16.5A: Altered Gene Expression in Cancer

Cancer, a disease of altered gene expression, is the result of gene mutations or dramatic changes in gene regulation.

Learning Objectives

• Describe how cancer is caused by uncontrolled cell growth

Key Points

• Cancer results from a gene that is not normally expressed in a cell, but is switched on and expressed at high levels due to mutations or alterations in gene regulation.

• Alterations in histone acetylation, activation of transcription factors, increased RNA stability, increased translational control, and protein modification are all observed in cancer cells.

• Tumor suppressor genes, active in normal cells, work to prevent uncontrolled cell growth.

• Proto-oncogenes, which are positive cell-cycle regulators, can become oncogenes and cause cancer when mutated.

Key Terms

• **oncogene**: any gene that contributes to the conversion of a normal cell into a cancerous cell when mutated or expressed at high levels

• **proto-oncogene**: a gene that promotes the specialization and division of normal cells that becomes an oncogene following mutation

• **cancer**: a disease in which the cells of a tissue undergo uncontrolled (and often rapid) proliferation
Cancer: Disease of Altered Gene Expression

Cancer can be described as a disease of altered gene expression. There are many proteins that are turned on or off (gene activation or gene silencing) that dramatically alter the overall activity of the cell. A gene that is not normally expressed in that cell can be switched on and expressed at high levels. This can be the result of gene mutation or changes in gene regulation (epigenetic, transcription, post-transcription, translation, or post-translation).

Changes in epigenetic regulation, transcription, RNA stability, protein translation, and post-translational control can be detected in cancer. While these changes do not occur simultaneously in one cancer, changes at each of these levels can be detected when observing cancer at different sites in different individuals. Therefore, changes in histone acetylation (epigenetic modification that leads to gene silencing), activation of transcription factors by phosphorylation, increased RNA stability, increased translational control, and protein modification can all be detected at some point in various cancer cells. Scientists are working to understand the common changes that give rise to certain types of cancer or how a modification might be exploited to destroy a tumor cell.

Tumor Suppressor Genes, Oncogenes, and Cancer

In normal cells, some genes function to prevent excess, inappropriate cell growth. These are tumor suppressor genes, which are active in normal cells to prevent uncontrolled cell growth. There are many tumor suppressor genes in cells, but the one most studied is p53, which is mutated in over 50 percent of all cancer types. The p53 protein itself functions as a transcription factor. It can bind to sites in the promoters of genes to initiate transcription. Therefore, the mutation of p53 in cancer will dramatically alter the transcriptional activity of its target genes.

Another type of gene often deregulated in cancers are proto-oncogenes which are positive cell-cycle regulators. When mutated, proto-oncogenes can become oncogenes and cause cancer. Overexpression of the oncogene can lead to uncontrolled cell growth because oncogenes can alter transcriptional activity, stability, or protein translation of another gene that directly or indirectly controls cell growth. An example of an oncogene involved in cancer is a protein called myc. Myc is a transcription factor that is aberrantly activated in Burkett’s Lymphoma, a cancer of the lymph system. Overexpression of myc transforms normal B cells into cancerous cells that continue to grow uncontrollably. High B-cell numbers can result in tumors that can interfere with normal bodily function. Patients with Burkett’s lymphoma can develop tumors on their jaw or in their mouth that interfere with the ability to eat.
Proto-oncogenes Can Become Oncogenes: When mutated, proto-oncogenes can become oncogenes and cause cancer due to uncontrolled cell growth.