Precision Medicine:
Stories from the CRISPR Revolution

Kevin Davies PhD

Executive Editor, *The CRISPR Journal;*
Author, *Editing Humanity*

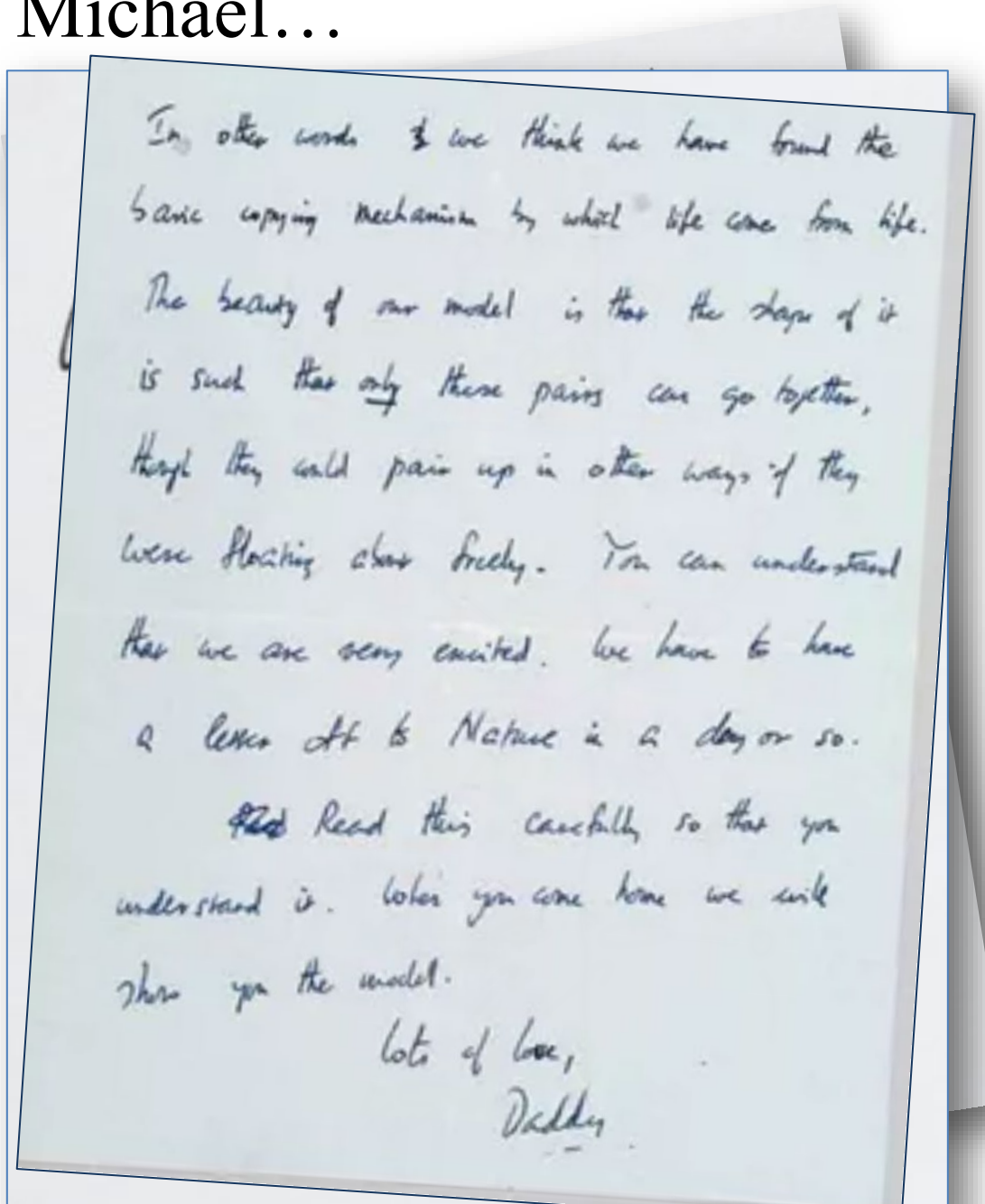
TACOS 2023
Scottsdale AZ


Welcome
TO THE
EAGLE
The most historic
pub in Cambridge
WHY NOT ENJOY A PINT WHERE
WATSON & CRICK ANNOUNCED
THE DISCOVERY OF
DNA
AND BE SURE TO CHECK OUT THE RAF BAR,
THE CEILING IS A MUST SEE.


DNA Double Helix 1953
"The secret of life"
For decades the Eagle was the local
pub for scientists from the nearby
Cavendish Laboratory.
It was here on February 28th 1953 that
Francis Crick and James Watson first
announced their discovery of how
DNA carries genetic information.
Unveiled by James Watson
25th April 2003

“My Dear Michael…

19 March 1953


In other words if we think we have found the basic copying mechanism by which life come 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 off to Nature in a day or so.

Read this carefully so that you understand it. Later 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’…”

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.

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

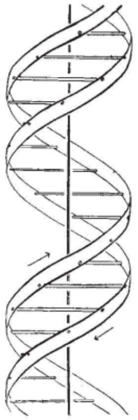
MOLECULAR STRUCTURE OF NUCLEIC ACIDS

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[1]. 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.



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

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 β-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[2] 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 is a residue on each chain every 3·4 A. 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, ...

... 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 eith... the other mem... guanine and cy... single chain do... way. However... formed, it follo... one chain is gi... chain is autom...

It has been f... of the amounts... of guanine to cy... for deoxyribose...

It is probabl... with a ribose s... the extra oxyg... der Waals cont...

The previous... ribose nucleic a... of our structure... compatible wit... be regarded as... against more e... in the following... of the details o... devised our str... 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

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.

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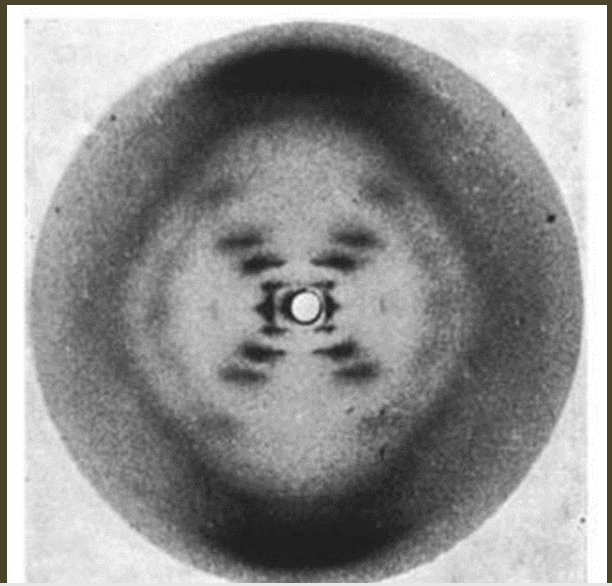
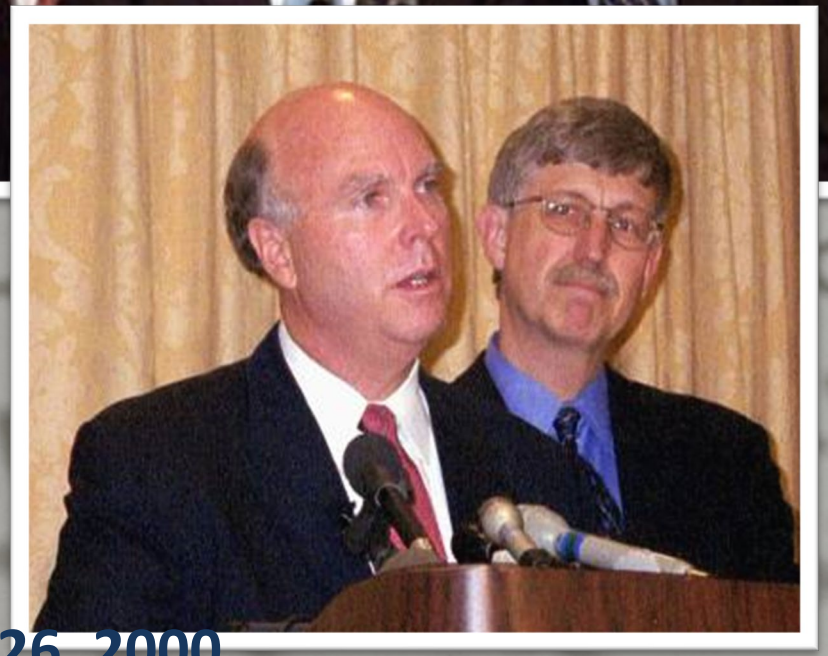
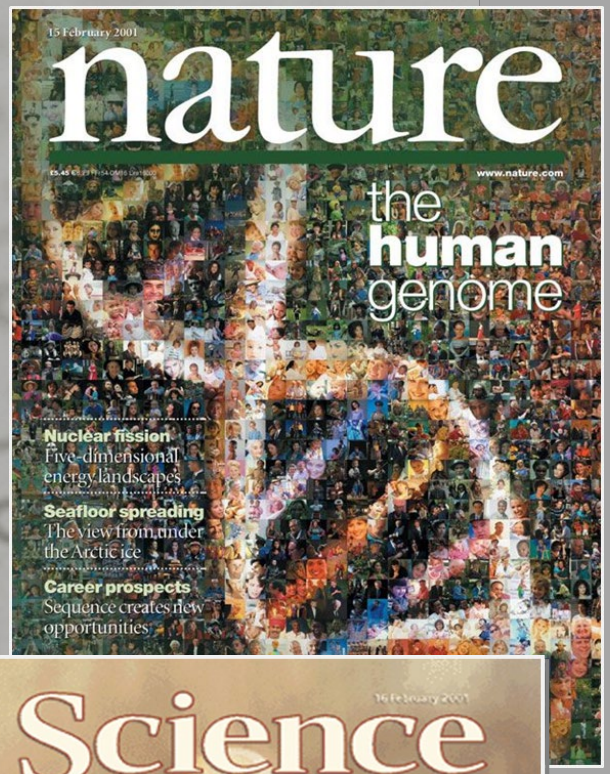
Photograph 51



The Human Genome (First Draft)

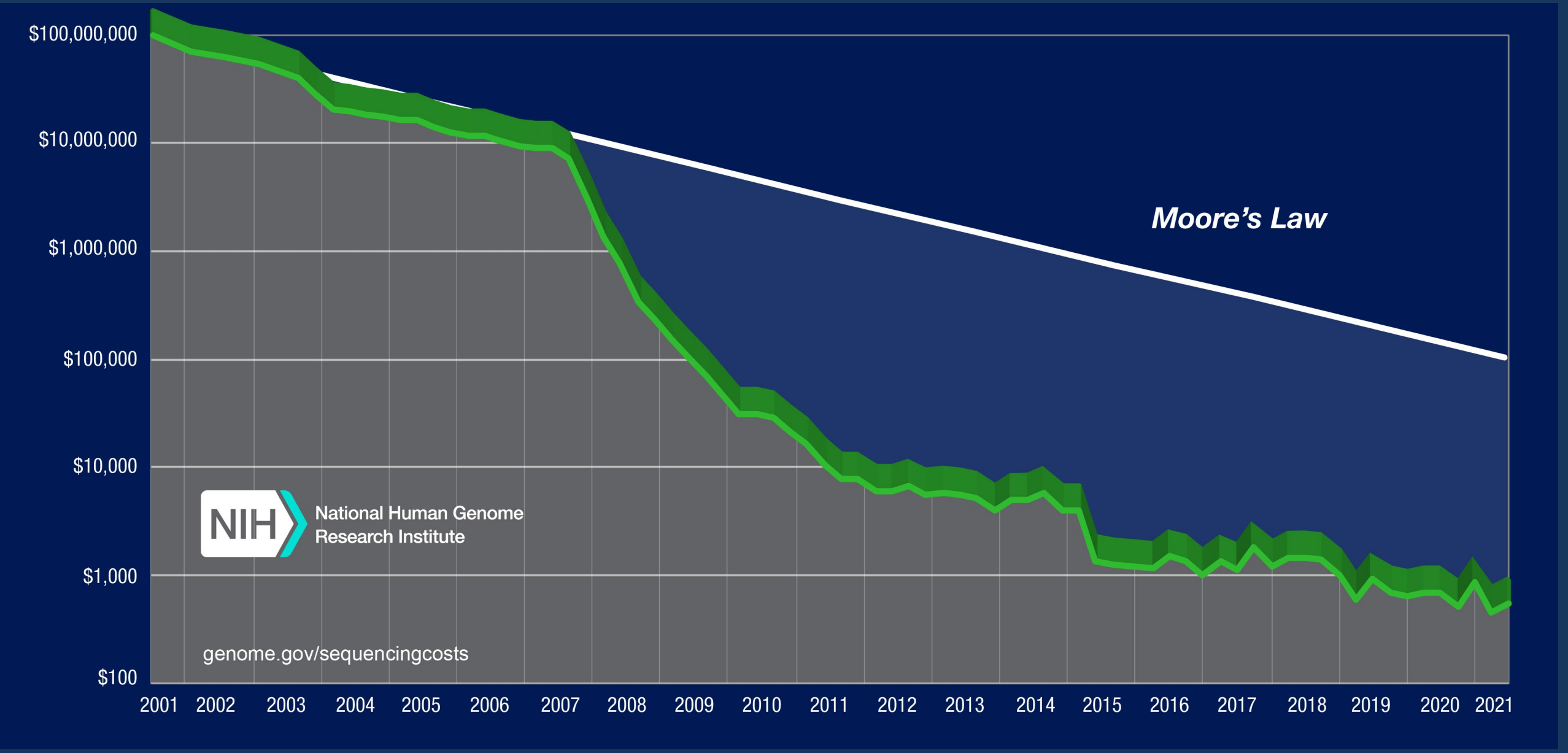




June 26, 2000

Sir Shankar Balasubramanian Sir David Klenerman

Cost Per Human Genome



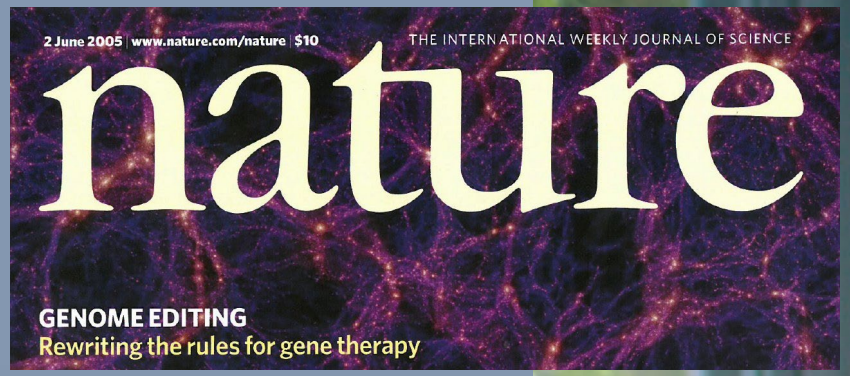
THE FASTEST DNA SEQUENCING >>> TECHNIQUE

Who
EUAN ASHLEY, ULTRA-RAPID GENOME TEAM

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

Where
UNITED STATES (STANFORD)

When
16 MARCH 2021



ARTICLES

Highly efficient endogenous human gene correction using designed zinc-finger nucleases

Fyodor D. Urnov[1], Jeffrey C. Miller[1], Ya-Li Lee[1], Christian M. Beausejour[1], Jeremy M. Rock[1], Sheldon Augustus[1], Andrew C. Jamieson[1], Matthew H. Porteus[2], Philip D. Gregory[1] & Michael C. Holmes[1]

Permanent modification of the human genome *in vivo* is impractical owing to the low frequency of homologous recombination in human cells, a fact that hampers biomedical research and progress towards safe and effective gene therapy. Here we report a general solution using two fundamental biological processes: DNA recognition by C_2H_2 zinc-finger proteins and homology-directed repair of DNA double-strand breaks. Zinc-finger proteins engineered to recognize a unique chromosomal site can be fused to a nuclease domain, and a double-strand break induced by the resulting zinc-finger nuclease can create specific sequence alterations by stimulating homologous recombination between the chromosome and an extrachromosomal DNA donor. We show that zinc-finger nucleases designed against an X-linked severe combined immune deficiency (SCID) mutation in the *IL2R*γ gene yielded more than 18% gene-modified human cells without selection. Remarkably, about 7% of the cells acquired the desired genetic modification on both X chromosomes, with cell genotype accurately reflected at the messenger RNA and protein levels. We observe comparably high frequencies in human T cells, raising the possibility of strategies based on zinc-finger nucleases for the treatment of disease.

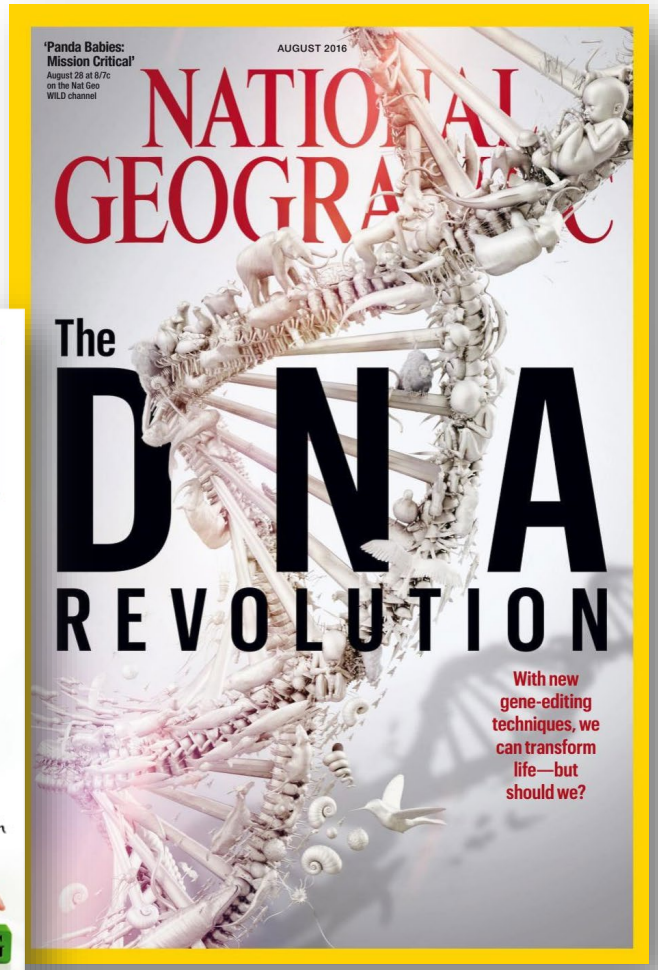
Courtesy:
HUMAN NATURE

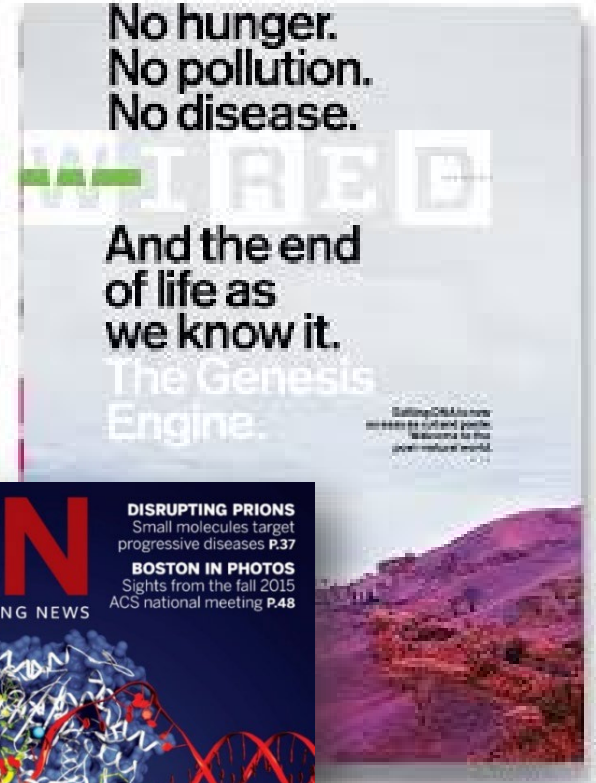
Fyodor Urnov
Innovative Genomics Institute

CRISPR


TIME
The Gene Machine
What the CRISPR experiments mean for humanity By Alice Park


The Economist
How Russians cope with recession
No-go for NGOs in China
Islamic State's taste for slavery
Commodities: the binge, the hangover
India's poet-politicians
Editing humanity
The prospect of genetic enhancement
High IQ
No baldness
Low risk of Alzheimer's, breast cancer and strokes
Perfect pitch
Sprinter
20/20 vision
A
T
G
C


'Panda Babies: Mission Critical'
August 28 at 8/7c on the Nat Geo WILD channel
AUGUST 2016
NATIONAL GEOGRAPHIC
The DNA REVOLUTION
With new gene-editing techniques, we can transform life—but should we?


No hunger.
No pollution.
No disease.
WIRED
And the end of life as we know it.
The Genesis Engine.

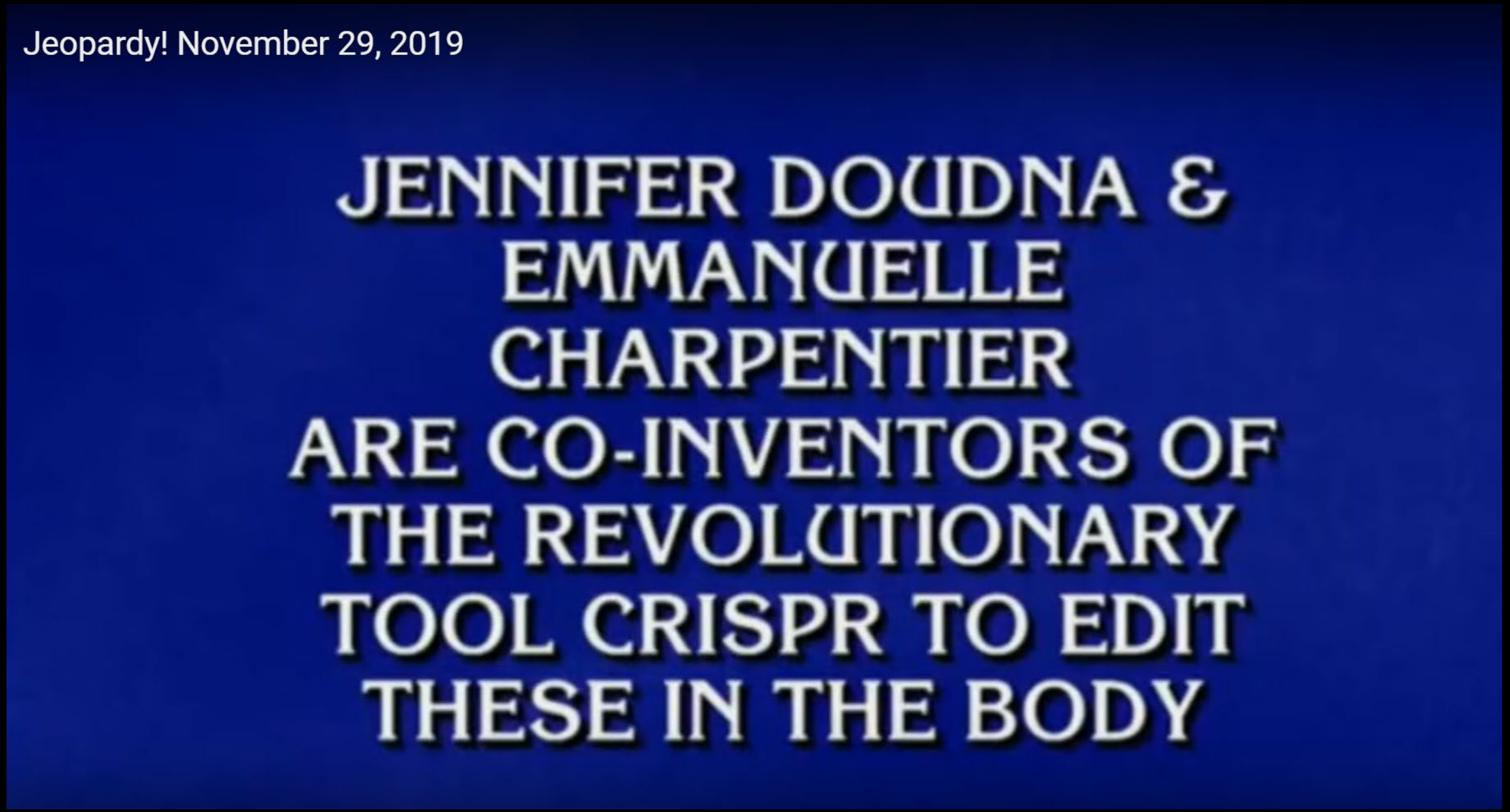

C&EN
CHEMICAL & ENGINEERING NEWS
SEPTEMBER 7, 2015
DISRUPTING PRIONS
Small molecules target progressive diseases P.37
BOSTON IN PHOTOS
Sights from the fall 2015 ACS national meeting P.48
EDITING THE GENOME
CRISPR/Cas9 takes gene manipulation into a new era P.14
PUBLISHED BY THE AMERICAN CHEMICAL SOCIETY


The risks of using CRISPR to edit embryos
ENERGYGUIDE
VWR
60 MINUTES Overtime

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.’

“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

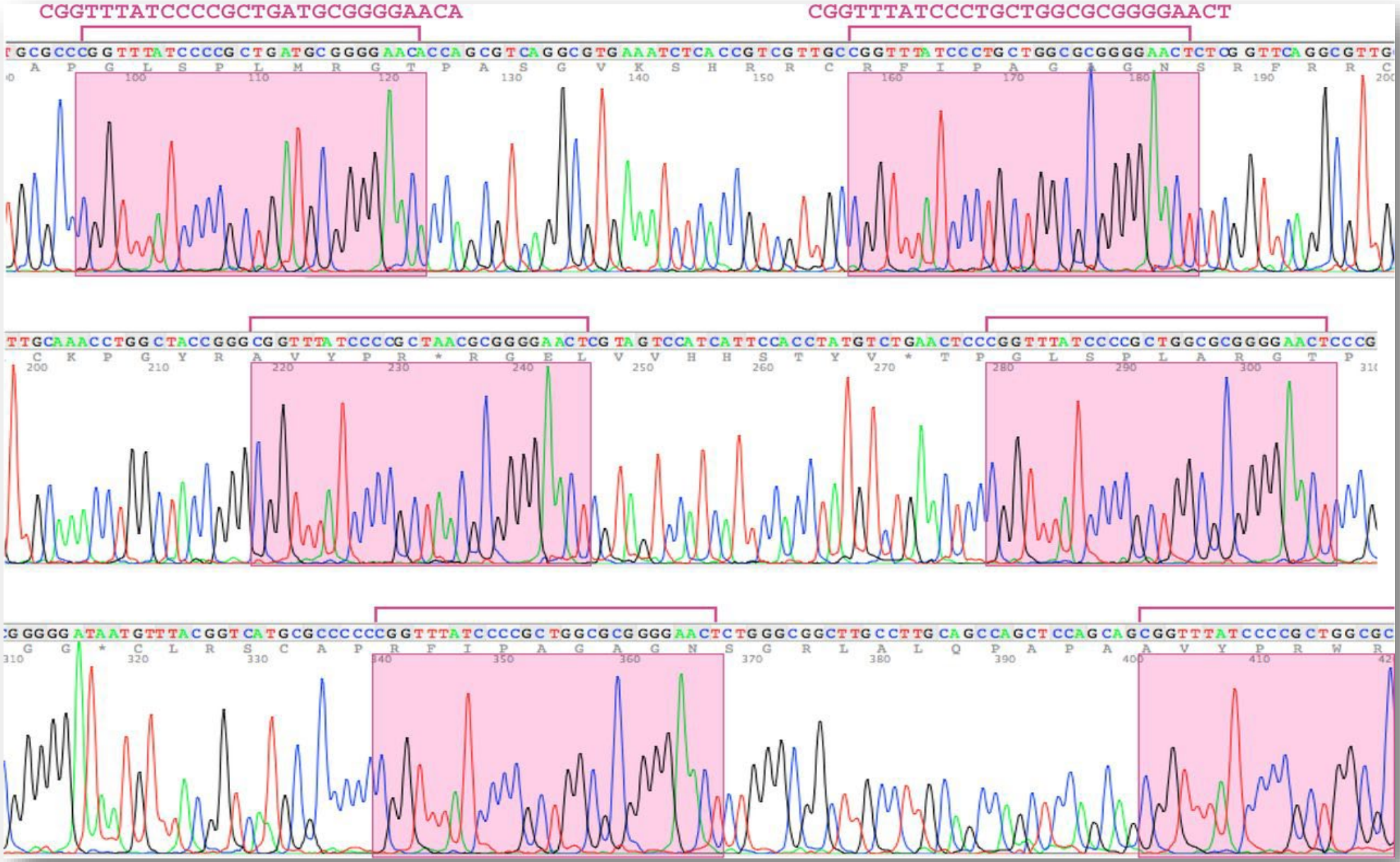
"for the development of a method for genome editing."

October 7, 2020

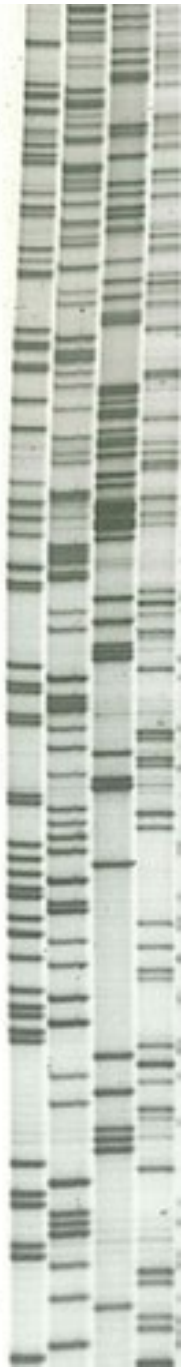

Stockholm
December 2022

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

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



Ishino Y. *et al*. *J. Bacteriol*. 2018



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.

JOURNAL OF MOLECULAR EVOLUTION

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]

Rodolphe Barrangou
NC State
EIC, *CRISPR Journal*

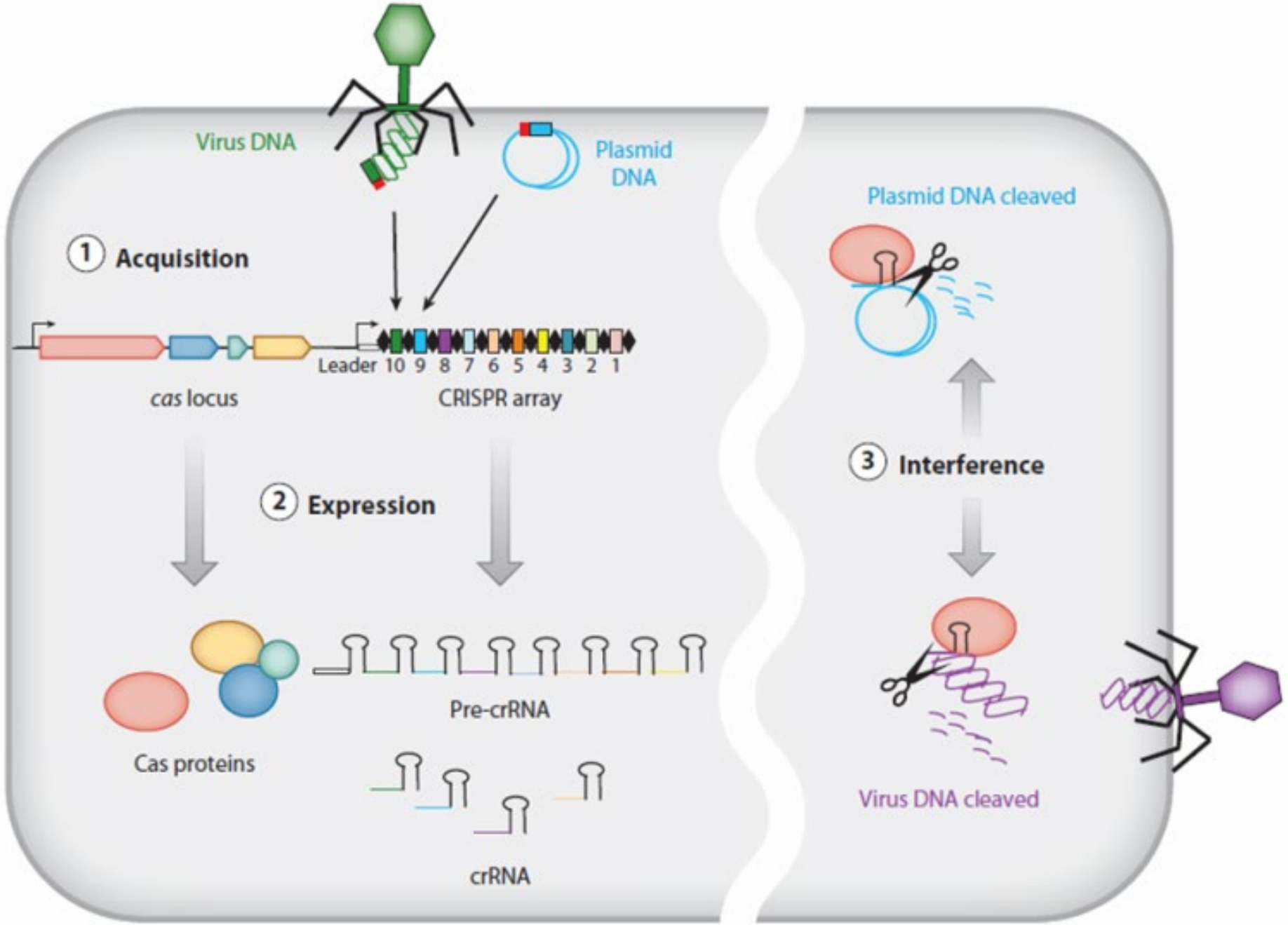
CRISPR Provides Acquired Resistance Against Viruses in Prokaryotes

Rodolphe Barrangou,[1] Christophe Fremaux,[2] Hélène Deveau,[3] Melissa Richards,[1] Patrick Boyaval,[2] Sylvain Moineau,[3] Dennis A. Romero,[1] Philippe Horvath[2]*

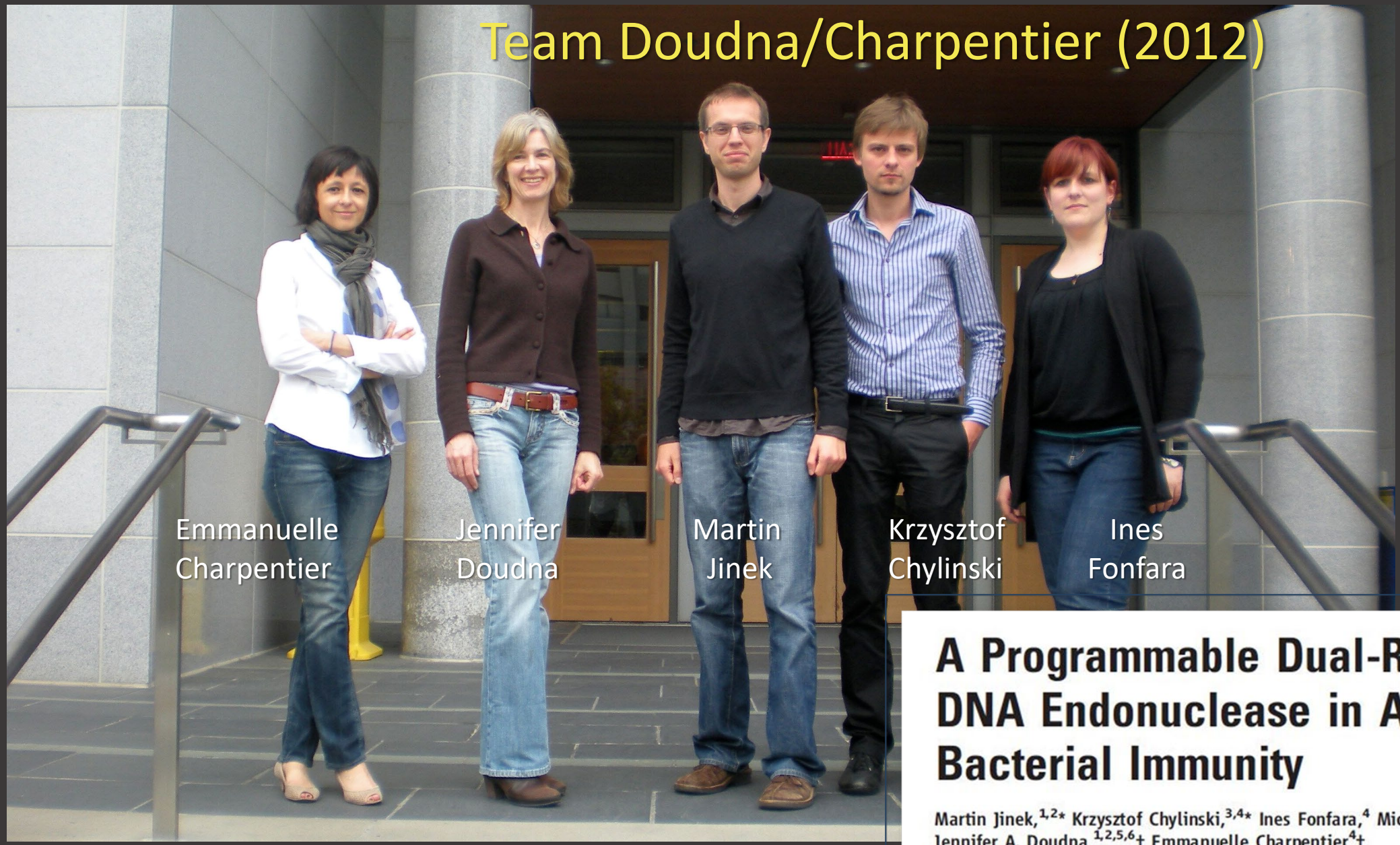
Science 2007

CRISPR

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



Team Doudna/Charpentier (2012)



Stanley Hall
UC Berkeley, 2012

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

Martin Jinek,[1,2*] Krzysztof Chylinski,[3,4*] Ines Fonfara,[4] Michael Hauer,[2†]
Jennifer A. Doudna,[1,2,5,6‡] Emmanuelle Charpentier[4‡]

Clustered regularly interspaced short palindromic repeats (CRISPR)/CRISPR-associated (Cas) syst
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

SARAH ZHANG 10.04.15 07:00 AM

The Battle Over Genome Editing Gets Science All Wrong

PNAS

Cas9–crRNA ribonucleoprotein complex mediates specific DNA cleavage for adaptive immunity in bacteria

Giedrius Gasiunas[a], Rodolphe Barrangou[b], Philippe Horvath[c], and Virginijus Siksnys[a,1]

[a]Institute of Biotechnology, Vilnius University, LT-02241 Vilnius, Lithuania; [b]DuPont Nutrition and Health, Madison, WI 5
and Health, F-86220 Dangé-Saint-Romain, France

Edited by Arthur Landy, Brown University, Providence, RI, and approved August 1, 2012 (received for review May 21, 20

"… these findings pave the way for the development of unique molecular tools for RNA-directed **DNA surgery**."

Sarah Zhang
WIRED 10.04.15

Kavli Prize
Oslo, Norway
Sept. 2018

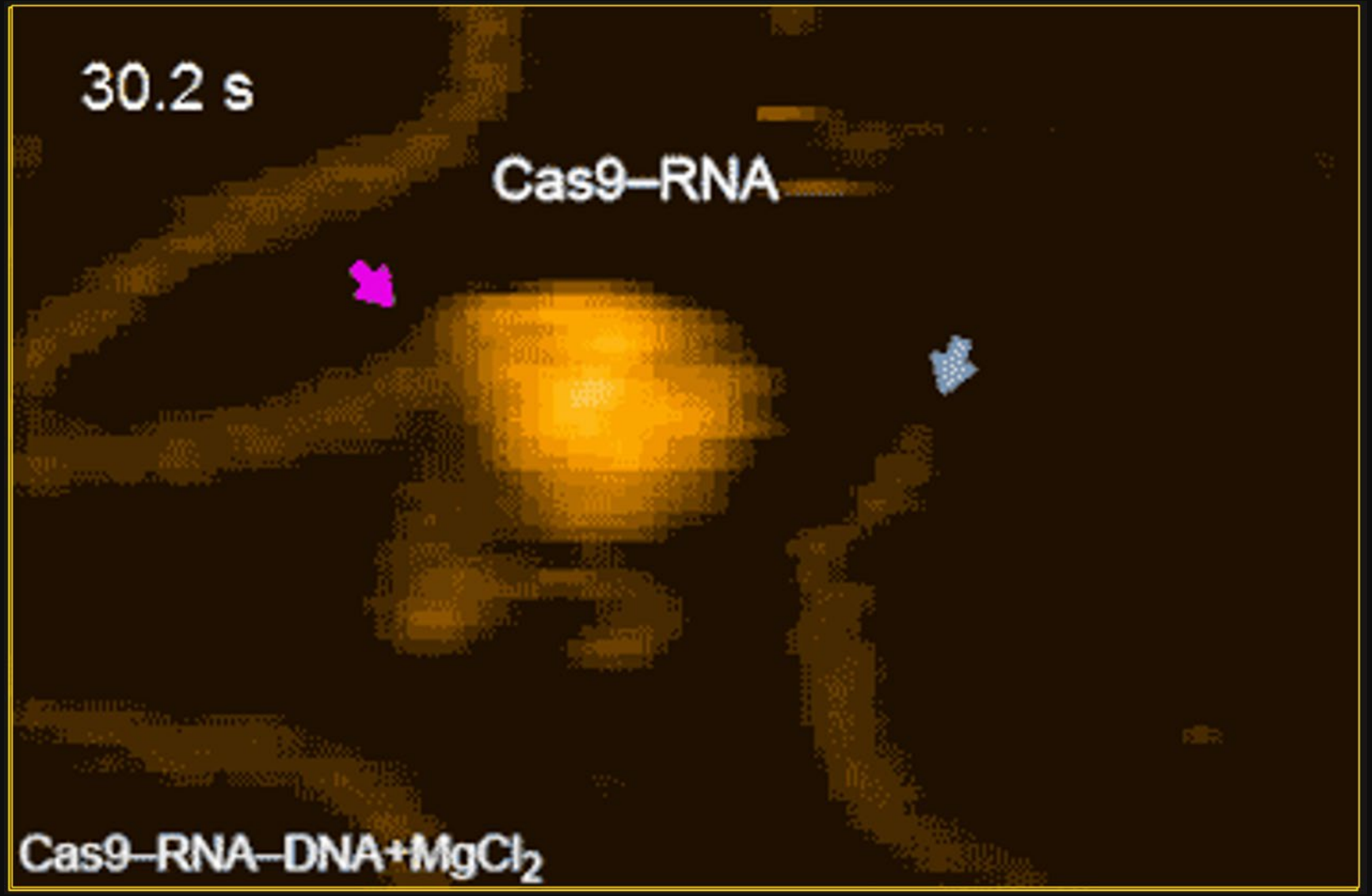
"… for the invention of CRISPR-Cas9, a precise nanotool for editing DNA"

Spot the Spelling Mistake

Cas Kramer
(Univ Leicester)

Lights. Camera. Action… **CUT!**

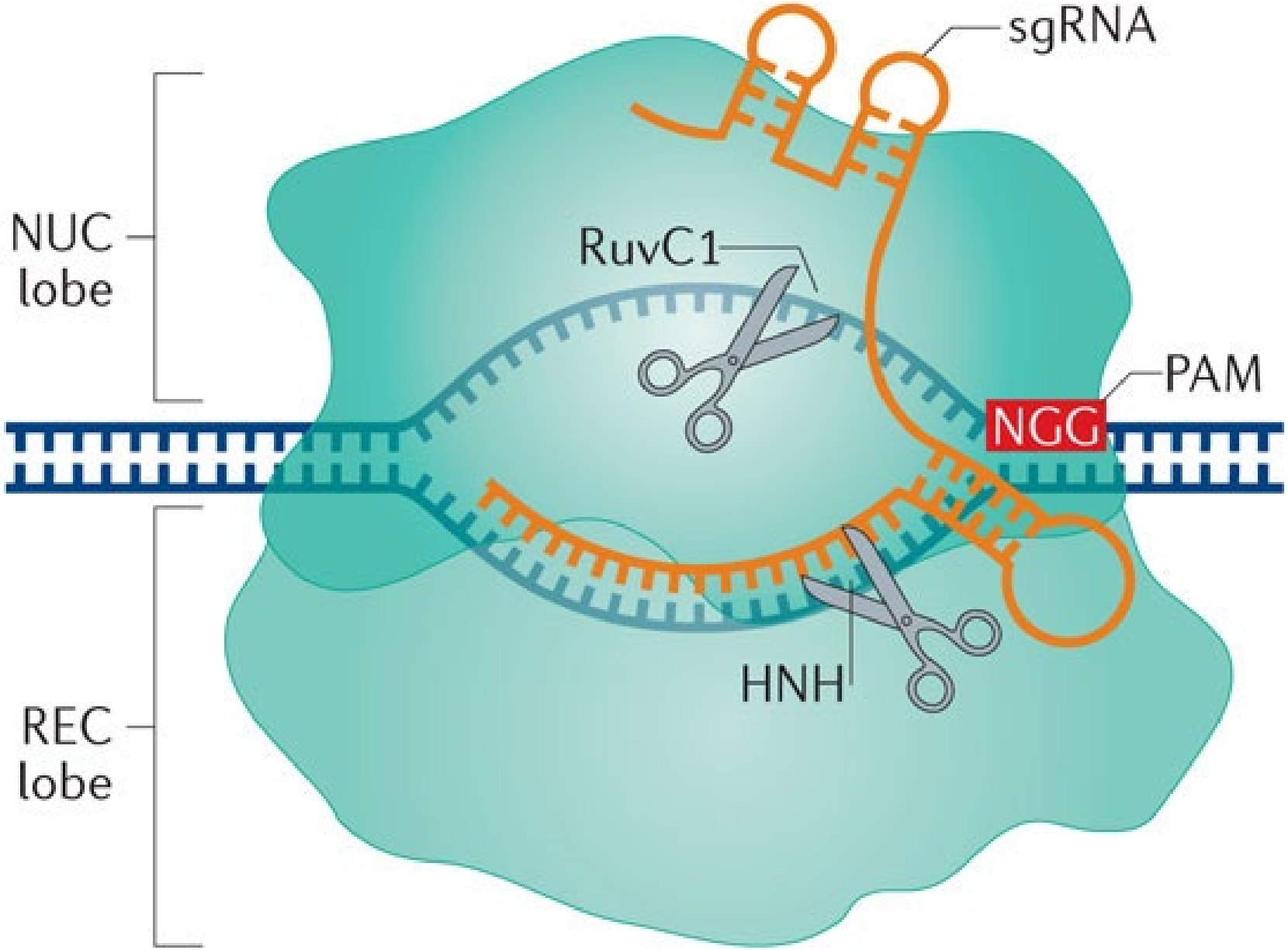
CRISPR-Cas9 visualized by high-speed atomic force microscopy



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

Hiroshi Nishimasu (Univ Tokyo)

The Genetic Scissors: Cas9 nuclease



Dominguez et al.
Nat Rev Mol Cel Biol. 2015

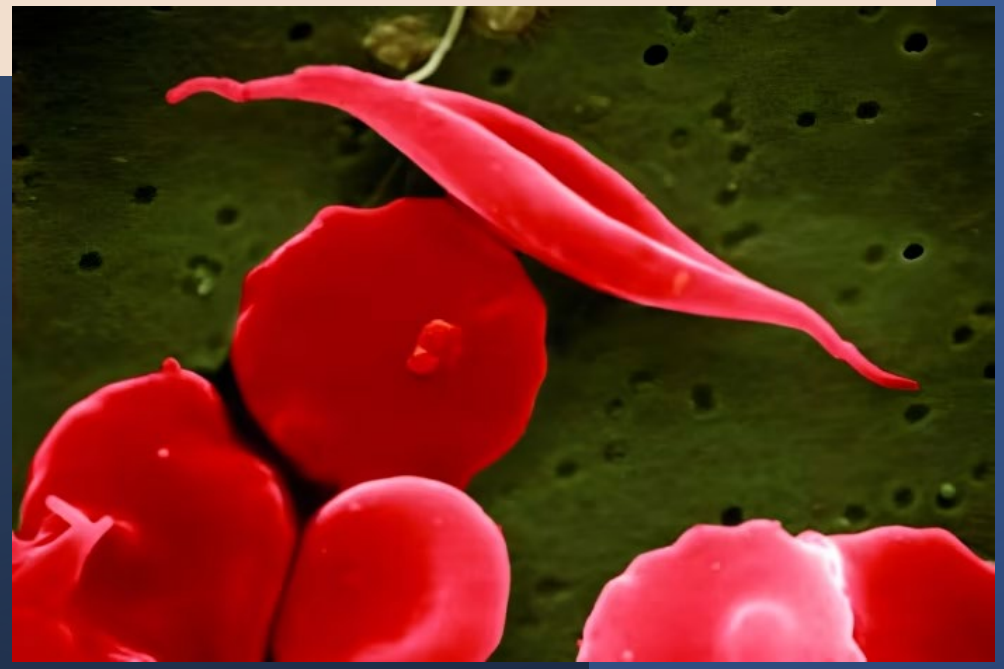
PUBLIC

PRIVATE

Biotech + Add to myFT

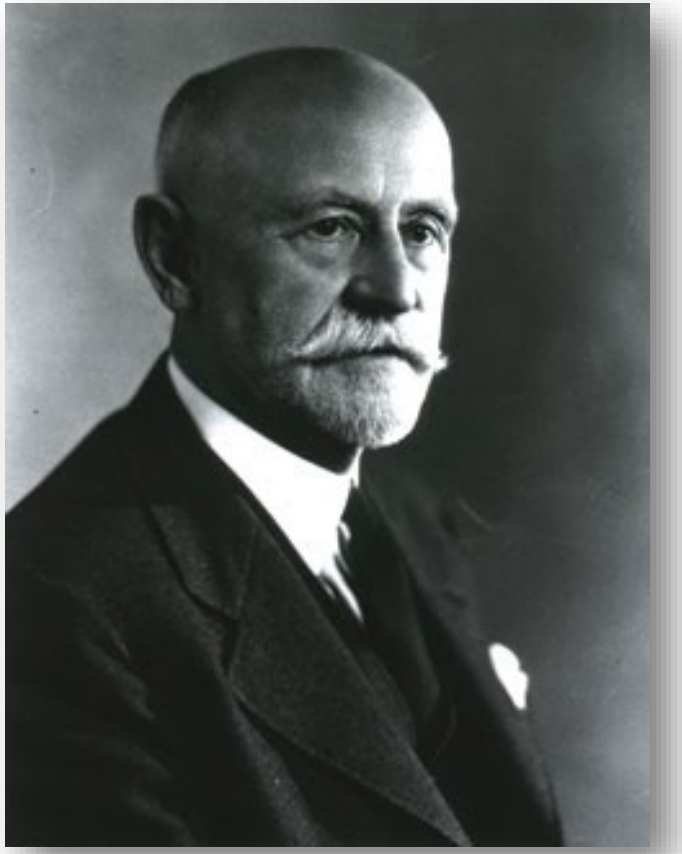
Revolutionary Crispr gene editing speeds from lab to treatment room

The first drug to make use of technology discovered only a decade ago will be with regulators by the end of the year



Financial Times
August 18, 2022

Sickle Cell Anemia: The First Molecular Disease



Dr James Herrick
Rush Presbyterian Hospital, Chicago

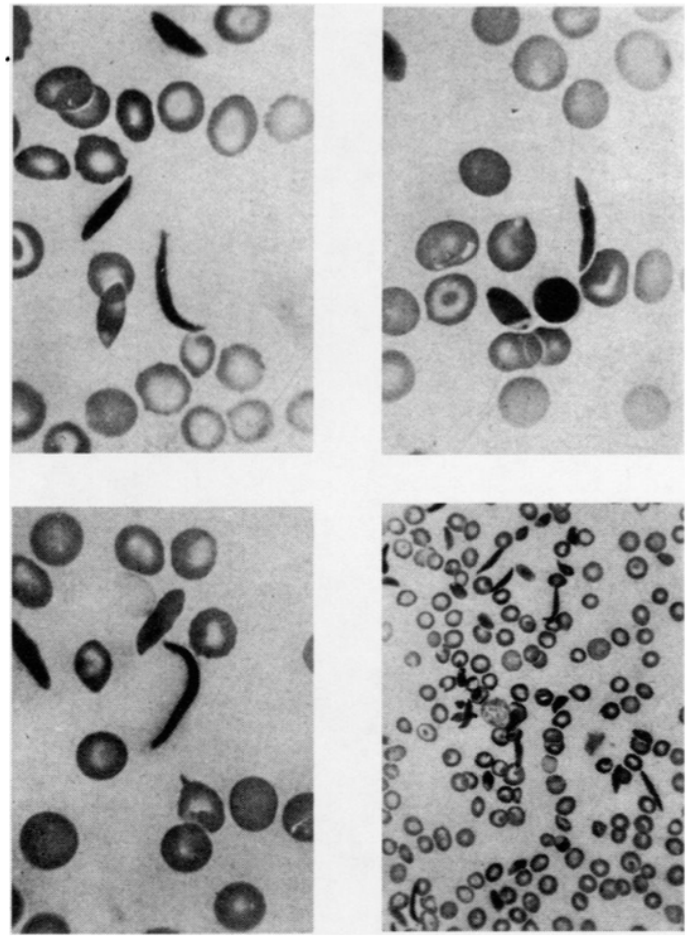


Figure 1. These photomicrographs show the peculiar elongated forms of the red corpuscles. Occasional shadow forms are seen with a few nucleated reds. The variations in shape and size are best made out in the low-power figure. The relatively number of white corpuscles and of normoblasts is not shown by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

Meredith Rizzo / NPR

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 of it.

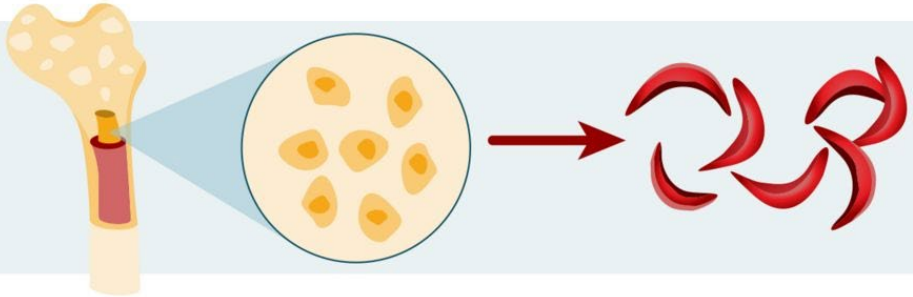
ORIGINAL ARTICLE BRIEF REPORT

CRISPR-Cas9 Gene Editing for Sickle Cell Disease and β-Thalassemia

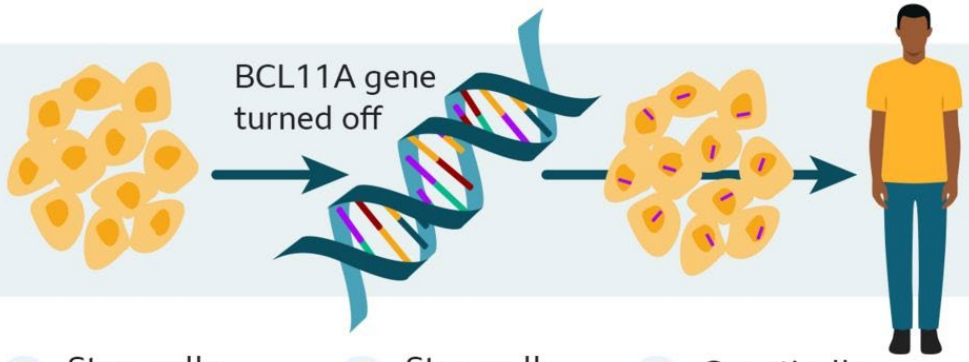
Haydar Frangoul, M.D., David Altshuler, M.D., Ph.D., M. Domenica Cappellini, M.D., Yi-Shan Chen, Ph.D., Jennifer Domm, M.D., Brenda K. Eustace, Ph.D., Juergen Foell, M.D., Josu de la Fuente, M.D., Ph.D., Stephan Grupp, M.D., Ph.D., Rupert Handgretinger, M.D., Tony W. Ho, M.D., Antonis Kattamis, M.D., Andrew Kernytsky, 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.

CRISPR Tx + Vertex | July 2019

How the treatment works



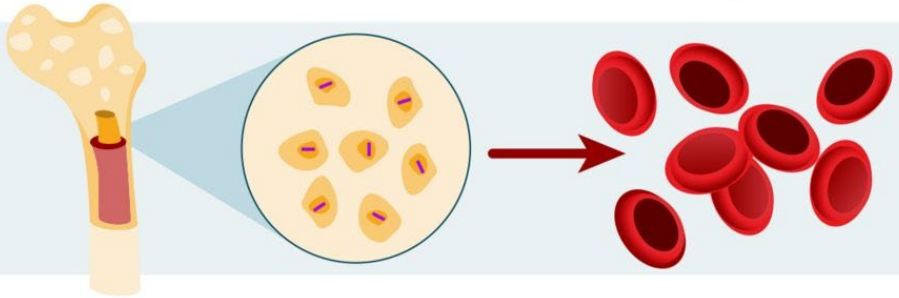
1 Jimi's stem cells in his bone marrow make diseased haemoglobin that can make red blood cells sickle-shaped



2 Stem cells extracted

3 Stem cells genetically modified

4 Genetically engineered stem cells given to Jimi



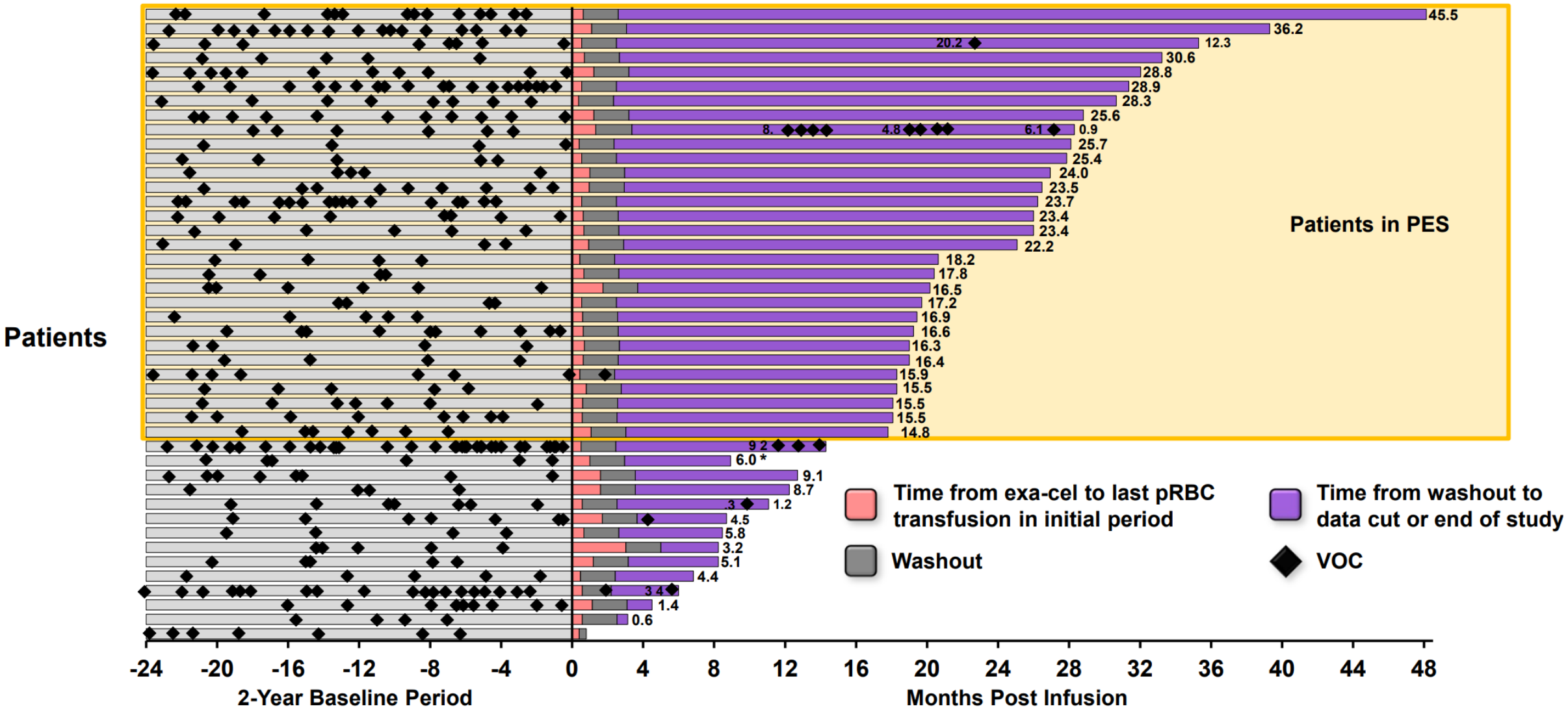
5 Engineered stem cells make healthy fetal haemoglobin and normal red blood cells

BBC

"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

Figure 9: Duration of Severe VOC-Free in Individual Patients Who Received Exa-cel (Studies 121 and 131, [SCD]FAS)



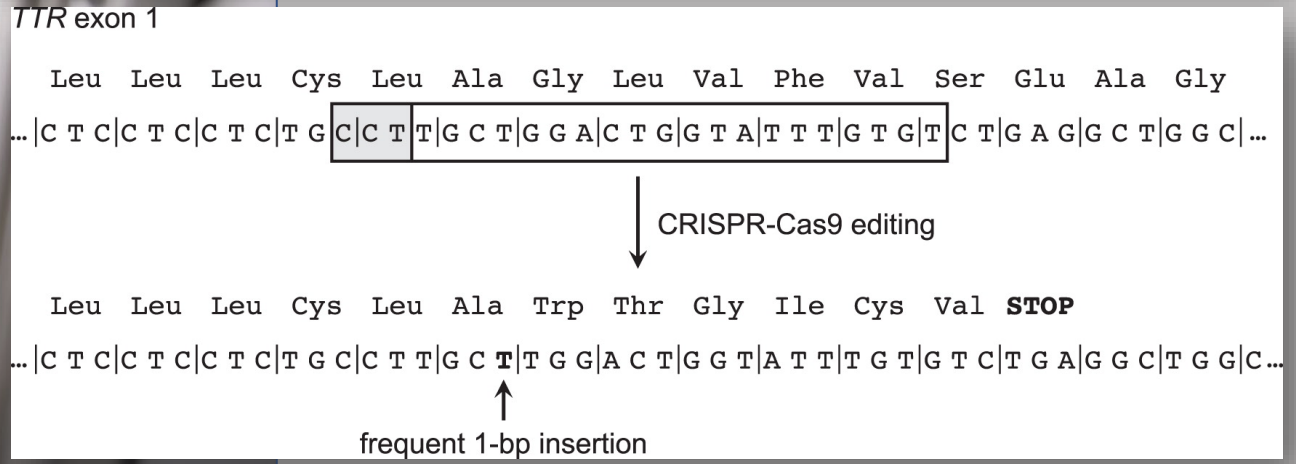
Vertex Pharmaceuticals (October 2023)

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.



Intellia THERAPEUTICS

NEJM June 2021

NEW ZEALAND / SCIENCE

Ground-breaking gene-editing treatment leaves patient feeling like they have 'a new body'

12:49 pm on 25 January 2023

Share this

Niva Chittock, Reporter
niva.chittock@rnz.co.nz

Being given a whole new body might sound like something from a sci-fi movie but a New Zealander [Judy Knox] says a new genetic treatment has felt just like that.

Hereditary angioedema is a rare immune deficiency that causes random, disabling and potentially lethal swelling…

Intellia Therapeutics chose New Zealand to be the first place to trial a ground-breaking gene-editing technology in late 2021 and 2022…

CRISPR for Leber's Congenital Amaurosis

Carlene Knight

STAT+

BIOTECH

Editas CRISPR treatment improved vision for one patient, but not others, early data show

Reprints

By Adam Feuerstein Sept. 29, 2021

editas MEDICINE

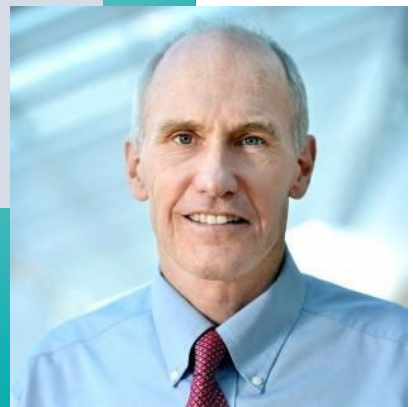
An epic clash of cultures in ancient Mesoamerica p. 968 | Music is another language pp. 974 & 1043 | A primordial body in the Kuiper Belt pp. 980 & 998–1000

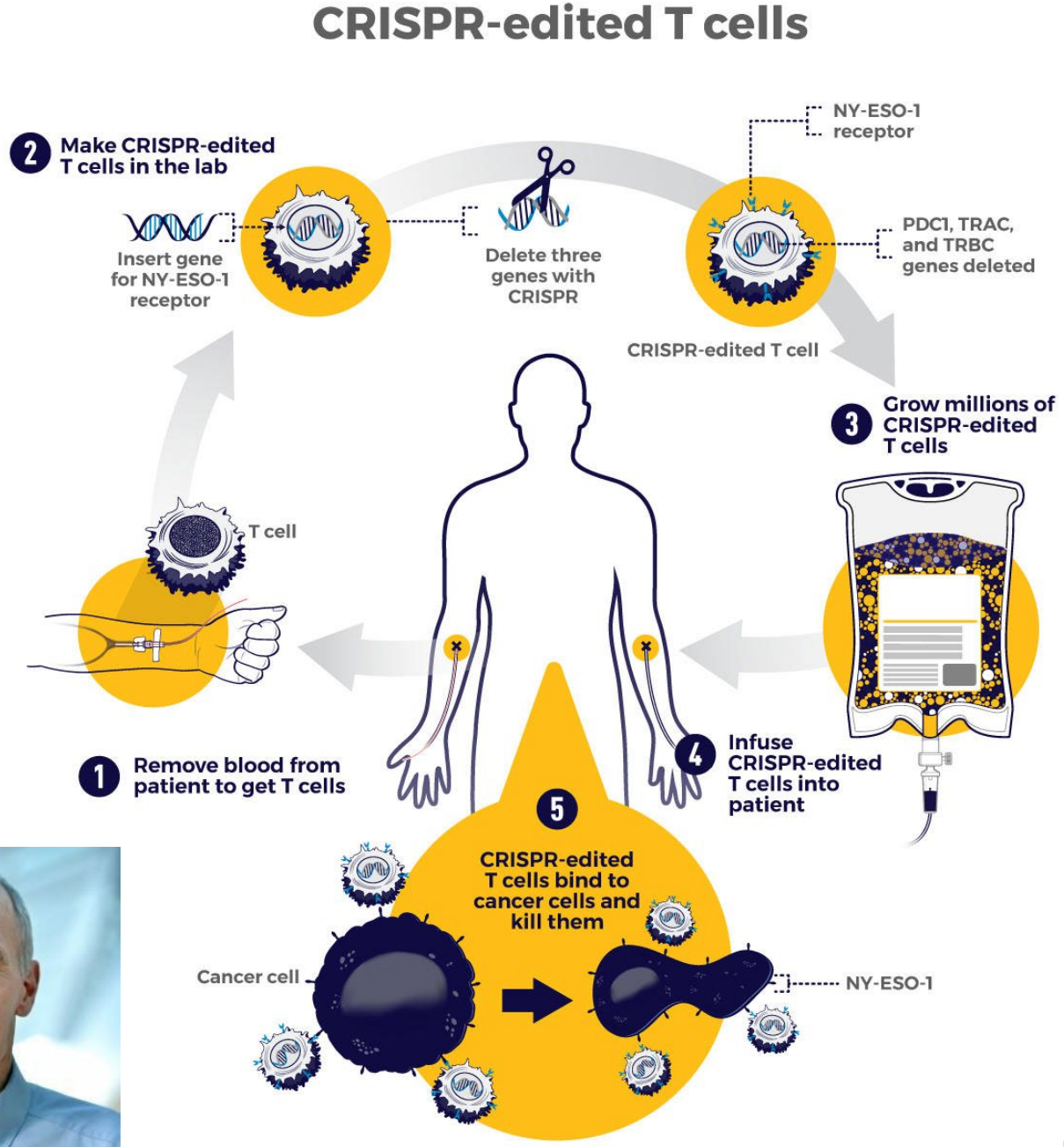
Science

$15
28 FEBRUARY 2020
sciencemag.org

AAAS

"… 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**."





NCI

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

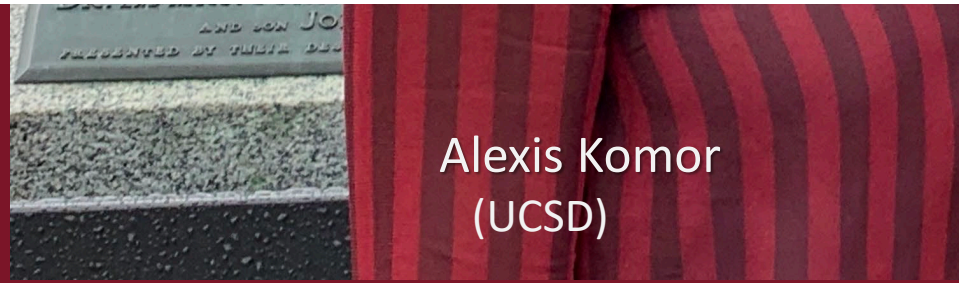
12 December 2022


David Liu
Broad Institute/HHMI

GuidePost

Programmable editing of a target base in genomic DNA without double-stranded DNA cleavage

Alexis C. Komor[1,2], Yongjoo B. Kim[1,2], Michael S. Packer[1,2], John A. Zuris[1,2] & David R. Liu[1,2]



Alexis Komor
(UCSD)

Programmable base editing of A·T to G·C in genomic DNA without DNA cleavage

Nicole Gaudelli
(Beam Therapeutics)

Nicole M. Gaudelli[1,2,3], Alexis C. Komor[1,2,3]†, Holly A. Rees[1,2,3], Michael S. Packer[1,2,3]†, Ahmed H. Badran[1,2,3], David I. Bryson[1,2,3]† & David R. Liu[1,2,3]

MEGAN MOLTENI SCIENCE 10.21.2019 11:00 AM

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.

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

Science Contents News Careers Jou

SHARE

12K

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

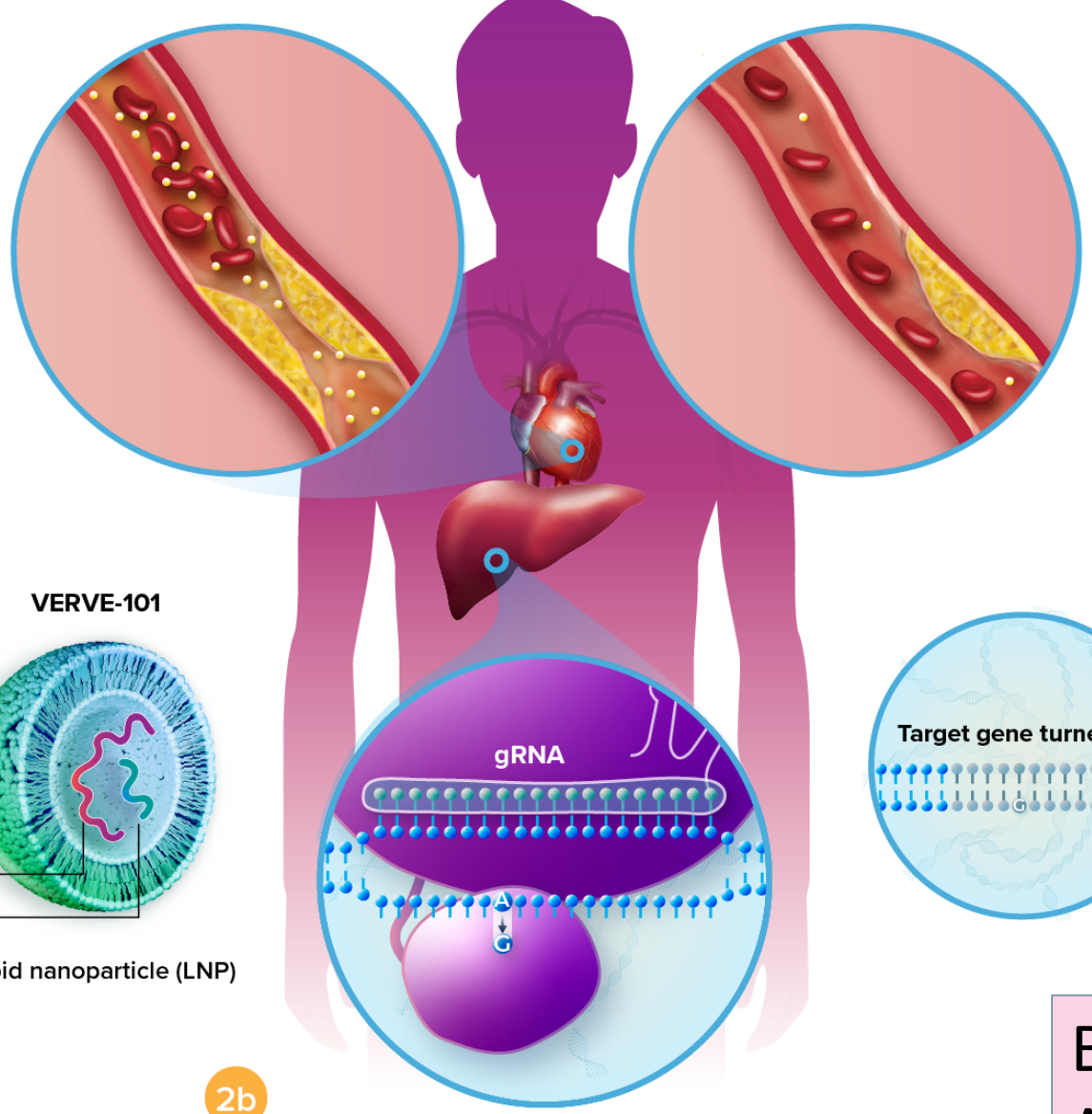
Verve Therapeutics demonstrates long-term LDL reduction for base editor therapy

*by **Alla Katsnelson, special to C&EN***

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

1

High blood LDL-C leads to clogged arteries in the heart resulting in ASCVD.



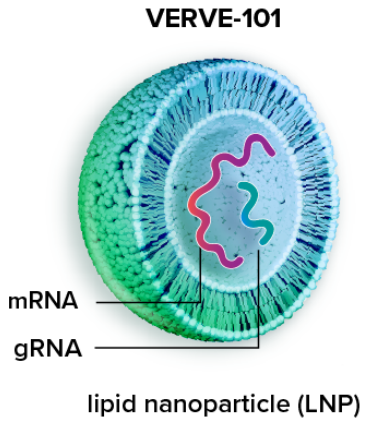
3

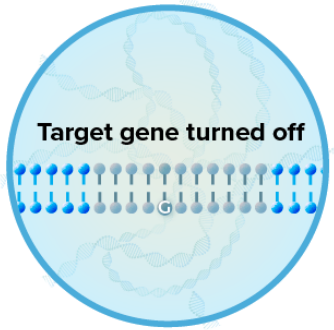
Turning off the *PCSK9* gene results in lower blood LDL-C lifelong, and thus treats ASCVD.

2a

We deliver our drug, VERVE-101, via intravenous infusion into the blood.

VERVE-101 gets taken up into the liver. The gRNA and mRNA are ultimately released inside the liver cells, into the cytoplasm.





2c

A single spelling change in the DNA sequence permanently turns off the *PCSK9* gene.

2b

The mRNA is translated into the base editing protein ABE which binds to the gRNA and together travel to the nucleus. Within the nucleus, this complex scans the DNA using the gRNA to find the target gene *PCSK9* and makes a specific A-to-G spelling change within the gene.

verve THERAPEUTICS

Base editing *PCSK9*: A potential “one and done” cure for heart disease?

CRISPR in the Clinic

Sponsor	Program	Disease	# patients	Notes
CRISPR Tx	exa-cel	Sickle cell/beta-thal	75	+ Vertex
	CTX110	CAR-T/B-cell malignancies	32	
	CTX130	CAR-T/solid tumors + blood	18	
	VCTX210	Type 1 diabetes	10	+ Viacyte
INTELLIA	2001	Transthyretin amyloidosis	27	+ Regeneron
	2002	Hereditary angiodema	10	
	5001	TCR-T-cell/AML	1+	
	OTQ923	Sickle cell	2+	
EDITAS	101	Leber congenital amaurosis 10	14	
	301	Sickle cell	2	
VERVE Tx	101	Familial hypercholesterolemia	4	*base editing*
CARIBOU	CB-010	CAR-T/non-Hodgkin lymphoma	9	
	CB-011	CAR-T/multiple myeloma	coming	
BEAM Tx	101	Sickle-cell	1+	*base editing*
	201	CAR-T/T-ALL	2+	
GRAPHITE BIO	nula-cel	Sickle-cell	1	*Abandoned

More than 200 patients have or are currently receiving CRISPR genome editing in clinical trials (Mar 2023)

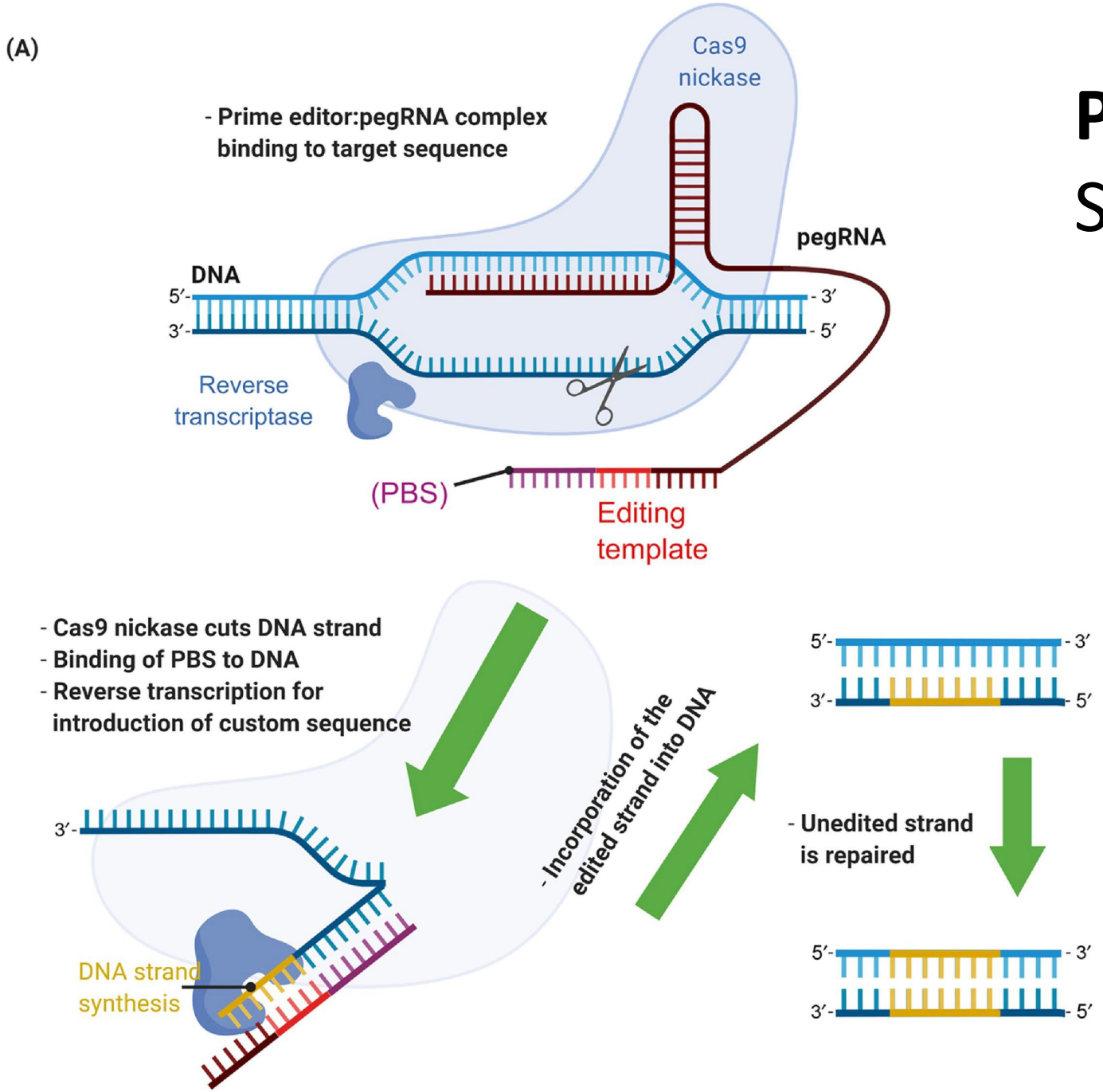
Cell Therapy | GEN Edge | Genome Editing | Gene Therapy | Stem Cells | Hematopoietic Stem Cells | Translational Medicine

Hit Pause: The Read-Across to Graphite Bio's CEDAR Sickle Cell Trial Suspension

Since voluntarily pausing the CEDAR trial upon reporting a serious and unexpected adverse event in the first patient dosed with GPH-101 (nula-cel), Graphite Bio has seen its share price tumble about 40% as questions persist as to what went wrong

By **Jonathan D Grinstein, PhD** - January 26, 2023

Prime Editing:
Search and Replace



prime medicine

Anzalone A. et al.
Nature 576, 149 (2019)

Genome Editing Goes Primetime

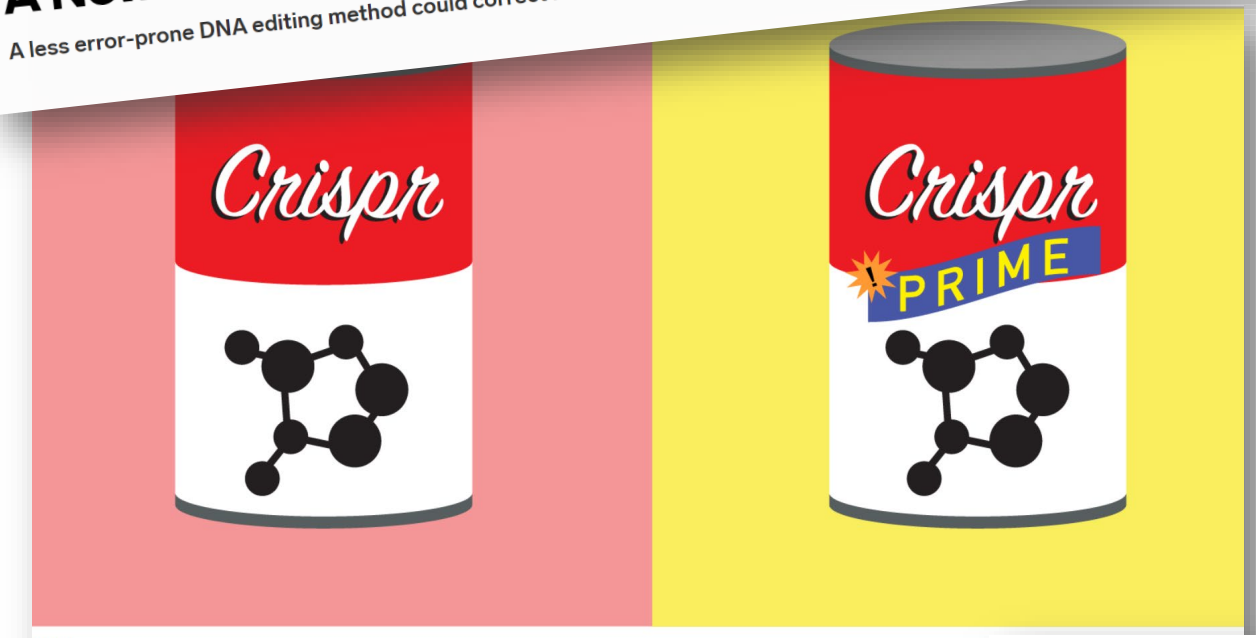
MEGAN MOLTENI SCIENCE 10.21.2019 11:00 AM

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.

New 'prime' genome editor could surpass CRISPR

By Jon Cohen | Oct. 21, 2019 , 11:00 AM



Tech Exclusives Insights Genome Editing CRISPR CRISPR-Cas9

Genome Editing Heads to Primetime

David Liu's lab introduces "prime editing", a new twist on genome editing that can introduce any base substitution without cleaving DNA.

By **Julianna LeMieux, PhD** - October 21, 2019 0

New CRISPR tool has the potential to correct almost all disease-causing DNA glitches, scientists report

By SHARON BEGLEY @sxbegle / OCTOBER 21, 2019

TECH

Biotechnology / CRISPR

The newest gene editor radically improves on CRISPR

New gene editing tool could fix most harmful DNA mutations

'Prime editing' more precise than Crispr-Cas9, but still needs time before use on humans

“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.”

Fyodor Urnov
New York Times
January 2023

Gene therapy can transform life for people with hemophilia. But some patients don't want it.

By Jonathan Saltzman Globe Staff, Updated January 29, 2023, 4:36 p.m.

Bobby Wiseman, 51, in the living room of his Rancho Cordova, Calif. home. JAKUB MOSUR/JAKUB MOSUR PHOTOGRAPHY

nature

PHARMACEUTICALS

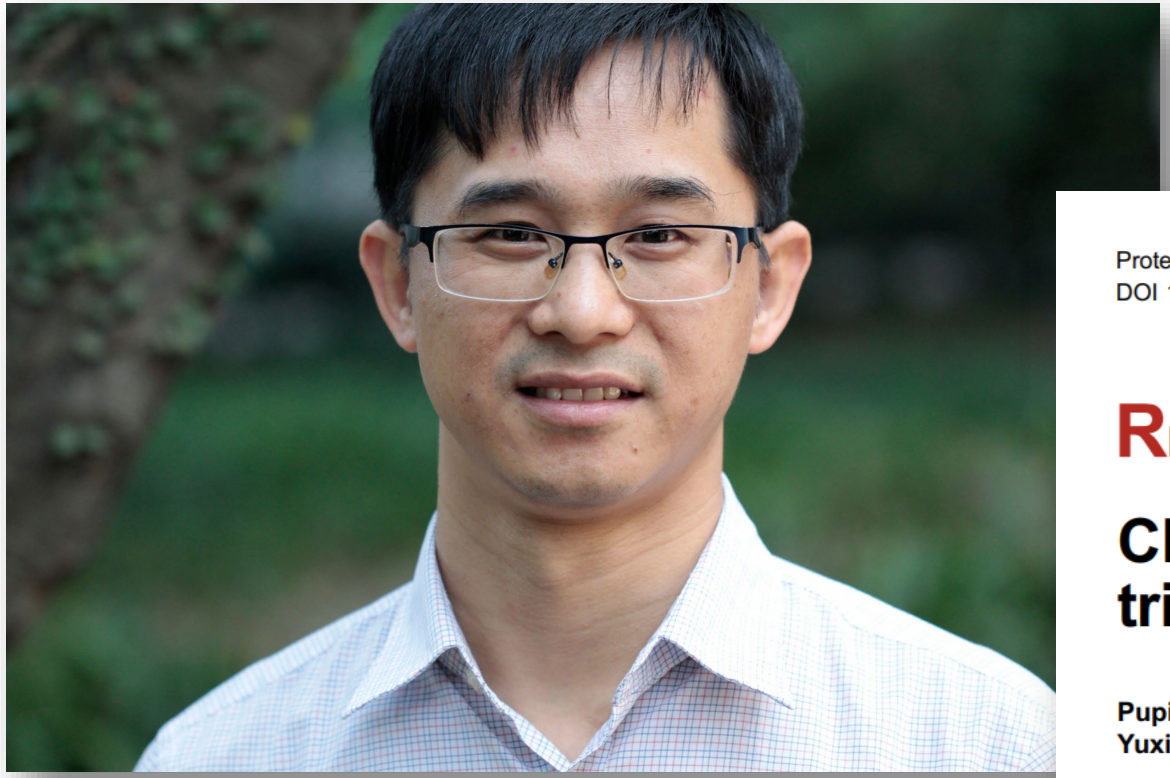
$3.5-Million Hemophilia Gene Therapy Is World's Most Expensive Drug

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
JURASSIC PARK
YOU DIDN'T STOP TO THINK IF YOU SHOULD

Chinese Scientists Edit Genes of Human Embryos, Raising Concerns

-- New York Times (2015)



Huang Junjiu
(Sun Yat-sen University)

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

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

Subject: Success!

Hi Steve,

Good News! The women is pregnant, the genome editing success! The embryo with CCR5 gene edited was transplanted to the women 10 days ago, and today the pregnancy is confirmed!

Regards,

JK

发自我的iPhone

- Email sent to Stephen Quake (Stanford), April 2018
- Similar emails sent to Craig Mello (UMass Chan Med Sch) and Mark DeWitt (UC Berkeley)

New York Times
April 14, 2019

“The Baby is Born”

Hi Stephen,

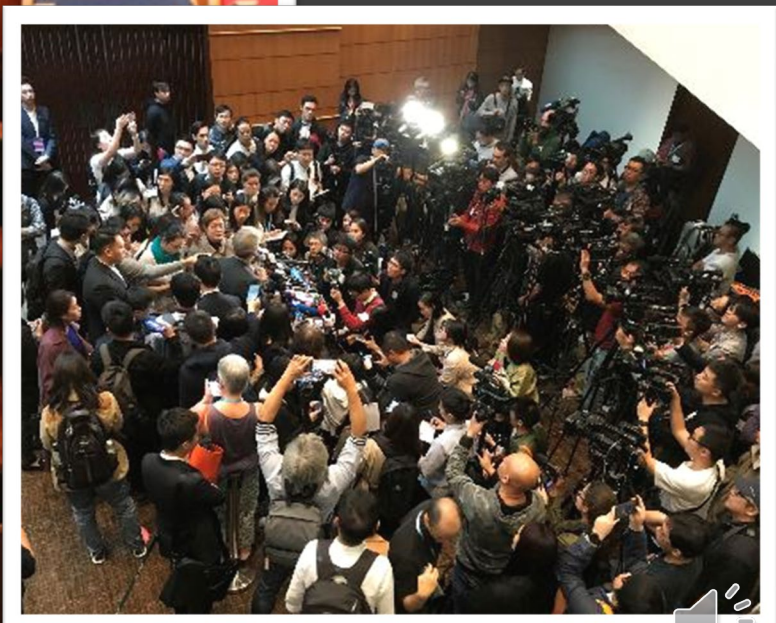
Great news! the baby is born (please keep it in confidential). I am coming to San Francisco this week, will you be available for a meeting? I can come to Stanford in Wednesday, Thursday or Friday. I want to get help from you on how to announce the result, PR and ethics.

Regards,
JK

Jiankui He
Associate Professor
Southern University of Science and Technology (SUSTech)
Lab website: www.sustc-genome.org.cn
贺建奎
南方科技大学生物系副教授

New York Times
April 14, 2019

Antonio Regalado
MIT Technology Review



HKU November 28, 2018


YULI YANG
University of Hong Kong
November 28, 2018


PAM
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
THE ROYAL SOCIETY
NATIONAL ACADEMY OF SCIENCES
NATIONAL ACADEMY OF MEDICINE

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


“ 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

Denis Rebrikov
Pirogov Medical University
Moscow

«Вчера было рано, завтра будет поздно. Власть надо брать сегодня».

“Yesterday was early, tomorrow will be late.
Power must be taken today.”

-- LENIN

Andrey Rudakov /
Bloomberg

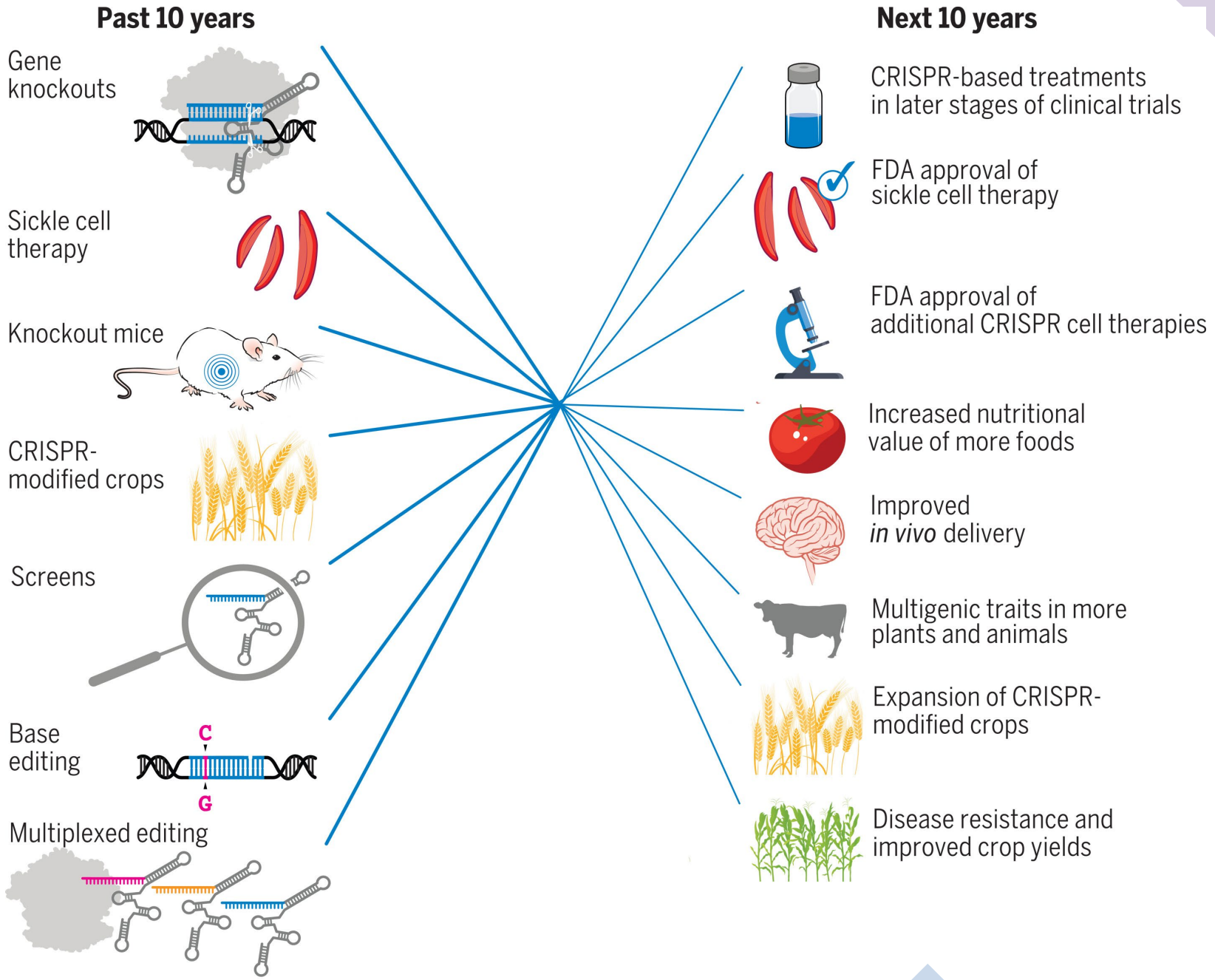
Who Wants a CRISPR Clinic?

From: "xxxxxxxx"<xxxxxxx>;
Date: Wed, Dec 5, 2018 01:18 PM
To: "hejk"<xxxxxxxxx >;
Cc: "xxxxxxxx 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 XXXXXXXX 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,
XXXXXXXXXXX
Business Director's Assistant
XXXXXX

Credit: William Hurlbut

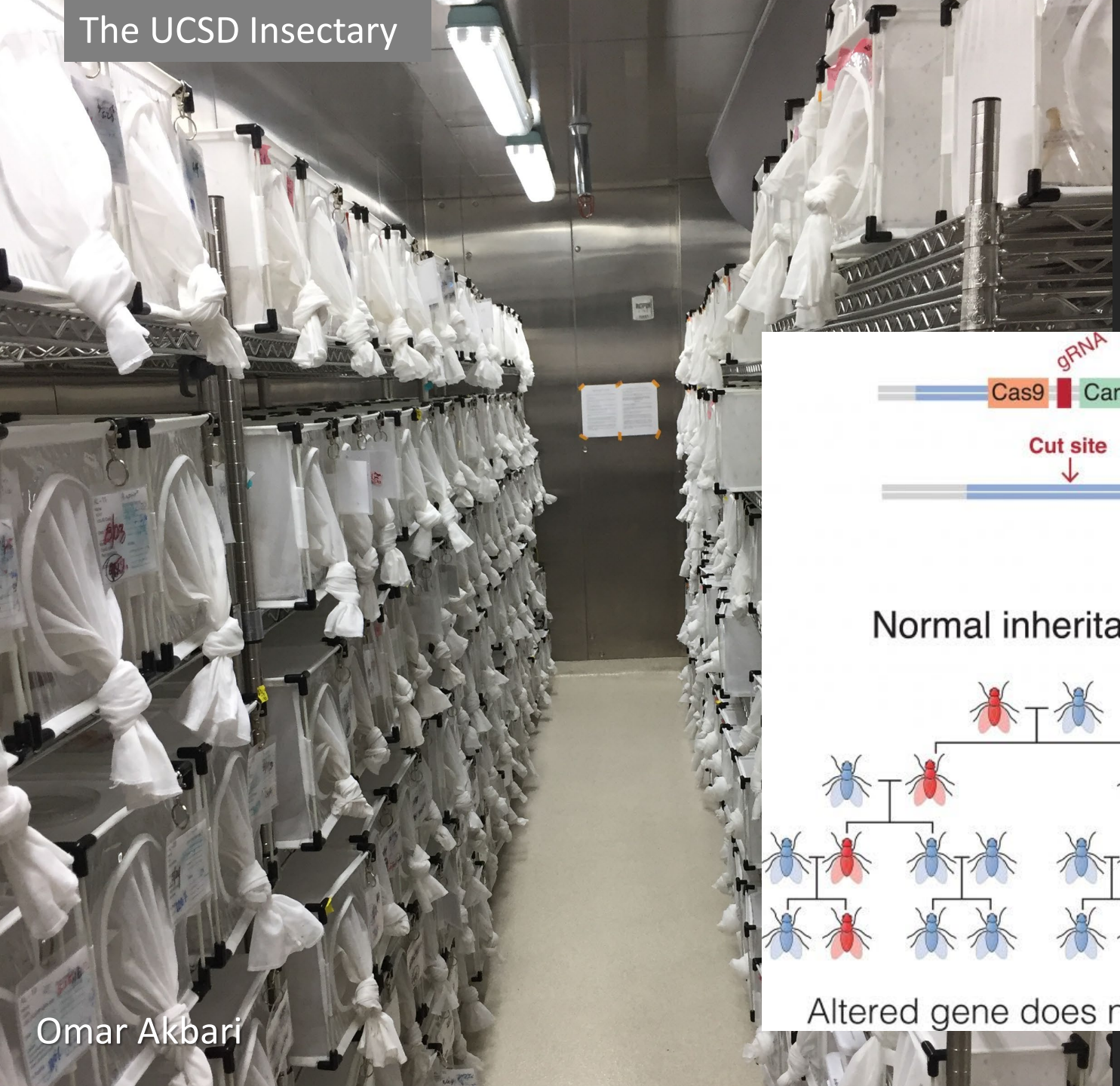

Past 10 years
Gene knockouts
Sickle cell therapy
Knockout mice
CRISPR-modified crops
Screens
Base editing
C
G
Multiplexed editing
Next 10 years
CRISPR-based treatments in later stages of clinical trials
FDA approval of sickle cell therapy
FDA approval of additional CRISPR cell therapies
Increased nutritional 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

REPORT

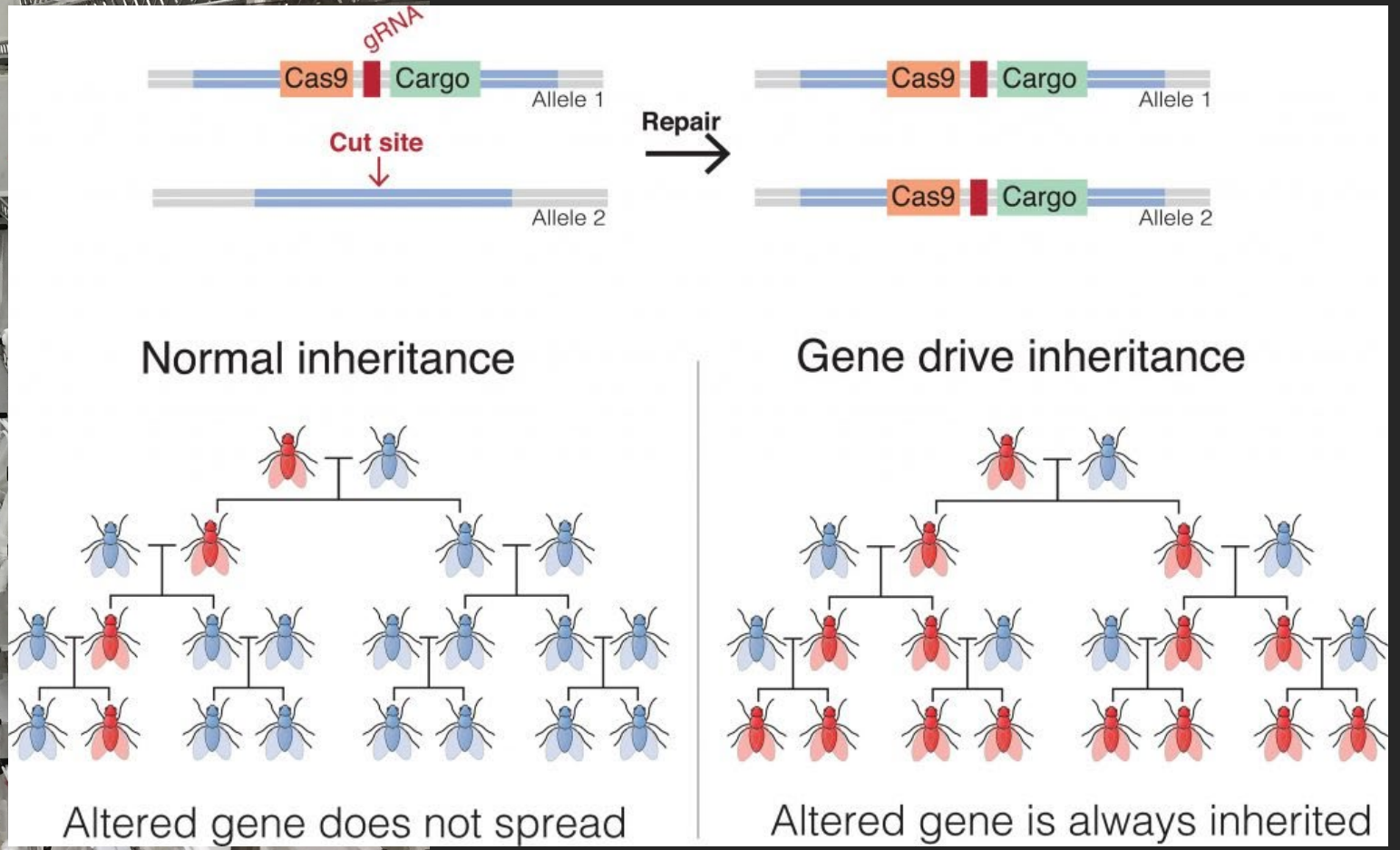
Inactivation of porcine endogenous retrovirus in pigs using CRISPR-Cas9

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

[1]*eGenesis, Inc., Cambridge, MA 02139, USA.*


The UCSD Insectary
Omar Akbari

GENE DRIVES


gRNA
Cas9
Cargo
Allele 1
Cut site
Allele 2
Repair
Cas9
Cargo
Allele 1
Cas9
Cargo
Allele 2
Normal inheritance
Gene drive inheritance
Altered gene does not spread
Altered gene is always inherited

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 is now on sale in Japan -- a tomato packed with an alleged increase in nutritional content.

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. Now, the tomatoes are ripe for sale.

sanatechseed®
For Tomorrow's Children and Earth

De-Extinction: Pleistocene Park?

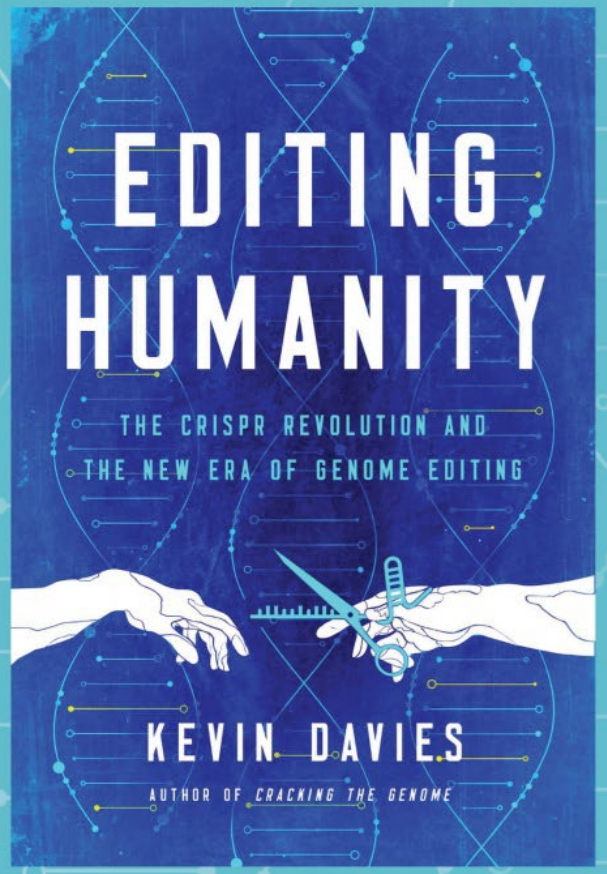
Eriona Hysolli
Medium December 2018

Brackett N. et al.
CRISPR Journal (April 2022).

Victoria Gray
London
March 2023

Royal Society

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.

E: davieskev@gmail.com
T: @KevinADavies

John Simon Guggenheim Memorial Foundation

Mary Ann Liebert, Inc.