The Effects of Chromatin and Epigenetics on Cancer and Tumorigenesis

Abstract

 For decades, it’s been believed that genetic and environmental factors primarily increase one’s risks of getting cancer – but what if there’s more? It’s common knowledge that environmental factors affect one’s chances of getting cancer – but there is also evidence to support that multigenerational genetic changes affect these chances as well. Because chromatin has been found to bring about mutations that bring cancer, chromatin and these epigenetic factors provide many paths and “on/off switches” for gene expression (Flahavan et al.). Typically, chromatin and epigenetic mechanisms serve to keep genes in check and stabilize them, but Flahavan et al. research whether or not the combination of certain states of chromatin combined with epigenetic mechanism actually lead to tumorigenesis, or the formation of tumors. Chromatin and its different states have the possibility of providing or preventing the introduction of tumors. These permissive or restrictive states of chromatin can make one’s epigenetic genome one that may or may not provide the proper landscape for the development of cancer. Flavahan *et al.*’s research on “Epigenetic plasticity and the hallmarks of cancer” has the potential to provide a greater understanding of what causes the formation of tumors and thus how to prevent them.

Introduction

 Epigenetics is the study of gene expression and heritable changes brought upon chemical reactions (commonly referred to as “on/off” switches). Epigenetics holds that one’s phenotypes are brought on by more than just the individual’s own genome and rather the epigenome, which is transgenerational (Flahavan et al.). With studies linking chromatin to different types of cancers, some genome projects have been investigating the role of epigenetics and different forms of chromatin in the development of tumors.

 Because chromatin regulators play a part in transcription (transcription factors), they are also vital in how genetic information is passed and bound to DNA sequences. Chromatin structures compact DNA and prevent and allow activation, creating a link between different states of restriction and giving way to cancer genes (Flahavan et al.).

In epigenetics, there are two main factors that affect genetic expression: DNA methylation and histone acetylation. DNA methylation is the process of methyl groups being added to a molecule of DNA, thus changing the sequence entirely (DNA methylation is referred to as the “off switch”). In contrast, histone acetylation affects whether or not the chromatin is accessible and acts as the “on switch” for gene expression (Weinhold). Chromatin restriction can often be due to DNA methylation. Because the odds of a good response to change are dependent on the expression of transcription factors, highly restricted or otherwise damaged forms of chromatin are crucial for the life of the cell.

 On chromosomes, there are loci that serve as specific sites of genes on chromosomes. These loci are assisted by transcription factors and chromatin. “Because any single locus can assume different transcriptional states in different cellular contexts, the chromatin state must be capable of responding to appropriate cues and conditions” (Flahavan et al.). When loci are rendered inactive, they serve to prevent bad activity in the area. Loci are necessary for responding to change. The ability of the locus to respond to changes in its environment properly is reinforced by transcription factors and the state of the chromatin and its own environment (Flahavan et al.). When the chromatin is too permissive or has too much plasticity, the loci can no longer properly respond to their own environment and prevent inappropriate activity.

 There are multiple forms of chromatin including heterochromatin and euchromatin. Euchromatin is more active during translation, while heterochromatin is considered less or inactive. While there exist restricted forms of chromatin, there are also permissive forms of chromatin that have the capability of allowing malignant cells to enter transcription. If these malignant forms of permissive chromatin are cloned through cell division, their fitness will be increased, possibly leading to tumorogenesis. This gives rise to genetic instability, which leads to hypermutation (Flahavan et al.). This exemplifies epigenetics and its plasticity (Flahavan et al.). This is crucial in the capability of chromatin to respond to its environment.

 An example of how epigenetic plasticity and permissive chromatic states can lead to cancer is the enhancer EZH2 and the histone H3K27. The EZH2 gene is vital in the development of an embryo and, when mutated or deactivated, may lead to a number of different cancers such as cancerous tumors and prostate cancer (Genetics Home Reference). According to Flahavan et al., the mutation or deactivation of this gene could lead to a highly permissive and potentially tumor-causing state of chromatin.

 Previously it was believed that tumors were allowed to progress almost exclusively due to genetics but recent studies have suggested that changes in chromatin and epigenetic changes such as demethylation cannot be dismissed as key characters in tumor formation and growth. Because of the steps epigenetics takes to silence or activate a gene, its affects on cancer are inarguable. According to Flahavan et al., approximately 50% of cancers are accompanied by mutations in chromatin proteins.

Recent Progress

 Despite the need for more advanced technology, some information has been given from the continued study of genetic, environmental, and metabolic stimuli and chromatin. Particularly helpful in this research is the study of anomalies in chromatin regulator gene mutations (Flahavan et al.). All of these anomalies serve to alter DNA methylation, which often silence genes in different cancer types (Kulia and Esteller). While these findings could simply be congruent with epigenetic mechanisms, the authors’ findings state that they “conclude that chromatin and epigenetic aberrations can confer wide-ranging oncogenic properties and may fulfill all of cancer’s hallmarks” (Flahavan et al.). While there is a need for technology in order to study this further, researchers are hopeful to find out more regarding tumorogenesis and offer possible strategies

Discussion

 There is still much to learn before more research can be done on the effects epigenetics have combined with chromatin. Despite this, there has been some success in learning about cancer epigenetics. According to Flahavan et al., further research will require more advanced technology for an in depth look into epigenetics and chromatin and their effects on tumorogenesis, including models.

 As established in in the Recent Progress, Flahavan et al.’s findings have been consistent with their hypothesis thus far, but there is still much to be learned before anything conclusions can be drawn. Researchers hope to eventually provide some therapeutic strategy for eliminating and correcting these cells.

References

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