Transcriptional regulation

Prokaryotes regulate transcription-lac operon:
Lac operon is a negative regulation which means repressors impede access to RNA polymerase to the promoters. The lac operon has two binding sites one cap site before the promoter, other one is for the lac repressor. when cells are provided with lactose and lack glucose. The concentration of cAMP increases in the cell which causes the CAP to bind with the CAP site. The lactose is converted to allolactose by one of the few existing beta-galactosidases. The allolactose acts as an inducer molecule that binds to a specific site on the Lac repressor. Which causes a conformational change that results in dissociation of the repressor from the operator. Release of the operator by lac repressor allows expression of the lac operon genes and leads to a 10^3-fold increase in the concentration of beta-galactosidase. So there is high transcription. When cells are provided with lactose and glucose, the concentration in cells is low so CAP will not bind to the cap site. In this case, although the repressor is released from the operator, there is only a low transcription level. When there is no lactose in the cell, the repressor binds with the operator. There is no mRNA transcription.s.

Regulation of translation in eukaryotic cell
-transcription factor: TF contains at least two domains. One is the DNA-binding domain and the other is the activation or repression domain.

Hormone-dependent gene activation——Upon hormone binding to the Ligand-Binding Domain (LBD) of a dimeric nuclear receptor, a conformational shift occurs that the inhibitor is released a activates the receptor. This activation facilitates the dimerization of the receptor, meaning it pairs with another similar receptor to form a functional unit that can bind to DNA. Once bound to DNA, the activated dimeric receptor, functioning as a transcription factor (TF), can regulate the transcription of adjacent genes, leading to altered gene expression in response to hormonal signals. This mechanism is essential for the precise control of gene activity in different tissues, reflecting the complex interplay between hormones and gene regulation.

-Tissue-specific gene expression is when genes are turned on only in specific cell types to perform unique functions. This is regulated by DNA sequences like enhancers and promoter-proximal regions that control when and where a gene is expressed. Enhancers are binding sites for proteins that increase the likelihood of transcription, while promoter-proximal regions are close to the gene's start site and help in recruiting the transcription machinery. These elements work together to ensure that a gene's expression pattern matches the functional needs of the tissue.

DNA-methylation: promoter hypermethylation acts to silence genes. In contrast, promoter hypomethylation is associated with active genes. Methyl groups can physically impede the binding of transcription factors. There is a CpG island which is commonly found in 5’ regions of genes it plays an important role in DNA methylation. CpG islands are genomic regions rich in CG dinucleotides that are often located near gene promoters and remain typically unmethylated to ensure active transcription of nearby genes; however, their methylation can lead to gene silencing, which is recognized by Methyl-CpG-binding proteins to bind with methyl CpG binding domains(MBD) that can read this epigenetic change and influence gene expression either directly or through the recruitment of other effector proteins.

Maintenance methylation is a critical cellular process for preserving the methylation pattern of the DNA during cell division. DNA Methyltransferase 1 (DNMT1) is the enzyme responsible for this process and is ubiquitously expressed in mammalian cells. It ensures that the methylation is

faithfully copied from the parent strand to the daughter strand after DNA replication, allowing the cell's epigenetic inheritance and maintaining its identity and function across generations of cells.

De novo methylation is initiated by enzymes such as Dnmt3a and Dnmt3b, which are responsible for establishing new methylation patterns on DNA during early embryonic development. This process follows the erasure of previous methylation marks post-fertilization, allowing the embryo to reset its epigenetic state. Sequence-specific DNA binding proteins guide these enzymes to their target sites, ensuring that methylation occurs in a precise and regulated manner, which is essential for proper development.

Genomic imprinting is an epigenetic mechanism established during gamete formation and early embryonic development, dictating that only one allele of a gene is active depending on its parental origin. For instance, the H19 gene is actively expressed from the maternal allele, while its paternal counterpart is imprinted, or silenced. In contrast, the gene for Insulin-like growth factor 2 (Igf2) is expressed from the paternal allele, with the maternal allele being imprinted and suppressed. This selective expression is crucial for developmental regulation, as Igf2 plays a key role in growth, and H19 influences various developmental pathways. The timing of these imprinting events ensures the orchestrated expression of growth and developmental genes in the embryo.

Two regulatory sequences are critical for the differential expression of these genes: an enhancer (downstream from the H19 gene) and an insulator (called the imprinting control region [ICR], located between the H19 and Igf2 genes). The enhancer (when bound by activators) can, in principle, activate either of the two genes. The enhancer cannot activate the Igf2 gene on the maternal chromosome because on that chromosome, the ICR binds a protein, CTCF, that blocks activators at the enhancer from activating the Igf2 gene On the paternal chromosome, in contrast, the ICR element and the H19 promoter are methylated. In that state, the transcriptional machinery cannot bind the H19 promoter, and CTCF cannot bind the ICR. As a result, the enhancer now activates the Igf2 gene. The H19 gene is further repressed on the paternal chromosome by the binding of MeCP2 to the methylated ICR. This, as we have seen, recruits histone modifiers that repress the H19 promoter.

Methylation of both alleles means that expression of Igf2 and repress H19 maternally and paternally will cause a Beckwith-Weidemann Syndrome (BWS). Failure of methylation of both alleles means that the repression of Igf2 and expression of H19 in maternally and paternally. this will cause Beckwith-Weidemann Syndrome (BWS)