Gene editing in embryos is fraught with scientific and ethical issues

December 2 2015, by Patrick Western

Genetic changes to embryos will not only affect the person that embryo becomes but also all their descendants. Credit: anna gutermuth/Flickr, CC BY-NC-ND

Recent technological advances have revolutionised our ability to manipulate the genetic code, allowing us to specifically edit individual genes. Gene editing offers exciting potential for disease therapies but application of the technology in embryos also raises many ethical and scientific issues.

Humans—and all other mammals—reproduce through sperm and eggs (germ cells) that transmit a single copy of each parent's chromosomes to the offspring. When an embryo forms at conception, it has a mix of genes from both germs cells, producing a child who's a biological reflection of the parents.

Sometimes, harmful mutations or changes in a gene sequence are transmitted by the germ cells and have deleterious effects in the embryo or in later life. In recent decades, genetic screening has allowed detection of particular genetic aberrations in early embryos. This has allowed us to avoid some of the harmful consequences of specific damaging mutations through pregnancy termination.

While genetic screening poses complex ethical questions, it's safe and doesn't introduce changes to genes that affect the baby or the baby's future children. By contrast, gene editing affects both.

Risking off-target effects

Gene-editing technologies have introduced the possibility of altering individual genes in eggs or sperm, or immediately after fertilisation in the earliest human embryos. This has the potential to correct gene mutations that underlie inherited disease.

But such germline gene therapy doesn't only affect the individual germ cells or embryo that has been treated; any changes will be transmitted to the future children of that individual.

This is highly controversial as it raises major safety concerns and the spectre of introducing "designer" mutations, in which specific genetic traits could be modified according to parents' requirements.

Clearly, there are fundamental social and ethical considerations involved

that preclude the use of gene editing in the human germline or in human embryos. But critical questions also surround safety and the potential biological impacts of gene editing if it were to be applied in humans.

The most obvious risk of editing embryo genes is the potential for errors or of introducing off-target genetic effects. Off-target effects occur when gene technology mistakenly hits a DNA sequence that's not the intended target.

While gene editing can be very specific, even minor errors or off-target effects are unacceptable in human embryos as they could harm the developing fetus or cause disease in adulthood. Off-target sites can also include the surprisingly large proportion of DNA sequence that lies between genes and plays important roles in gene regulation.

Critically, changes to any of these sequences will then be inherited by future generations.

The epigenetic black box

Other concerns surround potential effects on the way genes are regulated in the embryo. Although we've made unprecedented advances in biotechnology, we're only beginning to understand the complex biological systems that regulate fetal formation and influence lifelong health.

While gene sequence is paramount, additional information provided around the DNA is also crucial for development. One such example is the epigenetic code, which controls whether the thousands of genes contained in each cell are switched on and off in the correct combination, in the correct tissue, over a lifetime.

Epigenetic information contained in each cell type is passed to each new

cell as it divides to maintain or renew each tissue. This code ensures the long-term identity of cell types and the proper function of the tissue and organs they constitute.

Two important epigenetic issues arise in the context of editing embryo genes. First, environmental stimuli, such as chemicals, drugs or even diet, can alter epigenetic mechanisms. Second, disruptions in this code can lead to disease, a concept that is best illustrated in cancer development.

Importantly, both the sperm and egg transmit epigenetic information to the newly fertilised embryo. This epigenetic information affects development, health and even behaviour in the offspring.

Growing evidence indicates certain environmental stimuli alter epigenetic state in the germline and significantly affect outcomes not only in children, but also in grandchildren. Despite this, we have little understanding of how these effects are mediated in the developing embryo.

Cause for caution

While gene editing may be designed to correct a very specific genetic mutation, the change must be made in an embryo culture environment – that is, in the lab. Although embryo culture conditions are carefully controlled, we still have no way of properly measuring the potentially complex impacts of the gene-editing process on the embryo

Importantly, any negative effects may not be limited to the actual edit; they may also result from the gene-editing process, which requires the use of specific enzymes, chemicals and reagents in an artificial culture environment. These too may alter epigenetic state and other mechanisms in the embryo.

Despite the rapid progress and undeniable power of gene-editing technologies, we're still in the early stages of understanding the impacts of these processes on the genetic and epigenetic state of embryos and the future health and development of the person they become. The ethical issues surrounding germline gene therapy in humans are also enormous (more on that in The Conversation tomorrow).

If such technology were ever to be applied to the human germline for medical purposes, these issues would need to be addressed with the greatest stringency.

This story is published courtesy of The Conversation *(under Creative Commons-Attribution/No derivatives).*

Source: The Conversation