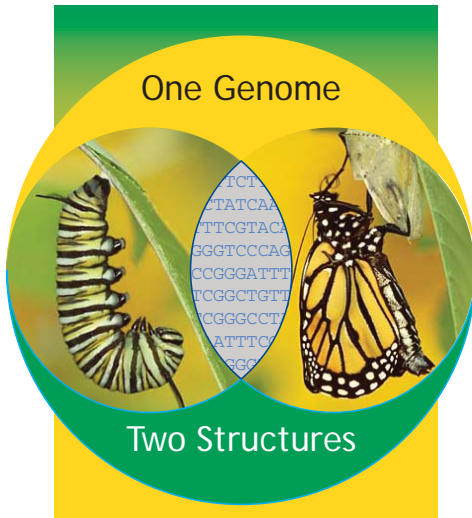


Epigenetics



THE CATERPILLAR AND THE BUTTERFLY: ONE Genome - TWO Structures

When the caterpillar changes into a butterfly, its genome – its basic genetic sequence – does not change. The differences between its two forms result from turning on and off different genes.

These changes in GENE EXPRESSION (turning a gene on) and GENE SILENCING (turning a gene off), which do not change the underlying DNA sequence, are collectively referred to as EPIGENETICS.

In some cases – the caterpillar and butterfly, for example – these changes are normal and expected and may be required for development.

But diet, environmental effects or even pre-natal factors can create unintended, reversible chemical modifications that mark a gene to be expressed or to be silenced. Some of these epigenetic changes may be benign. But when they allow cells to multiply uncontrollably, the result can be cancer!

Examples of Epigenetic Factors Involved with Cancer:

Histone deacetylase (HDAC) removes acetyl groups from genes. When specific genes that are supposed to limit cell growth lose acetyl groups, these genes are silenced, and the cell grows out of control.

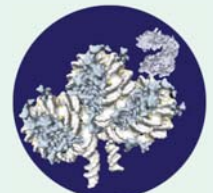
DNA methyltransferase (DNMT) causes increased methylation of genes and can silence genes called tumor suppressors, which restrain cell growth, again allowing the cell to grow out of control.

How Tumor Suppressor Genes Are Silenced

In a normal cell, genes shaped into structures called nucleosomes are “read” by proteins in the cell to create the desired protein (the tumor suppressor).

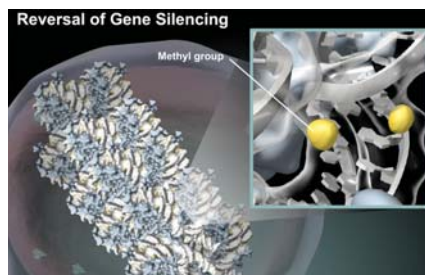


But nucleosomes can be packed closer together by epigenetic modifications made by HDAC and DNMT. This tight packing makes it difficult for the cell to read the genes. Because the gene is now silenced, the protein is no longer made and cannot regulate cell growth.

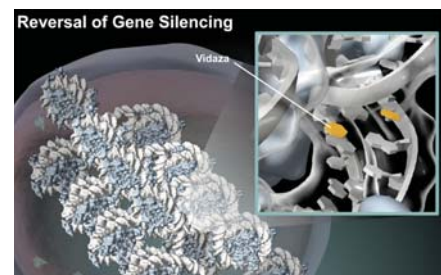


Vidaza® and Cancer Epigenetics

Vidaza is a demethylating agent. The Vidaza molecule becomes part of the gene structure, blocking the effect of DNMT. By limiting methylation of tumor suppressor genes, VIDAZA allows cells to grow and function normally. Vidaza is used to treat Myelodysplastic Syndromes (MDS).



Methyl groups silence a gene.



VIDAZA blocks the addition of methyl groups. The gene is expressed.