

Should We Synthesize a Human Genome?

By Drew Endy & Laurie Zoloth

10 May 2016

At Harvard today an invitation-only group of mostly scientists, lawyers, and entrepreneurs, ~150 in total, met to discuss if and how to synthesize from scratch an entire human genome – the heritable genetic material that in nature is transferred from parents to children. The meeting was originally organized to focus on “deliverables and industry involvement” with the primary goal of the project being “to synthesize a complete human genome in a cell line within a period of ten years.”

Synthesis refers to the construction of a genome starting from simple chemicals. Such a synthetic genome could then be tested in a laboratory by replacing the existing genome within a human cell. All this would still be far removed from making a synthetic human. However, the possibility of making a human cell whose genome is realized from only digital information and raw materials should trigger broader considerations.

For context, total synthesis of a human genome has become plausible at an accelerating rate. Thanks to new production techniques developed since 2003 the cost of assembling the genetic material encoding genes, the “building blocks” of life, has decreased from four dollars to just three cents per individual letter or “base pair” of deoxyribonucleic acid (DNA). As a result, the estimated initial cost of printing the DNA fragments encoding a 3 billion base pair human genome has dropped from \$12 billion to \$90 million. If cost reductions continue apace this price would approach \$100,000 within 20 years. However, such dramatic additional cost reductions might never be realized without overwhelming demand.

Advocates of synthesizing a human genome therefore argue that some open, collaborative “grand challenge” is needed to drive development of such technologies. While we strongly agree that sustained improvements in DNA construction tools are essential for advancing basic biological science and improving public health we are skeptical that synthesizing a human genome is an appropriate demand driver. We recall how controversies associated with many of the earliest genome synthesis projects produced unintended consequences. For example, a project that made polio virus from scratch in 2002 led to cancelled public funding for DNA synthesis research, unwittingly hindering research across diverse and unrelated fields, as policy makers struggled to imagine how such a technology could ever be controlled. From a simple technical perspective, we argue that synthesis of less-controversial and more-immediately useful genomes and also greatly improved sub-genomic synthesis capacities (e.g., real-time plasmid printing) should be pursued; alternatives that would deliver broad and diverse benefits.

Other topics on today’s agenda included changing the human genome itself. For example, could scientists synthesize a modified human genome that is resistant to all natural viruses? They likely could, for purely beneficial purposes, but what if others then sought

to synthesize modified viruses that overcame such resistance? Might doing so start a genome engineering arms race? And, what of even greater changes that can be imagined? In a world where human reproduction has already become a competitive marketplace, with eggs, sperm and embryos carrying a price, it is straightforward to brainstorm various uses of human genome synthesis capacities. For example, would it be OK to sequence and then synthesize Einstein's genome? If so how many Einstein genomes would it be OK to make and install in cells, and who would get to make and control these cells? What if the project was a joint collaboration between Israel and Iran?

Returning to our primary question, just because something becomes possible, how should we determine if it is ethical to proceed?

Given that human genome synthesis is a technology that could be used to completely redefine the core of what now joins all of humanity together as a species, we argue that discussions of making such capacities real, like today's Harvard conference, should not take place without open and advance consideration of whether and under what circumstances it is morally right to proceed. When the first actors at the table mostly have a significant material interest in proceeding, everyone, not just those in the room, risks out-of-control competition between public and private interests, ethical conflicts of interest, and temptations to manipulate human subject consent. Pluralistic, public, and deliberative discussions are instead the best appropriate way to frame paths forward.

In closing, we note that the narrative of creation of the human is the central narrative for many religious communities. To create a human genome from scratch would be an enormous moral gesture whose consequences should not be framed initially on the advice of lawyers and regulators alone. The perspectives of others including self-identified theologians, philosophers, and ethicists from a variety of traditions should be sought out from the very beginning. Critical voices representing civil society, who have long been skeptical of synthetic biology's claims, should also be included. The creation of new human life is one of the last human-associated processes that has not yet been industrialized or fully commodified. It remains an act of faith, joy, and hope. Discussions to synthesize, for the first time, a human genome should not occur in closed rooms.

Drew Endy, Associate Professor of Bioengineering at Stanford University and President of the BioBricks Foundation, is the author of "Synthetic Aesthetics: Investigating Synthetic Biology's Designs on Nature" and co-founder of Gen9, Inc., a DNA construction company. Laurie Zoloth, Professor of Religious Studies, Bioethics, and Medical Humanities is the past president of both the American Academy of Religion and the American Society for Bioethics and Humanities.

endy@stanford.edu

lzoloth@northwestern.edu