Science Media Centre Fact Sheet

Epigenetics

What is epigenetics?
'Epigenetics' refers to the study of heritable changes in cells that occur with no underlying changes to the underlying genetic code. These changes involve chemical modifications that alter gene expression and effectively result in genes being either switched 'on' (expressed) or 'off' (silenced).

How does it work?
Genes are switched on or off through a number of modifications that act as chemical tags, labelling which genes should be switched on or off.
The various mechanisms by which epigenetic changes take place are still being determined, but the main mechanisms that have been identified so far are:-

- Modification of DNA by methylation (see below)
- Modification of proteins associated with DNA by a variety of different processes. The best understood class of such proteins are the histones which are a major component of the chromatin complex that makes up chromosomes
- Binding of non-coding RNA to specific DNA sequences

How is it different to genetics?
Genetics is based on the study of the genetic code - the DNA sequence that provides the basic blueprint for life. This blueprint is essentially the same in all cells in any individual, even though our bodies comprise specialised organs and tissues with very different functions. Epigenetic processes provide the molecular basis for cells to undergo such differentiation and development. In a similar vein to the Human Genome Project, the Human Epigenome Project is now seeking to identify the full (vast) range of epigenetic modifications that are present in the human genetic code (see http://www.epigenome.org/index.php)

Why is it important?
Aberrant epigenetic changes have been implicated in a broad range of pathologies, including cancer, diabetes and mental illnesses (see sections below). It is well established that mutations in the genetic code can result in disease, but scientists are now also increasingly implicating gene expression changes in certain disease processes. The study of epigenetics could therefore provide a whole new range of drug targets for the treatment of disease that were not previously available, as well as new means of understanding how such diseases come about.

Key terms

DNA
Deoxyribonucleic acid (DNA) is the chemical that contains the genetic instructions used in the development and functioning of all known living organisms. DNA molecules are a long-term store of information, often compared to a set of blueprints with the instructions needed to construct other components of cells, such as proteins and RNA molecules.

DNA methylation
A type of chemical modification of DNA that can be inherited and subsequently removed without changing the original DNA sequence. This modification can lock, or silence, that genes. For example, if methylation silences a gene that normally would control cell growth or prompt the cell to commit suicide, then the cell will grow unchecked – the hallmark of cancer.

Histone proteins
The chief protein components of chromatin. Histones bind to DNA, help give chromosomes their shape, and help control the activity of genes. More than 10 different types of modification to histones are known including acetylation methylation, ubiquitination and phosphorylation. These can occur at multiple sites and can constitute epigenetic instructions.

Gene expression
Not every gene is expressed in every cell. Expression refers to whether the protein coded by a gene is expressed or not. The genetic code is "interpreted" by gene expression, and the properties of the expression products give rise to the organism's phenotype

Phenotype
The observable morphological, biochemical, and physiological characteristics of an individual, either in whole or with respect to a single or a few traits, as determined by a combination of the genotype and the environment

Genotype
The genotype of a person is her or his genetic makeup. It can pertain to all genes or to a specific gene.

Chromatin
Chromatin is the complex combination of DNA, RNA, and protein that makes up chromosomes.

Transgenerational epigenetic effects
The physiological and behavioural transfer of information across generations. For example, fathers who took up smoking before puberty had sons who were more likely to be obese (see below)

<u>Examples and related topics</u>

Epigenetics and cancer

- Aberrant gene function (genetic) and altered gene expression patterns (epigenetic) are key features of cancers and appear to cooperate at all stages of cancer development. Indeed, epigenetic alterations can participate in the earliest stages of neoplasia, including stem/precursor cell contributions.
- Epigenetic changes lead to altered chromatin structure with a wide range of effects including aberrant gene silencing (e.g. of tumour suppressor genes, cell cycle control genes) and may also lead to a predisposition to genomic instability (e.g by disruption of chromosome replication control).
- Inhibitors of two epigenetic processes (histone deacetylation and DNA methylation) have already found clinical utility in the treatment of certain cancers, providing

proof that epigenetic processes have therapeutic relevance. Recent advances in our understanding of epigenetics processes provide the opportunity to develop more selective agents acting on new epigenetic targets.

Epigenetics and the environment

- Mothers who were pregnant on 9/11 had altered levels of the stress hormone cortisol in the blood of their babies, suggesting events in the womb might be responsible. As an embryo develops, it is subject to external influences and experiences epigenetic changes, enabling a developing animal to adapt to its environment.
- In the Avon Longitudinal Study of Parents and Children in Bristol, fathers who took up smoking before puberty had sons who were more likely to be obese.

Epigenetics and mental health

- The brains of people who commit suicide are chemically different to those who die from other causes. People who had a serious depressive disorder and had committed suicide had DNA chemically modified by DNA methylation. The rate of methylation in the suicide brains was almost 10 times that of the other control group, and the gene that was being shut down was a chemical message receptor that plays a major role behaviour.

Sources of further information
Science: http://www.sciencemag.org/feature/plus/sfg/resources/res_epigenetics.dtl
Epigenetics website: http://www.epidna.com/
Human Epigenome Project: http://www.epigenome.org/index.php
The Epigenome: http://www.epigenome-noe.net/aboutus/epigenetics.php

Produced with guidance from CellCentric
http://www.cellcentric.com/index.php

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