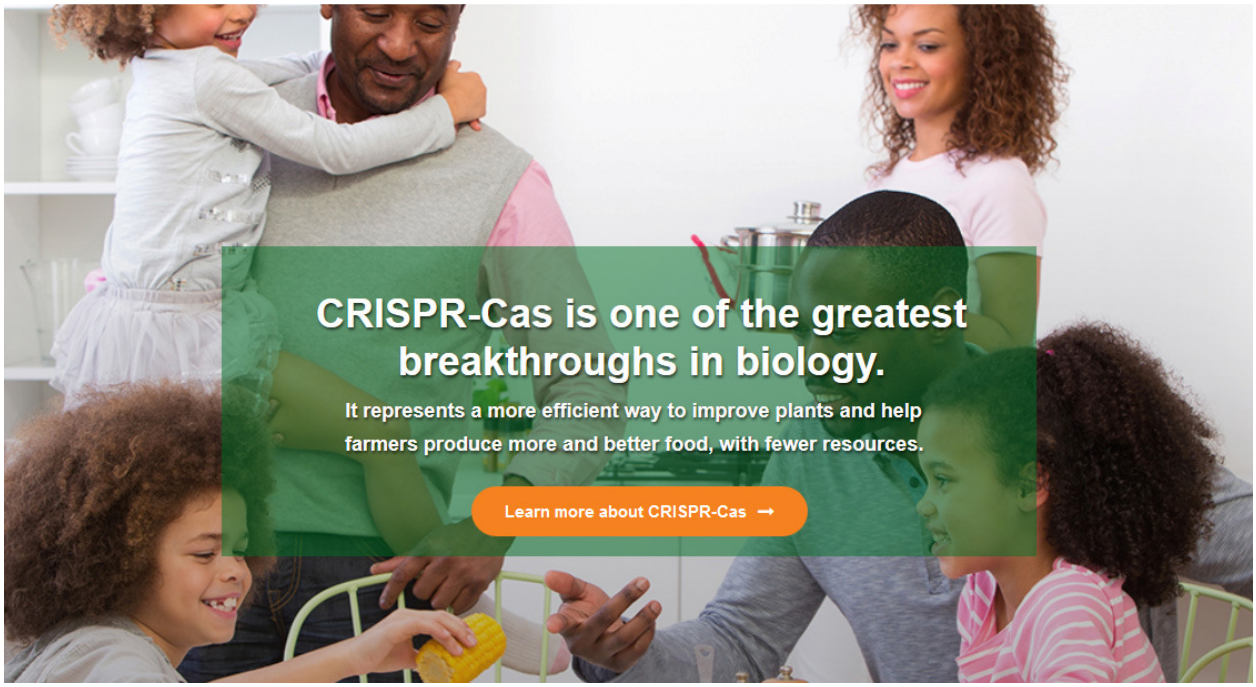
Canadian Friends Service Committee (QUAKERS)

SYNTHETIC BIOLOGY: 2018 UPDATE



Screenshot of a website made by chemical company DowDuPont to explain a key synthetic biology technique

Combining life sciences, computer science, and engineering, techniques called “synthetic biology” are developing rapidly. Many scientists and corporations hope to create increasingly novel life forms. We read claims like in the near future, “Designing genomes will be a personal thing, a new art form as creative as painting or sculpture.”[1]

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 the rapidly advancing field of synthetic biology.

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 http://quakerservice.ca/SyntheticBiology

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

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We like to offer very different perspectives at the start of each synthetic biology update. Here are two viewpoints about the ease of using synthetic biology in small labs or among do-it-yourself (DIY) hobbyists.

"I like to call it democratizing technology. It means that laboratories don't have to be particularly skilled in protein engineering, they don't have to have a lot of money to spend on this technology because it's relatively inexpensive to use, and scientists don't have to have a lot of training to do this." - Jennifer Doudna[2]

"The DIY buzz that synbio is exciting, fun, and empowers each person to tinker with life suggests that everyone has the right to play the game pretty much the way they want. That serves powerful corporate and academic interests because it means no one has much right to participate in decisions about common, enforceable rules." - Colleen Cordes[3]

A synthetic biology team at the international Genetically Engineered Machines competition. CC-BY iGEM Foundation/Justin Knight

Here are two views about gene drives (designed to force an engineered trait to be inherited by a population in the wild):

"Because gene drives rapidly spread genetic modifications through animal populations, they have the potential to alter entire species and wipe out diseases such as malaria." - *Nature* editorial on gene drives[4]

"Lab biosafety lapses in recent years such as the release of foot and mouth disease at the Pirbright Institute, the cover-up of lab-acquired human infections at Texas A&M University and subsequent scandal, and the loss (and later finding, under inadequate containment) of viable smallpox spores by the US Department of Health and Human Services more than amply demonstrates the potential for mistakes... at some of the very institutions that here endorse ramped up gene drive experiments." - Edward Hammond posting on a UN Convention on Biological Diversity online forum[5]

Intense debate continues about how powerful a gene drive could be and whether or how to proceed. Some have said that organisms in the wild will evolve resistance, so introduced genes will not continue to spread indefinitely.[6] However two recent computer models suggest that a gene drive could overcome such natural resistance. In the words of one of the researchers, if their models are correct then "if even a small number of organisms with a gene drive are released to a large wild population, it's likely that the drive element could spread within that population and to neighboring populations."[7]

At least one of the major champions of gene drives in conservation, synthetic biologist Kevin Esvelt, has now called his very public enthusiasm "an embarrassing mistake" and started urging a more cautious approach[8] (but still not calling for a moratorium on gene drive research to make time for discussion and establishing international regulations, something many, including CFSC, have called for[9]).

The key international body discussing the implications of synthetic biology gene drives that might irreversibly alter a whole species in the wild, is the UN Convention on Biological Diversity (CBD). We've participated in online forums and an expert group within the CBD, raising the need for a precautionary approach to various applications of synthetic biology, especially gene drives.

Access to information requests recently demonstrated that many scientists and some governments (including Canada), participated in the CBD in a coordinated way, with support from well-financed PR firms.[10] There's clearly a strong attempt to push powerful new technologies like gene drives ahead as quickly as possible.

We would welcome scientists and governments to be transparent about their positions on these important issues, and about the sources of those positions. Are they based in careful review of the evidence and recognition of what is known as well as what is unknown, uncertain, and ambiguous? Are they based on personal conviction? On talking points generated by public relations experts? On personal ability to financially benefit from the deployment of gene drives? Muddying these very different sources

of information makes it difficult to know who's voice we're hearing in these debates, undermining our confidence in the honesty and value of the process.

The possible conflicts of interest of many trusted scientific advisors have recently been an area of major attention. For instance of 13 advisors named to a panel to give the US government expert information about synthetic biology, nine had potential financial interests in promoting the use of synthetic biology with minimal regulation. Some of these conflicts were disclosed, while others were not.[11]

Kirsten Brown writes, "What's undoubtedly true is that money plays a significant role in science. And rarely has there been as much money at stake as with CRISPR, the nascent gene-editing technique that promises to cure everything from genetic disease to global famine by allowing researchers to easily cut and paste particular genes." Her piece explains a major controversy that played out in the summer of 2017 when a paper about off-target effects of CRISPR was published and then strongly criticized and rebutted.[12] So far the general narrative about CRISPR remains that it offers "unprecedented precision"[13] but that debate is also far from concluded.

A flurry of media attention was generated by controversial researcher Shoukhrat Mitalipov and his lab at Oregon Health and Science University (OHSU) when the team created edited human embryos with the synthetic biology technique CRISPR.

Many major news sources, like *The New York Times*, were excited about the research, calling it a "breakthrough,""a major milestone," and describing it as a success. The *Times* did note briefly the ethical questions this research raises, but did so in a way that largely minimized them.[14]

STAT News, to its credit, focused its reporting on what the research actually found. *STAT*'s coverage emphasized that the paper in question discovered something *far more limited* than the framing by the *Times* and other sources suggested. *STAT*'s piece explained that the actual finding was that creating "designer babies" may be impossible with current techniques.

The belief was previously that genes for designed traits may be readily inserted into the human genome. "In fact, the researchers found the opposite: They were unable to insert a lab-made gene.... 'This is the main finding from our study,' Mitalipov said: Embryos' natural preference for a parent's gene 'is very strong, and they won't use anything else.'"

In addition to more clearly explaining what the research findings were, the *STAT News* coverage also explained the legal framework and the ethical concerns in a more meaningful way.[15]

Are we ready for the implications of using synthetic biology techniques in humans?

The National Academies of Sciences and National Academy of Medicine in the US have given their opinion that clinical trials using synthetic biology in humans in ways where the edited genes may be passed on to future generations should be permitted.[16] Marcy Darnovsky of the Center for Genetics and Society noted, "Although [the reports' recommendations are] couched in apparently cautionary language, they actually constitute a green light for proceeding with efforts to modify the human germline — that is, to engineer the genes and traits that are passed on to future children and generations."[17]

Darnovsky called the research at OHSU "a pivotal point in the push toward genetically modified humans." She highlighted that the research is clear in its objective of marketing to fertility clinics, not sticking to the realm of scientific discovery to increase understanding. She also shared her concerns with the process the researchers used,

> A small group of scientists and closed committees have taken it upon themselves to move forward with reproductive germline modification technologies, scorning repeated calls by scientists, scholars, regulatory bodies, and civil society organizations around the world to keep this use of genetic engineering off limits. Mitalipov and his collaborators were clearly aware of the widespread calls for democratic deliberation and public engagement on this matter, but flagrantly disregarded them.[18]

Some went further. Jaydee Hanson of the International Center for Technology Assessment immediately called for the US government to develop laws prohibiting genetic engineering of humans and for funding to OHSU to be stopped until their research into human genetic engineering ceases.[19]

The Guardian's science editor Ian Sample gave his take on the debate, that "the conditions genome editing would help are rare, and our understanding of genes is still too poor for it to be widely used."[20]

But Alex Lee asked the provocative question, "What gives someone without an incurable condition such as blindness the right to stand in the way of potentially life-saving treatments?" For Lee, debate about the ethics of the OHSU research is fear mongering. "This is a good and promising breakthrough, not something to fear."[21]

David King of Human Genetics Alert expressed the opposite position - that these techniques will inevitably lead to eugenics if research like that done at OHSU is not stopped.

> [Critics of this kind of research] are regularly lumped in with religious reactionaries or anti-abortion campaigners. I am neither. If you peel away the hype, the truth is that we already have robust ways of avoiding the birth of children with [debilitating genetic] conditions, where that is appropriate, through genetic testing of embryos.... It's time we provided some critical scrutiny and stopped parroting the gospel of medical progress at all costs.[22]

Note that this research was conducted in the US, while in Canada it would have been illegal. However Françoise Baylis, Research Chair in Bioethics and Philosophy at Dalhousie University, reports that pressure is on the Canadian government to change Canadian law. The argument being put forward is that, "Canadian researchers may fall behind on the international scene."[23]

As in the debate described above, we regularly hear about synthetic biology in the context of impressive medical cures that are said to be imminent. For instance see the *Scientific American* article *Microbes with Rewired DNA Turn into Patient-Saving Drugs*.[24] A recent major international study commissioned by *The Lancet* is also worth paying attention to though. It found several pervasive and deeply troubling trends in medicine. Most strikingly, "A common tragedy in both wealthy and poor countries is the use of expensive and sometimes ineffective technology while low-cost effective interventions are neglected."[25]

Any discussion of synthetic biology in medicine might therefore raise questions like, "What effective interventions already exist?" or "What could be done to make low-tech interventions more effective instead of applying such a high-tech synthetic biology fix?" In some cases synthetic biology may make genuine sense. In other cases, it may be getting attention thanks to its newness or slick marketing, not because it is the best possible intervention.

SynBioWatch's new database of synthetic biology ingredients has over 350 entries, showing how about 75 ingredients are found across various products already on the market, like cosmetics, supplements, flavors, and fragrances.[26]
http://database.synbiowatch.org

At the end of June, Canada made a new submission about synthetic biology to the Convention on Biological Diversity. In the submission Canada revealed the state of tracking and regulation with respect to biodiversity. For instance, "No specific research, cooperation or activities have been identified by Federal Government Departments on the benefits and potential adverse effects of organisms, components or products of synthetic biology on biodiversity."

Agriculture and Agri-Food Canada recognized the potential for "Unforeseen second- and third-order impacts on biodiversity and local flora/fauna" and said that,

> The effects/impacts of an organism, component or product of synthetic biology on the organisms and species native to a particular region or ecosystem should be assessed using

> science-based criteria according to a precautionary approach, including an evaluation of any health, safety, and, where necessary, socioeconomic considerations, as per the mandate of CBD and its Protocols.[27]

It is unclear *how* Canada is applying the "precautionary approach" one of its departments suggests should be used. From what we can gather it appears that Canada reviews safety testing data submitted by industry to the relevant regulatory body, treating the products of synthetic biology as it would any non-synthetic biology product, and does not do any further follow up to monitor or evaluate the effects after approval.

As one example of why this approach to precaution seems inadequate, at least in some cases, synthetic microalgae has recently been tested in an open-air pond (in the US).[28] The civil society group Biofuelwatch issued a statement saying that "these tests in fact confirmed, that GE microalgae will almost certainly escape into the wild from open air ponds. Once escaped, these single celled organisms can become air or water borne, and disperse widely, or even globally. There is no telling what impact they will have and no way to reverse their dispersal once it occurs."[29] Even if this assessment is exaggerated, the precautionary approach would be to take seriously and plan for such possibilities, rather than to just hope for and expect the best (that synthetic biology microalgae won't spread or evolve and is essentially the same as other microalgae, for instance).

The World Anti-Doping Agency is concerned about athletes using synthetic biology to enhance their performance. The agency will be banning all gene editing techniques like CRISPR, but it's unclear that they'd have the means to test for them. This is still hypothetical as there's no proof that synthetic biology techniques can be used to improve athletic performance.[30]

The fact of it being untested hasn't stopped "biohackers" like Josiah Zayner and Brian Hanley. They believe in synthetic biology so much that they've started injecting themselves with edited DNA, for example trying to promote muscle growth. Zayner is encouraging others to follow his lead, having produced a "DIY Human CRISPR Guide," and various videos on the subject. He claims to have received messages from hundreds of people interested in self-experimentation with synthetic biology. Self-experimentation is not illegal, but US government regulators have tried to dissuade it, issuing strong warnings about the unknowns.[31]

The US Office of the Director of National Intelligence has announced a program seeking to detect if an organism has been developed using synthetic biology techniques. The project aims to create "tools and technologies that can be generalized across species to detect signatures that a biological system has been engineered."[32]

Among the many uses of synthetic biology in animals, cows are being developed that can withstand heat stress and still produce "great quality meat." Scientists are apparently developing the synthetic biology

cows in response to climate change[33] (itself contributed to by the industrial agricultural raising of cows in particular!).

Nearly every article about synthetic biology discusses the promises. A few consider the risks, and fewer still mention the unknowns or bigger issues of concern. But another angle is mentioned even less frequently - is the synthetic biology industry booming the way so many have said it will? We don't know what the future will hold, but it seems so far the industry has been over-sold. If we look at gene editing companies, they've offered a safe investment over the last two years (but haven't taken off). However when looking at the seven major synthetic biology companies trading on stock exchanges, an analyst says they're down 66% (as of November 17, 2017) from two years ago.[34]

A Chinese company claims to have used synthetic biology techniques to edit and clone dogs. A spokesperson said this could, "benefit pet owners who have formed a strong bond with their dogs. It will be too painful for them to see their dogs pass away. A cloned dog would be able to help with that."[35]

Researchers were able to encode malware into physical strands of DNA. This means that "when a gene sequencer analyzes [the DNA] the resulting data becomes a program that corrupts" the computer running the gene sequencer.[36]

Canadian Friends Service Committee was part of the fascinating conference *Redesigning the Tree of Life: Synthetic Biology and the Future of Food*. Audio and slides are now online and you will not find a more thought-provoking set of speakers about the regulatory, ethical, and spiritual implications of synthetic biology. http://quakerservice.ca/SB2018

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

APPENDIX:

Canadian Yearly Meeting of the Religious Society of Friends (Quakers) recommends that Friends work on this concern in the following ways:

1. That CYM affirm the seven principles identified in Principles for the Oversight of Synthetic Biology, a document that makes many important recommendations, and continue to work with the Biotechnology Reference Group of the Canadian Council of Churches (BRG) on discerning ways 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. That CYM request that Canadian Friends Service Committee (CFSC), with the help of concerned groups such as the ETC Group and the BRG, provide Canadian Quakers with an annual, easily understandable update on synthetic biology;
3. That CYM request CFSC, and encourage Monthly Meetings, to find opportunities to link with other faith and community groups, and with Indigenous peoples, to share insights and discernment about synthetic biology; and
4. That CYM encourage CFSC and Quaker Meetings in Canada to engage with other faith groups and interested parties, including organizations involved in research and/or manufacture in synthetic biology, to hold and/or participate in conferences that address ethical, spiritual, social, and economic aspects of synthetic biology.

http://www.quakerservice.ca/syntheticbiology

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