is regulated by two proteins: CAP and the lac repressor. To summarize therefore, Gene expression is regulated at the level of transcription and translation. Induction is seen in catabolic enzymes, while repression is seen in genes of biosynthetic pathways. And two regulatory proteins CAP and lac repressor exercise dual control in the regulation of lac genes. Thank you.