



An early human embryo, the focus of controversy.

BIOETHICS

Embryo engineering alarm

Researchers call for restraint in genome editing

By Gretchen Vogel

Asilomar. The word conjures up not only stunning California coastline but also vexing questions posed by new, potentially world-changing technologies. In 1975, the Asilomar conference center hosted a meeting where molecular biologists, physicians, and lawyers crafted guidelines for research that altered the DNA of living organisms. Now, scientists are calling for another Asilomar—this time to discuss the possibility of genetically engineered human beings.

In 1975, the notion of someday using recombinant DNA to design human babies was too remote to seriously consider, says David Baltimore, a molecular biologist and president emeritus of the California Institute of Technology in Pasadena, who helped organize the first Asilomar meeting. What's changed now is the explosion of powerful new genome-editing technologies such as CRISPR-Cas9, zinc fingers, and TALENs. They have made it easy for anyone with basic molecular biology training to insert, remove, and edit genes in cells—including sperm, eggs, and embryos—potentially curing genetic diseases or adding desirable traits. “The time has come where you can’t brush that possibility aside,” Baltimore says.

Rumors are rife, presumably from anonymous peer reviewers, that scientists in China have already used CRISPR on human embryos and have submitted papers on their results. They have apparently not tried to establish any pregnancies, but the rumors alarm researchers who fear that such papers, published before broad discussions of the risks and benefits of genome editing, could

trigger a public backlash that would block legitimate uses of the technology.

“If there were a rogue laboratory in the world somewhere that could get access to embryos, in principle it would be possible,” says Jennifer Doudna, a molecular biologist at the University of California, Berkeley, who helped develop CRISPR. Even before rumors surfaced, she organized a January meeting with scientists, ethicists, and law experts to discuss what steps the scientific community could take to ensure the technology would be used safely and ethically.

In two commentaries, one published online this week in *Science* (<http://scim.ag/DBaltimore>) and one in *Nature* last week, two groups of scientists take a stab at recommendations. In *Nature*, one of the researchers who helped develop zinc-finger nucleases, Edward Lanphier, and four colleagues call for a moratorium on any experiments that involve editing genes in human embryos or cells that could give rise to sperm or eggs. “Should a truly compelling case ever arise for the therapeutic benefit of germline modification, we encourage an open discussion around the appropriate course of action,” they write.

In the *Science* commentary, which grew out of the January meeting, Doudna, Baltimore, and 16 colleagues stop short of a blanket moratorium. They call on scientists to “strongly discourage ... attempts at germline genome modification for clinical application

in humans,” but leave open the possibility of research with human cells as long as they are not used to establish a pregnancy.

Most of the signatories of the *Science* commentary think such experiments could answer legitimate scientific questions, Doudna says. Editing genes in germ cells could help researchers understand certain kinds of infertility, for example, and altering the genes in one-celled embryos could shed light on the earliest stages of human development.

But scientists don't yet understand all the possible side effects of tinkering with germ cells or embryos. Monkeys have been born from CRISPR-edited embryos, but at least half of the 10 pregnancies in the monkey experiments ended in miscarriage. In the monkeys that were born, not all cells carried the desired changes, so attempts to eliminate a disease gene might not work. The editing can also damage off-target sites in the genome.

Those uncertainties, together with existing regulations, are sufficient to prevent responsible scientists from attempting any genetically altered babies, says George Church, a molecular geneticist at Harvard Medical School in Boston. Although he signed the *Science* commentary, he says the discussion “strikes me as a bit exaggerated.” He maintains that a de facto moratorium is in place for all technologies until they're proven safe. “The challenge is to show that the benefits are greater than the risks.”

Doudna and others are not so sure current regulations suffice. Although many European countries ban germline genetic engineering in humans, the United States and China do not have such laws. Research with private funds is subject to little oversight in the

United States, although any attempts to establish a pregnancy would need approval from the U.S. Food and Drug Administration. In China, any clinical use is prohibited by the Ministry of Health guidelines, but not by law.

Whether or not another Asilomar meeting is called, the topic has caught the attention of

several science policy groups, including the Nuffield Council on Bioethics, the Hinxton Group, and the National Academy of Sciences. Church hopes such discussions will tackle a question that he says both commentaries avoid: “What is the scenario that we're actually worried about? That it won't work well enough? Or that it will work too well?” ■

With reporting by Jocelyn Kaiser, Dennis Normile, and Christina Larson.

Past pauses

Biologists have called for research moratoriums before.

- 1975 Recombinant DNA studies
- 1997 Human reproductive cloning
- 2012 Influenza gain-of-function studies

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