Editorial Note Volume
2020 | Volume 6 Issue.3

[ISSN: 2472-1158]

Journal of Clinical Epigenetics

Extended Abstract

An ultimate theory on Epigenetics in Mammalian Reproduction with Emphasis on Human Reproduction

Kaur K

Centre For Human Reproduction, 721, G.T.B. Nagar Jalandhar-144001, Punjab, India

Introduction:

Epigenetic mechanisms play a fundamental role in controlled development and gene expression in different types of cells of an organism, carrying the same genomic DNA sequence. These mechanisms control differences in the gene expression that are mitotically heritable although not altering the primary DNA sequence [1]. A large number of proteins write, read or erase particular epigenetic modifications and thus define where and when the transcriptional machinery can access the primary DNA sequence to drive normal growth and differentiation in the developing embryo along with the fetus. Different type of epigenetic marks work in concert to drive appropriate gene expression. These are DNA methylation at CpG dinucleotides, covalent modifications of histone proteins, noncoding RNA's (ncRNA) along with other complementary mechanisms contributing to higher order chromatin organization, within the cell nucleus. There are two special examples e.g., chromosome inactivation and genome imprinting, which explains how 2016 Vol. 2 No. 4: 20 Journal of Clinical Epigenetics ISSN 2472-1158 2 This article is available in: http://www.clinical-epigenetics.imedpub.com/ important are the epigenetic mechanisms in regulating correct patterns of gene expression during early development chromosome inactivation basically is an example of dosage compensation in females leading to monoallelic expression of a huge number of X linked genes in female. Genome imprinting is a process in which special genes carrying epigenetic marks from parents of origin have the capacity for getting monoallelic parent of origin specific cell types at specific times of development. In germ cells in development as well as in embryo, there is genome wide reprogramming which is responsible for erasure as well as reestablishing of the correct epigenetic patterns. In contrast to these naturally occurring processes, the processes used in induced pluripotent stem cells from somatic cells are quite different [2], reviewed by Huang et al[3]. Changes in epigenetics can occur by different mechanisms and lead to infertility and imprinting disorders. Genetic as well as environmental factors impact genetic marks, which develop phenotypic differences varying from normal variation to human disease [4]. Both environmental factors e.g., starvation as well as artificial reproductive technologies (ART) have been shown to affect the epigenome of the embryo e.g., of the epigenetic changes which are associated with maternal starvation in fetal life can remain throughout adulthood, contributing to late onset disorders e.g., CVS disorders and type 2 diabetes mellitus [5-9].

This work is partly presented at 12th International Conference and Expo on Proteomics and Molecular Medicine November on 26-28, 2018 held at Dublin, Ireland

Editorial Note Volume
2020 | Volume 6 Issue.3

[ISSN: 2472-1158]

Journal of Clinical Epigenetics

Extended Abstract

Epigenetic marks

There is lot of crosstalk between various epigenetic marks like DNA methylation, histone modifications, NC RNA to regulate epigenome [10-11]. The ENCODE project, was a large collaborative one, which was developed to define all of the functional elements in the human genomes, got published recently having big datasets regarding histone modifications, transcription etc. These data point to both global as well as regional changes which overlap regarding epigenetic features, which in combination regulate gene expression [12].

DNA methylation

DNA methylation is one of the most studied mechanisms [13]. Methylation is associated with gene silencing through binding of methylation sensitive DNA binding proteins and or by interacting with various modifications of histone proteins, which modulate access of gene promoters to transcriptional machinery [14]. Basically DNA methylation in eukaryotic species involves the transfer of a methyl group to the cytosine of the CpG dinucleotide.

Histone modifications:

Chromatin has a basic unit which is made up of an octamer of histone proteins, 2 each of H2A, H2B, H3 and H4, DNA wraps around this core which gives stability to the structure along with capacity to regulate gene expression. Each core histone within a nucleosome has a globular domain along with a very dynamic N-terminal tail extending from the globular domain. They have tails which can cause a number of post translational modifications, which induce acetylation, methylation, phosphorylation, ubiquitylation, sumoylation. ADP and ribolysation proteins isomerization, citrullization, butyration, propionylation, and glycosylation [15]. 11 histone post translational modifications, were analyzed in the ENCODE project data, which includes acetylation along with methylation which mark active as well as regressive chromatin, besides modifications which were associated with transcription. They identified different chromatin stages which induced an active, bimodal, and inactive, each of which has different functional properties [15]. Bimodal data in which a combination of active and repressive marks are there, in the chromatin, of the promoter region of the gene, helps in reprogramming changes in gene expression which might be expected during early development, when differentiation and specification occur [16].

Regulatory ncRNAs

Eukaryotic gene transcripts, upto75% of genomic DNA, roughly 3% of these transcripts encode for proteins, of which main are ncRNAs, which are classified based on their size and function [12,15,17]. They include small interfering RNA (Si RNA), micro RNA (miRNA) and long noncoding RNA (lncRNA), which have important roles in gene expression, regulation at various levels, like transcription, degradation of mRNA, splicing and translation [18]. Si RNA's are double stranded RNA (dsRNA), which

This work is partly presented at 12th International Conference and Expo on Proteomics and Molecular Medicine November on 26-28, 2018 held at Dublin, Ireland

Editorial Note Volume
2020 | Volume 6 Issue.3

[ISSN: 2472-1158]

Journal of Clinical Epigenetics

Extended Abstract

mediates posttranscriptional silencing, which is in part done by inducing heterochromatin to recruit histone deacetylase complexes [19]. MiRNA are class small 18-24 nucleotides in length [20-22]. Linc RNA, a subset of lncRNA shows high conservation across different species. They have been shown to guide chromatin modifying complexes to specific genomic loci establishment of and participating in cell types-specific epigenetic states. In embryonic development, especially by lncRNA regulated by the pluripotent transcription factors like OCT4 and NANOG facilitate cell lineage specific gene expression [23]. They also play an important role in development processes of X chromosomal inactivation and genome imprinting [24]. The Role of long noncoding RNA (lncRNA) in dosage compensation In species with genetic sex determination such as XX female, XY male system in mammals and in the ZW female; ZZ male system in birds, males and females have a difference in sex chromosome-linked gene dosage which has resulted in the evolution of dosage compensation mechanism in mammals which is realized by the inactivation of one of the X chromosomes through coating by a lncRNA called Xist (Xinactive specific transcript). The 19 kilobase long transcript Xist is only transcribed from inactive X chromosome and coats hundreds of genes. Prior to inactivation an lncRNA that is antisense to Xist called Tsix is down regulated from one of the X chromosomes resulting in the Xist and inactivation of the X chromosome. On the active X, the maintenance expression of Tsix prevents the full-length Xist expression and X linked gene expression is unaffected (reviewed by Moran [25]). This phenomenon on dosage compensation in mammals is clearly regulated by lncRNAs. But in other groups such as birds there is no inactivation of one sex chromosome of the homogametic sex.

Results:

However there is potential involvement of lncRNAs in dosage compensation in chicken as well. Chickens and other birds have a ZZ male, ZW female sex chromosome system. 2016 Vol. 2 No. 4: 20 Journal of Clinical Epigenetics ISSN 2472-1158 © Under License of Creative Commons Attribution 3.0 License 3 The Z-linked transcription factor gene DMRT1 is thought to play a role in avian sex determination by directing testis development in Zz embryos. Overexpression of DMRT1 induces the male specific genes HEMGN, SOX9 and AMH (Figure 1) [26]. MHM is a 2.2 kilobase sequence absent in other birds and MHM is located within a region of Z chromosome which corresponds to hyper acetylation of histone H4 which is associated with increased gene expression or second hypothesis MHM may regulate by in male cells ZZ MHM is hyper methylated and transcriptionally silent, whereas in female cells Z which is hypo methylated and transcribed. Being near DMRT1, it is suggested it may influence to dampen DMRT1 in female cells, by MHM lncRNA coating the chromosome adjacent to DMRT locus, inducing local chromatin conformational changes which may interfere by TF binding [2]-7further reviewed by Rastetter et al. Special Types of Epigenetic.

This work is partly presented at 12th International Conference and Expo on Proteomics and Molecular Medicine November on 26-28, 2018 held at Dublin, Ireland

Editorial Note Volume
2020 | Volume 6 Issue.3

[ISSN: 2472-1158]

Journal of Clinical Epigenetics

Extended Abstract

Conclusions:

Basically epigenetic mechanisms control development and regulate gene expression in various types of cells of the organism, each carrying similar DNA sequence. In simple language, nucleotide of DNA are letters of the complicated text and these epigenetic labels or marks are the spaces, punctuations, sentences, paragraphs and styles which gives meaning to this complicated text. Here we have tried to discuss the epigenetic markers like DNA methylation at CpG dinucletotide, covalent modifications of histone proteins and details of noncoding RNAs including long ncRNAs, miRNA. Besides importance of lncRNAs has been discussed in dosage compensation in X linked genes with role of Xi and further the value of genome imprinting in ART and various disorders like BWS, RSS or both. Further role of environmental stressors in stresses. Role of famines in both Chinese as well as Dutch famines highlights immediate changes [3,6,156] and effects on future generations [171,172]. Epigenetic information can be inherited through the mammalian germ line and represents a plausible Tran's generational carrier of environmental information. Carone et al. carried out expression 2016 Vol. 2 No. 4: 20 Journal of Clinical Epigenetics ISSN 2472-1158 © Under License of Creative Commons Attribution 3.0 License 9 profiling screen for genes in mice that responded to paternal diet. Offspring of males fed a low protein diet exhibited increased hepatic expression of many genes involved in lipid and cholesterol biosynthesis and decreased levels of cholesterol esters, relative to the offspring of males fed a control diet. Epigenomic profiling of offspring livers revealed numerous modest 20% conjugates in cysteine methylation, depending on paternal diet including reproductive changes in methylation over a liker or enhancer for the key lipid regulator para. These results in conjunction with recent epidemiological data indicate that paternal diet can affect cholesterol and lipid metabolism in offspring and define a model to study environment reprogramming in the human genome [173]. Environmental pollutants and medications may affect fetal epigenetic marks e.g., is in choline intake in pregnancy increased placental promoter methylation of cortisol regulation genes CRH and NR3I leading to improved stress response in children by lowering cortisol levels in H-P-A axis. Thus future of epigenetics research lies in understanding the effects of interaction of epigenetics and environment emphasis on fetal programming, understanding and uncovering role of medicine and nutrition and assesses risk for adult onset disease.

This work is partly presented at 12th International Conference and Expo on Proteomics and Molecular Medicine November on 26-28, 2018 held at Dublin, Ireland