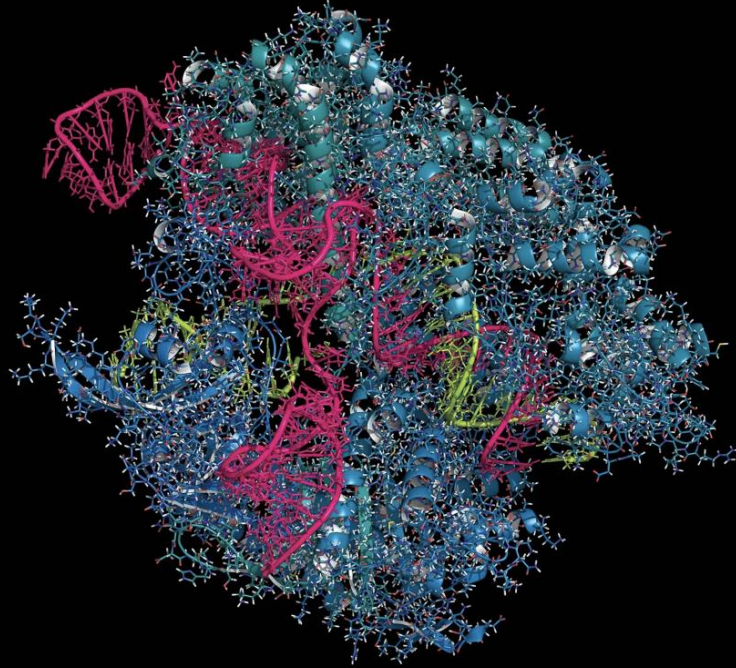


AUSTIN FORUM

ON TECHNOLOGY & SOCIETY

Connect. Collaborate. Contribute.™



Gene Editing: A 2024 Update with Dr. Ilya Finkelstein and Dr. Stephen C. Ekker

October 1, 2024

Welcome to the Austin Forum on Technology & Society!

We cover emerging, disruptive, and pervasive technologies to help you understand how these technologies will influence and impact society, and how you can be a positive contributor to that!



Bryan Port

Director

Center for Government & Civic Service

Austin Community College

bryan.port@austincc.edu

We have 6 ways to learn, share, connect!

Live monthly events	Online content
Presentation + Networking events • Expert presenter-focused • In-person and online—hybrid • Recording and slides posted online	Workshops • Offered by Austin Forum partners and friends • Free, or with special discounts for AF attendees • Designed to accelerate technical understanding, expertise
Meetup discussion events • Participatory for everyone • In-person <i>only</i> • Never recorded—speak freely!	Podcasts: Austin Forum Upload (<i>hiatus</i>) • Audio only • Conversation formats • Hosted in all major podcast stores, AF website
Book discussion events • Participatory for everyone • Online <i>only</i> • Never recorded—speak freely!	Slack Community, Website, Newsletter • Get updates and register for events • Learn more about the Austin Forum • Ask questions, share, etc. (Slack)

Our Partners Make Austin Forum Possible!

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AUSTIN FORUM
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Welcome to our newest annual partner!



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Before we get started, join our slack

Why join the Austin Forum Slack workspace?

- ✓ Continue and deepen the conversation after Austin Forum events
- ✓ Find new opportunities for collaboration, mentoring, working, and more
- ✓ Learn about other local events and relevant Tech & Society opportunities
- ✓ Because this gives *everyone* in our community—online and in-person—the *same* way to ask questions!

How?

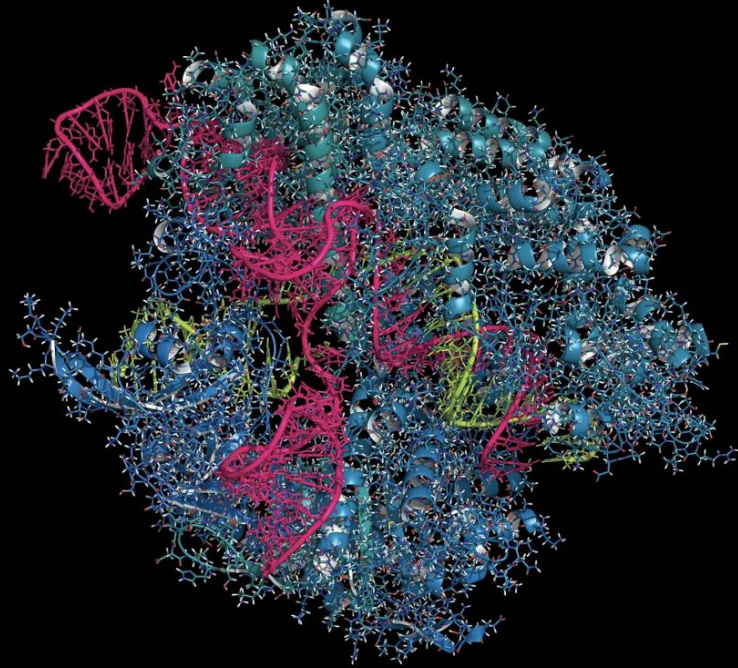
1. Open a web browser
2. Go to: www.austinforum.org/slack
3. Click “Join the Austin Forum Slack Workspace”
4. Enter your email address
5. Check your email to confirm Slack invitation
6. Enter your name and click “Create Account”
7. You’re in! You can use the Slack mobile app now, too.
8. Add channels to your view using **+ Add channels**)

And now, our featured presentation...

Please:

- ✓ *Respect our speakers & audience*
- ✓ *Ask questions* in the AF Slack in the **#event-questions** channel.
One person will win a SXSW badge!
- ✓ *Learn, think, and enjoy!*





Gene Editing: A 2024 Update with Dr. Ilya Finkelstein and Dr. Stephen C. Ekker

October 1, 2024

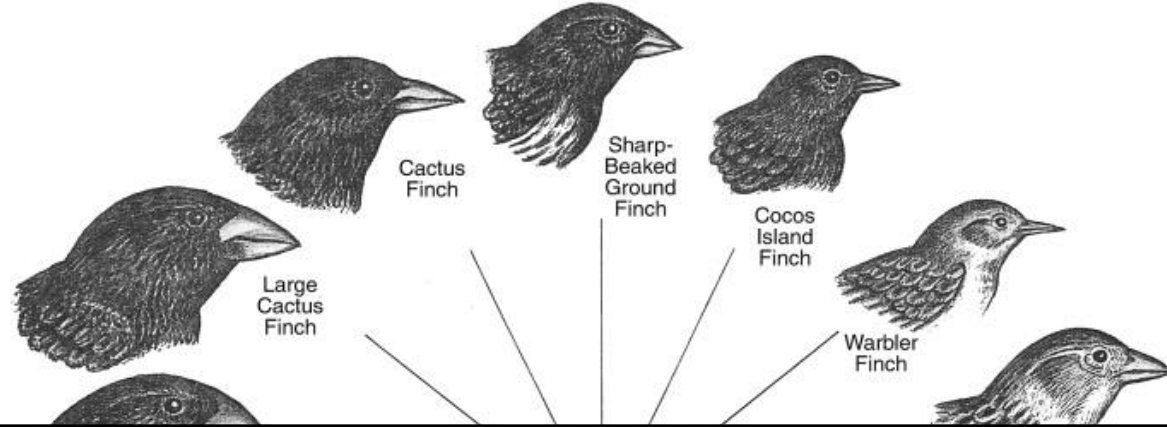
Gene Editing: A 2024 Update



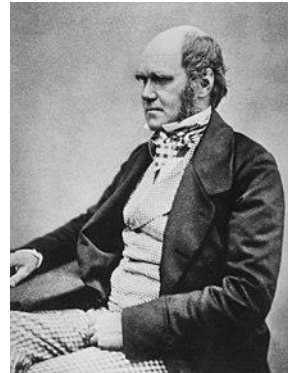
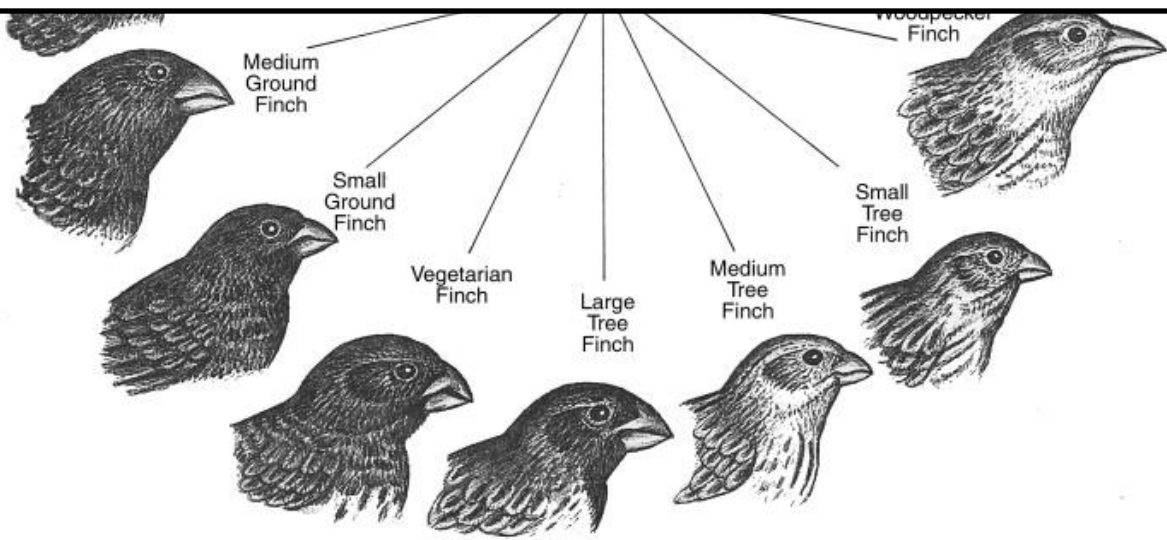
Dr. Ilya Finkelstein
The University of
Texas at Austin



Dr. Stephen C. Ekker,
The University of
Texas at Austin



Seeing this [...] diversity of structure in one small, intimately related group of birds, one might really fancy that [...] one species had been taken and modified for different ends.



The New York Times

Scientists Can Design 'Better' Babies. Should They?

Swift Gene-Editing Method May Revolutionize Treatments for Cancer and Infectious Diseases

NEWS | 30 November 2018

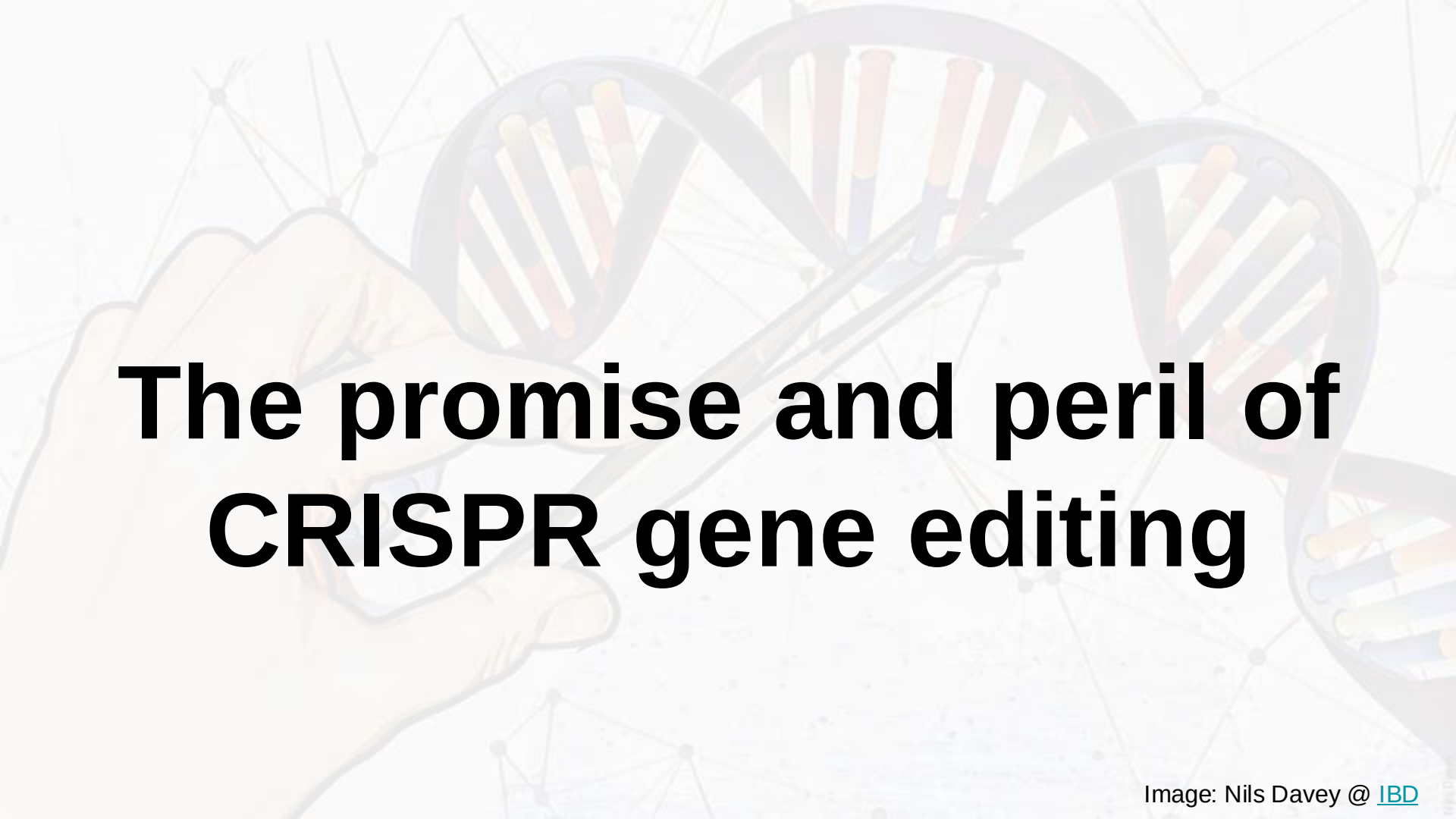
First CRISPR babies: six questions that remain

Startling human-genome editing claim leaves many open questions, from He Jiankui's next move to the future of the field.

The Economist

A new technique for manipulating genes holds great promise—but rules are needed to govern its use



The background features a stylized illustration of a hand holding a DNA double helix. The DNA structure is composed of two intertwined strands, one colored in shades of blue and purple, and the other in shades of orange and yellow. The hand is depicted in a light skin tone, with fingers gently gripping the DNA. The entire scene is set against a light gray background with a subtle pattern of interconnected lines and dots, suggesting a molecular or network structure.

The promise and peril of CRISPR gene editing

2013: CRISPR-Cas9 used to edit human cells

2013: Gene-edited mice

2015: Pigs resistant to swine flu

2017: Pigs for human organ transplants

2017: Viable edited human embryo (US)

2018: First human trials (US & Europe)

2021: First engineered humans born (HIV-resistant?)

2023: First CRISPR treatment for sickle cell disease

CRISPR



2014: Disease-resistant wheat

2015: Herbicide-tolerant canola

2022: Over 40 engineered crops

Image: Kelsey King @ [Ensia](#)



A humble beginning to the CRISPR age of biology

```
TGA AAATGGGA GGAGTTC TACCGCAGAGGCGGGGGA ACTC AAGTGATATCCATCATCGCATCCAGTGCGCC (1,451)
(1,452) CGGTTTATCCCCGCTGATGCGGGGGAACAC AGCGTCAGGCGTGAAATCTCACCGTCGTTGC (1,512)
(1,513) CGGTTTATCCCTGCTGGCGCGGGGGA ACTC CGGTT CAGGCGTTGCAAACCTGGCTACCGGG (1,573)
(1,574) CGGTTTATCCCCGCTAACGCGGGGGA ACTC TAGTCCATCATTCACCTATGTCTGAACTCC (1,634)
(1,635) CGGTTTATCCCCGCTGGCGCGGGGGA ACTC (1,664)
```

consensus: CGGTTTATCCCCGCT^{GG}_{AA}CGCGGGGGA ACTC

“An unusual structure was found ... Five highly homologous sequences of 29 nucleotides were arranged as direct repeats with 32 nucleotides as spacing.”



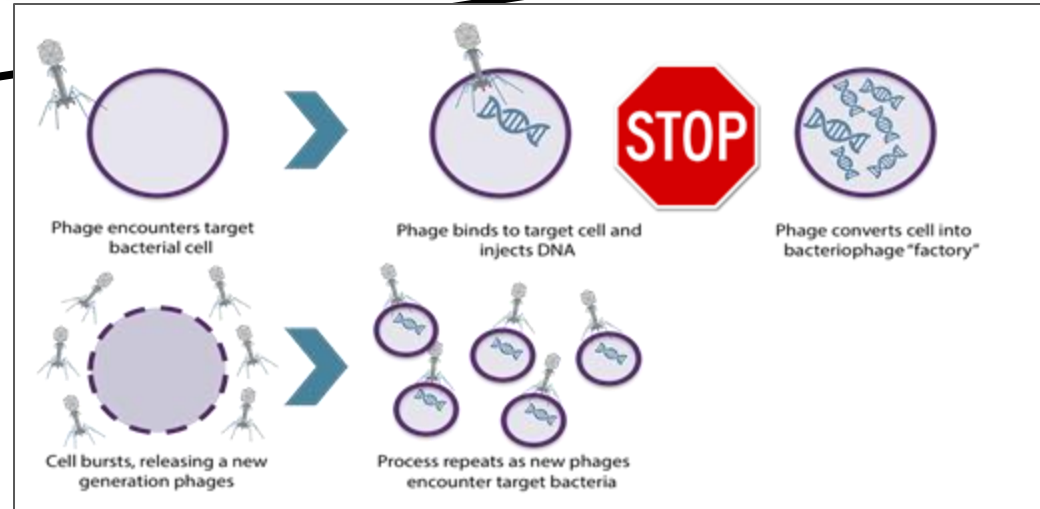
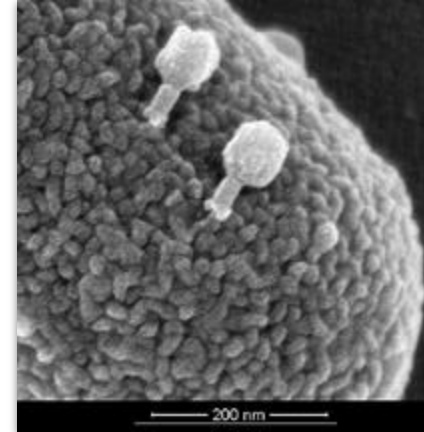
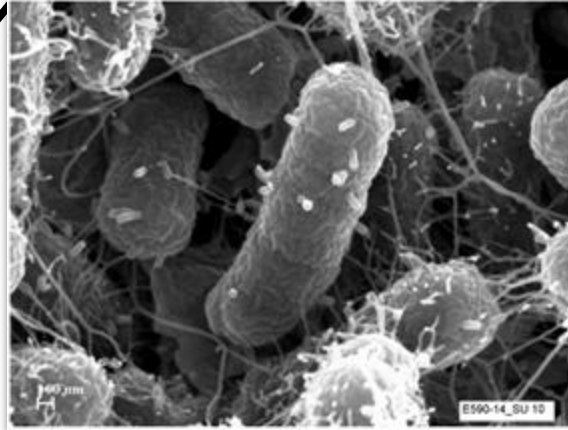
The authors suggest that spacers are the traces of past invasions by extrachromosomal elements, and hypothesize that they provide the cell immunity against [...] infection.

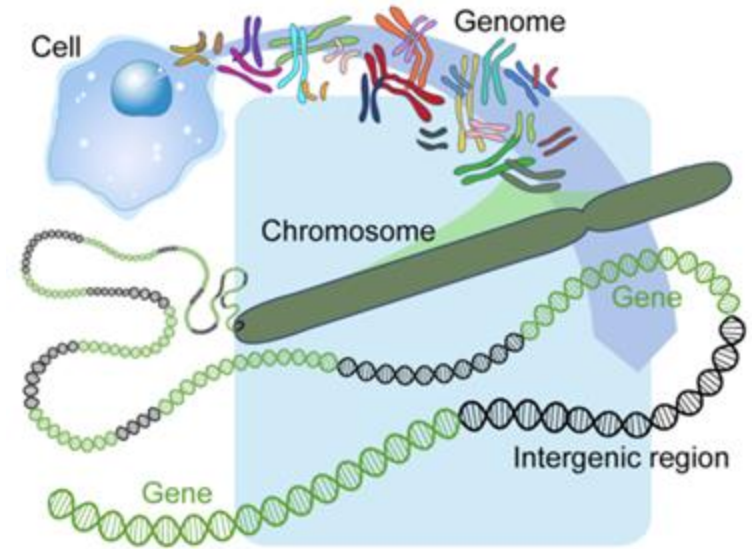
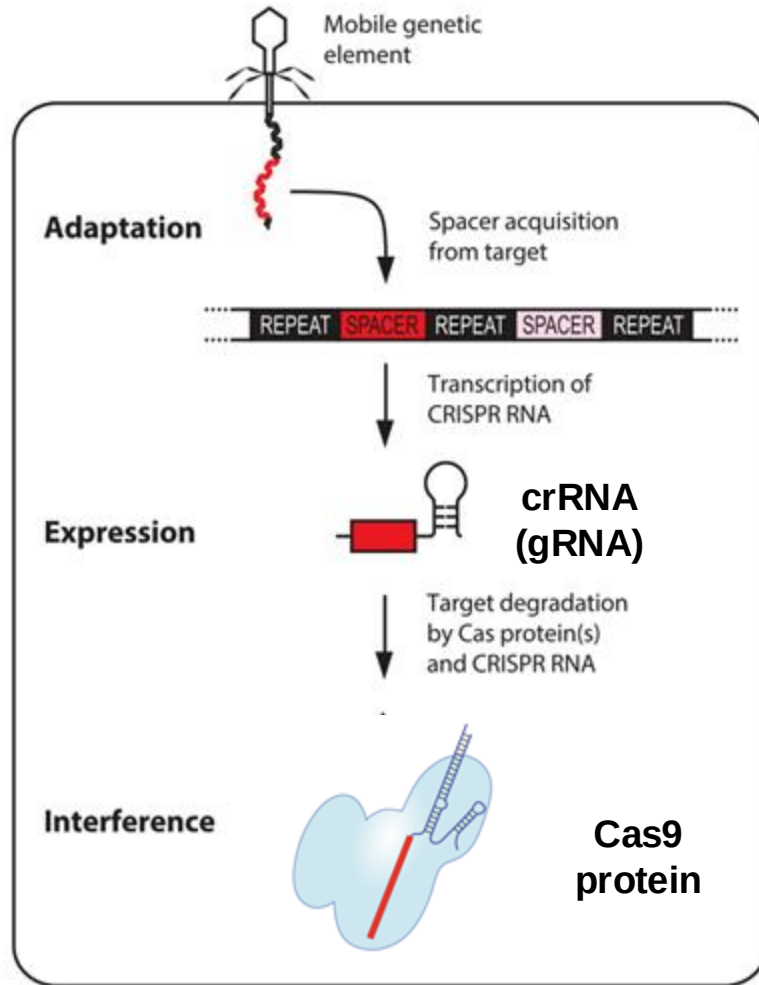
Fundamental curiosity-driven research is a public imperative!





DANISCO.





CRISPR-Cas proteins can be used in any organism!

- Gene knockout (deletion)
- Gene replacement (editing)
- Chromosome inactivation

Technical hurdles to genome editing

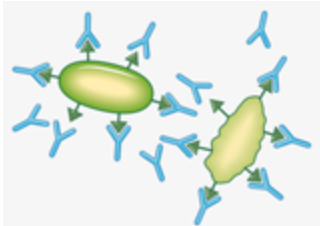
Unanticipated (off-target) edits

Species	T3 phage	Escherichia coli	Drosophila melanogaster	Homo sapiens	Paris japonica
Genome Size	170,000 bp	4.6 million bp	130 million bp	3.2 billion bp	150 billion bp
Common Name	 Virus	 Bacteria	 Fruit fly	 Human	 Canopy Plant

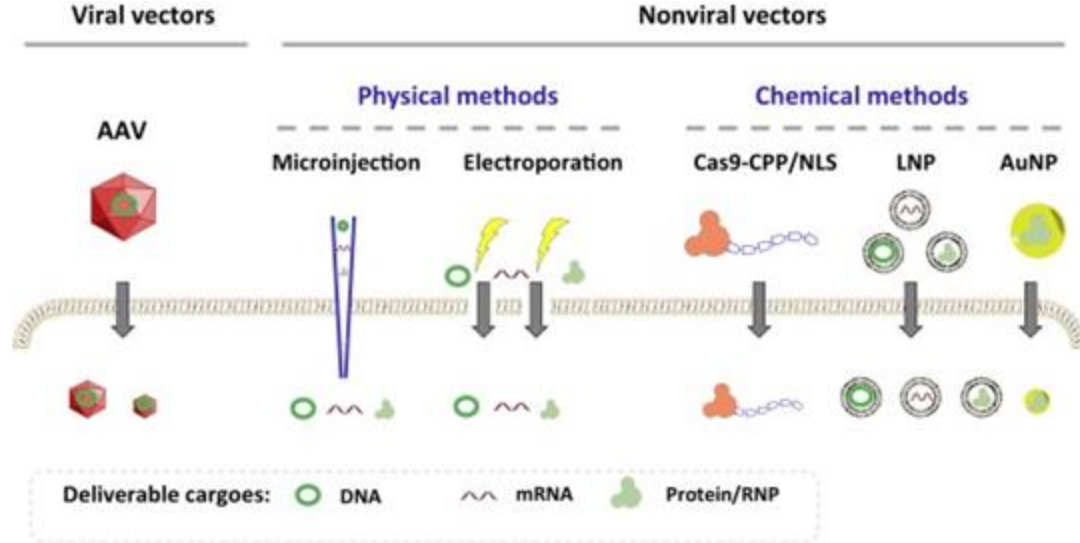
Solutions:

- Engineer/find more precise Cas9s
- Select target genes very carefully
- Verify all edits by other means

Unanticipated immune response

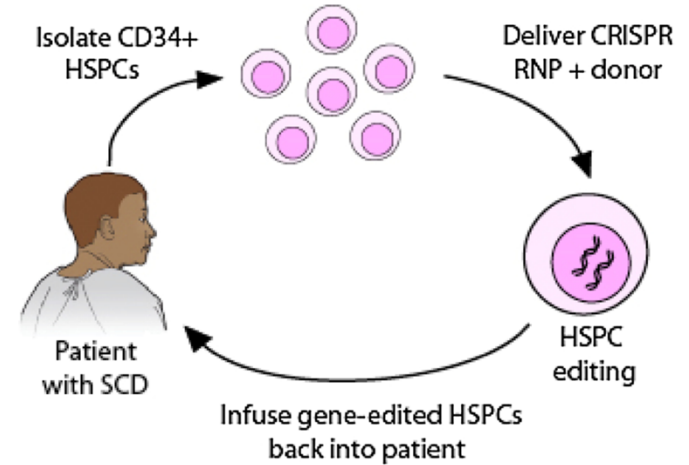


Delivery to cells



Cost

Victoria Gray: First sickle cell patient treated with CRISPR



Ex vivo engineering of hematopoietic stem and progenitor cells (HSPCs) followed by transplantation

Casgevy priced at \$2.2 million per patient in the US

Table 1. These 12 genomic therapies were selected from the FDA's list of 27 approved cellular and gene therapy (CGT) products, as of December, 16, 2022.

Therapy	Date Approved	Drug Description	Disease	Price
KYMRIA - Novartis Pharmaceuticals Corporation	8/30/2017	CD19-directed autologous CAR T-cells (ex vivo)	follicular lymphoma	\$475,000 [28]
YESCARTA - Kite Pharma, Inc. (Gilead)	10/18/2017	CD19-directed autologous CAR T-cells (ex vivo)	large B-cell lymphoma, a type of non-Hodgkin lymphoma	\$373,000 [29]

Can we afford these therapies?

Myers Squibb Company		(ex vivo)		
ABECMA - Celgene Corporation, a Bristol-Myers Squibb Company	3/26/2021	BCMA-directed autologous CAR T-cells (ex vivo)	multiple myeloma	\$419,500 [34]
CARVYKTI - Janssen Biotech, Inc.	2/28/2022	BCMA-directed autologous CAR T-cells (ex vivo)	multiple myeloma	\$465,000 [35]
ZYNTEGLO - bluebird bio, Inc.	8/17/2022	Autologous HSP cells modified with a LVV carrying a form of the β -globin gene (ex vivo)	β -thalassemia	\$2.8 M (USA) [36] \$1.8 M* (EU)
SKYSONA - bluebird bio, Inc.	9/16/2022	Autologous HSP cells modified with a LVV carrying a functional ABCD1 gene (ex vivo)	cerebral adrenoleukodystrophy	\$3.0 M [37]
HEMGENIX - CSL Behring LLC	11/22/2022	AAV carrying a form of the factor IX gene (in vivo)	Hemophilia B	\$3.5 M [38]
ADSTILADRIN - Ferring Pharmaceuticals A/S	12/16/2022	AAV carrying a functional interferon alfa-2b gene (in vivo)	Non-Muscle Invasive Bladder Cancer	not available

Only those FDA-approved therapies that derive their therapeutic effect as a result of modification to the human genome, including addition of a transgene, are included in this list. Imlygic (talimogene laherparepvec) from BioVex, Inc. was excluded as it did not squarely fit the criteria. Date approved corresponds to the date of the FDA's BLA approval letter. The drug description includes whether the genomic modification is executed in vivo or ex vivo.

CAR chimeric antigen receptors, AAV adeno-associated virus, HSP hematopoietic stem and progenitor, LVV lentiviral vector.

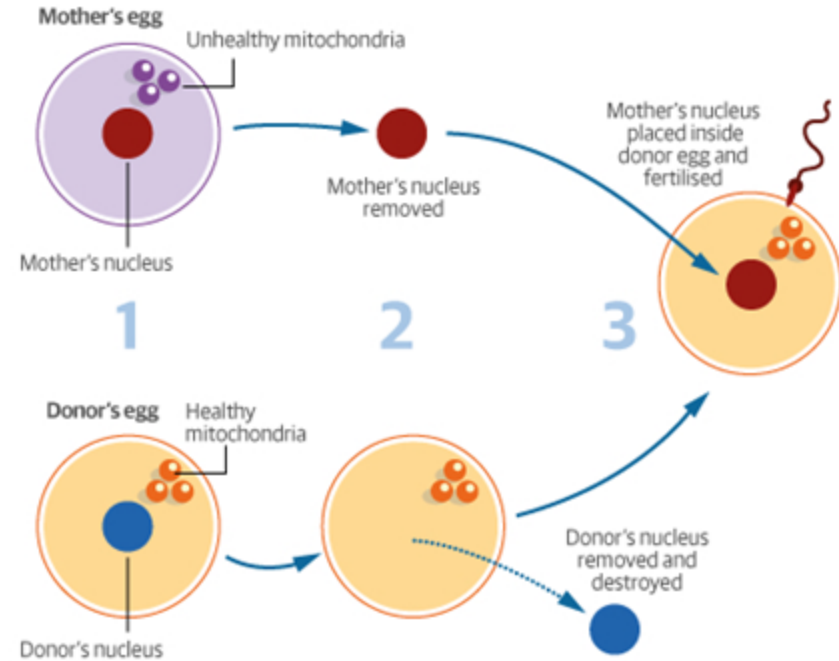
*After EMA approval and price setting, Bluebird Bio pulled out of the EU.

Future outlook: long term (5+ years)

- De novo “genome-write”
 - Already shown for viruses, bacteria, yeast
 - Human genome-write mostly a ‘cost’ problem
- Chromosome / genome transplant therapy
 - Synthetic genome transfer
- De-extinction of related species (?)
 - Woolly mammoth DNA in modern elephants
- Weaponized gene drives (?)

Method 2 Maternal spindle transfer

Repair is done before fertilisation



1978

NASA Scientist,
Dr David Brin asked:

**What if you could code
DNA like you can edit
text on a word
processor?**





- Therapy?
- Bioweapon?



- Both?

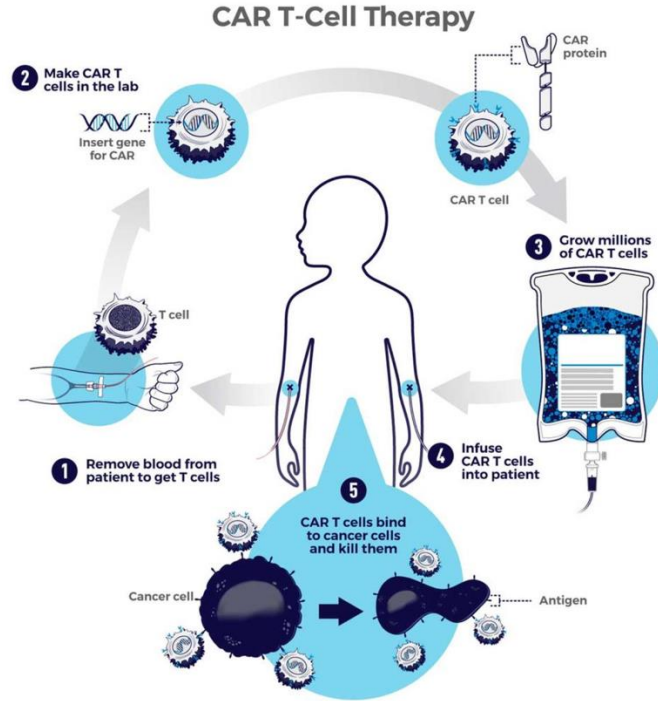
The Human Body is the Bottleneck for Therapies

- 37 Trillion 'Flash Drives' to 'edit'
- 1 per cell.



The Human Body is Also Amazing for Therapies

- By targeting key systems:
 - Blood (sickle cell disease)
 - Muscle (DMD)
 - Cancer (CAR-T)

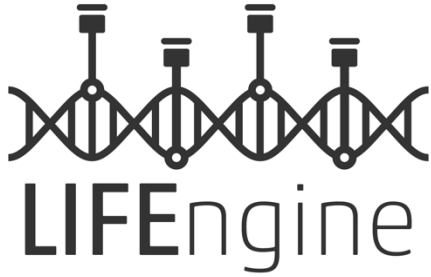


1985, Dr Carl Woese (UIUC) asked me:

**Why spend the rest of your life coding
computers...**

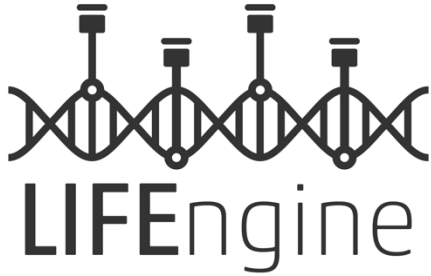
When you could code life?

Disclosures



Disclosures

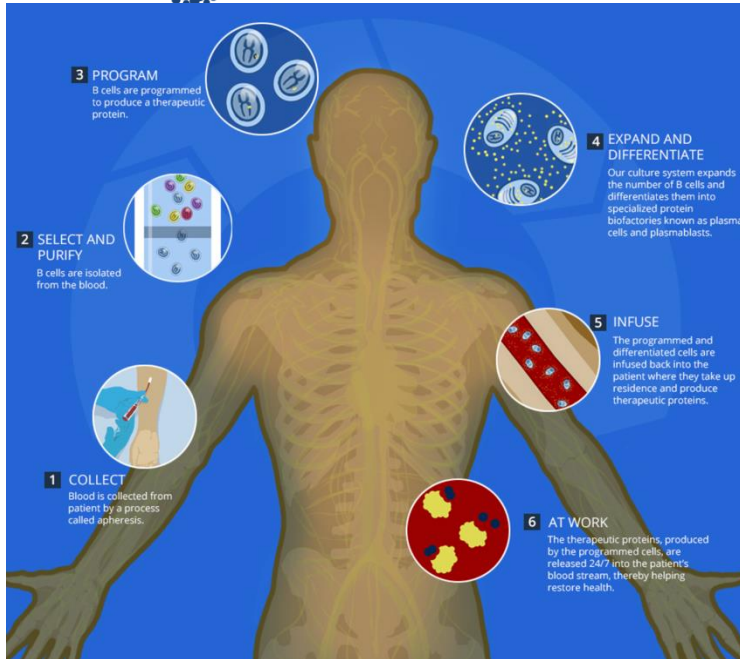
'Coding' life for Innovation & Impact



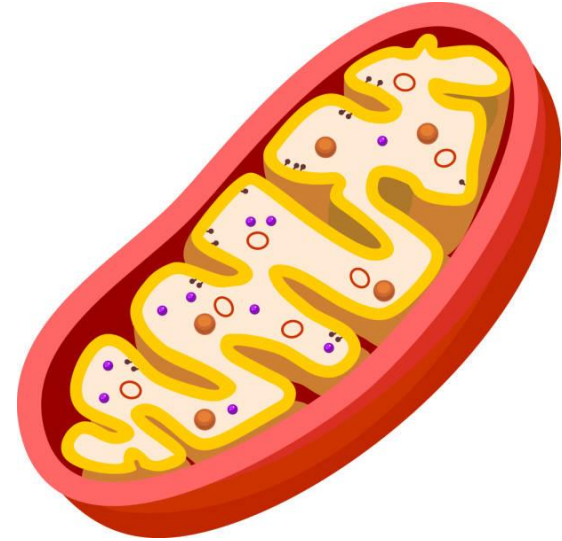
Rare Disease Therapies



IMMUSOFT



primera
THERAPEUTICS



Adding therapeutic genes to B Cells

Fixing Faulty Mitochondria

Curing Cancer in Pets and Their People

- Using Gene Editing and AI for Designing New Living Therapies



LEAH
LABORATORIES



Fighting Climate Change



Recombinetics: heat-tolerant Angus beef



Forjazul: Salt-tolerant seaweed

NASA Scientist,
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What are YOUR Answers?

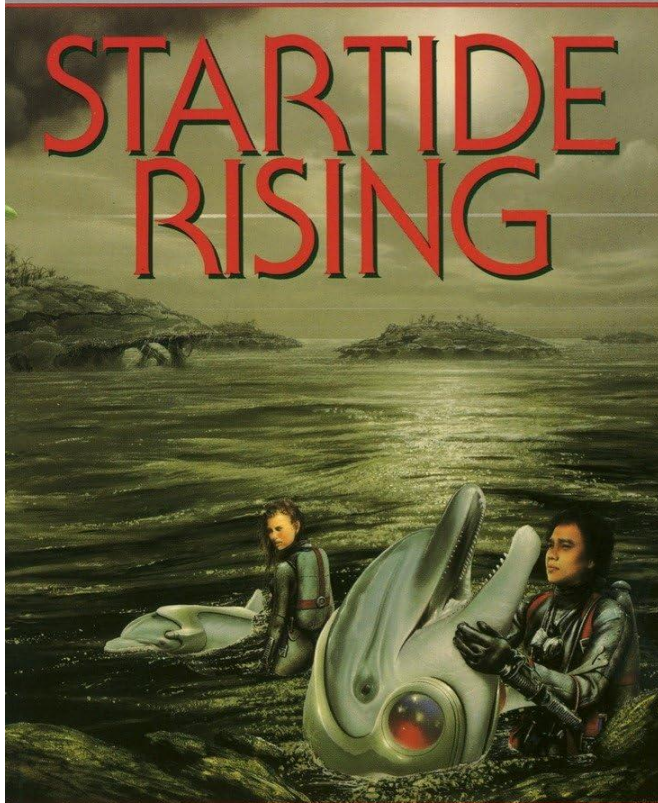
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BANTAM BOOKS
WINNER OF THE HUGO AND NEBULA AWARDS
DAVID BRIN
THE NEW YORK TIMES BESTSELLING AUTHOR OF *THE POSTMAN*



AN UPLIFT NOVEL

nature.com

24 September 2012



B. BEVAN/ARDEA.COM

Custom gene editing rewrites zebrafish DNA

A powerful approach that enables targeted genome editing in the zebrafish is demonstrated in *Nature* this week.

Latest news

- ▶ [NIH retires research chimps at troubled facility](#)
- ▶ [Chilean scientists oppose funding-agency relocation](#)
- ▶ [Outcry over jailed Russian chemist](#)

More news from [nature](#) ▶

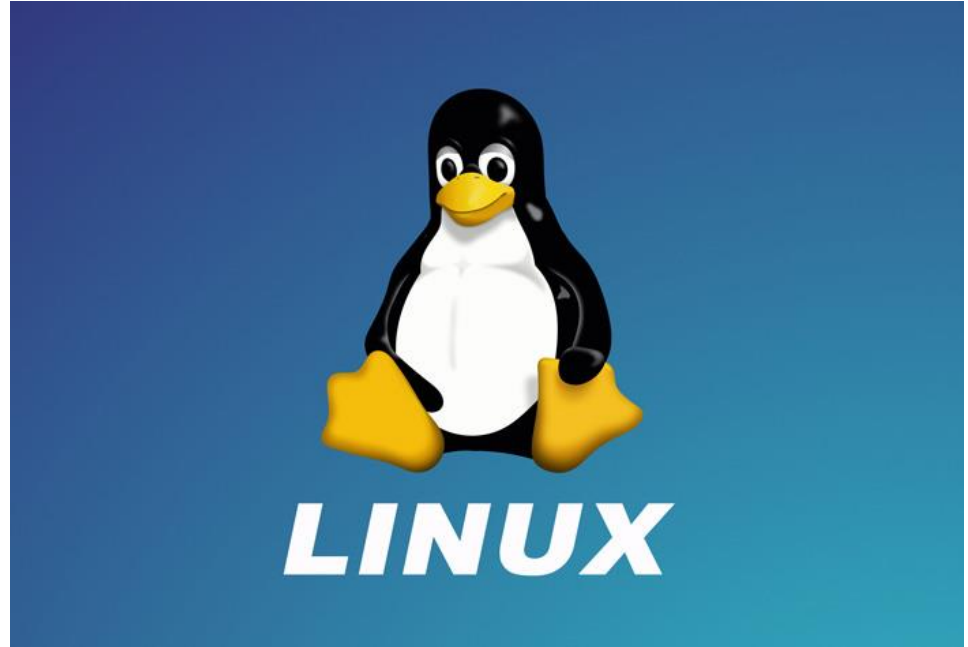
So what's next?



So what's next?



Great hardware



Open Source Software

So what's next?

- 'LINUX' for CRISPR

MEDTECH

Profluent combines LLMs and CRISPR for open-source AI gene editing project

By **Conor Hale** · Apr 23, 2024 2:00pm

CRISPR

Artificial Intelligence

generative AI

gene editing





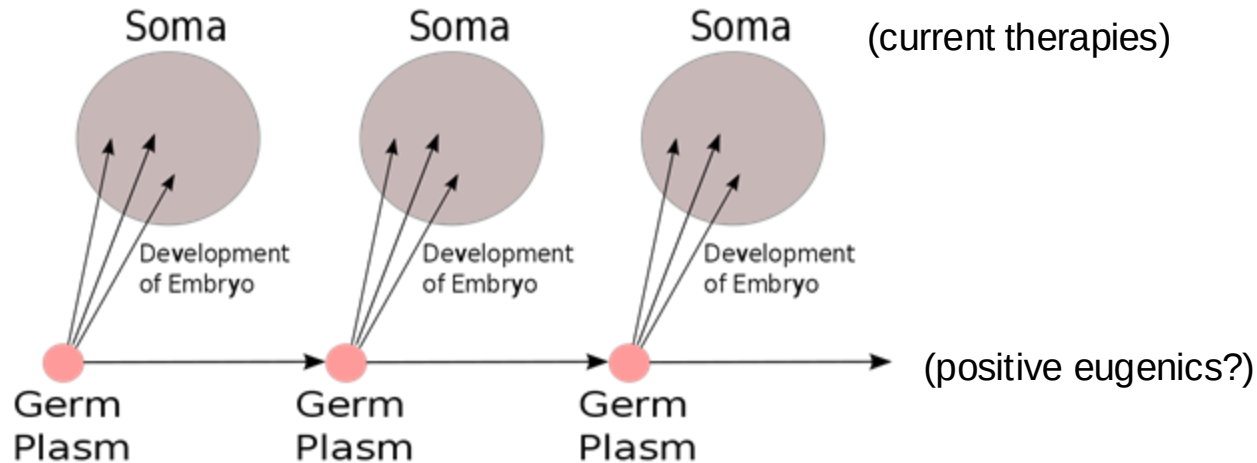
Ethics, Policy and CRISPR- Based Technology

Two Technologies

- **Gene editing:** CRISPR offers a more powerful technique than a host of earlier methodologies.
- **Gene drives:** how supra-Mendelian inheritance results in rapid spread of a gene in a population.

Ethics of Human Gene Editing

- Difference between germ-line and somatic cells.
- Weismann barrier:



Ethics of Somatic Cell Gene Editing

- If we accept modern medicine, there are no in-principle ethical problems.

Problem is safety and efficacy.

THE TIMES
December 19, 2007

Boy gets leukaemia after gene treatment to cure 'bubble baby syndrome'

- 3 year-old with X-linked severe combined immunodeficiency (X-SCID) - immune system fails to develop
- Treated with genetically modified virus to correct the faulty DNA that causes X-SCID
- Inserting the replacement DNA activated another gene that promotes cancer
- Now an acknowledged risk of gene therapy

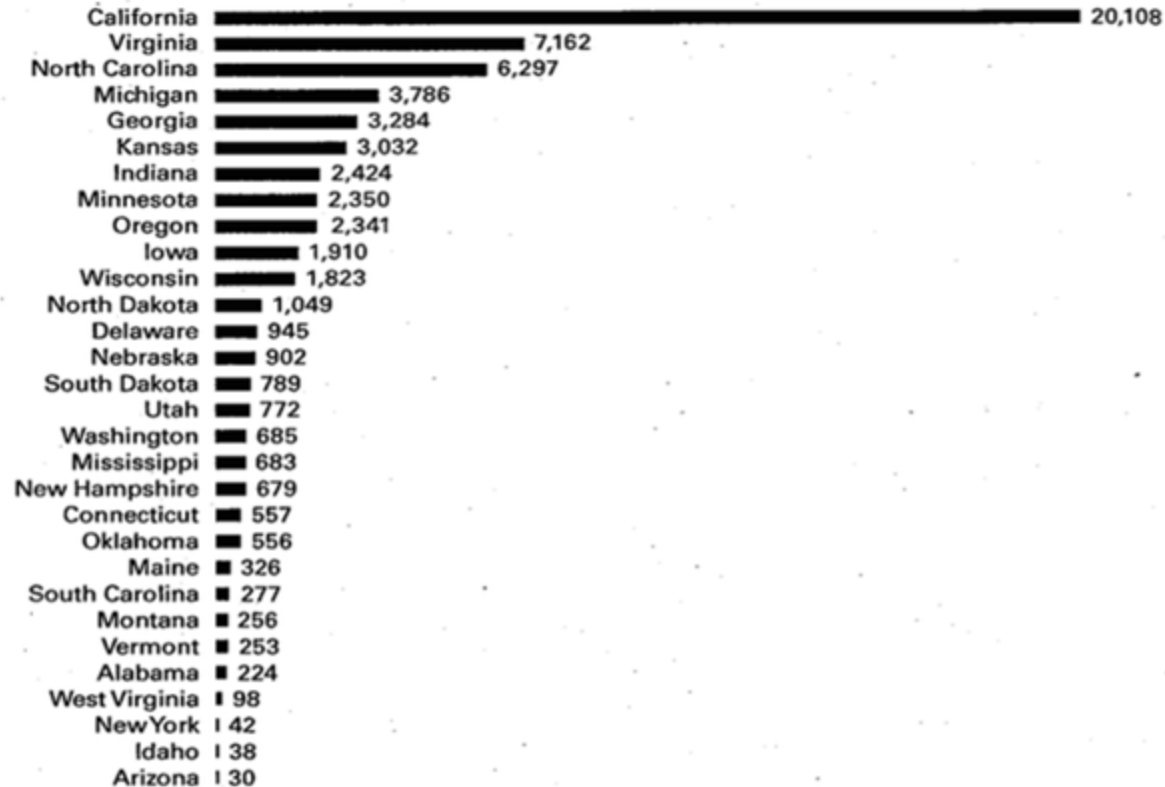
CLINICAL RESEARCH
Gene Therapy a Suspect In Leukemia-like Disease
Also seen in 4 / 11 patients in a French trial
One has died while 3 are in remission

Retrovirus vector

Germ-line editing: Burden of U.S. History

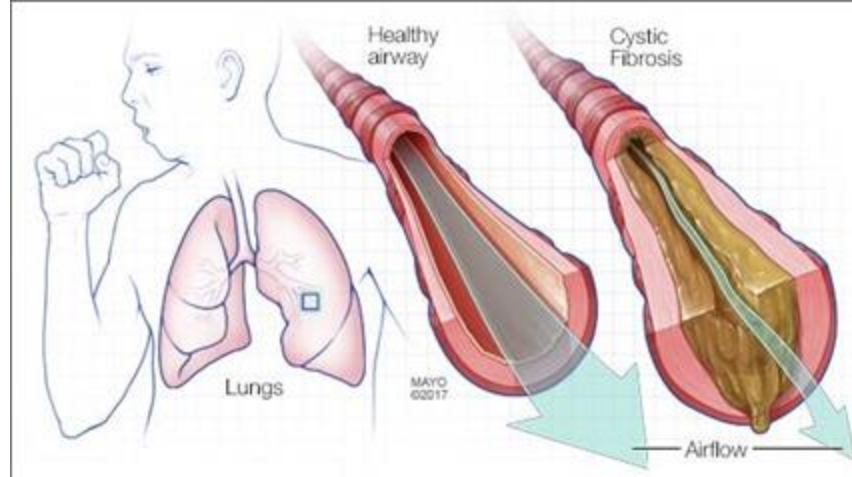


Context: Forced Sterilization in the U.S.



Negative versus Positive Eugenics

- **Negative eugenics:** Remove undesirable (e.g., disease) alleles from population.
- Elimination of genetic diseases from the human population?



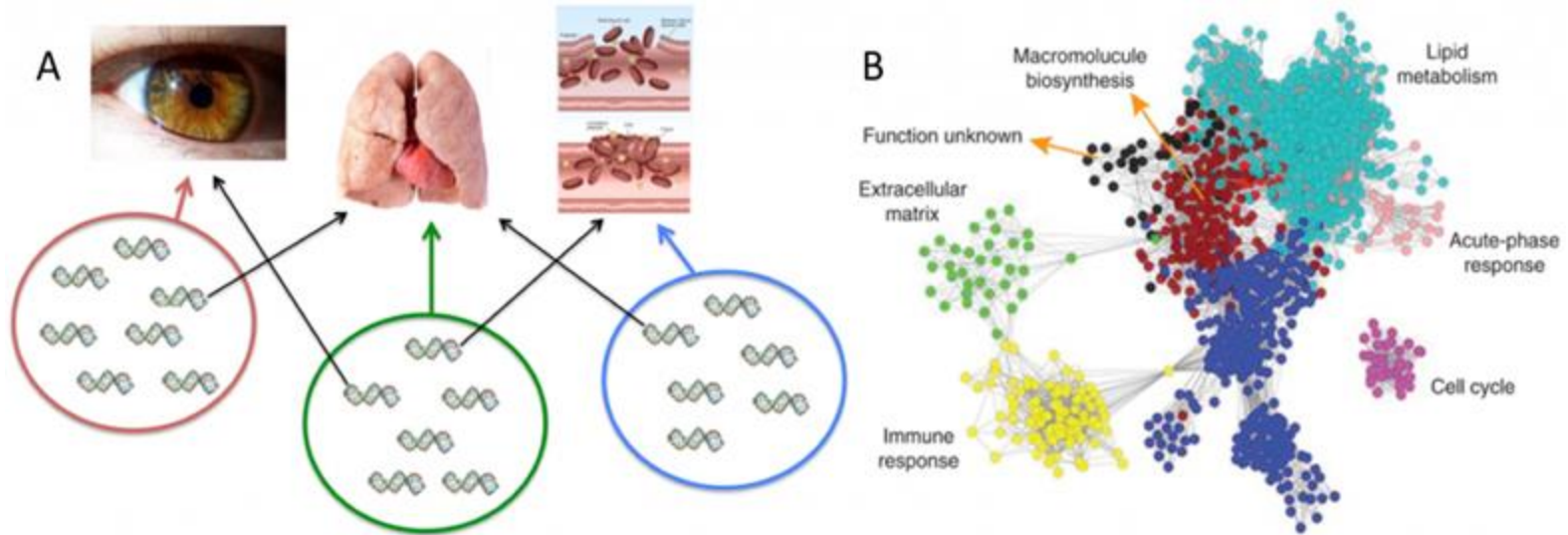
Positive Eugenics and Designer Babies: Who Decides?



Should We Select for Polydactyly?

Biology Makes Positive Eugenics Difficult

- Epistasis and Pleiotropy



Core Problem:



From *Science*.

Morals of the Story

- Somatic cell gene therapy is here, but at what cost?
- Germline gene therapy—deserves public discussion.
- Designer babies with enhanced traits?
 - Technically possible; extremely risky
 - Would you do it?

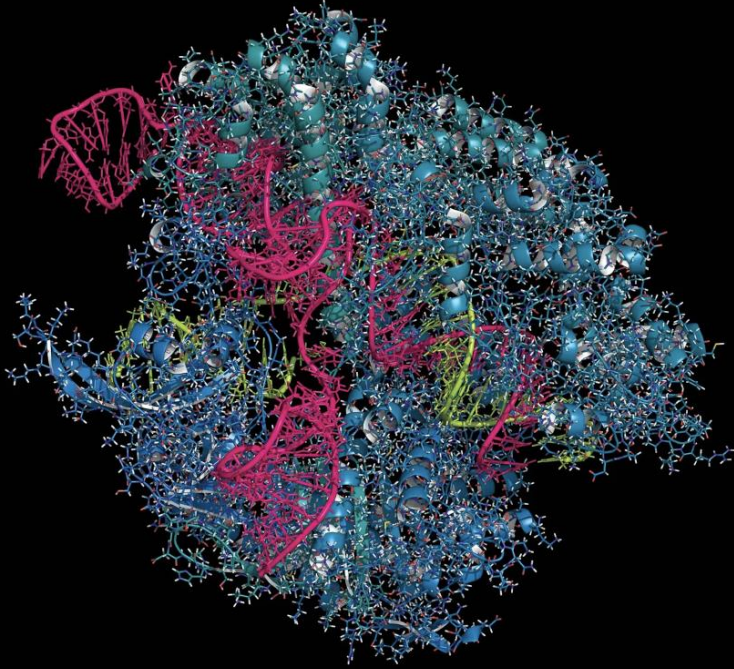


Thank you!



Stephen C. Ekker, PhD
stephen.ekker@gmail.com
[@scekker](#)

Ilya Finkelstein, PhD
ilya@finkelsteinlab.org



Q&A for

**Gene Editing: A 2024
Update with Dr. Ilya
Finkelstein and
Dr. Stephen C. Ekker**

***What was the most important thing you
learned tonight?*** (30 sec)

1 2 3 4 5 6 7 8 9 10

11 12 13 14 15 16 17 18 19 20

21 22 23 24 25 26 27 28 29



[← Back to All Events](#)

QUANTUM COMPUTING MEETUP

REGISTER

Thursday, October 3, 2024

6:30 PM – 8:30 PM

Remedy

360 Nueces Street, Austin, TX, 78701, United States

EVENT SUMMARY

Quantum computing promises the potential to solve tremendously challenging real-world problems that are unaddressable by traditional, or classical, computing machines today, tomorrow, and maybe forever. However, while the principles of quantum mechanics are well understood, building reliable, large-scale quantum computing presents tremendous engineering challenges. Furthermore, discovering optimal quantum computing algorithms and developing effective quantum computing applications is also important if quantum supremacy--or quantum advantage, or quantum value--compared to classical computing is to be achieved. Still, while we're in the early days of quantum computing, there are exciting developments and tantalizing results almost weekly that provide reasons for great optimism (and.

[← Back to All Events](#)

DISCUSSION OF "DIGITAL EMPIRES: THE GLOBAL BATTLE TO REGULATE TECHNOLOGY"

[REGISTER](#)

[AGENDA](#)

7:15 - 8:30 p.m. Discussion

[EVENT SUMMARY](#)

Moderated by Austin Forum executive director [Jay Boisseau](#). In "Digital Empires," Bradford argues that the world is on the cusp of a new era of geopolitical competition, one that will be fought over the control of data and technology. She identifies four digital empires—the United States, China, the European Union, and the United Kingdom—that are vying for dominance in this new realm.

Bradford's book is a timely and important contribution to our understanding of the global competition for

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Upcoming **presentation** topics include

- Smart cities & places
- Tech for health, happiness & helping
- Programming Quantum computers
- and more!!!

We are changing venues for the presentation events, to ACC Rio Grande in the Center for Government & Civic Service! (Free parking, streaming/recording, beer!)



Plus:

- In-person **meetups & workshops**
- Online **book discussions**
- **Podcasts**

Donate Your Unused Tech

- If you have computers, tablets, or smartphones no longer being used, please help those in need
- Bring your devices to any in-person event, and we'll donate to our worthy charities!



Austin Forum Team!



Jay Boisseau
Executive Director



Allison Warner
Managing Director



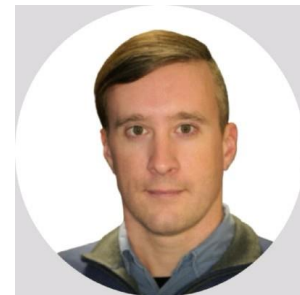
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Web/UX Designer



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Podcast Engineer



Chris Ashton
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and colleagues!*

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