Aalto University
School of Chemical
Technology

Synthetic biology
(Course CHEM-E8125), spring 2023

Future and ethics

Prof. Merja Penttilä,

Genome sequencing

Profs. Shankar Balasubramanian and
David Klenerman (Univ. Cambride, UK)

Millenium prize 2020
(18.5.2021)
Next generation of sequencing
(NGS, Illumina).
1 million € by the Technology
Academy Finland (TAF).

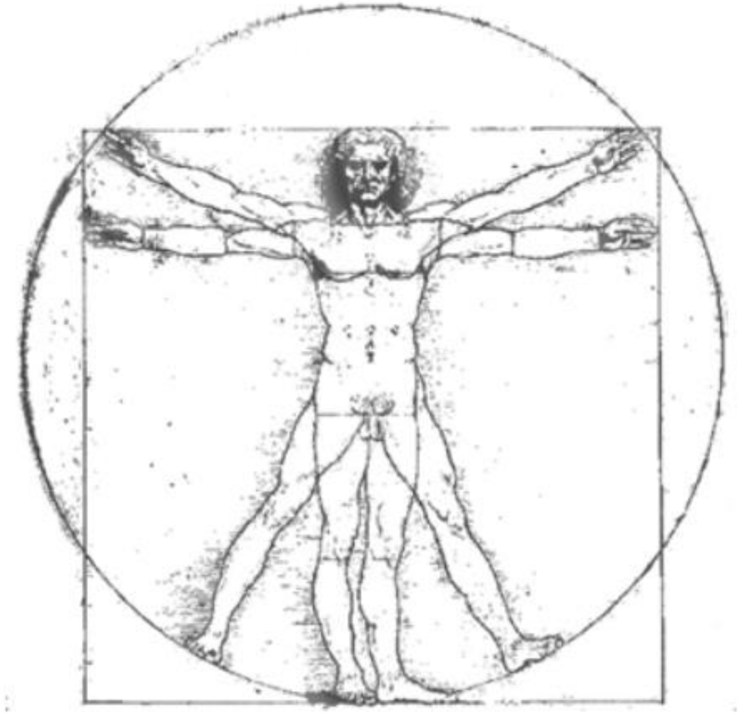
A **million-fold improvement in speed and cost** when compared to the first sequencing of the human genome. In 2000. Sequencing of one human genome took over 10 years and cost more than a billion dollars. Today, the **human genome can be sequenced in one day at a cost of $1,000** and more than a million human genomes are sequenced at scale each year.

Synthetic genomes

Synthetic human genome

- The goal is to launch GP-write project with $100 million in committed support –
  $1 billion estimate for total cost in 10 years

- Main focus in expanding DNA synthesis technologies



GP-Write project

Aims

- **Writing and building** variations on large Giga-base (Gb) **animal and plant genomes**, including the human genome
- **Understand** the **functional properties** and phenotypic consequences of the genome sequences
- Transform the quality of **DNA tools**, assembly **methods**, automated infrastructure, artificial intelligence, standards and data management systems
- Massively **reduce the cost** of writing and editing new genomes and creating DNA at scale
- **Disseminate broadly** information and knowledge generated through publicly available databases on the Internet to promote rapid application of research results
- Drive **development and commercialization** of new related technologies
- Address the **ethical, legal and social issues** that arise from the project.

- **Note:** The target is viable mammalian (human) cells, not a "human"

Synthetic human genome

The New York Times

Scientists Talk Privately About Creating a Synthetic Human Genome

The Lost Gardens of Emily Dickinson

Humans and Mastodons Coexisted in Florida, New Evidence Shows

Pfizer Blocks the Use of Its Drugs in Executions

MATTER

Climate Change and the Case of the Shrinking Red Knots

SCIENCE

Scientists Talk Privately About Creating a Synthetic Human Genome

By ANDREW POLLACK MAY 13, 2016

Sixty trays can contain the entire human genome as 23,040 different fragments of cloned DNA.

James King-Holmes/Science Source

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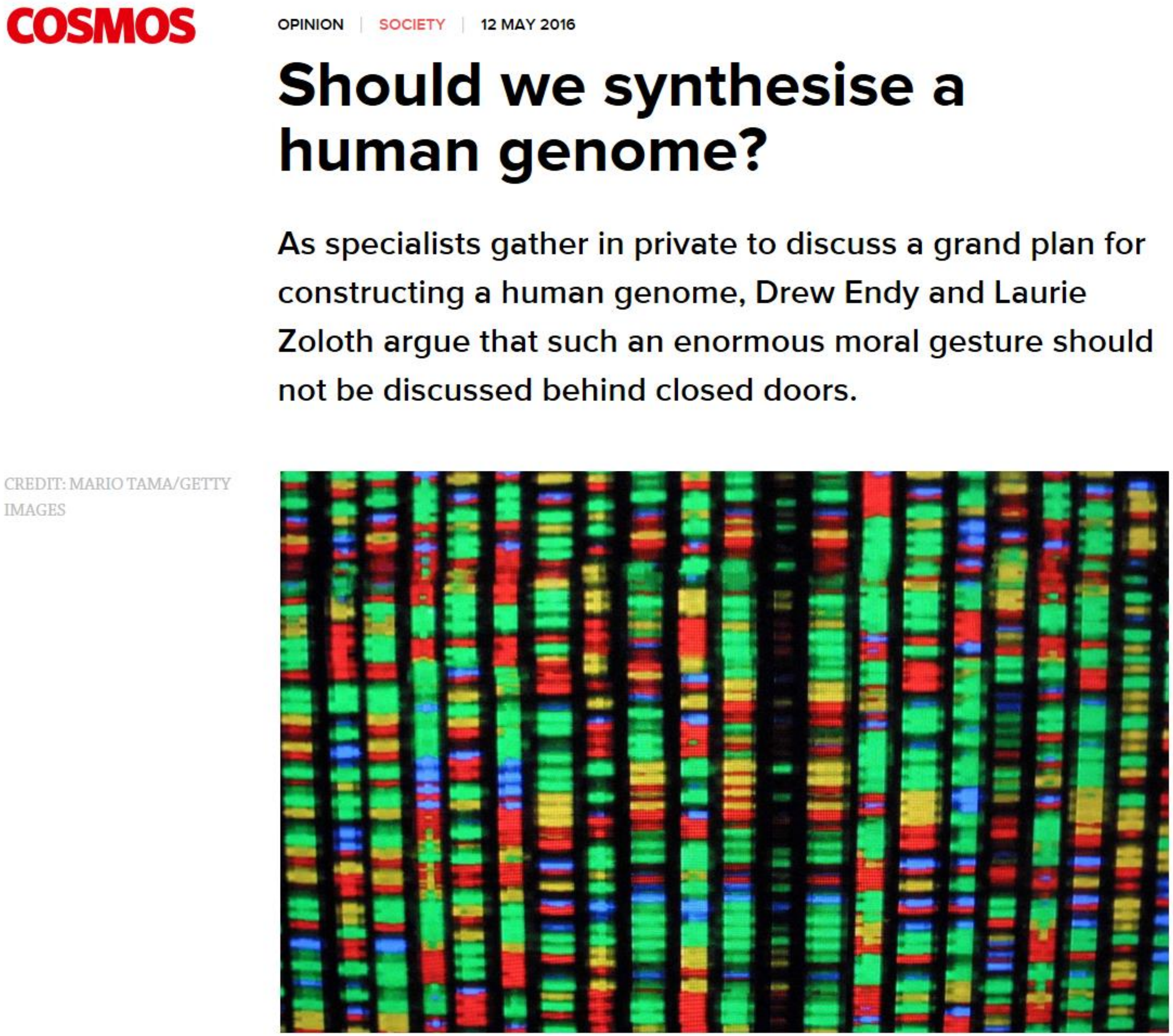


COSMOS

OPINION | SOCIETY | 12 MAY 2016

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.

CREDIT: MARIO TAMA/GETTY IMAGES

Synthetic human/animal genome - Critique

- Not feasible and not the most urgent thing to achieve
- The estimated initial cost of making the 3000 Mbp DNA human genome has dropped from $12 billion to $90 million.
- Who funds the project? NIH initially not positive.
- Religious criticism for scientists playing God.
- Who owns the synthetic genome and who could profit from it?
- Who’s genome to be synthesized (functionality)?

Research moves on, anyways

GP-Write project - Subproject

Virus proof mammalian cells

- Replacement of redundant codons in all genes, removal of corresponding tRNA genes.
- Viruses cannot not proliferate. Recoded cells would be immune.
- Ultrasafe cell line needs at least 400 000 changes, from all 20,000 genes
- 10 years' project.

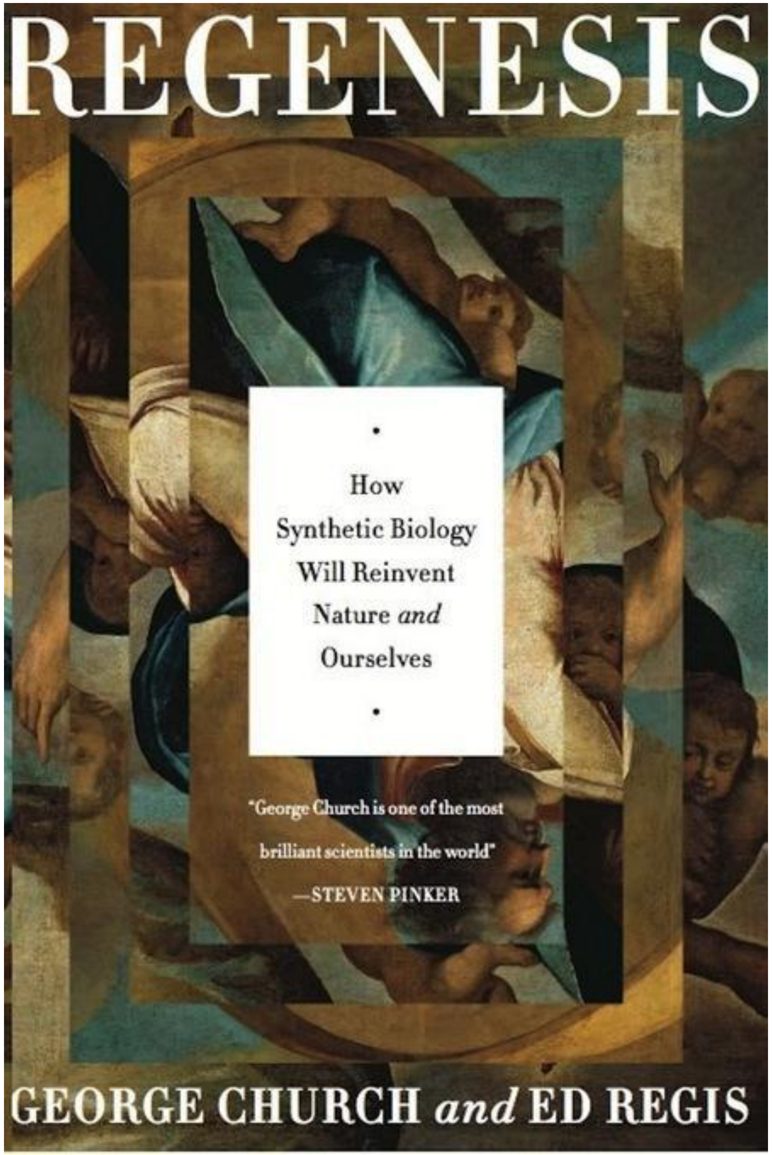
Virus proof *E.coli*

- G. Church removing 6 more codons, total of 62 000 changes in the *E.coli* genome.

Useful efforts to make virus-free cells that can be used for human medicine production. No viral contamination.

Engineeringbiologycenter.org

What about other animals?



REGENESIS

How Synthetic Biology Will Reinvent Nature *and* Ourselves

"George Church is one of the most brilliant scientists in the world"
—STEVEN PINKER

GEORGE CHURCH *and* ED REGIS

Gene-editing record smashed in pigs

Researchers modify more than 60 genes in effort to enable organ transplants into humans.

Sara Reardon

06 October 2015 *NATURE* | NEWS

Geneticist George Church has co-founded a company that is developing genetically modified pigs to grow organs for human transplant

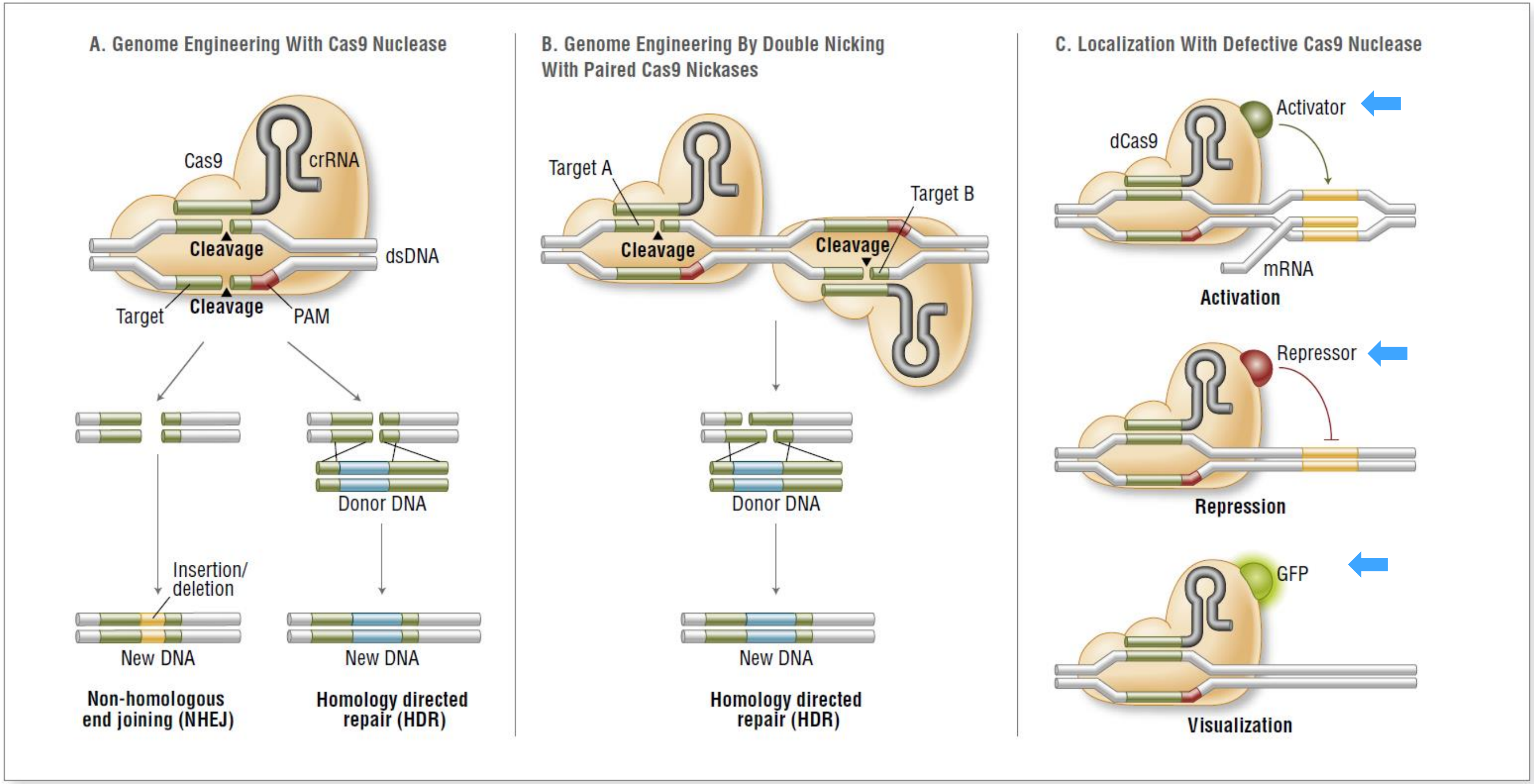
From a synthetic bacterium to synthetic mammals…. How does this differ from classical breeding?

Mammoth revival, mammophants? Recently extinct butterflies?

Is it OK to "rebuild" living organisms (vs. storing in data banks). Species have been stored as bits in genomic databanks.

CRISPR
A very powerful technology

CRISPR/Cas9 genome engineering



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NEB on-line

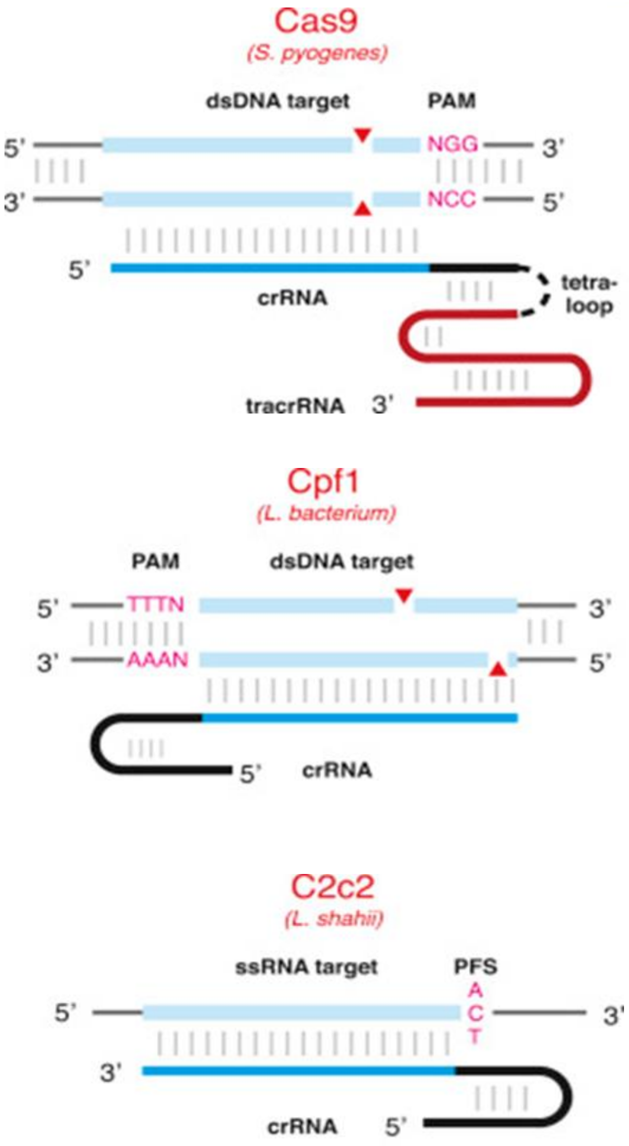
Alternative gene editing enzymes

Cas9
- Cas9 makes "blunt" cuts
- ~100 nucleotide gRNA
- Cut upstream of PAM

Cpf1
- Only a 42-nt short CRISPR RNA (crRNA)
- Cpf1 cleaves in a staggered fashion (directional gene transfer)
- Cut downstream of PAM
- Low off-target editing rates

C2c2
- RNA-guided RNA cleavage
- Single guide RNA

***Natronobacterium gregoryi* Argonaute (NgAgo):**
- Single strand DNA-guided endonuclease
- Creates site-specific DNA double-strand breaks
- Does not require a protospacer-adjacent motif (PAM)
- Findings disputed and paper retracted



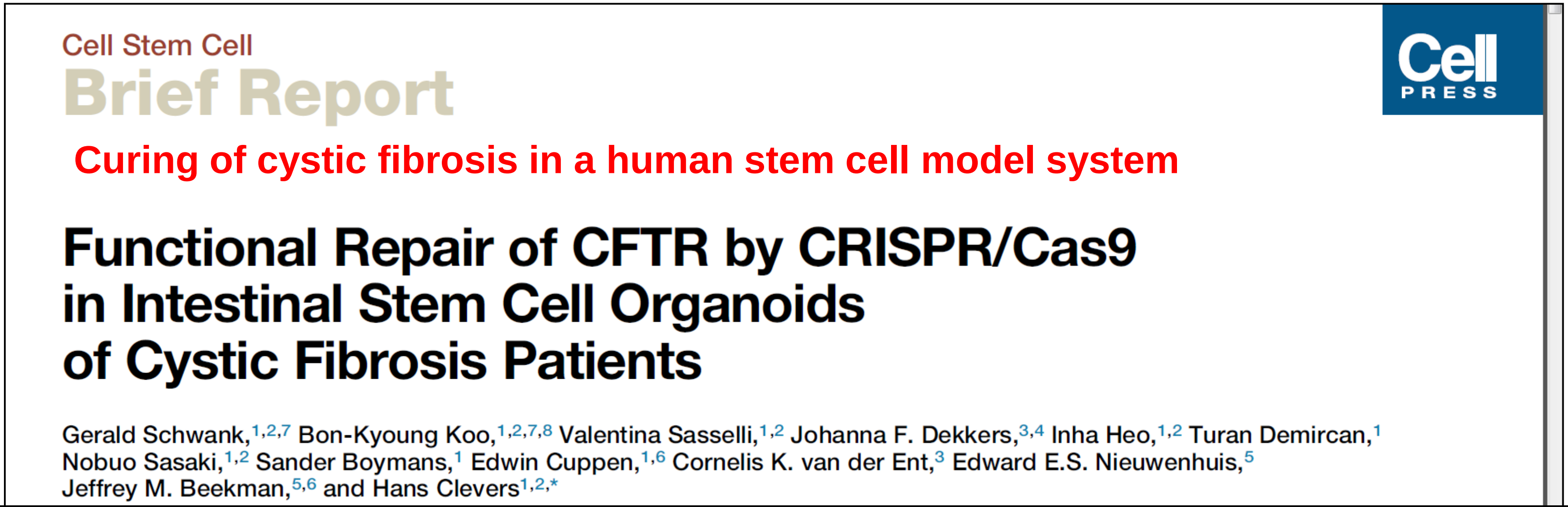
Ann Ran, Analytical Biochemistry, 2016

CRISPR regulation

- In the future: Any cultivable and transformable microbe will become engineerable? (genome sequence and growth conditions known)
- GMO legistlation even on transiently transformed strains where no foreign DNA is left behind (self cloning)?
- EU took a stand in 2018. CRISPR considered as GMO. Complaints being made. Discussions ongoing in 20212023.
- Some countries such as Netherlands and Sweden have made the decision that regardles of the method, organisms where no foreign DNA is left behind are not considered GMO. This decision is conditional to the EU level decision.

CRISPR concerns

- Robust wild type strains with genetic modifications escape to nature (intentionally or unintentionally) (in contrast to laboratory strains that typically contain a large number of compromising mutations)
- Infection of humans or e.g. cattle or crops
- Effects on biological diversity
- Legistlation has challenges to keep in the pace with technology developments



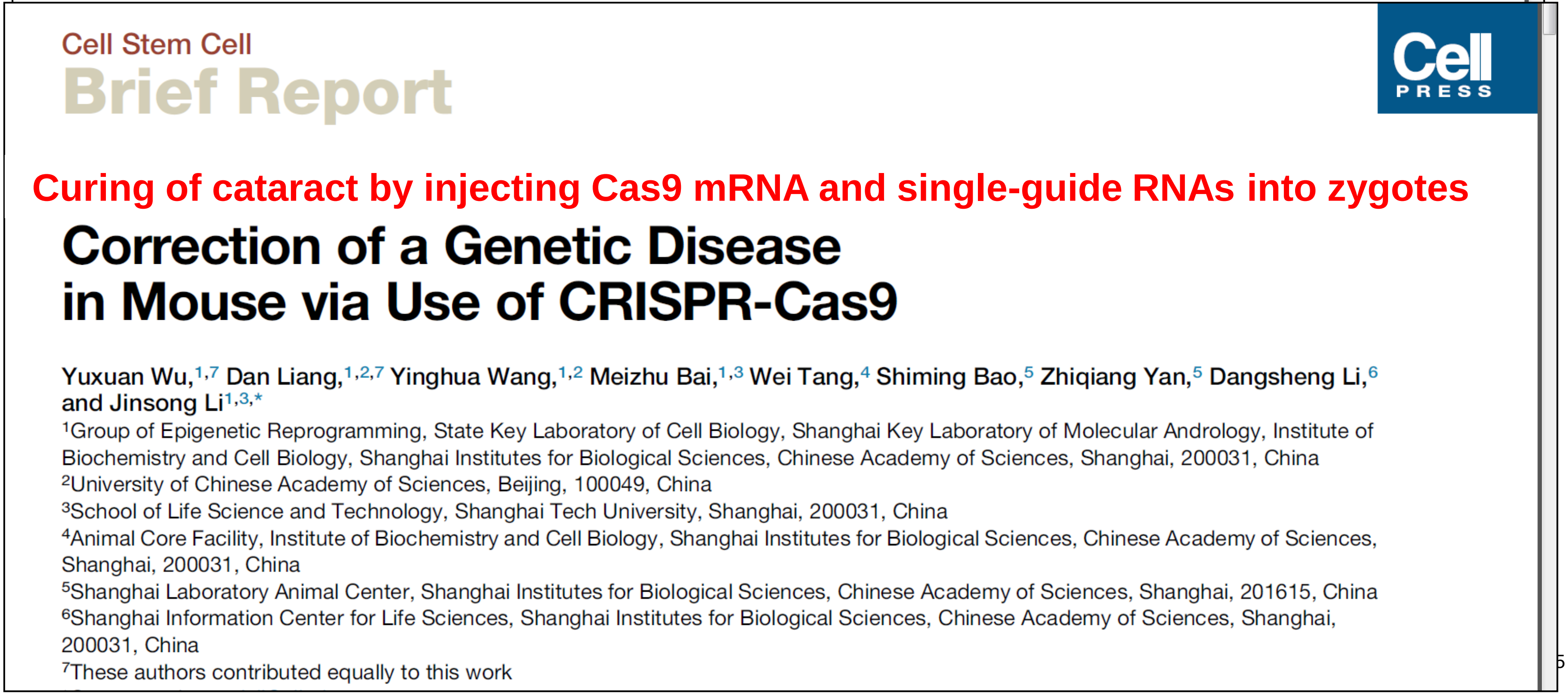
Cell Stem Cell

Brief Report

Curing of cystic fibrosis in a human stem cell model system

Functional Repair of CFTR by CRISPR/Cas9 in Intestinal Stem Cell Organoids of Cystic Fibrosis Patients

Gerald Schwank,[1,2,7] Bon-Kyoung Koo,[1,2,7,8] Valentina Sasselli,[1,2] Johanna F. Dekkers,[3,4] Inha Heo,[1,2] Turan Demircan,[1] Nobuo Sasaki,[1,2] Sander Boymans,[1] Edwin Cuppen,[1,6] Cornelis K. van der Ent,[3] Edward E.S. Nieuwenhuis,[5] Jeffrey M. Beekman,[5,6] and Hans Clevers[1,2,*]



Cell Stem Cell

Brief Report

Curing of cataract by injecting Cas9 mRNA and single-guide RNAs into zygotes

Correction of a Genetic Disease in Mouse via Use of CRISPR-Cas9

Yuxuan Wu,[1,7] Dan Liang,[1,2,7] Yinghua Wang,[1,2] Meizhu Bai,[1,3] Wei Tang,[4] Shiming Bao,[5] Zhiqiang Yan,[5] Dangsheng Li,[6] and Jinsong Li[1,3,*]

[1]Group of Epigenetic Reprogramming, State Key Laboratory of Cell Biology, Shanghai Key Laboratory of Molecular Andrology, Institute of Biochemistry and Cell Biology, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, Shanghai, 200031, China

[2]University of Chinese Academy of Sciences, Beijing, 100049, China

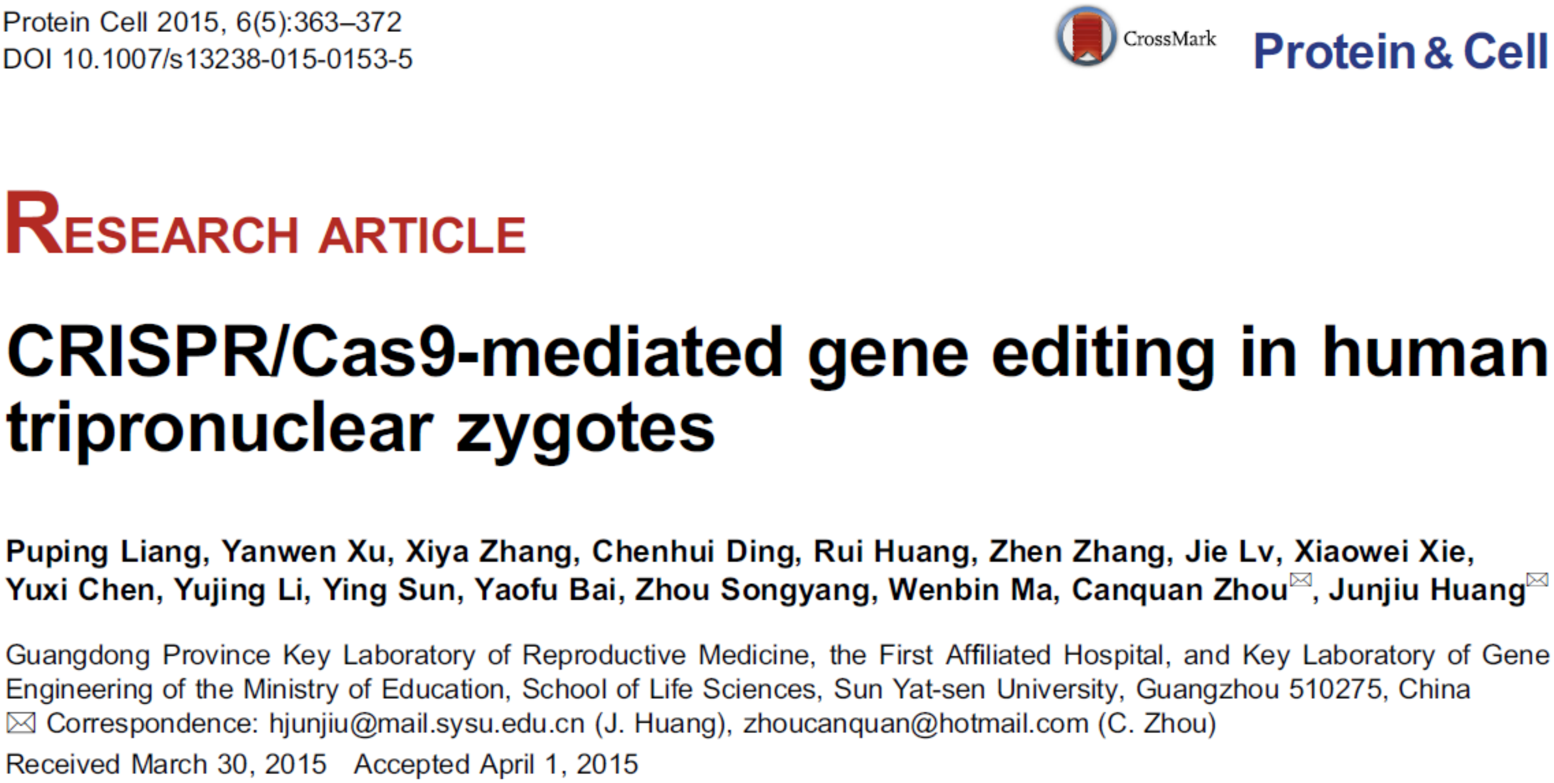
[3]School of Life Science and Technology, Shanghai Tech University, Shanghai, 200031, China

[4]Animal Core Facility, Institute of Biochemistry and Cell Biology, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, Shanghai, 200031, China

[5]Shanghai Laboratory Animal Center, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, Shanghai, 201615, China

[6]Shanghai Information Center for Life Sciences, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, Shanghai, 200031, China

[7]These authors contributed equally to this work



Protein Cell 2015, 6(5):363–372
DOI 10.1007/s13238-015-0153-5

Protein & Cell

RESEARCH ARTICLE

CRISPR/Cas9-mediated gene editing in human tripronuclear zygotes

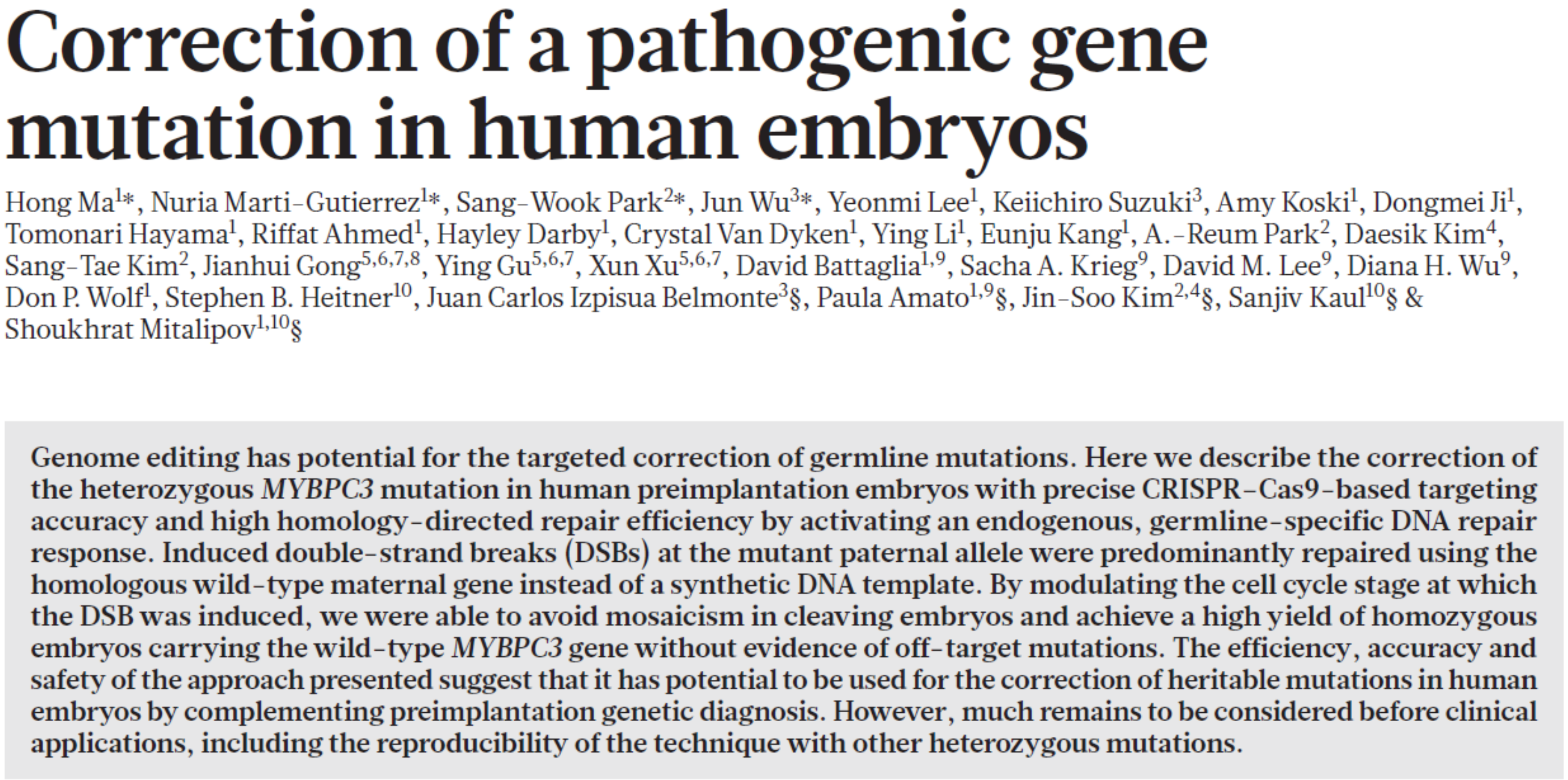
Puping Liang, Yanwen Xu, Xiya Zhang, Chenhui Ding, Rui Huang, Zhen Zhang, Jie Lv, Xiaowei Xie, Yuxi Chen, Yujing Li, Ying Sun, Yaofu Bai, Zhou Songyang, Wenbin Ma, Canquan Zhou✉, Junjiu Huang✉

Guangdong Province Key Laboratory of Reproductive Medicine, the First Affiliated Hospital, and Key Laboratory of Gene Engineering of the Ministry of Education, School of Life Sciences, Sun Yat-sen University, Guangzhou 510275, China
✉ Correspondence: hjunjiu@mail.sysu.edu.cn (J. Huang), zhoucanquan@hotmail.com (C. Zhou)

Received March 30, 2015 Accepted April 1, 2015

First example of engineering of an embryonic cell
Rejected from Nature and Science

Tripronuclear cells:
- Egg cell fertilized by two sperm cells
- Cannot grow into a fetus



Correction of a pathogenic gene mutation in human embryos

Hong Ma[1]*, Nuria Marti-Gutierrez[1]*, Sang-Wook Park[2]*, Jun Wu[3]*, Yeonmi Lee[1], Keiichiro Suzuki[3], Amy Koski[1], Dongmei Ji[1], Tomonari Hayama[1], Riffat Ahmed[1], Hayley Darby[1], Crystal Van Dyken[1], Ying Li[1], Eunju Kang[1], A.-Reum Park[2], Daesik Kim[4], Sang-Tae Kim[2], Jianhui Gong[5,6,7,8], Ying Gu[5,6,7], Xun Xu[5,6,7], David Battaglia[1,9], Sacha A. Krieg[9], David M. Lee[9], Diana H. Wu[9], Don P. Wolf[1], Stephen B. Heitner[10], Juan Carlos Izpisua Belmonte[3]§, Paula Amato[1,9]§, Jin-Soo Kim[2,4]§, Sanjiv Kaul[10]§ & Shoukhrat Mitalipov[1,10]§

Genome editing has potential for the targeted correction of germline mutations. Here we describe the correction of the heterozygous *MYBPC3* mutation in human preimplantation embryos with precise CRISPR–Cas9-based targeting accuracy and high homology-directed repair efficiency by activating an endogenous, germline-specific DNA repair response. Induced double-strand breaks (DSBs) at the mutant paternal allele were predominantly repaired using the homologous wild-type maternal gene instead of a synthetic DNA template. By modulating the cell cycle stage at which the DSB was induced, we were able to avoid mosaicism in cleaving embryos and achieve a high yield of homozygous embryos carrying the wild-type *MYBPC3* gene without evidence of off-target mutations. The efficiency, accuracy and safety of the approach presented suggest that it has potential to be used for the correction of heritable mutations in human embryos by complementing preimplantation genetic diagnosis. However, much remains to be considered before clinical applications, including the reproducibility of the technique with other heterozygous mutations.

- The researchers found no evidence of off-target genetic changes, and generated only a single mosaic in an experiment involving 58 embryos.

- The United States does not allow federal money to be used for research involving human embryos, but the work is not illegal if it is funded by private donors.

24 August 2017 | VOL 548 | NATURE | 413

CRISPR in medicine
Safety and ethical concerns

Off-target effects

- Unintentional development of cancer or other diseases

Desperate people are ready for desperate actions

- Commercial interest

Designer babies

- Curing inhereted diseases (can already now be screened for)
- Engineering for ”improved” properties (few simple traits exist)
- Difficulty to predict environmental factors/effects
- Sooner or later someone will edit germline ...
  - Jiankui He claimed that he had created the first genetically edited humans, female babies known as Lulu and Nana, presented at Second International Summit on Human Genome Editing in November 2018. Jianku claimed to have implanted embryos that were successfully modified with a mutation in the CCR5 with the intent of **preventing HIV transmission**. Jiankui's position at Southern University of Science and Technology has been terminated and he was immediately sent to house arrest for his work and was even considered to face death penalty. Resulted in prison for 3 years and a fine of 430 000 US dollars.

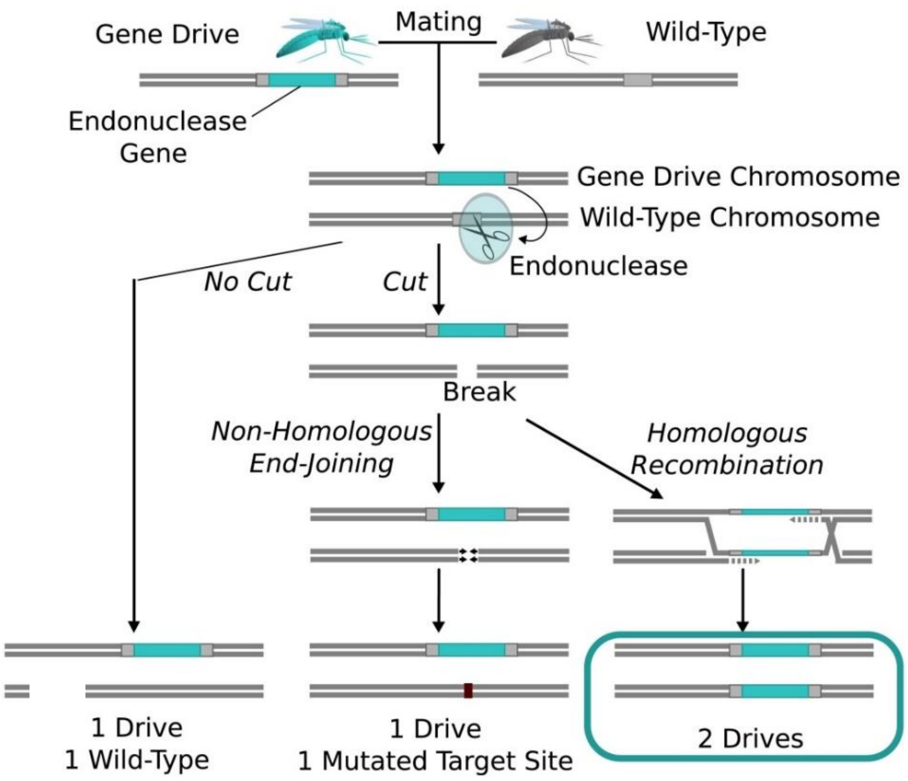
  -> WHO launced in 2019 a global registry to track research on genome editing.

- Balance of risks and benefits?
- Speed of development a big challenge.

Gene drives !

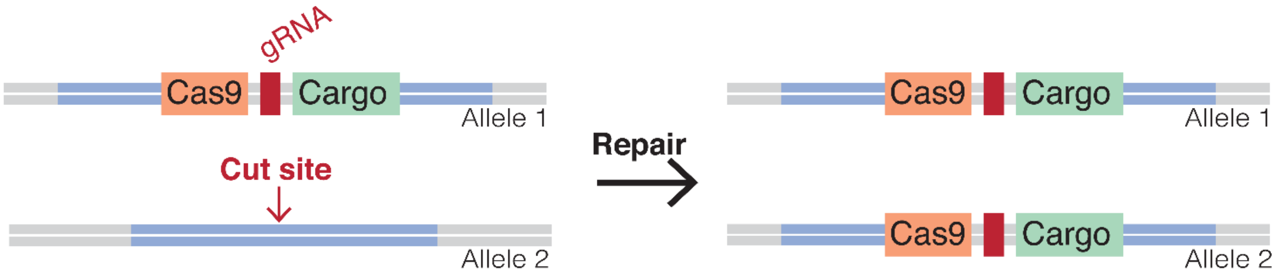
Gene drives

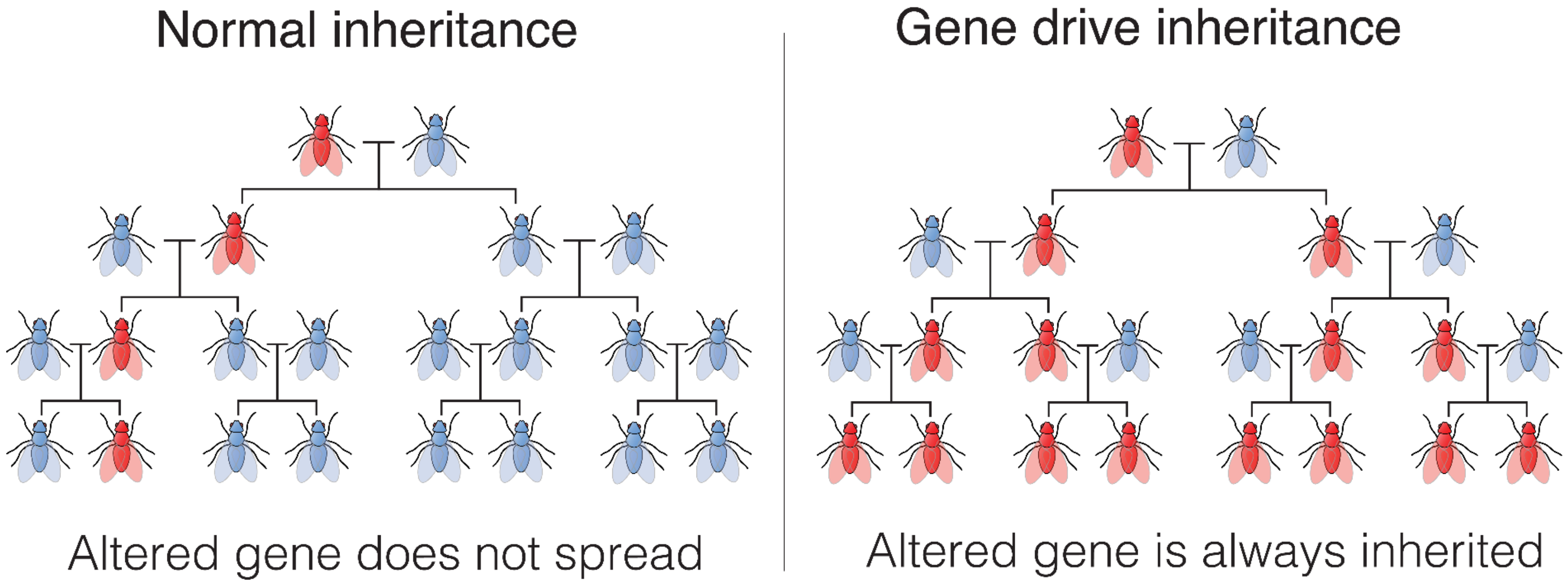
- Spreading of a genotype to every off-spring
- CRISPR/Cas9 mediated process
- Works for sexually reproducing organisms
- Requires fast reproduction for efficient spreading



Kevin M Esvelt et al. eLife Sciences 2014;3:e03401

Gene drives





Altered gene does not spread

Altered gene is always inherited

Kevin M Esvelt et al. eLife Sciences 2014;3:e03401

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Preventing malaria spread by mosquito populations using gene drives

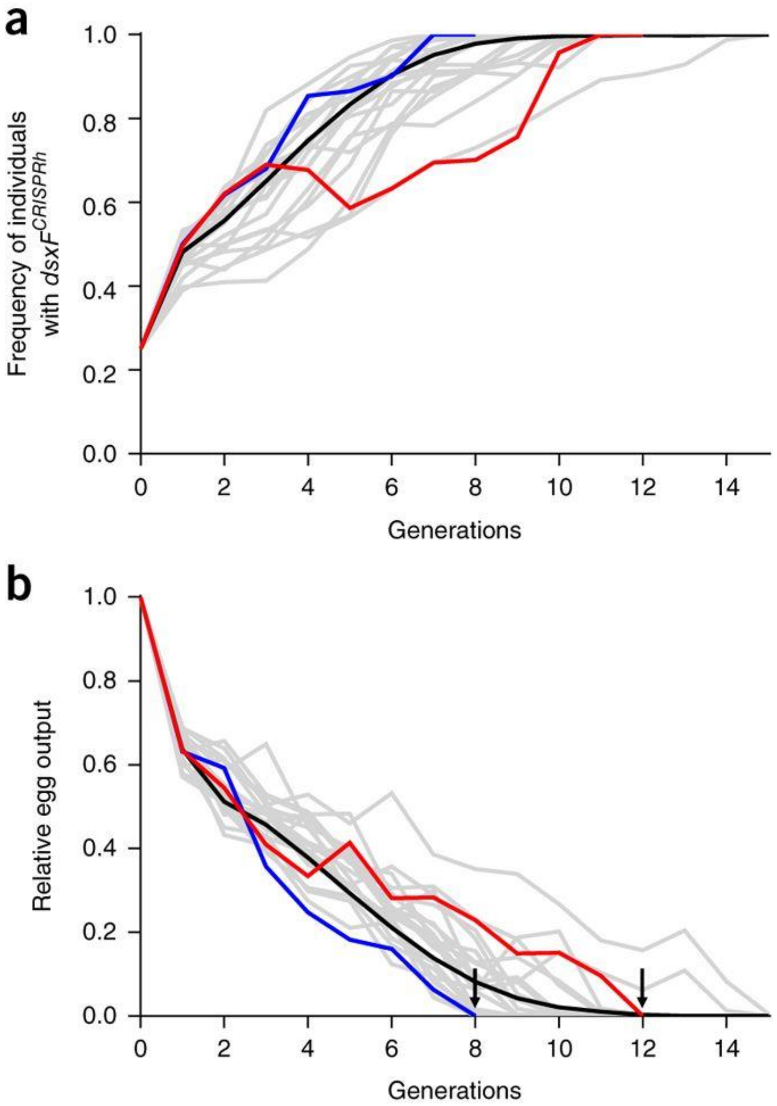
A CRISPR–Cas9 gene drive targeting *doublesex* causes complete population suppression in caged *Anopheles gambiae* mosquitoes

Kyros Kyrou et al. Nature Biotechnology **volume 36**, pages 1062–1066 (2018)

- Bill & Melinda Gates Foundation, Target Malaria project

Abstract

In the human malaria vector *Anopheles gambiae*, the gene *doublesex* (*Agdsx*) encodes two alternatively spliced transcripts, *dsx-female* (*AgdsxF*) and *dsx-male* (*AgdsxM*), that control differentiation of the two sexes. The female transcript, unlike the male, contains an exon (exon 5) whose sequence is highly conserved in all *Anopheles* mosquitoes so far analyzed. We found that CRISPR–Cas9-targeted disruption of the intron 4–exon 5 boundary aimed at blocking the formation of functional AgdsxF did not affect male development or fertility, whereas **females homozygous for the disrupted allele showed an intersex phenotype and complete sterility**. A CRISPR–Cas9 gene drive construct targeting this same sequence spread rapidly in caged mosquitoes, reaching **100% prevalence within 7–11 generations while progressively reducing egg production to the point of total population collapse**. Owing to functional constraint of the target sequence, no selection of alleles resistant to the gene drive occurred in these laboratory experiments. Cas9-resistant variants arose in each generation at the target site but did not block the spread of the drive.



Two cages were set up with a starting population of 300 wild-type females, 150 wild-type males and 150 $dsxF^{CRISPRh}$/+ males, seeding each cage with a $dsxF^{CRISPRh}$ allele frequency of 12.5%. (**a**) The frequency of $dsxF^{CRISPRh}$ mosquitoes was scored for each generation. The drive allele reached 100% prevalence in both cage 2 (blue) and cage 1 (red) at generation 7 and 11, respectively, in agreement with a deterministic model (black line) that takes into account the parameter values retrieved from the fecundity assays. Twenty stochastic simulations were run (gray lines) assuming a maximum population size of 650 individuals. (**b**) Total egg output deriving from each generation of the cage was measured and normalized relative to the output from the starting generation. Suppression of the reproductive output of each cage led the population to collapse completely (black arrows) by generation 8 (cage 2) or generation 12 (cage 1).

Next:

- Burkina Faso, Uganda, Mali
- Local mosquito strains
- Engineered strains to be tested in (closed) real nature field conditions 2024

Gene drives: Safety and ethical concerns

- The fear of dual use (malicious) or unintended mistakes

David Gurwitz, Tel Aviv University, Israel (Science, commentary letter)

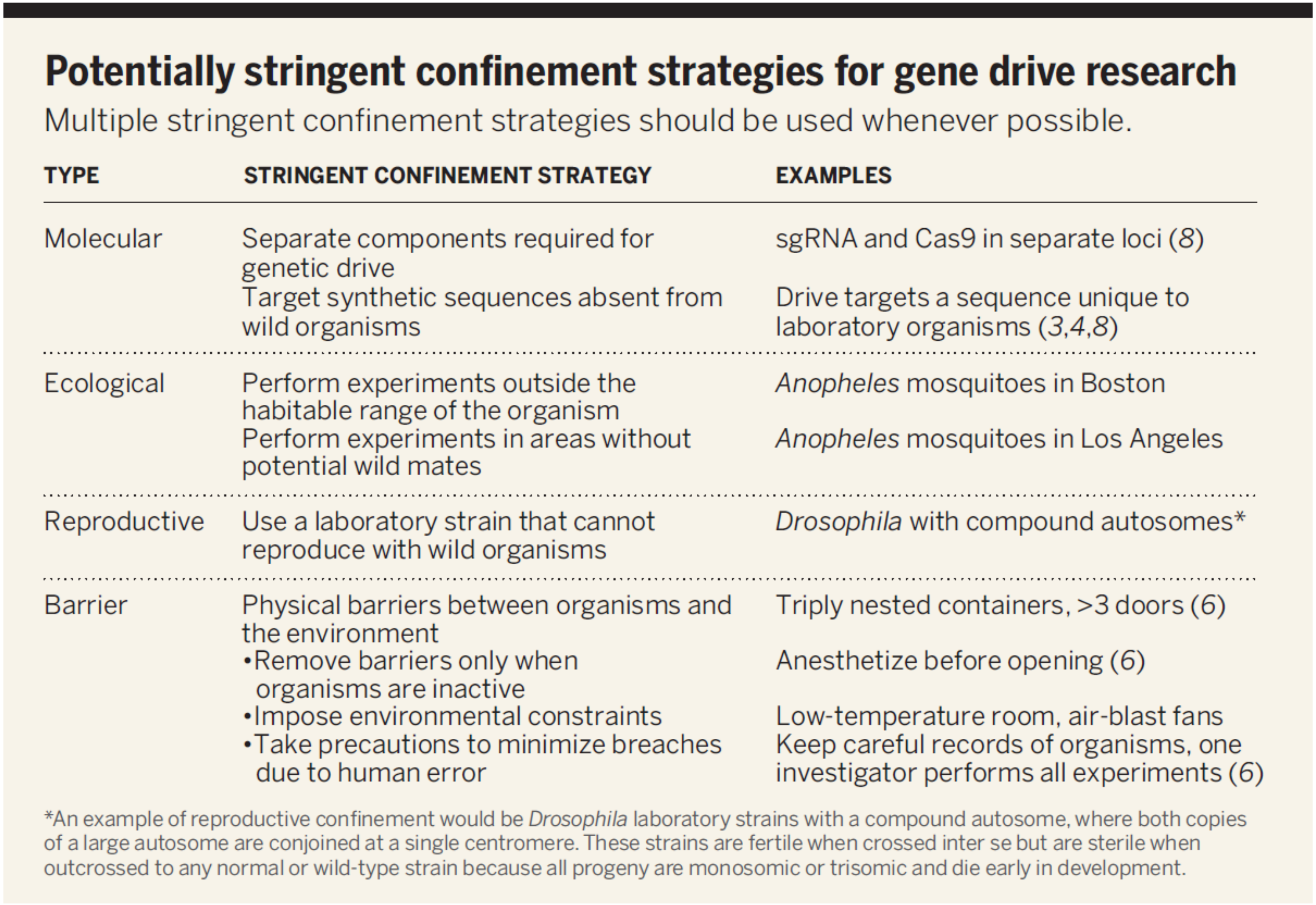
- Carrying bacterial toxins to humans
- Attacks on crop plants

His proposal: Keep the recipies for gene drive engineering secret
(in analogy to the nuclear bomb 70 year secrecy period)

Ken Oye/Kevin Esvelt reply:

- Technology at the moment still difficult to master in new organisms
- Secrecy would also compromise development of ”positive” applications and counter measures
- Secrecy fuels suspicion and affects ”learned” discussion on the topic
- Balance of potential misuse and benefits

Gene drives



Potentially stringent confinement strategies for gene drive research

Multiple stringent confinement strategies should be used whenever possible.

TYPE	STRINGENT CONFINEMENT STRATEGY	EXAMPLES
Molecular	Separate components required for genetic drive	sgRNA and Cas9 in separate loci (*8*)
	Target synthetic sequences absent from wild organisms	Drive targets a sequence unique to laboratory organisms (*3,4,8*)
Ecological	Perform experiments outside the habitable range of the organism	*Anopheles* mosquitoes in Boston
	Perform experiments in areas without potential wild mates	*Anopheles* mosquitoes in Los Angeles
Reproductive	Use a laboratory strain that cannot reproduce with wild organisms	*Drosophila* with compound autosomes*
Barrier	Physical barriers between organisms and the environment	Triply nested containers, >3 doors (*6*)
	•Remove barriers only when organisms are inactive	Anesthetize before opening (*6*)
	•Impose environmental constraints	Low-temperature room, air-blast fans
	•Take precautions to minimize breaches due to human error	Keep careful records of organisms, one investigator performs all experiments (*6*)

*An example of reproductive confinement would be *Drosophila* laboratory strains with a compound autosome, where both copies of a large autosome are conjoined at a single centromere. These strains are fertile when crossed inter se but are sterile when outcrossed to any normal or wild-type strain because all progeny are monosomic or trisomic and die early in development.

Akbari et al, Science

28 AUGUST 2015 • VOL 349 ISSUE 6251 **927**

Jennifer Doudna’s dream

- Jennifer Doudna (Univ. California, Berkeley), inventor of CRISPR and founder of several startup companies, had a dream in 2016 that Adolf Hitler wanted her CRISPR recipe
- In her book A Crack in Creation she wrote that she feared gene editing could come to the world’s attention, as atomic power did, in a mushroom cloud. “Could I and other concerned scientists save CRISPR from itself … before a cataclysm occurred
- In 2016, the US intelligence agencies designated gene editing as a potential weapon of mass destruction. The Defense Advanced Research Projects Agency (DARPA) put out a call (Programme “Safe Genes”, $65 million) for new ways to control or reverse the effects of gene-editing technology.
- **More than 40 anti-CRISPR proteins present on phages have already been found, many by Doudna’s lab. Other teams are having success locating conventional chemicals that can inhibit CRISPR. Amit Choudhary of Harvard Medical School (Boston) with funding from DARPA, has found two drugs that prevent gene-editing when mixed with human cells.**

Anti-CRISPR: discovery, mechanism and function

April Pawluk, Alan R. Davidson, & Karen L. Maxwell

Nature Reviews Microbiology volume 16, pages 12–17 (2018)

Biocontainment

Biological means to prevent synbio organisms to interact with natural environment

- killer switches
- synthetic reactions
- hybrid/synthetic life

(science fiction note: fight of synthetic molecules vs. as now occurs in nature)

NOTE: Industrial biotechnology is carried out in contained bioreactors. Safety as with any GMO (?).

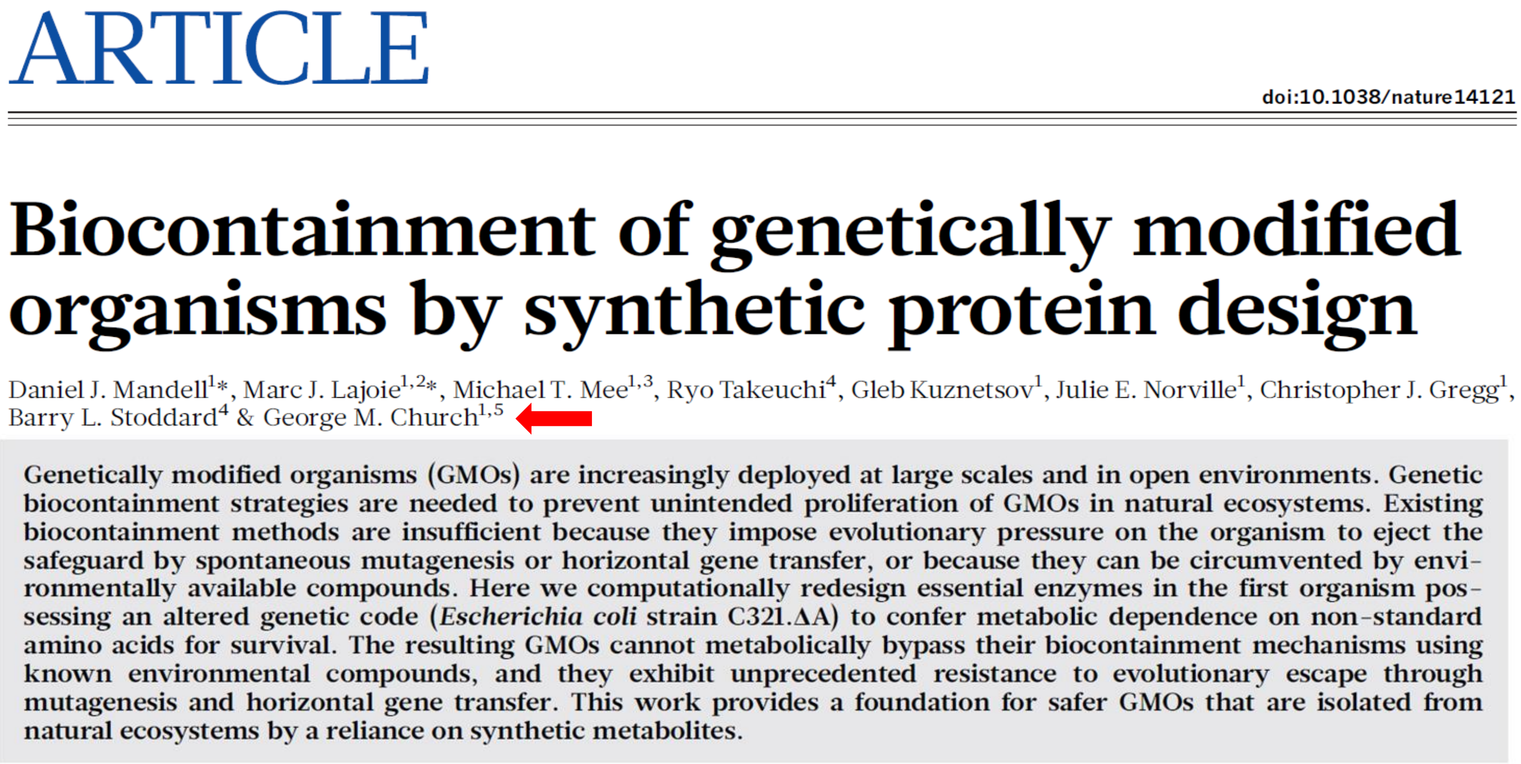
Biocontainment

An effective biocontainment strategy should protect against

- **Mutagenic drift**
  - Evolution is a never-ending process
  - The system must be resistant to mutations

- **Environmental supplementation**
  - Growth of the organisms requires a substance that does not exist in nature

- **Horizontal gene transfer**
  - Sterility causing genetic combinations
  - Non-complementary genetic codes (XNA)



ARTICLE

doi:10.1038/nature14121

Biocontainment of genetically modified organisms by synthetic protein design

Daniel J. Mandell[1]*, Marc J. Lajoie[1,2]*, Michael T. Mee[1,3], Ryo Takeuchi[4], Gleb Kuznetsov[1], Julie E. Norville[1], Christopher J. Gregg[1], Barry L. Stoddard[4] & George M. Church[1,5]

Genetically modified organisms (GMOs) are increasingly deployed at large scales and in open environments. Genetic biocontainment strategies are needed to prevent unintended proliferation of GMOs in natural ecosystems. Existing biocontainment methods are insufficient because they impose evolutionary pressure on the organism to eject the safeguard by spontaneous mutagenesis or horizontal gene transfer, or because they can be circumvented by environmentally available compounds. Here we computationally redesign essential enzymes in the first organism possessing an altered genetic code (*Escherichia coli* strain C321.ΔA) to confer metabolic dependence on non-standard amino acids for survival. The resulting GMOs cannot metabolically bypass their biocontainment mechanisms using known environmental compounds, and they exhibit unprecedented resistance to evolutionary escape through mutagenesis and horizontal gene transfer. This work provides a foundation for safer GMOs that are isolated from natural ecosystems by a reliance on synthetic metabolites.

- A large number of essential protein encoding genes made to incorporate unnatural amino acids into proteins
- Only cells that get the unnatural amino acids from the growth medium can survive
- Reversion mutants extremely unlikely
- Escape frequencies $10^{-9} – 10^{-11}$

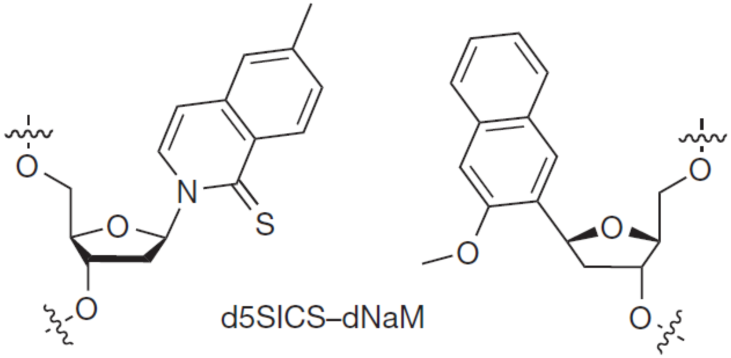
Containment through non-complementary code

Nature. 2014 May 15
doi:10.1038/nature13314

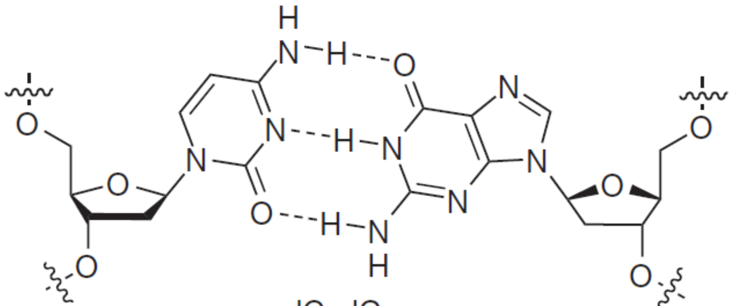
A semi-synthetic organism with an expanded genetic alphabet

Denis A. Malyshev[1], Kirandeep Dhami[1], Thomas Lavergne[1], Tingjian Chen[1], Nan Dai[2], Jeremy M. Foster[2], Ivan R. Corrêa Jr[2] & Floyd E. Romesberg[1]

- Hydrophobic nucleobases d5SICS and dNaM
- Pairing mediated by hydrophobic interactions
- Only one of each molecule was incorporated into an extrachromosomal DNA
- The novel nucleotides were not recognized as lesions by the cellular DNA repair pathway
- The unnatural-base-pair-containing DNA is replicated, without *E. coli* cell growth being significantly affected
- The novel nucleotides added to cells (Safety)



d5SICS–dNaM



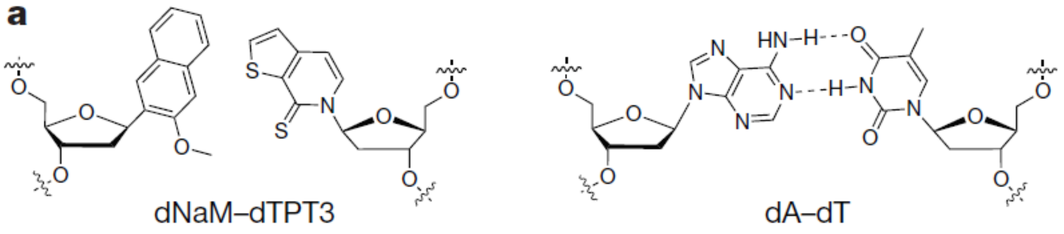
dC–dG

LETTER

doi:10.1038/nature24659

A semi-synthetic organism that stores and retrieves increased genetic information

Yorke Zhang[1], Jerod L. Ptacin[2], Emil C. Fischer[1], Hans R. Aerni[2], Carolina E. Caffaro[2], Kristine San Jose[2], Aaron W. Feldman[1], Court R. Turner[2] & Floyd E. Romesberg[1]



- Bacterial cells able to both replicate and read unnatural DNA into a functional protein

LETTER

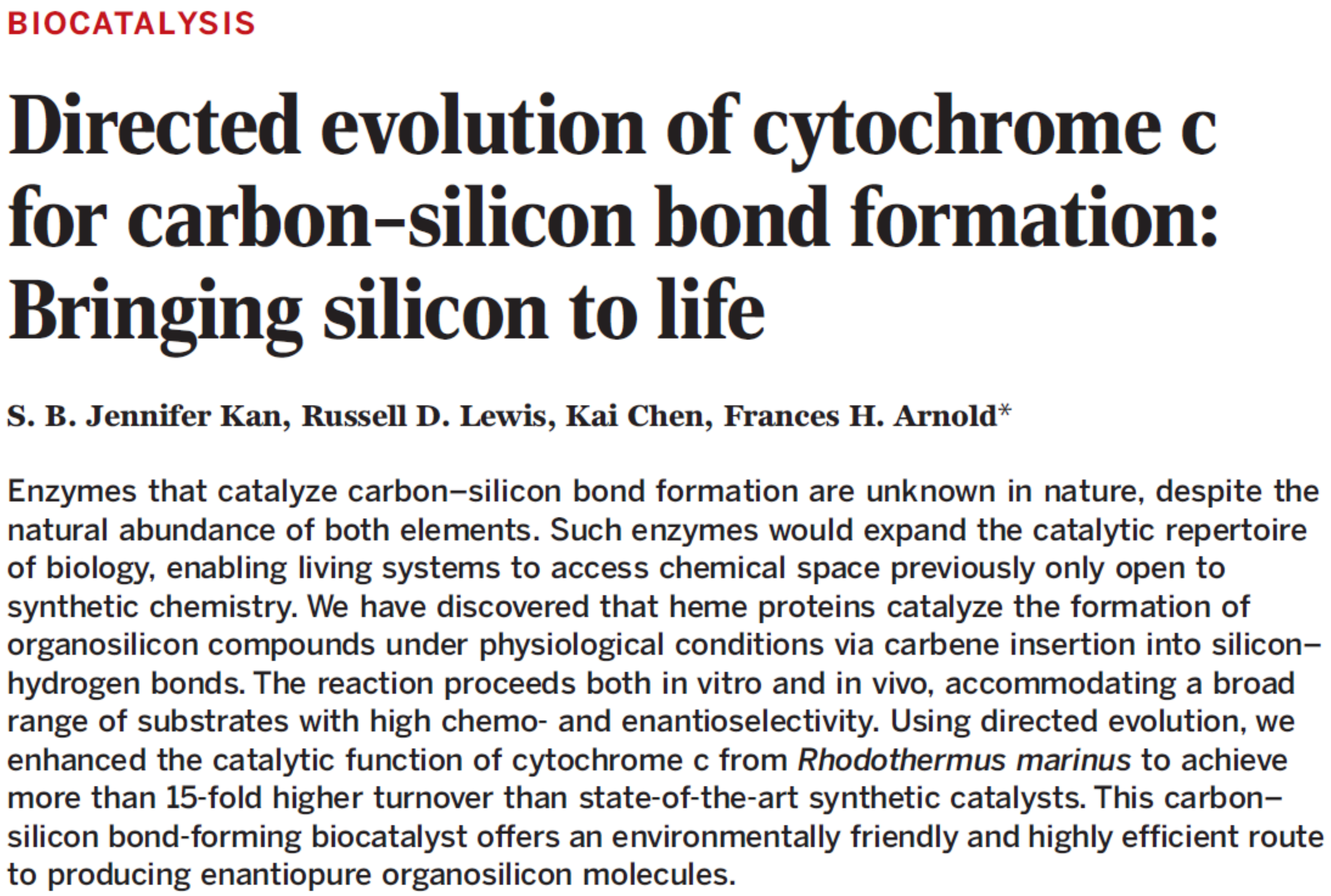
doi:10.1038/nature24659

A semi-synthetic organism that stores and retrieves increased genetic information

Yorke Zhang[1], Jerod L. Ptacin[2], Emil C. Fischer[1], Hans R. Aerni[2], Carolina E. Caffaro[2], Kristine San Jose[2], Aaron W. Feldman[1], Court R. Turner[2] & Floyd E. Romesberg[1]

- *In vivo* transcription of DNA containing dNaM and dTPT3 into mRNAs
- Two different unnatural codons and tRNAs with cognate unnatural anticodons
- Efficient decoding at the ribosome for site-specific incorporation of natural or non-canonical amino acids into green fluorescent protein.
- Interactions other than hydrogen bonding can contribute to every step of information storage and retrieval.

Hybrid life?



BIOCATALYSIS

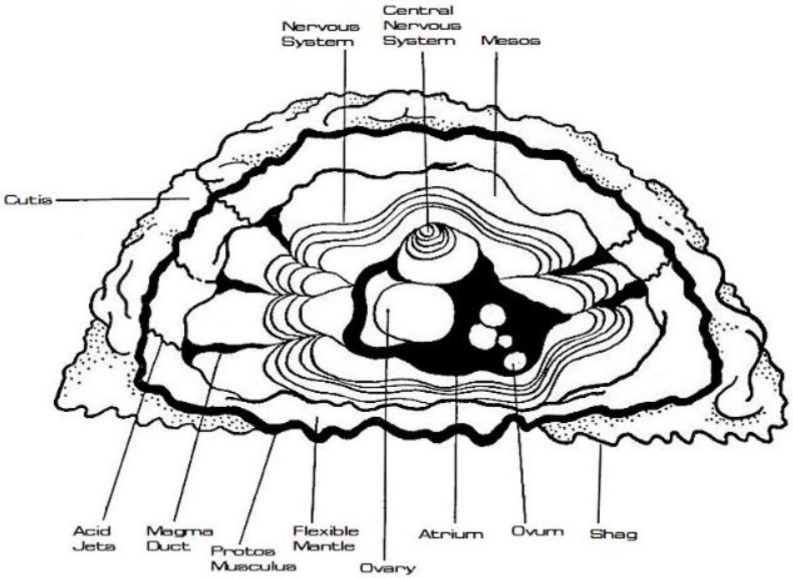
Directed evolution of cytochrome c for carbon–silicon bond formation: Bringing silicon to life

S. B. Jennifer Kan, Russell D. Lewis, Kai Chen, Frances H. Arnold*

Enzymes that catalyze carbon–silicon bond formation are unknown in nature, despite the natural abundance of both elements. Such enzymes would expand the catalytic repertoire of biology, enabling living systems to access chemical space previously only open to synthetic chemistry. We have discovered that heme proteins catalyze the formation of organosilicon compounds under physiological conditions via carbene insertion into silicon–hydrogen bonds. The reaction proceeds both in vitro and in vivo, accommodating a broad range of substrates with high chemo- and enantioselectivity. Using directed evolution, we enhanced the catalytic function of cytochrome c from *Rhodothermus marinus* to achieve more than 15-fold higher turnover than state-of-the-art synthetic catalysts. This carbon–silicon bond-forming biocatalyst offers an environmentally friendly and highly efficient route to producing enantiopure organosilicon molecules.

Hybrid life?

- Science-fiction authors have already imagined alien worlds with silicon-based life (e.g. Horta creatures in Star Trek)



General

General rules for increased likelihood for intended harmful use

Ease of use

- ✓ If a technology is easier to use, and it is common, it is more likely to be used.

Barriers to use

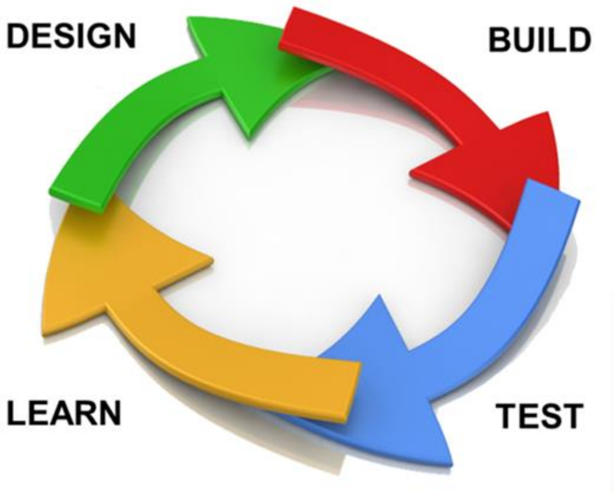
- ✓ Challenges even in one of the aspects of the design-build-test-learn cycle technologies can significantly hamper the likelihood of success of establishing complex systems.
- ✓ At the same time, novel innovations can rapidly remove barriers.

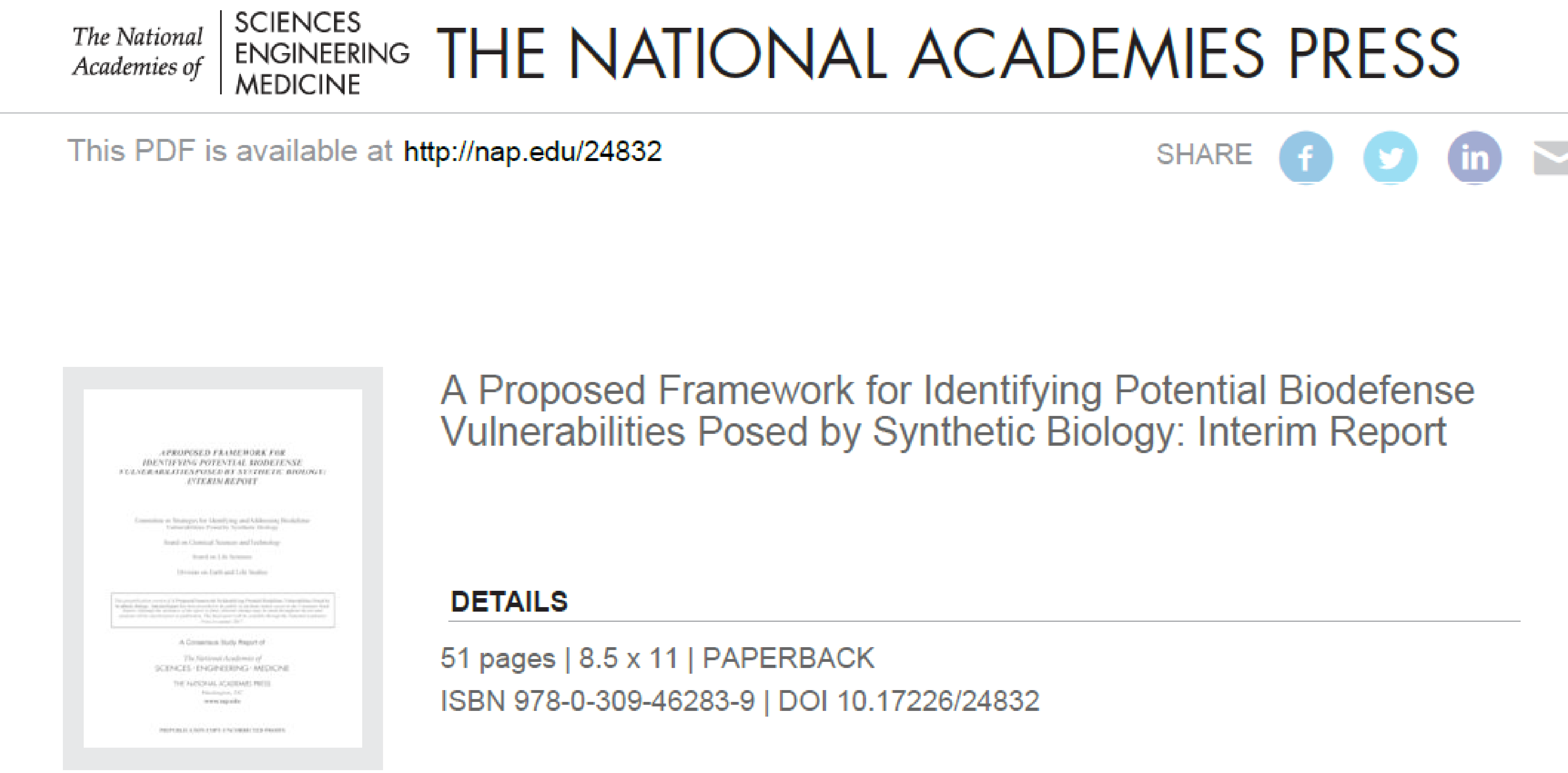
Synergy with other technologies:

- ✓ DBTL cycle-technologies support each other
- ✓ Even small advances in part of the technologies can have a cumulative positive effect

Cost

- ✓ High cost has a restrictive effect on the most non-professonial actors, but not necessary on professonial ones





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A Proposed Framework for Identifying Potential Biodefense Vulnerabilities Posed by Synthetic Biology: Interim Report

DETAILS

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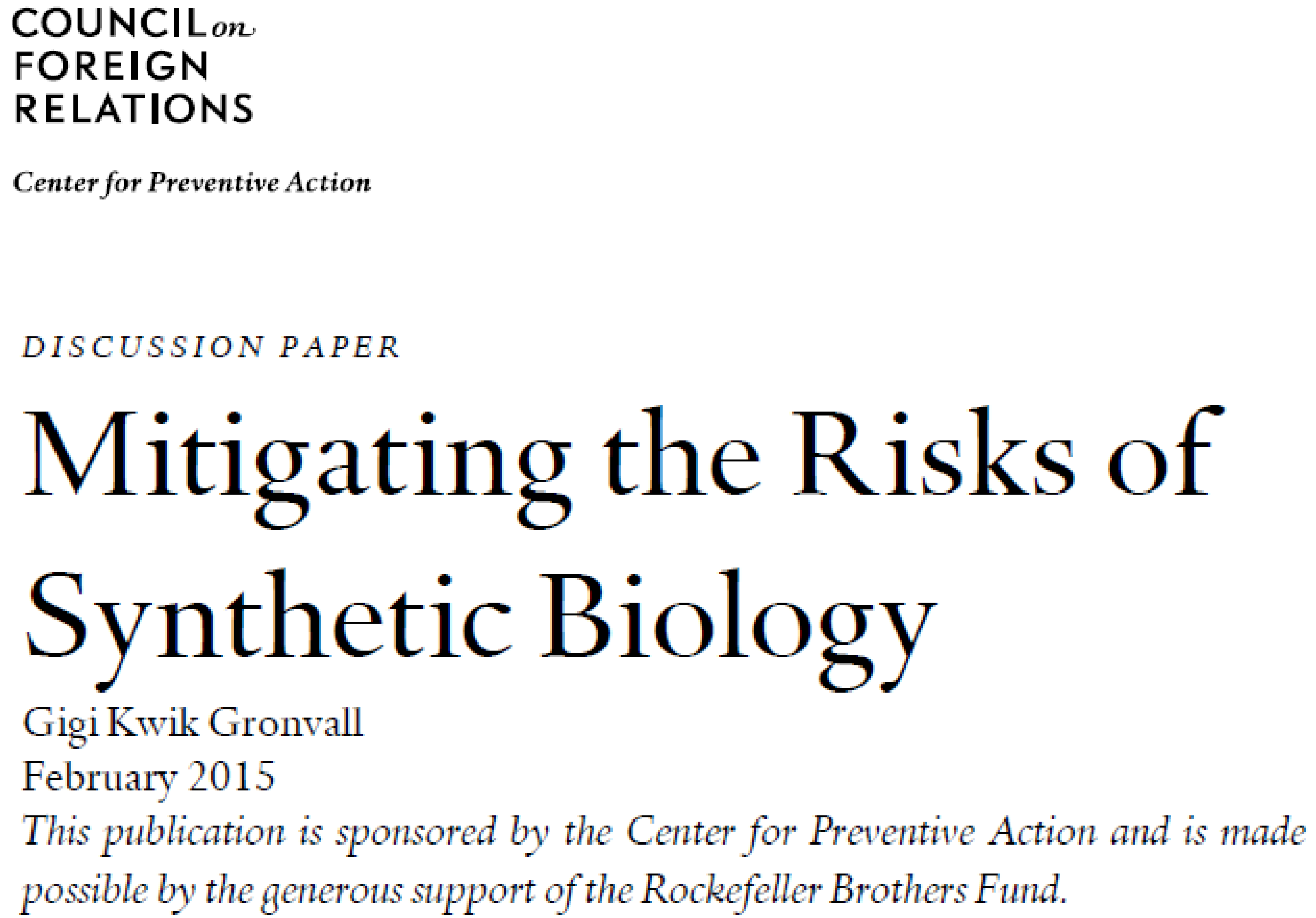

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DISCUSSION PAPER

Mitigating the Risks of Synthetic Biology

Gigi Kwik Gronvall
February 2015

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Guiding Ethical Principles in Engineering Biology Research

Rebecca Mackelprang, Emily R. Aurand, Roel A. L. Bovenberg, Kathryn R. Brink, R. Alta Charo, Jason A. Delborne, James Diggans, Andrew D. Ellington, Jeffrey L. “Clem” Fortman, Farren J. Isaacs, June I. Medford, Richard M. Murray, Vincent Noireaux, Megan J. Palmer, Laurie Zoloth, and Douglas C. Friedman*

ACS Synthetic Biology 2021; https://doi.org/10.1021/acssynbio.1c00129

I. seek to create products or processes that benefit people, society, or the environment;

II. consider and weigh the benefits of research against potential harms;

III. incorporate equity and justice in the selection and implementation of engineering biology education, research, development, policy, and commercialization;

IV. seek to openly distribute the results of early stage research and development;

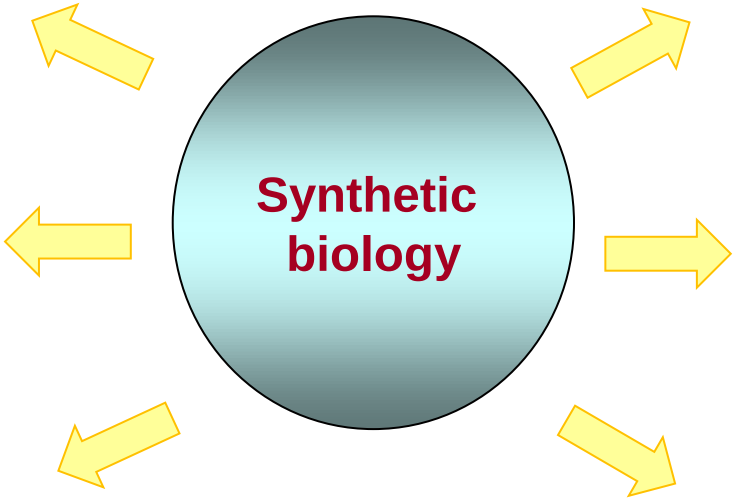
V. protect the rights of individuals associated with engineering biology, including the freedom of inquiry of researchers and the free and informed consent of research participants; and

VI. support open communication between engineering biology researchers and the stakeholders who might be affected by research, development, and the deployment of new technologies.

Concluding remarks

- Synthetic biology aims to make biology easier to engineer
- A central goal is rational design, so that biological traits, functions, and products can be generated in a predictable way (writing the code of the biological system).
- Synthetic biology will have a huge impact on biotechnology, medicine and manufacturing (biointelligent manufacturing).
- Like any technology, synthetic biology may be misused.
- The intentional or accidental mismanagement of synthetic biology technologies could result in loss of life as well as ecological and agricultural damage.
- Effective governance of the technology is a global challenge

Synthetic biology increases our understanding of the limits of life and enables applications that are important for the humankind



Minimalistic cells

- Genes essential for life
- Synthia

New genetic codes

- DNA with four bases correspomding to an amino acid instead of three bases
- Synthetic amino acids

”Hybrid organisms”

- Traits from other species

Replacemnet of oil in industrial production

- Chemicals, fuels, materials with cell factories

Healthy and sufficient nutrition

- Better food crops by plant biotechnology
- CellAg

Biological precision medicines and human spare parts

- Efficient drug production
- Tailored stem cells and organoids

Do It Yourself scientist related issues

- DIYbio.org (https://diybio.org/) founded 2008
- Mission of establishing a vibrant, productive and safe community of DIY biologists.
- Mission the belief that biotechnology and greater public understanding about it has the potential to benefit everyone.
- Question about safety? Ask a professional biosafety expert your question now: http://ask.diybio.org

More information on synbio

BioBuilder.org

Kate Amadala (Build-a-Cell, Twitter journal clubs)

SynBioBeta Built with Biology (FB, Twitter..

TED Talk https://www.youtube.com/watch?v=8DDgHq9ewOo

Synthetic Biology with Dr. George Church

https://www.youtube.com/watch?v=WZwRe6ht8yg

“I think the biggest innovations of the twenty-first century will be the intersection of biology and technology. A new era is beginning, just like the digital one [...]”

(Steve Jobs, 2009)

Exam

Important is to understand the concepts and technologies of synthetic biology (not the tiny details)

Have a nice summer !

BioGarage

- Community creation
- Open inspiring laboratory space
- Low-threshold bioengineering
- Interdisciplinarity
- Linking with international garages
- Science pitches, Bio-Slush, etc
- BD mentoring & support

New location at Tietotie 1 soon!

Aalto University
School of Chemical
Technology

"Guided tours for politicians"

"We would like to learn more in the lab"

"Normal people cloning would make them understand GMOs"

"A realistic option for start-ups"

"Proper place where biohazardous waste is treated correctly"

Opening event at Design Factory 27.9.2019
iGEM team demonstrating DNA isolation

Jenny and Antti Wihuri Foundation support for the Centre of Young Synbio Scientists (Prof. Merja Penttilä)

Contact nina.pulkkis@synbio.fi