TRIALS OF UNNATURAL SELECTION

Human genetic enhancement: not such a good idea?

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Two months have passed since the Second International Summit on Human Genome Editing was held in Hong Kong. Two days before the meeting began, He Jiankui, a young Chinese scientist, dropped a media bombshell on an unprepared world. Posting five videos on YouTube, He announced to a shocked web audience that twin girls had been born with DNA that he had modified using the CRISPR-Cas9 technique.

As I write this article during the last week of January, some important news has emerged. So here are the latest updates on the "CRISPR babies" case. Firstly, the Chinese authorities have totally disavowed He's experiment. According to the Chinese news agency Xinhua, an official investigation has been conducted, finding that He acted alone and in secret. As a result, he has been fired from his university post and will be prosecuted for violating "ethical principles" and perhaps some Chinese laws. His experiments have been suspended, but the twin girls already born and the woman carrying the other child edited by He will now be cared for by government health facilities.

Secondly, in Davos, where the World Economic Forum is currently being held, an announcement has been made by Dr. Dzau, president of the U.S. National Academy of Medicine: the world's three most authoritative Academies of Sciences – American, British and Chinese – and a number of other important scientific institutions, have agreed to establish an international commission with a view to drawing up stringent guidelines for the use of the CRISPR-Cas9 technique in genome editing (which in the future could include the editing of human embryos for implantation in the uterus) and to monitor its application. The final conclusions of the Hong Kong Summit are thus confirmed: He's conduct has been condemned as unscrupulous and "irresponsible" from both an ethical and a scientific point of view.

However, the international genome editing community appears determined to proceed towards modifying the DNA of human embryos in order to avoid serious genetic diseases, “in the absence of valid clinical alternatives". The idea − which has been around for years but whose spread has been enormously accelerated by the discovery of the CRISPR-Cas9 technique – is to achieve "human genetic enhancement” (a term used thousands of times more frequently than “improvement”, thus ‘greenwashing’ a word too often associated with eugenics) by editing germline DNA (embryos, eggs and sperm).

Scientists are divided on this fundamental issue. Those in favour (among them the great majority of researchers working with CRISPR-Cas9) see this technique as a powerful tool for human genetic improvement. Once all the problems that make the procedure unsafe and unpredictable have been successfully overcome, then a great prospect − the elimination of genetic diseases − could become a reality. Germline editing not only modifies the DNA of the individual treated with CRISPR − in this case we speak of somatic modification − but the changes are also inherited by all of his/her descendants. Thus, carriers of genes of often lethal diseases will be able to generate offspring who are free of the disease and will not pass it on to their children.

Certainly, such a promise is tempting. It is therefore worth examining in depth the arguments against germline gene modification.

Let us imagine that in a few decades our level of scientific knowledge will make it possible to modify the human germline with tools considered "safe". Let us also imagine that in that distant (?) future our growing reliance on technological solutions has made it culturally acceptable to modify not only the "defective" genes that cause diseases, but also the genes that influence aesthetic traits or − who knows – aspects of intelligence in human embryos.

It is hard to imagine that there would not be scientists who, motivated by ambition or interest, would be eager, like He, to satisfy the wishes of potential parents. Of course, this type of service, even if it were not entirely legal or performed in more permissive countries, would be accessible only to the wealthiest in society. But the mere possibility of wealthy parents having children with the characteristics they

choose, points to a disquieting future in which socio-economic differences would be translated into genetic ones. This would further widen the gap between rich and poor, exacerbating conflicts within a society already marked by deep inequalities. According to some bioethicists, permitting human germline modification would be equivalent to opening a "Pandora's box" in societies where money and consumerism already play far too dominant a role. To describe this situation, a new term has been coined: ‘consumer eugenics’, accentuating a trend that is already gaining momentum.

Nowadays the word ‘eugenics’ is banned: all too often in the last century it was associated with practices condemned by history as brutal crimes. However, we must not forget that its etymological meaning is precisely the "genetic improvement" now being talked about, including of course the improvement of human beings.

It is true that the current idea of human genetic improvement is not based on the concepts of “lower races and classes" that in the past led to such terrible consequences. And yet, having made the necessary distinctions, we must not close our eyes to the possible social repercussions of any scientific choice. Science both reflects and determines social realities, intertwined as it is with the ideas and socio-economic conditions of its age. Therefore the whole of society, within and outside the scientific community, needs to be involved in making informed decisions, and must not be excluded from choices of such magnitude.

Another important perspective from which to examine the question is a more strictly biological one. It is being said that human germline gene editing will be used only to modify genes that, when present with two copies in the DNA, cause lethal diseases such as cystic fibrosis, thalassemia or Tay-Sachs disease. Let’s consider for a moment a fundamental aspect of natural selection as conceptualized by Darwin's theory: it is the environment that brings about selection of living organisms. In other words, it will be ever-changing - and therefore unpredictable - environmental conditions (natural and social) that determine whether possessing certain genes is an advantage or a disadvantage for a given individual. So the most advantageous thing for a population (of any species of organism) exposed to important environmental changes is the presence within it of great genetic diversity; this guarantees that at least a part of the population will be able to

survive and reproduce under novel conditions. In other words, for any given organism no genetic constitution is absolutely better than any other; it can be better only relative to the environment in which the organism lives.

This also explains why, after thousands of years of human evolution and therefore of natural selection, certain "harmful" genes are still present in our DNA. For example, carrying two copies of the thalassemia gene is a lethal condition, but having only one copy protects people from malaria in swampy areas. The gene which, when present in two copies, causes cystic fibrosis, if present in a single copy gives resistance against the cholera bacterium. Similarly, a single copy of the Tay-Sachs disease gene protects against tuberculosis. A further example is the *CCR5* gene that He edited in the twin girls. If deactivated, it is supposed to prevent the HIV virus from entering into the body's cells. But the same gene also seems to have a protective action against other viral diseases, such as West Nile fever and influenza (endemic in China).

These examples also highlight another fundamental aspect of our genetic endowment: rarely does a gene influence a single trait. As a general rule, the way in which DNA works could be summarized as follows: many genes-to-many traits (the opposite of the one-to-one correspondence posited as the central dogma of the biology on which genetic engineering is based). As recent research shows, DNA works as a network of mutual relationships between genes and the environment.

The influence exerted by the environment on human DNA is now so clearly proven that a new branch of biology, named 'epigenetics', has been created to study it. Stated in another way, the purpose of epigenetics is to study all the external factors that control the way in which genes function. Environmental factors, such as food, drugs, exposure to toxic substances, as well as to emotions and behaviours, cause changes in the structure of our DNA, leading some genes to be active and others inactive, without modifying their sequence (as the gene editing does). And numerous recent studies have shown that the structural changes that control gene "expression" are passed down to the offspring along with the gene sequences.

If these complex interactions/effects are not taken into account, all attempts to improve the human genetic endowment by modifying the sequence of embryos' DNA may in the long run expose our species to the risk of reducing its genetic

diversity, based as they are on criteria that, as far as we now know, are highly questionable.

The complexity of living systems calls for a reversal of perspective: the quality of the environment should be the focus of every attempt to improve human health, and we should put the maximum effort into safeguarding variability and unpredictability as intrinsic properties, the very source of life in all living things.

Taking the opposite direction by permitting human germline modification is very unwise, since it risks reducing in unpredictable and dangerous ways the real wealth of our species: its biodiversity. Not everything that can be done should be done, and in such choices lies the very essence of human freedom.