Disputing Lamarckian epigenetic inheritance in mammals

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Abstract

A recent study finds that changes to transcription and DNA methylation resulting from in utero exposure to environmental endocrine-disrupting chemicals are not inherited across generations.

Epigenetic reprogramming

All mammals develop from a single cell, the zygote, which is made up of an egg and a sperm head, both of which contain a haploid genome. At the time of fertilization, the DNA of both egg and sperm is packaged into chromatin, and each has its own epigenetic (DNA methylation and histone modification) state related to the previous functional requirements of these cell types. Once fertilization occurs, it is necessary that these epigenetic marks undergo extensive reprogramming for a complex multicellular organism to develop and differentiate. A similar period of extensive reprogramming of the epigenome has been shown to occur in the primordial germ cells during the development of the mature gametes. Some genes, called imprinted genes, are known to escape the epigenetic reprogramming in the early embryo and maintain the epigenetic state established in the gametes of the parents. This observation has supported the idea that perhaps some loci can escape both the reprogramming that occurs during early development and that which occurs during the development of mature gametes, thereby enabling Lamarckian inheritance. The evidence that this happens is scant, but has attracted much attention.

In a recent study published in Genome Biology, Iqbal and colleagues [1] have investigated the epigenetic changes that occur in response to endocrine disruptors and find that these changes are corrected by germline reprogramming events in the next generation.
difficult to publish negative results, no matter how important those negative results might be. The end result is that the published studies supporting Lamarckian inheritance seem to be uncontested to those outside the field. As a result, many people who are unfamiliar with the molecular sciences and who may be less able to critically assess the evidence are getting an incomplete story.

Epigenetic consequences of exposure to endocrine disruptors

Iqbal and colleagues [1] specifically set out to identify any transcriptional changes or DNA methylation changes that could explain the reported transgenerational effects of in utero exposure to endocrine disruptors in mice. They hypothesized that for epigenetic changes to be passed to a grandchild (G2), the endocrine disruptors must have their effects on the epigenome of the germ cells in the first generation (G1) while in utero. In other words, the effects of exposure must occur while the developing G1 embryo is in the uterus of the G0 female. In addition, to affect further generations, such as the great-grandchild, the modifications must persist in the germ cells of the G2 grandchild, who was not exposed to endocrine disruptors at any point during development.

The authors [1] used expression arrays on mRNA purified from germ cells to study global expression patterns, and several methods to study DNA methylation at imprinted loci, at CpG islands and at promoters. They detected changes in transcription and methylation in the G1 germline immediately after exposure to the chemicals. Contrary to previous hypotheses, they found that these epigenetic changes did not persist into the G2 germline. In addition, they looked for effects of these chemicals on the establishment of genomic imprints but found no persistent abnormalities in DNA methylation at the differentially methylated regions of imprinted genes. Previous studies [12] have reported that the process of genomic imprinting is perturbed by in utero exposure to endocrine disruptors in further generations. Of course, it is impossible to completely rule out any vestigial epigenetic marks or any vestigial effects on the mRNA population, but Iqbal and colleagues [1] have carried out a detailed and extensive study. They conclude that although the endocrine disruptors exert direct epigenetic effects in the exposed fetal germ cells, these are corrected by reprogramming events in the next generation.

This paper [1] provides a citable reference for the ‘doubters’ of Lamarckian inheritance in mammals and, as such, is a valuable contribution to this ongoing debate.

Competing interests
The author declares that she has no competing interests.

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