



## It's not all in my DNA

By David Baulcombe

In the past an individual's foibles would have been put down to their 'nature' but in modern parlance it would be 'in their DNA'. A Google search for 'it's in my DNA' reveals that the sequence of A, C, G and T is used as an excuse for all sorts of personal peculiarities including falling in love. It seems that the success of modern genetics and the technology of DNA analysis has turned the man in the street into a hardline genetic determinist.

However, the technology that has so effectively identified genes affecting Huntington's chorea, various cancers, and other diseases has also revealed that there is a complex relationship between the nature of an organism and its DNA sequence. There is, apparently, another layer of information, additional to the DNA sequence and genetics.

The term 'epigenetics' is often used to describe this second informational layer. Epigenetics was originally an abstract concept but now we know that the epigenetic status of a gene is influenced by the types of protein that are associated with DNA in chromosomes. When the chromosomes divide, this epigenetic status is replicated. Epigenetic information is therefore similar to genetic information in that it is carried from one cell generation to the next, but it is not directly associated with particular motifs in the DNA sequence. This new understanding has implications throughout biology. It affects our understanding of disease in people, will allow new approaches to the improvement of food crops, and revolutionises thinking about evolution.

As a botanist I have selected cases from plant research to illustrate the phenomenon of epigenetics because they may be useful indicators of epigenetics in animals. We know that what is true for peas is also true for people in genetics; the same principle is likely to apply in epigenetics.



A classic example comes from the toadflax populations studied by Linnaeus in the eighteenth century illustrated in this beautiful photograph provided by Enrico Coen. The normal toadflax has flowers like those of the snapdragon, with bilateral symmetry (left), but Linnaeus identified a variant form with radially symmetric flowers (right)

that he named after the Greek name for monster – *Peloria*. Two hundred years later Enrico Coen at the John Innes Centre in Norwich used modern

molecular biology to identify a gene that affects floral symmetry; he named it *cycloidea*. Surprisingly the sequence of the *cycloidea* DNA is exactly the same in the two different plant types. The crucial difference is 'epigenetic' rather than genetic: the variant flowers had an epigenetic mutation or 'epimutation' that alters the expression of the *cycloidea* gene without changing the DNA sequence.

A second example is from my own laboratory. It involves plants that fluoresce green under ultraviolet (UV) light. Chlorophyll in normal plants is red-fluorescent under UV but our experimental plants were genetically modified and they carried a gene for a green-fluorescent protein from jellyfish. The green fluorescence in these plants masked the chlorophyll. I hope that the slightly exotic nature of these plants does not distract from the essential point that the fluorescence is simply a traffic light for gene expression. If the plants were green under UV light the gene was active; if they were red, the gene was silent. This photograph illustrates a leaf under UV light in which the jellyfish gene is silent in the region around the veins.



The green fluorescence was lost when we infected these plants with a special type of virus. This result was not surprising because the virus in these experiments was designed to silence the jellyfish gene. However, when we collected seed, we were surprised to find that the gene remained silent in several subsequent generations. This persistent silencing came about not because the virus was carried between generations. We could also rule out the idea that the gene was lost or that its DNA sequence had changed. Again, the effect was epigenetic: the virus caused a silencing epimutation in the jellyfish gene that remained stable through several generations.

When we first carried out these experiments I thought that heritable epimutations would be restricted to rare examples in nature and to contrived laboratory situations. However, it now turns out that varieties of the same species may have many epigenetic differences affecting many genes. Consequently the fitness of plants in the wild is affected by both genetic mutations and epimutations. There would be selection for plants with beneficial epimutations and selection against those with a damaging effect—just as with genetic mutations.

The involvement of epimutations in evolution has major implications for the way that evolution might operate because, unlike genetic mutations, they may not be random. The experiment with the jellyfish gene showed how a virus can target an epimutation to a particular gene and it is possible that the same type of targeting can occur with natural epimutations. One could envision, for example, that stressed plants

might accumulate epimutations in genes affecting resistance to stress. These epimutations could act as a 'memory' of the stressful time and could be passed on to subsequent generations. If that is the case then evolution of stress-resistant plants would accelerate. My laboratory is now searching for evidence that such targeted epimutation occurs with natural genes.

Daniel Dennett in *Darwin's Dangerous Idea* described how different types of evolutionist invoke either skyhooks or cranes as the machinery of evolution. Skyhooks have a purpose: they raise evolution from one level to the next. Cranes, by contrast, do not have a driver and they are not directed: they raise evolution randomly and there is an advance if there happens to be a platform in a suitably elevated place. It is important to point out that targeted epimutations do not imply skyhooks. The molecules that target the epimutations will have been genetically determined and their existence will have been a consequence of random genetic mutation and natural selection. Epimutations, therefore, are extensions to the arm of a crane and epigenetics is a derivative of conventional genetics.

Aside from this academic discussion about evolution, there are also practical consequences of epimutations. In medicine, for example, it is now necessary to look for both epimutations and genetic mutations to explain diseases and complex conditions that do not correlate with simple genetic markers. Similarly a crop-plant breeder may choose to develop new varieties by selecting for both genetic and epigenetic markers.

In the longer term I expect further understanding of epigenetics to influence thinking about the distinction between nature and nurture. Epimutations can be induced by the environment and so result from nurture but, because they persist through cell divisions or even across multiple generations, they are also a component of nature. I hope that, eventually, we will be able to use our understanding to identify and avoid environments in which damaging epimutations are introduced.

Epigenetics might also change popular song. Instead of 'I love you because it's in my DNA' it would be more appropriate to sing 'because I am epimutated'. The lyrics could explain, for example, that a visit to Birmingham in 1959 had affected the epigenetics of a neural stem cell, that this had altered brain circuitry to create, finally, an obsession with Aston Villa, sad-eyed ladies of the lowland, or whatever else the song is about. The scope for poetic expression is vast. Lyricists will be surely grateful although the rhyming might prove tricky.

Cambridge has an excellent track record of epigenetics research and there is an Epigenetics Club that meets two or three times each term. There are normally two international or local speakers followed by informal discussions. All are welcome. Details are available from:

<http://talks.cam.ac.uk/show/index/24992>

<http://www.facebook.com/pages/Cambridge-Epigenetics-Club/175666299116450>.

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