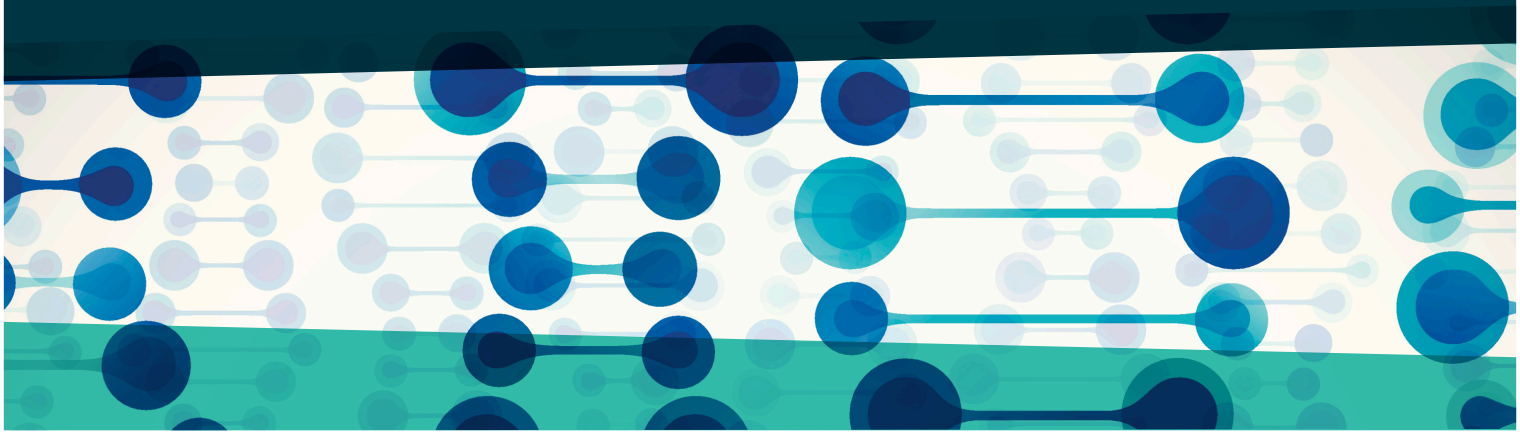
Australian Government
National Health and Medical Research Council



Epigenetics and health

Epigenetics has recently become a popular explanation for complex diseases of unknown origin. Epigenetics is the study of mechanisms that control how genes are switched 'on' and 'off' without any changes in the actual DNA of the cells.

The term 'epigenetics' ('outside' or 'above' genetics) was coined in the 1940s by Conrad Waddington, a biologist who was keen to understand how cells changed during development. At that time, scientists only understood that switching specific sets of genes on and off did not involve changing the primary DNA sequence, the linear arrangement of the DNA bases adenine (A), thymine (T), cytosine (C) and guanine (G).

What is epigenomics?

In the 1980s, researchers discovered that the cytosine (C) base of mammalian DNA could undergo a simple molecular modification called methylation. Changes in the amount and position of this DNA methylation was linked with the on and off state of genes and DNA methylation became a possible mechanism to explain the development of mammals.

DNA methylation is known as an epigenetic mark. Other epigenetic marks were later identified and included changes to the proteins that package the long strands of DNA into a condensed structure called chromatin. Today, scientists can identify both DNA methylation and changes to chromatin with great accuracy.

The complete set of epigenetic modifications to the genetic material of a cell is called the epigenome. The epigenome varies in different cell types. The mechanism by which epigenetic marks are placed at specific locations along genes is poorly understood at this stage. Detailed information about human epigenomes is available online in publicly available databases, e.g. www.genome.ucsc.edu. Another website of interest is the International Human Epigenome Consortium, http://ihec-epigenomes.net. These databases provide a powerful resource for those working in this area.

Could epigenomics help us to understand disease?

The epigenome of an individual is determined in part by the inherited DNA sequence and in part by the environment, although there is debate about the relative contribution of each of these factors. A quick online search will reveal many articles suggesting, even stating, that the environment can influence an individual's health through epigenetic changes. Certainly, there are studies that reveal a link between a particular epigenetic mark at a particular genome location and a specific disease. For example, the epigenome of cells in a tumour is very different from those in the neighbouring healthy tissue. However, it is not yet clear if these epigenetic changes actually cause the formation of tumours and more research is needed in this area.

One day, scientists hope they will be able to alter the epigenome and turn genes on and off in a way that would improve health outcomes for people. However, this type of manipulation is some way off because we do not yet know which epigenetic marks activate genes and we do not know how to change epigenetic marks at specific locations.

Is the epigenome useful as an indicator of disease?

Although we do not yet understand exactly how epigenetic changes drive disease in humans, we can use powerful techniques to record in detail the molecular state of the genome in individuals. This information enables scientists to infer whether genes will be active or inactive and such information can be used to indicate disease, or future disease, in an individual. Biological indicators (or markers) of disease are known as biomarkers. This field is essentially an extension of the 'genome revolution' and will be particularly useful for diagnosis of diseases that are acquired and not inherited.

Is the epigenome inherited?

By its nature, the epigenome is influenced by the genome (that is, the DNA sequence) and given the genome of individuals is inherited, the epigenomes of related individuals are more similar than those of unrelated individuals. The idea of inherited epigenetic marks has raised the interest of the general public. The concept is that environmental events to which parents were exposed could alter epigenetic marks in the sperm or egg and these epigenetic changes could then be inherited and influence the biology of the offspring. However, studies that prove this concept in humans are extremely difficult.

In general, epigenetic marks are cleared between each generation to allow the fertilised egg to develop into any cell type. At this stage, we do not know if there are locations in the human genome where acquired epigenetic marks are not cleared.