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Comments

Technique discussion of CRISPR babies --A comment to Jiankui He's research

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On November 25th, 2018, both the *MIT Technology Review* and *Associated Press* reported that *Dr. Jiankui He*, a Chinese biophysical researcher, has created two CRISPR babies. The gene editing babies, named *Lulu* and *Nana*, were genetically modified to resist HIV infection[1,2]. This news immediately initiated enormous concerns in both science world and society. Later, *Dr. He* revealed more data regarding his research[3]. Here, I would like to discuss this research from technical angle.

Initially, I thought that *Dr. He*'s research was simply crazy, which is not very uncommon in biological research area. In fact, it has been scolded for years that some talented scientists behave abusively in the lab. Nonetheless, the disclose of *Dr. He*'s data shows that instead of homology-directed recombination (HDR), non-homologous end joining (NHEJ) was induced by CRISPR/Cas9 in the twins' embryos. NHEJ is uncontrollable DNA repair mechanism and mostly used in gene knock out study of animals and plants [4]. To avoid unexpected effects (e.g. off-target effects) caused by the mutation, it is often required that at least two independent mutant lines are characterized with same phenotype to confirm the research discovery.

The whole experimental design of *He*'s research showed unbelievable underqualification in both science and ethics. Obviously, *Dr. He* has considered the off-target effects of CRISPR/Cas9 system, but the single-cell sequencing technology used to exclude off-target effects, which can only cover 80% of the whole genome, was not sufficient to ensure safety [5]. Moreover, the truncated C-C chemokine receptor 5 (CCR5) in *Lulu* (-4/+1) is completely different from the CCR5Δ32 discovered in European, leaving potential risks of creating a toxic protein and unwanted effects that are impossible to foresee. As for *Nana*, the -15/wt heterozygous genotype would not give protection against HIV.

Knowing the above information, *Dr. He* still pushed the project forward and created *Lulu* and *Nana*. The innocent twins have to suffer from unnecessary risks for pointless research. As we are fully aware that gene editing will eventually be adopted in clinical practices, it is very unlikely that we would induce NHEJ in any human cells. The random mutations caused by NHEJ would easily result in disastrous outcomes. Also, besides the fact that *Nana*'s genes cannot possibly give her protection against HIV, researchers have already developed multiple strategies to protect newborn from vertical transmission [6]. Moreover, in *Dr. He*'s research, it is the twins' father infected with HIV. It is very rare that HIV would transmit from father to child vertically, and the semen wash technology can almost ensure the child free from transmission [7].

In recent years, it is more and more emphasized that antibiotics should be used with caution, because the bacteria can easily adapt and become drug-resistant. As for virus, the mutation rate is much faster than bacterial. CDC has recommended an annual flu shot vaccine due to the constantly changing of virus. In HIV, although CCR5Δ32 homozygotes show strong immunity against HIV-1, the fact that X4 viruses can infect CCR5Δ32 homozygotes should not be ignored [6]. If gene editing technology were widely used in HIV resistance, strings like X4 that can circumstance CCR5Δ32 would undoubtedly propagate and cause new problems in a short time.

In conclusion, *Dr. He*'s research is not purposed to push the limit of science. Scientists have been dreaming about gene editing for decades, and we are so lucky to be born in the best time. Let us not mess this up. As researchers, we should

always remember that the final purpose of science is to serve this world and make it a better place.

Competing interests

The authors declare that they have no competing interests.

Acknowledgments

None

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