EXTREME GENETIC ENGINEERING and the HUMAN FUTURE

Reclaiming Emerging Biotechnologies for the Common Good

CENTER FOR GENETICS AND SOCIETY

Friends of the Earth

Acknowledgements

This report was drafted by Pete Shanks, M.A., consulting researcher with the Center for Genetics and Society, and completed with significant contributions from Dana Perls, M.C.P., Friends of the Earth-U.S.

We would also like to thank the following individuals for their review of and contributions to this report: Lisa Archer, Friends of the Earth-U.S.; Marcy Darnovsky, Ph.D., and Elliot Hosman, J.D., Center for Genetics and Society; Jim Thomas, ETC Group; Gregor Wolbring, Ph.D., University of Calgary; Rachel Smolker, Ph.D., BioFuels Watch; Ed Hammond, M.A./M.S., Third World Network; M.L. Tina Stevens, Ph.D., Alliance for Humane Biotechnologies; Donna Dickenson, Ph.D., for inspiring the report's subtitle; and Richard Hayes, Ph.D., former director of the Center for Genetics and Society.

About Center for Genetics and Society

The Center for Genetics and Society is a nonprofit information and public affairs organization working to encourage responsible uses and effective societal governance of human genetic and reproductive technologies and other emerging technologies. The Center supports benign and beneficent medical applications of these technologies, and opposes those applications that objectify and commodify human life and threaten to divide human society. A resource list of articles and statements about human germline gene editing can be found at **www.geneticsandsociety.org**

About Friends of the Earth

Friends of the Earth-U.S., founded by David Brower in 1969, is the U.S. voice of the world's largest federation of grassroots environmental groups, with a presence in 75 countries. Friends of the Earth works to defend the environment and champion a more healthy and just world. Through our 45-year history, we have provided crucial leadership in campaigns resulting in landmark environmental laws; precedent-setting legal victories; and groundbreaking reforms of domestic and international regulatory, corporate and financial institution policies. **www.foe.org**

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Executive Summary

The idea of genetically modified children was once the stuff of science fiction, but recent developments in genetic engineering and "synthetic biology" could make it a reality. Scientists are bringing together a new generation of technologies that enable them to artificially redesign life — everything from yeast cells to people. And now, with recently developed techniques for "gene editing," the prospect of redesigning humans is much closer.

This is a brief overview of the current range of synthetic biology techniques and approaches, particularly gene editing, that are being proposed for use on humans. We discuss the challenges and concerns that arise from these proposals, including their unprecedented ethical, social and health implications.

Researchers hail synthetic biology – a new set of genetic engineering techniques – as "the future of manufacturing, engineering and medicine."[1] Amid big dreams are fast-paced investments. The synthetic biology market is expected to reach close to $39 billion by 2020.[2] Already products of synthetic biology, such as synthetic biology-derived vanillin, stevia and oils, are entering food and consumer products ahead of independent environmental and safety assessments, oversight and labeling — a worrying precedent for human applications.

But much more far-reaching proposals are in the pipeline. For example, one prominent synthetic biologist, Stanford's Drew Endy, has asked, "What if we could liberate ourselves from the tyranny of evolution by being able to design our own offspring?"[3]

Prominent voices, including some scientists working in the field, are deeply concerned about the unforeseen consequences that human genetic engineering could have. Some believe there are lines that should not be crossed, especially attempts to create genetically modified human beings (sometimes called "designer babies"), and suggest that the risks to individuals and to society will never be worth any supposed benefit. Others argue that if it's "safe," anything goes. A few even hypothesize that humanity will have a moral duty to genetically "enhance" our children if the technology and underpinning genetics progress.

No matter which opinion one holds, everyone needs to be aware of these new technologies and be able to engage in decisions about what is safe, ethical and beneficial.

There is a dearth of oversight for the rapidly emerging frontier of this merger of engineering and biology. Historic precedent demonstrates that failure to ensure transparency, democratic input and practical regulatory oversight can give license to unethical research that manifests with unintended consequences resulting in harm. Only in retrospect have these transgressions been made public.

For example, over a period of 40 years between 1932 and 1972, the U.S. Public Health Service and the Tuskegee Institute engaged in unethical research, telling hundreds of black men that they were receiving treatment for syphilis, when in fact researchers were studying the impacts of the disease as it went untreated.[4] In the 1940s, U.S. government medical researchers infected people in Guatemala with gonorrhea and syphilis without consent.[5]

More recently, there have been instances where either self-regulation has failed or scientists have not cooperated with government regulators. For example, some fertility clinics have routinely failed to follow existing professional guidelines regarding payment for women's eggs, social sex selection and the number of embryos transferred.[6] Cases of fraud and abuse have been documented from unregulated, unlicensed stem cell clinics that continue to proliferate, particularly off-shore.[7] In the late 1990s and early 2000s, several patients died as a result of unexpected reactions in gene therapy experiments.[8] In the follow-up to that tragedy, the National Institutes of Health discovered that "only 35 to 37 of 970 serious adverse events" in one kind of gene therapy trial were reported as required.[9]

The implications and potential impacts of gene editing are vast and in many cases, irreversible.

Executive Summary (continued)

We need broad-ranging, inclusive discussions that expand beyond the ivory towers of academia or corporate-funded experts in the field, and that actively involve and integrate the perspectives of the public, including civil society organizations, labor unions, the faith community and others. The Center for Genetics and Society and Friends of the Earth-U.S. advocate that everyone should have a voice in such monumental decisions about the future direction of humanity. Open, meaningful and full public participation at every level is essential and must include consideration of the wide-ranging ethical, social and economic impacts of these technologies alongside currently uncertain predictions around safety.

We are already seeing attempts to pave the way for genetically engineered humans. Consider this sequence of recent events:

- In April 2015, researchers from Sun Yat-sen University reported that they had used gene editing techniques to alter human embryos,[10] the first time in history this is known to have occurred.[11]
- In April and May 2015, many U.S. scientists, as well as the White House, National Institutes of Health and other agencies, called for a moratorium on experimenting with human embryos, and the National Academies of Sciences announced plans for a meeting to discuss the implications of this research in December 2015.[12]
- In September 2015, a group of six major UK research funders and the Hinxton Group, an international consortium on stem cells and ethics, both released statements advocating for gene editing research in human embryos.[13]
- Also in September 2015, a team of researchers affiliated with the Francis Crick Institute applied to the UK's Human Fertilisation and Embryology Authority for a license to begin genome editing research in human embryos.[14]

Together, these developments suggest that researchers may be much closer to heritable human applications of gene editing than previously thought, and that addressing the related social, environmental, health and ethical concerns is now critical.

Recent genetic engineering discussions have focused on CRISPR/Cas9, a molecular complex intended to "edit" a genome by cutting out and/or splicing in parts of DNA sequences. This technique (which is not yet perfected, but is rapidly being refined) is promoted as a promising tool to prevent genetic diseases.

Using gene editing at the request of health-impacted patients with specific diseases, often referred to as "somatic" gene therapy, may be a worthwhile goal, if it is in fact feasible, and if the implications of such procedures are fully understood and accepted. But using the same techniques to modify embryos in order to make permanent, irreversible changes to future generations and to our common genetic heritage — the human germline, as it is known — is far more problematic.

Even the developers of the CRISPR/Cas9 tool are concerned about how others may use it. One of the discoverers, University of California, Berkeley researcher Jennifer Doudna, said:

> *"Once the discovery is made, it's out there. Anybody with basic molecular biology training can use it for genome editing. That's a bit scary."*[15]

In order to fully understand the implications of these technologies, there are essential questions that must be addressed:

- What might be the unforeseen consequences of editing DNA, about which scientists still understand very little?
- What if something goes wrong? With gene "editing" there is no simple "undo" button.
- Which of the proposed human engineering applications could address important problems?
- How can we avoid harms caused by a rush for new opportunities for profit?

Executive Summary (continued)

- What are the risks of intervening in a patient's genome?
- Who has access and will benefit from these proposed applications?
- How do we evaluate assumptions about disease prevention, disabilities or the social creation of genetically modified humans?
- What is ethical, and who decides?

The potential human applications of synthetic biology tools, such as gene editing, put big questions on the table. It is important to look at the assumptions we are making and to quickly raise awareness about how these technologies may impact our own DNA and health, and that of future generations.

Findings and Key Concerns

- There are significant scientific, environmental, health and ethical challenges to the human applications of synthetic biology, which currently include reengineering the human microbiome, gene drives, xenotransplantation and gene editing.
- Science and biotechnology developed in the context of private funding, public investment, intellectual property and commercial pharmaceuticals is subject to systemic incentives to rush newly discovered technologies to market, regardless of their social utility and ahead of appropriate, transparent assessment and oversight.
- Heritable genetic modification in humans, also known as human germline intervention, is exceedingly difficult to justify on medical grounds, and carries enormous risks, both for individuals and society.
- Some of those who are advocating for moratoria on editing the human germline nonetheless limit discussions of "ethics" to questions of scientific risk (safety), and fail to significantly consider social, ethical and legal risks.
- The advent of human germline intervention could lead to the development of new forms of social inequality, discrimination and conflict. Among the risks of heritable genetic modification is the possibility of a modern version of eugenics, with human society being divided into genetic "haves" and "have-nots."
- Dozens of countries, including many of those with highly developed biotechnology sectors, have explicitly banned heritable human genetic modification, as has the Council of Europe's binding 1997 Convention on Human Rights and Biomedicine.

A Call to Action

We call for:

- National and international prohibitions on the use of gene editing and synthetic biology to alter the human germline for reproductive purposes. This call is especially relevant in those countries, like the U.S., that have not already enacted such a prohibition.
- Explicit and expansive public engagement on the human applications of synthetic biology, including consideration of not just safety thresholds, but also of social and ethical concerns.
- An ongoing, transparent, democratic process with which to evaluate and appropriately regulate new, emerging and proposed human applications of synthetic biology. This broad public oversight will hold scientists and entrepreneurs accountable to responsible regulation of these potentially hazardous technologies.
- Increased investment in more socially just and less risky solutions to environmental, health and social problems.

Executive Summary Endnotes

1 Bryan Johnson, "Why Synthetic Biology Will Be The Future of Manufacturing, Engineering and Medicine," SynBioBeta, last modified May 5, 2015, http://synbiobeta.com/why-synthetic-biology-will-be-the-future-of-manufacturing-engineering-and-medicine/.

2 Camille Delebecque and Jim Philp, "Training for synthetic biology jobs in the new bioeconomy," Science, June 2, 2015, http://bit.ly/1QpqP83.

3 Michael Specter, "A Life of Its Own," The New Yorker, last modified September 28, 2009, http://www.newyorker.com/magazine/2009/09/28/a-life-of-its-own.

4 "U.S. Public Health Service Syphilis Study at Tuskegee." Centers for Disease Control and Prevention. Last accessed 15 October 2015. http://www.cdc.gov/tuskegee/timeline.htm.

5 Robert Bazell, "U.S. apologizes for Guatemalan STD experiments." NBC News, last modified October 1, 2010, http://www.nbcnews.com/id/39456324/ns/health-sexual_health/t/us-apologizes-guatemala-std-experiments/#.ViJxIs4rX2B.

6 Pete Shanks, "The Limitations of Voluntary Guidelines," Biopolitical Times, last modified August 21, 2012, http://www.biopoliticaltimes.org/article.php?id=6356.

7 Paul Knoepfler, "How Much Do Stem Cell Treatments Really Cost?" The Niche, last modified February 22, 2015, https://www.ipscell.com/2015/02/stemcelltreatmentcost/.

8 Paul Gelsinger and Adil E. Shamoo, "Eight Years After Jesse's Death, Are Human Research Subjects Any Safer?," Hastings Center Report 38, no. 2 (2008): 25–27, http://www.thehastingscenter.org/Publications/HCR/Detail.aspx?id=82.

9 Larry Thompson, "Human Gene Therapy Harsh Lessons, High Hopes," FDA Consumer, Sept-Oct 2000, http://permanent.access.gpo.gov/lps1609/www.fda.gov/fdac/features/2000/500_gene.html. See also Marcy Darnovsky, "Protecting research subjects from a broken system," Biopolitical Times, last modified April 8, 2008, http://www.biopoliticaltimes.org/article.php?id=4009.

10 Liang et al., "CRISPR/Cas9-mediated gene editing in human tripronuclear zygotes," Protein & Cell 6, (May 2015): 363-372, published online April 18, 2015, http://link.springer.com/article/10.1007%2Fs13238-015-0153-5.

11 Antonio Regalado, "Engineering the Perfect Baby," MIT Technology Review, last modified March 5, 2015, http://www.technologyreview.com/featuredstory/535661/engineering-the-perfect-baby/.

12 "About Human Germline Gene Editing," Center for Genetics and Society, http://www.geneticsandsociety.org/article.php?id=8711.

13 Kate Kelland, "Medical specialists urge more debate on gene-editing technology," Reuters, last modified September 2, 2015, http://www.reuters.com/article/2015/09/02/us-health-genes-editing-idUSKCN0R14WH20150902. See also "Statement on Genome Editing Technologies and Human Germline Genetic Modification," The Hinxton Group, http://www.hinxtongroup.org/Hinxton2015_Statement.pdf.

14 Daniel Cressey, Alison Abbott, Heidi Ledford, "UK scientists apply for license to edit genes in human embryos," Nature, last modified September 18, 2015, http://www.nature.com/news/uk-scientists-apply-for-licence-to-edit-genes-in-human-embryos-1.18394.

15 Joe Palca, "In Hopes of Fixing Faulty Genes, One Scientist Starts with the Basics," NPR, last modified October 13, 2014, http://www.npr.org/sections/health-shots/2014/10/13/354934248/in-hopes-of-fixing-faulty-genes-one-scientist-starts-with-the-basics.