UK Approves First Studies Using New Gene Editing Technique

Feb. 1, 2016
A Powerful New Tool for 'Editing' the Human GenomeDNA Sequencing Company Wants to Develop a Cancer Blood Test

A U.K. researcher will be the first to use a precise but controversial new gene-editing technology called CRISPR to alter the genes in a human embryo.

In a nondescript office in London, a small group of experts and patient advocates have made a momentous decision that could forever change the human condition. The U.K.'s Human Fertilization and Embryo Authority (HFEA) decided to approve a researcher's request to use CRISPR to permanently change DNA in a human embryo.

It's the first time the technology, which has taken the medical world by storm, has been sanctioned for use on human embryos. The team of scientists led by Kathy Niakan, a biologist at Francis Crick Institute, will attempt to edit out bits of DNA that prevent an embryo from developing properly—which may answer important questions about infertility. The embryo would not be allowed to survive beyond 14 days—meaning they wouldn't be implanted into a woman's womb and grown into live babies.

"I promise you she has no intention of the embryos ever being put back into a woman for development," Robin Lovell-Badge, group leader at the Crick Institute, told TIME. "That wouldn't be the point. The point is to understand things about basic human biology. We know lots about how the early mouse embryo develops in terms of how various cell lineages give rise to the embryo or to [other] tissue that make up the placenta. But we know very little about how this happens in the human embryo."

Still, the experiment raises serious questions about how the powerful technique should be used. CRISPR opens the door to an unprecedented level of control over the human genome. Older techniques for editing DNA have been blunt and unreliable at best; CRISPR, on the other hand, is quickly emerging as the precision blade to those butter-knife approaches.

CRISPR allows scientists to precisely snip out and replace genes, and for the first time, the newly green-lit experiment will apply this to the so-called germline cells in an embryo—the DNA in an embryo so early in its development that all of its resulting cells will carry the change—and pass it on to the next generation. Monday's decision has been eagerly anticipated by scientists around the world.

In the United States, federal laws prohibit the National Institutes of Health from funding human-embryo-based research that uses CRISPR, and leading scientists have called for a moratorium on the use of the technology on human embryos.

Since CRISPR popped into biology labs in 2012, scientists have been using it in research studies as they try to splice and dice genes from cells—but not live embryos. They've used it to cut out everything from the mutation responsible for sickle cell anemia to HIV. Its relatively simple process means that nearly every molecular biology lab, and IVF clinic, for that matter, already has the proper equipment to use CRISPR.

But none have dared to alter the germline genome until Chinese researchers attempted it—to the horror of many western scientists—last April. (The results were disappointing, perhaps because the embryos they

used were abnormal which, say some experts, are not the ideal test for CRISPR.) Niakan asked the HFEA in September to consider what she hopes will be a more successful version of germline gene editing using CRISPR.

Trying to Answer Infertility's Mysteries

Niakan trained in the United States and studies early embryo development and infertility. The environment for such research is more of a wild west in the U.S. Only since 2009, when President Obama lifted a previous ban on embryo-based research, can scientists in the U.S. use NIH money to study embryos donated from IVF procedures. (They can't use CRISPR on them, however—at least not for now.) But studies on human embryos with private funding are left unregulated.

The U.K., on the other hand, has been at the forefront of genetic engineering feats, from pioneering the IVF process to creating a welcome environment for the study of embryonic stem cells, the early cells that develop into all of the tissues in the human body. U.K. authorities have also OKed the creation of human embryos for research purposes only.

Niakan wants to use CRISPR to study a series of genes that mouse studies strongly suggest may be involved even in creating the early human embryo. CRISPR, she says, will allow her to clip out each gene of interest and then observe what happens to the resulting embryos. By tracking which types of cells continue to grow and develop, she can determine which genes are critical to which specific types of tissues in the early embryo.

Ultimately, it's possible that if Niakan learns which specific genes in healthy embryos help them implant successfully in the uterus and grow to term, that knowledge could help infertile couples start families. The genetic pathways Niakan identifies wouldn't necessarily mean that women would have to undergo CRISPR treatments, but it could lead to drugs that capitalize on the CRISPR findings, by either enhancing or reducing the effects of certain genes.

For Niakan, CRISPR is the ideal way answer her scientific questions. HFEA requires that scientists using human embryos for research rely on the most efficient methods possible, and she anticipates that CRISPR will allow her to successfully make the genetic changes she needs in eight out of every 10 embryos she studies.

A Question of Precedent

HFEA, in weighing their decision, had to consider questions far beyond Niakan's scientific ones. While scientists focus on CRISPR's incredible power to answer biological questions, for almost anyone else, CRISPR raises the notion of designer babies, made-to-order genetic traits and so forth. If CRISPR can successfully change the genome of an embryo, it could forever alter the human gene pool—and diversity in the gene pool is an important part of keeping a species healthy. Intentionally manipulating that pool could have unpredictable consequences on our ability to fight disease, our life expectancy, and more—for good and for ill.

HFEA's decision also sets an important precedent for the future use of CRISPR, and how other scientists in labs around the world will put it to use. The ability to manipulate the human genome with such precision and relative ease raises inevitable questions about the how far this intervention can and should go. Any discussion about genetic manipulation, whether it's the genetic engineering that was made possible when scientists first discovered the biological scissors that could cut DNA in the 1970s, to testing for genetic mutations and now CRISPR, all lead to questions about man playing god.

Niakan is using CRISPR to study genes responsible for infertility, but the technology could just as easily be used to dictate which genes an embryo should, or shouldn't have. It's relatively straightforward to decide that the gene that causes sickle cell anemia, for example, a devastating blood disorder that requires people to get regular transfusions of healthy blood cells, should be snipped out. But what about a gene involved in short stature? Or grey hair?

The Crick Institute's Lovell-Badge says that makes him uncomfortable about how CRISPR might be applied outside of the U.K. Any IVF clinic, for example, already has the means to use CRISPR to edit genomes of the embryos they implant — they just need to order the right genetic cassettes to cut out and replace whichever genes they desire. In the U.S., because IVF clinics aren't regulated, any private IVF clinic could theoretically start to employ CRISPR and promise parents-to-be their own customized baby. "That really scares me because you can imagine someone with a big ego whether it's a patient or a clinician wanting to be the first to do this type of thing," he says.

In the U.K., IVF clinics are strictly regulated by laws that would deter such editing. Even if technicians used CRISPR to genetically edit an embryo's DNA, it would be illegal to implant that altered embryo into a woman. Violators could be fined or imprisoned. There are also strong regulations surrounding how human embryonic stem cells should be studied and handled, and these laws provide a precedent for "knowing where the boundaries are in the U.K. so there is confidence that as long as you are doing things approved by HFEA then you know you're not stepping over any boundaries," says Lovell-Badge.

Those boundaries will continue to change, as the latest approval shows. The challenge isn't in decoding the science of manipulating the human genome. It's in making sure that those interventions are done in a responsible and socially acceptable way.