

## Letter to the Editor

### Ethical and scientific issues of gene-edited twin by clustered regularly interspaced short palindromic repeats (CRISPR) Cas9 technology

#### Bilir et al. Gene-edited twin by CRISPR-Cas9

Esra Bilir<sup>1</sup>, Emine Elif Vatanođlu Lutz<sup>2</sup>, Mustafa Levent Özgönül<sup>3</sup>

<sup>1</sup>Koç University Faculty of Medicine, İstanbul, Turkey

<sup>2</sup>Department of Medical History and Ethics, Koç University Faculty of Medicine, İstanbul, Turkey

<sup>3</sup>Department of Medical History and Ethics, Akdeniz University Faculty of Medicine, Antalya, Turkey

**Adress for Correspondence:** Emine Elif Vatanođlu Lutz,  
Phone: +90 543 635 31 71 e-mail: drvatanolu@yahoo.com ORCID: orcid.org/0000-0003-3156-4733

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To the Editor,

In November 2018, He Jiankui, a Chinese biophysicist at Southern University of Science and Technology, announced through an online video that the first gene-edited twin girls were born without chemokine receptor type 5 (CCR5) that achieved by using CRISPR-Cas9 due to the father being infected with human immunodeficiency virus (HIV) aiming to create HIV resistant offspring. Although the goal of creating humans with HIV resistant gene seems very reasonable and needs to be appreciated, he did not receive any credits but the contrary because he acted against the fundamental principles of medical practice “First do no harm”, Nuremberg Code stating one must not conduct research on humans without animal experiment, and the Helsinki Declaration (HD) concerning human enhancement and intervention in the human embryo(1). HD is the main ethical document of World Medical Association which regulates the ethical norms all clinical research in all fields in the world.(1)

This issue was criticized by the authorities in the world because gene-edited human embryos by CRISPR-Cas9 has never been approved to reach birth because of its unpredictable side effects, and also it is technically still imperfect(2). The first question should be directed to He is that without ethical committee approval how he managed to start and complete this “experiment” on human embryos. The weakness of institutional board control and national legal regulations regarding using gene-editing technologies in humans might have enabled him to perform this “experiment”. However, he acted against basic international rules of scientific research, especially, involving humans. Although He is not a medical doctor, the team must include a gynecologist to perform oocyte pick-up who should have informed the authorities and also disabled him to contact with the couple claimed to be the parents of the twin. It remains unclear

whether the team obtained informed consent by fully explaining the consequences and possible unpredictable side effects of using CRISPR-Cas9.

There are also major scientific limitations to CRISPR-Cas9 technology. It is not 100% effective for inserting new gene(s) or deleting gene(s) and also might lead to unwanted mutations that potentially are harmful to the humans(3). Some scientists also reported concerns about neurological deficits after knockdown of CCR5 by CRISPR-Cas9(4). The twin girls were claimed to be free of CCR5 gene; however, it is known that CCR5 is not the only way for HIV to enter the cells. Since HIV is not only physically and psychologically debilitating, but culturally and socially devastating too, this case can be considered as a promising option for the people infected with HIV(5). They have rights to reproduce and have healthy offspring, nevertheless, it should be achieved by well-established methods, not by experimental and possibly harmful technologies.

In conclusion, there is an urgent need for legal regulations to control the usage of CRISPR-Cas9 on humans that both international and national authorities should prepare. In Turkey all regulations are based on HD. It is suggested and very important that all innovative clinical research fields should be first harmonized according to the ethical standards of HD.

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