



La lettre du Collège de France

8 | mars 2014
Collège de France Newsletter n°8

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Electronic version

URL: <https://journals.openedition.org/lettre-cdf/2010>
DOI: 10.4000/lettre-cdf.2010
ISSN: 2109-9219

Publisher

Collège de France

Printed version

Date of publication: 1 March 2014
Number of pages: 30-31
ISSN: 1628-2329

Electronic reference

Catherine de Lange and Edith Heard, ““We can’t undo what our parents have given us in terms of our genes””, *La lettre du Collège de France* [Online], 8 | mars 2014, Online since 11 August 2015, connection on 17 August 2022. URL: <http://journals.openedition.org/lettre-cdf/2010> ; DOI: <https://doi.org/10.4000/lettre-cdf.2010>

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“We can’t undo what our parents have given us in terms of our genes”

Catherine de Lange and Edith Heard



- 1 **The Epigenetics professor and Royal Society fellow explains why she is concerned about too much faith invested in her field**
- 2 When something isn’t working, Edith Heard is the kind of person who will try to fix it. And at the top of her list might well be the reputation of her subject – epigenetics. At a recent science festival, James Watson, outspoken co-discoverer of the structure of DNA, publicly blasted the fashionable research field, pronouncing that “epigenetics is used for a lot of crap”. That might not be her choice of language, but – perhaps surprisingly, having dedicated her career to epigenetics – Heard would, to some extent, agree. “I get the feeling that people want to believe epigenetics is going to solve our genetic

problems, that we can somehow undo what our parents have given us in terms of our genes," she says. "I think that's a fallacy." Heard is head of genetics and developmental biology at the Institut Curie in Paris, and if she is concerned about the hype surrounding her subject it may be because she has seen it propelled into the limelight from obscurity during the course of her career. When Heard was at university, she had never heard of it. "Epigenetics was not on the agenda."

- 3 Growing up in London, it wasn't until she began her degree in natural sciences at Cambridge in the mid-80s that Heard's attention turned to biology. This was a time when great leaps were being made in molecular biology, in particular our understanding of early development, and how embryos form and are controlled by genes. "I really felt there was a buzz... it was one of these scientific revolutions that people talk about," she says.
- 4 Encouraged by her apparent talent for biology, and by the need to do "something useful" with her science, Heard went on to do a PhD in cancer research at the Imperial Cancer Research Fund in London. It was here that she got her first glimpse of epigenetics in action. "I realised that cancer cells are a mess... DNA wasn't enough to explain all the changes that occur."
- 5 It is this idea that is now beginning to capture the imagination of the press and the public. Epigenetics – the idea that persistent changes can occur to genes without altering the actual sequence of DNA – has become not only a buzzword, but also an antidote to the genetic determinism of the early twenty-first century. Back then, thanks largely to the efforts of the Human Genome Project, DNA came to be seen as the "blueprint for life". Epigenetics, on the other hand, offers the tantalising hope that our genetic code is more of a rough guide that we can revisit later and amend, for example by switching certain genes on or off.
- 6 While this is certainly true – and scientists such as Heard are only just beginning to truly understand the mechanisms involved – much has been made of the idea that such changes can be caused by the environment and passed on to subsequent generations. Too much, Heard says. "People are going around saying that any environmental influence that can change your gene expression pattern we can call epigenetic. And from that people are saying that what you eat and drink, or what you breathe, will actually influence not just you but maybe even your children and grandchildren." This may happen in plants, and in some other organisms, but in humans, Heard says, "there is no good evidence that this can be heritable across several generations. It's overhyped".
- 7 Her desire to witness the true processes of epigenetics in part led Heard to Paris, along with some more personal reasons – it wasn't just biology that had grabbed her attention at Cambridge; she had also fallen in love with a French PhD student. By happy coincidence, Paris was also home to the Pasteur Institute, and one of the main labs trying to solve the riddle of one of the most fundamental manifestations of epigenetics – X chromosome inactivation.
- 8 First discovered by British scientist Mary Lyon in 1961, X-inactivation is the process by which one of a woman's X chromosomes is shut down during development, because they have two of them, whereas men have just one. This is essential to survival, and is perhaps one of the clearest examples of epigenetics – the genes are all still there, intact, in the right order, but half of them are unnecessary. They are switched off, and

this change persists from one cell division to the next. "No one really understood how it worked," says Heard, "so that's what I spent the next nine years in Paris doing."

- 9 Specifically, she wanted to find out what causes one X chromosome to be switched off and one to stay on, even though they share the same cell nucleus. She wondered whether their positioning in the nucleus was related to these epigenetic changes. "I realised we were never going to work out what was going on unless we could actually look inside individual cells."
- 10 She needed to catch epigenetics in the act. Having set up her own lab in Paris, Heard set about devising new techniques to image the DNA using fluorescent dyes. The efforts paid off. Within just a few months, "it was obvious that there were amazing things happening that we hadn't conceived of". Now she could see for the first time exactly when and where X-inactivation was happening, which led to some huge breakthroughs. One of them was the discovery that X chromosome inactivation happens not once, but twice, during development – first in all cells designated to building the placenta, then again in some cells sent off to build the embryo. "I remember almost feeling dizzy thinking, I can't believe this is actually the way it happens."
- 11 The finding has big implications for stem-cell research, much of which focuses on reverting cells that have already been designated a function back to their naive, embryonic state. "It was incredible because it showed this plasticity. You can take a cell that has made all sorts of decisions, stable decisions you would think, and yet it can undo them all in a couple of cell cycles."
- 12 Understanding the intricate processes behind epigenetics also offers hope for treating diseases, most notably cancer. In this respect, Heard believes her field deserves some of the hype, as there is scope to change the action of our genes, especially when they go awry in tumour formation, through the use of epigenetic drugs. "Now the big question in cancer is how much of the change is epigenetic?"
- 13 Yet Heard points out that even epigenetic changes are likely to have a genetic trigger in the first place. "Even our epigenetic changes are genetically driven. The code of genetics is the code. It's the only code." But now with epigenetics, "people are hoping we can pray our way out of faulty genes".
- 14 So how does Heard expect to fix this problem? She hopes her recent elections to professor of the Collège de France and Royal Society Fellowship might help. The French role is particularly important, she says, as she has to give nine public lectures on her subject a year. "It's our duty as scientists to pass on the right messages. I don't want to say epigenetics isn't exciting ... [but] there's a gap between the fact and the fantasy. Now the facts are having to catch up."
- 15 *Source: The Observer, Sunday 23 June 2013*
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EDITH HEARD

Epigenetics and Cellular Memory