

## **EFFECTS OF RELATIONSHIP BETWEEN ENVIRONMENTAL FACTORS AND EPIGENETICS ON HEALTH RISKS**

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### **ABSTRACT**

Environmental pollutants and other harmful factors cause serious changes in genes. However, sometimes changes can occur only in chromatin structure and gene expression, without any changes in DNA sequence. In this case, many epigenetic mechanisms such as DNA methylation and histone modification, acetylation, ubiquitination, and sumoylation are mentioned. Additionally, another important feature of an epigenetic change lies in the fact that it may be inherited. Environmental factors that have serious effects on especially during pregnancy lead to many diseases, including cancer. However, the severity and phenotypic effects of the diseases vary depending on the environment. These factors can be count as air pollution, metal ions, polluted drinking water, UV radiation, tobacco and alcohol consuming and more. In this study, the effects of environmental pollutants on genes and epigenetics have been reviewed.

**Keywords:** Genes, environmental pollutants, Epigenetics; DNA methylation

### **1. INTRODUCTION**

Epigenetics, examine the rearrangement of gene expression by inherited changes in chromatin structure although there is no change in the DNA sequence. Many epigenetic mechanisms such as DNA methylation, histone modifications, and acetylation can modify the genome functioning[1].Epigenetic changes can also be reversible besides inherited changes that last for generations[2]. There is evidence in the literature that environmental influences also play a role in these epigenetic changes. According to recent studies, it has been determined that there are some environmental toxic substances that alter the methylation profile of genes.

Exposure to these substances can cause epigenetic changes and thus lead to health concerns regarding various diseases.

Although there are many epigenetic mechanisms such as acetylation, phosphorylation, ubiquitination, sumoylation and methylation, two particularly important mechanisms inherited can be mentioned in detail DNA methylation and histone modification. DNA methylation is a chemical inherited change in DNA that causes 5-methyl cytosine by adding the methyl group to the C (Cytosine) base in CpG islands. This covalent modification has a prominent role in preserving genome integrity by transcriptional silencing of recurrent DNA sequences. DNA methylation also takes a part in processes such as gene expression regulation, genomic imprinting and X chromosome inactivation. Among the modifications that occur in histones, acetylation and methylation of H3 and H4 are the leading ones[1]. While DNA methylation suppress the transcription, histone acetylation activates transcription[3].

Epigenetic mechanisms are quite significant regarding the talent of transcription factors to regulate DNA binding regions. Studies have shown that DNA methylation occurring in large regions of the genome and in the early stages of life is affected by environmental events. Environmental signals affect the individual's learning, cognition, memory and mood by altering gene expression[4]. Gene-environment interactions affect diseases and can cause the alterations on the phenotypic expression of a genetic trait. Some people may be more susceptible to oxidative damage and therefore to cardiovascular diseases caused by air pollution due to the genetic polymorphism they carry. It is thought that DNA damage and mutations may occur and increase the risk of disease, depending on environmental exposure[1].

## 2. DISCUSSION

There are studies and evidences that genotoxic agents cause DNA damage. For example, it has been determined that high doses of dioxin have carcinogenic effects and cause translocations, and ionizing radiation also increases germinal mutations [1]. There are many other environmental factors that affect epigenetic regulations, particularly DNA methylation. For example, according to a study, it has been found that exposure to asbestos increases methylation in pleural tissues[5]. In a study conducted on rats, it was determined that arsenic is associated with DNA hypomethylation of malignancy that develops in liver epithelial cells. Arsenic exerts its carcinogenic effect by suppressing the expression of DNA methyltransferase genes *DNMT1* and *DNMT3A*. In our daily life, we are exposed to chromium, arsenic and other metal ions mostly for reasons such as professional obligation and drinking water. In a study conducted in the Indian population, it has been reported that high arsenic exposure resulted in the

hypomethylation of the *MT-ND6* gene in the mitochondrial genome [6]. In addition, air pollution is a serious cause of morbidity and mortality, especially causing asthma and cardiovascular diseases. Steel mills, highways and diesel exhaust gases are important sources of air pollution. In studies conducted on mice, it was found that the frequency of mutations was increased in the sperm of mice exposed to polluted air[7].It can be clearly said that the ratio of chemicals contained in air and water in the city and the countryside is not the same.

Another environmental factor that changes the level of DNA methylation is metal ions. Among these metal ions, chromium, cadmium and nickel reduce DNA methylation levels, particularly nickel suppresses gene expression[5]. There is increasing evidence that metal exposure causes DNA mutations, and the impacts of metals may be more than just altering DNA sequence or gene expression [7]. Bisphenol A, which is used in plastic production, which has a great place in our lives, is also effective in tumorigenesis with DNA methylation change. In addition, it was emphasized that tobacco use, alcohol and drug abuse also cause epigenetic changes and hypermethylation of the promoter region was observed in the lung tissue of especially smokers. [5]. Similarly, in another study, it was found that the *HERP* gene promoter region was hypermethylated in individuals who suffers with alcohol dependence [8]. According to the data obtained from animal experiments, nutritional supplements and xenobiotic chemicals can epigenetically alter certain regions of the genome both in the prenatal and postnatal period [9]. Nutrition and diet also affect the epigenetic regulation of gene expression. Abnormal epigenetic markers accumulate and activate tumorigenesis and are thought to be effective in colorectal cancer formation [10]. In addition to environmental factors such as toxins and chemicals that cause diseases with epigenetic changes, there are also environmental factors including nutrition-diet components, lifestyle, exercise, physical activity that change the genome constructively [7].

Meiotic epigenetic inheritance (MEI) has been widely discussed recently, as it can enable the transfer of epigenetic factors such as DNA methylation, histone modifications or RNA to subsequent generations via gametes. The role of DNA methylation in meiotic epigenetic inheritance is still not fully understood, but it is clear that histone modifications, tRNA and microRNAs affect the gene regulation of the offspring. In this context, genome-wide studies are important for the clearer understanding of these regulations [11].Xenobiotics such as environmental pollutants, heavy metals and therapeutic drugs cause mitochondrial dysfunction through epigenetic changes resulting from mtDNA methylation. Gene expression alterations that occur in this way are thought to be associated with mitochondrial dysfunction as well as aging, neurodegenerative disorders, circadian rhythm changes and cancer[6]. In another study, it was shown that it is associated with placental

global DNA methylation levels in people living in polluted cities in the first trimester of pregnancy and therefore in fetuses exposed to polluted air particles. However, it has been emphasized that more studies are needed on the effects of environmental pollutants on early development of the fetus and susceptibility to disease [12]. There are also studies in the literature that support the role of epigenetic abnormalities in cancer development and progression. In addition, studies strengthen the view that DNA methylation, histone modifications, chromatin remodeling, and microRNA may be potential determinants of cancer development [13]. A harmful environmental factor UV radiation, damages essential biomolecules such as DNA, proteins and lipids, thereby activating genotoxic stress. DNA damage caused by UV exposure leads to serious problems such as pyrimidine dimers, DNA double strand breaks and oxidative damage, and ultimately cause various diseases, particularly cancer [14].

In conclusion, there are numerous studies in the literature examining the relationship between exposure to environmental chemicals and epigenetics, but much more studies are needed due to the complex and heterogeneous nature of epigenetics.

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