What is synthetic biology and why care about it?

It's happening right now. Many scientists, technology-enthusiasts, and corporations hope to *create novel life forms*. They seek to move from evolution through natural selection into a moment of ever more human-conceived and designed life.

Combining life sciences, computer science, and engineering, an entire field sometimes called "synthetic biology" is developing. It uses a suite of powerful techniques with names like "CRISPR." As with many new technologies, governments have failed to keep pace. The public doesn't provide input into the far-reaching decisions companies make. There's limited regulation.

Canadian Friends Service Committee is the peace and social justice agency of Quakers in Canada. Grounded in our values of peace, integrity, equality, simplicity, and respect for all creation, we are led to respond to synthetic biology. We are particularly interested in the social, ethical, and spiritual implications, which go well beyond the technology itself. See an overview of our hopes and concerns at https://quakerservice.ca/SBIssues

CFSC's specific mandate is listed in the Appendix. It includes sharing easily accessible updates about synthetic biology to raise public awareness. Find out more at https://quakerservice.ca/SyntheticBiology

Please share any thoughts or feedback (however brief or detailed)**:** matt@quakerservice.ca

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Editing Humans

"Human-focused biotech and persuasion form a single system: for the biotech to be adopted, the public has to accept it first."[1]

Harvard Professor George Church holds up a molecular model. CC-BY Steve Jurvetson

For years George Church has earned tremendous amounts of attention for synthetic biology. Media latched on to talk of "de-extincting" the wholly mammoth and whipped it up into grossly exaggerated articles promising far more than Church's research does (see https://quakerservice.ca/SBUpdate2017 for more on that).

But earlier this year Chinese scientist He Jiankui may have surpassed Church to become the most famous synthetic biologist on the planet, although not in the way He seems to have expected.

The sudden uproar happened when He claimed to have edited the DNA of twin baby girls who had already been born by the time an announcement about this human experimentation was made.

Before his data was published He used a PR firm to release a series of YouTube videos seeking to cast his research in a positive light. Yet the general reaction was anything but positive. Oxford professor Julian Savulescu called He's work "monstrous."[2] Xu Nanping, vice minister of the Chinese Ministry of Science and Technology, said it was "extremely abominable in nature."[3]

Most scientists were negative, but much more reserved. Meagan Lizarazo, Executive Vice President of the International Genetically Engineered Machines (iGEM) competition (iGEM seeks to make synthetic biology fun by pitting teams of students against each other to create original synthetic organisms), said:

> *We are stunned and disappointed by Dr. He's actions, particularly as a former iGEM team leader. Conducting human genome engineering — and further, doing so without proper research or backing from the broader scientific community — is a clear violation of iGEM's standards as well as those of the scientific community at large. Had this project been proposed within the iGEM competition, it would have been disqualified for violating iGEM's policies.*[4]

One of the few people who came to He's defence was Church, who brushed aside concerns, saying in an interview, "As long as these are normal, healthy kids it's going to be fine for the field and the family," while admitting that there was no medical benefit to the children from He's experiment.[5]

The fact that CRISPR causes off-target effects (such as removing unintended sections of DNA) has been documented in various studies.[6] Will this impact the girls' health in the future? Some scientists, like Church, feel that it won't. Others are more cautious. Two studies published in 2018 raised the possibility that CRISPR editing might even cause cancer.[7] We simply don't have the experience or data to know what will happen to the twins, nor their offspring.

Tests in mice suggest the edit (to delete a gene called CCR5) may have altered the twins' brains in unpredictable ways. (Some speculate it could wind up enhancing their cognitive abilities.)[8] It also appears, from a presentation He gave, that his use of CRISPR failed to make even his *intended* edits, as both twins seem to still have some normal copies of the CCR5 gene. The girls' parents would have had to know about all of these risks and unknowns in order to provide meaningful consent for the experiment, and reports suggest that they were not properly informed.[9]

American synthetic biologist Michael Deem was listed with He as one of the authors on a paper about the experiment. (The paper was submitted to *Nature* in late November, 2018 but was rejected due to ethical concerns.) Reports suggest that Deem was present when the parents gave their consent to participate in the study, and that his credentials as a respected figure at a prominent US college may have helped persuade the parents that the experiment was safe.

Deem's lawyers have denied that he was present in China to talk to the parents, but this contradicts an earlier quote from Deem, published by the Associated Press. What exactly Deem's involvement was, and whether or not he broke any US laws by failing to bring his part in the experiment to a Rice University ethics committee, remains to be determined.[10]

In a statement following an internal investigation, the Southern University of Science and Technology said that He had been fired, and confirmed earlier reports that the experiment was done in secret and without proper authorization or ethics reviews.[11] A parallel investigation by the Chinese government concluded that He had intentionally evaded oversight and had forged ethics papers. Chinese officials stated that He would be punished.[12] Disturbingly, reports have circulated stating that if found guilty of corruption or bribery, He would face a maximum sentence of the death penalty.[13]

Although He kept most people and authorities in the dark, he did seek guidance from multiple scientists. To most he spoke theoretically, but some, like Craig Mello of the University of Massachusetts, were aware of He's having already proceeded with human experimentation. Mello said in an email to He, "You are risking the health of the child you are editing ... I just don't see why you are doing this." But he continued to serve as an adviser to He's synthetic biology company, and did not make his concerns about the experiment public.[14]

While He was, so far as we know, the first to edit human babies, prior to this, several studies in China had edited the DNA of adults, as we've previously reported.[15] Troublingly, a recent article states that researchers *are not tracking the long-term health of these experiment participants* and have lost touch with them![16]

Regulating human editing

Canadian Friends Service Committee made a statement about He's human experimentation that read in part:

> *He Jiankui's work demonstrates that individuals can circumvent the weak processes and often voluntary guidelines in place and make far-reaching decisions about their synthetic biology work. This is dangerous. We are deeply concerned about the potential grave and unknown harms that even well-meaning researchers could cause, and we call again for a renewed focus on* precaution.[17]

We also joined hundreds of organizations and individual academics in signing a joint statement to the organizers of an important conference, the Second International Summit on Human Genome Editing.[18]

> *The undersigned individuals and organizations wish to express our dismay and outrage at He Jiankui's claims of creating genetically engineered babies. ...His actions violate a key provision of the concluding statement issued at the First International Summit on Human Gene Editing in 2015, that such dangerous experiments should not proceed until there was broad societal consensus in their favor.*
>
> *That statement was intended to reassure civil society that the scientific community could regulate itself and prevent such reckless behavior. If the organizers of this week's summit in Hong Kong wish to demonstrate that science is not out of control, and is worthy of public trust, now is the time for them and the rest of the international scientific community to act.*
>
> *We urge that they (1) condemn in clear terms the rogue actions of the researcher who has taken it on himself to make a hugely consequential decision that affects all of us; and (2) call on governments and the United Nations to establish enforceable moratoria prohibiting reproductive experiments with human genetic engineering.*
>
> *Such policies are necessary in order to ensure that we do not get into a run away international competition for primacy in reproductive genetic engineering, leading to a new form of eugenics. If the summit and other scientific bodies do not act, it will fall to civil society and policy makers to do so, in order to ensure the avoidance of disastrous consequences for global society.*

The Summit did condemn He's research, but did not call for governments or the UN to establish enforceable moratoria.[19] So far most of the scientists who expressed deep concerns about He's experiment seem to have kept silent about improving regulations. An editorial in *Nature* proposed better information sharing via "a global registry (or national registries) set up by funders or governments to record preclinical research that involves gene editing in human embryos."[20] Two prominent US Academies are preparing an international commission on the topic of human genetic engineering, with Britain and China having already indicated they will participate.

There are many issues to deal with. For instance, one "key question, virtually unaddressed in the many CRISPR discussions and reports and white papers so far, is what specific scientific tests must be done to determine whether edits made in a human embryo are 'safe.'"[21]

At CFSC, we feel that robust discussions involving people with diverse perspectives and expertise are urgently needed.[22] There also needs to be an international legal framework with consistent and enforceable rules. This will be a *major* challenge, given the powers of biotech lobby groups seeking to prevent or limit regulation, and the fact that CRISPR is inexpensive and readily accessible.

Mindsets: broad vs narrow, ethical vs unrestricted, holistic vs reductionistic

We recognize the potential for great benefits from synthetic biology, but remain deeply concerned by how research and commercialization are currently unfolding. A dangerously narrow mindset that doesn't consider broader ecological or social impacts, that seeks to control and dominate life, and that has given rise to many horrors including eugenics (the idea "that science should be used to control human reproduction in order to breed preferred types of people"[23]), remains all too present.

What has, until recently, been the stuff of science-fiction – the dangers of babies having their heritable traits edited, being designed to be stronger, prettier, or more obedient – could one day become reality. We emphasise *could*, because at CFSC we don't believe in technological determinism. Societies have successfully curtailed the use of technologies, and if there is a will, that could happen here.

Also this field suffers from a great deal of exaggeration about precision. Some scientists offer the metaphor of the cell being a machine, with readily changeable parts. But this may distort and understate the complex interactions within the cell.

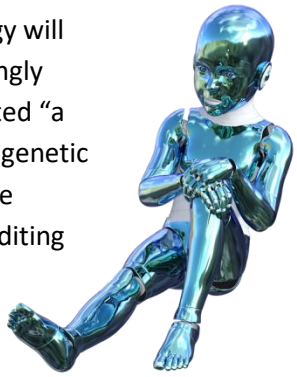
We might think we understand a gene in isolation, but genes don't exist in isolation. Studies in yeast suggest that almost all of the genes may be necessary to keep the cell alive, and researchers admit to being baffled by many of the interactions among these yeast genes: "…it's not random. We just don't understand how the cell is connected." Some scientists argue that such research is relevant to humans, where "a wide array of genes may be subtly influencing traits that we don't normally associate with them."[24]

So exactly how genes function and interact with each other remains a complex and poorly-understood topic. One theory proposes that, for some traits at least, *tens of thousands of genes* may each be contributing small effects.[25] Also, our environments and life experiences may have their own very

significant impacts on the expression of our genes.[26] These and other issues mean that exactly what is technically feasible in engineering humans is very unclear and may be much less predictable than some are assuming.

What might the future hold?

What we *have* already seen – apparently-successful research into creating animals like dogs and horses that are stronger and faster than usual[27] – suggests that the chances are high that some parents may seek out these types of edits for their children. Some folks are already looking to move forward with further human experimentation. (Undesirable, unexpected effects have also been found in gene edited animals, such as pigs that grew extra vertebrae, cattle that died prematurely, and rabbits that grew enlarged tongues.[28])



Do-It-Yourself biohackers Bryan Bishop and Max Berry believe that technology will continually speed up the slow process of evolution and give humans increasingly incredible powers (a belief called "transhumanism"). They claim they've started "a company focused on the production of designer babies and human germline genetic engineering." The pair say their company already has "an initial parent-couple customer" but are just beginning animal trials and remain years away from editing human babies. Some suggest that the science behind these claims is unsound, and wonder if the pair are really just trying to get attention (and possibly raise money) by being so provocative.[29]

The use of synthetic biology in humans plays out as artificial intelligence and big data make dramatic advances. "AI is increasingly used to map and measure our biological functions. Most corporate AI platforms already have access to our online behaviour, relationships, health and emotional states – but, increasingly, they will acquire baseline information about our vital signs, organs and genomes."[30] This raises all sorts of serious concerns about dystopian systems of control and manipulation.

All this makes one thing starkly clear: our current weak regulations embolden reckless human experimentation, creating the potential for many gravely disturbing scenarios. This will continue until strong and enforceable regulations are in place.

Gene drives

While editing humans has long been the stuff of science fiction, one application of gene editing may be so powerful that most of us never would have *imagined* it. It's called a "gene drive" and in theory it could force an engineered trait through an entire population *in the wild*. Needless to say, this continues to be a major topic of debate. (See https://quakerservice.ca/SB2018 for more background on gene drives.)

Sharm El Sheikh, Egypt, was the site of important debates about regulating gene drives. CC-BY Marc Ryckaert

When parties to the UN Convention on Biological Diversity met in Egypt in November 2018 the regulation of gene drives was a contentious topic. Civil society called for a moratorium on gene drive research until sufficient regulation is in place, but in the end that call was unsuccessful. The 196 countries present did agree to stronger rules about the use of gene drives, including ensuring the free, prior and informed consent of any affected Indigenous peoples or local communities.

The agreement calls for case-by-case risk assessment and for risk management procedures to be put in place. But as we've previously discussed, in the case of new uses of synthetic biology we're dealing not only with *risks* (a term for those which have been observed and are already well known) but also with *ambiguity* about how to define and measure the extent of potential impacts, and *uncertainty* about what may happen. There are also many *unknowns* (we don't know what we don't know) in terms of possible effects on ecosystems, social impacts, or even how gene drives could undermine the ways we think about life, making it seem more disposable.

Gene drive research has been conducted for the first time in the lab in mammals (mice). The success rate suggests that releasing a gene drive into wild populations of mammals would be ineffective. "It would take many generations for the gene drive to spread through an entire rodent population, leaving ample time for species to evolve resistance."[31] But research continues, with stated goals ranging from one day eradicating invasive species to ending Lyme disease.

Target Malaria says it's trying to crash mosquito populations through gene drives. It secured permission to release genetically modified (but not gene drive) mosquitoes in two villages in Burkina Faso as an early test. The study is paying villagers small amounts to be bitten by mosquitoes (it also promises to pay for their treatment if they get malaria).[32] Some in the community are supportive of these tests, but others have unaddressed concerns. Activists protested Target Malaria's activities and released a short documentary that calls into question the claim of working closely with affected communities and obtaining their free, prior and informed consent.

A Question of Consent: Exterminator Mosquitoes in Burkina Faso

https://www.youtube.com/watch?v=nD_1noCf2x8&feature=youtu.be

Last year tests releasing millions of (non-gene drive) genetically modified mosquitoes in Grand Cayman apparently failed to produce the intended reduction in mosquito populations.[33] But there may be viable alternatives to these approaches. Last summer Paraguay was certified malaria-free. The South American nation pursued successful policies including building front-line health workers' skills and ensuring universal free malaria treatment. The Director General of the World Health Organization said, "Success stories like Paraguay's show what is possible. If malaria can be eliminated in one country, it can be eliminated in all countries."[34]

Bioweapons

We've previously reported on how gene drives could be used as potent bioweapons.[35] But there may be much simpler uses for synthetic biology that are also incredibly deadly. Researchers at the University of Alberta created horsepox (a virus related to the extinct smallpox) from scratch "by stitching together fragments of mail-order DNA in just six months for about $100,000." Alarmingly, when the research was published it also included details on how to repeat it. This suggests that many labs would today be able to synthesize a very potent virus relatively easily. Reportedly the research team alerted Canadian authorities to the nature of their work and none raised any objections.[36]

The US military remains a major funder of synthetic biology research, with interests such as engineering marine bacteria to react in detectable ways "for the purpose of tracking enemy submarines." Air Force research scientist Claretta Sullivan says, "Our team is looking at ways we can reprogram cells that already exist in the environment to create environmentally friendly platforms for generating molecules

and materials beneficial for defence needs." Other examples of military research include attempts to create "living camouflage."[37]

Skin products

A start up company says it will use synthetic biology to design yeast that excretes a chemical called gadusol, which various animals produce as natural "sunscreen." The company hopes to start trials of this new synthetic biology sunscreen soon.[38] This is far from the only synthetic biology product we may soon or already be rubbing on our skin. In another case, an edited silkworm is creating "human collagen" which is already being used in commercial skincare products.[39]

Patents

One promise of synthetic biology is increased control of life. But who will have that control? A study done in June 2018 suggests that it could be a small handful of companies in just a few countries. For instance, the study found that a single company, BASF, owns "half of all existing patents for genes from marine species."[40]

Clothes

A 2018 report from ETC Group and Fibershed critiques the various applications of synthetic biology in clothing, raising concerns such as that advertising is misleading, that the livelihoods of 225 million farmers may be at risk, and that engineered organisms can produce various environmental harms. Among the most jaw-dropping areas of current research, some are envisioning combining nanotechnology, 3D printing, and synthetic biology to one day have "fabrics that see, hear, sense, communicate, store and convert energy, regulate temperature, monitor health, and change color."[41] An artist has also been working with leather – made from *human skin* grown in the lab.[42]

Plants, food, science, and uncertainty

We'll wrap up with a discussion of another key area of synthetic biology research – editing plants. In late 2017 Canadian Friends Service Committee was part of the fascinating conference *Redesigning the Tree of Life: Synthetic Biology and the Future of Food*.

We had the privilege to hear not only from experts with various types of hopes and concerns and from folks tracking the regulation of synthetic biology, but also from leading synthetic biologist Drew Endy, who has a very positive vision of the field's potential, as well as his own fears. The diversity of views expressed greatly enriched the conference. (For audio and slides see: http://quakerservice.ca/SB2018)

CFSC Associate member Anne Mitchell at the *Redesigning the Tree of Life* conference, November, 2017

Unlike with editing humans, where debates often take into account certain ethical and social questions, many folks promote synthetic biology (and older GMO techniques) in food as if it were free from any ethical issues and urgently necessary to save humanity. This line of thought often holds that all sorts of pressing problems can best be solved through editing plants at a massive scale.

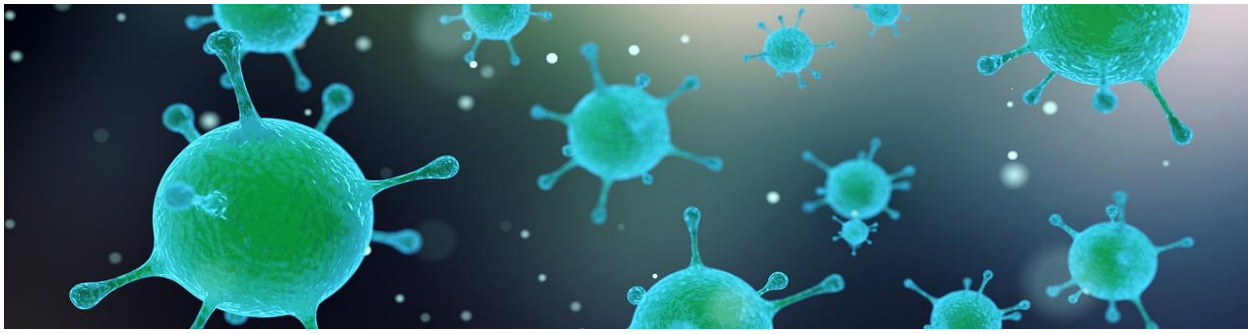
Such molecular-level thinking rarely seems to recognize the extent of the uncertainties and unknowns at play. Often, there's no acknowledgement of the role of current technologies in *creating* the problems named, or that new technologies may create new problems (predictable or unforeseen). That the problems have social, ecological, and political dimensions is also too often ignored. (Inequality, over-consumption, colonialism, and so on are not common words used in these analyses.)

There *is* some mention of the social dimension of new technologies, but that tends to be stated as a complaint that anti-science fear mongering or "fundamentalism" is impeding innovative and safe biotech.

To be sure, there *is* anti-science fear mongering out there. Yet it's troubling when the discussions get so simplistic and polarized as to suggest that either one whole-heartedly accepts synthetic biology solutions or humanity is doomed.

There can be many reasons to support or to oppose any new technology. How we consider the issues, what we choose to focus on and what we choose to ignore, makes a big difference to the decisions we later make. Some arguments against synthetic biology can be overly pessimistic and anti-science. But some arguments in favour can, even if the science behind them is sound, still lead to myths about the necessity of biotech solutions.[43] What studies get done and don't get done can also be heavily influenced by industry, which funds many research institutions and in some cases applies significant pressure on researchers to discourage them from looking into issues like health risks.[44]

A great deal of synthetic biology research is being done on foods and other editing of plants' genes.[45] A project called "Harnessing Plants for the Future" seeks to develop a "super plant that will both provide food and store carbon dioxide in its roots."[46] Some are promoting genetically engineered trees as the best/only way to conserve forests.[47] And companies are trying to use synthetic biology techniques to make crops hardier, for instance by engineering resistance to viruses. A 2018 paper suggests one possible unintended consequence of this latter approach though. The team was surprised by nature's rapid creation of a new virus through a genetic mutation.[48]



Appendix

In 2014 Canadian Yearly Meeting, the national body of Quakers in Canada, asked Canadian Friends Service Committee, the peace and social justice agency of Quakers in Canada, to work on synthetic biology in the following ways:

1. By affirming the seven principles identified in Principles for the Oversight of Synthetic Biology, a document that makes many important recommendations, and supporting attempts to implement the seven principles:
    i. Employ the precautionary principle;
    ii. Require mandatory synthetic biology-specific regulations;
    iii. Protect public health and worker safety;
    iv. Protect the environment;
    v. Guarantee the right-to-know and democratic participation;
    vi. Require corporate accountability and manufacturer liability; and
    vii. Protect economic and environmental justice.
2. By providing Canadian Quakers and the general public with an annual, easily understandable update on synthetic biology;
3. By finding opportunities to link with other faith and community groups, and with Indigenous peoples, to share insights and discernment about synthetic biology; and
4. By engaging with other faith groups and interested parties, including organizations involved in research and/or manufacture in synthetic biology, hold and/or participate in conferences that address ethical, spiritual, social, and economic aspects of synthetic biology.

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