An overview of epigenetics

Epigenetics is studying of the mechanism by which all the mitotically and meiotically changes in the pattern of inherited gene expression occur in the lack of modifications or alterations in the nucleotide composition of a specified gene. The controlled of genes are activated or repressed with no change in DNA epigenetically.

Important for studying “ Epigenetics”

The most important permissive and suppressive factors in controlling the expressed genome via gene transcription are epigenetic modifications of chromatin and DNA. The methylation of DNA and the posttranslational modification of histone proteins in chromatin are the two main epigenetic mechanisms, which are regulated by distinct, but coupled, pathways. It is apparent that a central regulator of cellular development and activation is the epigenetic state. Human pathologies, including in inflammatory and neoplastic disorders suggests a key role for epigenetics in. The profound effects on the expression of specific genes by epigenetic modification can be influenced by environmental factors and nutritional factors throughout life. These may be passed on to following generations with potentially harmful effects. Alterations of epigenetic profiles are associated in many cancers that leading to altered genes expression involving in cell development or differentiation. The epigenetic dysregulation proposed as a potential explanation in neoplastic and autoimmune diseases increase in frequency with increasing age. Some studies in monozygotic twins support of this hypothesis, revealed increasing epigenetic differences with age. In key inflammatory response genes, differences in methylation status of CpG sites, gene silencing, and other epigenetic regulatory mechanisms have been

observed. In the pathogenesis of common human diseases, the importance of the epigenetic modification of genome is possible to be as important as that of traditional genetic mutations. The understanding of this area of biology is possible to rise quickly in the near future supporting by our advances in technology.

Types of “ Epigenetics”

Epigenetic events have been identified and classified into several different types. These are relating to remodeling of chromatin structure as a way to control gene expression with the role of DNA methylation in these structural alterations. The most important epigenetic event in controlling and importantly maintaining the pattern of gene expression during development is likely to be the DNA methylation. Besides, acetylation, methylation phosphorylation, ubiquitylation and sumoylation of histone proteins are another DNA modification events knowing to effect epigenetic phenomena.

Histone modification

Gene transcription in mammalian cells take place in the chromatin context (a nucleosome composed of 2 molecules each of histones H2A, H2B, H3, and H4 wrapped around by 147 base pairs of DNA) however it does not occur on naked DNA. As a consequence, modifications to the chromatin and the histones themselves impact gene expression.

A globular C-terminal domain and an unstructured N terminal tail are composed to form the core histones. The histone proteins occur primarily on the N-terminal tail although a variety of modifications occur throughout the

histone protein. Several of these alterations are enzymatically reversible. Acetylation, phosphorylation, ubiquitination, and methylation are included in modifications of histone H3 and H4 tails.

Normally, the genetic importance of all these modifications is not well-understood; however transcription, DNA repair, DNA replication and chromatin condensation are known to be influenced by these modifications. Combinations of histone modifications can be used to predict changes in gene expression testing by a “ histone code” hypothesis. For instance, transcriptionally active DNA is associated with lysine acetylation, whereas the special effects (i. e., repression or activation of transcription) of arginine and lysine methylation differ by number of methyl groups, location of the amino acid and nearness to a gene promoter.

Histone acetylation involved the histone acetyl transferases (HATs) which are co-activators rather than DNA-binding moieties underlines require for regulation, flexibility with alternative strategies in modifiable chromatin and the basal transcriptional machinery. Histone acetyl transferases complexes have power over classical co-activator activity, i. e., they promote TATA box binding protein (TBP) or other common transcription factor associated with the basal promoter. A lot of of the HATs are constituents of large multi-subunit complexes are recruited to the promoters through interaction with DNA-bound activator proteins.

Histone phosphorylation involving Serine of histone H3 has also appeared as a significant modification, including in chromosome condensation and transcriptional activation during mitosis. Since transcription activation and

chromosome condensation are predictable to involve differing physical alterations of chromatin, that is, opening of chromatin during transcription and closing of chromatin throughout mitosis), that the same alteration is concerned in both routes is conditional support for the alterations-as-binding surfaces more willingly than direct alteration of chromatin.

Histone ubiquitination is fusion the ranks of essential modifications. Primary, Lysine 120 contained by the histone H2B carboxy-terminal tail is used as a substrate for the Rad6 ubiquitin ligase. This modification is important to meiotic and mitotic growth, even though it is not clear up till now whether it is involved in transcription. Secondly, the TBP-associated complex TFIID contains TafII250 has been demonstrated to have histone H1 ubiquitination action; it may be involved in transcription by adding to its long list of enzymatic actions (Protein kinase and HATs actions).

Histone methylations are divided into two types, targeting either lysine or arginine residues. Histone methylases are recruited to promoters as co-activators or depressors whereas histone arginine methylation is involved in gene activation.

Histone lysine methylation is catalysed by a cluster of enzymes which are called histone methyl transferases (HMTase). The responsibility of the SET domain family of lysine HMTase involved in hetero-chromatic gene silencing is especially exhilarating. The cysteine-rich regions border this domain. There come out to be complicated interaction between diverse modifications on different sites of the histone tails of H3 and H4, several of which work

opposing to regulate the alteration from an inactive chromatin state to an active one.

DNA Methylation

The alteration of DNA by adding of a methyl group can change the chromatin by resulting to a more compact structure, and thus silencing gene expression. The informations of how DNA methylation influences gene transcription are slowly being determined, but it is obvious that the basic mechanism works by modifying protein-DNA interactions. Methylation shows to control the gene expression via affecting the interactions with DNA of both specific transcriptional factors and chromatin proteins. The binding of protein factors can interfere by methylation at specific sites, involving several recognized to be necessary for RNA synthesis.

Methylation of adenine and cytosine bases causing DNA modification. Enzymatically modification of DNA at the 5th carbon position of cytosine (C) residues to 5-methylcytosine is preponderantly in the context of CpG dinucleotides. For lots of genes, in the 5′ regulatory region methylation is adequate for inhibition of gene activity.

Furthermore, gene re-activation can be induced by treatment of cells with 5-azacytidine, a potent demethylating agent. Removal of methyl group from the DNA can activate the cis-acting sequences which can lead to re-activation of the gene sequence.

Chromatin remodeling and DNA methylation

Chromatin remodeling proteins play an important role in the control of gene expression despite the fact that DNA methylation and histone modifications

are also clearly important for this process. For instance, the gene expression, replication, DNA repair, and recombination require the SNF2 family of chromatin remodeling proteins acts in these various cellular processes. SNF2 family members include 7 helicase domains however not demonstrate separating activity of helicases in the classical strand. As an alternative, these proteins modify the structure of chromatin causing disruption of the histone and DNA contacts by utilizing of ATP. In the background of gene expression, SNF2 family members play a role to function in transcriptional repression in addition to activation depending on the SNF2 factors and the proteins by which it works together.

Applications of “ Epigenetics”

Recent information has recognized a relationship between epigenetic processes and disease while epigenetics plays a critical role in the maintenance, control and regulation of gene expression causing many differentiation states of cells in an organism. Most important is the relation among epigenetics and cancer which has been recommended to be a causative factor in almost half of all cancers. Changing in the methylation condition of tumor suppressor genes (TSG) and the progression of many types of cancers has been demonstrated.