Experiences leave behind epigenetic traces in our genetic material

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Credit: Swiss National Science Foundation

An ideological dispute is taking place in biology. And it's about a big topic that's central to everything: heredity. In his epoch-making book On the Origin of Species of 1859, Darwin wrote of the reigning ignorance about how differences between individuals come about. It was only with 'modern evolutionary synthesis' in the 1940s that people became convinced that heredity functions through genetics – in other words, that the characteristics of living creatures are passed on to the next generations through their genetic substance, DNA.

This perspective was helpful in providing a focus for research in the ensuing decades, which brought about extraordinary discoveries. As a result, many aspects of the form and function of living creatures can now be explained. But already in the 1950s, different observations called into question the seemingly exclusive control of the genes. For example, maize kernels can have different colours even if their DNA sequence is identical.

Plants remember aridity

Further investigations brought to light the fact that when individuals with identical genetic material have a different outward appearance, this can be traced back to different degrees of activity on the part of the genes. Whether a particular section of DNA is active or not – i.e., whether it is read – depends to a decisive degree on how densely packed the DNA is.

This packing density is influenced by several so-called epigenetic mechanisms. They form a complex machinery that can affix or detach tiny chemical attachments to the DNA. Here, the rule applies that the tighter packed the DNA, the more difficult it is to read – and this means that a particular gene will be more inactive.

Living creatures can adjust to a volatile environment by steering their epigenetic mechanisms. In this manner, for example, the epigenetic machinery can ensure that plants can deal better with a hot or arid climate if it at some point they already had to live through a similar situation. So in this sense, the epigenetic markings in the genetic material form a kind of 'stress memory' of the plants. This much is today a matter of consensus among biologists.

Doubts on heredity over generations

Several studies, however, suggest that the descendants of stressed plants are also better prepared against the dangers already faced by their ancestors. "However, these studies are a matter of controversial debate," says Ueli Grossniklaus, the director of the Department of Plant and Microbial Biology at the University of Zurich. Like many other epigeneticists who are involved in deciphering these mechanisms, he believes that, "since the evidence is patchy, we can't yet say to what degree acquired characteristics can be transmitted in stable form over several generations." So it still remains to be proven whether epigenetics actually brings organisms long-lasting advantages and thus plays a role in evolution. It's an attractive idea, thinks Grossniklaus, but it's still to be demonstrated.

It's not just in plants that results on the heredity of epigenetic markings are causing a stir – the same is true in mice. In order to investigate the possible long-term effects of severe childhood trauma, for example, the research group led by Isabelle Mansuy, a professor of neuro-epigenetics at the University of Zurich and ETH Zurich, has been taking mouse offspring away from their mothers for three hours each day, just a few days after being born.

Male mice pass on trauma

When they reach adulthood, the mice subjected to a difficult infancy displayed behavioural disorders and the corresponding chemical traces in their genetic material. For example, when compared with control mice who were always allowed to remain with their mothers, the traumatised mice spent significantly more time in the brightly lit section of their cage than in the dark section.

The behaviour of these mice has allowed the researchers to deduce that the traumatised animals showed symptoms of depression and yet, at the same time, less fear. "They seem to seek danger, such as we often observe in US war veterans who suffer from post-traumatic stress," says Mansuy.

Astonishingly, Mansuy's research team has observed the same behavioural abnormalities in the offspring of these traumatised male mice – even where the young mice were never separated from their non-traumatised mothers. Obviously, the sperm contains an epigenetic signal that is also able to codetermine the gene activity of their offspring.

Cancelling out epigenetic memories

This is precisely what causes the greatest unease among many experts. They argue that the genetic material is subjected to epigenetic reprogramming to such a high degree during the maturation of the sperm, and afterwards in the fertilised ovum, that this erases most of the epigenetic markings acquired during the mouse's life.

"I agree", says Mansuy, "but it is also proven that some markings survive this reprogramming." There are also other epigenetic mechanisms. In addition to the hereditary material from DNA, sperm also contains a complex collection of small and micro-RNA molecules that can intervene in the epigenetic mechanism, thereby playing an important role in the intergenerational regulation of gene activity.

Mansuy believes that her experiments, along with those carried out by others, have served to prove at least in principle the existence of epigenetic inheritance mechanisms. She also reckons that epigenetics may in part explain why there is a familial predisposition to many complex illnesses such as diabetes, cancer and mental illness, even though these inheritance patterns cannot be explained by classical genetics.

In comparison with other genetic mutations, epimutations occur roughly a thousand times more often, as Detlef Weigel's group at the Max Planck Institute for Developmental Biology showed in their 2011 investigation of 30 generations of thale cress (Arabidopsis thaliana).

Furthermore, epimutations are fundamentally reversible. Perhaps this is why epigenetic traces in our genetic material are transmitted to the next generation, and sometimes also to the generation after that, but then usually disappear again. It is probably just this transitory and uncertain characteristic that nurtures the current disputes – and will probably continue to nurture them until biology has finally understood in full the complex epigenetic machinery of inheritance.

Provided by Swiss National Science Foundation

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