

EDITORIAL

Australia Advances Epigenetics Research in Human Disease

The field of epigenetic research and its role in human disease has finally come of age with the realisation that epigenetics heralds great promise for insights into disease mechanisms and a new class of disease biomarkers and novel therapeutic targets. Whilst genetics is concerned with the sequence of DNA coding for a gene, epigenetics relates to how cells maintain and transmit the way in which that sequence is read or interpreted and this is orchestrated by clever strategies for packaging of DNA into the nucleus. Each human diploid cell contains approximately 2 metres of DNA if stretched end-to-end; yet the nucleus of a human cell, which contains the DNA, is only about 6 µm in diameter. This is geometrically equivalent to packing 40 km of extremely fine thread into a tennis ball! The complex task of packaging DNA is accomplished by chromatin modeling proteins that bind to and fold the DNA, generating a series of coils and loops that provide increasingly higher levels of organisation, preventing the DNA from becoming an unmanageable tangle. Amazingly, although the DNA is very tightly folded, it is compacted in a normal cell in a way that allows it to easily become available to the many enzymes in the cell that replicate it, repair it, and express specific genes in a tissue-specific manner.

There are three major epigenetic players involved in gene regulation: **DNA methylation** – the methylation of cytosine residues that are next to guanine residues (CpG sites); **histone modification** – the modification of histones that form part of and regulate the structure of the chromatin; and **non-coding RNA** – RNA that does not code for protein but mediates gene regulatory processes. Deregulation of any of these epigenetic players has the potential to have a deleterious impact on control of gene expression and chromatin accessibility leading to a diseased state, such as cancer.

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This Showcase on Research features articles from four internationally recognised Australian groups that are spearheading the field of human epigenetic research and provide examples of the current state of epigenetic biology and its potential utility in the diagnosis and treatment of human disease. John Mattick *et al.* describe the exciting new findings that non-coding RNAs (ncRNAs) are involved in the regulation of chromosome structure and chromatin architecture. Rebecca Hinshelwood and Susan Clark describe the role that epigenetics plays in cancer. Deregulation of the DNA methylation and histone modification pattern of the genome is a common hallmark of oncogenesis and these changes are involved in the silencing of tumour suppressor genes and the activation of oncogenes. Sam El-Osta describes recent work that links epigenetic deregulation to heart disease, showing that hyperglycemic memory may be mediated by changes in chromatin modification and as such, points toward the concept that previous early life events and nutritional status can result in a predisposing susceptibility to environmental insults. David Ravine highlights the various human diseases that are underpinned by epigenetic changes in the development of complex, non-Mendelian diseases such as diabetes, asthma, epilepsy and neuropsychiatric disorders such as autism, bipolar disease and schizophrenia. The recent and ongoing discovery of new epigenetic mechanisms is fuelling the development of epigenetic therapies, some of which are already in clinical use today.

These articles demonstrate the exciting state of epigenetic research in human disease in Australia and internationally and highlight the importance of the Human Epigenome Project that aims to generate tissue-specific DNA methylation reference profiles of the human genome to provide the basis for new insights into disease pathways.

Cover Illustration

In Australia, research into understanding epigenetic regulation and human disease is being conducted by four internationally recognised research groups located in Brisbane, Sydney, Melbourne and Perth.

Image courtesy of Rebecca Hinshelwood and Susan Clark (Garvan Institute of Medical Research).

Epigenetics

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