Top scientists hold closed meeting to discuss building a human genome from scratch

WENDY MAEDA/THE BOSTON GLOBE

George Church, professor at Harvard Medical School, was one of the organizers of a meeting on synthetic genomes.

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Over 130 scientists, lawyers, entrepreneurs, and government officials from five continents gathered at Harvard this week for an "exploratory" meeting to discuss the topic of creating genomes from scratch — including, but not limited to, those of humans, said George Church, Harvard geneticist and co-organizer of the meeting.
The meeting was closed to the press, which drew the ire of prominent academics.

Synthesizing genomes involves building them from the ground up — chemically combining molecules to create DNA. Similar work by Craig Venter in 2010 created what was hailed as the first synthetic cell, a bacterium with a comparatively small genome.

The meeting was held Tuesday "to discuss the concept of an international project focused on large genome synthesis as the next chapter in our understanding of the blueprint of life," according to a consensus statement from the organizers provided by Church.

In recent months, Church has been vocal in saying that the much-hyped genome-editing technology called CRISPR, which is only a few years old and which he helped develop, would soon be obsolete. Instead of changing existing genomes through CRISPR, Church has said, scientists could build exactly the genomes they want from scratch, by stringing together off-the-shelf DNA letters.

The topic is a heavy one, touching on fundamental philosophical questions of meaning and being. If we can build a synthetic genome — and eventually, a creature — from the ground up, then what does it mean to be human?

"This idea is an enormous step for the human species, and it shouldn't be discussed only behind closed doors," said Laurie Zoloth, a professor of religious studies, bioethics, and medical humanities

at Northwestern University.

In response, she co-authored an article with Drew Endy, a bioengineering professor at Stanford University, calling for broader conversations around the research.

Church said that the meeting was originally going to be "an open meeting with lots of journalists engaged." It was supposed to be accompanied by a peer-reviewed article on the topic. But, he said, the journal (which Church declined to identify) wanted the paper to include more information about the ethical, social, and legal components of synthesizing genomes — things that were discussed at the meeting.

So Church and the other organizers were in a bind — should they keep the meeting open to the public and break the embargo, or close the meeting so as not to break the embargo of the scientific journal.

"This is a major journal," Church said. "So we can't push them around."

They chose to respect the embargo.

"I'm not sure that was the best idea," Church said Thursday night.

Church said that when the article is published — "it could be any day now" — a video of the entire meeting will be available to the public.

But a different narrative appeared during the week on social media. Endyposted a tweet that included a screenshot appearing to be a message from the meeting organizers. It said, in part, "We intentionally did not invite the media, because we want everyone to speak freely and candidly without concerns about being misquoted or misinterpreted as the discussions evolve."

Endy could not be reached for comment Thursday night.

Should we synthesise a human genome?

As specialists gather in private to discuss a grand plan for constructing a human genome, Drew Endy and Laurie Zoloth argue that such an enormous moral gesture should not be discussed behind closed doors.

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At Harvard today, an invitation-only group of about 150 scientists, lawyers, and entrepreneurs, met to discuss if and how to construct from scratch an entire human genome – the heritable genetic material that in nature is transferred from parents to children.

The meeting was originally organised to focus on "deliverables and industry involvement" with the primary goal of the project being "to synthesise a complete human genome in a cell line within a period of 10 years".

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 realised from only digital information and raw materials, should trigger broader considerations.

For context, total synthesis of a human genome is becoming 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 $4.00 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 three billion base pair human genome has dropped from $12 billion to $90 million.

If cost reductions continue in the way they have been, then this price would approach $100,000 within 20 years. However, such dramatic additional cost reductions might never be realised without an overwhelming demand.

Advocates of synthesising 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 sceptical that synthesising a human genome is an appropriate demand driver.

We recall how controversies associated with many of the earliest genome synthesis projects delivered unintended consequences.

For example, a project that made polio virus from scratch in 2002 generated such fear that public funding for improving DNA synthesis tools was cancelled, unwittingly harming research across diverse and unrelated fields while policy makers struggled to imagine how such tools could ever be controlled.

We argue that the synthesis of less controversial and more immediately useful genomes along with greatly improved sub-genomic synthesis capacities (for example, the real-time printing of plasmids the casettes that transfer genes between cells) should be pursued instead.

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up far stranger uses of human genome synthesis.

These are alternatives that would deliver broad and diverse public benefits.

Other topics on today's agenda included changing the human genome itself. For example, could scientists synthesise 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 synthesise 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 easy to make up far stranger uses of human genome synthesis capacities.

Would it be OK, for example, to sequence and then synthesise Einstein's genome? If so how many Einstein genomes should be made and installed in cells, and who would get to make them?

Taking a step back, just because something becomes possible, how should we approach determining if it is ethical to pursue?

Given that human genome synthesis is a technology that can 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 it is morally right to proceed.

When the first people at the table mostly have significant and direct material interests in proceeding, everyone, not just those in the room, risk 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.

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 sceptical 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 industrialised or fully commodified. It remains an act of faith, joy, and hope.

Discussions to synthesise, for the first time, a human genome should not occur in closed rooms.

Drew Endy is Associate Professor of Bioengineering at Stanford University.

Laurie Zoloth is a professor of medical ethics and humanities at Northwestern University, Chicago.