



Unintended Effects of Genetic Manipulation

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After Reported 2018 Birth of Two Genetically-Engineered Babies in China, Calls for Moratorium on Human Germline Engineering Grow

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Responding to a widely condemned experiment reported last year as resulting in the birth of two genetically-engineered babies in China, an international group of prominent genetic-engineering researchers, other scientists, and ethicists has called for a voluntary “global moratorium on all clinical uses of human germline editing.”

Proposing the moratorium in March, 2019, in the prestigious journal *Nature*, the group defined germline editing as “changing heritable DNA (in sperm, eggs or embryos) to make genetically modified children.” They said they were not calling for a permanent ban, but a fixed period — possibly five years — during which individual governments would voluntarily declare that they would not allow the clinical use of human germline engineering. The group urged that governments use that time to develop an “international governance framework” for the future — which they also advised should be voluntary, not the subject of a binding treaty. What that framework would look like, they suggested, could be based on broadly inclusive societal discussions about “the technical, scientific, medical, societal, ethical and moral issues that must be considered before germline editing is permitted.”

Their action echoes other concerned responses, including stronger calls for not just a moratorium on clinical applications of human genome engineering, but also on related experimentation in research labs. One of the earliest and strongest responses was organized by the Center for Genetics in Society and Human Genetics Alert. It was published just two days after the news broke in late November in Hong Kong — where the Second International Summit on Human Genome Editing was about to convene — that the Chinese biophysicist He Jiankui claimed to have engineered changes in the genome of two human embryos that were then implanted in the womb of a woman who he said had recently given birth to twin girls.

The two organizations immediately coordinated a statement signed by more than 100 leaders of civil-society groups — including Craig Holdrege, co-founder and director of The Nature Institute — urging: (1) The summit organizers and the larger scientific community to clearly condemn what He had done as reckless and socially irresponsible, and (2) The United Nations and individual governments “to establish enforceable moratoria prohibiting reproductive experiments with human genetic engineering.” More civil-society leaders and organizations have signed that call since it was first published.

“Such policies are necessary,” the civil-society leaders stated, “in order to ensure that we do not get into a runaway international competition for primacy in reproductive genetic engineering, leading to a new form of eugenics.”

By contrast, the group of researchers and ethicists whose call was published in *Nature* in March did not call for any halt in such experimentation, or for a moratorium that would be enforceable internationally. Their focus was limited to a moratorium on actually applying such

techniques in embryos that are intended to be implanted and carried to term, and to voluntary action by individual governments. They added that “clinical germline editing should not proceed for any application without broad societal consensus on the appropriateness of altering a fundamental aspect of humanity for a particular purpose.” By “societal consensus” they appeared to be referring to consensus within the nation in which such work would be carried out, after an international framework existed.

Germline editing techniques, this group warned, “are not yet safe enough or effective enough to justify any use in the clinic,” nor are the long-term biological consequences for either an individual or the human species as a whole of such inherited genetic changes well understood. “There is wide agreement in the scientific community that, for clinical germline editing, the risk of failing to make the desired change or of introducing unintended mutations (off-target effects) is still unacceptably high,” the group noted. For example, He said he was trying to engineer a particular genetic change to confer future resistance to AIDs, if the babies subjected to the engineering as embryos were exposed to the HIV virus after birth. But that particular genetic change might also be associated with a higher chance of experiencing complications or death from influenza or the West Nile virus, if the twins later contracted either of those, according to the group of researchers and ethicists.

Leaders of the second international summit, at the end of their November meeting, issued a statement that “proceeding with any clinical use of germline editing remains irresponsible at this time.” They too warned of the unintended effects of He’s work, although they did not mention him by name. But the rest of their statement included a number of references that seemed to envision a future where human germline engineering may well be safely regulated and ethically performed. More than 40 countries have legally prohibited human-germline modification, and a binding international treaty of the Council of Europe also prohibits it, according to the Center for Genetics in Society. In the U.S., federal agencies, such as the National Institutes of Health, are prohibited from supporting research into human germline engineering that uses human embryos. But such research, funded by other sources, continues in the U.S., as it does elsewhere.

In the same issue of *Nature*, two top leaders of the National Institutes of Health — Francis S. Collins, its Director, and Carrie D. Wolinetz, its Acting Chief of Staff and Associate Director for Science Policy — wrote a letter voicing their support for the international call for a moratorium on clinical applications of human germline engineering. They also, however, made a point of suggesting that scientists should not assume that any such moratorium would or should turn out to be only temporary.

“We think that human gene editing for reproductive purposes carries very serious consequences — social, ethical, philosophical and theological,” Wolinetz and Collins wrote. “Such great consequences deserve deep reflection. A substantive debate about benefits and risks that provides opportunities for multiple segments of the world’s diverse population to take part has not yet happened. Societies, after those deeper discussions, might decide this is a line that should not be crossed. It would be unwise and unethical for the scientific community to foreclose that possibility.”

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