



## La lettre du Collège de France

8 | mars 2014  
Collège de France Newsletter n°8

---

### Epigenetics and Cellular Memory

Excerpts from the Inaugural Lecture - 13 December 2012

Edith Heard

---



#### Édition électronique

URL : <https://journals.openedition.org/lettre-cdf/1921>

DOI : 10.4000/lettre-cdf.1921

ISSN : 2109-9219

#### Cet article est une traduction de :

Épigénétique et mémoire cellulaire - URL : <https://journals.openedition.org/lettre-cdf/1603> [fr]

#### Éditeur

Collège de France

#### Édition imprimée

Date de publication : 1 mars 2014

ISSN : 1628-2329

#### Référence électronique

Edith Heard, « Epigenetics and Cellular Memory », *La lettre du Collège de France* [En ligne], 8 | mars 2014, mis en ligne le 01 avril 2015, consulté le 17 août 2022. URL : <http://journals.openedition.org/lettre-cdf/1921> ; DOI : <https://doi.org/10.4000/lettre-cdf.1921>

---

Ce document a été généré automatiquement le 17 août 2022.

Tous droits réservés

---

# Epigenetics and Cellular Memory

Excerpts from the Inaugural Lecture - 13 December 2012

Edith Heard

---

## RÉFÉRENCE

Source: La lettre, no. 36, May 2013

- 1 In the late 1980s and early 1990s, we witnessed a revival of the term “epigenetics”, which also took on new meaning. The semantic shift stemmed from the realization that certain changes in gene expression are transmitted through multiple cell divisions, even across generations in certain cases, without changes in the DNA sequence itself.
- 2 As early as 1971, Eduardo Scarano showed that it was the processes of modification rather than mutation of the DNA sequence that explained this stable transmission of the genes’ particular states of activity. Such modifications were demonstrated shortly afterwards, in particular the methylation of one of the four DNA bases, cytosine. Furthermore, it very quickly appeared that this methylation is transmitted via cell division and is significantly often associated with a stable gene silencing. In 1994, the Australian geneticist Robin Holliday proposed that epigenetics be redefined as the study of changes in gene expression transmissible through cell division, even across generations, without changes in the DNA sequence. This led to the idea that “epigenetic” modifications were transmissible or even heritable regulatory signals that were added to the information carried by the DNA sequence.
- 3 In 1961, the British mouse geneticist Mary Lyon, noted that female mammals, who have two X chromosomes, unlike males with only one X and a Y chromosome, show unusual “mosaic” phenotypes of the coat-colour. Where do these female-specific mosaic phenotypes come from? Lyon suggested that they resulted from random inactivation of one of the two X chromosomes in each of the early embryo cells, followed by the stable transmission, that is, the memorization, of this silent state during the successive cell divisions. When the two X chromosomes carry different forms of the same gene, controlling for example coat-colour, the random inactivation of one of these two chromosomes and the clonal expansion of the cells thus produced results, in the adult individual, in a juxtaposition of patches of cells, each with a different phenotype. Lyon thus posited, that the “sex chromosome” identified by the cytologist Murray Barr in the nucleus of the female cells corresponds to the inactive X.





- 4 In 1975, Art Riggs proposed that the inactivation of the X and its stable transmission through cell divisions was based on the methylation of DNA. This hypothesis was supported by the findings that the regulatory regions situated near the genes are indeed methylated on the inactive X. Other researchers subsequently discovered that this methylation is faithfully reproduced after replication of the DNA, via specific enzymes known as “maintenance” DNA methyltransferases. Better still, these enzymatic activities can be blocked by drugs and this can lead to reactivation of some of the genes carried by the inactive X chromosome.
- 5 Another example of unexpected heredity in mammals is the “parental imprint”. In 1986, two embryologists, Davor Solter and Azim Surani, each carried out seminal work in nuclear transplantation in the oocytes of mice. The aim was to obtain embryos carrying two genomes of maternal origin (gynogenotes) or two genomes of paternal origin (androgenotes). In both cases, they found an early embryonic lethality, even though the maternal and paternal genomes carried the same genetic information. Here again, it was rapidly found that DNA methylation is instrumental in the functional non-equivalence of genomes of maternal and paternal origin. This differential methylation is established in the germinal lineage of the parents and is transmitted to their offspring, which maintain it.
- 6 These two striking examples illustrate an essential point of the processes of epigenetic memorization linked to development: in mammals the inactivation of the X as a parental imprint is erased with each generation. This reprogramming, or *tabula rasa*, is indispensable for a new life cycle to begin.

- Inaugural Lecture published by Éditions Fayard and online at [www.books.openedition.org/cdf/2252](http://www.books.openedition.org/cdf/2252)

- The video of the Inaugural Lecture is available online at [www.college-de-france.fr](http://www.college-de-france.fr), on the professor's page.

---

AUTEUR

**EDITH HEARD**

Epigenetics and Cellular Memory