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Epigenetic 'Memory' Key to Nature Versus Nurture

ScienceDaily (July 25, 2011) — Researchers at the John Innes Centre have made a discovery, reported this evening (24 July) in *Nature*, that explains how an organism can create a biological memory of some variable condition, such as quality of nutrition or temperature. The discovery explains the mechanism of this memory -- a sort of biological switch -- and how it can also be inherited by offspring.

The work was led by Professor Martin Howard and Professor Caroline Dean at the John Innes Centre.

Professor Dean said: "There are quite a few examples that we now know of where the activity of genes can be affected in the long term by environmental factors. And in some cases the environment of an individual can actually affect the biology or physiology of their offspring but there is no change to the genome sequence."

For example, some studies have shown that in families where there was a severe food shortage in the grandparents' generation, the children and grandchildren have a greater risk of cardiovascular disease and diabetes, which could be explained by epigenetic memory. But until now there hasn't been a clear mechanism to explain how individuals could develop a "memory" of a variable factor, such as nutrition.

The team used the example of how plants "remember" the length of the cold winter period in order to exquisitely time flowering so that pollination, development, seed dispersal and germination can all happen at the appropriate time.

Professor Howard said: "We already knew quite a lot about the genes involved in flowering and it was clear that something goes on in winter that affects the timing of flowering, according to the length of the cold period."

Using a combination of mathematical modelling and experimental analysis the team has uncovered the system by which a key gene called FLC is either completely off or completely on in any one cell and also later in its progeny. They found that the longer the cold period, the higher the proportion of cells that have FLC stably flipped to the off position. This delays flowering and is down to a phenomenon known as epigenetic memory.

Epigenetic memory comes in various guises, but one important form involves histones -- the proteins around which DNA is wrapped. Particular chemical modifications can be attached to histones and these modifications can then affect the expression of nearby genes, turning them on or off. These modifications can be inherited by daughter cells, when the cells divide, and if they occur in the cells that form gametes (e.g. sperm in mammals or pollen in plants) then they can also pass on to offspring.

Together with Dr Andrew Angel (also at the John Innes Centre), Professor Howard produced a mathematical model of the FLC system. The model predicted that inside each individual cell, the FLC gene should be either completely activated or completely silenced, with the fraction of cells switching to the silenced state increasing with longer periods of cold.

To provide experimental evidence to back up the model, Dr Jie Song in Prof. Dean's group used a technique where any cell that had the FLC gene switched on, showed up blue under a microscope. From her observations, it was clear that cells were either completely switched or not switched at all, in agreement with the theory.

Dr Song also showed that the histone proteins near the FLC gene were modified during the cold period, in such a way that would account for the switching off of the gene.

Funding for the project came from BBSRC, the European Research Council, and The Royal Society.

Professor Douglas Kell, Chief Executive, BBSRC said: "This work not only gives us insight into a phenomenon that is crucial for future food security -- the timing of flowering according to climate variation -- but it uncovers an important mechanism that is at play right across biology. This is a great example of where the research that BBSRC funds can provide not only a focus on real life problems, but also a grounding in the fundamental tenets of biology that will underpin the future of the field. It also demonstrates the value of multidisciplinary working at the interface between biology, physics and mathematics."