



## **New Australian Epigenome Alliance moves us towards a Brave New World**

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The human genome project has taken us only so far. We now know there are two metres of tightly compacted DNA, containing roughly 30,000 genes, coiled into the nucleus of each cell in our body. We understand the functions of some of these genes, and partly understand how, when and why they are switched 'on' or 'off'.

There is now a significant global push to understand changes that occur in the function of genes without a change in the genome sequence. This branch of research is known as 'epigenetics', and concerns itself with the multitude of chemical interactions that modify the DNA and how it is packaged in the cell. Epigenetic processes can change the behaviour of a gene without a change in the DNA sequence.

The Australian Epigenome Alliance, a national body attracting leading lights in the field, had its inaugural meeting in Sydney last week. The goal will be to make sure that Australia maintains its high international standing in epigenetics, and also engages in a continuing dialogue with experts around the world.

Professor Susan Clark, member of the Alliance and epigenetics specialist from the Garvan Institute of Medical Research, was the Australian contributor to a paper that appeared in *Nature* on 7 August. The paper describes the international epigenome project, outlining the work that has been done so far, and the large task that lies ahead.

"Epigenetics is the next frontier of understanding, and is very exciting," says Professor Clark. "Unfortunately, it's also very expensive. NIH, the national medical research funding body in the United States has committed US\$300 million to epigenetics research this year. European Union funding programs have committed 50 million euros (US\$79 million). The aim of our Alliance is to try and raise the research profile in this country, support initiatives to establish the infrastructure we need to do the work, and collaborate with colleagues overseas."

"The human genome project gave us the raw data. The human epigenome project will provide ways of interpreting that data. Or to put it another way, we have the words, and now we need the syntax or grammar to make sense of them."

Many of the epigenetic 'events' referred to as 'DNA methylation' and 'chromatin modification' result in activation or de-activation of a single gene. Methylation tells which genes to be active and which to be silent. Chromatin, responsible for the physical coiling or structuring of DNA, can make a gene available, or unavailable, for interaction with other molecules inside a cell.

At a very broad level, we know some of the environmental influencers, or triggers that change the epigenetic state. A mother's diet, for example, can dramatically affect expression of genes during development. Certain

illnesses cause significant, and predictable, epigenetic changes that are “heritable”, being passed on to other cells in the same person (sometimes to their detriment as in cancer) or to offspring.

Every human being starts off with the same epigenome, a set of instructions, like pre-written computer code, that bring about changes in our DNA at certain times. That’s how we differentiate from a single cell into a complex being. Some genes will be active for a brief period only, for a specific purpose. Others will always be functional, such as the insulin gene, if we are to remain healthy. If something goes wrong with the instructions, and therefore the genes that underlie them, we will suffer developmentally or else we will become ill.

Professor Clark stresses the importance of being able to correlate the DNA sequence with the DNA methylation profile and the chromatin modification profile in every cell. “We need to fully understand this roadmap in a normal cell if we’re going to understand the changes that take place in disease.”

“Take cancer, for example. You can have a change in one cell that gives rise to a survival advantage in that cell, making it replicate faster. The change comes about due to changes in the DNA methylation or chromatin structure, without any change in the DNA sequence itself.”

“We now have the tools to detect the chemical changes. The technology can detect changes in the DNA methylation of one cell in 10,000.”

“While we need to be able to detect change, and so diagnose disease, the real power of epigenetic research will be in altering DNA methylation patterns or chromatin modification, and preventing disease.”

## **ABOUT GARVAN**

The Garvan Institute of Medical Research was founded in 1963. Initially a research department of St Vincent's Hospital in Sydney, it is now one of Australia's largest medical research institutions with approximately 400 scientists, students and support staff. Garvan’s main research programs are: Cancer, Diabetes & Obesity, Immunology and Inflammation, Bone, and Neuroscience. The Garvan’s mission is to make significant contributions to medical science that will change the directions of science and medicine and have major impacts on human health. The outcome of Garvan’s discoveries is the development of better methods of diagnosis, treatment, and ultimately, prevention of disease.

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