CRS INSIGHT

CRISPR Gene Editing Research in Embryos Generates Scientific and Ethics Debate

September 12, 2017 (IN10773)

|

Related Authors

- John F. Sargent Jr.
- Amanda K. Sarata

View More...

|

John F. Sargent Jr., Specialist in Science and Technology Policy (jsargent@crs.loc.gov, 7-9147)
Amanda K. Sarata, Specialist in Health Policy (asarata@crs.loc.gov, 7-7641)
Judith A. Johnson, Specialist in Biomedical Policy (jajohnson@crs.loc.gov, 7-7077)

A recent experiment in the United States using the gene modification tool CRISPR to target a disease gene in human embryos has raised optimism about promising medical advances, generated scientific debate, and renewed debate about longstanding ethical issues.

Since 1996, Congress has prohibited the use of funds appropriated in the Labor-HHS-Education appropriations bill for "the creation of a human embryo or embryos for research purposes" or for "research in which a human embryo or embryos are destroyed, discarded, or knowingly subjected to risk of injury or death greater than that allowed for research on fetuses in utero under [federal law and regulations]." Use of private funds for such basic research is not prohibited. Implantation of CRISPR modified embryos as part of a clinical research study is essentially blocked, regardless of funding source, since Congress began prohibiting use of appropriated FDA funds for the agency's review of exemptions for such work in December 2015 (P.L. 114-113).

CRISPR Research in Human Embryos

In August 2017, an international team led by researchers at Oregon Health and Science University (OHSU) reported using CRISPR in viable human embryos to correct a genetic defect which causes hypertrophic cardiomyopathy (HCM), a leading cause of sudden death in young athletes. Research using CRISPR in human embryos had already been happening in other countries. Three previously published studies by researchers in China used CRISPR for genetic modification of both nonviable and viable human embryos. In February 2016, the United Kingdom's Human Fertilisation and Embryology Authority approved research that would use CRISPR-Cas9 to modify healthy human embryos to investigate the role of specific genes that are involved in early development. Three key challenges to the use of CRISPR in embryo gene editing are its effectiveness in making intended changes; the potential for off-target effects

(unintended modifications); and mosaics (embryos composed of both modified and unmodified cells).

With private funding and in privately funded facilities, OHSU scientists used CRISPR to attempt to increase the chance that an embryo would have the healthy version of the gene. DNA modification was accomplished by injecting sperm (which had a 50% chance of carrying the genetic variant) along with CRISPR-cas9 (cas9 is an enzyme that cuts DNA) and a healthy version of the gene template into human eggs. Embryos were analyzed for gene repair at a multi-cell stage. The experiment reportedly showed that 72.4% of the embryos had the healthy version of the gene (vs. the expected 50% without the use of CRISPR). The study's authors claim that the embryos' repaired gene is unexpectedly the maternal version rather than the template. There was no evidence of unintended DNA changes and the researchers found one mosaic embryo.

The results of this study—and specifically the claim that the embryo preferentially used self-directed repair as opposed to template-directed repair—has recently come under some criticism. A group of six geneticists, developmental biologists, and stem cell researchers released a preprint abstract that offers alternative explanations for the finding of self-repair; the OHSU authors are to offer a point-by-point response to the critique in coming weeks.

Ethical Context

The OHSU work modifies the germline—defined as eggs, sperm, or very early embryos—as opposed to somatic cells (cells of the body, changes to which are not passed to future generations), and thus raises several ethical considerations. There are a range of views on the moral status of the human embryo, which are relevant to all research on human embryos. Apart from that issue, modification of the human germline has long raised its own ethical considerations, including that changes to the germline would be passed on to future generations and therefore might alter the genetic makeup of the population in unintended or unforeseen ways. The American Medical Association's Code of Ethics states that germline manipulation could result in "unpredictable and irreversible results that adversely affect the welfare of subsequent generations."

Another ethical consideration with this research, although not unique to it, is that modification might be used for enhancement purposes rather than for curing or treating disease or restoring lost function. Enhancement concerns often are discussed in terms of the concept of "designer babies," meaning parents would select non-disease, preferred traits (e.g., intelligence) in their offspring.

Another ethical consideration is the possibility that differential access to the technology based on a lack of resources could create inequities. Some note the hypothetical future use of germline modification, likely expensive and only accessible to the wealthy, could produce a class of economically and socially advantaged people.

The scientific community's view on germline modification research has evolved since *the publication of the first Chinese experiment in April 2015*. The director of the National Institutes of Health wrote in April 2015, "[t]he concept of altering the human germline in embryos for clinical purposes has been debated over many years from many different perspectives, and has been viewed almost universally as a line that should not be crossed." A National Academy of Sciences/National Academy of Medicine (NAS/NAM) International Summit in late 2015 softened this position for the first time. It concluded with a statement rejecting the clinical use of germline modification unless certain criteria are met and stating that these have not yet been met, but noting that "as scientific knowledge advances and societal views evolve, the clinical use of germline editing should be revisited on a regular basis." In 2017, NAS/NAM issued a report that largely echoes the statement made at the International Summit, but softening the position a bit more. The report found that although germline modification is not ready for use in humans yet, the technology is advancing quickly, and that such research is "a realistic possibility that deserves serious consideration." However, the report lays out a number of stringent criteria that would need to be met prior to carrying out this research—assuming that current restrictions were to be lifted—including the absence of reasonable alternatives and restriction to preventing a serious disease or condition.