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To Study the Effect of Epigenetics on Human with Reopened to Different Regulatory Agents

[*1] Dr. Shailendra Choudhari

[*1] Associate Professor, Department of Botany, Balbhim Arts, Science and Commerce College Beed, Maharashtra, India.

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***Corresponding Author**
Dr. Shailendra Choudhari
Assistant Professor, Department of Botany, Balbhim Arts, Science and Commerce College Beed, Maharashtra, India.

Abstract
From the years, scientists have practiced to describe disorders caused by genetic and environmental factors. The function of epigenetics in human diseases has been examined from years ago. This review describes the effect of epigenetics on human by various methods. Epigenetics play an important role in evaluation and activity of natural immunity. The various effects such as diet obesity, physical activity, alcohol consumption, environmental pollutants, and psychological stress are responsible for epigenetics. Epigenetics is also refer as epigenomics. Epigentics control the gene expression by the cross talk of various epigenetic mechanism Such as DNA methylation (A stabilized alteration), Histone changes (which regulate reversibility), chromatic composition change and untranslated RNA, Each mechanism works in various way to control gene expression. The some of above mechanism could be convey to next generations.

Keywords: Humans, epigenetics, regulatory agent, arthritis, syndrome.

Introduction

A number of digestive disorders, such as Barrett's esophagus, cirrhosis, inflammatory bowel disease, and various gastrointestinal cancers, have been connected to aberrant epigenetic patterns. In fact, research on illnesses of the gastrointestinal tract and hepatobiliary tree has led to a number of fascinating findings concerning epigenetics in general. Hope and the promise of novel biomarkers for early cancer detection, prediction, prognosis, and therapy response are offered by epigenetic changes of DNA in cancer and precancerous lesions. A potential goal of cutting-edge therapeutic approaches and drug development is the reversal of epigenetic alterations. It is envisaged that cutting-edge diagnostic procedures, therapeutic plans, and even lifestyle changes will be founded on epigenetic mechanisms and applied to medical practice in the future.

In order to shed new light on the pathogenesis of autoimmune diseases and the potential for developing novel therapeutic approaches that target the epigenome, this paper reviews the significance of epigenetic alterations during the development of the most common autoimmune diseases affecting humans, including type 1 diabetes (T1D), systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), systemic sclerosis, Sjogren's syndrome, and systemic sclerosis.

Epigenetic Field and History

The word 'epigenetics' was firstly introduced in 1942 by Conrad Waddington. The Conrad Waddington was the British developmental biologist and embryologist. The Conrad Waddington was worked at Cambridge University. In past few years, many investigations proved that the epigenetic mechanism involved in regulation of all biological functions in the body from conception to death incorrect epigenetic signs can result in birth defects, childhood diseases or symptoms of disease in other terms of life Epigenetic mechanism are used to regulate development of an organism and their changes may cause various disorders such as cancer. Some of epigenetics marks are reversible. The DNA methylation mechanism can also be irreversible. The maintenance of proper cell growth, development, and differentiation depends heavily on epigenetic mechanisms, which are recognized for their capacity to control gene transcription and genomic stability. The definition of "epigenetics" is the mitotically/mitotically heritable changes

in gene expression caused by environmental stimuli, without affecting the DNA's base-sequence. The definition of "epigenetics" is the meiotically/mitotically heritable changes in gene expression caused by environmental stimuli, without affecting the DNA's base-sequence. Epigenetic alterations are kept as additional immune response regulators because genome-wide profiling in some circumstances is unable to fully explain the complicated biological processes in autoimmune diseases. Epigenetic dysregulation controls the functioning of immune cells, directly influencing the emergence of autoimmunity.

Greek for "epi" means "on or above," thus "epigenetic" refers to elements other than the genetic code. Epigenetic alterations to DNA control whether or not genes are activated. These alterations are connected to DNA and do not alter the order in which the DNA building blocks are organised. Your surroundings and behaviours, such as what you eat and how active you are, are just as cr ucial to your health as your genes. Your surroundings and behaviours, such as what you eat and how active you are, are just as crucial to your health as your genes. Epigenetics is the study of how environmental factors and behaviour can alter how your genes function. While epigenetic alterations are reversible and do not alter your DNA sequence like genetic changes do, they can alter how your body interprets a DNA sequence.

The requirement that the new epigenetic state must be initiated by a temporary mechanism distinct from the one needed to sustain it has most recently been added to this definition. The term "epigenetics," however, was used more generally (and less precisely) to classify all developmental events going from the fertilised zygote to the mature organism-that is, all of the controlled processes that start with the genetic material and shape the finished product. As you become older, both as a result of normal development and ageing and in reaction to your behaviours and surroundings, your epigenetics alter.

1. Growth and Epigenetics

Epigenetic alterations start to take place before birth. Despite sharing the same genes, your cells all appear and behave differently. Epigenetics plays a role in determining which function a cell, such as a heart cell, neuron cell, or skin cell, will have as you grow and develop.

2. Age and Epigenetics

Your epigenetic makeup evolves over time. Your epigenetic makeup at birth is different from what it is when you are a child or an adult.

3. Versatility and Epigenetics

Not all epigenetic modifications are long-lasting. In response to adjustments in behaviour or environment, some epigenetic modifications can be introduced or eliminated.

Gene expression refers to how often or when proteins are created from the instructions within your genes. While genetic changes can alter which protein is made, epigenetic changes affect gene expression to turn genes "on" and "off." Since your environment and behaviours, such as diet and exercise, can result in epigenetic changes, it is easy to see the connection between your genes and your behaviours and environment. Over the past ten years, an enormous amount of information and research has been published on the role of epigenetic mechanisms in the emergence of phenotypes and diseases. The goal of the current study is to introduce the reader to the discipline of epigenetics by highlighting some of the most important and thought- provoking research on the subject.

Epigenetics Modification

The ability of epigenetic changes to be passed down over generations (meiotic inheritance) and between mother and daughter cells (mitotic inheritance) is a key characteristic. The epigenetic alterations in a multicellular organism allow various adult cells to express particular genes that are necessary for the existence of each cell type and the transmission of information to the daughter cells. Epigenetic modifications frequently take place during the lifetime of an organism, but if they happen in g erm cells, they might be passed on to the following generation [10]. The regulation of histone modifications, heterochromatin states, paramutation, bookmarking, imprinting, gene silencing, X chromosome inactivation, position effect, changeable disorder or phenotypic severity, reprogramming, maternal attributes, carcinogenic processes, teratogenic effects, and cloning are all known to involve epigenetic processes. DNA methylation, histone modification, and noncoding RNA activity are the three main categories of epigenetic regulation.

1. DNA Methylation

Histone modification and non-coding RNA mediated gene expression control are two additional universal epigenetic processes that regulate the act ivity of DNA methylation, which suppresses gene expression in a variety of ways. The leading scientific journal Nature recently named 5mC the "fifth base," adding it to Adenine, Guanosine, Thymine, and unmethylated Cytosine [1]. Forty years after Hotchkiss' discovery, in the 1980s, the British molecular biologist Adrian Bird discovered regions in the genome characterized by a high frequency of cytosine-phosphate-guanine (CpG) dinucleotides, known as CpG islands. These regions are often associated with the promoter regions of genes and are critical for gene regulation. Bird's work revealed that methylation of CpG islands could lead to gene silencing (see below), a significant process in development and cellular differentiation [2].

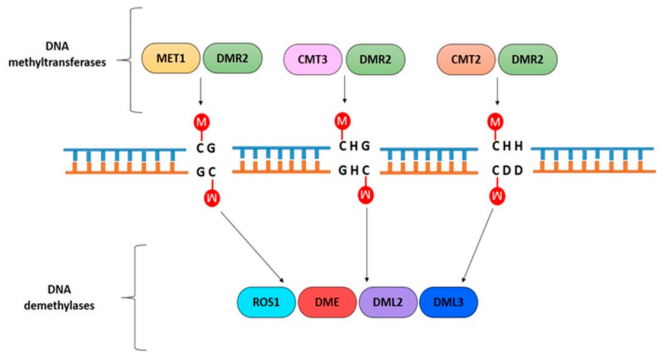

Fig 1: DNA Methylation Histone modification and non-coding rn

DNA methylation state is extremely stable and acts as a unique epigenetic memory for certain cells during all phases of the cell cycle. It might also control how histone codes are expressed and activated. At CpG sites, DNA methyltransferase enzymes mediate DNA methylation. By altering the binding of transcription factors or upregulating the binding of methyl-cpg binding proteins, it can also reduce gene expression. S-adenosyl methionine serves as a crucial methyl group donor inside of cells. Folic acid and B12, acting

through both passive and active processes, are thus key players in the re-methylation or attraction of the de-methylated form of S- adenosyl. Overall, DNA methylation, as a very outstanding epigenetic agent, could have an impact on chromatin alterations, gene expression, DNA faultlessness, and durability.

In the early 1960s, scientists observed that DNA methylation occurred in bacterial systems as a defense mechanism against bacteriophage infection [3]. Later, the transfer of a methyl group from S-adenosylmethionine (SAM) to DNA has been demonstrated in all living organisms, marking the beginning of our understanding of DNMTs function [4]. DNMTs are the enzymes that catalyze the transfer of a methyl group from SAM to the 5-carbon position of cytosine residues (5mC). Several types of DNMTs have been discovered, including DNMT1, DNMT3A, and DNMT3B, each with specific roles in establishing and maintaining DNA methylation patterns. The discovery of these enzymes and their metabolic pathway allowed the development of critical anticancer therapies based on the effect of Cytosine analogs to modulate DNA syntheses and methylation, such as cytarabine (AraC) and 5-azacytidine (AzaC) [5]. As all the epigenetic enzymes, DNMTs have a counterpart in the tento-eleven translocation (TET) proteins, which demethylates DNA through a series of intermediates starting from 5-hydroxymethylcytosine (5hmC) [6]. An imbalance between DNA methylation and demethylation may be at the basis of different human pathology, as discussed below.

2. Histone Modification

Histone modification, which encompasses acetylation, methylation, phosphorylation, is one method of controlling gene expression by chromatin remodelling. Numerous studies have examined acetylation, which has been demonstrated to be mediated by five families of mammalian histone acetyltransferase enzymes. Histone methylation and demethylation are epigenetic changes that can either increase or decr ease gene expression, particularly through changing the chromatin structure. A protein called a histone contributes to the chromatin structure, which is made up of DNA wrapped protein.

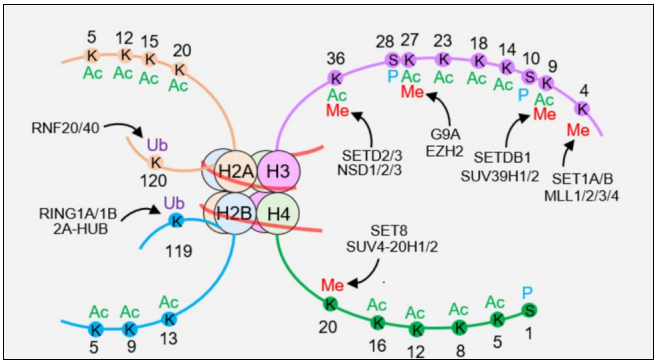

Fig 2: Histone Modifications and protein structure

Histone H1 is a linker, associating with the DNA as it enters and exits the nucleosome and stabilizes the chromatin structure [7]. In terms of mechanics, these operations are carried out either directly by modifying how nucleosomes interact with chromatin or inadvertently by enlisting effector proteins that have distinctive modules that can recognise distinct histone modifications in a sequence-dependent manner. The substrate specificity of the enzymes that catalyse the various covalent modifications as well as the enzymes that remove these marks to change the changes forms the fundamental basis of these epigenetic codes.

It is catalyzed by the Protein Arginine (R) Methyltransferases (PRMTs) family of enzymes, further divided into type I (PRMT1, 2, 3, 4, 6 and 8), II (PRMT5 and 9) and III (PRMT7) which may add one or two methyl groups [8] governing either chromatin relaxation or condensation [9]. Arginine methylation is reversible as well, but very few arginine demethylases have been identified so far [10, 11]. Phosphorylation, a critical histone modification, involves adding a phosphate group by kinases, such as the Aurora B family, to serine, threonine, or tyrosine residues. Histone phosphorylation can regulate chromatin condensation and gene expression and play a role in DNA damage repair and mitosis [12].

3. Non Coding RNA Activity

Non-coding RNAs are a group of RNAs that do not encode functional proteins and were initially thought to just control post-transcriptional levels of gene expression. The most prevalent regulatory RNAs, however, appear to be long non-coding RNAs, endogenous siRNAs, piRNAs, and miRNAs, according to a wide range of recent studies. Additionally, there is mounting evidence that regulatory non-coding RNAs are crucial for epigenetic regulation.

Housekeeping non-coding RNAs and regulatory non-coding RNAs are two categories for non-encoding RNAs (non-coding RNAs) that are not translated into proteins. According to size, regulatory RNA can be broadly categorised into two groups: long non-coding RNAs (lncRNAs) and short chain non-coding RNAs (siRNAs, miRNAs, and piRNAs) (Table I). Non-encoding RNAs have been implicated in epigenetic alteration in recent years, and numerous studies have demonstrated that they can affect gene and chromosomal expression to regulate cell development.

RNA molecules known as non-coding RNAs (ncRNAs) regulate the expression of genes but do not code for proteins. Examples include long non-coding RNAs (IncRNAs) and microRNAs (miRNAs). Messenger RNAs (mRNAs) can attach to miRNAs, which can cause their destruction or stop translation. By controlling the amount of functional mRNAs available, this can influence gene expression.

Epigenetics Abnormalities

Abnormal gene activity or inactivity can result from errors in the epigenetic process, such as the alteration of the incorrect gene or the failure to add a chemical group to a specific gene or histone. Genetic problems frequently result from altered gene activity, including that brought on by epigenetic mistakes. It has been demonstrated to be associated with a wide range of human illnesses, including several types of cancer, autoimmune diseases, and neurological disorders. (Fragile X syndrome as well as Huntington, Alzheimer, and Parkinson diseases and schizophrenia).

Environmental elements like nutrition, stress, pollutants, poisons, and lifestyle decisions (drinking alcohol, smoking) can affect epigenetic alterations. For instance, exposure to chemicals during pregnancy might cause epigenetic alterations that affect the child's health later in life. Additionally, dietary elements like folic acid and certain phytochemicals may have an effect on DNA methylation patterns. Everyday exposure to different environmental pollutants as a human can change our epigenome and have an impact on our health.

Cancer

Cancer is characterised by epigenetic alterations. Oncogenes, or genes that promote the growth of cancer, can be activated and tumour suppressor genes can be silenced as a result of abnormal DNA methylation and histone changes. To undo these alterations in cancer cells, epigenetic treatments including DNA methyltransferase inhibitors and histone deacetylase inhibitors are being created.

Cancer is significantly impacted by epigenetic changes. Many tumour suppressor functions can be rendered inactive by hypermethylation of promoter regions of tumour suppressor genes. Additionally, methylation levels are crucial for cell division, DNA repair, differentiation, death, metastasis, growth factor response, detoxification, and drug resistance. these characteristics have greatly advanced the use of methylation levels in the early identification of cancer [13].

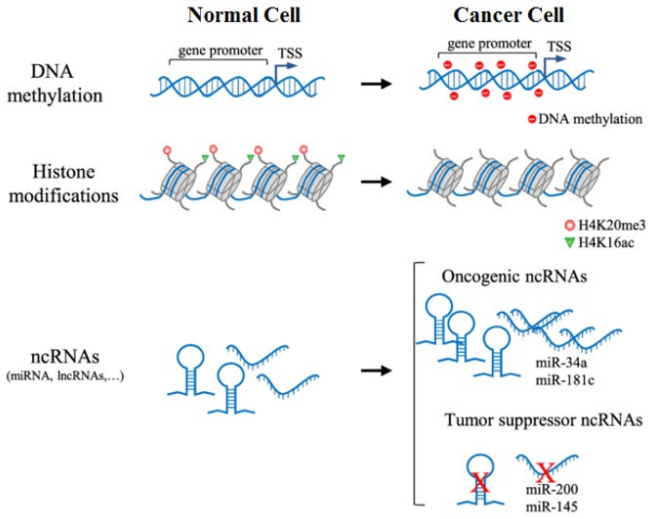

Fig 3: Cancer is characterised by epigenetic alteration

Promotor of methylation in different types of cancer such as breast cancer, gastric cancer, lung cancer, Liver cancer, intestinal cancer. Histone modifications in various types of cancer for example lung cancer, Non-small cell cancer, gastric cancer, prostate cancer, pancreatic cancer. There are several mutations that increase your risk of getting cancer. The chance of developing cancer is increased by some epigenetic modifications. For instance, getting breast and other cancers increases your risk if you have a mutation in the BRCA1 gene that stops it from functioning normally. Similar to this, more DNA methylation increases the chance of developing breast and other cancers by lowering the expression of the BRCA1 gene. The total DNA methylation levels in cancer cells are lower than in normal cells, despite the fact that cancer cells show higher DNA methylation at some genes. DNA methylation patterns can differ among cancers with similar appearances. The sort of cancer that a person has can be identified with the use of epigenetics, and it can also be used to identify tumours that are difficult to locate early. Cancers must be confirmed with other screening procedures because epigenetics alone cannot diagnose cancer [15]. Numerous epigenetic modifications have an impact on human health. Specific microbial infections can cause epigenetic modifications that can inhibit the immune system's abilities. Another significant component affecting epigenetic alterations is nutrition. Prenatal diet might affect a baby's epigenetics and increase their susceptibility to certain disorders.

1. Colorectal Cancer

The expression of specific genes is impacted by aberrant DNA methylation in colorectal tumours in areas close to those genes. Utilising stool samples, several commercial colorectal cancer screening assays search for aberrant DNA methylation levels at one or more of these DNA locations. It's crucial to be aware that the screening process must include a colonoscopy test if the test result is positive or abnormal.

2. Bladder Cancer

Two mechanisms are involved in epigenetic alterations in bladder cancer. Tumour suppressor genes, for example, contain open chromatin, unmethylated promoters, acetylated and active histones, and free nucleosomes in the region upstream of these genes.

3. Non-Small Lung Cancer

An unmethylated promoter known as IGFBP3 in non-small cell lung cancer (NSCLC) serves as a marker for the effectiveness of the chemotherapy drug Cisplatin. The cytochrome P450 variation CYP2C19*17 polymorphism necessitates greater valproic acid (VPA) dosages to achieve target plasma levels. Monitoring epigenetic modifications can also be used to assess the effectiveness of a treatment and the development of a disease. Following adjuvant Tamoxifen therapy, PITX2 methylation can be utilised to predict the main result for breast cancer patients. In comparison to bladder cancer patients who did not have hypermethylated p16 and got the same treatment, those who had p16 hypermethylation were less likely to experience a relapse after receiving IL2 therapy.

4. Prostate Cancer

In Western nations, prostate cancer affects more men than any other type of cancer, and its prevalence is rapidly rising globally. Prostate cancer cells have been found to have genome-wide DNA hypomethylation, which could alter the genome's structure and functionality. According to reports, people with metastatic prostate cancer have much lower levels of global hypomethylation than those with non-metastatic prostate cancer. The most frequent and well-studied epigenetic event in cancer, particularly prostate cancer, has been DNA hypermethylation. Numerous genes have been discovered to be hypermethylated in prostate cancer.

Autoimmune Diseases

In the growth and function of the immune system, epigenetic mechanisms are crucial. Numerous research that aim to explain a connection between epigenetic changes and the emergence of autoimmune illnesses have been published in the previous ten years. One can distinguish between systemic and organ-specific autoimmune disorders, which are the two primary categories. While in organ-specific diseases the immune response is focused on a particular organ, in systemic diseases the immune system assaults in a generalised fashion its own antigens in multiple organs. This paper reviews the significance of epigenetic alterations during the development of the most common autoimmune diseases affecting humans, including type 1 diabetes (T1D), systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), systemic sclerosis, Sjogren's syndrome, and systemic sclerosis.

1. Systrmic Lupus Erythematosus (SLE)

The autoimmune condition most closely associated with epigenetic alteration is SLE. It is more common in women

and is mostly brought on by T lymphocyte dysregulation, making it a challenging and complicated condition to treat. Autoantibodies against nuclear antigens can develop in any organ system or tissue, including the kidney and blood arteries, in SLE, a chronic autoimmune disease. Neutrophils and granulocytes from SLE patients were recently found to be completely hypomethylated, particularly at the interferon MX1 and IFI44L gene lloci.

2. Rheumatoid Arthritis (RA)

RA is a chronic, crippling inflammatory disease that causes diffuse joint destruction and destructive arthritis. Affected methylation states in T and B cells as well as synovial fibroblasts are epigenetic pathways involved in RA. Early investigations on methylation found that patients' T cells displayed an unusual pattern, resembling SLE, marked by global hypomethylation. In example, the anti-RA drug methotrexate (MTX) promoted FOXP3 expression through promoter demethylation, resulting in the increase of protective Treg cells.

Sjogren's syndrome

Dry mouth and eyes are caused by unknown salivary and tear glands. SS, an autoimmune condition that affects about four million people in the USA, is fairly common. This autoimmune disease is accompanied by blood autoantibody synthesis that is directed against different body tissues, causing an inflammatory reaction. Reduced DNA methylation of immune cells is one of the most researched epigenetic markers in SS, similar to other autoimmune illnesses. "Yin *et al*."

Epigenetics Therapy

A collection of disorders known as human tumours are brought on by a variety of factors, including advancing genetics and aberrant epigenetics. Epigenetic modifications are major contributors to carcinogenesis and the growth of cancer, according to an increasing number of studies. The development of epigenetic cancer treatment is a result of epigenetic alterations found in tumours. The goal of epigenetic therapy is to undo the epigenetic changes brought on by tumours and return the epigenome to normal. Though histone modifications and DNA methylation in gene transcription have made remarkable strides in recent years, the significance of epigenetic processes in cancer has not yet been fully clarified. However, significant progress has been made in the development of epigenetic medicines that target histone-modifying enzymes and chromatin [16].

Given that carcinogenesis is connected with numerous epigenetic alterations, combined epigenetic therapies have demonstrated promising results in the treatment of cancer patients. To get the most out of these medicines, specific genetic and epigenetic alterations related to cancer should be identified in each patient.

Conclusions

Present study revealed that the surface of the epigenetic landscape. And it summarizes the maximum vital ideas within the subject: beginning, organisation of DNA in chromatin, secondary and regulatory adjustments of DNA and DNA-associated proteins, enzymes that modulate chromatin feature, and their effect on gene expression. sooner or later, we highlighted the proposition that epigenetics can represent a treasured resource for the development of recent tablets for the remedy of continual illnesses and provided several examples. Many applicable factors have been revealed: the epigenetic modification of non-histone proteins, the role of metabolites inside the function of epigenetic enzymes, and the epigenetic position of RNA, which includes miRNAs and lengthy non-coding RNAs, to call some. However, we consider that this newsletter could provide physicians a taste of epigenetics and its ability for advancing medicinal drug. Tons extra is expected in the coming years, with epigenetics visible as a primary source of expertise in research into getting older and age-associated diseases.

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