Epigenetics

The information below comes from <https://www.boundless.com/biology/gene-regulation/gene-expression-can-be-controlled-through-chromatin-structure/introduction-to-epigenetics/>

(For a better understanding of the enormous implications of epigenetics to your own personal health and the health of your future children you are encouraged further to view the three very different videos found at <http://sciblogs.co.nz/code-for-life/2013/02/06/epigenetics-introductory-explanations/>.)

**Epigenetics** is the study of changes in gene expression caused by mechanisms other than changes in the underlying DNA sequence; hence the name "epi-genetics" (from the Greek word for "over" or "above"). Examples of such changes might be DNA methylation or histone deacetylation, both of which serve to suppress gene expression without altering the sequence of the silenced genes. These changes may remain through cell divisions for the remainder of the cell's life and may also last for multiple generations. However, there is no change in the underlying DNA sequence of the organism; instead, non-genetic factors cause the organism's genes to be expressed differently. Epigenetic changes, therefore, are reversible, unlike mutations of DNA.

The molecular basis of epigenetics is complex. It involves modifications of the expression of certain genes but not the basic structure of the DNA. Additionally, the chromatin proteins associated with the DNA may be altered. This accounts for why differentiated cells in a multicellular organism express only the genes that are necessary for their own function. Epigenetic changes are preserved when cells divide. Most epigenetic changes only occur within the course of one individual organism's lifetime, but if a mutation in the DNA occurs in the sperm or egg cell that results in fertilization, then some epigenetic changes are inherited from one generation to the next. This raises the question of whether or not epigenetic changes in an organism can alter the basic structure of its DNA.

DNA methylation is an important regulator of gene transcription. Genes with high levels of 5-methylcytosine in their promoter region are usually transcriptionally silent. DNA methylation is essential during embryonic development; in somatic cells, patterns of DNA methylation are generally transmitted to daughter cells with high fidelity. A large body of evidence has demonstrated that aberrant DNA methylation is associated with unscheduled gene silencing. Aberrant DNA methylation patterns have been associated with a large number of human malignancies and found in two distinct forms, hypermethylation and hypomethylation, compared to normal tissue. Hypermethylation is one of the major epigenetic modifications that repress transcription via the promoter region of tumour suppressor genes. Hypermethylation typically occurs at CpG islands in the promoter region and is associated with gene inactivation. Global hypomethylation has also been implicated in the development and progression of cancer through different mechanisms.

Chromatin structure and packaging of the genome are important for regulating cellular homeostasis. ROS-induced oxidative stress is involved in the multistage process of prostate cancer progression. In particular, there is a growing interest in the involvement of oxidative stress in the epigenetic regulation of gene expression and, specifically, in controlling DNA methylation. Agents that prevent the production and chronic accumulation of ROS may play an important role in the treatment of prostate cancer. Epigenetic alterations are clearly involved in prostate cancer initiation and progression. Hypermethylated genes can be used to detect early stages of prostate cancer. In addition to the use of epigenetic alterations as a means of screening, epigenetic alteration may help clinicians predict the risk of recurrence and drug resistance. A combinatorial approach of epigenetic therapy with antioxidant agents, along with standard radiotherapy and targeted anticancer therapy, may help in sensitization of tumors that are resistant to current approaches of treatment. Finally, a link between the biomarkers and therapy may have positive impact on health care.

Epigenetic modifications, such as DNA methylation, play an important role in the regulation of gene expression, primarily through their role in regulating chromatin structure and function. Defects in epigenetic factors are linked to several diseases. For example, Rett syndrome, a neurodevelopmental disorder, is caused by mutations in the gene encoding methyl-CpG-binding protein-2 (MECP2), and alpha-thalassemia/mental retardation X-linked (ATRX) syndrome is caused by mutations in ATRX, which encodes a member of the SWI/SNF family of chromatin remodeling proteins. Patients with ATRX syndrome exhibit severe mental retardation as well as alpha-thalassemia.

Epidemiological studies have established that genetic factors play a major role in the development of schizophrenia. However, the discordance rate for schizophrenia between monozygotic twins is approximately 50%, suggesting that epigenetic and/or environmental factors are also involved in the development of the disease. Despite extensive research, the molecular etiology of schizophrenia remains enigmatic. The methylation state of the genome undergoes highly dynamic changes, extensive demethylation and reconstruction, during early embryogenesis; yet, once established, it is very stable. Nevertheless, some epigenetic signals, including DNA methylation, can be transmitted from one generation to the next, and are influenced by environmental or intrinsic biological factors. Thus, DNA methylation and/or other epigenetic modifications of the genome may help explain the ambiguity of inherited schizophrenia and the role, if any, of environmental factors in the etiology of the disease.

You are encouraged to also see <http://www2.le.ac.uk/departments/genetics/vgec/schoolscolleges/epigenetics_ethics/Introduction> for an additional article about what epigenetics is and its implications for all of us. Furthermore, you are encouraged to be aware of future articles about the development of this field of study.