FEATURE ARTICLE

# Teaching High School Students About the Role of Epigenetics in Diseases

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**Abstract**

*Epigenetics shows how environmental factors and life experiences alter gene activity without changing the gene sequences. This review examines key epigenetic mechanisms such as DNA methylation, histone modifications, microRNAs, and long non-coding RNAs, and their roles in gene regulation. It also highlights the impact of maternal diet, stress, and toxin exposure on epigenetic marks. The paper discusses the role of epigenetics in diseases such as cancer and diabetes, presenting new avenues for diagnosis and treatment. Ethical, social, and legal challenges, including informed consent, discrimination, distributive justice, and transgenerational equity, are also explored. Additionally, the review suggests innovative teaching strategies for epigenetics, including interactive videos, simulations, storytelling, and case studies, to enhance student engagement. Ultimately, understanding epigenetics empowers informed health choices and promotes a healthier world by integrating these insights responsibly for the benefit of current and future generations.*

**Key Words:** *epigenetics; DNA methylation; histone modifications; non-coding RNAs; ethical issues; informed consent; discrimination; distributive justice; transgenerational equity.*

## ○ Introduction

Many may find it incredible that the lifestyle choices we make today extend beyond our own health, influencing the health of our descendants as well. Diseases are caused by both genetic and environmental factors. Genes contain instructions for making specific proteins, and changes in DNA sequences can produce defective proteins, resulting in diseases. Unlike genes, the epigenome provides a different set of instructions that determine whether genes are activated or silenced (Berdasco & Esteller, 2019). In the context of epigenetics, it is the changes in the epigenome and gene activity that lead to diseases, while there is no alteration in the DNA sequences or eventual amino acid sequences. In short, epigenetics is the study of the impact of environmental and lifestyle factors on gene activity and expression.

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Environmental factors such as diet and toxins can alter the epigenome, affecting susceptibility to diseases and health outcomes. Research into epigenetic changes offers valuable insights into how these factors contribute to the onset and development of diseases, as well as other phenotypes. These epigenetic alterations are reversible, prompting scientists to postulate that unraveling the intricacies of the epigenome holds tremendous potential for the prevention, diagnosis, and treatment of diseases (Berdasco & Esteller, 2019). However, the insights gleaned from epigenetics research could be misused for non-medical applications, such as employment and insurance, risking bias and stigmatization (Dupras et al., 2019, 2022).

The objectives of this paper are to educate students about the role of epigenetics in diseases and to enable them to recognize the impacts of their lifestyle choices on health. The first part of the paper examines the underlying mechanisms of epigenetics, the effects of environmental factors on the epigenome, and the role of epigenetic changes in various diseases. The second part addresses the ethical, social, and legal issues related to epigenetics and suggests strategies for teaching this topic. Please note that the information in this paper is specifically from a human and/or biomedical perspective.

## ○ Epigenetic Mechanisms

Chromatin is found in the nuclei of eukaryotic cells. It comprises DNA and proteins, and its basic units are called nucleosomes. Each nucleosome consists of DNA encircling a protein core, which contains eight histone proteins. In this section, we explore the molecular mechanisms that enable cells to alter the structure of chromatin. These chemical alterations, called epigenetic marks, can result in changes in gene expression. The epigenetic marks collectively form the epigenome of cells. We also examine how non-coding RNAs impact gene expression.

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### *DNA Methylation*

DNA methylation is an important epigenetic mechanism. DNA methyltransferase catalyzes the transfer of methyl groups to cytosine in DNA, leading to the formation of 5-methylcytosine. Methylation can occur at CpG sites throughout the genome, not just at promoters, and in these cases, it can be linked to either the activation or repression of transcription. DNA methylation is essential for processes such as X-chromosome inactivation and cellular differentiation (Gagnidze & Pfaff, 2022).

### *Histone Modifications*

In epigenetics, histones can be modified in various ways, each affecting chromatin structure and gene expression. Key types of histone modifications, collectively known as the histone code, include acetylation, methylation, phosphorylation, ubiquitylation, sumoylation, crotonylation, GlcNAcylation, and citrullination (Zhang et al., 2021). These modifications are dynamic and reversible, allowing cells to respond to different signals and environmental changes by altering gene expression patterns. In this section, we will elaborate on histone acetylation and methylation.

Histone acetyltransferases accelerate the transfer of acetyl groups from acetyl-CoA to the amino groups of lysine residues within histone N-terminal tails, neutralizing their positive charge. This reduction in charge weakens the bonds between histones and the negatively charged DNA, thereby opening the chromatin structure. As a result, transcription factors and RNA polymerase gain greater access to gene promoters, facilitating transcription. In contrast, histone deacetylases catalyze the removal of acetyl groups, causing the chromatin to become compact and inhibiting transcription (Gagnidze & Pfaff, 2022).

In the case of histone methylation, histone methyltransferase catalyzes the addition of methyl groups to the tails of histones, leading to the condensation of chromatin and the inhibition of transcription. Conversely, the removal of methyl groups from histone tails results in the opening of chromatin structure, thereby facilitating transcription.

### *Non-Coding RNAs*

There are at least nine types of short non-coding RNAs involved in gene regulation, of which microRNAs are just one type (Table 1). MicroRNAs are short, single-stranded, non-coding RNAs that control gene expression at the post-transcriptional level and are typically 18–25 ribonucleotides long. They decrease translation by binding to the 3' untranslated region of mRNAs. This complementary binding can lead to the degradation of mRNAs or the inhibition of translation. MicroRNAs play a regulatory role in processes such as cellular differentiation by selectively binding to multiple mRNA molecules within differentiation pathways. This process leads to the repression of specific genes while concurrently activating others, culminating in the transformation of a stem cell into a specialized cell (Yao et al., 2019).

Unlike microRNAs, long non-coding RNAs (lncRNAs) possess more than 200 ribonucleotides and control gene expression via diverse mechanisms. For example, some lncRNAs serve as guides, ushering enzymes to specific locations to affect DNA methylation and histone modifications. This can result in either a decrease or an increase in transcription. Other lncRNAs function as decoys, capturing transcription factors and preventing them from binding to DNA, resulting in a decrease in transcription. LncRNAs play crucial roles in cellular differentiation, organ development, and immune responses (Kazimierczyk & Wrzesinski, 2021).

**Table 1. Brief description of different types of short non-coding RNAs**

| Short non-coding RNAs | Brief description |
|---|---|
| MicroRNAs (miRNAs) | These are small RNA molecules that regulate gene expression post-transcriptionally by binding to complementary sequences on messenger RNAs (mRNAs), leading to their degradation or inhibition of translation. |
| Small Interfering RNAs (siRNAs) | These are double-stranded RNAs involved in the RNA interference (RNAi) pathway, where they guide the degradation of complementary mRNA sequences, effectively silencing specific genes. |
| Piwi-interacting RNAs (piRNAs) | These are the largest class of small non-coding RNAs in animal cells, primarily involved in regulating genetic elements in germ cells. |
| Small Nuclear RNAs (snRNAs) | These are involved in the splicing of pre-mRNA, a crucial step in the maturation of mRNA. |
| Small Nucleolar RNAs (snoRNAs) | These guide chemical modifications of other RNAs, particularly ribosomal RNAs (rRNAs), transfer RNAs (tRNAs), and snRNAs. |
| Small Cajal Body-specific RNAs (scaRNAs) | These are a subset of snoRNAs that specifically localize to Cajal bodies and are involved in the modification of snRNAs. |
| Endogenous Short-interfering RNAs (endo-siRNAs) | These are similar to siRNAs but are derived from endogenous sources within the cell and play roles in gene regulation and defense against transposons. |
| Trans-acting siRNAs (ta-siRNAs) | These are plant-specific siRNAs that regulate gene expression by guiding the cleavage of target mRNAs. |
| Repeat-associated small interfering RNAs (rasiRNAs) | These are involved in silencing repetitive elements and transposons, particularly in the germline. |

## ○ Effects of Environmental Factors on Epigenetic Marks

Epigenetic mechanisms can modify the DNA and histones of chromatin, influencing gene expression. Here, we explore how environmental factors can alter epigenetic marks through these mechanisms.

### *Maternal Diet*

Maternal diet plays a vital role in determining the epigenetic marks of a fetus, which control cellular differentiation, tissue development, and the baby's overall health. The nutrients consumed by an expectant mother can directly affect DNA methylation. For example, folate is necessary for supplying methyl groups needed for this process. Adequate folate intake is essential for preventing neural tube defects, while a deficiency can lead to abnormal DNA methylation patterns.

A diet rich in omega-3 fatty acids, antioxidants, and polyphenols may promote histone modifications. Omega-3 fatty acids can increase histone acetylation, enhancing the expression of neuroprotective genes and those involved in synaptic plasticity, neurogenesis, and anti-inflammatory responses. This results in improved cognitive outcomes, such as better memory, attention, and problem-solving skills in the offspring (Acevedo et al., 2019). Antioxidants and polyphenols, prevalent in fruits, vegetables, and whole grains, can protect against oxidative stress (Maugeri et al., 2024). They can influence histone modifications, regulating the expression of genes that respond to oxidative stress. This regulation includes the upregulation of genes encoding antioxidant enzymes, such as superoxide dismutase and glutathione peroxidase, which play a crucial role in neutralizing free radicals.

Epigenetic changes induced by maternal diet can persist throughout a child's life, influencing future health (Peral-Sanchez et al., 2022). Some studies suggest that the beneficial effects of maternal intake of folate, omega-3 fatty acids, antioxidants, and polyphenols can be passed on to subsequent generations through epigenetic inheritance (Maugeri et al., 2024). This highlights how a maternal diet can potentially affect three generations: the mother, the fetus, and the oocytes formed in the fetus. This underscores the transgenerational effects of epigenetic alterations due to environmental exposures.

### *Chronic Stress*

Chronic stress significantly affects DNA methylation patterns, impacting overall health. It initiates a series of physiological changes, including the secretion of stress hormones such as cortisol. Cortisol influences DNA methylation by affecting the enzymes that add or remove methyl groups, with the specific effects varying based on context, gene, and cell type. Changes in DNA methylation can influence several biological processes, including brain development and function. Gaining insight into these epigenetic processes is essential for developing methods to mitigate the effects of stress on general health (Schiele et al., 2020). These methods include psychotherapy, medications such as antidepressants, nutritional supplements such as folic acid or vitamin $B_{12}$, and lifestyle interventions such as meditation, yoga, or other relaxation techniques.

Individuals suffering from post-traumatic stress disorder (PTSD) are known to have extremely low levels of DNA methylation in ten differentially methylated regions (DMRs): *APOB*, *MUC4*, *EDN2*, *ZFP57*, *GPX6*, *CFAP45*, *AFF3*, *TP73*, *UBCLP1*, and *RPL13P*. Vinkers et al. (2021) conducted a study to determine whether successful treatment of PTSD can restore these epigenetic marks. The control group comprises 23 soldiers who have been exposed to trauma but remain healthy, while the experimental group consists of 21 soldiers who suffer from PTSD, undergo psychotherapy, and are in remission. Interestingly, the researchers found that successful treatment of PTSD resulted in increased DNA methylation in the ten DMRs, with *ZFP*57 showing the most consistent and significant increase related to PTSD symptom reduction, indicating the reversibility of epigenetic marks associated with the development of PTSD.

### *Toxins*

Formaldehyde is often present in wood products such as furniture; included in household products such as glues, paints, and lacquers; and used as a preservative in some medicines and cosmetics. The primary route of exposure to formaldehyde is through inhaling air containing this compound. Due to its high solubility in water, formaldehyde can permeate every cell within the body. A recent, high-impact study revealed that the body can produce formaldehyde endogenously when it metabolizes the artificial sweetener aspartame (Pham et al., 2023). The researchers discovered that formaldehyde could inhibit the MAT1A protein and cause a decrease in S-adenosyl-L-methionine, which is a universal donor of methyl groups, thereby leading to the demethylation of histones.

Cigarette smoke is toxic, comprising thousands of chemicals, including nicotine, hydrogen cyanide, formaldehyde, lead, arsenic, ammonia, nitrosamines, and polycyclic aromatic hydrocarbons. Cigarette smoking has been closely linked to reversible epigenetic modifications. Researchers have demonstrated that the *AHRR* gene, which commonly shows lower DNA methylation levels in smokers, undergoes a process of epigenetic restoration when smoking is ceased (Fang et al., 2023). However, the rate of recovery is non-uniform and varies with a smoker's history. Light smokers may see a return to non-smoker methylation levels within a year, while heavy smokers might need more than two years to observe similar changes. This suggests that the epigenetic marks due to cigarette smoke are not indelible but can be significantly altered with changes in behavior.

Although alcohol may be consumed in social settings, it is classified by the World Health Organization as a toxic substance. Studies have established a link between alcohol consumption and accelerated aging, as indicated by changes in DNA methylation status. Zindler et al. (2022) reported that aging is accelerated by 3.64 years in patients with alcohol use disorder (AUD) compared with a control group. These researchers were the first to provide evidence for the recovery effects of long-term abstinence from alcohol. When AUD patients abstain from alcohol for 12 months, their DNA methylation age decreases by 3.1 years, reinforcing the concept that epigenetic marks are reversible with changes in behavior.

## ○ Role of Epigenetic Changes in Diseases

Epigenetic changes play a significant role in embryonic development, the onset and progression of various conditions, and other biological processes such as aging. In this section, we examine how the dysregulation of epigenetic mechanisms can lead to cancer and diabetes.

### *Cancer*

Epigenetic mechanisms are pivotal in modulating the expression of oncogenes and tumor suppressor genes, which can either promote or suppress tumor development. DNA methylation serves as a key regulatory switch for both oncogenes and tumor suppressor genes. While hypomethylation activates oncogenes, hypermethylation

silences tumor suppressor genes. Together, these processes lead to the initiation and development of cancer (Pathak et al., 2023).

Several oncogenes are known to play critical roles in the development of various cancers in humans; two of the most significant ones are *MYC* and *BCL-2*. The *MYC* gene encodes the c-Myc transcription factor, while the *BCL-2* oncogene encodes a protein that promotes cell survival but inhibits apoptosis. DNA hypomethylation at the promoter regions leads to the overexpression of both oncogenes, resulting in uncontrolled cell division and other hallmarks of cancer (Nagaraja & Nagarajan, 2021). The *MYC* gene is linked to hepatocellular carcinoma, renal cell carcinoma, and lung adenocarcinoma. In contrast, the *BCL-2* gene is associated with chronic lymphocytic leukemia, multiple myeloma, Burkitt lymphoma, and non-Hodgkin's lymphoma.

Contrary to oncogenes, tumor suppressor genes such as *p53* and *RB1* protect the body from cancer. The *p53* gene is responsible for encoding the p53 protein, which plays crucial roles in cell cycle arrest, mending damaged DNA, and triggering apoptosis of cells containing irreparable DNA. Likewise, the *RB1* gene encodes the retinoblastoma protein, which inhibits cell cycle progression. However, the silencing of both tumor suppressor genes through DNA hypermethylation at the promoters results in the devastating collapse of these protective mechanisms, leading to the development of tumors. The *p53* gene is associated with a broad range of cancers, including bile duct cancer, brain cancer, breast cancer, colorectal cancer, liver cancer, lung cancer, and pancreatic cancer. In contrast, the *RB1* gene is implicated only in bladder cancer and eye cancer (Chen et al., 2020).

### *Diabetes*

Type 1 diabetes (T1D) is a chronic autoimmune disorder with a complex cause, potentially involving epigenetic regulation. Researchers from the University of Turku, Finland, discovered that children who develop T1D exhibit epigenetic changes at a very early stage of the disorder, long before autoantibodies against pancreatic β-cell antigens are detected in the blood. They collected blood samples at multiple time points from people diagnosed with T1D and control groups, even before the appearance of autoantibodies. In one study, Starskaia et al. (2022) reported altered DNA methylation in four genes, namely *IRF5*, *ARRDC2*, *PCBP3*, and *TRAF3*, in T cells from T1D individuals compared with the control group. In another study, aberrant microRNA expression was observed in the blood of people diagnosed with T1D compared with the control group (Suomi et al., 2022). These findings are extremely important and will enable researchers to develop blood-based biomarkers to identify children at risk of developing T1D before autoantibodies appear. The presence of autoantibodies indicates active autoimmunity, signaling that the immune system has failed to recognize and tolerate the body's own cells.

Researchers have long established that DNA methylation at 5,584 sites in the genome of pancreatic β-cells differs markedly between individuals diagnosed with type 2 diabetes (T2D) and those without the condition. However, it was only recently that Rönn et al. (2023) demonstrated that individuals with T2D exhibit the same DNA methylation patterns as those with elevated blood glucose levels but who are undiagnosed with T2D. This finding suggests that altered DNA methylation may contribute to the development of T2D. The study also identified 203 genes, including *CABLES1*, *FOXP1*, *GABRA2*, *GLR1A*, *RHOT1*, and *TBC1D4*, with altered DNA methylation in individuals with T2D compared with the control group. When researchers knocked out the expression of the *RHOT1* gene in cells from individuals without T2D, insulin secretion decreased, confirming the gene's importance for insulin secretion. Scientists are currently developing blood-based biomarkers that can predict who is at risk of developing T2D. If successful, physicians will be able to identify individuals with altered DNA methylation before they become ill. These individuals could then receive personalized lifestyle advice to decrease their risk of T2D or undergo epigenetic editing to correct the activity of certain genes.

## ○ Role of Epigenetics in Embryonic Development

While epigenetic modifications can occur throughout a person's life, those that happen during embryonic development are especially crucial (Wilkinson et al., 2023). Different genes need to be activated or deactivated at specific times to ensure that developmental processes occur in the correct sequence. Additionally, genes must be expressed in the appropriate cells and tissues. This spatial control ensures that cells differentiate into the correct types and form the appropriate structures in the right locations. Each stage of this process is meticulously regulated by the expression of specific gene groups.

In mammals, the fusion of sperm and ovum results in the formation of a zygote. These gametes are highly specialized cells, each possessing a unique genome and epigenome. The resulting zygote inherits genomic DNA sequences from both the sperm and ovum. However, unlike genomic DNA, the epigenomes from both gametes are erased during the early stages of embryonic development, followed by new epigenome programming. This reprogramming occurs in two phases (Gopinathan & Diekwisch, 2022). The first phase takes place early in development, before embryo implantation, while the second phase occurs during gamete formation following the fetus's sex determination. In the first phase, epigenome reprogramming is essential for restoring totipotency, which is necessary for cellular differentiation in embryonic tissues and organogenesis. The second phase is crucial for the development of sex-specific gametes. Thus, epigenetic regulation during development is highly dynamic and mitotically inherited. The process of rebuilding the embryonic epigenome is significantly influenced by environmental factors.

## ○ Epigenetic Testing

Several biotech companies, such as Qiagen, Chronomics, EpigenCare, MyDNAge, and EpiMedTechGlobal, offer epigenetic test kits online to both the public and physicians. Some of these kits can estimate biological age by measuring DNA methylation, which may differ from chronological age. This information can be used to assess overall health and predict longevity. Additionally, there are test kits that measure exposure to tobacco smoke, empowering individuals with knowledge to protect their health. Some kits also analyze the methylation patterns of key genes implicated in stress responses and psychiatric disorders, including *NR3C1*, *FKBP5*, *BDNF*, *IL6*, and *OXTR*. These companies also provide test kits for the early detection of liver cancer, breast cancer, and cervical cancer (EpiMedTechGlobal, 2023). While there are kits available for the early diagnosis of Alzheimer's disease, it is important to note that they are still in the research phase and not yet available for clinical use (Zhang et al., 2023).

## ○ Ethical, Social, & Legal Issues of Epigenetics

The ethical issues related to genetic testing and epigenetic testing share several similarities, reflecting broader concerns about informed consent, privacy, and equity. Here are some key parallels: both genetic and epigenetic testing require comprehensive informed consent. Individuals must understand the implications of the tests, including potential outcomes and risks. The sensitive nature of genetic and epigenetic information raises significant privacy concerns, as there is a risk of unauthorized access to personal data, which could lead to discrimination or stigmatization based on genetic or epigenetic profiles. Additionally, there are concerns about equitable access to both types of testing; high costs can create disparities, potentially leaving marginalized groups without access to beneficial technologies.

The ethical issues related to genetic testing and epigenetic testing differ in one major way, reflecting the distinct nature of the two fields. Genetic mutations are generally stable and inherited, leading to long-term implications for individuals and their descendants. In contrast, epigenetic changes can be reversible and influenced by lifestyle choices, which complicates ethical considerations. For example, if an individual has an epigenetic marker linked to a disease, they might feel pressured to change their behavior, raising questions about autonomy and personal responsibility.

### *Informed Consent*

Informed consent is essential for individuals undergoing epigenetic testing. However, informed consent in the context of epigenetics may be fraught with ethical concerns (Dupras et al., 2019). To begin with, both the vast amount and complexity of epigenetic information, which can be difficult for even experts to grasp, create a substantial challenge in ensuring participants are genuinely informed. For instance, the PubMed database indicates that around 50,000 peer-reviewed journal papers on 'epigenetics' have been published so far, with more than 19,000 of them published since 2013. Next, the traditional consent process may not be suitable for epigenetic testing. As epigenetics is a rapidly growing field, researchers need to modify the consent process to accommodate its dynamic and evolving nature. Finally, since the epigenetic data of participants might be similar to that of their family members, any disclosure will affect not only the participants but also their family members, who may not have consented to the tests (Santaló & Berdasco, 2022).

### *Risk of Stigmatization & Discrimination*

With developments in epigenetic testing, physicians can diagnose diseases at a very early stage, allowing patients to start treatment promptly and increase their chances of full recovery. For instance, Zhang et al. (2023) reported that changes in DNA methylation can be detected in the blood and cerebrospinal fluid of individuals with Alzheimer's disease (AD) many years before the onset of clinical symptoms. Therefore, changes in DNA methylation can serve as biomarkers for the early detection, monitoring, and treatment of AD. While we reap the benefits of epigenetic advances, ethical concerns arising from the non-medical use of epigenetic data by various stakeholders, including employers and insurers, cannot be overlooked. As these stakeholders tap into such information to further their agendas, biases and discrimination based on epigenetic data are likely to pose a threat in the future, undermining the principle of equality (Dupras et al., 2019).

Employers may refer to epigenetic data when making decisions related to recruitment and promotions. Individuals with epigenetic biomarkers of desirable traits may be preferred over those with undesirable traits, such as accelerated biological age, depression, smoking, and alcohol consumption. In certain situations, these markers could be viewed by employers as forewarnings of future health concerns, prompting unjustified changes to job positions and pay (Dupras et al., 2022). Despite its potential, the application of epigenetic data in the employment sector remains mostly theoretical and is a subject of intense debate. Most discussions emphasize the importance of regulating any future use of such data to safeguard individuals' rights and prevent misuse (American Civil Liberties Union, 2024).

Insurers began exploring epigenetic testing for life insurance underwriting in 2020. The Society of Actuaries (2020) published a white paper detailing how epigenetics may impact the life insurance industry. Industry experts strongly believe that epigenetics is likely to be adopted because it has the potential to enable more precise underwriting and offer more personalized life insurance premiums. Shapo and Masar III (2020) argue that epigenetic testing, which is non-invasive and can be done using saliva samples, provides accurate information about an individual's current health status, helping with accurate risk classification and underwriting. They also contend that using epigenetic data aligns with regulatory goals of transparency and fairness. However, while such a practice would benefit low-risk individuals, those at higher risk based on their epigenetic profiles would be penalized by having to pay exorbitant premiums. Ironically, these high-risk individuals, who need insurance coverage the most, could be deterred from taking out life insurance (Dupras et al., 2019).

Recently, Lloyd et al. (2023) published an insightful article suggesting that the reversible nature of epigenetic marks could serve as a point of intervention, potentially paving the way for compassion and justice in life trajectories. As described earlier, epigenetic changes caused by smoking, alcohol consumption, and PTSD are reversible, with DNA methylation levels showing recovery upon cessation, abstinence, and successful treatment, respectively (Fang et al., 2023; Vinkers et al., 2021; Zindler et al., 2022). Recent research also shows that accelerated biological aging can be reversed through promising epigenetic reprogramming strategies, which involve DNA methyltransferase and histone deacetylase inhibitors (Pereira et al., 2024). In view of these findings, employers or insurers could encourage individuals who smoke, consume alcohol, or suffer from stress disorders to undergo appropriate treatments such as nicotine replacement therapy, rehabilitation programs, or psychotherapy. Once they have fully recovered from their conditions, as confirmed by epigenetic tests, they could be given another chance to be hired, promoted, or insured. This could go a long way toward developing a caring society.

According to the United Nations High Commissioner for Refugees (2024), approximately 123 million people were forcibly displaced worldwide due to persecution, conflict, violence, or human rights violations. This figure includes 68 million internally displaced persons, 38 million refugees, 8 million asylum seekers, and 6 million individuals in need of international protection. These displaced individuals, often lacking identity documentation, attempt to obtain asylum seeker or refugee status in countries such as Australia, Germany, and the United States. Since those under 18 often have access to additional resources and protection that can make it easier for them to become refugees compared with adults, some individuals falsely claim to be minors. There has been ongoing discussion about

using epigenetic clock-based tests to verify age claims; however, this approach raises significant ethical concerns (Dupras et al., 2019). It is noteworthy that these tests reveal the biological age rather than the chronological age. Since potential asylum seekers and refugees usually live in horrendous conditions, including starvation, overcrowding, fear, and diseases, their biological age is likely to exceed their chronological age. Hypothetically speaking, a minor difference of a few months could unfairly deny asylum to someone who is genuinely 17.8 years old, even if the biological age is found to be 18.2. This demonstrates the risks associated with using epigenetic clock-based tests to determine the destiny of individuals. Despite its potential for age estimation, epigenetic testing must be further refined to be reliably used in human rights contexts (Abbott, 2018).

### *Achieving Distributive Justice*

Achieving distributive justice is crucial for fostering fairness in society, particularly in the realm of health equity. Health disparities among socioeconomic groups are significantly influenced by variations in environmental and lifestyle factors, which can lead to unequal health outcomes (Martin et al., 2022). For instance, marginalized communities often face higher exposure to pollutants and limited access to nutritious food, exacerbating their health challenges. Santaló and Berdasco (2022) highlight the ethical implications of these disparities, noting that certain demographics disproportionately bear the burden of chronic diseases linked to epigenetic changes.

To address these issues, it is imperative that advancements in clinical epigenetics are made accessible to all populations, ensuring that no group is unfairly disadvantaged (Dubois et al., 2020). This can be achieved through targeted public health initiatives that prioritize research funding for conditions prevalent in underserved communities. Additionally, government policies must actively promote healthy living environments by implementing regulations that reduce environmental toxins, enhance access to healthcare, and support community-based wellness programs (Chiapperino, 2018). By creating equitable conditions for health, we can work toward a society where everyone has the opportunity to thrive, regardless of their socioeconomic background.

### *Transgenerational Equity*

There is growing evidence that parental exposure to environmental factors can influence the health of future generations through epigenetic regulation (Korolenko et al., 2023). This issue raises numerous ethical, social, and legal concerns.

Ethically, the current generation has a moral obligation to reduce harmful exposures that could affect the health of future generations. Moreover, the ethical principle of informed consent is relevant here. Typically, individuals have the right to be informed about and consent to any action affecting them. However, future generations, who will inherit the environmental conditions we create, cannot provide consent. This includes changes to the environment that may affect human health, such as pollution, climate change, and chemical exposure. Since future generations cannot consent to the risks we impose on them, we must act fairly and morally by minimizing these risks and harms to protect the health and well-being of those who cannot advocate for themselves (Santaló & Berdasco, 2022).

Socially, understanding epigenetic regulation could lead to public health initiatives aimed at reducing exposure to harmful environmental factors. Additionally, there may be a need for increased education on how lifestyle choices can have long-term effects on the health of one's descendants (Meloni & Müller, 2018).

From a legal perspective, stricter regulations on environmental pollutants might be implemented to safeguard the health of future generations. Additionally, epigenetics may provide molecular evidence linking past chemical exposures to health conditions, potentially aiding in civil liability cases and offering compensation for environmental harms. However, the difficulty of quantifying the harm with certainty may complicate the application of epigenetics in the courtroom (O'Connell & Karpin, 2020).

### *International Legal Frameworks Governing Epigenetics*

International legal frameworks are beginning to take shape as epigenetics continues to advance and intersect with health, human rights, and bioethics. The major legal frameworks are as follows:

- The World Medical Association (2013) developed the Declaration of Helsinki. It provides ethical principles for medical research involving human subjects, including guidelines for informed consent and risk-benefit assessments that are directly applicable to epigenetic studies.
- The European Union (2018) passed the General Data Protection Regulation (GDPR). While not specific to epigenetics, the GDPR sets stringent requirements for handling personal data, including genetic and epigenetic data.
- The UNESCO International Bioethics Committee (2021) has published a report on the principles of protecting future generations in the realm of epigenetics.
- The World Health Organization (2022) provides guidance and fosters international cooperation on genetic and epigenetic research, focusing on ethical issues, public health implications, and regulatory standards.

The rapid progress in epigenetic research creates major hurdles for global legal frameworks. As our understanding of epigenetics increases, regulations for epigenetic research and applications must evolve accordingly. There must also be consistency and uniformity in the legal systems across all countries to foster global collaboration. Hence, international bodies, governments, researchers, and bioethicists must work together to refine the legislation.

## ○ Strategies for Teaching Epigenetics

### *Aligning Learning Outcomes with NGSS*

The learning outcomes for the high school topic on "Epigenetics" align with several elements of the Next Generation Science Standards (NGSS). Here's how they correspond:

1. High School (HS)-Life Sciences (LS) 1-1: Structure and Function - Explaining how epigenetic mechanisms regulate gene expression relates to understanding the structure and function of biological molecules.
2. HS-LS1-2: From Molecules to Organisms - Describing how environmental factors alter the epigenome connects to the interactions between organisms and their environments.
3. HS-LS1-3: Developing and Using Models - Explaining how epigenetic changes can lead to diseases like cancer and diabetes involves modeling biological processes and their implications for health.

4. HS-LS1-4: Cell Growth and Division - Discussing the role of epigenetics in embryonic development ties into understanding how cells grow and differentiate.
5. HS-Engineering, Technology, and the Applications of Science (ETS) 1-1: Engineering Design - Discussing ethical, social, and legal issues related to epigenetics reflects the need for responsible engineering practices and societal considerations in scientific advancements.

These outcomes emphasize the integration of life sciences and engineering practices, fostering a comprehensive understanding of how epigenetics impacts health and society.

In the future, researchers will continue to elucidate the differences in the epigenomes of individuals diagnosed with certain conditions compared with those without these conditions. They could then develop blood-based biomarkers for the early diagnosis, monitoring, and treatment of these conditions.

### Interactive Videos

Teachers can share the following videos. They are highly engaging and animated, explaining epigenetics in a simple and accessible way.

- The Epigenome at a Glance: Available at https://learn.genetics.utah.edu/content/epigenetics/intro, this video serves as a great introduction to epigenetics.
- Epigenetics: Can we control our Genes? Available at https://www.bbc.com/reel/playlist/conversation-starters?vpid=p0gm1jv6, this video explores the concept of epigenetics and whether we can control our genes.
- The Epigenetics of Identical Twins: Available at https://learn.genetics.utah.edu/content/epigenetics/twins, this video shows that many environmentally induced differences are reflected in the epigenomes of identical twins.
- Epigenetics: Available at http://www.pbslearningmedia.org/resource/biot09.sci.life.gen.epigenetics/epigenetics/, this video highlights the role of epigenome in gene expression and explains why identical twins, despite sharing the same genes, become more epigenetically dissimilar as they age.
- What does Epigenetics have to do with Honeybees? Available at https://www.youtube.com/watch?v=2uiB8Fg8iRg, this video explains the mechanism of DNA methylation using the example of honeybee colonies, where DNA methylation solely determines whether a larva develops into a queen or worker.

### Storytelling

Teachers can share stories of real people and how the environment has impacted their epigenetics. This personalizes science and makes it more tangible. For example, introduce students to the NASA Twins Study involving identical twin astronauts Scott and Mark Kelly (Garrett-Bakelman et al., 2019). Scott was on the International Space Station for 340 days, while Mark stayed on Earth. The study observed significant epigenetic changes, particularly in DNA methylation patterns, in pathways related to immune function and oxidative stress during Scott's time in space. While a large portion of these modifications normalized following Scott's return to Earth, around 9% of the epigenetic shifts persisted even 6 months after the mission, suggesting that some epigenetic marks are more easily reverted than others.

### Case Studies

Researchers have previously noted that the majority of identical, or monozygotic, twins develop differently over time, even though they share the same genes. These differences in phenotypes could be explained by the accumulation of different life experiences, resulting in variations in their epigenomes. For instance, in a study of identical twins, Duncan et al. (2022) found that siblings with more than 150 minutes of physical activity a week had smaller waistlines and body mass indices compared with their sedentary siblings. This correlated with differences in their epigenomes: only the sedentary twins had epigenetic marks associated with cardiovascular conditions, stroke, and T2D. Teachers can reinforce the importance of environmental factors in the development of identical twins by utilizing a case study titled "Identical Twins, Identical Fates? An Introduction to Epigenetics" (National Center for Case Study Teaching in Science, 2012). The case chronicles the life trajectories of two identical twins, where one is afflicted with schizophrenia while the other is not, illustrating the significance of environmental factors on disease susceptibility.

### Assessment

Assessing the learning outcomes for the high school topic on "Epigenetics" can be done through various methods that align with the NGSS standards. Below are some effective assessment strategies:

1. Formative Assessments
   a. Quizzes and Tests: Short quizzes can assess students' understanding of key concepts, such as the role of epigenetic mechanisms and their impact on gene expression.
   b. Class Discussions: Engaging students in discussions about how environmental factors influence the epigenome can help gauge their comprehension and ability to connect concepts.
2. Project-Based Assessments
   a. Research Projects: Students can conduct research on specific epigenetic changes and their implications for health, presenting their findings through reports or presentations.
   b. Model Creation: Students can create models to illustrate how epigenetic changes lead to diseases, demonstrating their understanding of biological processes.
3. Practical Applications
   a. Case Studies: Analyzing real-world case studies related to epigenetics can help students apply their knowledge to practical scenarios, such as the effects of maternal diet on offspring.
   b. Ethical Debates: Organizing debates on the ethical implications of epigenetic research can assess students' understanding of the social and legal issues involved.
4. Summative Assessments
   a. Final Projects or Papers: A comprehensive project or paper that synthesizes their learning about epigenetics, including its mechanisms and implications, can serve as a capstone assessment.
   b. Presentations: Students can present their research or models to the class, allowing for peer assessment and feedback.

5. Self-Assessment and Reflection
    a. Reflection Journals: Encouraging students to maintain journals where they reflect on what they have learned about epigenetics can provide insights into their understanding and personal connections to the material.

These assessment methods not only evaluate students' knowledge but also encourage critical thinking and application of concepts in real-world contexts.

## ○ Conclusion

Understanding epigenetics enables us to make well-informed decisions about our lifestyles that benefit both our health and that of future generations. For instance, Li et al. (2018) reported that individuals who adopt healthy lifestyles live more than a decade longer than those who do not. Researchers have completed numerous epigenome-wide association studies using patterns of DNA methylation and histone modifications that differ between healthy individuals and people diagnosed with diseases. Such data opens new avenues for the prevention, detection, diagnosis, and treatment of various conditions. Therefore, unraveling the mysteries of the epigenetic code paves the way to a healthier future. As we continue to advance our knowledge of epigenetics, ethical concerns may arise. Hence, we must integrate these insights into society responsibly, ensuring that the benefits of epigenetic discoveries are maximized while the potential risks, such as discrimination, are reduced.

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