

# Human genome editing

- Sep 26, 2016

A type of genetic engineering called genome editing is receiving worldwide attention as a technique that can produce amazing progress in medicine and improvement of agricultural products. But the technique, which precisely alters genetic sequences, has raised ethical and social questions. Given the move to strongly push research on genome editing in Japan, including human genome editing, it is imperative that the government and academic societies concerned work out strict rules because the technique at this stage is not fully reliable and its ethical, legal and social ramifications are not completely known.

In genome editing, targeted DNA in a cell is cut away at a specific location to inactivate a problematic gene or to insert a replacement DNA sequence for replacement or repairs in order to produce a desired result. While DNA is a substance that contains genes, a genome refers to the entirety of hereditary information contained in genes and chromosomes in cells. In humans, a copy of the entire genome — more than 3 billion DNA base pairs — is contained in all cells that have a nucleus. Since the accuracy of genome editing at present is not high enough and inaccurate editing can happen, there is a view that genome editing is not an established technique. The current mainstream method in genome editing is programming a complex made up of a guide RNA and a certain type of protein to target a problematic gene in DNA.

In April last year, news that Chinese scientists edited the DNA of human embryos — the first time this has been done — shocked the world and touched off a debate because of the ethical implication of such endeavors. A team of researchers at Sun Yat-sen University in Guangzhou injected 86 nonviable embryos with a complex called CRISPR/Cas 9 to modify the gene responsible for beta thalassemia, a fatal blood disorder. Of the embryos, 71 survived and 54 of them were genetically tested. It was found that just 28 were successfully spliced, but that only a fraction of them contained the replacement genetic material. The researchers also detected a number of “off-target” mutations apparently caused by the injection of the CRISPR/Cas 9 complex.

Apparently prompted by what the Chinese team did, the Cabinet Office’s life ethics study group of experts in April issued an interim report that condoned basic genome editing research on manipulating genes in fertilized human embryos but said returning an embryo whose problematic gene has been

modified through genome editing to a womb is not acceptable. The Science Council of Japan in July started discussions by a committee of specialists on issues related to medical research and treatment that applies genome editing to fertilized human embryos and reproductive cells, and plans to issue a report or proposal by fall 2017. Early this month, the Japanese Society for Genome Editing issued a statement that basically agreed with the government study group's position.

The government study group, composed of 15 experts on life sciences, law and ethics, specifically said that basic research is acceptable for such purposes as finding out the roles played by genes at an early stage of embryonic development with the help of genome editing, developing methods to treat congenital hard-to-cure diseases and improving assisted reproductive technologies. But it called on researchers to limit their research to the first two weeks of a human embryo's development and to dispose of such embryos after their research is over. It also said that researchers should consider whether it is possible to use animal embryos instead of human embryos.

The group flatly turned down clinical use of human genome editing at this stage, citing the risks of inaccurate or incomplete editing such as off-target mutations and mosaicism or interminglement of modified and unmodified genes, as well as the difficulty to predict what effects gene alteration will have on other genes and to examine risks that future generations may face as a result of genetic alterations in embryos that will be passed from generation to generation.

Because the group's report has no binding power, the possibility cannot be ruled out that ethics committees of research institutes could permit human genome editing research beyond the scope mentioned by the report. The government and academic societies need to start working to develop binding guidelines or legal regulations that control human genome editing research by fully taking into consideration not only the ethical but also the social problems the technique can cause.

An international summit on human gene editing held in December in Washington, hosted by the U.S. National Academy of Sciences, the U.S. National Academy of Medicine, the Chinese Academy of Sciences and Britain's Royal Society, issued a statement which pointed out that "permanent genetic 'enhancements' to subsets of the population could exacerbate social inequalities or be used coercively." The statement stressed that "it would be irresponsible to proceed with any clinical use of germ-line editing" unless the relevant safety and efficacy issues are solved by fully weighing risks, potential benefits and alternatives, and unless there is broad societal consensus about the appropriateness of the

proposed application. It also called for putting all clinical use of human genome editing “under appropriate regulatory oversight.”

Human genome editing could have serious consequences depending on the level of its reliability and the way it is used. Theoretically it is even possible to use the technique to produce “designer babies.”

The government study group’s decision to make a manual to oversee the clinical use of human genome editing is meaningful. But given the technique’s potential benefits and risks, which are both of great consequence, there is a strong need for a wide range of the public, including ordinary citizens, lawmakers, bureaucrats, scientists, and legal and ethics experts, to carry out informed and detailed discussions so that human genome editing can truly contribute to enhancing the well-being of all people.

<http://www.japantimes.co.jp/opinion/2016/09/26/editorials/human-genome-editing/>