16.5B: Epigenetic Alterations in Cancer

Common in cancer cells, silencing genes, which occur through epigenetic mechanisms, include modifications to histone proteins and DNA.

LEARNING OBJECTIVES

Describe the role played by epigenetic alterations to gene expression in the development of cancer

KEY TAKEAWAYS

Key Points

- The DNA in the promoter region of silenced genes in cancer cells is methylated on cytosine DNA residues in CpG islands.
- Histone proteins that surround the promoter region of silenced genes lack the acetylation modification that is present when the genes are expressed in normal cells.
- When the combination of DNA methylation and histone deacetylation occur within cancer cells, the gene present in that chromosomal region is silenced.
- Epigenetic changes that are altered in cancer can be reversed and may, therefore, be helpful in new drug and therapy design.
Key Terms

• **epigenetic**: the study of heritable changes in gene expression or cellular phenotype caused by mechanisms other than changes in the underlying DNA sequence

• **methylation**: the addition of a methyl group to cytosine and adenine residues in DNA that leads to the epigenetic modification of DNA and the reduction of gene expression and protein production

• **acetylation**: the reaction of a substance with acetic acid or one of its derivatives; the introduction of one or more acetyl groups into a substance

Cancer and Epigenetic Alterations

Cancer epigenetics is the study of epigenetic modifications to the genome of cancer cells that do not involve a change in the nucleotide sequence. Epigenetic alterations are as important as genetic mutations in a cell's transformation to cancer. Mechanisms of epigenetic silencing of tumor suppressor genes and activation of oncogenes include: alteration in CpG island methylation patterns, histone modifications, and dysregulation of DNA binding proteins.

**Epigenetic Alterations in Cancer Cells**: In cancer cells, silencing genes through epigenetic mechanisms is a common occurrence. Mechanisms can include modifications to histone proteins and DNA associated with these silencing genes.

Silencing genes through epigenetic mechanisms is very common in cancer cells and include modifications to histone proteins and DNA that are associated with silenced genes. In cancer cells, the DNA in the promoter region of silenced genes is methylated on cytosine DNA residues in CpG islands, genomic regions that contain a high frequency of CpG sites, where a cytosine nucleotide occurs next to a guanine nucleotide. Histone proteins that surround that region lack the acetylation modification (the addition of an acetyl group) that is present when the genes are expressed in normal cells. This combination of DNA methylation and histone deacetylation (epigenetic modifications that lead to gene silencing) is commonly found in cancer. When these modifications occur, the gene present in that chromosomal region is silenced. Increasingly, scientists are understanding how these epigenetic changes are altered in cancer. Because these changes are temporary and can be reversed (for example, by preventing the action of the histone deacetylase protein that removes acetyl groups, or by DNA methyl transferase enzymes that add methyl groups to cytosines in DNA) it is possible to design new drugs and new therapies to take advantage of the reversible nature of these processes. Indeed, many researchers are testing how a silenced gene can be switched back on in a cancer cell to help re-establish normal growth patterns.

Genes involved in the development of many other illnesses, ranging from allergies to inflammation to autism, are also thought to be regulated by epigenetic mechanisms. As our knowledge deepens of how genes are controlled, new ways to treat these diseases and cancer will emerge.