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Research Article

The role of epigenetic in cancer cases

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Abstract-Epigenetics is an emerging field of biology that concerns the elements that control gene expression, but do not change the DNA sequence. This topic was selected because of its relevance in several biological processes and diseases such as cancer [1]. Which of our genes and gene regulator regions are and are not turned on (or off) is, in no small measure due to changes (epigenetic ones) to the DNA such as DNA methylation, histone modification and non-coding RNA activity [2,3]. In contrast to genetic mutations, which change the underlying DNA code permanently, reproducible, reversible modifications due to epigenetics can be appealing targets for therapeutics [3].

Cancer is fiendishly complex and hard to understand and treat. It would be in relation with the positive of proliferation and dissemination of tumoral cells. Although the gene mutations have been considered as the predominant force driving cancer, the emerging insights on epigenetics have shown that the epigenetic alterations take center stage during cancer initiation and progression [4]. These changes may play on the cancer initiation and progression by way of activating oncogenes, inactivating tumor suppressor genes, promoting the tumor microenvironment, etc [5]. Epigenetic modifications and changes in epigenetic patterns need to further be understood to work on the novel diagnosis tools, prognosis and personal medications as well so for the better patient survival [6,7].

Keywords: Epigenetic, Cancer, Cancer Cases.

I. UNDERSTANDING EPIGENETICS

Epigenetics is a fascinating area of science that explores how genes are regulated from their DNA code. The term "epigenetics" comes from the Greek prefix "epi-", which means "on top of" or "above" [8], it refers to the changes in gene function that occur independently of changes to the DNA sequence. Some factors that can influence these changes may be related to the external environment, the types of food eaten, stressors, and relationships with others. Epigenetics are 'the changes in gene activity that are not caused by changes to gene sequences'; that are known to affect development earlier and later in life, as well as disease risk [9].

Flexibility and reversibility is one of the most interesting parts of epigenetics. Whereas mutations are permanent changes to the DNA code, epigenetic changes can be tacked on or taken off by environmental

signals. This plasticity allows cells to cope with dynamic changes in their environment, an essential feature in processes such as embryonic development, cell differentiation and tissue repair. For example, during development, epigenetic changes switch on or off and, and directly a stem cell to become muscle, brain or blood cell [10].

Additionally, epigenetic control is essential for cellular identity and function. Every cell type in the body has its own set of chemical tags, which make up an "epigenome," that tells a cell's machinery whether to read the genetic recipe and make a particular protein. This epigenetic encoding ensures, for instance, that muscle cells have the genes that they need to contract, while nerve cells have the genes that they need to transmit chemical signals. Deregulation of epigenetic code and deviation from what the normal could be implemented may lead to a wide variety of pathologies, including cancer [11].

Furthermore, the epigenetic modification can be inherited from one generation to the next, which is referred to as transgenerational inheritance. In addition, studies have found that environmental exposures of the parents, such as diet and stress, can send signals to the offspring's genome, leading to epigenetic changes that impact the offspring's health and risk of disease. This is a key piece of information for the understanding of the genetic nature/nurture interaction [12].

And knowing more about epigenetics also lets us know important things about how genes work in concert with the environment to change our biology. It also paves the way for exploring new therapeutics for modulating disease by targeting epigenetic changes. The prospect of pioneering biomarkers for the early detection of diseases and personalised medical treatment employing patient specific epigenetic profile is expected by using an epigenetic-mapping-related strategy [8].

II. MECHANISMS OF EPIGENETIC CHANGES

Epigenetic changes are changes to the genome that affect gene expression without changing the sequence of the DNA. These mechanisms involve non-coding RNA regulation, histone modification, as well as DNA methylation. All of these mechanisms are important for determining which genes are to be turned on or off and together coordinate cellular responses and promote genomic stability [8].

DNA Methylation

DNA methylation is one of the best studied means of epigenetic regulation. It involves methylation of the fifth carbon of the cytosine ring of a CpG dinucleotide. Enzymes that transfer a methyl group from SAM to DNA are known as DNA methyltransferases (DNMTs) in this process. These methyl groups can inhibit gene expression, as they can prevent transcription factors and other gene regulatory proteins from binding to DNA [1].

Key Functions of DNA Methylation: Gene Silencing: Methylation of CpG islands, regions rich in CpG dinucleotides within gene promoter regions, can result in gene silencing. That's because transcription factors and other proteins that help turn genes on and off have a more difficult time getting to methylated DNA [7]. X-Chromosome Inactivation: In mammalian females, one of the X chromosomes is inactivated to ensure equivalent dosage between the two sexes. This de-activation works primarily via DNA lhalliation [13],

Genomic Imprinting: An imprinted gene is one that exhibits parent-of origindependent expression. Methylation marks on DNA are established in germ lines and are maintained until the end of life to ensure appropriate patterns of gene expression [14].

Silencing of Transposable Elements: Transposable elements are DNA sequences that can move from one genomic position to another. DNA methylation functions as a restrainer of these elements to maintain the genomic integrity [15].

DNA Methylation in Cancer

Derangement of DNA methylation patterns is a hallmark in many cancers. Such abberancies may result in hyper/hyopmethylation.

Hypermethylation: This occurs often at CpG islands near the promoter regions of tumor suppressor genes, leading to their inactivation. Inactivate of the tumor suppressor genes is a critical step in cancer development [7].

Hypomethylation: global or at specific sites may lead to the activation of oncogenes and expression of normally suppressed transposable elements. Hypomethylation can facilitate genomic instability and carcinogenesis [13].

Therapeutic Implications

Its reversible nature generates interest in using DNA methylation as a therapeutic target in cancer. The drugs — DNA methyltransferase inhibitors (DNMTis) — are designed to undo abnormal patterns of methylation. Azacitidine and decidabine are two drugs used to treat selected types of haematological cancers. These drugs appear promising to enhance the outcome of the cancer treatment as they reactivate silencing tumor suppressor genes and hence reduce genomic instability [1].

III. HISTONE MODIFICATION

Histone modification is an important epigenetic regulating process and refers to the chemical modifications being added to the histone proteins. Histones are the primary proteins around which DNA winds, to form the nucleosomes, which are the basic building blocks of chromatin. Such modification could change the accessibility of DNA to transcription factors and other regulatory proteins and thereby gene expression [16].

Guiding Marks on the Histones

There are many types of histone modifications, each with specific impacts on the structure of chromatin and gene expression. The most common modifications include:

Acetylation: Acetyse groups (CoCH3) are added to lysine residues of histone tails by histone acetystransferases (HATS). Acetylation neutralizes the positive charge of histones, and this reduce their ability to attract the negatively charged DNA, and generate a more open chromatin conformation that facilitates gene transcription [17].

Phosphorylation: Phosphate groups (PO) are added by kinases to serine and threonine residues. Numerous ramifications of phosphorylation including effects on chromatin structure and DNA damage response and cell cycle control [18].

Ubiquitination: The addition of ubiquitin molecules to lysine residues of histones is catalyzed by ubiquitin ligases. Ubiquitination may communicate histone degradation or modify the chromatin structure for the regulation of gene expression [19].

Sumoylation: The attachment of small Ubiquitin-like modifier (SUMO) proteins to lysine residues can reorganize the chromatin structure and gene expression, which is often correlated with gene silencing [19].

Histone Code Hypothesis

The histone code hypothesis suggests that specific combinations of histone modifications—histone marks—create a code that is read by other proteins to control gene expression. Such histone modifications can subtly modulate gene expression in a combinatorial and context-dependent manner. For instance, acetylation at one location and methylation at another of the same histone tail may have opposing effects on gene transcription [16].

Histone Modification in Cancer

Cancer is frequently associated with abnormal histone modifications, which can cause carcinogenesis by changing gene expression:

Histone Acetylation: Low level of histone acetylation, usually resulting from the upregulation of histone deacetylases (HDACs), is associated with gene silencing and carcinogenesis. On the other hand, high levels of acetylation can activate oncogenes [20].

Histone Methylation: Disordered histone methylation modifications, including the overexpression of HMTs or the deletion of histone demethylases, can upregulate or downregulate cancer-related genes [19].

IV. NON-CODING RNAS

Non-coding RNAs (ncRNAs) are RNA molecules that do not get translated into proteins but play important roles in controlling gene expression at several levels, including chromatin structure, transcription, RNA processing, and translation. They are widely categorized into three types based on their size and function: microRNAs (miRNAs), long non-coding RNAs (lncRNAs), and small interfering RNAs (siRNAs) [21].

Micro RNAs (miRNAs) are small (20-24 nucleotides) RNA molecules that regulate gene expression at the post-transcriptional level. These short RNAs base pair to complementary sites in target messenger RNAs (mRNAs) and induce their degradation or repress translation. Through modulation of the stability and translation of mRNAs, miRNAs are able to regulate gene expression in numerous cellular processes including development, differentiation and apoptosis [22].

In cancer, miRNA's oncogenic or tumor suppressor functions have been profoundly addressed. For example, an increased expression of miRNAs such as oncomiRs, would be able to reduce a tumor suppressor genes expression leading to cancer growth. Tumor-suppressor miRNAs would presumably be downregulated to allow overexpression of oncogenes, conversely [23].

Long non-coding RNAs (lncRNAs) are a diverse group of RNA molecules over 200 nucleotides in length that regulate gene expression at many levels. They have been implicated in shaping chromatin, and acting at the levels of transcription and mRNA post-transcriptional processing. LncRNAs can function as ‘scaffolds’ to recruit multiple proteins to form functional complexes, or act as ‘decoys’ to sequester regulatory proteins from their targets [24].

lncRNAs have been shown to participate in tumor development and progression in cancer through regulating important biological processes, including cell proliferation, invasion and metastasis. Some lncRNAs may act like oncogenes promoting the expression of cancer-related genes or as tumor suppressors that repress oncogenic signaling pathways [25].

Small interfering RNAs (siRNAs) are small RNA duplexes involved in RNA interference (RNAi) mechanisms, which lead to the repression of specific genes. siRNAs originate from larger double-stranded RNA molecules that are processed and sequestered into the RNA-induced silencing complex (RISC). The RISC uses one strand of siRNA to direct cleavage of homologous mRNAs and to decrease gene expression [22].

Non-coding RNAs in Cancer: Dysregulation of ncRNAs is frequent in various malignancies. Incorrect expression of miRNAs, lncRNAs, and other ncRNAs can alter normal gene expression pattern which leads to tumor development. For example, the miR-34 family of miRNAs is typically decreased in cancer, resulting in overexpression of genes that promote cell growth and survival. Similarly, the lncRNA HOTAIR is frequently overexpressed in breast cancer, which is linked with a poor prognosis and metastasis [21].

V. CHROMATIN REMODELING

Chromatin remodeling is an important epigenetic regulatory process that includes dynamically modifying chromatin structure to regulate access to genetic information. Chromatin, which is made up of DNA wrapped around histone proteins, may exist in two states: tightly packed (heterochromatin) and loosely packed (euchromatin). The degree of compaction affects the accessibility of DNA to transcription factors and other regulatory proteins, hence controlling gene expression [26].

ATP-dependent chromatin remodeling complexes perform chromatin remodeling by repositioning, ejecting, or restructuring nucleosomes using the energy released during ATP hydrolysis. To change DNA-histone interactions, these complexes have the ability to modify nucleosomes, evict nucleosomes from the DNA, or move nucleosomes along the DNA. The following are the primary categories of chromatin remodeling complexes:

1. SWI/SNF Complexes: To increase DNA accessibility for transcription, these complexes slide and expel nucleosomes. The relevance of SWI/SNF components in preserving genomic integrity is highlighted by the frequent observation of mutations in these components in a variety of malignancies [27].

2. ISWI Complexes: These complexes organize nucleosome placement along the DNA and mainly aid in nucleosome sliding. ISWI complexes are essential for transcription, DNA replication, and DNA repair [28].

3. CHD Complexes: CHD (Chromodomain-Helicase-DNA-binding) complexes are engaged in chromatin remodeling and are distinguished by the existence of chromodomains that detect particular histone modifications. CHD complexes control gene expression and chromatin structure throughout development and differentiation [29].

4. INO80 Complexes: These complexes perform transcription, replication, DNA damage repair, and nucleosome removal and repositioning function. In order to preserve genomic stability [28].

Mechanisms of Chromatin Remodeling

Chromatin remodeling complexes modify chromatin shape and control gene expression through a number of mechanisms:

1. **Nucleosome Sliding:** Certain DNA sequences can be exposed or obscured by nucleosomes being repositioned along the DNA by chromatin remodeling complexes. Transcription factors and other regulatory proteins can enter or exit target genes through this sliding process [27].

2. **Nucleosome Ejection:** Certain remodeling complexes have the ability to push nucleosomes out of the DNA, forming nucleosome-free areas that make it easier for transcription factors to bind and start transcription [28].

3. **Nucleosome Restructuring:** Remodeling complexes have the ability to modify nucleosome structure, which can change how DNA and histone proteins interact. Depending on the situation, this reorganization might either increase or decrease gene expression [29].

Chromatin Remodeling in Cancer: A common characteristic of many malignancies is the dysregulation of chromatin remodeling. Changes in chromatin structure, abnormal expression of remodeling complexes, and mutations in chromatin remodeling genes can all lead to carcinogenesis. For instance, a number of malignancies, such as lung, ovarian, and breast tumors, commonly include mutations in the components of the SWI/SNF complex. These alterations have the potential to alter gene expression and chromatin accessibility, which would aid in the growth and survival of cancer cells [30].

VI. EPIGENETIC CHANGES IN DIFFERENT TYPES OF CANCER

Epigenetic changes can contribute to the initiation and spread of cancer by activating oncogenes or silencing tumor suppressor genes.

Breast Cancer: Breast cancer growth and progression are significantly influenced by epigenetic modifications, including DNA methylation, histone modification, and miRNA expression. Without changing the DNA sequence, these modifications can have an impact on gene expression. For example, tumor suppressor gene silence due to hypermethylation can accelerate the development of cancer. Epigenetic markers that may be used as prognostic and diagnostic tools are still being researched [31].

Lung Cancer: Environmental contaminants are important risk factors for lung cancer, and the epigenetic modifications they cause play a crucial role in the development of lung cancer. Normal cells can become cancerous by changing gene expression, which is facilitated by DNA methylation, histone modifications, and non-coding RNAs. Potential biomarkers for the detection and therapy of lung cancer are being investigated, including epigenetic markers such as DNA methylation patterns of genes including AHRR and F2RL3 [32].

Prostate Cancer: Histone alterations and DNA methylation that impact gene expression are hallmarks of prostate cancer. Prostate cancer has been linked to aberrant epigenetic processes that affect several genes, including DNA hypermethylation and altered histone acetylation. The potential of these epigenetic modifications as targets for diagnosis and treatment is being investigated [33].

Colorectal Cancer The occurrence and progression of colorectal cancer are controlled by epigenetic alterations including the methylation of DNA and modifications to histones. These changes could lead to the loss of tumour suppressor gene function or the overexpression of oncogenes that is a characteristic of cancer proliferation. The researchers finally hope to find epigenetic markers for colorectal cancer which can lead to early diagnosis and treatment [34].

Leukemia: Leukemia is largely driven by epigenetic modifications, such as DNA methylation and histone modifications. These changes may lead to tumor suppressor gene silencing and oncogene activation helping the development and progression of leukemia. Investigations are currently focusing on the possibility that leukemia diagnosis, prognosis, and treatment can be based on epigenetic markers [34].

VII. THE ROLE OF ENVIRONMENTAL FACTORS

The environment plays a major role in epigenetic modifications that may influence gene expression and contribute to the development and progression of cancer. These factors (stress, pollution exposure, diet) can induce epigenetic changes, such as histone modifications, DNA methylation, or variations in non-coding RNAs. For the establishment of cancer prevention and treatment approaches, details on the interplay of environmental factors and the epigenome are essential [35].

Diet: The epigenome is largely influenced by dietary elements. DNA methylation pathways depend on nutrients such as folate, vitamin B12, and other methyl-donating factors. The mRNA levels and DNA methylation status in the blood may be sensitive to a diet with high levels of particular compounds. For example, it has been shown that consumption of cruciferous vegetables, such as those containing compounds such as sulforaphane, may impact DNA methylation and histone acetylation which might decrease the risk of cancer. Nevertheless low sugar and high processed diets can increase the chances of cancer due to unfavourable epigenetic changes [36].

Pollutants: Environmental toxins such as air pollution, heavy metals and poisons, could push DNA's chemistry toward cancerous epigenetic change. For instance, modifications in the DNA methylation of genes associated with lung cancer have been associated with tobacco smoke exposure. Air pollution particles may also change miRNA expression and histones paltry, which may then modify gene expression and promote cancer. The identification of at-risk populations and the development of

strategies to mitigate their influence could be facilitated by acquiring a better understanding of the epigenetic impact of pollutants [37].

Stress: Chronic stress can lead to epigenetic changes in gene expression that promote cancer. Genes involved in the immune response and the stress response may have altered histone modifications and DNA methylation due to cortisol. Such changes may lead to an abnormal immune response, increasing susceptibility to cancer. In addition, the stress-related epigenetic marks may even be inherited by offspring, possibly affecting their health and disease risk [38].

VIII. EPIGENETIC BIOMARKERS FOR EARLY DETECTION

Histone alterations and DNA methylation patterns are examples of epigenetic biomarkers that provide a possible path for cancer early diagnosis. By identifying abnormal epigenetic alterations that occur before tumor development, these biomarkers allow for prompt detection and treatment. For instance, early-stage lung and colorectal malignancies have been found to have hypermethylation of the CDKN2A gene promoter. One non-invasive technique for identifying these changes is liquid biopsies that examine the methylation patterns of circulating tumor DNA (ctDNA). These methods lower the dangers connected with invasive treatments while also facilitating early identification [1].

Diagnostic Techniques: Clinical practice is progressively adopting advanced diagnostic methods that include epigenetic biomarkers. A popular technique for identifying DNA methylation is bisulfite sequencing, which enables single-base precision of methylation patterns. Other methods that can characterize genome-wide epigenetic alterations in a high-throughput way are array-based approaches and methylation-specific PCR (MSP). Real-time methylation analysis is possible with emerging techniques like nanopore sequencing. Furthermore, as epigenetic biomarkers that may be found in physiological fluids, microRNAs (miRNAs), which are tiny non-coding RNAs with regulatory functions, are being researched to provide an additional level of diagnostic accuracy [39].

Prognostic Value: In addition to being useful for early diagnosis, epigenetic biomarkers are essential for determining the course of disease. Certain histone modification patterns and methylation profiles can reveal information about the prognosis of patients and the aggressiveness of tumors. For instance, hypermethylated MGMT gene promoter in glioblastoma is associated with better outcome with alkylating agents, emphasizing the prognostic significance of the gene. There is a possibility that the effectiveness of histone deacetylase (HDAC) inhibitors as therapeutic drugs could be affected by epigenetic profiles. With the inclusion of such a biomarker in "standard" practice, one can achieve more accurate patient stratification and patient-specific treatment regimens [2].

IX. EPIGENETIC THERAPIES AND TREATMENT STRATEGIES

By acting via DNA and chromatin reversible modifications, epigenetic treatments have completely reshaped cancer treatment as we know it. In the dynamic of treatment, in comparison to the traditional treatment, the epigenetic drugs are able to modify the tumor microenvironment and awaken dormant tumor suppressor genes which delay the spread of the cancer. These methods not only enhance the efficiency of treatment, but also offer possible strategies to overcome drug resistance.

DNA Methylation Inhibitors: The most widely-studied group of epigenetic drugs are the DNA methylation inhibitors, decitabine and azacitidine. These compounds reduce hypermethylation of gene promoters and induce expression of silenced tumor suppressor genes by inhibiting DNA methyltransferases (DNMTs). These drugs have achieved significant clinical success and are indicated for hematologic malignancies including acute myeloid leukemia (AML) and myelodysplastic syndromes (MDS). For example, decitabine has been shown to reinstate the expression of genes associated with apoptosis and cell cycle regulation, such as DAPK and p15INK4B [40].

Histone Deacetylase Inhibitors: Inhibitors for the enzyme Histone deacetylase (HDAC) are also promising epigenetic therapies. Drugs such as vorinostat and romidepsin increase histone acetylation leading to a relaxed chromatin configuration and activation of transcription of tumor suppressor genes. HDAC inhibitors are in development for solid tumors and are now FDA approved for CTCL. In addition to the direct effects on tumour cells, HDAC inhibitors modulate the immune system, and immune cells are more capable of fighting malignancies [41].

Combination Therapies: In cancer, combination therapies via integrating conventional therapy and epigenetic drugs have emerged as a powerful strategy. Together, DNA methylation and HDAC inhibitors act in synergy to reactivate genes that neither one alone can do. Moreover, promising results have emerged from the combination of epigenetic drugs with immune checkpoint inhibitors, such as immune checkpoint inhibitors. For example, the results of preclinical studies have demonstrated better and enhanced T cell-mediated responses when azacitidine is combined with anti-PD-1 antibodies. Such an integrated approach makes conceivable the overcoming of resistance mechanisms and the delivery of tailored therapy based on the individual epigenetic profile of a patient [42].

X. FUTURE DIRECTIONS IN EPIGENETIC RESEARCH

Fast-paced advances in the prevention and treatment of cancer are driven by new technologies and findings from the rapidly evolving fields of genomics and epigenetics. Embracing these advances could lead to better therapeutic impact, diagnostic accuracy, and even avenues for understanding cancer biology.

Emerging Technologies: Novel tools change how cancer epigenomes are decoded. Single-cell sequencing technology enables researchers to study the epigenetic modifications in individual cells, thereby making it possible to identify tumor heterogeneity and the dynamic process of cancer progression. Moreover, real-time functional role analysis of DNA methylation and histone marks is enabled by methods such as CRISPR-dCas9 that combines CRISPR techniques with epigenetic modifiers. Besides making it easier to identify over-complex patterns in large datasets, predict how an illness develops and how a therapy will work, the 43 syndrome of things artificial intelligence AI and epigenomics is also revolutionizing the flavor of science.

Room for Improvement: In the field of epigenetic research, there is room to make discoveries that could dramatically change cancer treatment. One focus is on the discovery of new epigenetic biomarkers that can predict the response to immunotherapy and therefore better classify patients. A related intriguing opportunity is the development of second-generation epigenetic drugs that are more specific and have fewer side effects. For instance, selective inhibitors of BET (bromodomain and extra-terminal domain) proteins are under investigation for their ability to epigenetically control transcriptional regulators in cancer. Furthermore, investigations into RNA epitranscriptome—chemical modifications and modifications to RNA sequences—expands our understanding of gene regulation and its implications in cancer therapy [44].

REFERENCES

1. Jones, P. A., & Baylin, S. B. (2007). The epigenomics of cancer. Cell, 128(4), 683-692.

2. Sharma, S., Kelly, T. K., & Jones, P. A. (2010). Epigenetics in cancer. Carcinogenesis, 31(1), 27-36.

3. Lu, Y., Chan, Y.-T., Tan, H.-Y., Li, S., Wang, N., & Feng, Y. (2020). Epigenetic regulation in human cancer: the potential role of epi-drug in cancer therapy. Molecular Cancer, 19:79.

4. Mancarella, D., & Plass, C. (2021). Epigenetic signatures in cancer: proper controls, current challenges and the potential for clinical translation. Genome Medicine, 13:23.

5. Baylin, S. B., & Jones, P. A. (2011). A decade of exploring the cancer epigenome - biological and translational implications. Nature Reviews Cancer, 11(10), 726-734.

6. Feinberg, A. P., & Tycko, B. (2004). The history of cancer epigenetics. Nature Reviews Cancer, 4(2), 143-153.

7. Esteller, M. (2008). Epigenetics in cancer. New England Journal of Medicine, 358(11), 1148-1159.

8. Bird, A. (2007). Perceptions of epigenetics. Nature, 447(7143), 396-398.

9. Goldberg, A. D., Allis, C. D., & Bernstein, E. (2007). Epigenetics: a landscape takes shape. Cell, 128(4), 635-638.

10. Ptashne, M. (2013). Epigenetics: core misconcept. Proceedings of the National Academy of Sciences, 110(18), 7101-7103.

11. Heard, E., & Martienssen, R. A. (2014). Transgenerational epigenetic inheritance: myths and mechanisms. Cell, 157(1), 95-109.

12. Jablonka, E., & Raz, G. (2009). Transgenerational epigenetic inheritance: prevalence, mechanisms, and implications for the study of heredity and evolution. The Quarterly Review of Biology, 84(2), 131-176.

13. Robertson, K. D. (2005). DNA methylation and human disease. Nature Reviews Genetics, 6(8), 597-610.

14. Cedar, H., & Bergman, Y. (2009). Linking DNA methylation and histone modification: patterns and paradigms. Nature Reviews Genetics, 10(5), 295-304.

15. Gopalakrishnan, S., Van Emburgh, B. O., & Robertson, K. D. (2008). DNA methylation in development and human disease. Mutation Research/Fundamental and Molecular Mechanisms of Mutagenesis, 647(1-2), 30-38.

16. Kouzarides, T. (2007). Chromatin modifications and their function. Cell, 128(4), 693-705.

17. Bannister, A. J., & Kouzarides, T. (2011). Regulation of chromatin by histone modifications. Cell Research, 21(3), 381-395.

18. Strahl, B. D., & Allis, C. D. (2000). The language of covalent histone modifications. Nature, 403(6765), 41-45.

19. Chi, P., Allis, C. D., & Wang, G. G. (2010). Covalent histone modifications—miswritten, misinterpreted and mis-erased in human cancers. Nature Reviews Cancer, 10(7), 457-469.

20. Dawson, M. A., & Kouzarides, T. (2012). Cancer epigenetics: from mechanism to therapy. Cell, 150(1), 12-27.

21. Esteller, M. (2011). Non-coding RNAs in human disease. *Nature Reviews Genetics*, 12(12), 861-874.

22. Bartel, D. P. (2004). MicroRNAs: genomics, biogenesis, mechanism, and function. Cell, 116(2), 281-297.

23. Calin, G. A., & Croce, C. M. (2006). MicroRNA signatures in human cancers. Nature Reviews Cancer, 6(11), 857-866.

24. Rinn, J. L., & Chang, H. Y. (2012). Genome regulation by long noncoding RNAs. Annual Review of Biochemistry, 81, 145-166.

25. Wapinski, O., & Chang, H. Y. (2011). Long noncoding RNAs and human disease. Trends in Cell Biology, 21(6), 354-361.

26. Varga-Weisz, P. D., & Becker, P. B. (2006). Regulation of higher-order chromatin structures by nucleosome-remodelling factors. Current Opinion in Genetics & Development, 16(2), 151-156.

27. Kadoch, C., & Crabtree, G. R. (2015). Mammalian SWI/SNF chromatin remodeling complexes and cancer: Mechanistic insights gained from human genomics. Nature Reviews Cancer, 15(9), 338-351.

28. Clapier, C. R., & Cairns, B. R. (2009). The biology of chromatin remodeling complexes. Annual Review of Biochemistry, 78, 273-304.

29. Längst, G., & Manelyte, L. (2015). Chromatin remodelers: from function to dysfunction. Genes, 6(2), 299-324.

30. Wilson, B. G., & Roberts, C. W. M. (2011). SWI/SNF nucleosome remodellers and cancer. Nature Reviews Cancer, 11(7), 481-492.

31. Huang, Y., Nayak, S., Jankowitz, R., Davidson, N. E., & Oesterreich, S. (2011). Epigenetics in breast cancer: what's new?. Breast Cancer Research, 13, 1-11.

32. Zhang, A., Luo, X., Li, Y., Yan, L., Lai, X., Yang, Q., ... & Wang, J. (2024). Epigenetic changes driven by environmental pollutants in lung carcinogenesis: a comprehensive review. Frontiers in Public Health, 12, 1420933.

33. Li, L. C., Carroll, P. R., & Dahiya, R. (2005). Epigenetic changes in prostate cancer: implication for diagnosis and treatment. Journal of the National Cancer Institute, 97(2), 103-115.

34. Quintanal-Villalonga, Á., & Molina-Pinelo, S. (2019). Epigenetics of lung cancer: a translational perspective. Cellular Oncology, 42(6), 739-756.

35. Herceg, Z., & Vaissière, T. (2011). Epigenetic mechanisms and cancer: an interface between the environment and the genome. Epigenetics, 6(7), 804-819.

36. Lim, U., & Song, M.-A. (2012). Dietary and lifestyle factors of DNA methylation. Methods in Molecular Biology, 863, 359-376.

37. Hou, L., Zhang, X., Wang, D., & Baccarelli, A. (2012). Environmental chemical exposures and human epigenetics. International journal of epidemiology, 41(1), 79-105.

38. Denhardt, D. T. (2018). Effect of stress on human biology: Epigenetics, adaptation, inheritance, and social significance. Journal of cellular physiology, 233(3), 1975-1984.

39. Esteller, M. (2007). Epigenetic gene silencing in cancer: the DNA hypermethylome. Human molecular genetics, 16(R1), R50-R59.

40. Issa, J. P. J. (2007). DNA methylation as a therapeutic target in cancer. Clinical Cancer Research, 13(6), 1634-1637.

41. Prince, H. M., Bishton, M. J., & Harrison, S. J. (2009). Clinical studies of histone deacetylase inhibitors. Clinical cancer research, 15(12), 3958-3969.

42. Topper, M. J., Vaz, M., Marrone, K. A., Brahmer, J. R., & Baylin, S. B. (2020). The emerging role of epigenetic therapeutics in immuno-oncology. Nature Reviews Clinical Oncology, 17(2), 75-90.

43. Buenrostro, J. D., Wu, B., Litzenburger, U. M., Ruff, D., Gonzales, M. L., Snyder, M. P., ... & Greenleaf, W. J. (2015). Single-cell chromatin accessibility reveals principles of regulatory variation. Nature, 523(7561), 486-490.

44. Zoghbi, H. Y., & Beaudet, A. L. (2016). Epigenetics and human disease. Cold Spring Harbor perspectives in biology, 8(2), a019497.