The Involvement of Epigenetic Mechanisms in Malignant Tumor Gene Transmissions

Mischa Marie Perzanowski

Abstract:

Epigenetics studies physiological changes resulting from gene expression mutations instead of genetic code self-alterations, stating that the environment is responsible for the chemicals that influence and attach to genes. Notably, epigenetic mechanisms maintain the regular development of expression patterns relating to tissue genes specifically. The abnormal epigenetic modifications of specific oncogenes, as well as tumor suppressor genes, may result in uncontrollable cell growth and division, modified gene function, and cancerous mutations. Recently, technological progress has begun to characterize cancerous molecular epigenetic changes, which in turn have driven drug research and development. An example of a type of epigenetic drug and treatment would be cancer growth inhibitors, which function to reactivate tumor suppressor genes, blocking the growth factors that activate uncontrollable cell division and growth, restoring normal cell functions. Research studies have realized that epigenetic mechanisms must be transmitted during cell division, leading to a greater understanding of gene mutations. This study aimed to review how tumor cells transmit their epigenetic features to daughter cells while maintaining the malignant phenotype, resulting in cancerous growth. Through an intensive process in which I collected data and gathered materials for quantitative analysis, the study concluded that the three trademark epigenetic mechanisms of DNA methylation, hereditary chromatin structures, and timings of DNA replications were the cause of such successful transmission.

Introduction:

Epigenetic research is full of challenges and obstacles which contribute to research gaps. These hindrances include a need for more investigations into the interplay between the different epigenetic mechanisms, difficulty justifying relationships between epigenetic changes and their outcomes, and limitations related to specific methodologies and data analysis. As this study focused on the hereditary factors of epigenetics within cancer, overcoming the largely unexplored transgenerational effects of epigenetic mechanisms was the most prominent obstacle. As a result, the initial hypothesis of this study was formulated from a basic yet fundamental biological standpoint: that the processes of meiosis and mitosis were critical in the transfer of malignant epigenetic coding genes after the production of daughter cells. Specifically, meiosis gives rise to four unique daughter cells by dividing the germ cells within gamete-producing organisms. Meiosis requires at least five MMR proteins, specifically MSH4, MSH5, MLH1, MLH3, and PMS2, to facilitate homologous chromosome recombination and division. Furthermore, mitosis replicates the chromosomes of meiotic proteins instead of meiosis, which divides into two new nuclei due to re-expression. However, this part of the cell cycle can have catastrophic oncogenic (cancerous) consequences, as seen in how aberrant expressions are common within tumors. Finally, these genes enable oncogenesis since genetically unstable cancers alter healthy mitosis processes to strengthen tumors in order to avoid lymphatic and treatment pressures.

When examining the relationship between cancer and epigenetics, DNA methylation, the roles of histones, chromatins, their modifications, and DNA replication become apparent. Genetics-wise, DNA methylation can suppress genes via proteins involved in blocking transcription factors. Notably, modified methylation tissue patterns resulting from differentiated cells commonly occur in the DNA of cancer cells. One prominent pattern includes hypomethylation on the genome. Another pattern would be the opposite, which is the centralized regions of hypermethylation on CpG island locations.

Less studied than DNA methylation's role in cancer, covalent histone modification and exchange regulate cancer dysregulations. Histones work independently to monitor gene expressions and localize themselves depending on the function to create an overarching signaling network. When histones malfunction, they may either activate oncogenes or inactivate tumor suppressor genes at either level of global genomes or localized gene regions. These studies contribute to the relationship involving cancer, epigenetics, and chromatins. Therefore, scientific understanding of the oncogenic process becomes more evident through added complexities.

Lastly, DNA replication proteins assist in tumor growth and can be divided into three categories. The first would be initiation, where replisomes, which are lengthy replication proteins, unwind the DNA helix, DNA's typical physical, coiled-up structure. The second variety would be elongation, where replisomes supply nucleotides that add to a DNA strand's growth. Finally, the third classification would be termination, where replisomes disperse due to an intersection. Typical DNA replication is critical in regulating the normal underlying functions of all physiological processes in order to ensure genetic stability. Despite this, flawed DNA replication results in mutations, deviated cell cycles, exacerbated genetic copies, and potentially cancer.

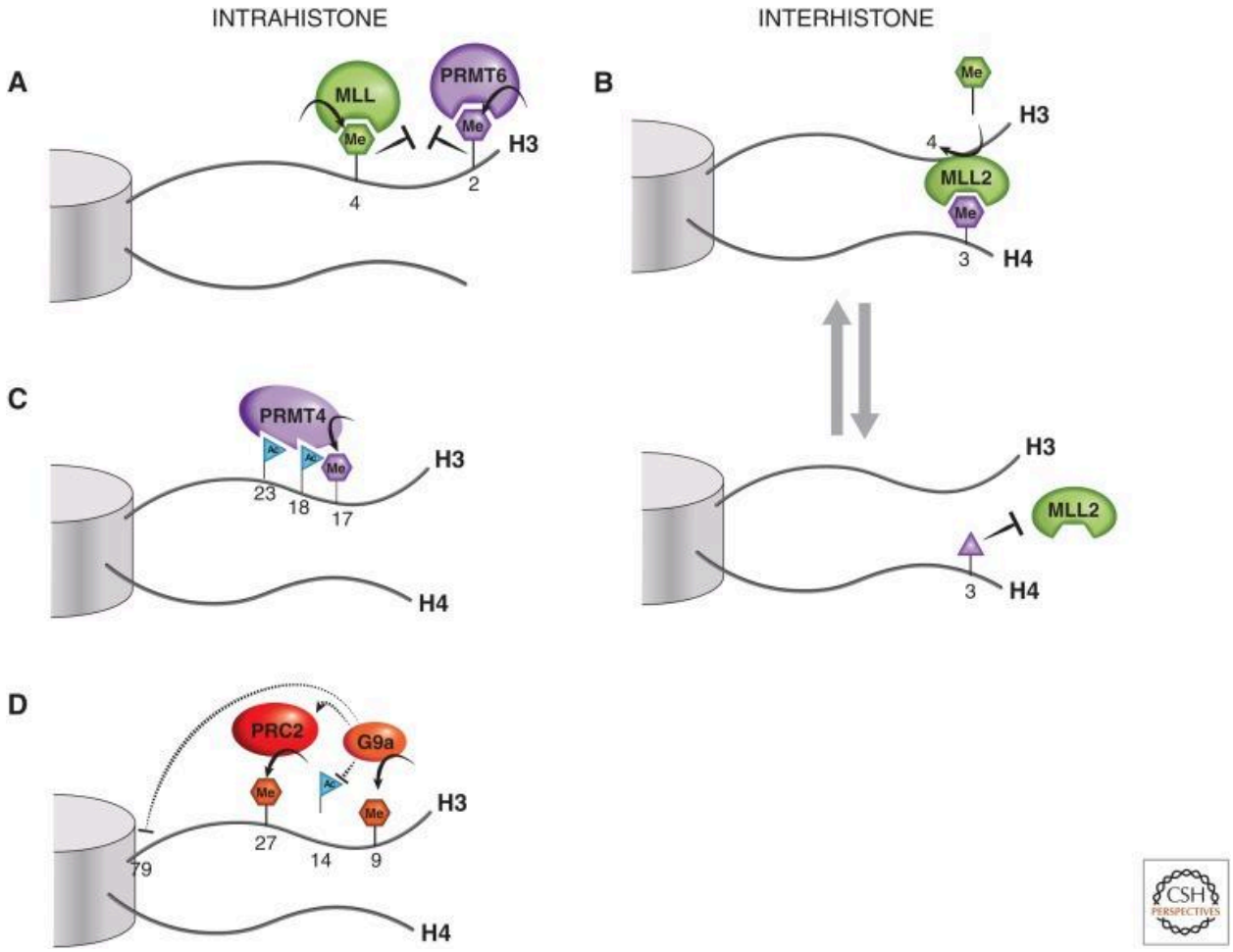
DNA Methylation:

DNA methylation may be responsible for the potential inactivation of tumor suppressor genes (TSGs). The more cancerous hypermethylation promoters are present, the less so are TSGs. For instance, breast and ovarian cancers lose their TSG of BRCA1 as a result of hypermethylation enablement (Esteller 2000). Furthermore, those affected by renal cell carcinoma become vulnerable to further malignancies as a result of flawed DNA methylation silencing the TSG VHL. Abnormal TSGs evidently contribute to genetic instability and mutations as their loss of function results in unkept cell cycles.

Tumorigenesis studies discovered the responsible genetic modifications, such as mutations, terminations, and, most notably, DNA recombination. A trait that has come to define cancer cells for years has been hypomethylation on the global genome as well as within sparsely dense CpG regions. Notably, these processes of hypomethylation portray an inverse relationship with the occurrence of hypermethylation at CpG islands, which instead are compact with DNA density. Unfortunately, cancers take advantage of the situation since they are known to be modifiable. Notably, cancer patients who partake in chemo or radiotherapeutic treatments directly confront cancer progression by resisting cancer's adaptive responses.

Hereditary Chromatin Structures:

Flawed hereditary chromatin structures and histone modifications interfere with the genome and with gene expression, potentially leading to cancer. Recently, deviant modifying enzymes, which typically function to maintain genetic information, have resulted in the numerous histone mutations that contribute to tumorigenesis and metastasis through epigenetic involvement. Further research has made it possible for several histone mutations to be well-studied and categorized into either modifications correlated to active transcription or those with blocked genes. For example, H3K4me3 would fall under the former and H3K27me3 the latter (Yang 2022). Despite ongoing and notable efforts contributing to a vast archive recording the types of histone modifications, fundamentals have yet to be cemented.



Caption: A depiction of histone addition, removal, or recognition (histone tail crosswalk) involving intra-histones (A, C, D) and inter-histones (B). (Audia, 2016).

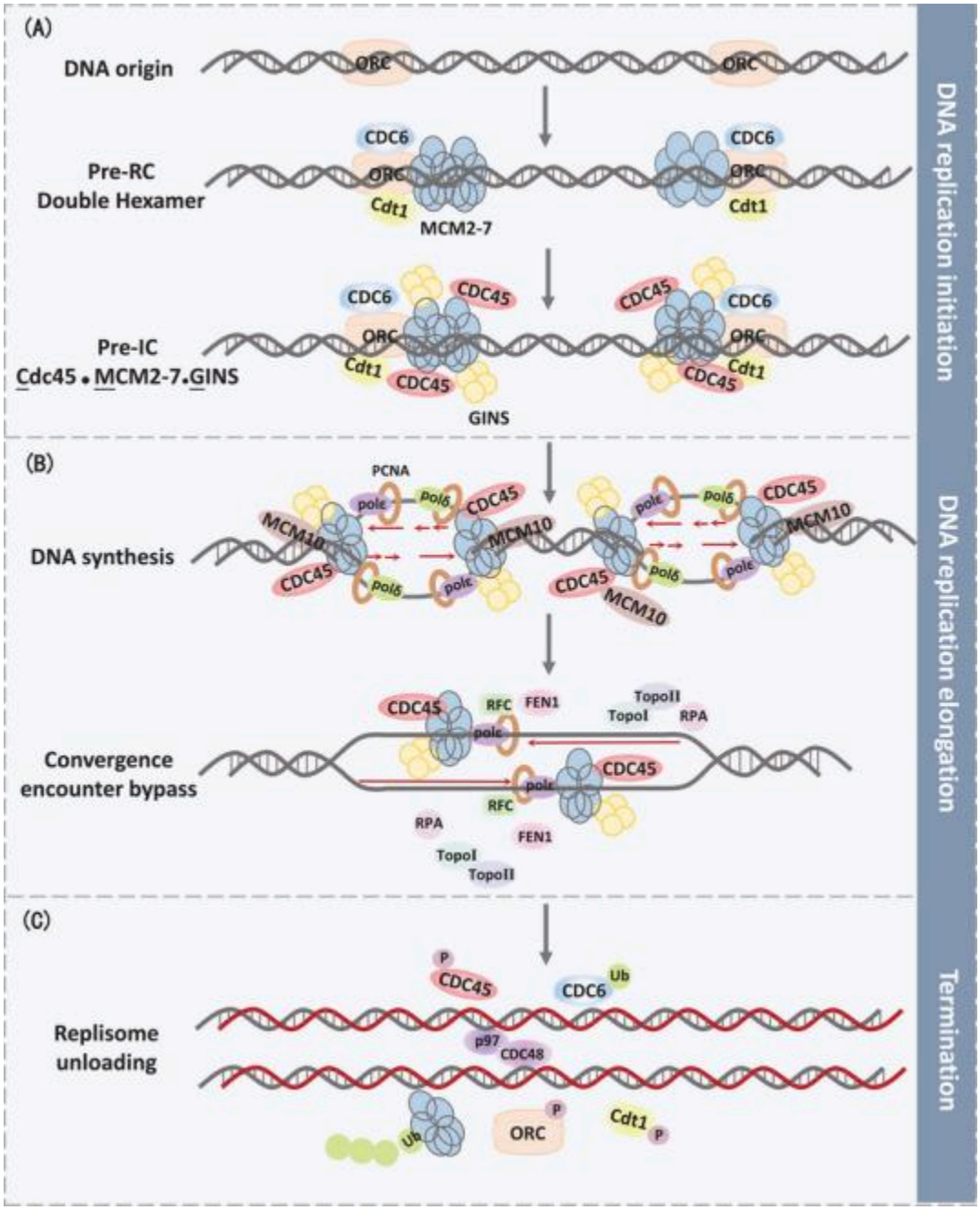
Meanwhile, to focus on a particular kinetic mechanism (enzyme modifier) that has been recorded as commonly responsible for mutating histone genes, resulting in modified chromatin methylation patterns and, therefore, the spread of tumorigenesis and metastasis would be to focus on HDAC. HDAC assumes the position of a driver of cancer progression due to overexpression and enhanced activity. Typically, HDAC alters histone acetylation and maintains the oncogenetic expressions of p300 and CBP20 (Yang, 2022). The histone mentioned above,

notably, contains the capability to transform cancerous cells back to normal functioning. Furthermore, the oncogenes discussed above are partially responsible for developing and growing hematologically based malignant tumors. Once more, however, further research is needed to capitalize on the reversible abilities of acetylation histone to the point where such abilities occur regardless of the type of alteration.

DNA Replication:

Finally, DNA replication typically drives cancer, which strengthens over time. This process occurs through genetic alterations during increased stem cells, which assist in the growth of tissues and organs. These malignant alterations can either be divided into one of two categories. The first category consists of modifications that enable cancer, initiate carcinogenesis, and destabilize the gene, which promotes uncontrollable chromatid division and genome copying. These factors contribute to cancer cells with increased drug resistance. The second group of cancerous transformations has been coined as "germ cell neoplasia" (Vassilev 2017), which causes pluripotent yet immature stem cells to mislocate to ectopic sites, producing tumors. The accumulation of either genetic mutation initiates an overarching process of a present cancer development well into adulthood.

When DNA replicates multiple times along with uncontrollable genome copying processes, the result is either polyploidy (when a cell contains an extra set of chromosomes) or aneuploidy (when a cell has one missing or one extra chromosome). Accordingly, both of these conditions can provide cancerous cells with extra genetic copies, strengthening them in order to resist treatments such as chemotherapy aggressively. Fortunately, though, this means that DNA replication can potentially reveal inhibitors as chemotherapeutic targets to terminate cancer cell origins. While cancers take advantage of an unstabilized genome regarding their formation and survival, a discovered minimum of 42 genes have proved critical in prohibiting enhanced DNA replication within varying types of cancers (Vassilev, 2017). However, such a type of cancer that has yet to be researched and determined whether or not included within the list of attributes would be germ cell cancers. Nonetheless, these findings and genes create the potential for new cancer-selective therapies, in which treatment would focus on targeting a gene that disrupts the genome and damages DNA by utilizing a second gene (one of the 42 genes) essential to restoring DNA's normal state.



Caption: A schematic DNA replication diagram involving initiation, elongation, and termination. (Song, 2023).

Conclusion:

This study hypothesis suggested that the processes of meiosis and mitosis were critical in the transfer of malignant epigenetic coding genes after the production of daughter cells. While both cell cycle processes play notable roles in the spread of cancerous cells, they both fell out of the discussion and focus once further research discovered the more essential aspects of epigenetic involvement in tumor growth and transmission of malignant phenotypes: DNA

methylation, chromatin structures and histone modifications, and DNA replication. As the three main mechanisms driving epigenetics assist in the spread of cancer, all three processes are involved in varying cancer types from beginning to end, with situations depending on their situational alterations and mutations. While there are obstacles in regards to researching the exact role epigenetics play due to a lack of investigation on the interplay of different epigenetic mechanisms, difficulties in justifying relationships between epigenetic changes, and their outcomes and limitations related to specific methodologies and data analysis, the significance of the information that epigenetics reveals in how the cancer phenotype is driven can't be understated. All three of these mechanisms provide insight into how the malignant phenotypes of cancers transfer down to their daughter cells. While DNA methylation continues to receive copious amounts of investigation and coverage, further research on chromatin structures and histone modifications could lead to discovering treatments and procedures critical in reversing malignant histones back into cells with regular functions regardless of the type of alteration. Furthermore, research on the timing of DNA replication would enhance efforts in exploring a new cancer-selective therapy that targets genes that prevent genome stability and employs a second gene to repair DNA damage. The future of epigenetic research is promising since, as of right now, research can explain the biology of cancer and its causes for growth, and with continued research, a new focus on tailored treatments and personalized medicines is within the realm of possibility.

Citations:

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