GOVERNING BENEFITS AND RISKS OF EMERGING BIOTECHNOLOGIES
RETROSPECTIVE AND CURRENT CASES
10:05-10:25 AM 17 FEBRUARY 2022

Professor Kenneth A. Oye
MIT Political Science and Data Systems and Society

OUTLINE

Risk Governance Under Uncertainty: Permissive, Precautionary, Adaptive

Retrospective and Current Biotechnology Cases

- Agriculture: Genetically Engineered Plants and Animals
- Industry: Synthesis of Biofuels, Fragrances, and Drugs
- Medicine: SCGT, Regenerative Medicine, HGGT
- Environment: Gene Drives

A Closing Conundrum: Governing Risks with Information Hazards

The research, conferences and workshops on which this presentaiton is based have been supported by the Netherlands Rijksinstituut voor Volksgezondheid en Milieu; the US Defense Advanced Research Projects Agency, US National Science Foundation Molecular and Cellular Biology, the MIT Center for Biomedical Innovation, the International Risk Governance Council and Richard Johnson.

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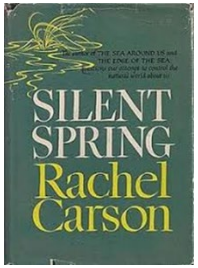
APPROACHES TO RISK GOVERNANCE UNDER UNCERTAINTY

Permissive

Allow innovation unless environment, health, security are clearly compromised
After-the-fact reaction if crisis materializes; backlash may limit innovation
Examples: DDT, post-Fukushima nuclear shutdown, US stasis on gene therapy



Precautionary

Limit innovation unless environment, health and security are clearly protected
Diversion of innovation to less regulated areas may heighten risks
Examples: EU on GMOs, US on stem cell research, Y2K

Planned Adaptive

* Prepare: Fund research to inform priors on benefits and risks
* Discriminate: Foster initial applications with most favorable priors
* Observe: Harvest and process information from initial experience
* Adapt: Learn from experience and update/correct practices

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WHY BIOENGINEERING IS CHANGING SO FAST

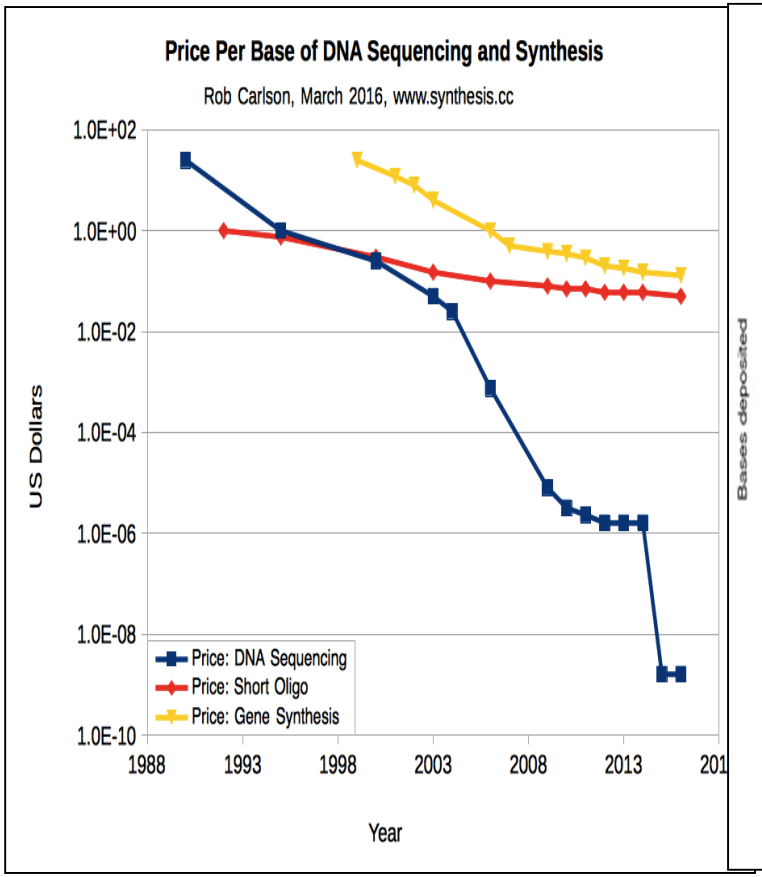
ENABLING TECHNOLOGIES DEVELOPING AT EXTRAORDINARY RATES

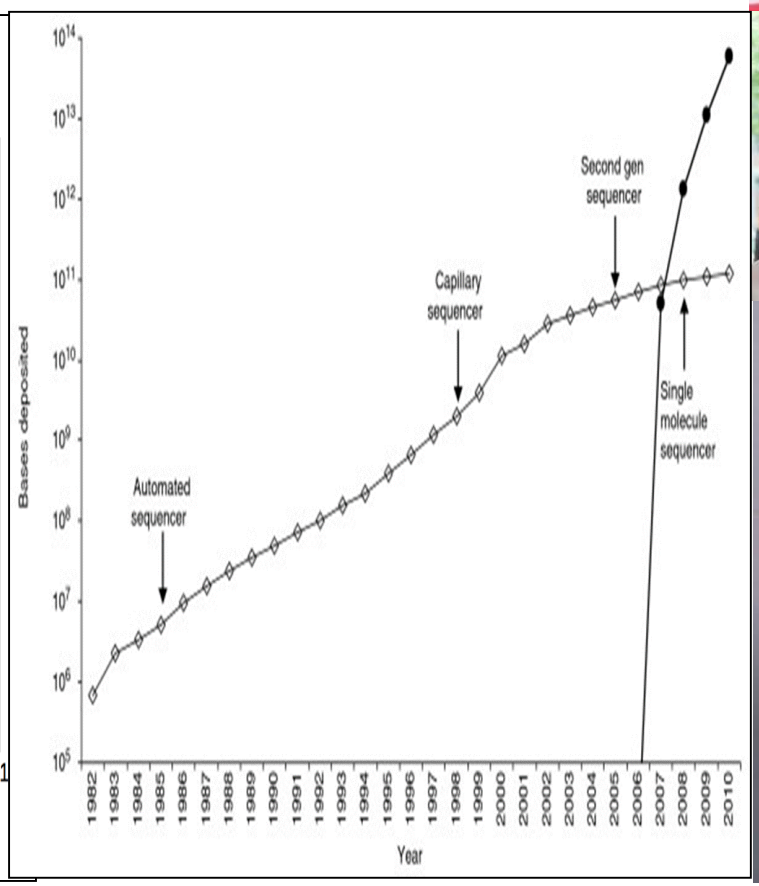
Making DNA: Cost and speed of DNA synthesis

Reading DNA: Cost and speed of DNA sequencing

Characterizing and Designing DNA: AI and data storage

Editing DNA: From zinc fingers and talens to CRISPR and base editing





Cost of DNA Synthesis & Sequencing

Info Deposited in Data Bases

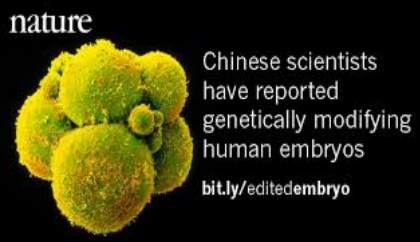
Design/Editing Tools

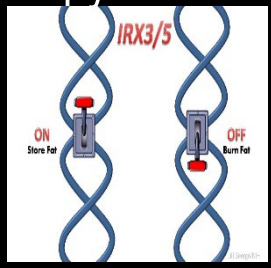
EMERGING APPLICATIONS

AGRICULTURE — GM Crops and Livestock N Fixation, Glowing Plants, Aquabounty

INDUSTRY — Synthesis of Organic Materials Fuel, Flavors, Drugs

MEDICINE — Regenerative Medicine, Somatic and Germline Cell Therapy





ENVIRONMENT — Remediation; Control Vector Borne Disease and Invasive Species

FISH STORY: DEVELOPERS AND REGULATORS LIMIT RISKS

AQABOUNTY ATLANTIC SALMON WITH POUT AND CHINOOK GENES

FOOD SAFETY: FDA compared non-GE farmed and GE salmon, with focus on estradiol, testosterone, 11-ketotestosterone, T3, T4 and insulin-like growth factor 1 (IGF1)) + complete compositional analysis.

ENVIRONMENT: FDA issued "Finding of No Significant Impact" (FONSI)

Physical containment: All fish in land based tanks with safeguards

Geophysical containment: High water temp or bad water quality g

Biological containment – organism design

- Adults sterile triploid (diploid broodstock)
- Adults all female
- Fitness disadvantage relative to wild type due to limited food

EMERGING APPLICATIONS

AGRICULTURE

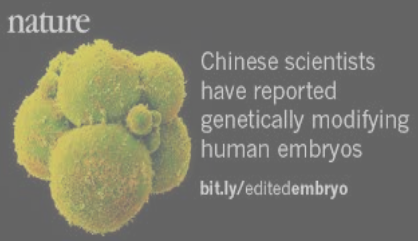
GM Crops and Livestock N Fixation, Glowing Plants, Aquabounty

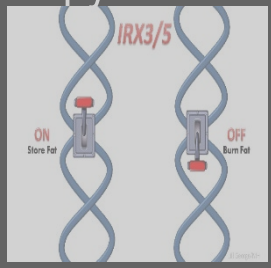
INDUSTRY

Synthesis of Organic Materials Fuel, Flavors, Drugs

MEDICINE

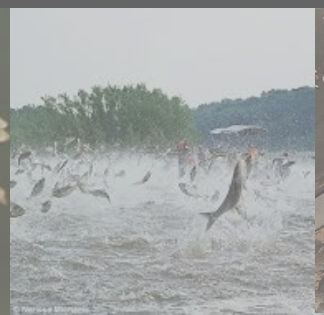
Regenerative Medicine, Somatic and Germline Cell Therapy





ENVIRONMENT

Remediation; Control Vector Borne Disease and Invasive Species



INDUSTRIAL APPLICATIONS: MAKING LOW VALUE MATERIALS

SGI, Sapphire, Algenol — synthesis of biofuels

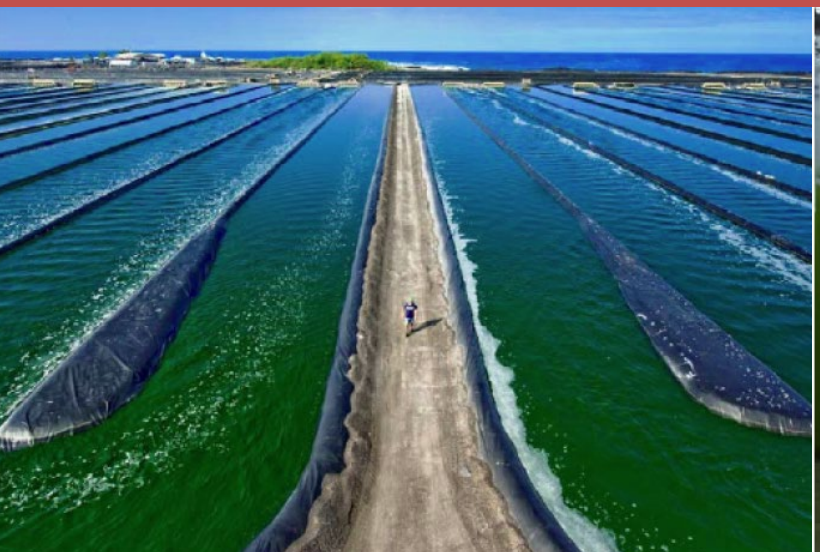
Universal Biomining — extraction and effluent treatment

Economics > low cost containment > environment release probable

Environmental effects

- Fitness / reproduction / propagation
- Horizontal gene flow
- Mutation > effects on fitness, gene flow?

Raceways and Sluices



Plastic Bags

Surface Ponds

ALGAE BIOFUELS CONTAINMENT WORKSHOP

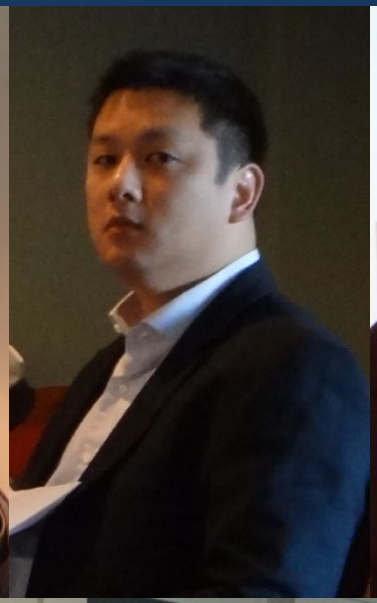
SYNTHETIC GENOMICS®

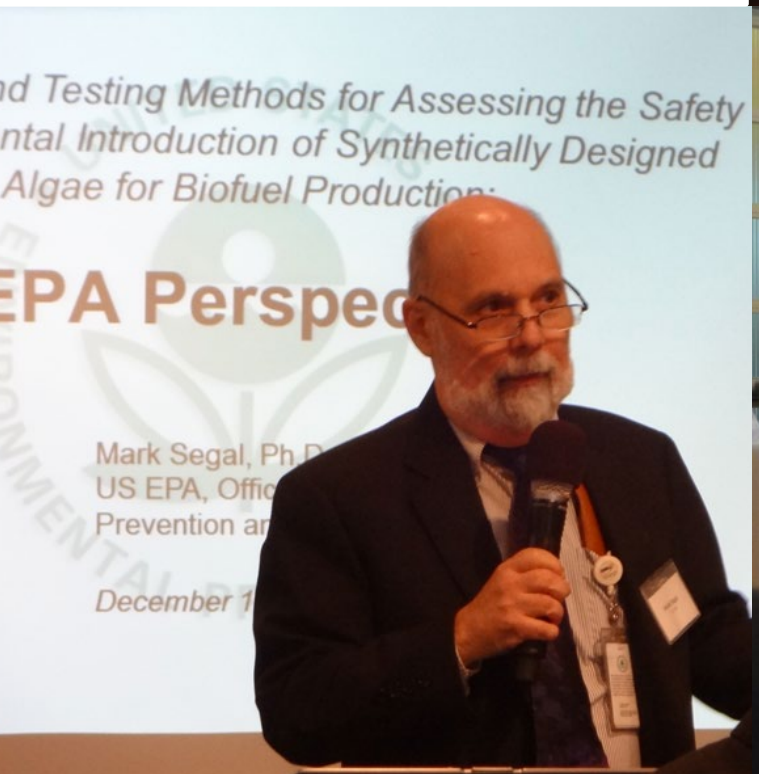
ALGENOL BIOFUELS

HARNESSING THE SUN TO FUEL THE WORLD™

Sapphire Energy

Agilent Technologies





TECHNOLOGISTS DESIGN TO LIMIT RISKS OF RELEASE

Daisuke Kiga: Synthetic Amino Acids

Biocontainment Design: Church and Isaacs Labs

Unfilled gap - independent systematic demonstration and testing

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]

LETTER

doi:10.1

Recoded organisms engineered to depend on synthetic amino acids

Alexis J. Rovner[1,2], Adrian D. Haimovich[1,2]*, Spencer R. Katz[1,2]*, Zhe Li[1,2], Michael W. Grome[1,2], Brandon M. Gass Miriam Amiram[1,2], Jaymin R. Patel[1,2], Ryan R. Gallagher[1,2], Jesse Rinehart[2,3] & Farren J. Isaacs[1,2]

US EPA FUNDS RESEARCH ON IMPROVED METHODS OF TESTING

First grants awarded July 2021

EPA United States Environmental Protection Agency

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Research Grants

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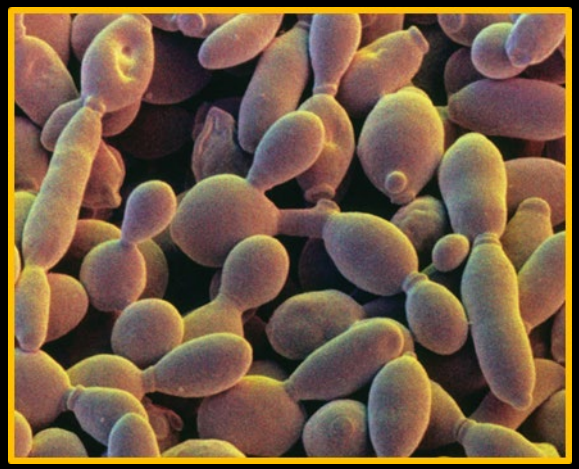
- Funding Opportunities
- Research Areas

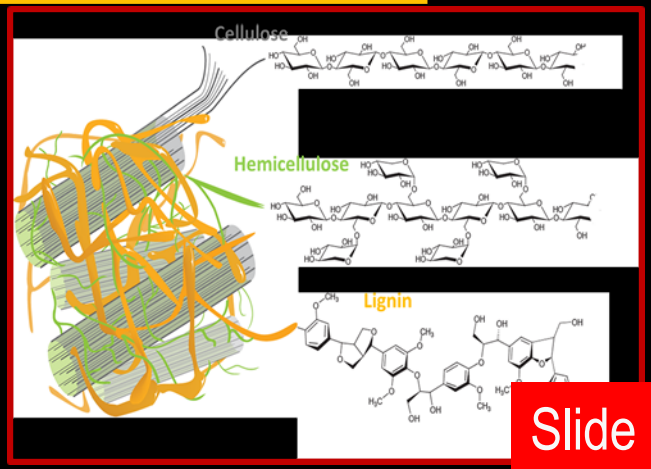
Assessment Tools for Biotechnology Products

INDUSTRIAL APPLICATIONS: MAKING HIGH VALUE MATERIALS

Keasling/Amyris/Sanofi	amorphadien, artemisinen
Prather	glucaric acid
Evolva	vanillin
Smolke, Dueber, Martin, Facchini	reticuline, hydrocodone, morphine

evolva





OPIATE PRODUCTION IN YEAST DUEBER, MARTIN, SMOLKE

Benefits: Ability to vary scaffolds, control intermediates, create novel analgesics
Hazard: Production beyond control of cartels and law enforcement
Technical Measures: markers, finicky strains, unappealing final product
Policy Measures: lab security, licensing, synthesis screening

nature International weekly journal of science

Illegal use of opiates such as heroin and morphine affects more than 16 million people worldwide.

Regulate 'home-brew' opiates

The research community and the public require a fast, flexible response to the synthesis of morphine by engineered yeasts, urge **Kenneth Oye**, **Tania Bubela** and **J. Chappell H. Lawson**.

Every year, thousands of students from across the world compete to build biological systems from pre-existing parts in a competition organized by the International Genetically Engineered Machine (iGEM) Foundation. Last November, to spark discussion on security and health risks raised by synthetic biology, FBI Special Agent Edward You presented an example: the production of opiates from sugar by yeast (*Saccharomyces cerevisiae*) that has been genetically modified.

You's hypothetical scenario is becoming a reality. One week after the iGEM competition, two developers of opiate-producing yeast strains approached us, specialists in biotechnology policy. They had results in advance of publication, and requested advice on how they might maximize the benefits of their research while mitigating the risks. Now, published papers by these researchers — John Dueber at the University of California, Berkeley, and his colleagues[1], and Vincent Martin ▶

Science

SYNTHETIC BIOLOGY

Complete biosynthesis of opioids in yeast

Stephanie Galanie,[1] Kate Thodey,[2] Isis J. Trenchard,[2] Maria Filsinger Interrante,[2] Christina D. Smolke[2]*

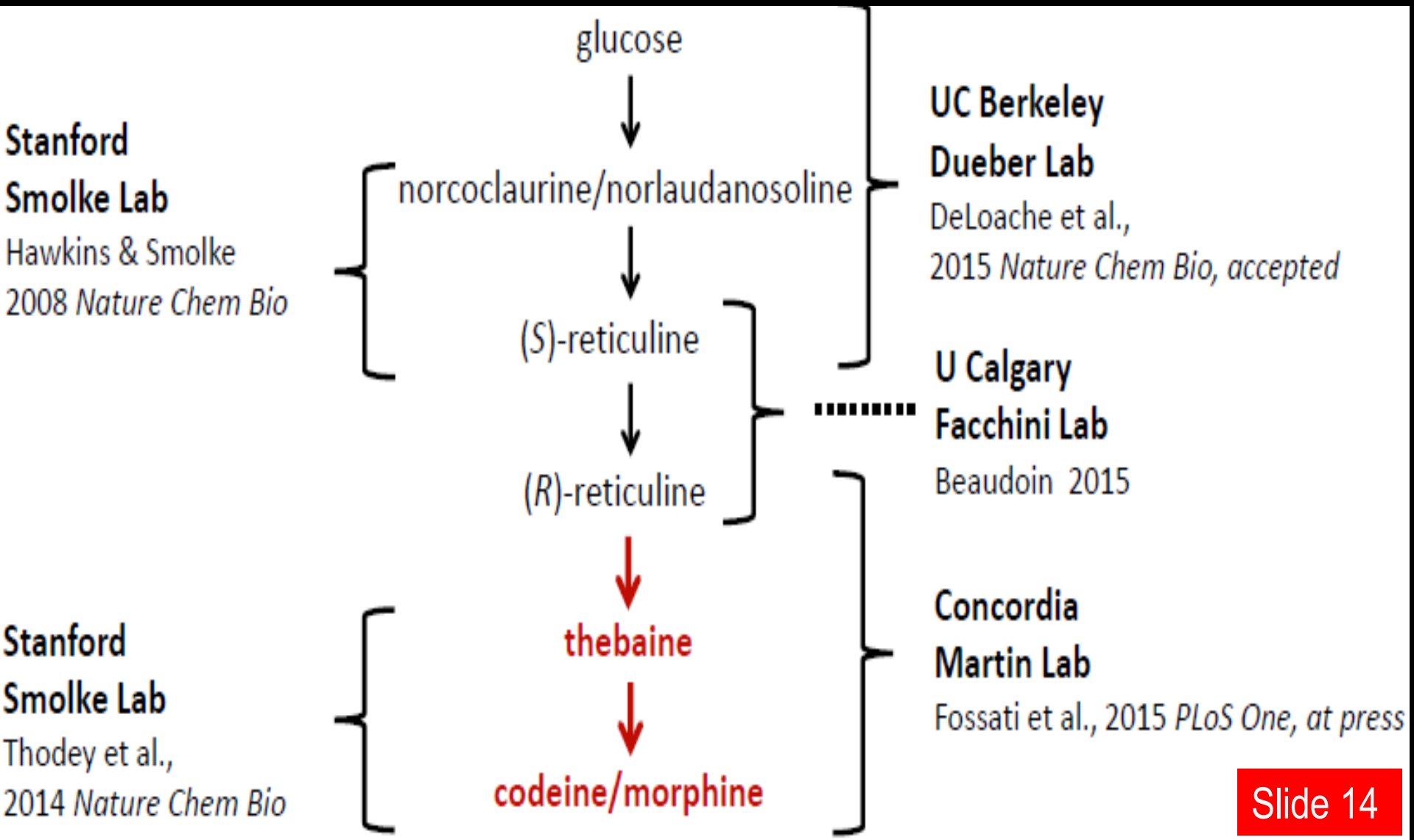
Opioids are the primary drugs used in Western medicine for pain management and palliative care. Farming of opium poppies remains the sole source of these essential medicines, despite diverse market demands and uncertainty in crop yields due to weather, climate change, and pests. We engineered yeast to produce the selected opioid compounds thebaine and hydrocodone starting from sugar. All work was conducted in a laboratory that is permitted and secured for work with controlled substances. We

Slide 13

OPIATE PRODUCTION IN YEAST: TWO RESEARCH GROUPS

Smolke, Thodey, Hawkins (Stanford)

Dueber (UCB), Facchini (Calgary), Martin (Concordia)



(NOT) BREWING BAD

PERSONNEL SECURITY

Psychological disorders

- Psychopathy
- Borderline personality disorder
- Narcissistic personality disorder

Other Risk Factors

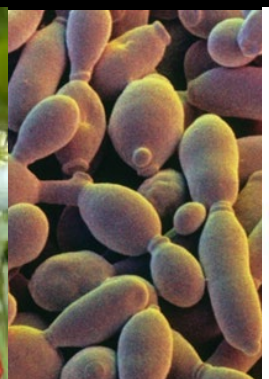
- Financial stress
- Status insecurity
- Sleep deprivation
- Perceived unfairness

LAB SECURITY

- Entry and exit control
- Materials access
- Inventory management
- Information controls

REDUCE APPEAL OF STRAINS

- Insert markers for traceability
- Make hard to cultivate
- Stop short of opiates
- Make distasteful to consume



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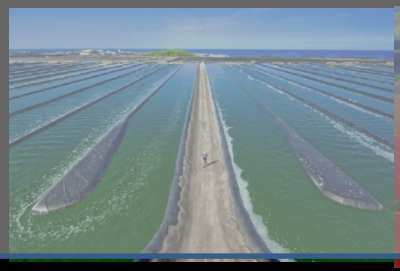
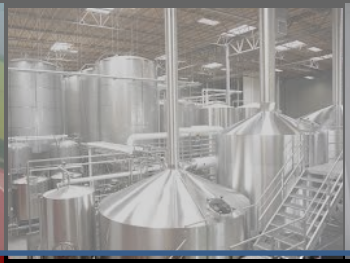
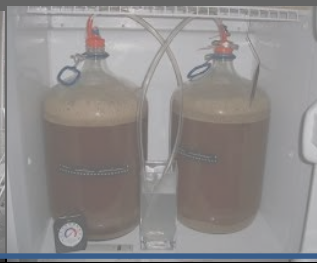
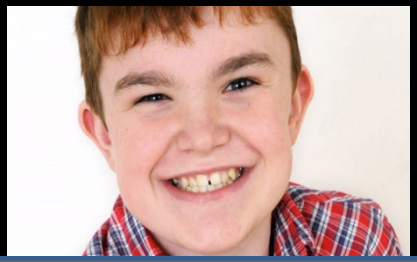
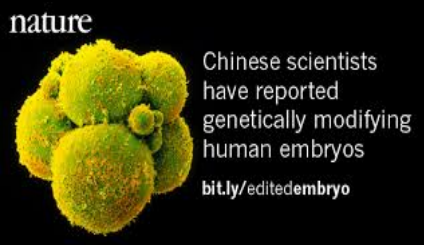


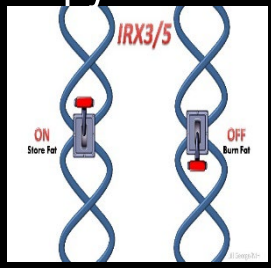




MEDICINE — Regenerative Medicine, Somatic and Germline Cell Therapy







ENVIRONMENT — Remediation; Control Vector Borne Disease and Invasive Species


Penn gene therapy destroyed teen's lungs

How a worried mother [illegible] what went wrong

Public Interest Group Calls for Public Disclosures in Gene Therapy Death

Jolee Mohr, with husband Robb and daughter Toree in 2006, died after two injections of a gene therapy. The cause is not yet known. Photo courtesy of Mohr Family

Contact: Osagie Obasogie
510-625-0819, ext 310

Troubling new revelations have emerged this week in the death of an Illinois woman in a gene therapy trial for arthritis, prompting the Center for Genetics and Society to call on the federal government to consider firmer regulatory action.

The death of 36-year-old Jolee Mohr in a gene transfer experiment sponsored by Targeted Genetics Corporation of Seattle raises important concerns about other participants in the 20 study locations across the country, and about participants in clinical trials of gene therapy and

doi:10.1038/nature16526

High-fidelity CRISPR–Cas9 nucleases with no detectable genome-wide off-target effects

Benjamin P. Kleinstiver[1,2*], Vikram Pattanayak[1,2*], Michelle S. Prew[1], Shengdar Q. Tsai[1,2], Nhu T. Nguyen[1], Zongli Zheng[3] & J. Keith Joung[1,2]

CRISPR–Cas9 nucleases are widely used for genome editing but can induce unwanted off-target mutations. Existing strategies for reducing genome-wide off-target effects of the widely used *Streptococcus pyogenes* Cas9 (SpCas9) are imperfect, possessing only partial or unproven efficacies and other limitations that constrain their use. Here we describe SpCas9-HF1, a high-fidelity variant harbouring alterations designed to reduce non-specific DNA contacts. SpCas9-HF1 retains on-target activities comparable to wild-type SpCas9 with >85% of single-guide RNAs (sgRNAs) tested in human cells. Notably, with sgRNAs targeted to standard non-repetitive sequences, SpCas9-HF1 rendered all or nearly all off-target events undetectable by genome-wide break capture and targeted sequencing methods. Even for atypical, repetitive target sites, the vast majority of off-target mutations induced by wild-type SpCas9 were not detected with SpCas9-HF1. With its exceptional precision, SpCas9-HF1 provides an alternative to wild-type SpCas9 for research and therapeutic applications. More broadly, our results suggest a general strategy for optimizing genome-wide specificities of other CRISPR-RNA-guided nucleases.

Unexpected mutations after CRISPR–Cas9 editing *in vivo*

To the Editor: CRISPR–Cas9 editing shows promise for correcting disease-causing mutations. For example, in a recent study we used CRISPR-Cas9 for sight restoration in blind *rd1* mice by correcting a mutation in the *Pde6b* gene[1]. However, concerns persist regarding secondary mutations in regions not targeted by the single guide RNA (sgRNA)[2]. Algorithms generate likely off-target sites for a given gRNA, but these algorithms may miss mutations. Whole-genome sequencing (WGS) has been used to assess the presence of small insertions and deletions (indels)[3] but not to probe for single-nucleotide variants (SNVs) in a whole organism. We performed WGS on a CRISPR–Cas9-ed[illegible] identify all off-target mutations and found an une[illegible] number of SNVs compared with the widely accepted assumption

VERSION 1.5

CURRENT SOMATIC CELL GENE THERAPY (SCGT)

Single gene alterations to cure thalassemia, cystic fibrosis, hemophilia.

800+ SCGT now under development

Bluebird LentiGlobin BB305 for β-thalassaemia approved by EMA FDA

bluebirdbio™

VERSION 2.0
REGENERATIVE MEDICINE

REPLACE

Engineer differentiated tissue/organ

Insert/transplant in subject

- Tracheal implants - Macchiarrini
- Retinal Tissue Implant – Kurimoto

REGENERATE

Trigger internal healing in subject

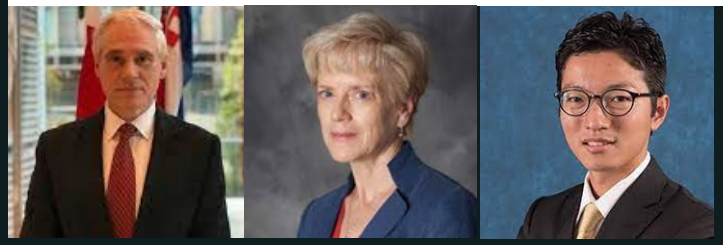
Insert extracellular matrix, modified stem cells

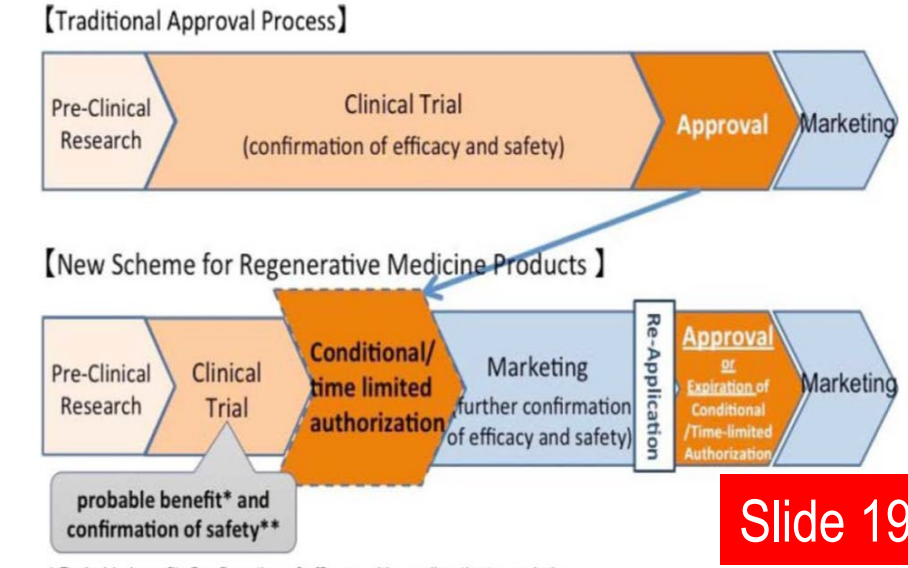
- Own cord blood stem cells
- Donor stem cells, marrow
- Procymal for graft-versus-host disease

PMDA "Conditional Time Limited Authorization"

Pharmaceuticals Licensing and Reimbursement in the European Union, United States, and Japan

KA Oye[1], HG Eichler[2], A Hoos[3], Y Mori[4], TM Mullin[5] and M Pearson[6]





Slide 19

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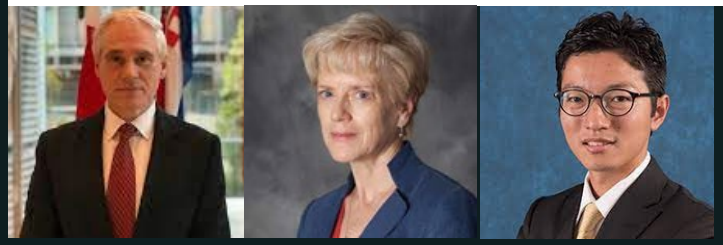

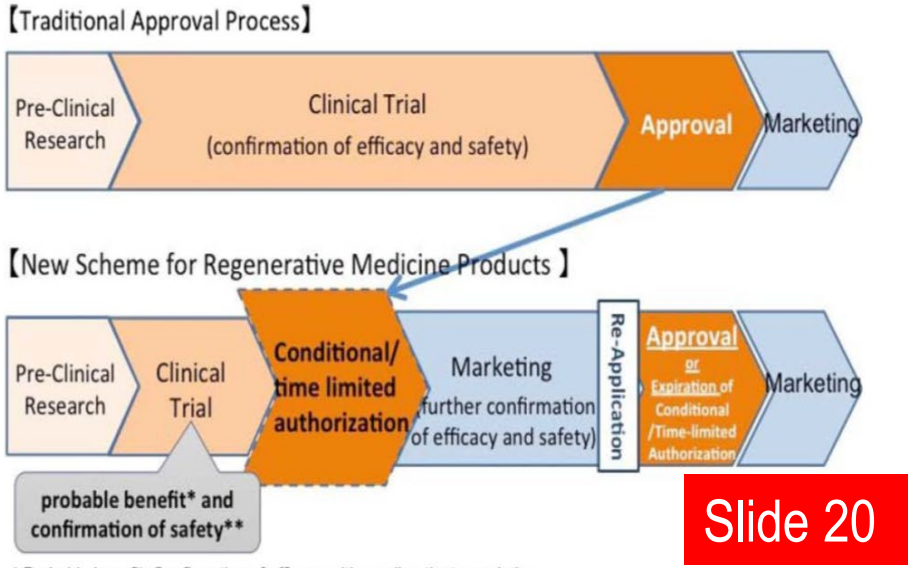

VERSION 3.0 GERMLINE GENE THERAPY (GGT)

SCGT works in individual, GGT changes in germline will be heritable

- Huang@Sun Yat-sen edited β-thalassaemia gene 28 embryos. Experiment failed with many off-target effects (4/2015 Protein&Cell)
- Zhang@Broad Improved Cas9 Specificity (12/2015 Science)
- Joung@MGH Hi-fi CRISPR no off-target effects (1/2016 Nature)
- Mitalipov@Oregon GGT pathogen in human embryo (8/2017 Nature)
- HGP Write – ultra-safe cells with codon knockout to limit gene flow

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

CrossMark 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

GENOME EDITING

Rationally engineered Cas9 nucleases with improved specificity

Ian M. Slaymaker,[1,2,3,4]* Linyi Gao,[1,4]* Bernd Zetsche,[1,2,3,4] David A. Scott,[1,2,3,4] Winston X. Yan,[1,5,6] Feng Zhang[1,2,3,4]†

The RNA-guided endonuclease Cas9 is a versatile genome-editing tool with a broad range of applications from therapeutics to functional annotation of genes. Cas9 creates double-strand breaks (DSBs) at targeted genomic loci complementary to a short RNA guide. However, Cas9 can cleave off-target sites that are not fully complementary to the guide, which poses a major challenge for genome editing. Here, we use structure-guided protein engineering to

nature International weekly journal of science

NATURE | ARTICLE

日本語要約

Correction of a pathogenic gene mutation in human embryos

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

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BEYOND THERAPEUTICS

OLYMPIC ENHANCEMENTS

- SIZE
- SPEED
- AGILITY
- PAIN THRESHOLD
- JOINT STRENGTH
- EYE-HAND COORDINATION
- DEPTH PERCEPTION

MILSPEC ENHANCEMENT

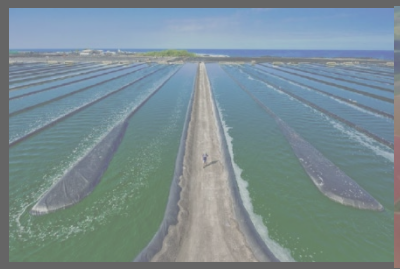
- PAIN THRESHOLD
- TOLERANCE OF SLEEP LOSS
- VISUAL ACUITY
- PARALLEL PROCESSING
- COURAGE
- POSITIVE OWN GROUP AFFECT
- NEGATIVE OUT-GROUP AFFECT

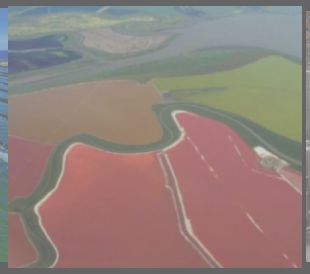
WHICH ENHANCEMENTS ARE IN FACT FEASIBLE? ETHICAL?

EMERGING APPLICATIONS

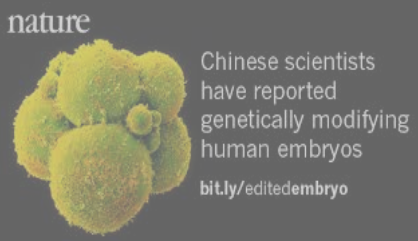
AGRICULTURE — GM Crops and Livestock — N Fixation, — Glowing Plants, Aquabounty

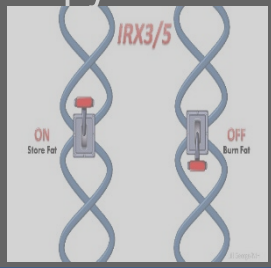
INDUSTRY — Synthesis of Organic Materials — Fuel, Flavors, Drugs





MEDICINE — Regenerative Medicine, Somatic and Germline Cell Therapy





ENVIRONMENT — Remediation; Control Vector Borne Disease and Invasive Species

Sciencexpress Policy Forum

Regulating gene drives

Kenneth A. Oye,[1,2*†] Kevin Esvelt,[3*] Evan Appleton,[4] Flaminia Catteruccia,[5,6] George Church,[3] Todd Kuiken,[7] Shlomiya Bar-Yam Lightfoot,[2] Julie McNamara,[2] Andrea Smidler,[5,8] James P. Collins[9]

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Regulatory gaps must be filled before gene drives could be used in the wild

Genes in sexually reproducing organisms normally have, on average, a 50% chance of being inherited, but some genes have a higher chance of being inherited. These genes can increase in relative frequency in a pop-

nome engineering that uses the CRISPR nuclease Cas9 to cut sequences specified by guide RNA molecules (5, 6). This technique is in widespread use and has already engineered the genomes of more than a dozen species. Cas9 may enable "RNA-guided gene drives" to edit nearly any gene in sexually reproducing populations (1).

To reduce potential negative effects in advance of construction and testing, Esvelt et al. have proposed several novel types of drives (1). Precision drives could exclusively affect particular species or subpopulations by targeting sequences unique to those groups. Immunizing drives could block the spread of unwanted gene drives by preemptively altering target sequences. Reversal drives could overwrite unwanted changes introduced by an initial drive or by conventional genome engineering, even restoring the original sequence. However, ecological effects would not necessarily be re-

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WHAT IS A GENE DRIVE ?

Mendelian: 50% odds genetic alteration will pass to next generation
IFF fitness or reproductive edge, THEN propagate

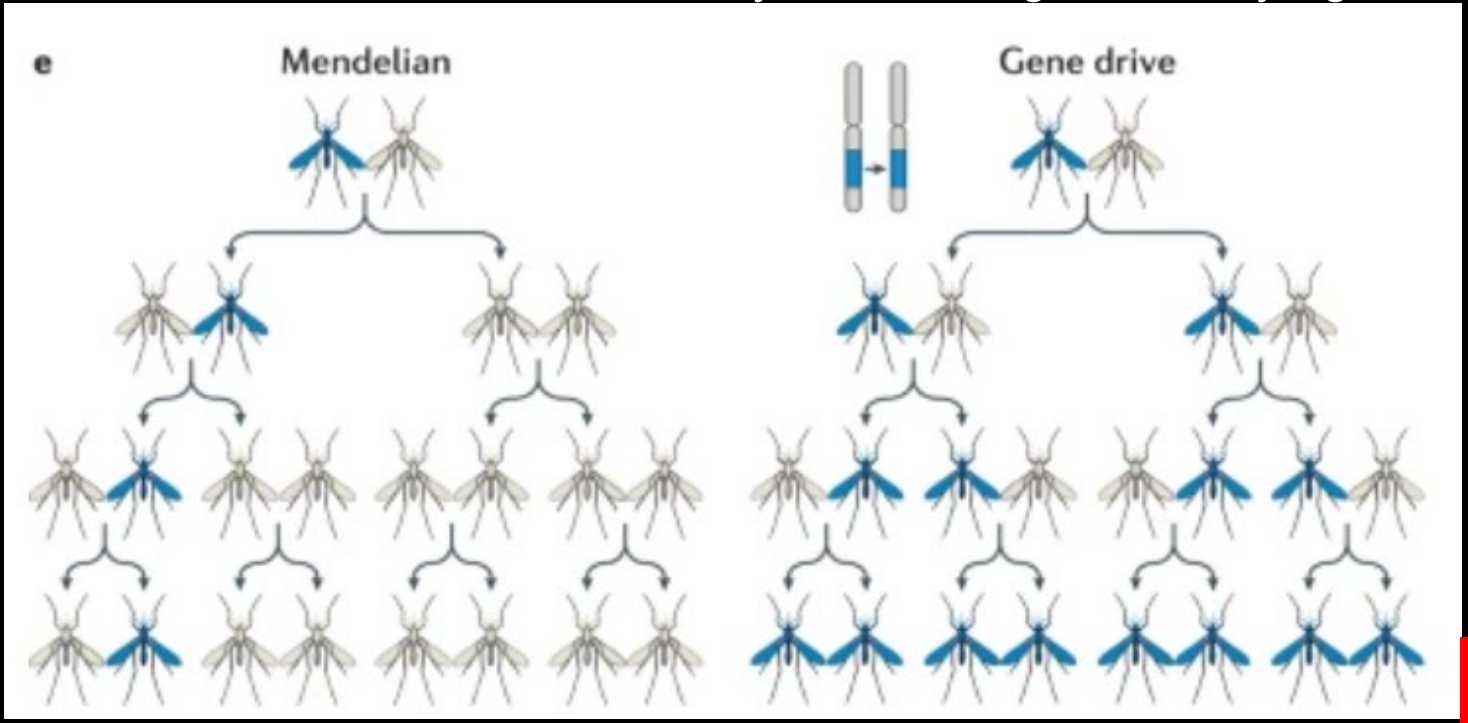
Gene drive: 99.5% odds alteration will pass to next generation (caveat)
Edit whole population without fitness or reproductive edge

FOR WHAT APPLICATIONS?

Environment: Control invasive species

Agriculture: Cut herbicide/pesticide resistance, eradicate pests

Health: Control vector borne diseases by eradicating or modifying vector



ENVIRONMENTAL ISSUES

Mutation of gene drives inevitable, will alter effects
Lateral gene transfer may reduce discrimination
Immunization and reversal may not be effective
Diseases borne by vectors will evolve
Environmental effects will vary by species and alteration

SECURITY ISSUES

Gain-of-function enabling ability to host diseases
Suppression of crops and livestock in traditional agriculture
Suppression of pollinators and other keystone species
Immunization drives may protect self and allies from effects
Reversal drives may be withheld for economic or political gain
Security implications uncertain - note ingenuity and creativity

(MOST) WIZARDS ARE ACTING RESPONSIBLY

Code of Conduct, Use IP to Enforce, Open Access to Data

RESEARCHERS CODE OF CONDUCT SCIENCE AUGUST 2015

BIOSAFETY

Safeguarding gene drive experiments in the laboratory

Multiple stringent confinement strategies should be used whenever possible

By **Omar S. Akbari[1,2], Hugo J. Bellen[3,4], Ethan Bier[5,*], Simon L. Bullock[6], Austin Burt[7], George M. Church[8,9], Kevin R. Cook[10], Peter Duchek[11], Owain R. Edwards[12], Kevin M. Esvelt[8,*], Valentino M. Gantz[5], Kent G. Golic[13], Scott J. Gratz[14], Melissa M. Harrison[15], Keith R. Hayes[16], Anthony A. James[17], Thomas C. Kaufman[10], Juergen Knoblich[11], Harmit S. Malik[18,19], Kathy A. Matthews[10], Kate M. O'Connor-Giles[14,20], Annette L. Parks[10], Norbert Perrimon[9,21], Fillip Port[6], Steven Russell[22], Ryu Ueda[23,24], Jill Wildonger[25]**

Gene drive systems promote the spread of genetic elements through popula-

fore used institutionally approved stringent barrier methods. Only one experimenter

research involving potential gene drive systems while formal national guidelines are developed. Although we cannot claim to represent all researchers, we share a commitment to the safe and responsible development of gene drive technology. Although we differ in our assessments of the types of precaution needed, we recognize that any single confinement strategy could fail. We therefore unanimously recommend that future studies use a combination of stringent confinement strategies (see the table) whenever possible and always use safeguards adequate for preventing the unintentional release of synthetic gene drive systems into natural populations.

RECOMMENDATIONS. RNA-guided gene drive systems are created by the germline a DNA cassette and a single synthetic guide RNA (sgRNA)

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Potentially stringent confinement strategies for gene drive research

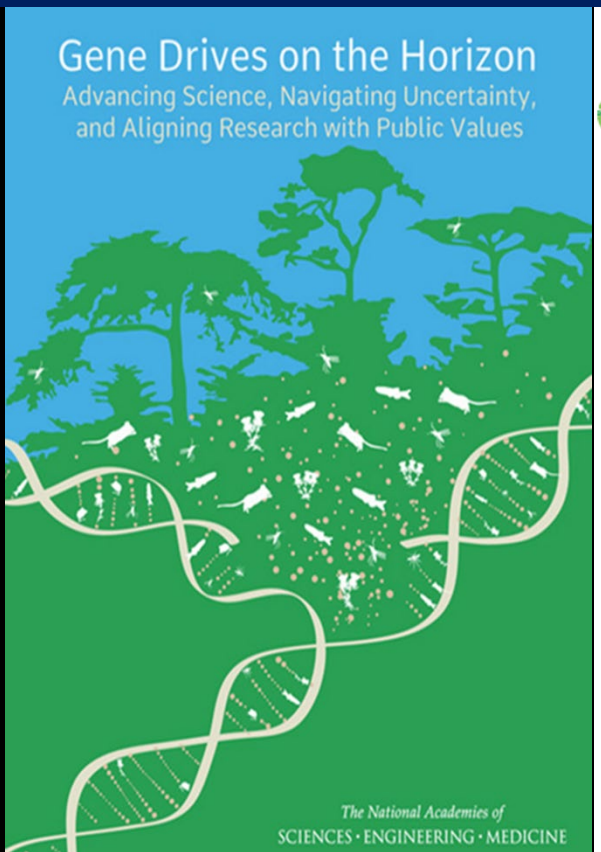
Multiple stringent confinement strategies should be used whenever possible.

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 outcrossed to any normal or wild-type strain because all progeny are monosomic or trisomic and die early in develop

ACADEMICS, GOVERNMENTS AND NGOS DELIBERATE

UN Biological Weapons Convention Meeting of Experts Geneva August 2014
International Experts Group on Biosecurity Regulation, Berlin 2015
National Academy of Sciences, Consensus Committee, Washington DC 2016
European Union Synergene Amsterdam, June 2016
OECD Gene Editing Workshop, Ottawa October 2016
IUCN World Conservation Congress Hawaii September 2016
UN Convention on Biodiversity COP13 Cancun December 2016
UN Convention on Biodiversity SBSTTA-22 and SBI-2 Montreal July 2018
NIH Novel and Exceptional Technologies Advisory Committee Gene Drive Group 2021
Outreach Network for Gene Drive Research August 2021



GOVERNING BENEFITS AND RISKS OF EMERGING BIOTECHNOLOGIES
RETROSPECTIVE AND CURRENT CASES
10:05-10:25 AM 17 FEBRUARY 2022

Professor Kenneth A. Oye
MIT Political Science and Data Systems and Society

OUTLINE

Risk Governance Under Uncertainty: Permissive, Precautionary, Adaptive

Retrospective and Current Biotechnology Cases

- Agriculture: Genetically Engineered Plants and Animals
- Industry: Synthesis of Biofuels, Fragrances, and Drugs
- Medicine: SCGT, Regenerative Medicine, HGGT
- Environment: Gene Drives

A Closing Conundrum: Governing Risks with Information Hazards

The research, conferences and workshops on which this presentaiton is based have been supported by the Netherlands Rijksinstituut voor Volksgezondheid en Milieu; the US Defense Advanced Research Projects Agency, US National Science Foundation Molecular and Cellular Biology, the MIT Center for Biomedical Innovation, the International Risk Governance Council and Richard Johnson.

INFORMATION HAZARDS: A CONUNDRUM

Information should be shared among biotechnology geeks to validate work and to provide building blocks for scientific advance.

Information should be shared with biosecurity policy wonks and biosafety officers to enable effective risk management.

Information should not be shared with malevolent or negligent actors to reduce the risk of harmful applications.

Compartmentalization of information is difficult / impossible.

Risk Analysis, Vol. 39, No. 5, 2019 DOI: 10.1111/risa.13235

Perspective

Information Hazards in Biotechnology

Gregory Lewis,[1,*] Piers Millett,[1] Anders Sandberg,[1] Andrew Snyder-Beattie,[1] and Gigi Gronvall[2]

With the advance of biotechnology, biological information, rather than biological materials, is increasingly the object of principal security concern. We argue that both in theory and in practice, existing security approaches in biology are poorly suited to manage hazardous biological information, and use the cases of Mousepox, H5N1 gain of function, and Botulinum toxin H to highlight these ongoing challenges. We suggest that mitigation of these hazards can be improved if one can: (1) anticipate hazard potential before scientific work is performed; (2) consider how much the new information would likely help both good and bad actors; and (3) aim to disclose information in the manner that maximally disadvantages bad actors versus

PAST EXAMPLES?
How to make mammal-to-mammal transmissible strains of avian flu (2012)

Airborne Transmission of Influenza A/H5N1 Virus Between Ferrets

SANDER HERFST, EEFJE J. A. SCHRAUWEN, MARTIN LINSTER, SALIN CHUTINIMITKUL, EMMIE DE WIT, VINCENT J. MUNSTER, ERIN M. SORRELL, THEO M. BESTEBROER, DAVID F. BURKE, [...] RON A. M. FOUCHIER +4 authors Authors Info & Affiliations

SCIENCE • 22 Jun 2012 • Vol 336, Issue 6088 • pp. 1534-1541 • DOI: 10.1126/science.1213362

Experimental adaptation of an influenza H5 HA confers respiratory droplet transmission to a reassortant H5 HA/H1N1 virus in ferrets

Masaki Imai, Tokiko Watanabe, Masato Hatta, Subash C. Das, Makoto Ozawa, Kyoko Shinya, Gongxun Zhong, Anthony Hanson, Hiroaki Katsura, Shinji Watanabe, Chengjun Li, Eiryo Kawakami, Shinya Yamada, Maki Kiso, Yasuo Suzuki, Eileen A. Mahe

Nature **486**, 420–428 (2012) | Cite this

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EDITORIAL
July/August 2020 Volume 11 Issue 4 e01868-20
https://doi.org/10.1128/mBio.01868-20

Rethinking Gain-of-Function Experiments in the Context of the COVID-19 Pandemic

Michael J. Imperiale [a], **Arturo Casadevall** [b]

[a]Department of Microbiology and Immunology, University of Michigan, Ann Arbor, Michigan, USA
[b]Department of Molecular Microbiology and Immunology, Johns Hopkins Bloomberg S
Health, Baltimore, Maryland, USA

CURRENT EXAMPLES?
How to synthesize horsepox (2018), How to make COVID variants (2021)

PLOS BIOLOGY

PLOS Biology | https://doi.org/10.1371/journal.pbio.3001091 February 25, 2021

METHODS AND RESOURCES

A plasmid DNA-launched SARS-CoV-2 reverse genetics system and coronavirus toolkit for COVID-19 research

PLOS ONE

Published: January 19, 2018 • https://doi.org/10.1371/journal.pone.0188453

RESEARCH ARTICLE

Construction of an infectious horsepox virus vaccine from chemically synthesized DNA fragments

Ryan S. Noyce[1], Seth Lederman[2], David H. Evans[1]*

1 Department of Medical Microbiology & Immunology and Li Ka Shing Institute of Virology, University of Alberta, Edmonton, Alberta, Canada, 2 Tonix Pharmaceuticals, Inc., New York, New York, United States of America

Technologists have a duty to engage with risks of their own work*
*Note: with info hazards responsible conduct is even more critical

Duty: Those proposing/conducting/funding research have a duty to evaluate actions with reference to both legal standards and ethical norms

Concrete Obligations that Follow from Duty:

101 Align own work with law/norms based on existing knowledge
201 Encourage others to align their work with laws/norms
301 Identify important gaps in knowledge and fill gaps through research
401 Identify gaps in legal coverage and join in debate on gaps

Engage <u>early</u> in order to allow time to:

101	Modify own work to fit law/norms	before tech designs lock in
201	Organize to improve conduct of others	before bad conduct locks in
301	Initiate research on benefits/risks	in time to inform choices
401	Evaluate and influence policy	before policy designs lock in

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