World Journal of Pharmaceutical Science and Research
www.wjpsronline.com
Review Article
ISSN: 2583-6579
SJIF Impact Factor: 5.111
Year - 2025
Volume: 4; Issue: 2
Page: 64-73

A STUDY ON DIFFERENTIATED OF EPIGENETICS AND GENETICS

Masna Ramya*

Assistant Professor, UCT, Osmania University, Tarnaka, Hyderabad, Telangana.

Article Received: 21 January 2025 | | ***Article Revised: 10 February 2025*** | | ***Article Accepted: 03 March 2025***

***Corresponding Author: Masna Ramya**
Assistant Professor, UCT, Osmania University, Tarnaka, Hyderabad, Telangana.
DOI: https://doi.org/10.5281/zenodo.15109121

How to cite this Article: Masna Ramya (2025). A STUDY ON DIFFERENTIATED OF EPIGENETICS AND GENETICS. World Journal of Pharmaceutical Science and Research, 4(2), 64-73. https://doi.org/10.5281/zenodo.15109121

ABSTRACT

Epigenetics refers to heritable phenotypic changes that do not alter the DNA sequence but arise from modifications in chromatin structure. These modifications, including histone alterations and DNA methylation, shape the epigenetic profile, influencing cell memory, fate, and mammalian development. Unlike the static genetic code, the epigenetic code is dynamic, varying across tissues and over time due to aging, disease, or environmental factors. Ongoing research explores the interplay between histone modifications, DNA methylation, and RNA interference in contexts such as cancer, X chromosome inactivation, and genomic imprinting.

KEYWORDS: Epigenetics, chromatin modifications, DNA methylation, cell fate, cancer.

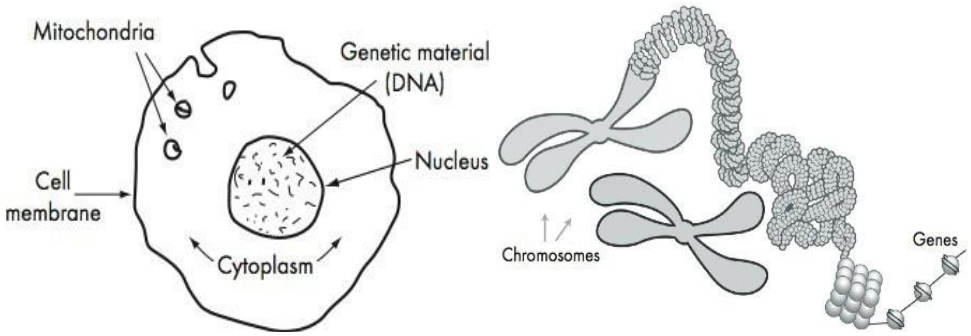
INTRODUCTION

Epigenetics is the study of heritable changes in the phenotype of a cell or organism that are not encoded in the DNA of the genome. The molecular basis of an epigenetic profile arises from covalent modifications of the protein and DNA components of chromatin. The epigenetic profile of a cell often dictates cell memory and cell fate and, thus influences mammalian development. The epigenetic code is hypothesized to be the combined effects of histone modifications and DNA methylation on gene expression. While the genetic code for an individual is the same in every cell, the epigenetic code is tissue- and cell-specific, and may change over time as a result of aging, disease or environmental stimuli (e.g., nutrition, life style, toxin exposure) (1). Cross-talk between histone modifications, DNA methylation or RNAi pathways are being studied in such areas as cancer, X chromosome inactivation, and imprinting.

GENES AND CHROMOSOMES

Our bodies are made up of millions of cells. Each cell contains a complete copy of a person's genetic plan or blueprint. This genetic plan is packaged in the cells in the form of genes. Chromosomes can be thought of as being made up of strings of genes. The chromosomes, and therefore the genes, are made up of the chemical substance called DNA

(**D**eoxyribo **N**ucleic **A**cid). The chromosomes are very long thin strands of DNA, coiled up like a ball of string. The DNA making up each chromosome is usually coiled up tightly. If we imagine it stretched out, it would look like beads on a string Each of these beads is called a ***gene.*** Each gene is a piece of genetic information, Thousands of genes make up each chromosome. Since the chromosomes come in pairs, there are two copies of the genes. The exception to this rule applies to the genes carried on the sex chromosomes: the X and Y.

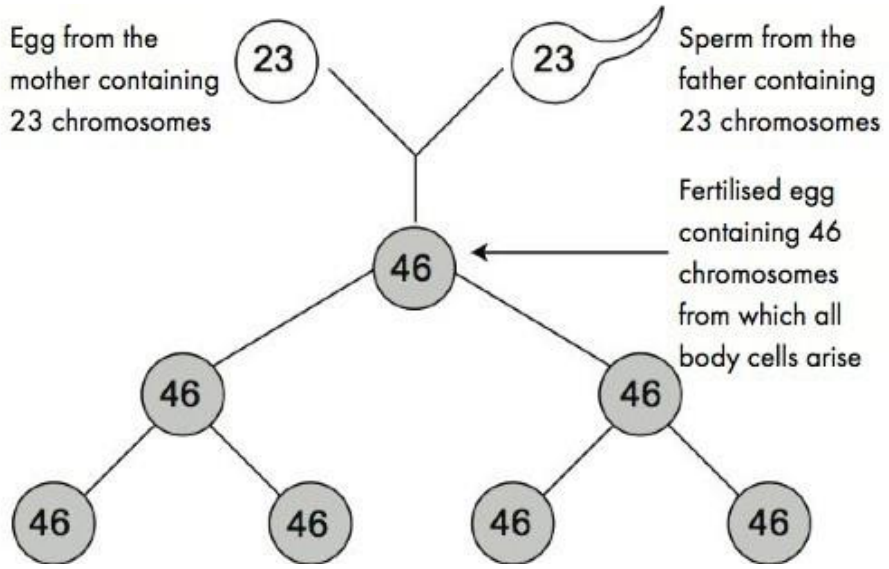


Genes are also located in very small compartments called *mitochondria* that are randomly scattered in the cytoplasm of the cell outside the nucleus.

Chromosomal material extracted from cell nuclei of eukaryotic cells is called chromatin. It contains equal amount of DNA and proteins. Mainly histone proteins are present. Chromatin is 2 types Heterochromatin & Euchromatin Heterochromatin is densely packed inactive chromatin, Euchromatin is lightly packed active chromatin.

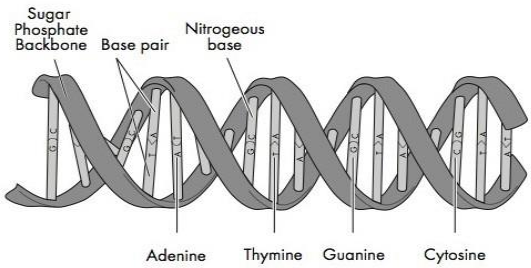
CHROMOSOMES

The chromosomes are made up of DNA. During nuclear division, the DNA (as chromatin) in nucleus is coiled into very tight compact structures called chromosomes. These are rod-shaped structures made of protein and DNA In their body cells, humans have 46 chromosomes, made up of 23 pairs. There are 44 chromosomes called *autosomes* that are numbered from 1 to 22 according to size from the smallest to the largest as well as the two sex chromosomes: X and Y .Women's chromosomes are described as 46, XX; men's as 46, XY. A mother passes 23 chromosomes to her child through her egg and a father passes 23 chromosomes through his sperm.



Each chromosome consist of two very long thin strands of DNA chains twisted into the shape of a double helix and are located in the nucleus (the 'control centre') of our body cells.All of the DNA in the cell (in the nucleus and the mitochondria) make up the **genome.**

Genes make up only about 1% of the genome all of the 20,000 or so genes contain a different `packet' of information necessary for our bodies to grow and work.



The genetic information is in the form of a chemical (DNA) code (the ***genetic code***) The DNA code is made up of very long chains of four basic building blocks (*nucleotide bases*): **A**denine (A) and **G**uanine (G), and **T**hymine (T) and **C**ytosine (C). A chromosome consists of two of these DNA chains running in opposite directions; the bases pair up to form the rungs of a ladder twisted into the now famous double helix.

Pairing of the bases follows strict rules: base A can only pair with base T, and vice versa; and base G can only pair with base C, and vice versa. Roughly three billion of these base pairs of DNA make up the human genome. In the DNA information, each 'word' is a combination of three of these four chemical 'letters' A, G, C and T (a triplet).

The DNA that makes up the genes is often called '*coding DNA*'. The DNA 'string' between each of the genes in a chromosome is often called '*non-coding DNA'*.

EPIGENETIC VS GENETIC

EPIGENETIC		**GENETICS**
1.	Epigenetics is defined as heritable changes in gene expression without a change in the DNA sequence itself	Genetics Study of genes(DNA&RNA)
2.	Emphasizes on heritable changes in the molecular machinery for gene expression patterns.	Emphasizes on heritable changes of characters
3.	Deals with gene expression among the population of cells.	Deals with traits of individuals in a population
4.	Regulates awakening/silencing of gene expression	Reinforces dominance/recessive nature of traits
5.	Goes with chromatin	Revolves around genes
6.	Deals with the regulatory units of chromatin viz., epialleles.	Deals with the functional units of DNA as alleles.
7.	Focuses on transgenerational expression of genes in the across individuals. successive generations of cellular population	Envisages the transgenerational expression of traits Facross individuals
8.	Handles with the cellular genome and chromatin remodeling	Handles with either single or constellation of genes
9.	Elaborates on cellular differentiation, gene imprinting and cellular pathobiology	Elaborates on genetic profiles in a population.
10.	Profusely depends on mitotic inheritance	Exclusively depends on meiotic inheritance.

11.	Describes epigenetic marks, packaging and modification of chromatin	Describes test crosses and back crosses to validate genes
12.	Changes are often reversed	Genetic changes are stable and rarely reversed
13.	"Epigenome" generally refers to the complete set of characteristics of epigenetic pathways in an organism.	The term "genome" that defines the complete set of genetic information contained in the DNA of an organism.

EPIGENETIC CHANGES

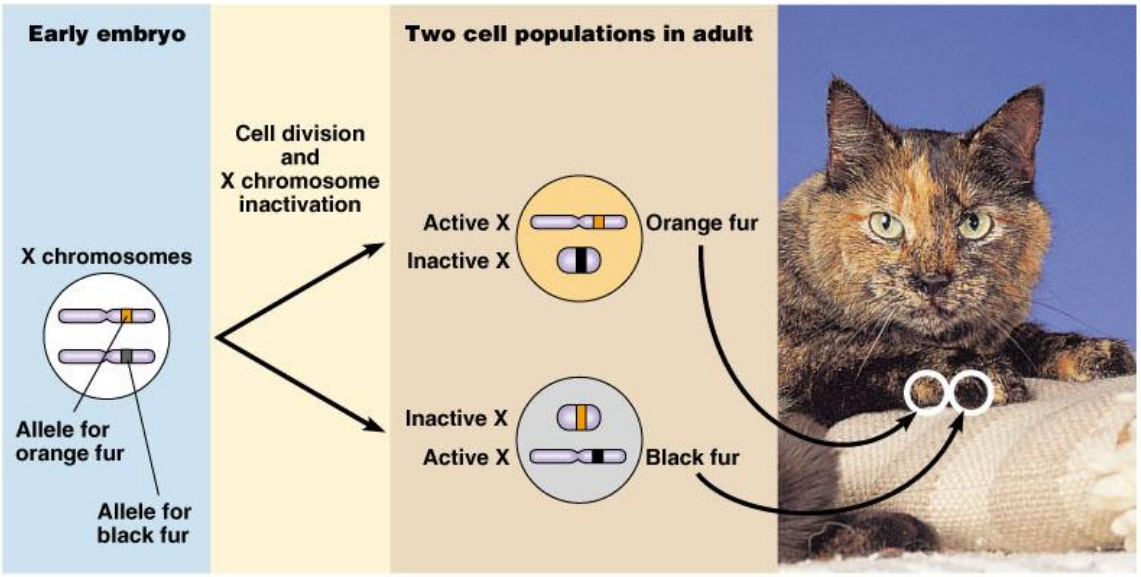
Epigenetic changes are genetic changes that are heritable but not depend on DNA sequence changes. They depend on modification of the DNA. Epigenetics changes occurs due to x chromosome inactivation and genetic imprinting.

X CHROMOSOME INACTIVATION

X inactivation involves the attachment of methyl (CH3) groups to cytosine nucleotides on the Xchromosome. One of the two X chromosomes has an active *XIST* gene (X-inactive specific transcript). This gene produces multiple copies of an RNA molecule that almost cover the X chromosome. This initiates X inactivation.

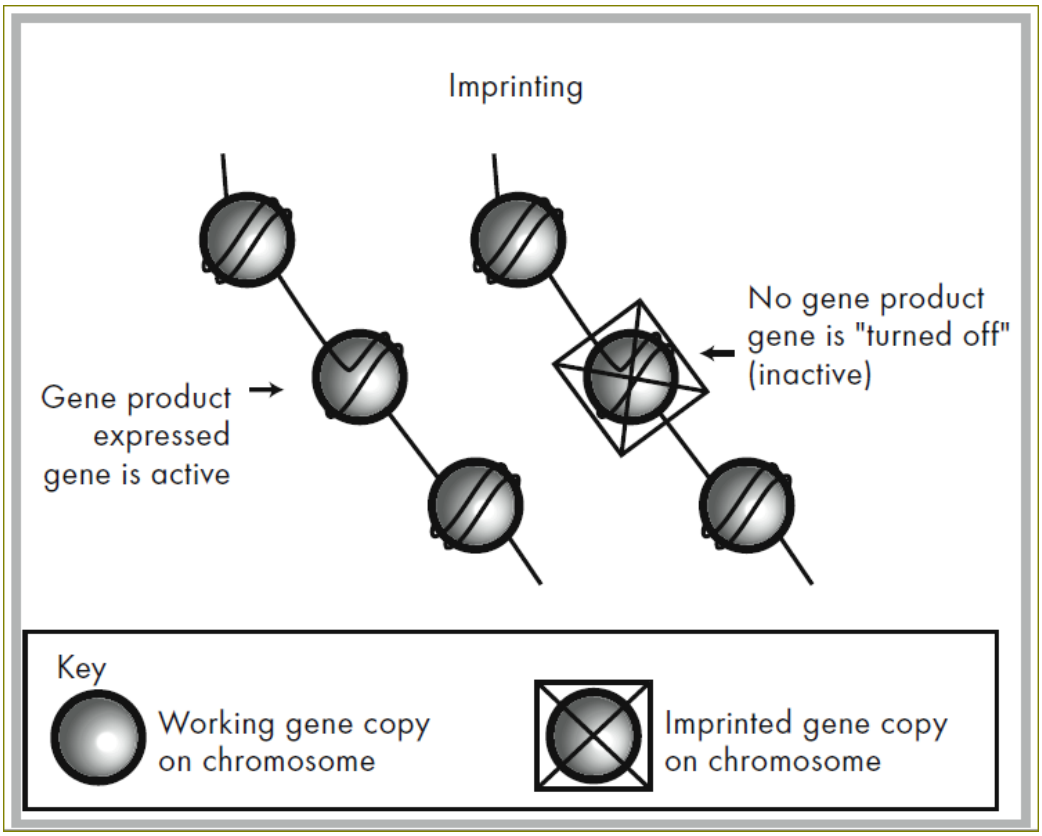
X chromosome inactivation is the epigenetic system where'stamping' of the genetic information enables men and women to have equal expression of the genes carried on the X chromosome; despite the fact that women have two X chromosome copies and men have only one - in addition to a Y chromosome.

Example: the orange and black pattern on tortoiseshell cats is due to patches of cells expressing an orange allele while others have a nonorange allele.



GENETIC IMPRINTING

The epigenetic system of 'stamping'the genetic information that occurs according to whether it is inherited from the mother or the father. This system is called '***genetic imprinting'.***The information in certain genes is active only when it passes to a child through the sperm or the egg. This system of being 'stamped' according to the paternal or maternal origin of a gene copy is called '***genetic imprinting'.***



Genetic imprinting (or *genomic imprinting*) is the name given to this modification process., if the gene copy is modified, it will be turned off in that person and the cells will not produce any product from that imprinted gene copy. Genetic imprinting occurs in the ovary or testis early in the formation of the eggs and sperm. Some genes are imprinted so that they are switched off or inactive only if they are passed down through an egg cell; others will be inactivated only if they are passed down through a sperm cell. Imprinting will then occur again in the next generation when that person produces his or her own sperm or eggs. Some chromosomes do not contain imprinted genes. While imprinting is not a common epigenetic mechanism controlling gene expression in humans, it is an important one and provides interesting new insights into the mechanisms of gene expression.

Uniparental disomy

Uniparental disomy (UPD) occurs when an individual receives both copies of a chromosome from one parent only. Therefore the child inherits some of the genes from one parent only (*uniparental*) rather than the usual situation where one copy of each gene is inherited from the father, and the other from the mother (*biparental inheritance*). Where the chromosome involved in the UPD is imprinted, there may be implications for that individual. For instance, if there is UPD for chromosome 15, there are different possible outcomes If both copies of chromosome 15 are inherited from the mother (*maternal UPD*), a genetic condition called **Prader Willi** syndrome occurs If both copies of chromosome 15 are inherited from the fatherB(*paternal UPD*) a different genetic condition called **Angelman** syndrome occurs These two distinctly different conditions have features including intellectual impairment and characteristic facial features. Other conditions that may be caused by UPD and imprinting effects include Beckwith-Wiedemann syndrome (an overgrowth condition) and Russell-Silver syndrome (featuring growth delay).

DISEASES

DISEASES	DNA METHYLATION	HISTONE MODIFICATION	OTHERS	TREATMENT
AGE	DNA METHYLATION	_	_	DIET
MENTAL DISORDERS Behavior Disorders	DNA METHYLATION	HISTONE METHYLATION ACETYLTION, PHOSPHORYLATION	_	Diet Trichostatin A
Alzheimer's Disorde	DNA METHYLATION	HISTONE ACETYLTION	_	5-azacytidine and Decitabine HDAC inhibitor
Schizophrenia	_	HISTONE ACETYLTION	_	HISTONE" DEACETYLASE INHIBITORS
PARKINSONS DISEASE	DNA METHYLATION	HISTONE MODIFICATION	MICRO RNA	HISTONE" DEACETYLASE INHIBITORS
CANAER COLON CANCER	DNA METHYLATION	_	__	DNMT 3b (DNA METHYL TRANFERASSE 3b), Zebularine
PRIMARY TUMERS	DNA METHYLATION (hypo methylation)	HISTONE MODIFICATION	_	DNA methylation initiaters5-azadeoxycytidine (5AZA) & HDAC inhibitors
Type 2 diabetes mellitus	DNA METHYLATION	_	_	DNA METHYLATION INHIBITERS

EPIGENETIC ROLE IN CANCER TREATMENT

The major epigenetic changes that take place during the development of cancer are the aberrant DNA methylation of genes that suppress tumor genesis and histone modifications of chromatin.

DNA METHYLATION AND CANCER

In normal cells, the pattern of DNA methylation is conserved after DNA replication and cell division by the methylation of cytosine by a maintenance DNA methylase (DNMT1). DNA methylation of genes occurs primarily in the promoter region that contain CpG islands, which are defined as a 1 kb stretch of DNA that contains this sequence at a higher frequency than the rest of the genome. The methylation of CpG islands in the promoter region silences gene expression and is a normal event that occurs in cells to regulate gene expression. However, when aberrant DNA methylation of tumor suppressor genes occurs in tumors, it is implicated in neoplastic transformation. The aberrant methylation of genes that suppress tumor genesis appears to occur early in tumor development and increases progressively, eventually leading to the malignant phenotype. Genes involved in every step of tumor genesis can be silenced by this epigenetic mechanism.

Table 1: Hallmarks of cancer and different types of genes silenced by aberrant DNA methylation.

Hallmarka (acquired capability)	Gene silenced by DNA methylation	Gene function
Insensitivity to antigrowth signals	p16CDKN2A	Cyclin-kinase inhibitor induce differentiation cell cycle arrest
Self-sufficiency in growth signalsEvading apoptosis	RARb Cote´ et al. (1998) Sigma 14-3-3 RASSF1A Capase-8 TMS1 DAP-kinase p14ARF	Regulation Ras pathway Initiate apoptosis Proapoptosis Proapoptosis Proapoptosis
Limitless replicative potential Sustained angiogenesis	Rb Thrombospondin-1	Tumor suppressor gene Angiogenesis inhibitor stimulate angiogenesis
Increased invasion And metastasis	E-cadherin TIMP3	Suppress metastasis Inhibit metastasis DNA missmatch repair
Genome instability (enabling characteristic)	hMLH1 MGMT BRCA1	Repair alkylated guanine Repair DNA damage

DAP-kinase - Death Associated Protein kinase;

MGMT-O_6 - Methylguanine DNA ethyltransferase;

RARb - Retinoic acid Receptor-b2;

Rb - Retinoblastoma;

TIMP3 - Tissue Inhibitor of Metallo Proteinase-3;

VHL -Von Hippel–Lindau tumor suppressor gene.

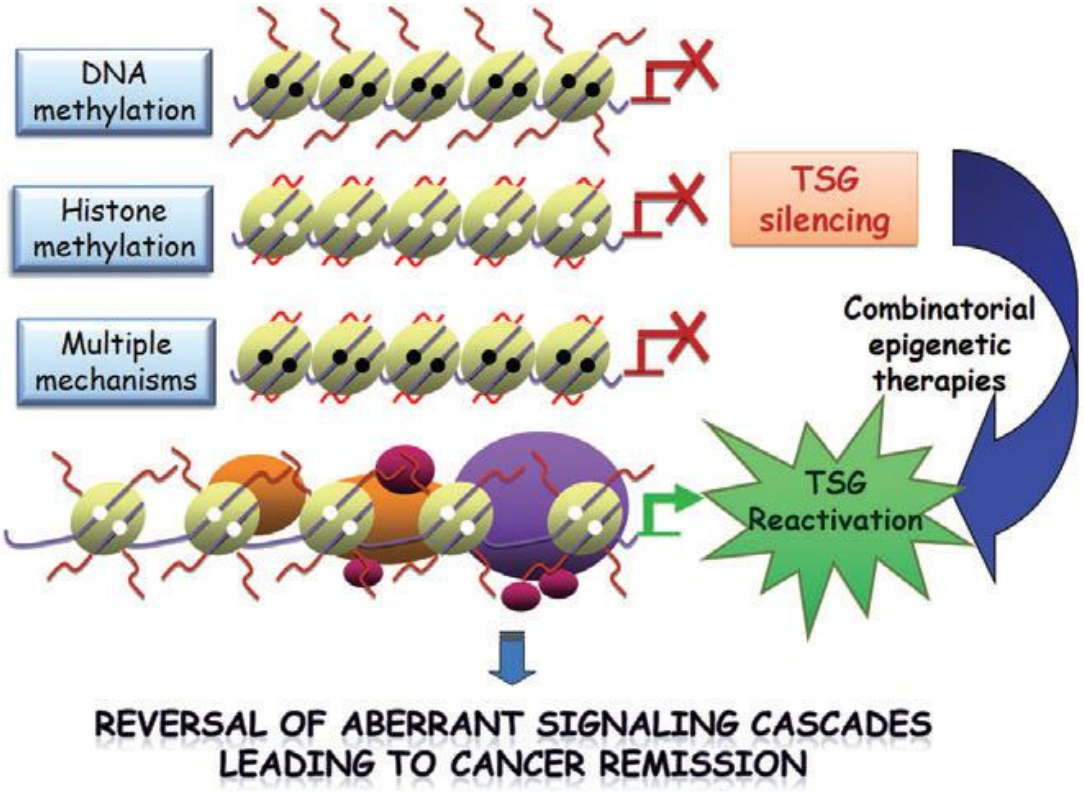


Figure Novel approach for cancer therapy.

In cancers, tumor suppressor gene (TSG)s can be epigenetically silenced by DNA-, histone-methylation or combined mechanisms. Combinatorial epigenetic therapies targeting these machineries should reactivate these genes by chromatin remodeling and reverse the aberrant signaling cascades leading to cancer remission. Black and white circles indicate methylated and unmethylated CpG sites, respectively. Red and brown lines indicate tails of methylated and unmethylated H3K27 resulting in compacted and relaxed chromatin states, respectively.

POSSIBLE MECHANISMS THAT PRODUCE ABERRANT DNA METHYLATION

It is not clear what are the molecular events that lead to aberrant methylation. There are several hypotheses. It is possible that aberrant promoter hyper methylation is due to the infidelity of DNMT1. The substrate for this DNA methylase is hemi methylated DNA. Methylation occurs immediately after DNA replication with the primary function to ensure that the identical methylation pattern of the parental cell is passed on to each daughter cell.

DNMT1 is part of a multi protein DNA replication complex which may be prone to methylation errors. It is known that the human DNA polymerases replicate genomic DNA with very high fidelity, but do commit error sat a very low frequency Other DNA methylases that could be involved in aberrant DNA methylation are the de novo methylating enzymes DNMT3a and DNMT3b. These enzymes use unmethylated DNA as their template and play an important role in embryonic development the third possible mechanism responsible for gene hyper methylation could be due to a faulty repair mechanism of aberrantly methylated DNA. A human DNA demethylase has been identified. This demethylasehas the potential to function as a repair enzyme, which has the potential to correct aberrantly methylated CpG sequences. A fourth possible event to produce hypermethylation of CpG islands is related to chromosomal remodeling and implicates the aberrant methylation of lysine-9 of histone-3 in nucleosomes by histone methyltransferase.

Aberrant DNA methylated genes have been identified in each step of tumor genesis

(1) Self-sufficiency in growth signals;
(2) Evading apoptosis;
(3) Insensitivity to antigrowth signals;
(4) Tissue invasion and metastasis;
(5) Sustained angiogenesis; and
(6) Limitless replicative potential.

This long list of cancer-related genes plus the findings by genomic screening of a large number of aberrantly methylated CpG islands in different types of tumors(C ostello et al., 2000; Shi et al., 2002; Suzukiet al., 2002) indicate that epigenetic events play a key role in tumor genesis.

CHROMATIN STRUCTURE AND GENE EXPRESSION

The structure of chromatin can also play an important role with respect to the regulation of gene expression. Chromatin containing hypoacetylated lysines in histones has a compact structure that is repressive for transcription. Inhibitors of histone deacetylase (HDAC) can convert chromatin to an open structure and activate certain genes that inhibit tumor growth. These HDAC inhibitors also have potential in cancer therapy.

CROSS-TALK BETWEEN DNA METHYLATION AND HISTONE CODE

A ‘cross-talk’ between DNA methylation and histone deacetylation can occur and work in concert to silence gene expression. The molecular mechanism involves the attachment of a methylated CpG binding protein (MBP) to the methylated promoters and its recruitment of HDAC to form a complex that suppresses transcription. These two epigenetic modifications represent an interesting target for therapeutic intervention using 5AZA and HDAC inhibitors. These agents in combination have been shown to produce a synergistic reactivation of tumor suppressor genes and an enhanced antineoplastic effect against tumor cells, and should be investigated as a novel form of epigenetic therapy for cancer.

EPIGENETIC CHANGES AND DIAGNOSIS OF CANCER

Hypermethylation of the promoter region of cancerrelated genesp rovidesa tool for cancer diagnosis. Bisulfite treatment of DNA results in a deamination of cytosine to form uracil; 5-methyl-cytosine is resistant to thisch emical treatment.In some patients, dying tumor cells can release fragmentsof genomic DNA, which can be used as biomarkers for the diagnosis of cancer. Using MSP, it is possible to detect methylated genes released from tumors in the serum of patients.

REVERSIBILITY OF EPIGENETIC EVENTS PROVIDES A TARGET FOR CHEMOTHERAPEUTIC INTERVENTION

Genes that suppress tumorigenesis can be silenced by aberrant methylation and aberrant histone acetylation. Since these epigenetic events are reversible they can be potential targets for agents that inhibit DNA methylation or inhibit histone deacetylation. The potent and specific inhibitor of DNA methylation, 5AZA, has been demonstrated to reactivate most of these silent cancer-related genes in human tumor cells. It is unlikely that a single agent has the potential to cure malignant disease due to the rapid development of drug resistance to single drug therapy. The interaction of 5AZA with other agents that enhance its antineoplastic activity should also be investigated.

CONCLUSION

Epigenetic changes occur frequently during tumor development. The major changes are aberrant DNA methylation and histone modification in chromatin. Both these epigenetic events act in concert to silence the expression of genes that suppress tumorigenes is. The aberrant DNA methylation of some of these target genes can be used for early diagnosis of cancer using MSP. In addition, these epigenetic changes are potential targets for therapeutic intervention using inhibitors of DNA methylation and histone deacetylation. The synergistic activation of tumor suppressor genes and the synergistic in vitro antineoplastic activity by the combination of these epigenetic agents suggest that they have interesting potential for the chemotherapy of cancer.

BIBLIOGRAPHY

1. Bird, A. (2007). Perceptions of epigenetics.
2. Bjornsson, HT, Fallin, MD, & Feinberg AP (2004). An integrated epigenetic and genetic approach to common human disease.
3. Bradbury, J (2003). Human Epigenome Project: Up and running.
4. Epigenome Network of Excellence (n.d.)
5. Falls, JG, Pulford, DJ, Wylie, AA, & Jirtle, RL (1999). Genomic imprinting: Implications for human disease.
6. Mead, NM (2007) Nutrigenomics: The genome-food interface. Environmental Health Perspectives.
7. Robertson, KD (2005). DNA methylation and human disease. Nature Reviews – Genetics

8. Rodenheiser, D, & Mann, M (2006). Epigenetics and human disease: Translating basic biology into clinical applications.
9. Santos-Reboucas, CB & Pimentel, MMG (2007). Implications of abnormal epigenetic patterns for human diseases.
10. Schmidt, CW (2005). Critical Care: Applying genomics to inflammation outcomes.