

# DNA Surgery:

## Tales from the CRISPR Revolution



Kevin Davies PhD

Executive Editor, *The CRISPR Journal*;

Author, *Editing Humanity*

HSCO

Honolulu | 11.09.24

# AI IN PRECISION ONCOLOGY



Mary Ann Liebert, Inc. publishers

www.liebertpub.com/aipo

## DOUG FLORA, MD



AI in Precision Oncology  
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DOI: 10.1089/aipo.2023.28999.editorial

AI IN PRECISION ONCOLOGY

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## EDITORIAL

### Introducing *AI in Precision Oncology*

Douglas B. Flora\*

Welcome to *AI in Precision Oncology*, a pioneering peer-reviewed research journal rooted in the transformative power of artificial intelligence (AI) in oncology. This journal will serve as a robust platform for disseminating rigorous, groundbreaking, high-quality peer-reviewed research, review articles, and captivating frontmatter to support the interests, needs, and innovation in the field and industry.

My foremost goal as editor-in-chief, along with the goals of the incredible team of editorial board members, is to inform, innovate, and inspire. With this journal serving as a main resource in the field, we will support clinicians, researchers, AI experts, patients, and industry leaders with up-to-date advancements in the field while fostering an environment conducive to further innovation and collaboration. The genesis of the journal is fundamentally linked to my personal commitment to improving cancer care across the field by supporting AI-enabled health care systems that are accessible, efficient, and, most importantly, effective for everyone.

Along with this, *AI in Precision Oncology* will serve as a catalyst between worlds. The fusion of both AI-enabled technologies and precision oncology is advancing at an unprecedented pace; however, a divide currently exists between these technological strides and their pragmatic integration into clinical settings. Clinicians, rightly so, require a trove of evidence-based research to acquaint themselves with AI tools and understand the methodologies to incorporate them into their practice. With this journal serving as a foremost resource, and the exceptional research-based content we will provide to the community, we aspire to bridge this divide.

Furthermore, *AI in Precision Oncology* will serve as an educational compass for health care professionals who might be unacquainted with AI. The journal will provide

review articles, commentaries, tutorials, tools, protocols, and thought-leader profiles to inform health care professionals and allow a better understanding of the available tools and how to implement them and integrate them into their own clinical practices. AI can afford health care providers the luxury of time by automating time-consuming tasks that do not necessitate a human touch, such as data analysis or administrative chores.

Clinicians can then direct their time toward engaging more meaningfully with patients, improving patient satisfaction, and enhancing the quality of care by enabling more comprehensive and personalized consultations.

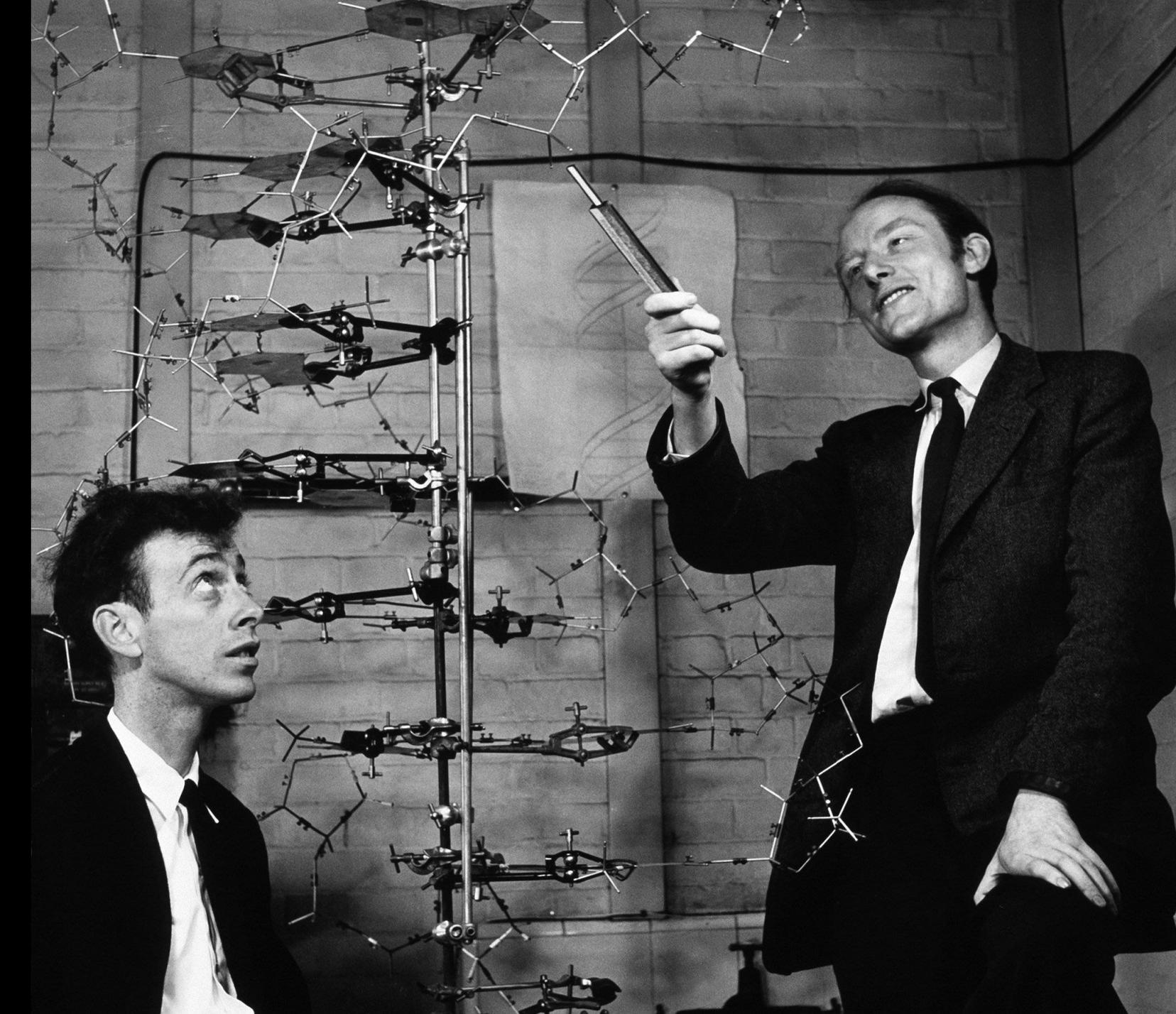
Our goal is to bring together researchers, clinicians, and industry experts to share their knowledge and experience in this rapidly evolving field. We warmly welcome a variety of article formats including original research articles, reviews, and perspectives on applying AI in cancer research, diagnosis, and treatment. Some of our key areas of interest include (but are not limited to):

- AI algorithms for cancer detection, diagnosis, and prognosis
- AI-based biomarkers for cancer screening and diagnosis
- AI-assisted imaging analysis for tumor detection and segmentation
- AI-guided treatment planning and personalized therapy
- AI-enabled drug discovery and development
- Machine learning and deep learning in cancer research
- Natural language processing for electronic health record analysis
- Ethical and regulatory issues in AI in precision oncology

# The Human Genome



Cas Kramer  
(Univ Leicester)



equipment, and to Dr. G. E. R. Deacon and the captain and officers of R.R.S. *Discovery II* for their part in making the observations.

- <sup>1</sup> Young, F. B., Gerrard, H., and Jevons, W., *Phil. Mag.*, **40**, 149 (1920).
- <sup>2</sup> Longuet-Higgins, M. S., *Mon. Not. Roy. Astr. Soc., Geophys. Supp.*, **5**, 285 (1949).
- <sup>3</sup> Von Arx, W. S., *Woods Hole Papers in Phys. Oceanog. Meteor.*, **11** (3) (1950).
- <sup>4</sup> Ekman, V. W., *Arkiv. Mat. Astron. Fysik. (Stockholm)*, **2** (11) (1905).

## MOLECULAR STRUCTURE OF NUCLEIC ACIDS

### A Structure for Deoxyribose Nucleic Acid

WE wish to suggest a structure for the salt of deoxyribose nucleic acid (D.N.A.). This structure has novel features which are of considerable biological interest.

A structure for nucleic acid has already been proposed by Pauling and Corey<sup>1</sup>. They kindly made their manuscript available to us in advance of publication. Their model consists of three intertwined chains, with the phosphates near the fibre axis, and the bases on the outside. In our opinion, this structure is unsatisfactory for two reasons: (1) We believe that the material which gives the X-ray diagrams is the salt, not the free acid. Without the acidic hydrogen atoms it is not clear what forces would hold the structure together, especially as the negatively charged phosphates near the axis will repel each other. (2) Some of the van der Waals distances appear to be too small.

Another three-chain structure has also been suggested by Fraser (in the press). In his model the phosphates are on the outside and the bases on the inside, linked together by hydrogen bonds. This structure as described is rather ill-defined, and for this reason we shall not comment on it.

We wish to put forward a radically different structure for the salt of deoxyribose nucleic acid. This structure has two helical chains each coiled round the same axis (see diagram). We have made the usual chemical assumptions, namely, that each chain consists of phosphate diester groups joining  $\beta$ -D-deoxyribofuranose residues with 3',5' linkages. The two chains (but not their bases) are related by a dyad perpendicular to the fibre axis. Both chains follow right-handed helices, but owing to the dyad the sequences of the atoms in the two chains run in opposite directions. Each chain loosely resembles Furberg's<sup>2</sup> model No. 1; that is, the bases are on the inside of the helix and the phosphates on the outside. The configuration of the sugar and the atoms near it is close to Furberg's 'standard configuration', the sugar being roughly perpendicular to the attached base. There



This figure is purely diagrammatic. The two ribbons symbolize the two phosphate-sugar chains, and the horizontal rods the pairs of bases holding the chains together. The vertical line marks the fibre axis.

is a residue on each chain every 3.4 Å. in the z-direction. We have assumed an angle of 36° between adjacent residues in the same chain, so that the structure repeats after 10 residues on each chain, that is, after 34 Å. The distance of a phosphorus atom from the fibre axis is 10 Å. As the phosphates are on the outside, cations have easy access to them.

The structure is an open one, and its water content is rather high. At lower water contents we would expect the bases to tilt so that the structure could become more compact.

The novel feature of the structure is the manner in which the two chains are held together by the purine and pyrimidine bases. The planes of the bases are perpendicular to the fibre axis. They are joined together in pairs, a single base from one chain being hydrogen-bonded to a single base from the other chain, so that the two lie side by side with identical z-coordinates. One of the pair must be a purine and the other a pyrimidine for bonding to occur. The hydrogen bonds are made as follows: purine position 1 to pyrimidine position 1; purine position 6 to pyrimidine position 6.

If it is assumed that the bases only occur in the structure in the most plausible tautomeric forms (that is, with the keto rather than the enol configurations) it is found that only specific pairs of bases can bond together. These pairs are: adenine (purine) with thymine (pyrimidine), and guanine (purine) with cytosine (pyrimidine).

In other words, if an adenine forms one member of a pair, on either chain, then on these assumptions the other member must be thymine; similarly for guanine and cytosine. The sequence of bases on a single chain does not appear to be restricted in any way. However, if only specific pairs of bases can be formed, it follows that if the sequence of bases on one chain is given, then the sequence on the other chain is automatically determined.

It has been found experimentally<sup>3,4</sup> that the ratio of the amounts of adenine to thymine, and the ratio of guanine to cytosine, are always very close to unity for deoxyribose nucleic acid.

It is probably impossible to build this structure with a ribose sugar in place of the deoxyribose, as the extra oxygen atom would make too close a van der Waals contact.

The previously published X-ray data<sup>5,6</sup> on deoxyribose nucleic acid are insufficient for a rigorous test of our structure. So far as we can tell, it is roughly compatible with the experimental data, but it must be regarded as unproved until it has been checked against more exact results. Some of these are given in the following communications. We were not aware of the details of the results presented there when we devised our structure, which rests mainly though not entirely on published experimental data and stereochemical arguments.

It has not escaped our notice that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material. Full details of the structure, including the conditions assumed in building it, together with a set of co-ordinates for the atoms, will be published elsewhere.

We are much indebted to Dr. Jerry Donohue for constant advice and criticism, especially on interatomic distances. We have also been stimulated by a knowledge of the general nature of the unpublished experimental results and ideas of Dr. M. H. F. Wilkins, Dr. R. E. Franklin and their co-workers at

“My Dear Michael...

19 March 1953

In other words I think we have found the basic copying mechanism by which life comes from life.

The beauty of our model is that the shape of it is such that only these pairs can go together, though they could pair up in other ways if they were floating about freely. You can understand that we are very excited. We have to have a letter to Nature in a day or so.

~~Read~~ Read this carefully so that you understand it. When you come home we will show you the model.

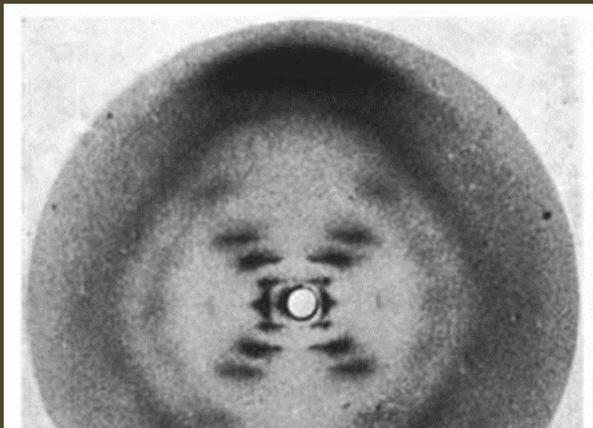
lots of love,  
Daddy

“Jim Watson and I have probably made a most important discovery...

Our structure is very beautiful. D.N.A. can be thought of roughly as a very long chain with flat bits sticking out. The flat bits are called the ‘bases’...”



**NICOLE KIDMAN**  
returns to the London stage  
in  
**PHOTOGRAPH 51**  
a new play by Anna Ziegler



Photograph 51



Rosalind Franklin  
(1920-1958)



# THE FASTEST DNA SEQUENCING >>> TECHNIQUE

## Who

**EUAN ASHLEY, ULTRA-RAPID  
GENOME TEAM**

## Where

**UNITED STATES (STANFORD)**

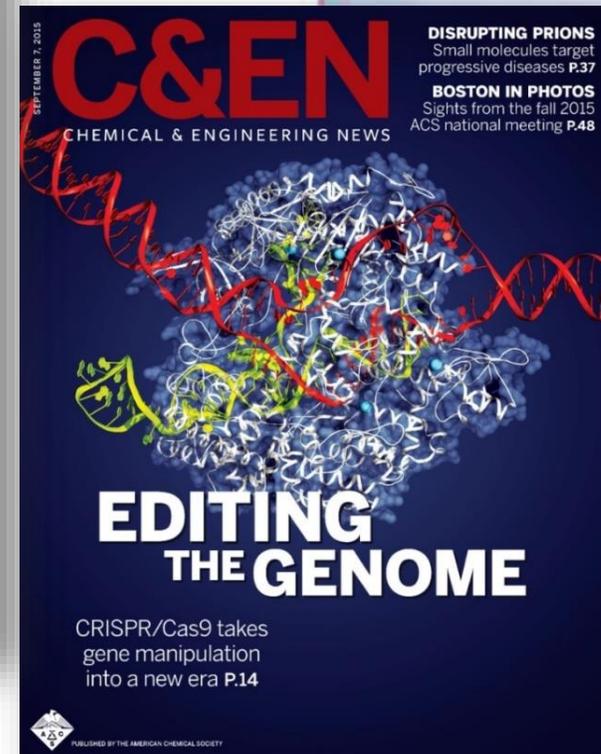
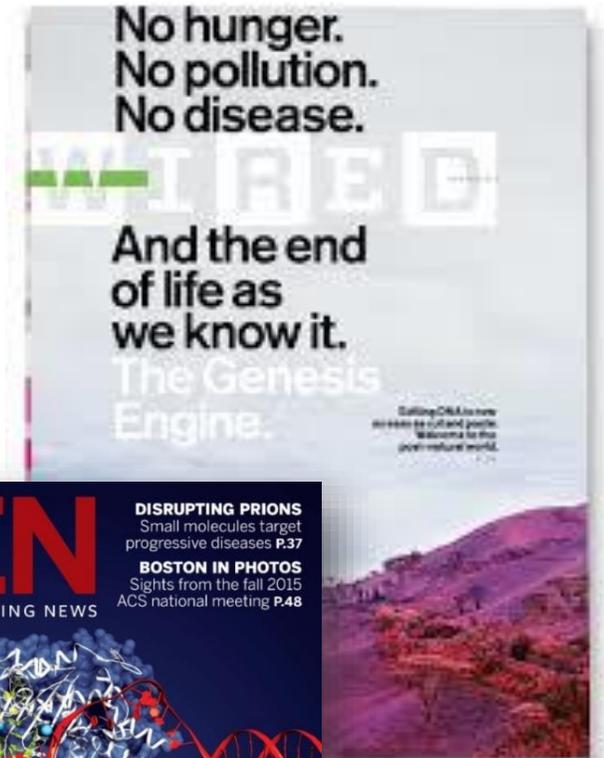
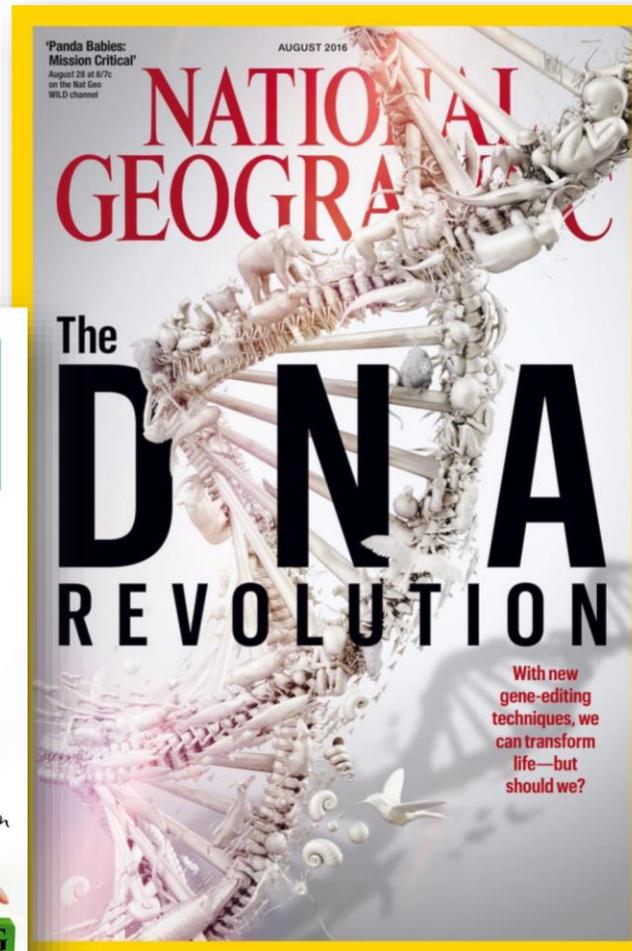
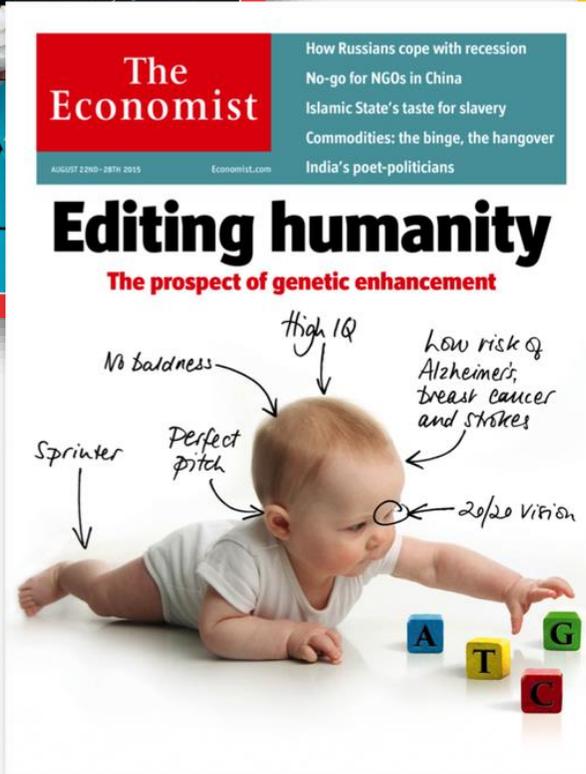
## What

**05:02:00  
HOUR(S):MINUTE(S):SECOND(S)**

## When

**16 MARCH 2021**

# CRISPR





In 1993, a breakthrough new technology, known as CRISPR, gave scientists a path to treat incurable diseases through genetic editing.

In 2016, due to its potential for misuse, the U.S. Intelligence Community designated genetic editing a 'Weapon of Mass Destruction and Proliferation.'

BIG  
MEETS  
BIGGER

DWAYNE JOHNSON  
**RAMPAGE**

SEE IT IN REALD 3D AND IMAX

APRIL 20

+ ADD TO CALENDAR

*“Are you familiar with CRISPR?”*

Jeopardy! November 29, 2019

**JENNIFER DOUDNA &  
EMMANUELLE  
CHARPENTIER  
ARE CO-INVENTORS OF  
THE REVOLUTIONARY  
TOOL CRISPR TO EDIT  
THESE IN THE BODY**



The Nobel Prize  
in Chemistry 2020  
awarded jointly to

Emmanuelle  
Charpentier  
&  
Jennifer A.  
Doudna

"for the development  
of a method for  
genome editing."

October 7, 2020



# An “unusual arrangement” in *E. coli* (1987)



Clustered Regularly Interspaced Short Palindromic Repeats



**Francisco Mojica PhD**  
(University of Alicante)  
Salterns of Santa Pola, Spain

**Asunto: Re: Acronym**

**Fecha:** Wed, 21 Nov 2001 16:39:06 +0100

**De:** "Ruud Jansen" <R.Jansen@vet.uu.nl>

**Empresa:** Diergeneeskunde

**A:** "Francisco J. Martínez Mojica" <fmojica@ua.es>

Dear Francis

What a great acronym is CRISPR.

I feel that every letter that was removed in the alternatives made it less crispy so I prefer the snappy CRISPR over SRSR and SPIDR. Also not unimportant is the fact that in MedLine CRISPR is a unique entry, which is not true for some of the other shorter acronyms.

## **Intervening Sequences of Regularly Spaced Prokaryotic Repeats Derive from Foreign Genetic Elements**

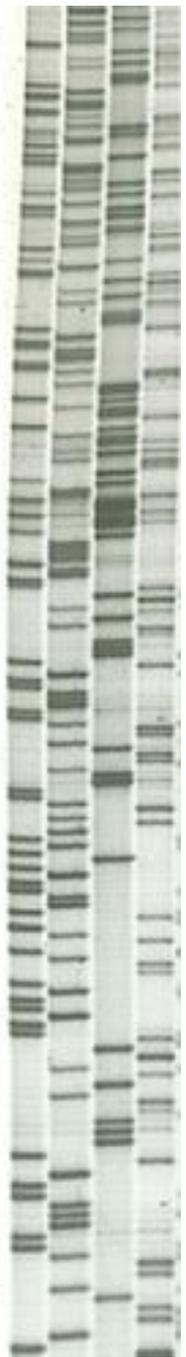
**Francisco J.M. Mojica, César Díez-Villaseñor, Jesús García-Martínez, Elena Soria**

División de Microbiología, Departamento de Fisiología, Genética y Microbiología, Universidad de Alicante, Campus de San Vicente, E-03080, Spain

Received: 6 February 2004 / Accepted: 1 October 2004 [*Reviewing Editor:* Dr. John Huelsenbeck]

JOURNAL OF **MOLECULAR  
EVOLUTION**

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Rodolphe Barrangou  
NC State  
EIC, *CRISPR Journal*



Science 2007

# CRISPR Provides Acquired Resistance Against Viruses in Prokaryotes

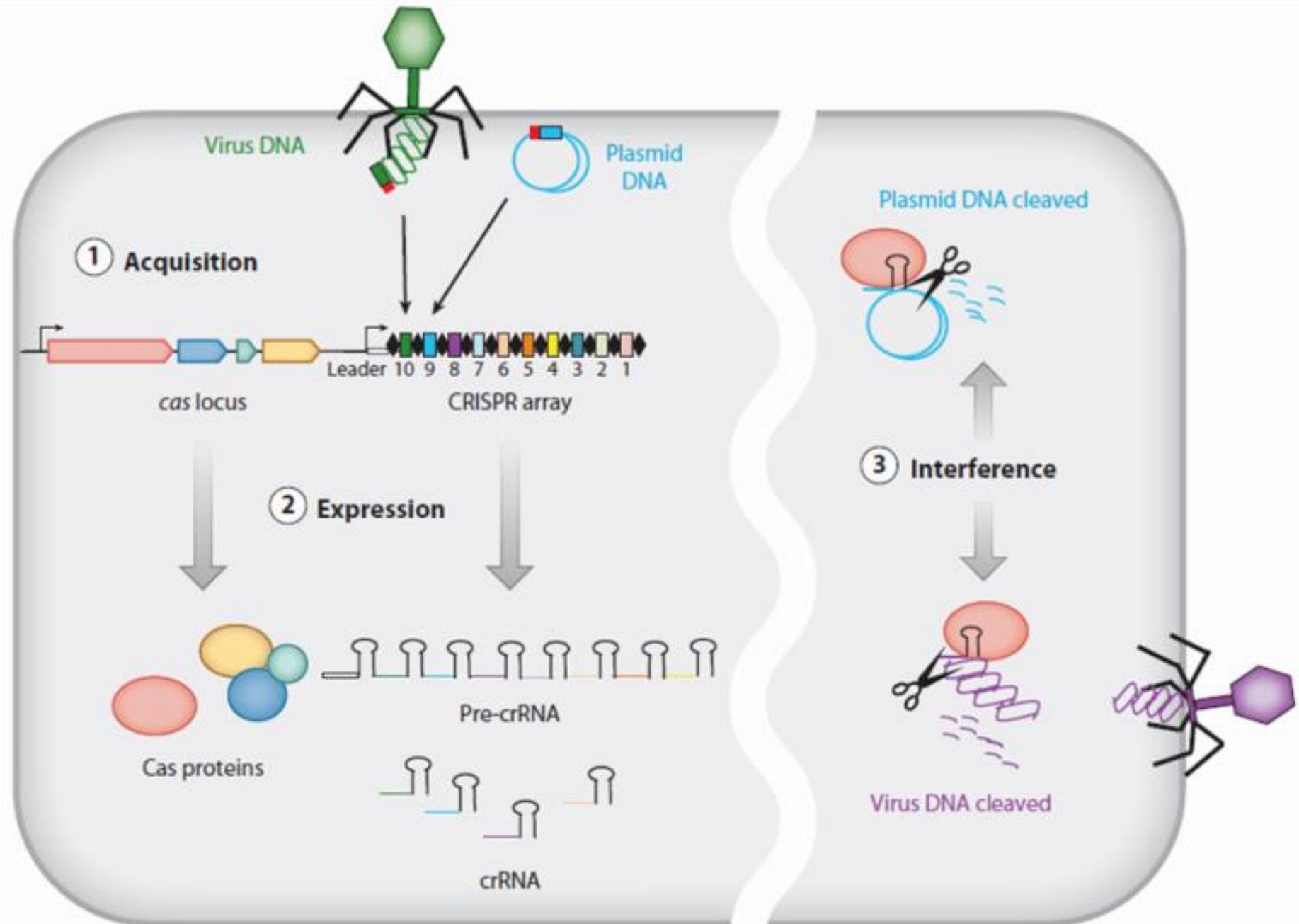
Rodolphe Barrangou,<sup>1</sup> Christophe Fremaux,<sup>2</sup> H el ene Deveau,<sup>3</sup> Melissa Richards,<sup>1</sup> Patrick Boyaval,<sup>2</sup> Sylvain Moineau,<sup>3</sup> Dennis A. Romero,<sup>1</sup> Philippe Horvath<sup>2\*</sup>



CHOOZIT<sup>®</sup> SWIFT 600

# CRISPR

... is a natural bacterial immune defense system that provides a means to recognize, remember and destroy viral invaders.



# Team Doudna/Charpentier

Emmanuelle  
Charpentier

Jennifer  
Doudna

Martin  
Jinek

Krzysztof  
Chylinski

Ines  
Fonfara

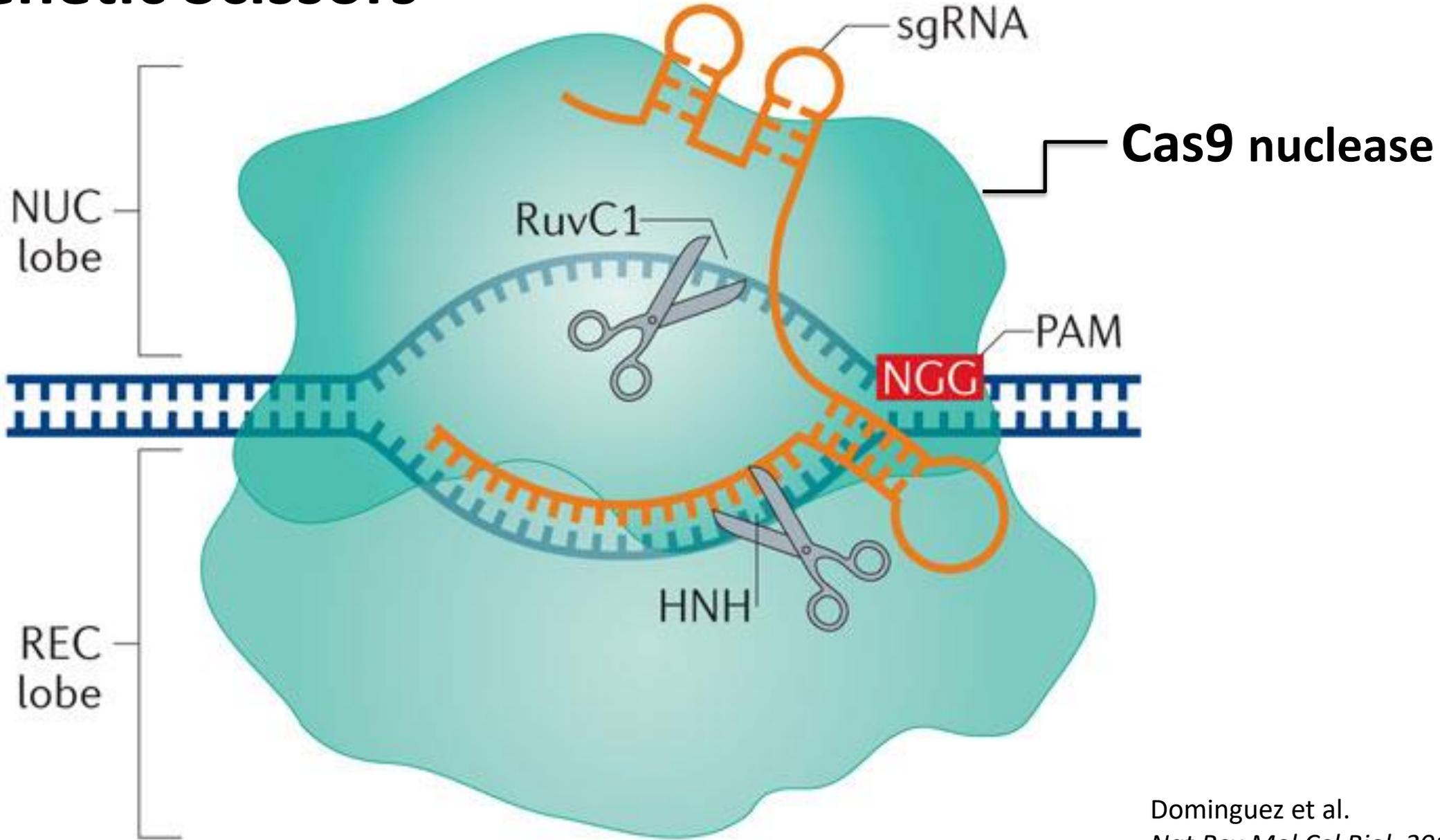
## A Programmable Dual-RNA-Guided DNA Endonuclease in Adaptive Bacterial Immunity

Martin Jinek,<sup>1,2\*</sup> Krzysztof Chylinski,<sup>3,4\*</sup> Ines Fonfara,<sup>4</sup> Michael Hauer,<sup>2,†</sup>  
Jennifer A. Doudna,<sup>1,2,5,6,‡</sup> Emmanuelle Charpentier<sup>4,‡</sup>

Clustered regularly interspaced short palindromic repeats (CRISPR)/CRISPR-associated (Cas) systems provide bacteria and archaea with adaptive immunity against viruses and plasmids by using CRISPR RNAs (crRNAs) to guide the silencing of invading nucleic acids. We show here that in

Stanley Hall  
UC Berkeley, 2012

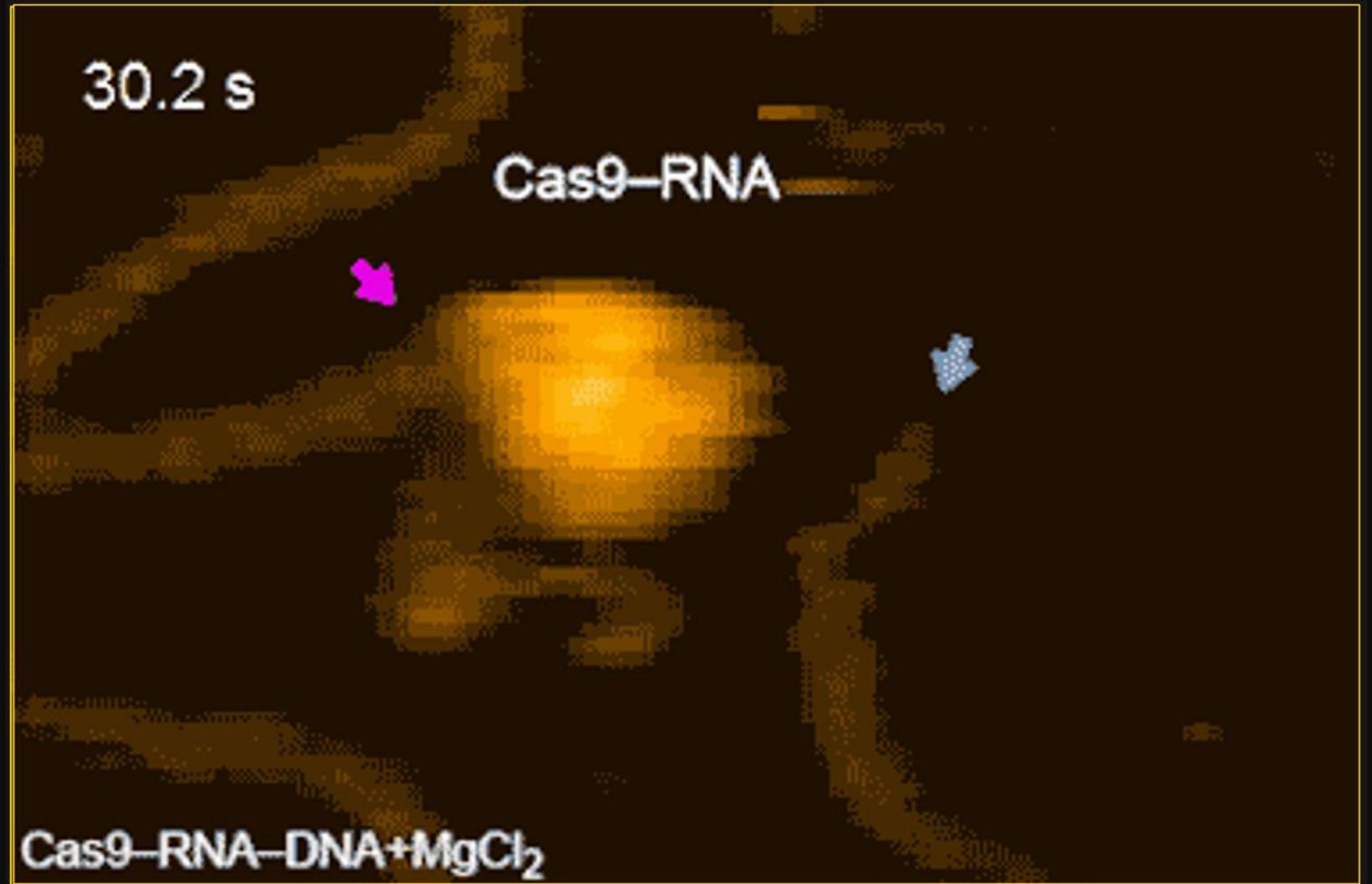
# The “Genetic Scissors”



Dominguez et al.  
*Nat Rev Mol Cel Biol.* 2015

Lights. Camera. Action... **CUT!**

CRISPR-Cas9  
visualized by high-  
speed atomic force  
microscopy



M. Shibata, H. Nishimasu *et al.*  
*Nature Communications* 8, 1430 (2017)

Hiroshi Nishimasu (Univ Tokyo)



PUBLIC



PRIVATE



# U.S. approves first gene-editing treatment, Casgevy, for sickle cell disease

PUBLISHED FRI, DEC 8 2023 • 11:19 AM EST | UPDATED FRI, DEC 8



Angelica Peebles  
@IN/ANGELICAPEEBLES/  
@ANGELICAPEEBLES



Annika Kim Constantino  
@ANNIKAKIMC

The First CRISPR Drug: Vertex Pharmaceuticals' Casgevy Wins U.K. Approval for Sickle Cell Disease

By Julianna LeMieux, PhD - November 16, 2023

## *F.D.A. Approves Sickle Cell Treatments, Including One That Uses CRISPR*

People with the genetic disease have new opportunities to eliminate their symptoms, but the treatments come with obstacles that limit their reach.

## The world's first CRISPR therapy is approved: who will receive it?

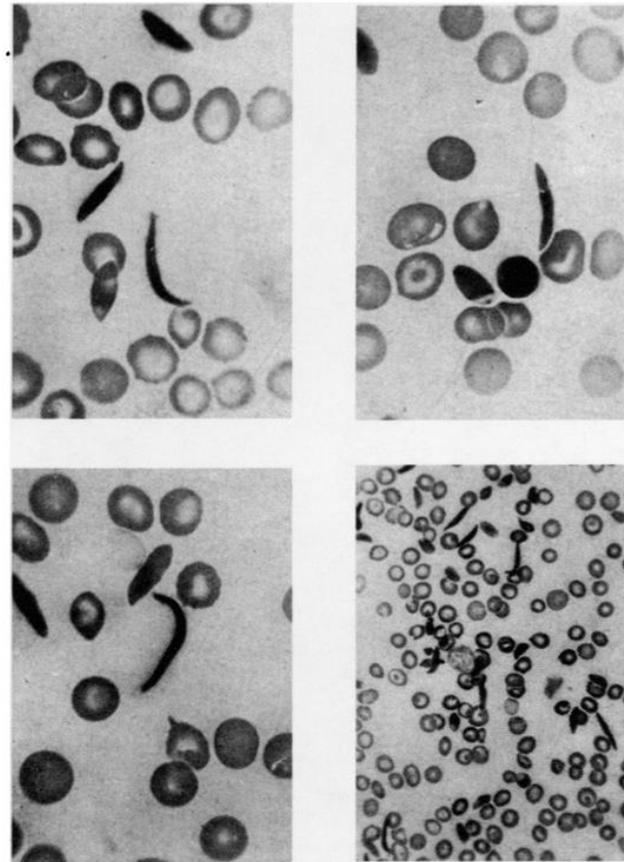
The go-ahead for Vertex's gene editing therapy in sickle cell disease and  $\beta$ -thalassemia is a historic milestone, but this one-time treatment is costly.

December 8, 2023

# Sickle Cell Anemia: The First Molecular Disease (1910)



**Dr James Herrick**  
Rush Presbyterian Hospital,  
Chicago



**Figure 1.** These photomicrographs show the peculiar elongated forms of the red corpuscles. Occasional shadow forms are seen with a few nucleated reds. The variations in shape and size are best made out in the low-power figure. The relatively number of white corpuscles and of normoblasts is not shown by these particular figures.



## Victoria Gray

Forest, Mississippi

First patient to receive CRISPR gene therapy for sickle-cell disease in the USA

- 46% total HbF
- 99.7% red blood cells contain some HbF.

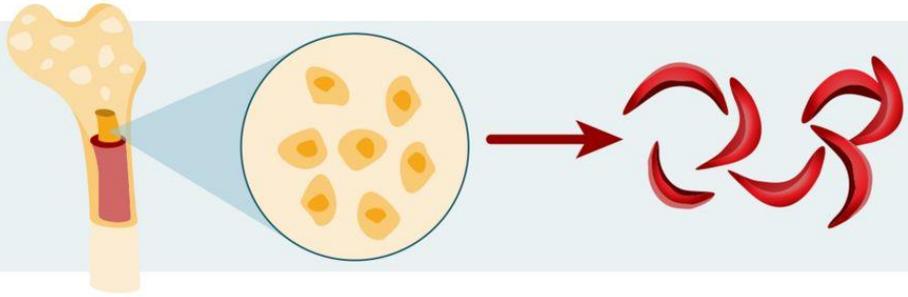
ORIGINAL ARTICLE BRIEF REPORT

### CRISPR-Cas9 Gene Editing for Sickle Cell Disease and $\beta$ -Thalassemia

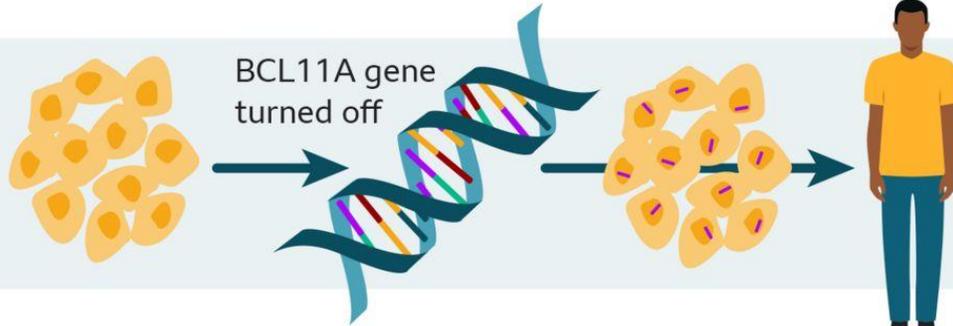
Haydar Frangoul, M.D., David Altshuler, M.D., Ph.D., M. Domenica Cappellini, M.D., Yi-Shan Chen, Ph.D., Jennifer Domm, M.D., Brenda K. Eustace, Ph.D., Juergen Foell, M.D., Josu de la Fuente, M.D., Ph.D., Stephan Grupp, M.D., Ph.D., Rupert Handgretinger, M.D., Tony W. Ho, M.D., Antonis Kattamis, M.D., Andrew Kernysky, Ph.D., Julie Lekstrom-Himes, M.D., Amanda M. Li, M.D., Franco Locatelli, M.D., Markus Y. Mapara, M.D., Ph.D., Mariane de Montalembert, M.D., Damiano Rondelli, M.D., Akshay Sharma, M.B., B.S., Sujit Sheth, M.D., Sandeep Soni, M.D., Martin H. Steinberg, M.D., Donna Wall, M.D., Angela Yen, Ph.D., and Selim Corbacioglu, M.D.

Frangoul *et al.* *NEJM* 384:252-260 (2021)

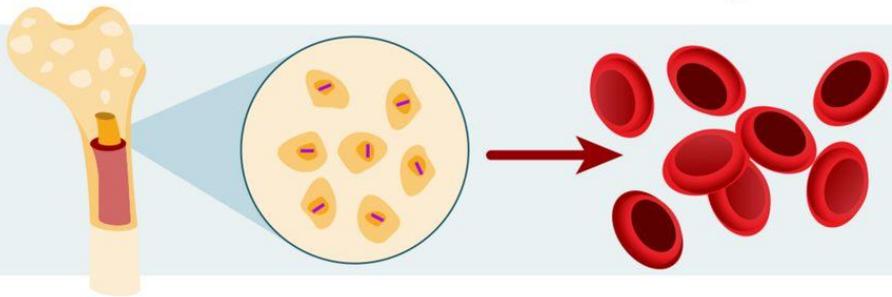
## How the treatment works



- 1 Jimi's stem cells in his bone marrow make diseased haemoglobin that can make red blood cells sickle-shaped



- 2 Stem cells extracted
- 3 Stem cells genetically modified
- 4 Genetically engineered stem cells given to Jimi



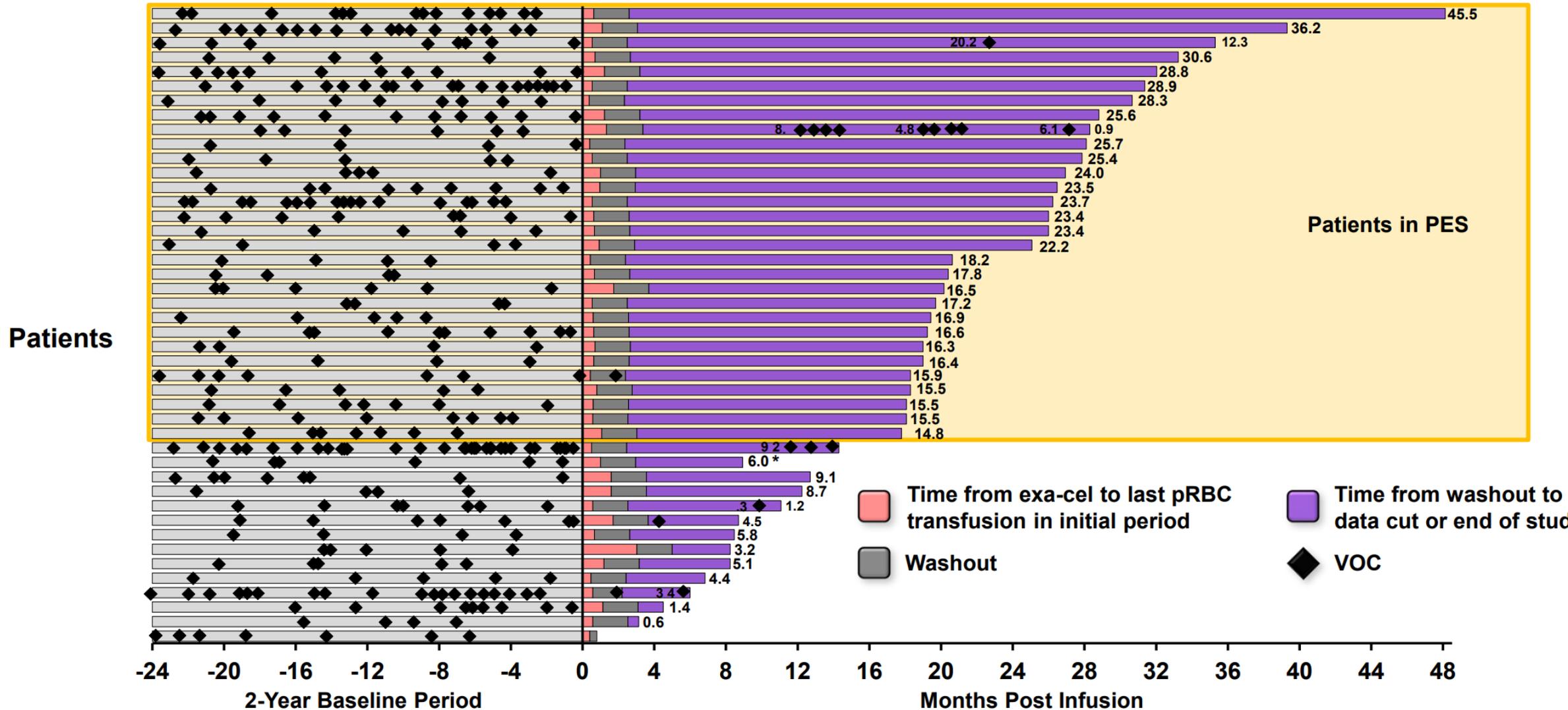
- 5 Engineered stem cells make healthy fetal haemoglobin and normal red blood cells



“I remember waking up without any pain and feeling lost, because my life is so associated with pain. It's just a part of who I am. It's weird now that I don't experience it anymore.”

– Jimi Olaghere

# Before and After: VOCs in Patients Receiving Exa-cel Therapy (Studies 121 and 131)



# In vivo Genome Editing

ORIGINAL ARTICLE

## CRISPR-Cas9 In Vivo Gene Editing for Transthyretin Amyloidosis

Julian D. Gillmore, M.D., Ph.D., Ed Gane, M.B., Ch.B., Jorg Taubel, M.D., Justin Kao, M.B., Ch.B., Marianna Fontana, M.D., Ph.D., Michael L. Maitland, M.D., Ph.D., Jessica Seitzer, B.S., Daniel O’Connell, Ph.D., Kathryn R. Walsh, Ph.D., Kristy Wood, Ph.D., Jonathan Phillips, Ph.D., Yuanxin Xu, M.D., Ph.D., Adam Amaral, B.A., Adam P. Boyd, Ph.D., Jeffrey E. Cehelsky, M.B.A., Mark D. McKee, M.D., Andrew Schiermeier, Ph.D., Olivier Harari, M.B., B.Chir., Ph.D., Andrew Murphy, Ph.D., Christos A. Kyratsous, Ph.D., Brian Zambrowicz, Ph.D., Randy Soltys, Ph.D., David E. Gutstein, M.D., John Leonard, M.D., Laura Sepp-Lorenzino, Ph.D., and David Lebwohl, M.D.



Genome Editing News Rare and Neglected Diseases

### “New Era of Medicine”: Researchers Publish First Positive Clinical Data for In Vivo Genome Editing in Humans

*Intellia, Regeneron candidate NTLA-2001 shows sustained reduction in protein-causing transthyretin (ATTR) amyloidosis after a single dose in six patients*

By Alex Philippidis · June 28, 2021 0

TTR exon 1

Leu Leu Leu Cys Leu Ala Gly Leu Val Phe Val Ser Glu Ala Gly  
 ...|C T C|C T C|C T C|T G|C C T|T G C T|G G A|C T G|G T A|T T T|G T G|T C T|G A G|G C T|G G C|...

↓ CRISPR-Cas9 editing

Leu Leu Leu Cys Leu Ala Trp Thr Gly Ile Cys Val **STOP**  
 ...|C T C|C T C|C T C|T G C|C T T|G C T|T G G A|C T G|G T A|T T T|G T G|T G T C|T G A|G G C|T G G C|...

↑ frequent 1-bp insertion

# Science

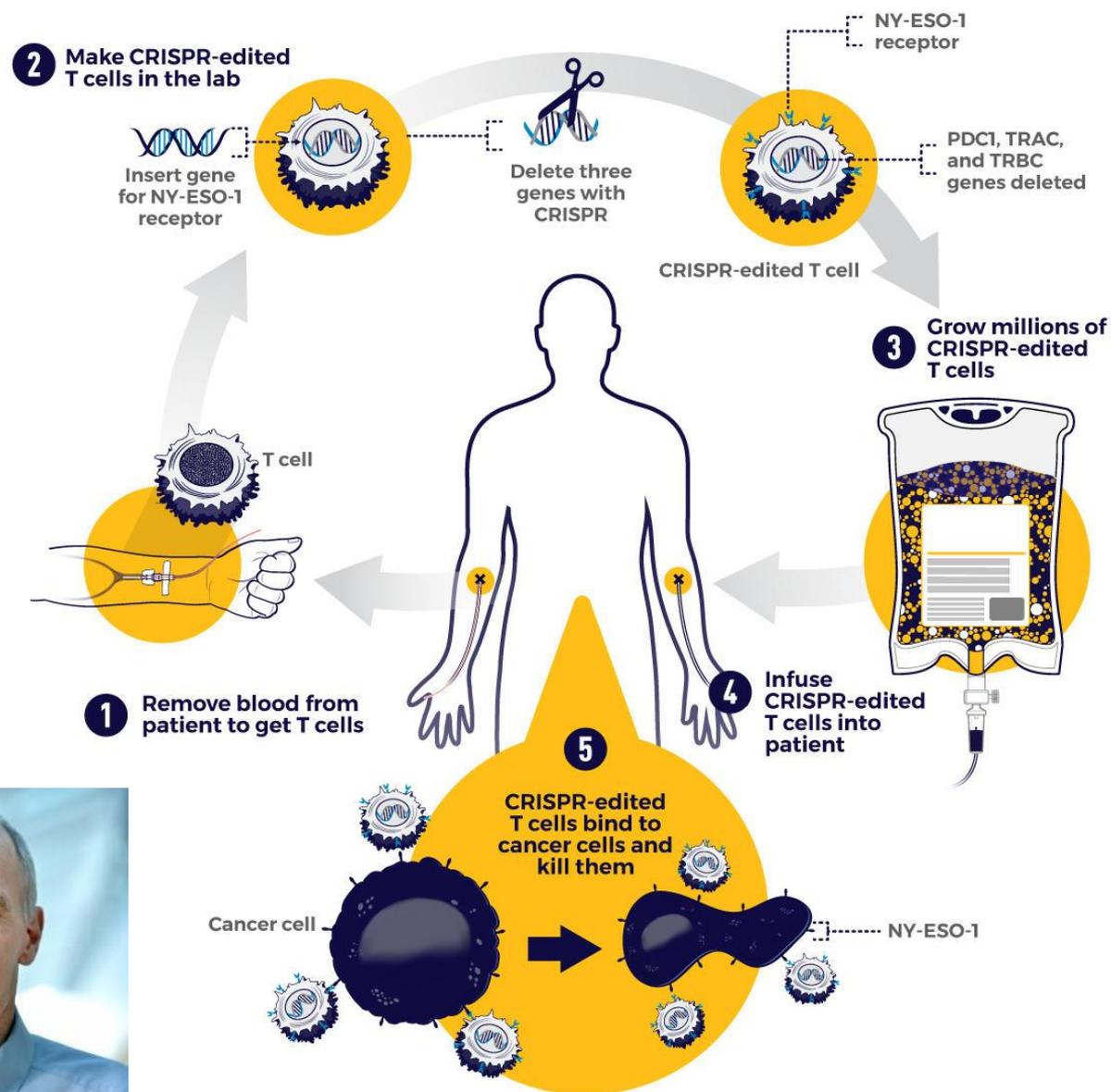
\$15  
28 FEBRUARY 2020  
sciencemag.org



“... Adoptive transfer of engineered T cells into patients resulted in durable engraftment with edits at all three genomic loci... Modified T cells persisted for up to 9 months, suggesting that immunogenicity is minimal under these conditions and **demonstrating the feasibility of CRISPR gene editing for cancer immunotherapy.**”



## CRISPR-edited T cells



# World-first use of base-edited cells to treat 'incurable' leukaemia



**Alyssa**

T-acute lymphoblastic leukemia

Bone Marrow Transplant Unit,  
Great Ormond Street Hospital,  
London

Diagnosed May 2021

Treated May 2022

Prof. Waseem Qasim

David Liu  
Broad Institute/HHMI



# A New Crispr Technique Could Fix Almost All Genetic Diseases

A less error-prone DNA editing method could correct many more harmful mutations than was previously possible.

RESEARCH HIGHLIGHT | 16 February 2023

## Genome editor tackles disease that can cause sudden death

Scientists repair a mutation that causes heart-muscle abnormalities and can kill without warning.

# Beam Therapeutics Cofounder And Crispr Scientist Publishes Research On New Sickle Cell Treatment In Mice



Leah Rosenbaum Forbes Staff

Innovation

I write about the business of healthcare.

SHARE



A 4-year-old with progeria, a syndrome with features of premature aging that stems from a mutated gene MARTIN ZABALA XINHUA/EYEVIN/REDUX

## 'Incredible' gene-editing result in mice inspires plans to treat premature-aging syndrome in children

By Jocelyn Kaiser | Jan. 6, 2021, 11:00 AM

## One-time CRISPR hit lowers cholesterol in monkeys

Verve Therapeutics demonstrates long-term LDL reduction for base editor therapy

by Alla Katsnelson, special to C&EN

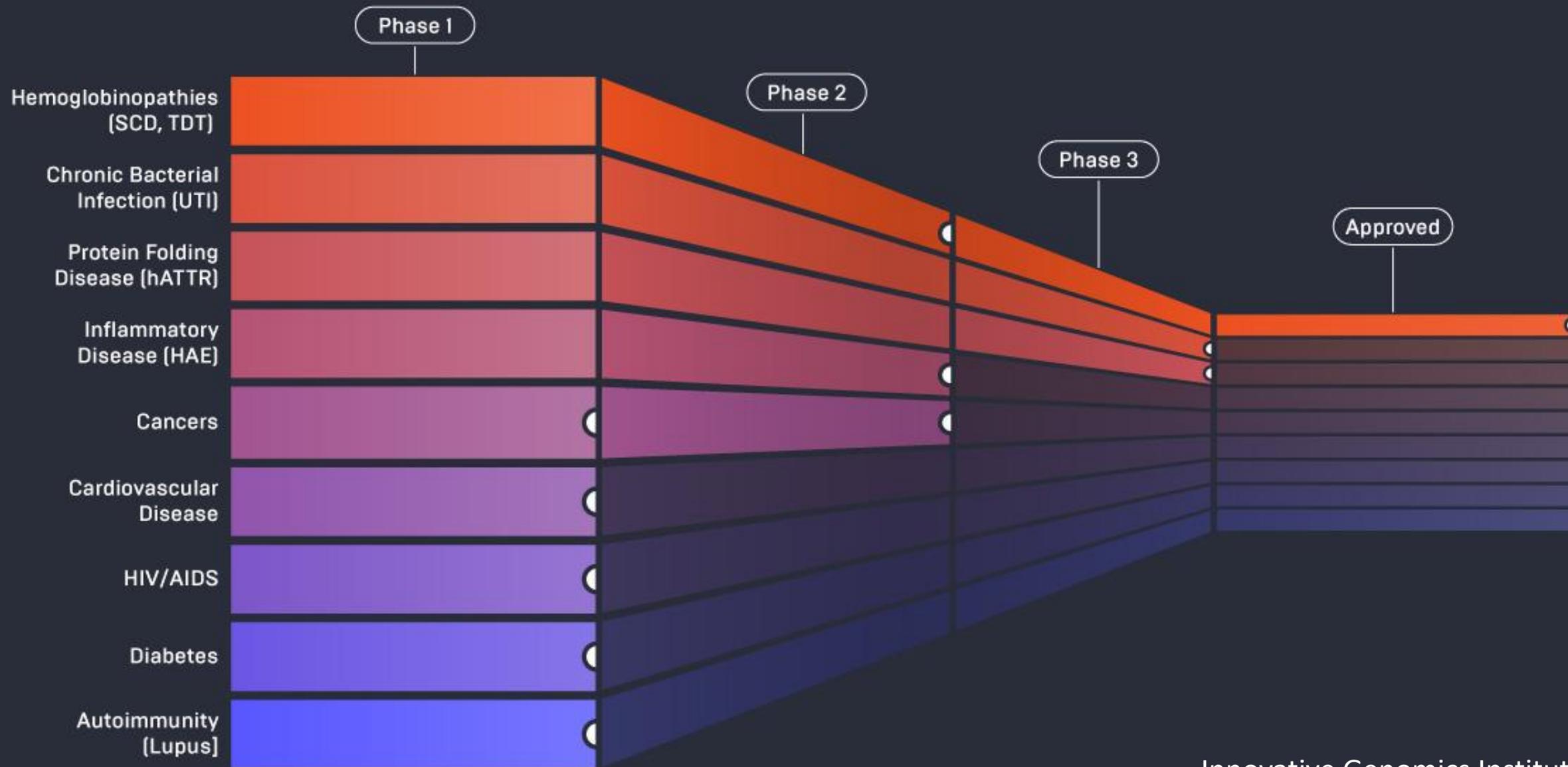
May 19, 2021 | A version of this story appeared in Volume 99, Issue 19



David Liu inside his office at the Broad Institute in Cambridge, MA. BOSTON GLOBE VIA

f  
t  
in

# CRISPR in Clinical Trials – 2024



“At this point, all hypotheticals, the words ‘potentially’ and ‘could’ or ‘in principle’ are gone. CRISPR is curative.

Two diseases down, 5,000 to go.”

— FYODOR URNOV (IGI 2024)

OPINION  
GUEST ESSAY

“The invention of CRISPR gene editing gave us remarkable treatment powers, yet no one should do a victory lap. Scientists can rewrite a person’s DNA on demand. But now what? Unless things change dramatically, the millions of people CRISPR could save will never benefit from it. We must, and we can, build a world with CRISPR for all.”



HEALTH AND SCIENCE

# New sickle cell gene therapies are a breakthrough, but solving how to pay their high prices is a struggle

2024•11:01 AM EST | UPDATED MON, FEB 26 2024•4:06 PM EST

SHARE [f](#) [X](#) [in](#) [✉](#)

## World's Most Expensive Drug Is Now \$4.25 Million Gene Therapy



The one-time treatment, Lenmeldy, is used to correct the underlying cause of a hereditary condition called early-onset metachromatic leukodystrophy. *Photographer: Eric Piermont/AFP/Getty Images*

nature

PHARMACEUTICALS

# \$3.5-Million Hemophilia Gene Therapy Is World's Most Expensive Drug

A hemophilia drug has the potential to save lives. But it cannot treat the most common form of the disease

**YOU WERE SO PREOCCUPIED WITH WHETHER OR NOT YOU COULD**



**YOU DIDN'T STOP TO THINK IF YOU SHOULD**

## The Journey of He Jiankui

2011



2007



2013

Heterogeneous Diversity of Spacers within CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats)  
-- **Jiankui He** & Michael W. Deem  
*Phys. Rev. Lett.* **105**, 128102 (Sept 2010)



Antonio Regalado  
*MIT Technology Review*





University of Hong Kong  
November 28, 2018

Embryo 1  
(Lulu)  
+1 bp / - 4 bp



Embryo 2  
(Nana)  
-15 bp / WT



**SECOND INTERNATIONAL SUMMIT ON  
HUMAN GENOME EDITING**

Convened by

The Academy of Sciences of Hong Kong 港科院

THE ROYAL SOCIETY

NATIONAL ACADEMY OF SCIENCES

NATIONAL ACADEMY OF MEDICINE



Hong Kong  
November 2018

# 15 Reasons Why

## SCIENCE

### **The CRISPR Baby Scandal Gets Worse by the Day**

The alleged creation of the world's first gene-edited infants was full of technical errors and ethical blunders. Here are the 15 most damning details.

ED YONG DEC 3, 2018

7. A few people knew about He's intentions but failed to stop him.
8. He acted in contravention of global consensus.
9. He acted in contravention of his own stated ethical views.
10. He sought ethical advice and ignored it.
11. There is no way to tell whether He's work did any good.
12. He has doubled down.
13. Scientific academies have prevaricated.
14. A leading geneticist came to He's defense.
15. This could easily happen again.

Ed Yong, *The Atlantic*  
Dec 3 2018

A photograph of Dr. He Jiankui, an elderly man with grey hair, wearing a dark suit, a blue and white striped shirt, and a red lanyard. He is surrounded by a crowd of people, many of whom are holding up smartphones and cameras to capture his image. In the foreground, several microphones from various news organizations are pointed towards him. The scene is dimly lit, with some light reflecting off the screens of the phones and the microphones. A green circle is visible in the upper left corner of the image.

“ How could Dr. He and [his] team change the gene pool of the human species without considering the need to consult other parts of the human species?”

-- Qiu Renzong

# Who Wants a CRISPR Clinic?

**From: "xxxxxxx" <xxxxxxx>;**  
**Date: Wed, Dec 5, 2018 01:18 PM**  
**To: "hejk" <xxxxxxxx >;**  
**Cc: "xxxxxxx xxxx" < >;**  
**Subject: CRISPR Gene Editing Embryology Lab Application Course**

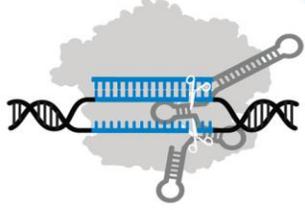
**Dear He Jiankui,**  
**Congratulations on your recent achievement of the first gene editing baby delivered by your application!**  
**My name is XXXXXXX, and I am the Business Director's Assistant at XXXXXXX Fertility & Gynaecology Center, in Dubai.**  
**Our Embryologist is interested in partaking in a course regarding CRISPR gene editing for Embryology Lab Application.**  
**Does your facility offer this type of course?**

**Kind regards,**  
**XXXXXXXXXXXX**  
**Business Director's Assistant**  
**XXXXXX**

# CRISPR at 10

## Past 10 years

Gene knockouts



Sickle cell therapy



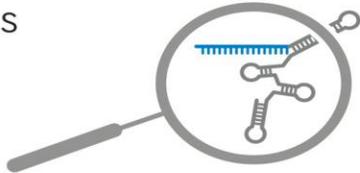
Knockout mice



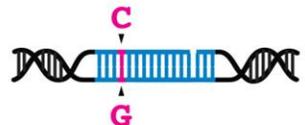
CRISPR-modified crops



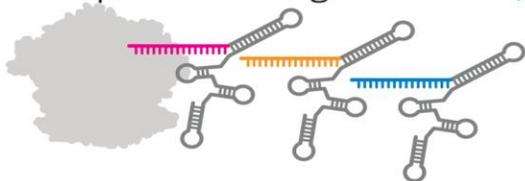
Screens



Base editing



Multiplexed editing



## Next 10 years

CRISPR-based treatments  
in later stages of clinical trials



FDA approval of  
sickle cell therapy



FDA approval of  
additional CRISPR cell therapies



Increased nutritional  
value of more foods



Improved  
*in vivo* delivery



Multigenic traits in more  
plants and animals



Expansion of CRISPR-  
modified crops



Disease resistance and  
improved crop yields



New hope for China's left-behind kids p. 1226

How pesticides should be regulated p. 1232

A twist on photoemission delay pp. 1239 & 1274

# Science

\$15  
22 SEPTEMBER 2017  
sciencemag.org

AAAS



## CRISPR PIGS

Eliminating endogenous retrovirus in a step toward xenotransplantation  
pp. 1238 & 1303

### REPORT

## Inactivation of porcine endogenous retrovirus in pigs using CRISPR-Cas9

Dong Niu<sup>1,2,\*</sup>, Hong-Jiang Wei<sup>3,4,\*</sup>, Lin Lin<sup>5,\*</sup>, Haydy George<sup>1,\*</sup>, Tao Wang<sup>1,\*</sup>, I-Hsiu Lee<sup>1,\*</sup>, Hong-Ye Zhao<sup>3</sup>, Yong Wang<sup>6</sup>, Yinan Kan<sup>1</sup>, Ellen Shrock<sup>7</sup>, Emal Leshia<sup>1</sup>, Gang Wang<sup>1</sup>, Yonglun Luo<sup>5</sup>, Yubo Qing<sup>3,4</sup>, Deling Jiao<sup>3,4</sup>, Heng Zhao<sup>3,4</sup>, Xiaoyang Zhou<sup>6</sup>, Shouqi Wang<sup>8</sup>, Hong Wei<sup>6</sup>, Marc Güell<sup>1,†</sup>, George M. Church<sup>1,7,9,†</sup>, Luhan Yang<sup>1,†,‡</sup>

<sup>1</sup>eGenesis, Inc., Cambridge, MA 02139, USA.

## First pig kidney transplant in a person: what it means for the future

The operation's early success has made researchers hopeful that clinical trials for xenotransplanted organs will start soon.



Nature March 2024

# Tomato is first CRISPR-edited food to go on sale in the world



ENVIRONMENT 24 September 2021

By [Michael Le Page](#)



Tomatoes with genes edited by CRISPR technology are now on sale in Japan  
Courtesy of Sanatech Seed

For the first time ever, you can now buy a food altered by [CRISPR gene editing](#) – at least, if you live in Japan, where the Sicilian Rouge High GABA tomato has just gone on sale.

“We started shipping the tomatoes on September 17,” says Minako Sumiyoshi at Japanese start-up Sanatech Seed, which is selling the tomatoes directly to consumers. She says demand for the tomatoes is “not too bad”.

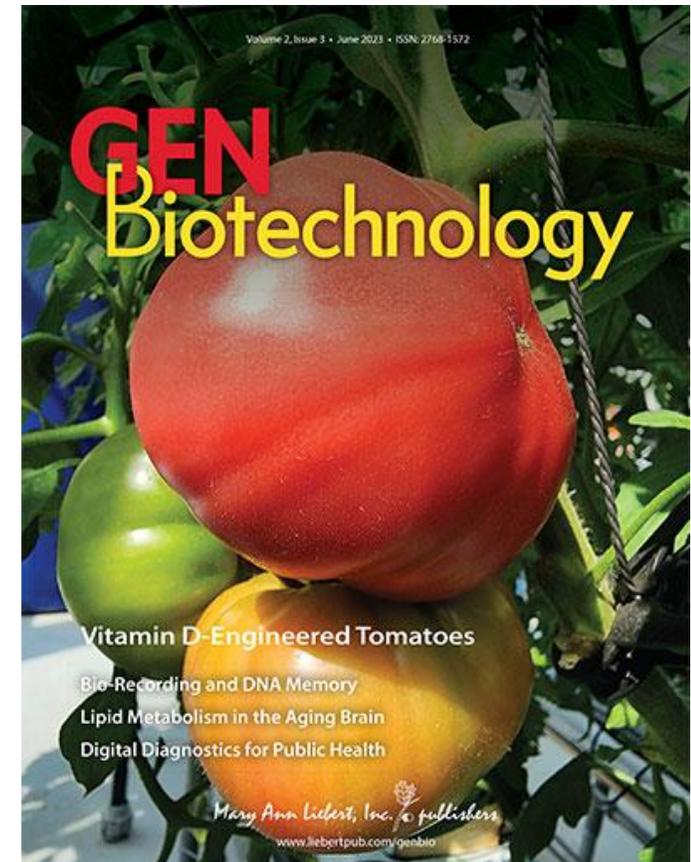
“It is a very significant milestone for CRISPR foods,” says ...

The first CRISPR gene-edited food on sale in Japan:

The **Sicilian Rouge High GABA** tomato, created by [Sanatech Seed](#), sold gene-edited seedlings to farmers in 2021 -- some 4,200 farmers took up the offer.



**sanatechseed®**  
For Tomorrow's Children and Earth





De-Extinction: Pleistocene Park?



Eriona Hysolli  
Medium December 2018

# Victoria Gray

London  
March 2023

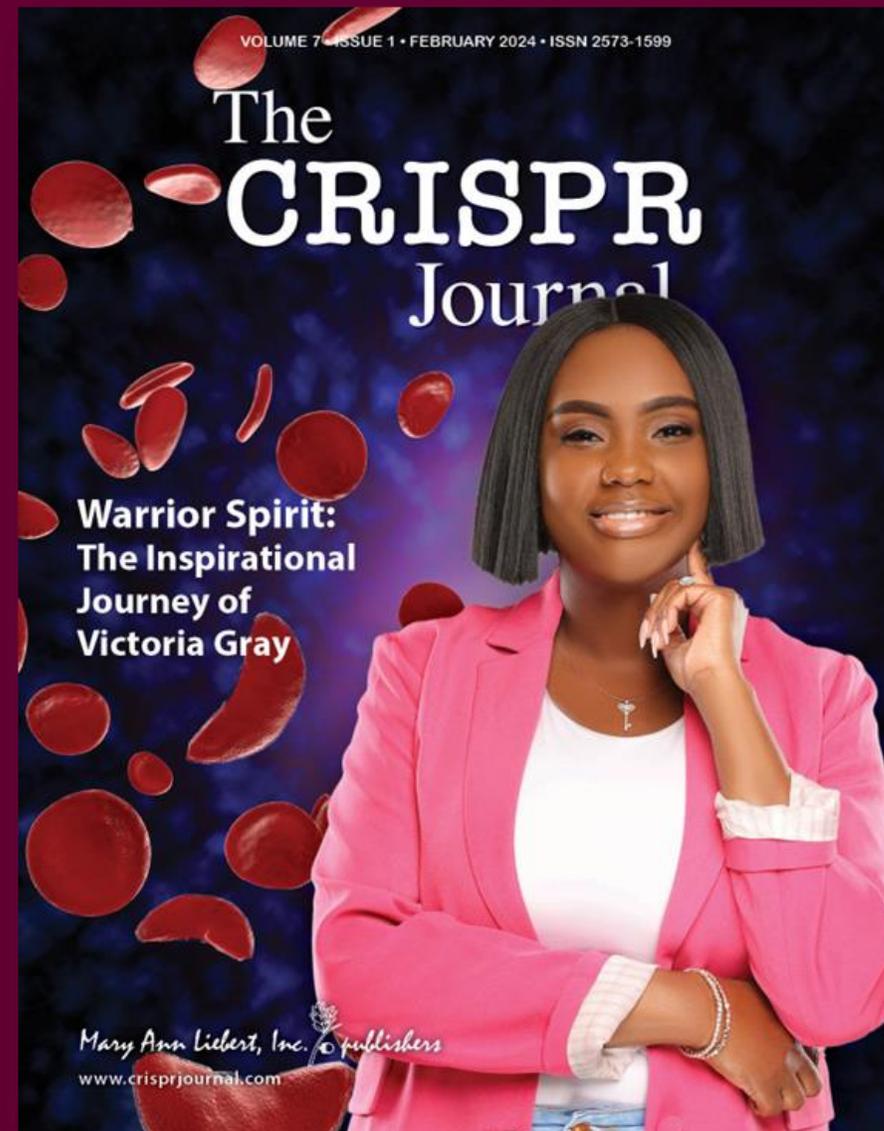


Royal  
Society

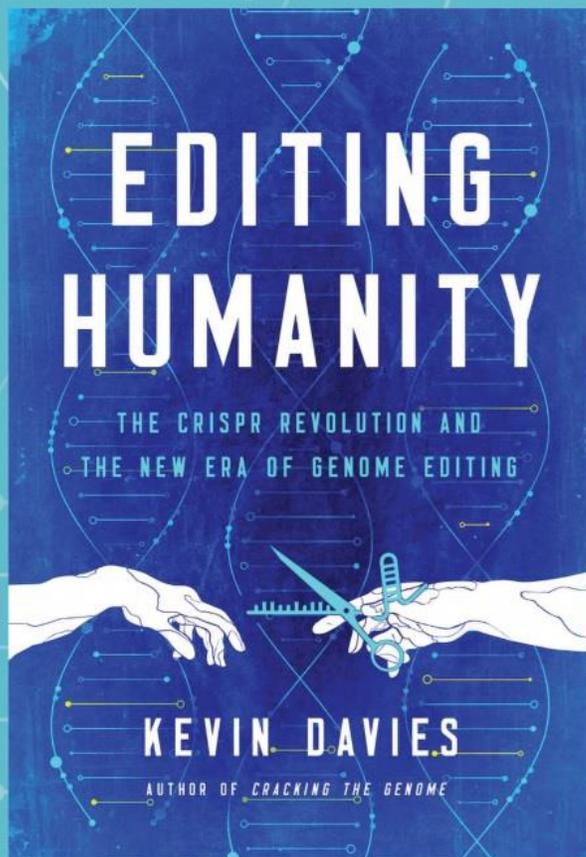
# Queen Victoria



MaxCyte / March 2024



THE AUTHOR OF *CRACKING THE GENOME* UNRAVELS  
ONE OF THE MOST IMPORTANT BREAKTHROUGHS  
IN MODERN SCIENCE AND MEDICINE.



“With great reporting and deep knowledge, science journalist Kevin Davies takes us to all the frontlines of CRISPR research, from gene editing to improved agriculture. It’s the scientific revolution of our era, and Davies gives us a close-up view of all the important players and exciting discoveries.”

— WALTER ISAACSON,  
author of *Steve Jobs* and  
*The Innovators*

*Davies dissects the implications CRISPR will have on our everyday lives and the lives of generations to come.*



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John Simon  
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