Proceed with caution: National Academies offers ‘qualified support’ for gene editing ‘abnormal’ embryos

Are so-called ‘designer babies’ one step closer to reality?

A joint National Academy of Sciences and National Academy of Medicine advisory panel issued a 250-page report on February 14 opening the door a crack to gene-edited embryos and permanently altering the human germline–a controversial issue among scientists and bioethicists.

The panel supported the modification of human embryos in instances in which there’s no other way to keep babies from acquiring genetic diseases that cause serious health complications or disabilities. Gene editing “for purposes other than treatment or prevention of disease and disability should not proceed at this time,” it concluded. The recommended safeguards would limit gene editing to addressing rare genetic disorders, such as Huntington’s disease, which occur when both members of a couple carry a Mendelian (single gene) disease-causing mutation.

Outlined in a presentation at the National Academy of Sciences in Washington, D.C., the report addressed safety, ethical and social considerations, and provided a platform for what it believed are responsible development and use of genome-editing technologies. Public discussions must “precede any decisions about whether or how to pursue clinical trials of such applications,” it recommended.

Mixed reaction

The panel specifically rejected germline changes that could make children smarter, stronger or more attractive, rather than just healthier–though everyone acknowledges that such a line is scientifically fuzzy. The focus of germline, or heritable genome editing, must be on “healthy babies, not designer babies,” said Alta Charo, committee co-chair and a professor of law and bioethics at the University of Wisconsin—Madison. For some populations, Charo said, heritable genome editing would allow parents to have genetically related children without passing on their known risk for genetic diseases.

The authors acknowledged that every nation has its own stance on genome modification, and that cultural and religious beliefs will affect how gene editing technologies are received by certain populations. Caution is needed, the committee warned, but caution does not necessarily mean prohibition.The orange-light recommendations were an attempt to encourage research in a field littered with ethical landmines. “They have closed the door to the vast majority of germline applications and left it open for a very small, well-defined subset. That’s not unreasonable in my opinion,” said Eric Lander, a genome researcher of the Broad Institute in Cambridge, Massachusetts known as encouraging of the research. But critics quickly emerged. “It changes the tone to an affirmative position in the absence of the broad public debate this report calls for,” said Edward Lanphier, CEO Sangamo Therapeutics in Richmond, California. He co-authored a *Nature* commentary in 2015 that called for a moratorium on clinical embryo editing, claiming that heritable human genetic modifications pose “serious risks” while the therapeutic benefits are “tenuous.”

Marcy Darnovsky, a philosopher and executive director of the Center for Genetics and Society in Berkeley, California, which is known for its hardline rejection of gene editing and many modern biotechnologies, was uncompromisingly critical of the panel's recommendations. "We're very disappointed with the report," she said. "It's really a pretty dramatic shift from the existing and widespread agreement globally that human germline editing should be prohibited."

CRISPR consequences

Fears concerning the inappropriate or abusive uses of gene editing have escalated since the development of the CRISPR/Cas9 technology in 2012. Some ethicists worry that only affluent members of society would have access to this technology, while others are concerned about unexpected health and social consequences that could result from cosmetic genetic tampering. Critics warn that human gene editing could result in off-target effects—accidental edits elsewhere in the genome—potentially resulting in irreversible disability or even death, although most scientists believe such effects would be rare and could be anticipated.

Committee co-chair Richard Hynes, a cancer researcher at the Massachusetts Institute of Technology, reminded the audience at the press conference that gene editing is not a new concept. Enormous advances in the field, especially the development of CRISPR, are responsible for making genome editing procedures cheaper, more precise, and much easier than in the past. These factors, in turn, have caused an explosion of interest in applications in three main areas: basic research, somatic cell edits and germline edits.

Where the research stands now

Clinical trials using edits on human somatic, or body cells, are already underway. It is now possible to "insert or delete single nucleotides, interrupt a gene or genetic element, make a single-stranded break in DNA … or make epigenetic changes to gene expression," according to the report. These types of edits only affect the patient being treated, whereas germline edits—on human sperm, eggs, or embryos—would be passed on to subsequent generations.

There are alternatives to germline gene editing, but for some groups these alternatives—such as selective abortion and destruction of affected embryos—are unacceptable. Another possibility is providing somatic cell treatment to children once they are born, but this comes with its own set of risks and ethical considerations. In certain situations, such as when a parent is homozygous for a harmful disease variant, there are no alternatives. This makes heritable genome editing the only option for some parents seeking genetically related offspring.

Currently in the United States, research trials using germline cells are unable to be considered due to Food and Drug Administration regulations on "research in which a human embryo is intentionally created or modified to include a heritable genetic modification."

General principles to guide the governance of human genome editing, given in detail in the full report, include the promotion of well-being; transparency and accessibility of information to all stakeholders; due

care; responsible science and adherence to the highest standards of research “from bench to bedside”; and respect for persons and the personal dignity of all individuals.

Given the accessibility of CRISPR, one could conceive of a future in which a form of genome editing black market could emerge to service those who would disregard such principles for profit or out of medical desperation. Genome editing laws are either lax or nonexistent in many countries. These legal disparities could potentially inspire the rise of a new kind of medical tourism. But for now, legally editing human germline cells remains in the distant future.

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