

**EPA Workshop on Epigenetics and Cumulative Risk Assessment
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EPIGENETICS GLOSSARY

Compiled from Multiple Online Sources

DEFINITION OF EPIGENETICS

Epigenetics: Literally, that which is "added to" genetics. The term is most commonly taken to refer to heritable changes in gene expression that do not result from changes in actual gene sequences. ("Heritable" here can refer not only to inheritance between parents and offspring, but also between parent and daughter cells.)

Epigenome: All the structures and processes of the cell that contribute to epigenetic regulation.

GENERAL CONCEPTS IN GENETICS AND EPIGENETICS

Allele: Human genes occur in pairs, one on each chromosome of a chromosome pair. The paired genes are called "alleles" and can have a differing form and significance. For instance, in the case of some flowers, the allele on one chromosome may produce a red petal color and the other a white petal color.

Chromatin: A complex of DNA and proteins of which chromosomes consist.

Chromosome: A structure containing DNA and protein and the unit of inheritance. Humans have 46 chromosomes, 22 pairs of non-sex chromosomes and either XX (females) or XY (males).

Gamete: A reproductive germ cell -- an egg cell in the female or sperm in the male. Reproductive germ cells are haploid, i.e., they carry only 23 chromosomes (only one chromosome from each of the 23 pairs).

Gene Expression: Most commonly this term refers to the production of messenger RNA (mRNA) using a DNA gene sequence as a template. The mRNA will (after various sorts of processing) be translated into a protein.

Genome: All the DNA in an organism or cell, especially with reference to the total sequence of nucleotide bases, or "letters" of the genetic code.

Imprinting: A genetic phenomenon by which certain genes are marked by biochemical modifications after conception so that only the gene copy inherited from one of the parents is expressed whereas the imprinted gene copy is silenced; for example, for certain genes only the copy inherited from the father will be expressed.

Messenger RNA (mRNA): Key intermediary molecule generated when a gene is expressed (i.e., when the information encoded in the gene is converted into a protein product by the cell); mRNA levels for a gene are used as an indicator of how "active" the gene is (i.e., how much of the protein is produced).

Phenotype: The observable physical traits or biochemical characteristics of an organism based on a combination of the organism's genes and environmental factors.

Promoter: A DNA segment located at the start of a gene's coding sequence that provides a binding site for the enzymes that initiate the first step in the process of gene expression (i.e., *transcription*).

Transcription: Biochemical process in which an intermediary molecule called messenger RNA is generated based on the genetic information of the DNA.

Transgenerational epigenetic inheritance: Parent-to-child inheritance of an environmentally induced change in the epigenetic program, without direct exposure of the child. The term 'transgenerational' is often used rather broadly to describe all environmental effects that can be transmitted from one generation to the next. However, it is important to distinguish parental (or intergenerational) effects, such as the impact of in utero exposure to particular nutritional, hormonal, or stress/toxin environments on the developing embryo and its germline (which will eventually produce grandchildren), from truly transgenerational effects that are found in generations that were not exposed to the initial signal or environment that triggered the change.

DNA METHYLATION

CpG island: Regions of DNA enriched for CG dinucleotides; CpG islands are typically 300-3000 bp long, located upstream of gene coding regions, and usually not methylated in normal cells.

CpG island shores: Regions of DNA that lie at the outskirts of CpG islands rather than in the islands itself. They have variable methylation and have been proposed to be enriched in methylation differences between tissue types or between normal and cancer samples.

CpG Site (Cytosine-phosphate-Guanosine site): A location within a DNA sequence in which a cytosine and guanine appear consecutively.

DNA Methylation: The addition of a methyl (CH₃) group to the DNA. It usually occurs at DNA cytosine nucleotides followed by guanosine (C-phosphate-G, CpG) and represses gene expression.

DNA methyltransferases (DNMTs): Enzymes that catalyze the transfer of a methyl group to DNA from S-adenosylmethionine.

Hypo/Hypermethylation: An increase/decrease in normal methylation levels.

HISTONE MODIFICATIONS

Histones: Proteins upon which DNA is tightly wound and whose function is to condense and package DNA in the nucleus.

Histone Modifications: Post-translational addition or subtraction of any one of several chemical groups to an individual amino acid of a histone. Depending on the chemical group involved, the modification is called methylation (addition of a methyl group), acetylation (addition of an acetyl group), phosphorylation, ubiquitination, sumoylation, and so on. These modifications can dramatically affect the electrical and other properties of the chromatin, and they play a major role in gene regulation. Histone modifications include the different types listed here below:

- **Histone Acetylation:** The covalent addition of an acetyl group (-COCH₃) to a macromolecule, most commonly protein lysine and arginine residues. When present on histones it neutralizes their positive charge allowing chromatin decompaction and enhanced gene expression.
- **Histone Methylation:** The addition of a methyl (CH₃) group to histone lysine or arginine residues which are repressive or activating depending on the residue and its position.

- **Histone Succinylation:** The addition of a succinyl group to a protein lysine residue on a histone. It alters the lysine charge from +1 to -1 but its exact role remains unknown.
- **(Histone) SUMOylation:** The addition of a Small Ubiquitin-like Modifier (SUMO) protein to a target protein. This modification is involved in trafficking proteins to the nucleus among many other processes.
- **Histone Ubiquitination:** The addition of one or a chain of ubiquitin proteins to a histone. It often targets the histone for degradation but can also alter its localization, conformation, or binding.

NON CODING RNAs

Non-coding RNA (ncRNA): RNA molecules that are not used as a template to produce proteins.

Long non-coding RNA (lncRNA): Non-protein coding RNAs that are 200 base pairs or longer that are highly regulated, but many of their functions remain to be characterized.

MicroRNA (miRNA): Single-stranded, non-protein coding RNAs about 21-24 nucleotides in length expressed in plants and animals. They bind to their target gene's 3' untranslated region and block transcription or promote degradation.

SOURCES

This glossary list was compiled and adapted by Andrea Baccarelli, Harvard School of Public Health from the following online sources:

A (mostly) nontechnical glossary of genetics, epigenetics, and molecular biology with a primary focus on the human being. By Stephen L. Talbott: http://www.netfuture.org/2012/glossary.htm#gene_expression

CpG site. From Wikipedia, the free encyclopedia. https://en.wikipedia.org/wiki/CpG_site

Environmental Epigenetics Glossary. Autism Speaks. <http://autismepigenetics.org/environmental-epigenetics-glossary/>

Epigenetics Glossary of Terms. Zymo Research. <http://www.zymoresearch.com/learning-center/epigenetics/glossary>

Epigenetics glossary, AbCam. <http://www.abcam.com/epigenetics/epigenetics-glossary>

Epigenetics Glossary, Alcohol Res. 2013; 35(1):114–116. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3860428/>

Epigenetics Glossary. In “What is Epigenetics”. <http://www.whatisepigenetics.com/glossary/>

Transgenerational Epigenetic Inheritance: Myths and mechanisms. By Edith Heard and Robert A. Martienssen. Cell 2014; 157(1):95-109.