Epigenetic reprogramming: Research discovers how epigenetic information could be inherited

January 24 2013

New research reveals a potential way for how parents' experiences could be passed to their offspring's genes. The research was published today, 25 January, in the journal *Science*.

Epigenetics is a system that turns our genes on and off. The process works by chemical tags, known as epigenetic marks, attaching to DNA and telling a cell to either use or ignore a particular gene.

The most common epigenetic mark is a methyl group. When these groups fasten to DNA through a process called methylation they block the attachment of proteins which normally turn the genes on. As a result, the gene is turned off.

Scientists have witnessed epigenetic inheritance, the observation that offspring may inherit altered traits due to their parents' past experiences. For example, historical incidences of famine have resulted in health effects on the children and grandchildren of individuals who had restricted diets, possibly because of inheritance of altered epigenetic marks caused by a restricted diet.

However, it is thought that between each generation the epigenetic marks are erased in cells called primordial gene cells (PGC), the precursors to sperm and eggs. This 'reprogramming' allows all genes to be read afresh for each new person - leaving scientists to question how epigenetic inheritance could occur.

The new Cambridge study initially discovered how the DNA methylation marks are erased in PGCs, a question that has been under intense investigation over the past 10 years. The methylation marks are converted to hydroxymethylation which is then progressively diluted out as the cells divide. This process turns out to be remarkably efficient and seems to reset the genes for each new generation. Understanding the mechanism of epigenetic resetting could be exploited to deal with adult diseases linked with an accumulation of aberrant epigenetic marks, such as cancers, or in 'rejuvenating' aged cells.

However, the researchers, who were funded by the Wellcome Trust, also found that some rare methylation can 'escape' the reprogramming process and can thus be passed on to offspring – revealing how epigenetic inheritance could occur. This is important because aberrant methylation could accumulate at genes during a lifetime in response to environmental factors, such as chemical exposure or nutrition, and can cause abnormal use of genes, leading to disease. If these marks are then inherited by offspring, their genes could also be affected.

Dr Jamie Hackett from the University of Cambridge, who led the research, said: "Our research demonstrates how genes could retain some memory of their past experiences, revealing that one of the big barriers to the theory of epigenetic inheritance - that epigenetic information is erased between generations - should be reassessed."

"It seems that while the precursors to sperm and eggs are very effective in erasing most methylation marks, they are fallible and at a low frequency may allow some epigenetic information to be transmitted to subsequent generations. The inheritance of differential epigenetic information could potentially contribute to altered traits or disease susceptibility in offspring and future descendants."

"However, it is not yet clear what consequences, if any, epigenetic inheritance might have in humans. Further studies should give us a clearer understanding of the extent to which heritable traits can be derived from epigenetic inheritance, and not just from genes. That could have profound consequences for future generations."

Professor Azim Surani from the University of Cambridge, principal investigator of the research, said: "The new study has the potential to be exploited in two distinct ways. First, the work could provide information on how to erase aberrant epigenetic marks that may underlie some diseases in adults. Second, the study provides opportunities to address whether germ cells can acquire new epigenetic marks through environmental or dietary influences on parents that may evade erasure and be transmitted to subsequent generations, with potentially undesirable consequences."

More information: 'Germline DNA Demethylation Dynamics and Imprint Erasure Through 5-Hydroxymethylcytosine', 25 January 2013, *Science*.

Provided by University of Cambridge