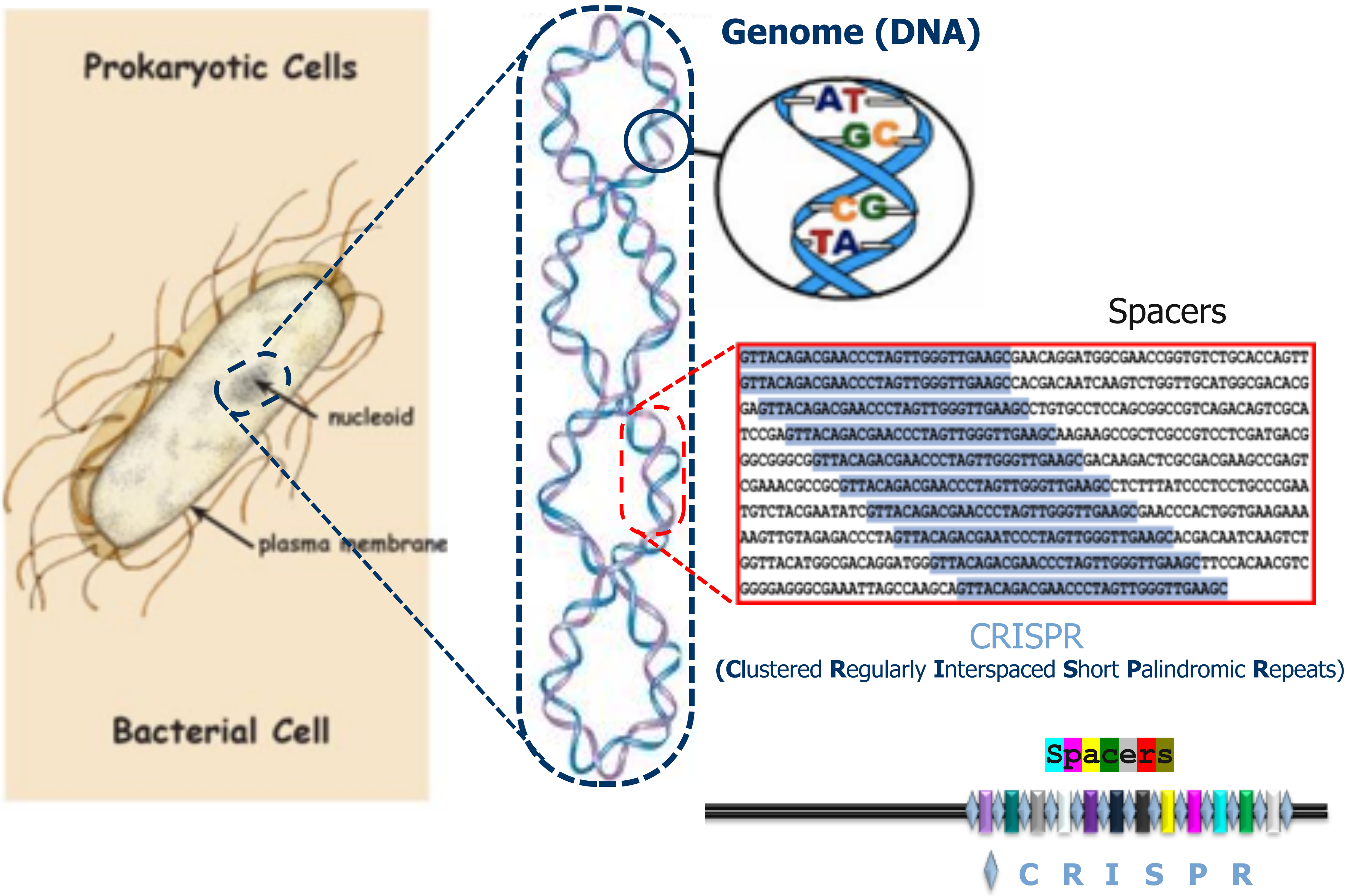
CRISPR systems: the advent of a new scenario in biological research

Francisco J. M. Mojica

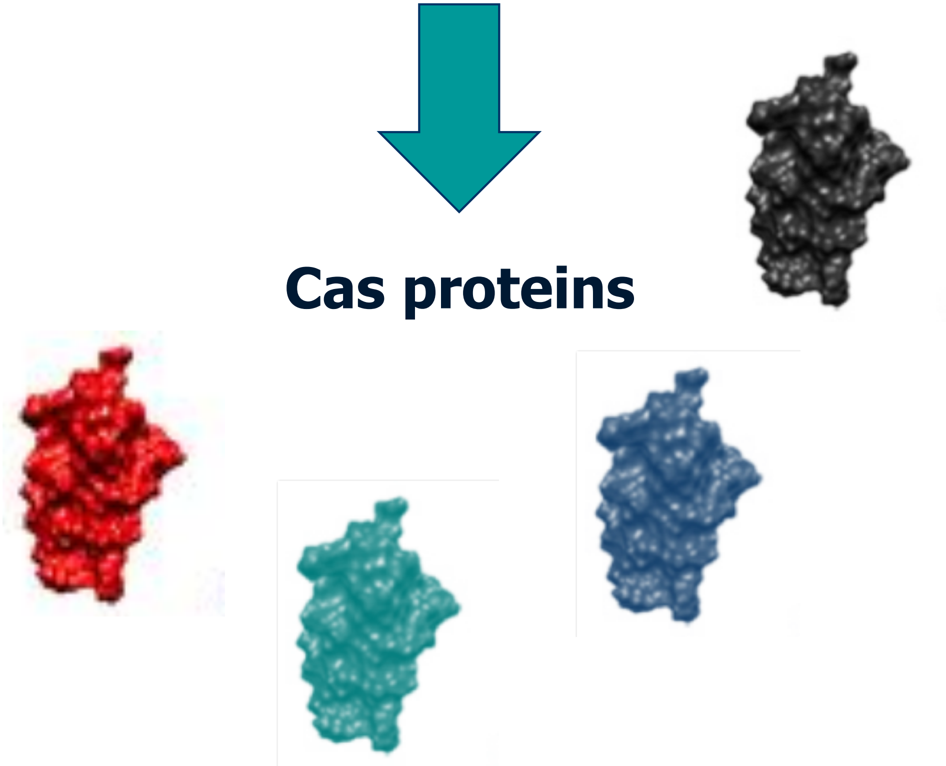
Universitat d'Alacant
Universidad de Alicante

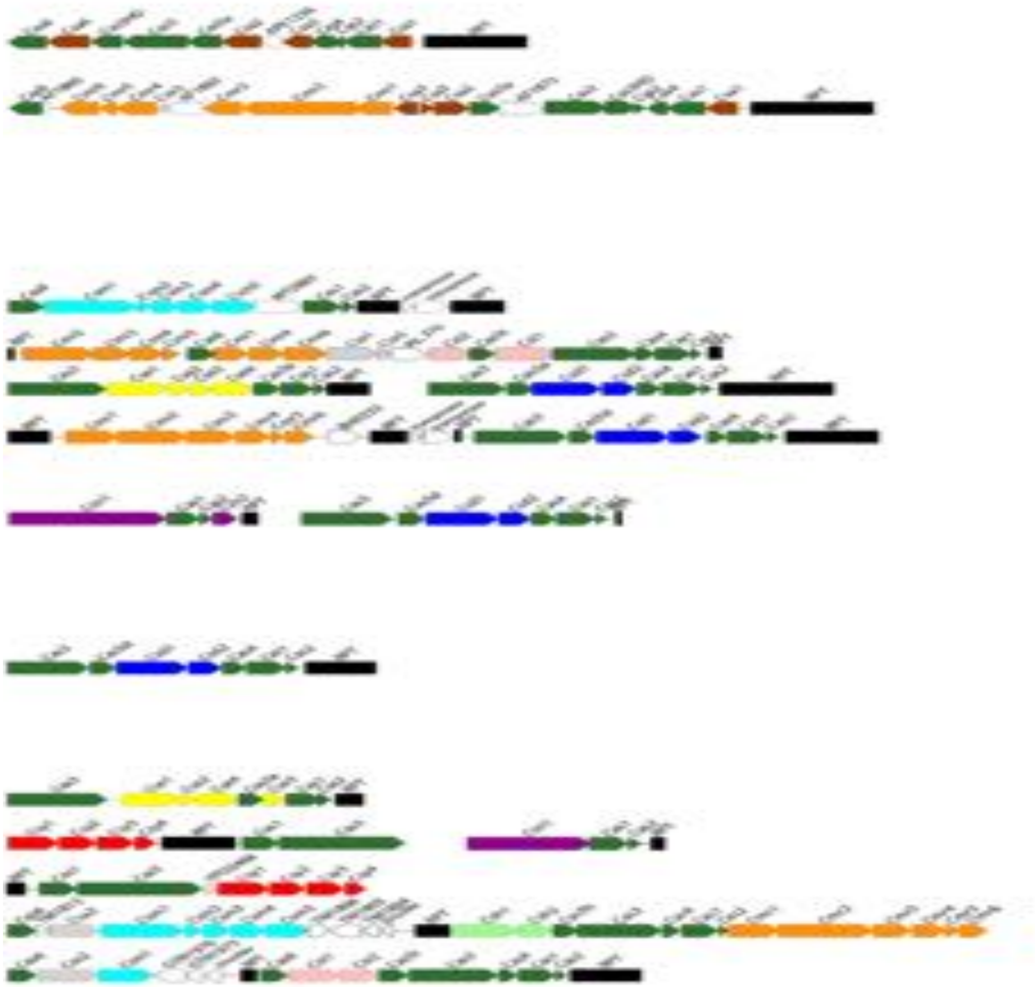
Components of the CRISPR systems



Prokaryotic Cells
nucleoid
plasma membrane
Bacterial Cell
Genome (DNA)
AT
GC
CG
TA
Spacers
GTTACAGACGAACCCTAGTTGGGTTGAAGCGAACAGGATGGCGAACCGGTGTCTGCACCAGTT
GTTACAGACGAACCCTAGTTGGGTTGAAGCCACGACAATCAAGTCTGGTTGCATGGCGACACG
GAGTTACAGACGAACCCTAGTTGGGTTGAAGCCTGTGCCTCCAGCGGCCGTCAGACAGTCGCA
TCCGAGTTACAGACGAACCCTAGTTGGGTTGAAGCAAGAAGCCGCTCGCCGTCCTCGATGACG
GGCGGGCGGTTACAGACGAACCCTAGTTGGGTTGAAGCGACAAGACTCGCGACGAAGCCGAGT
CGAAACGCCGCGTTACAGACGAACCCTAGTTGGGTTGAAGCCTCTTTATCCCTCCTGCCCGAA
TGTCTACGAATATCGTTACAGACGAACCCTAGTTGGGTTGAAGCGAACCCACTGGTGAAGAAA
AAGTTGTAGAGACCCTAGTTACAGACGAATCCCTAGTTGGGTTGAAGCACGACAATCAAGTCT
GGTTACATGGCGACAGGATGGGTTACAGACGAACCCTAGTTGGGTTGAAGCTTCCACAACGTC
GGGGAGGGCGAAATTAGCCAAGCAGTTACAGACGAACCCTAGTTGGGTTGAAGC
CRISPR
(Clustered Regularly Interspaced Short Palindromic Repeats)
Spacers
C R I S P R

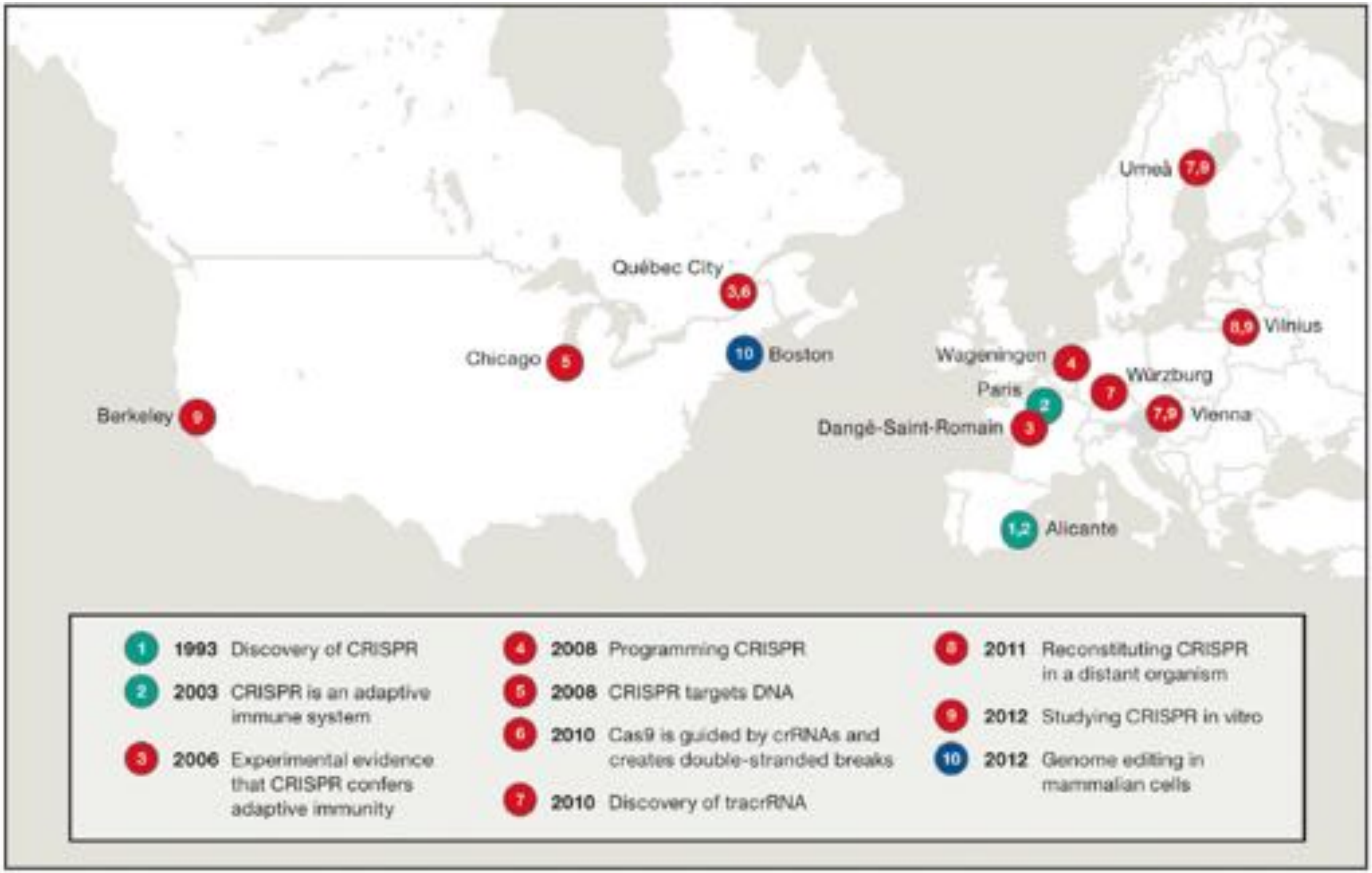
cas (**C**RISPR **as**sociated) **genes**





CRISPR System

Seminal Developments



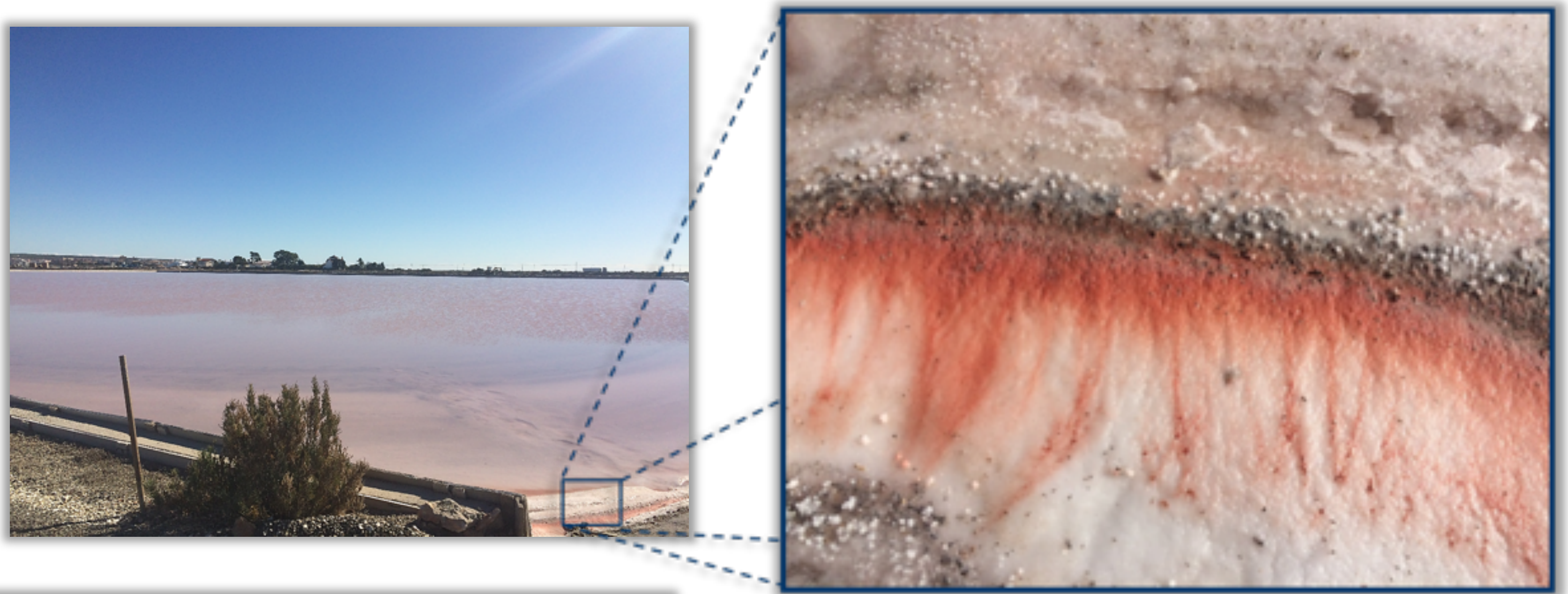
Cell

Leading Edge
Perspective

The Heroes of CRISPR

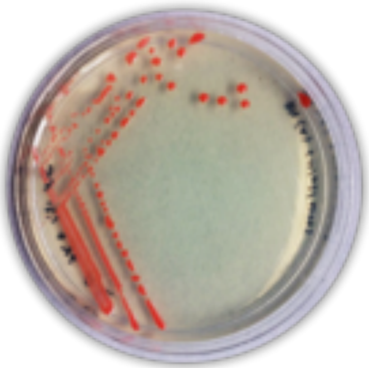
Eric S. Lander[1,2,3,*]

1990's: Haloadaptation in Archaea

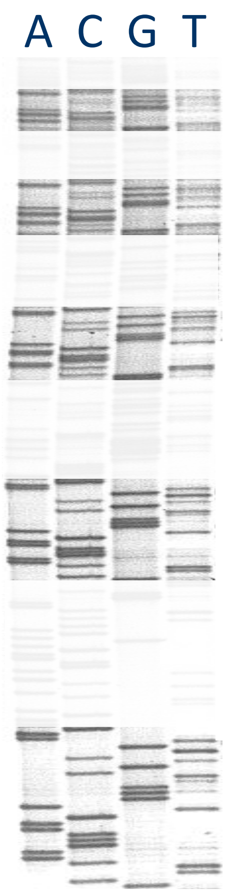


Salt marshes. Santa Pola (Alicante. SPAIN)

***Haloferax* spp.**

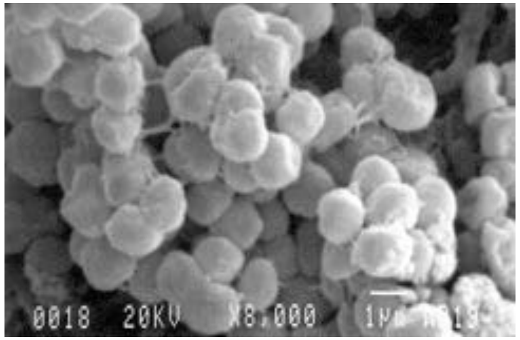


1993: Tandem Repeats in Archaea



Mojica. FJM. PhD. Thesis, 1993

***Haloferax* spp.**

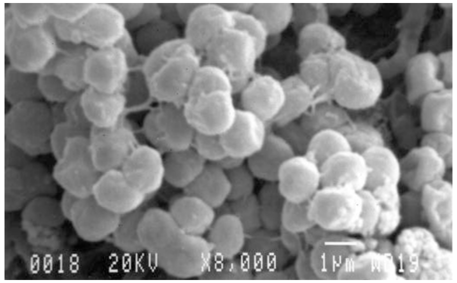


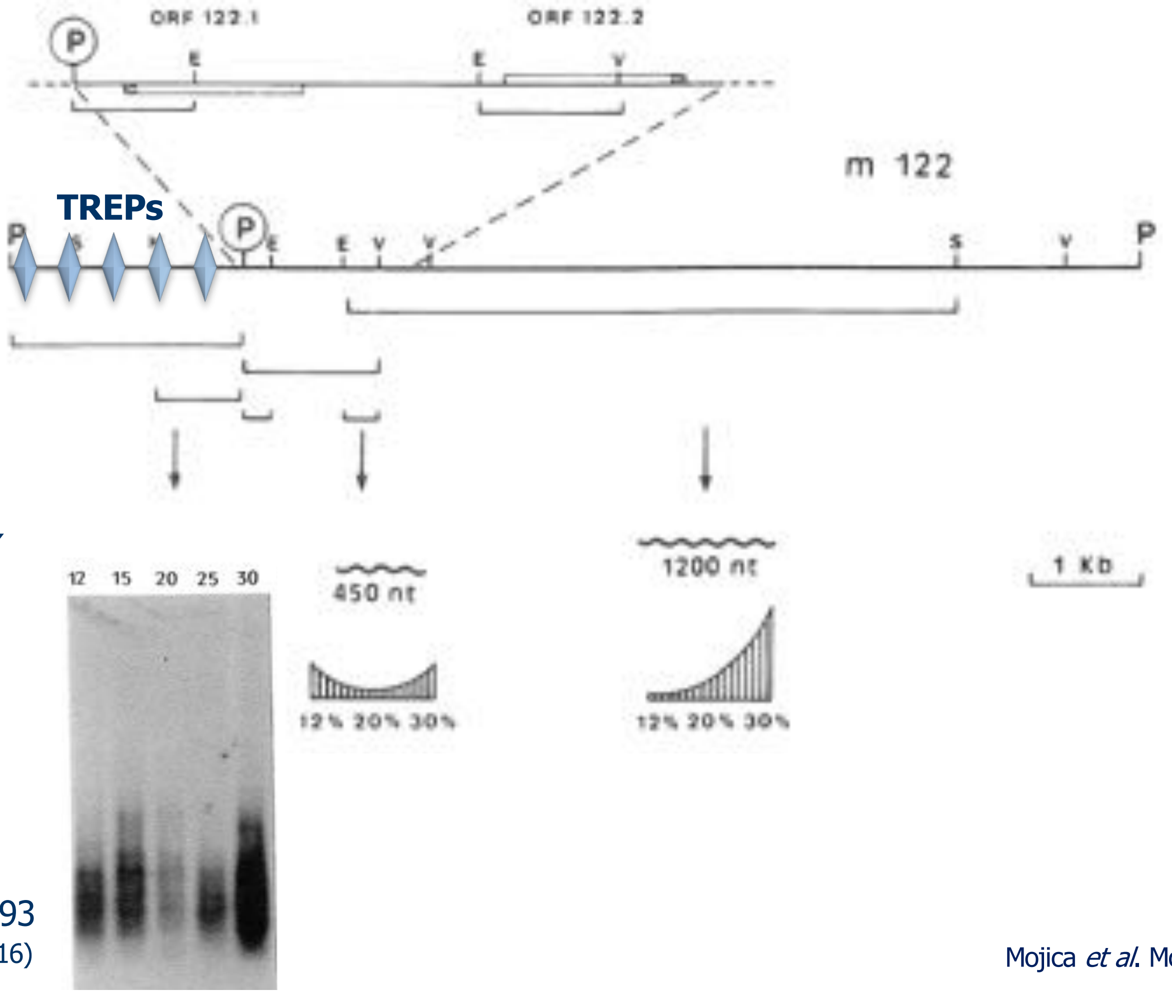
Boán, I.F. Universidad de Alicante

Mojica *et al.* Molecular Microbiology (1993)

1993-1995: TREPs' Activity

Haloferax mediterranei



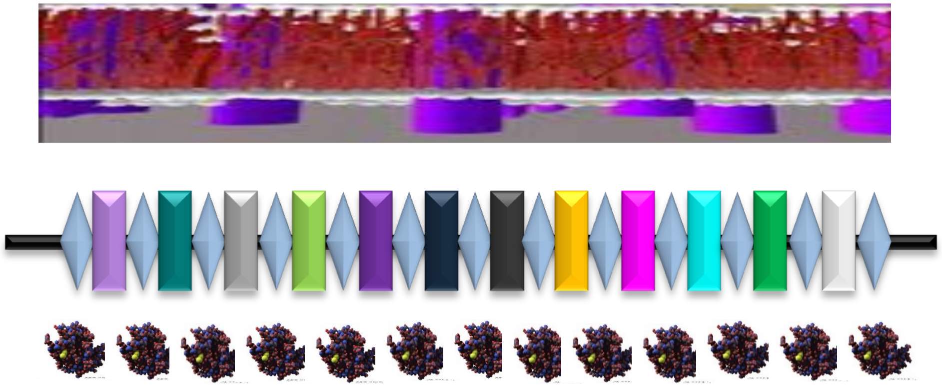


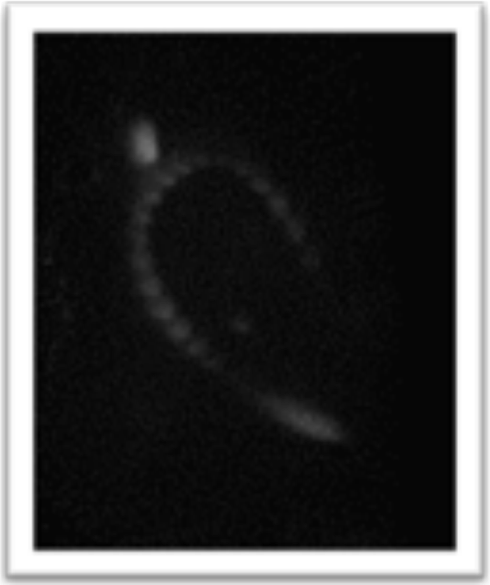
"Northern blot hybridization, using a HindIII-PstI fragment containing the last 12 repeats, revealed a long smear….with several differently sized blurred bands, resembling a highly processed RNA…"

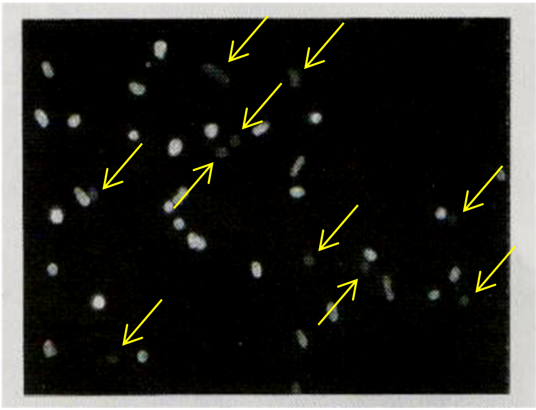
Mojica, FJM.; PhD Thesis. 1993
(Mojica & Rodriguez-Valera, FEBS J. 2016)

Mojica *et al*. Mol. Microbiol. (1993)

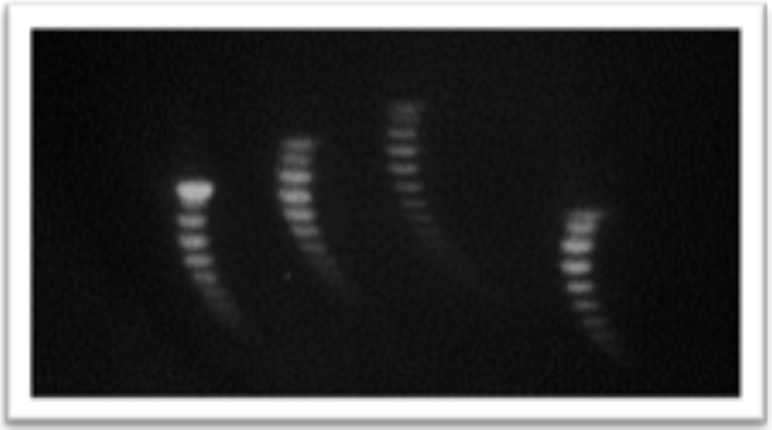
The enigmatic role of TREPs





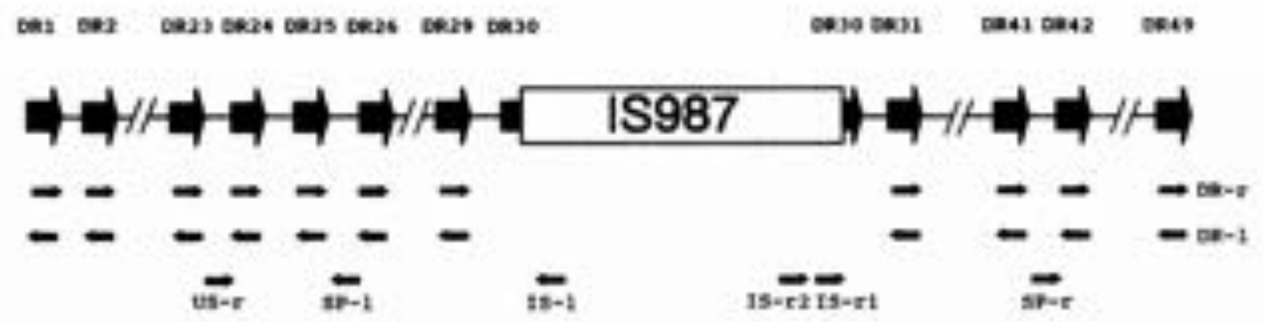


Mojica *et al.* Molecular Microbiology (1995)



Regularly spaced repeats in Bacteria

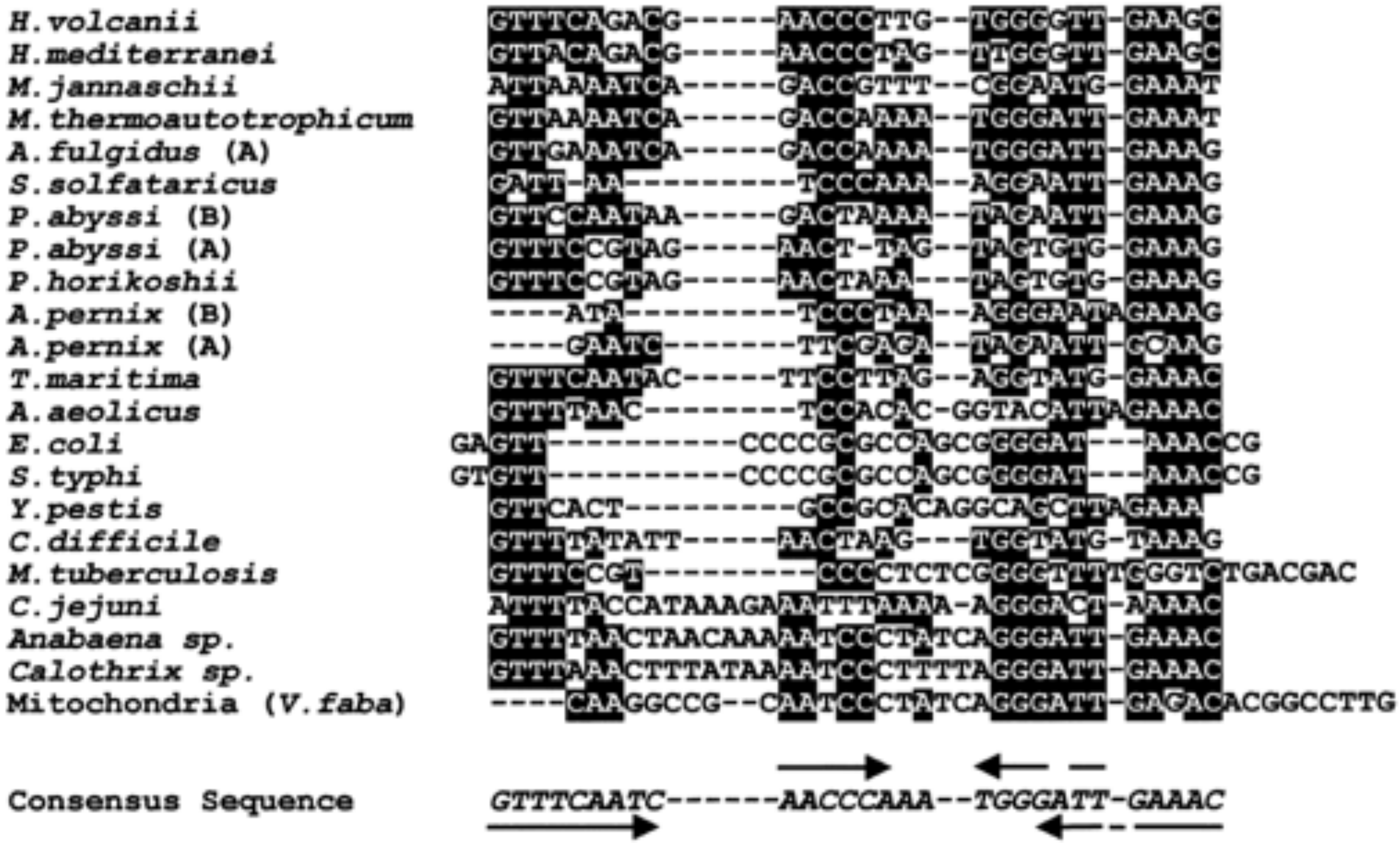
Ishino *et al.*, J. Bacteriol. 1987



Jan D.A. van Embden

Hermans *et al.*, Infect. Immun. 1991

2000: A new family of DNA repeats



Francisco J.M. Mojica *et al.* Molecular Microbiology (2000)

Clustered

Regularly

Interspaced

Short

Palindromic

Repeats

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.

Mojica & Garrett. CRISPR-Cas Systems 2013

"to avoid confusing nomenclature, Mojica *et al*. and our research group have agreed to use in this report and future publication the acronym CRISPR"

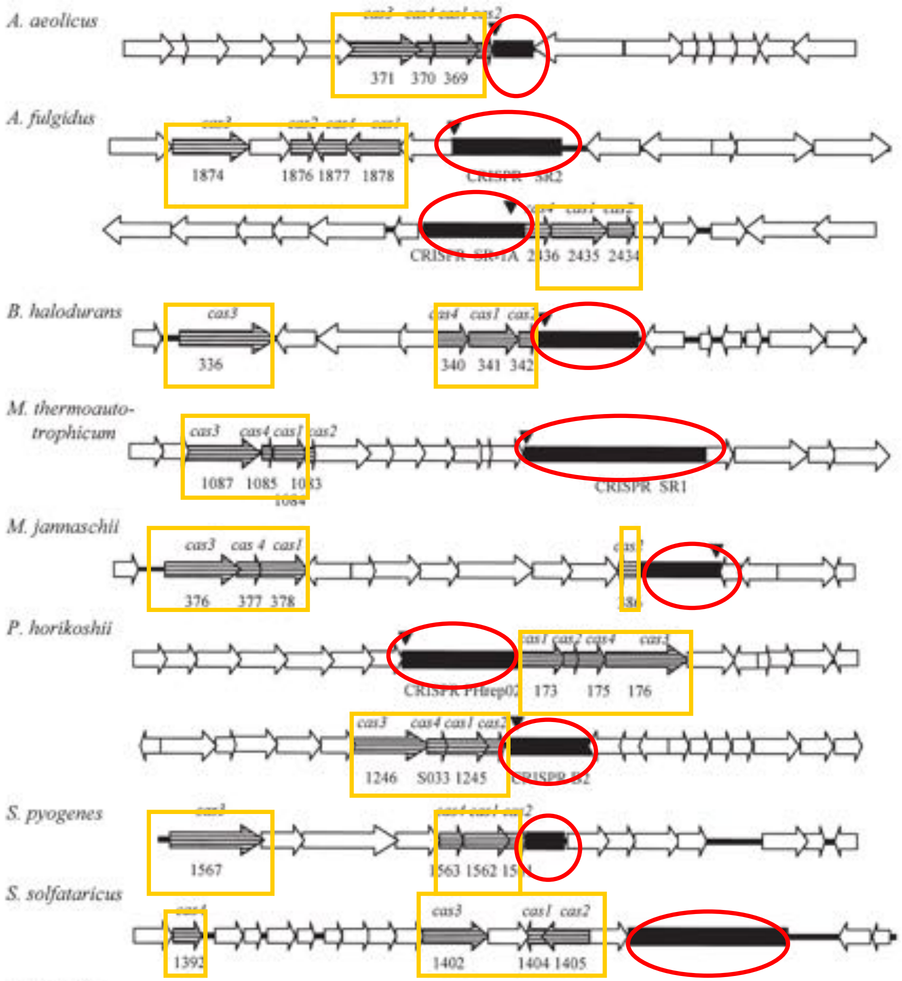
Jansen *et al*. Mol. Microbiol. 2002

2002: The *cas* genes

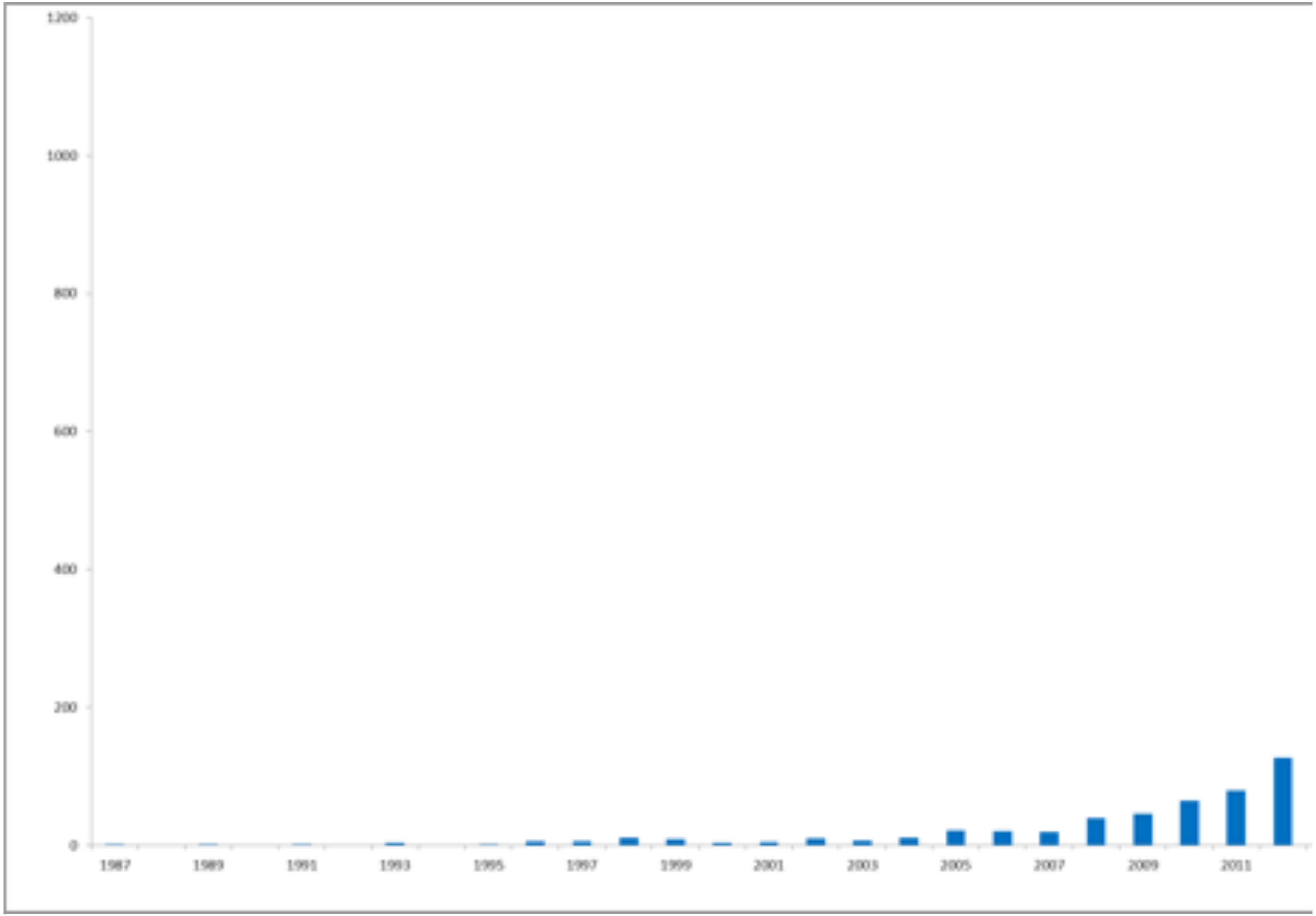
Molecular Microbiology (2002) **43**(6), 1565–1575

Identification of genes that are associated with DNA repeats in prokaryotes

Ruud. Jansen,[1*] Jan. D. A. van Embden,[2]
Wim. Gaastra[1] and Leo. M. Schouls[2]



CRISPR-Cas Publications



No. CRISPR/Cas papers

Year

DNA repeats as constituents of a prokaryotic immune system

We have identified mobile DNA elements (bacteriophages and conjugative plasmids) as the origin for spacers of the Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) of prokaryotes… **to propose a relationship between the CRISPRs and the immunity to foreign DNA**…, i.e. simply by deleting or inserting a spacer in a CRISPR loci would produce specific susceptibility or immunity respectively. **Immunity against these transmissible elements has a tremendous repercussion in biological, biotechnological and clinical sciences**.

Submitted to Nature, 2003

2005: The origin of spacers

J Mol Evol (2005) 60:174–182
DOI: 10.1007/s00239-004-0046-3

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

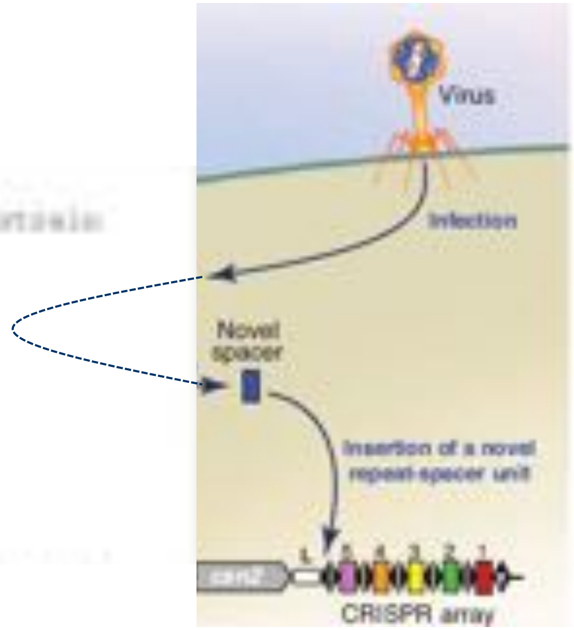
Mobile Genetic Elements

	Spacers (4500)	Phages (46)	Plasmids (10)
Chlorobium tepidum TLS	62		1
Clostridium tetani Massachusetts E88	62	1	
Corynebacterium efficiens YS-314T	22		1
Escherichia coli ECOR42	14		1
Escherichia coli ECOR44	10	1	
Escherichia coli ECOR47	17	1	
Escherichia coli ECOR49	11		1
Listeria innocua Clip11262	9	3	
Listeria monocytogenes EGD-e	4	1	
Methanothermobacter thermoautotrophicus ΔH	169	9	
Mycoplasma gallisepticum R	71		
Neisseria meningitidis Z2491 (serogroup A)	16		
Photorhabdus luminescens laumondii TT01	65	7	
Porphyromonas gingivalis W83	44		
Pyrobaculum aerophilum IM2	129		
Salmonella typhimurium LT2 SGSC1412	57	1	
Shigella sonnei 53G	3		
Streptococcus agalactiae NEM316	13	1	
Streptococcus agalactiae 2603V/R	25	1	1
Streptococcus pyogenes M1 GAS SF370	9	8	
Sulfolobus solfataricus P2	424	6	3
Sulfolobus tokodaii 7	471	2	2
Thermoanaerobacter tengcongensis MB4T	306		
Yersinia pestis CO-92 (Biovar Orientalis)	16	4	

Streptococcus pyogenes

<table>
<tr><th>Spacer</th><th>Gene</th><th>Prophage[a]</th><th>Activity</th><th>Alignment[b]</th></tr>
<tr><td>4-1</td><td>spyM3_1239</td><td>315.4</td><td>Unknown</td><td>gctgtgacattgcgggatgtaatcaaagtaaaa
||||||||||||||| |||||||||||| ||||
gctgtgacattgcggaatgtaatcaaagcaaaa</td></tr>
<tr><td>4-2</td><td>spyM3_0941</td><td>315.2</td><td>Capside protein</td><td>taaagcaaacctagcagaagcagaaaatgac
|||||| ||||||| |||||||||||| |||
taaagcgaacctagtagaagcagaaaacgac</td></tr>
<tr><td>4-3</td><td>spyM18_0741</td><td>Φ_{speC}</td><td>Methyltransferase</td><td>ctgatgtaattggtgattttcgtgatatgcttt
||||||||||||||||||||||||||||| ||
ctgatgtaattggtgattttcgtgatatgcctt</td></tr>
<tr><td>7-1</td><td>spyM3_1215</td><td>315.4</td><td>Endopeptidase</td><td>gcgctggttgatttcttcttgcgcttttt
|||||||||||||||||||||||||||||
gcgctggttgatttcttcttgcgcttttt</td></tr>
<tr><td>7-2</td><td>speM</td><td>Φ_{speLM}</td><td>Exotoxin</td><td>tatatgaacataactcaatttgtaaaaaa
|||||||||||||||||||||||||||||
tatatgaacataactcaatttgtaaaaaa</td></tr>
<tr><td>7-3</td><td>spyM18_0742</td><td>Φ_{speC}</td><td>Methyltransferase</td><td>aggaatatccgcaataattaattgcgctct
||||||||||||||||||||||||||||||
aggaatatccgcaataattaattgcgctct</td></tr>
<tr><td>7-4</td><td>hylP</td><td>315.3</td><td>Hyaluronidase</td><td>agtgccgaggaaaaattaggtgcgcttggc
||||||||||||||||||||||||||||||
agtgccgaggaaaaattaggtgcgcttggc</td></tr>
<tr><td>7-5</td><td>spyM3_1347</td><td>315.5</td><td>Unknown</td><td>aaatttgtttagcaggtaaaccgtgcttt
|||||||||||||||||||||||||||||
aaatttgtttagcaggtaaaccgtgcttt</td></tr>
</table>

Spacer
Protospacer



Spacer/Protospacer Incompatibility !!

- Strains with spacers are resistant to infection by the protospacer-carriers

- Absence of protospacer in the spacer-carrier strains

- immunity

plasmids. Remarkably, these extrachromosomal elements fail to infect the specific spacer-carrier strain, implying a relationship between CRISPR and immunity against targeted DNA. Bacteriophages and

- guided by CRISPR-RNA

activity could be executed by CRISPR-RNA molecules, acting as regulatory RNA that specifically recognizes the target through the homologous RNA-spacer sequence, similarly to the eukaryotic interference RNA.

Mojica *et al*. J. Mol. Evol. 2005

Acquired Immunity Against Viruses

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 VOL 315 23 MARCH 2007

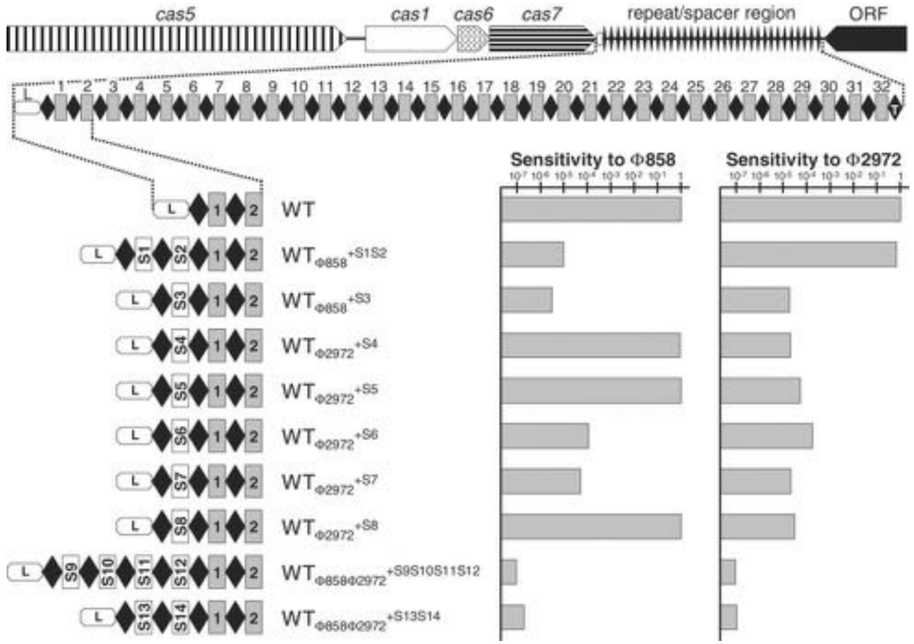
R. Barrangou

D. Romero

S. Moineau

P. Horvath

Fig. 1. Streptococcus thermophilus CRISPR1 locus overview, newly acquired spacers in phage-resistant mutants, and corresponding phage sensitivity.



Rodolphe Barrangou et al. Science 2007;315:1709-1712

Science AAAS

RNA-guided

Small CRISPR RNAs Guide Antiviral Defense in Prokaryotes

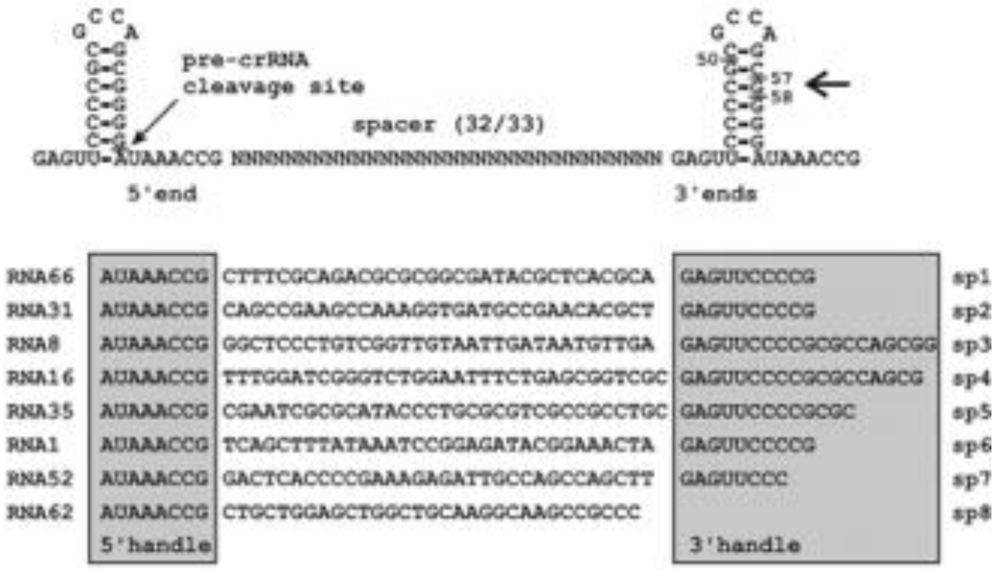
Stan J. J. Brouns,[1*] Matthijs M. Jore,[1*] Magnus Lundgren,[1] Edze R. Westra,[1] Rik J. H. Slijkhuis,[1] Ambrosius P. L. Snijders,[2] Mark J. Dickman,[2] Kira S. Makarova,[3] Eugene V. Koonin,[3] John van der Oost[1]†

SCIENCE VOL 321 15 AUGUST 2008

S. Brouns

E. Koonin

J. van der Oost

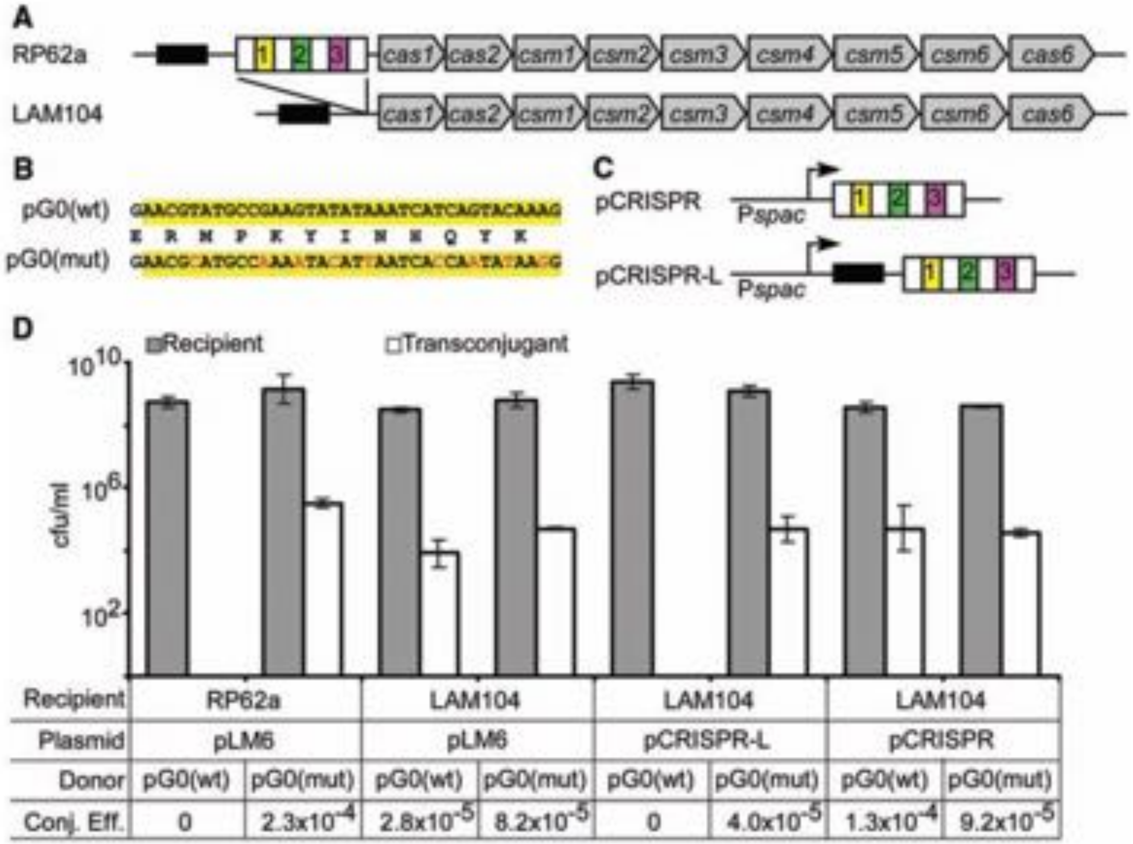


DNA Targeting

CRISPR Interference Limits Horizontal Gene Transfer in Staphylococci by Targeting DNA

Luciano A. Marraffini and Erik J. Sontheimer*

SCIENCE VOL 322 19 DECEMBER 2008

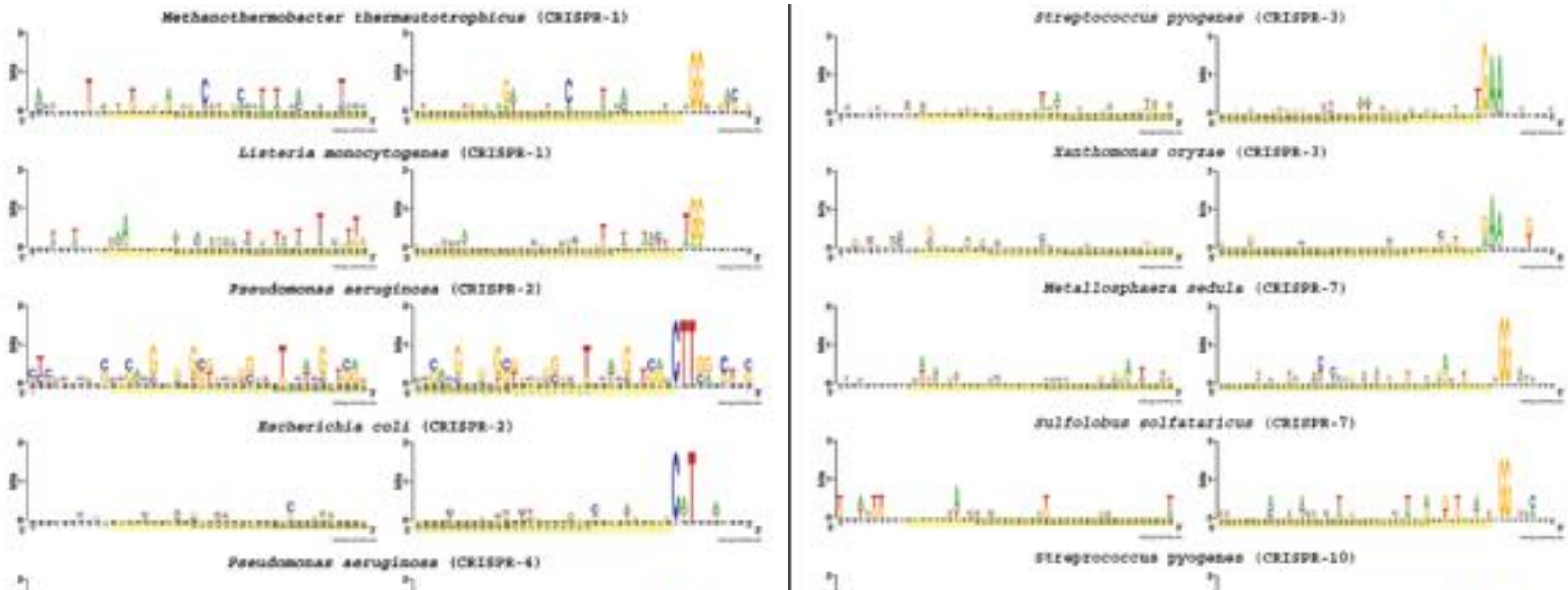


Protospacer Adjacent Motifs (PAMs)

Short motif sequences determine the targets of the prokaryotic CRISPR defence system

F. J. M. Mojica, C. Díez-Villaseñor, J. García-Martínez and C. Almendros

Microbiology (2009)



"PAMs will have to be considered in the development of the expected applications of the CRISPR system as an innovative molecular biology tool"

Immunity = Target Cleavage

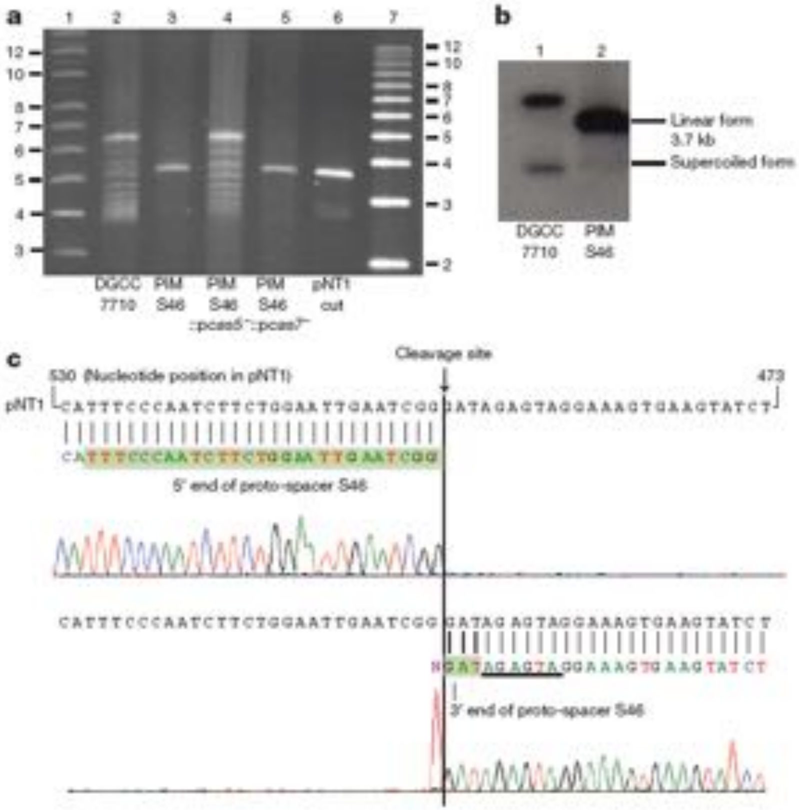
The CRISPR/Cas bacterial immune system cleaves bacteriophage and plasmid DNA

Nature (2010)

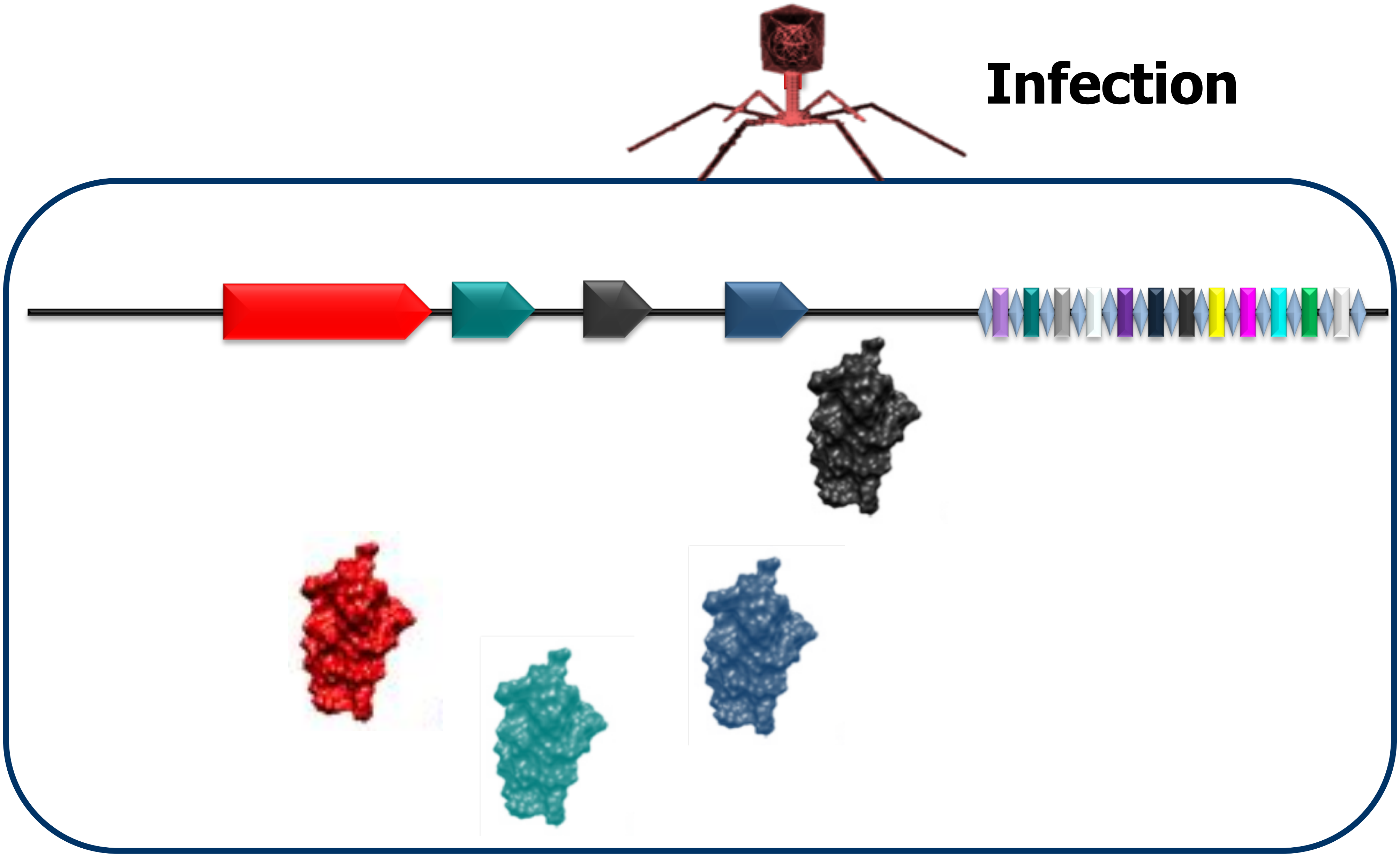
Josiane E. Garneau[1], Marie-Ève Dupuis[1], Manuela Villion[1], Dennis A. Romero[2], Rodolphe Barrangou[2], Patrick Boyaval[3], Christophe Fremaux[3], Philippe Horvath[3], Alfonso H. Magadán[1] & Sylvain Moineau[1]

S. Moineau

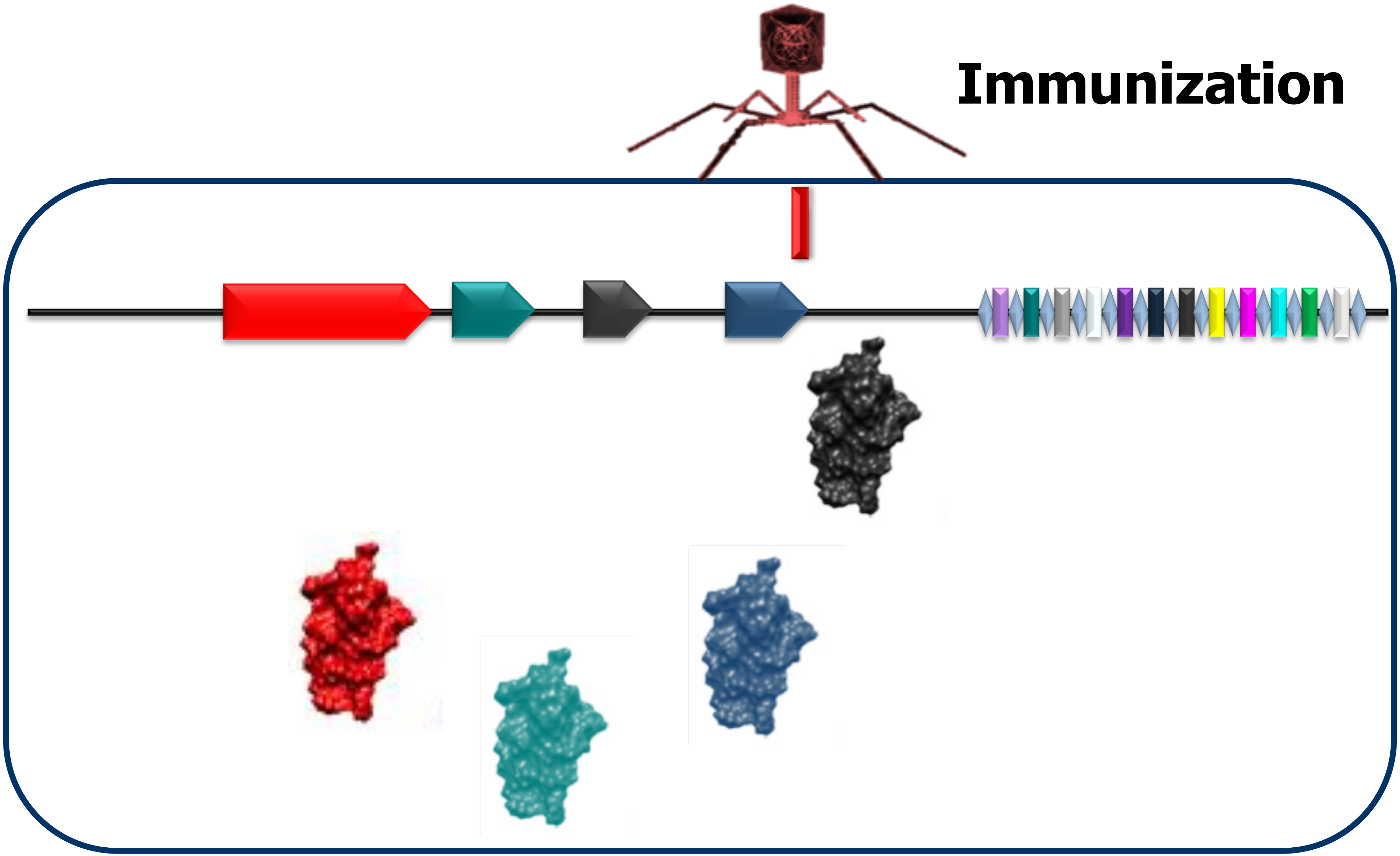
J. Garneau



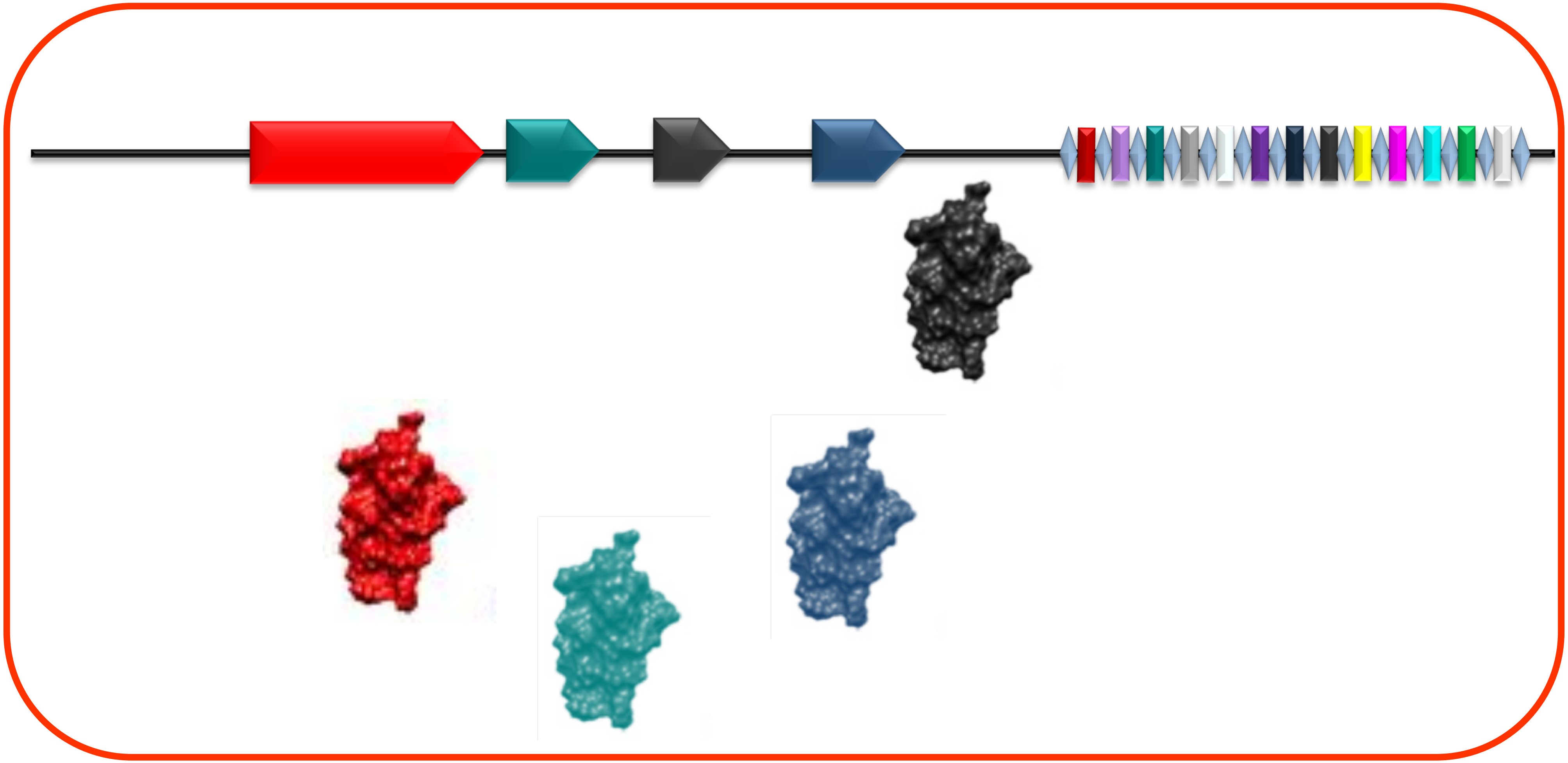
The CRISPR Mechanism


Infection

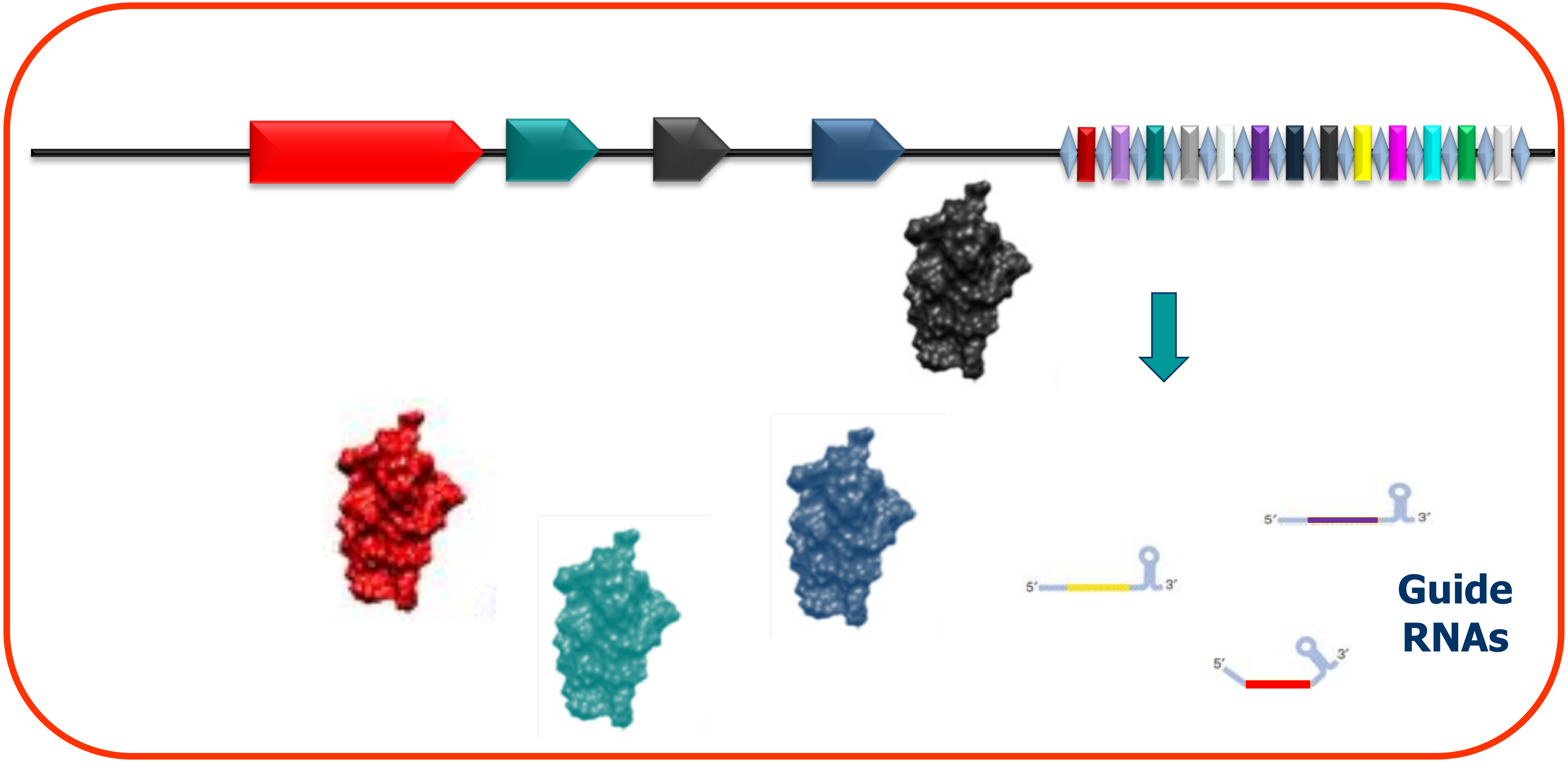
Immunization



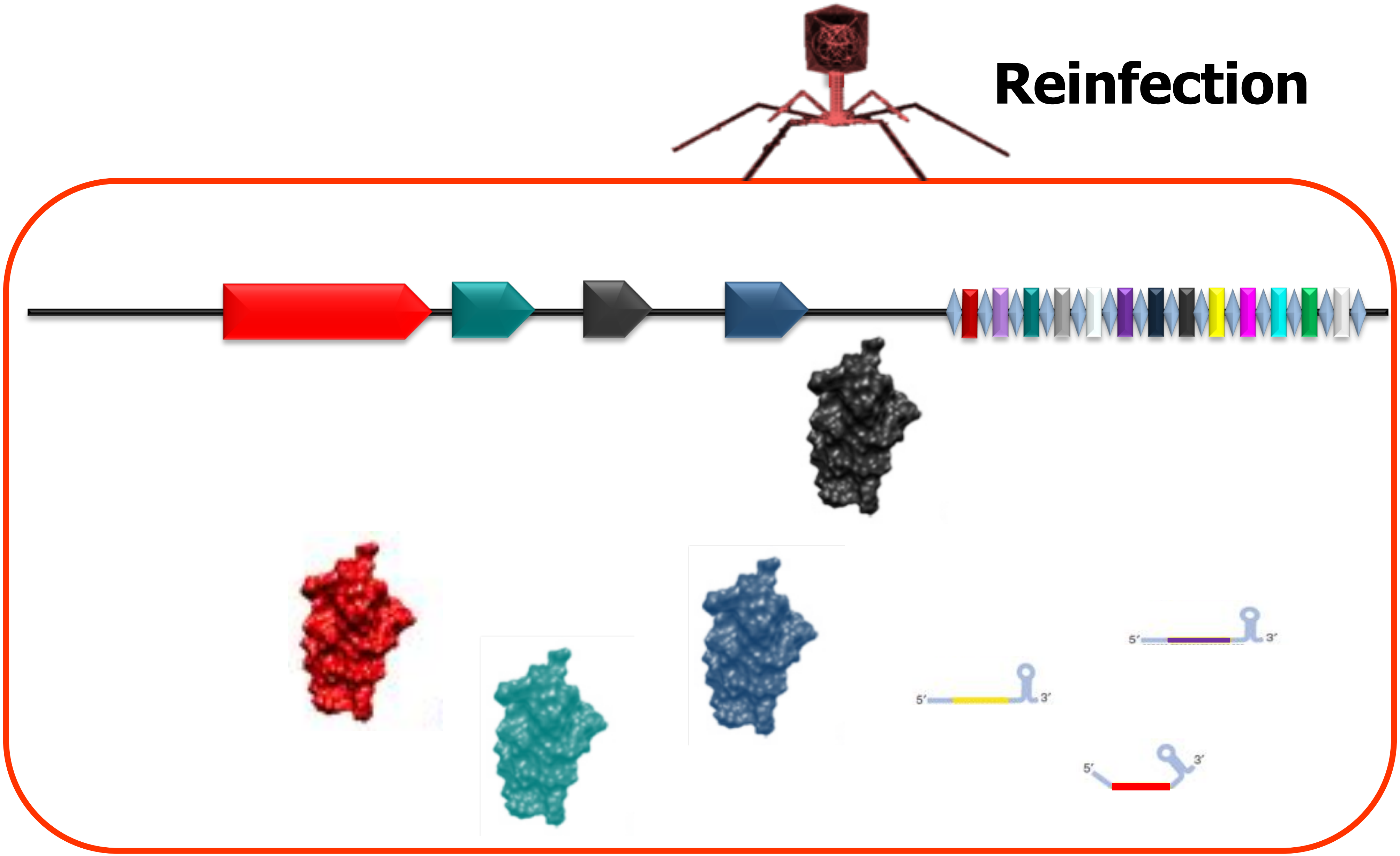
Immunized Cell



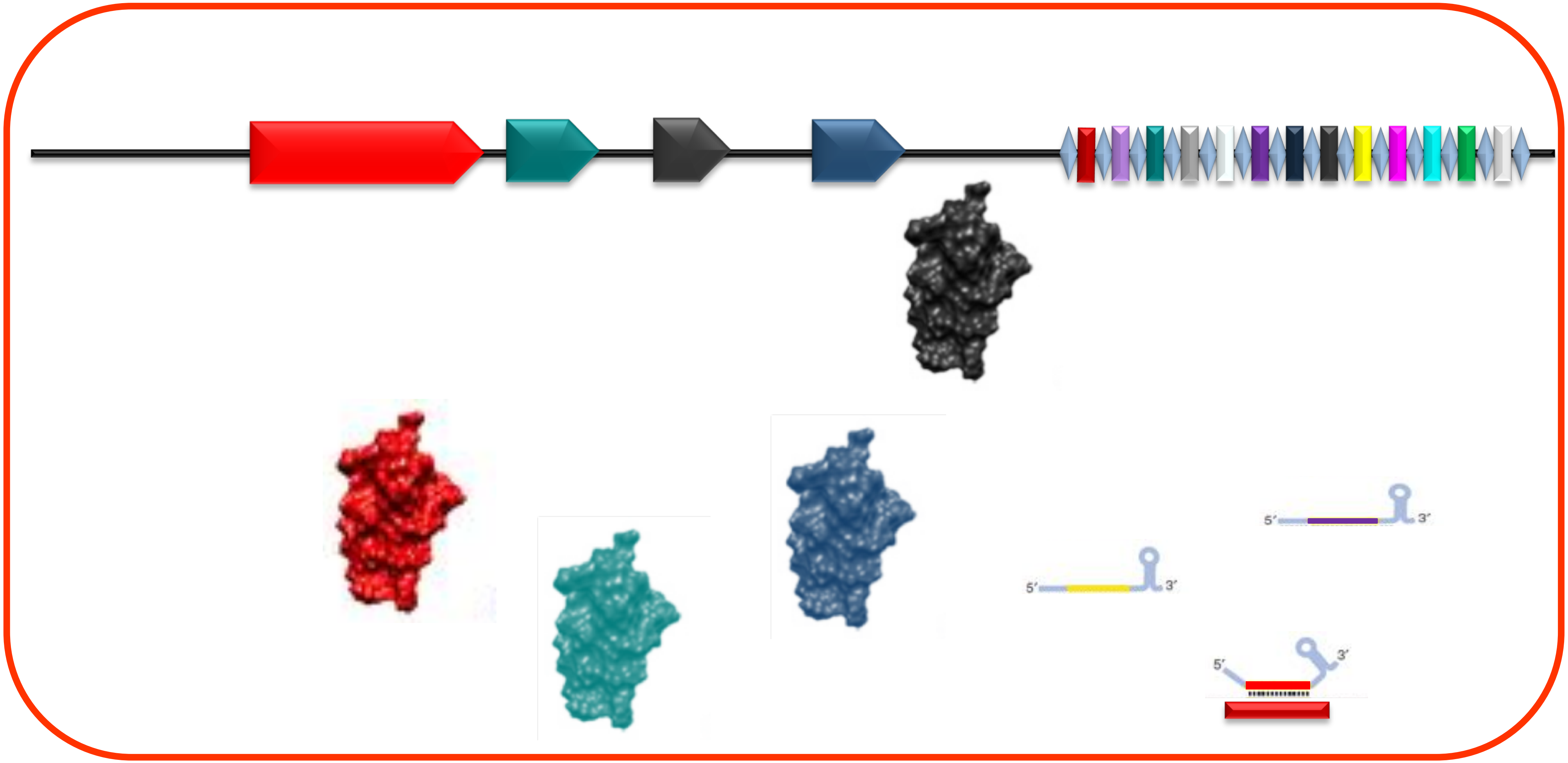
Guides production



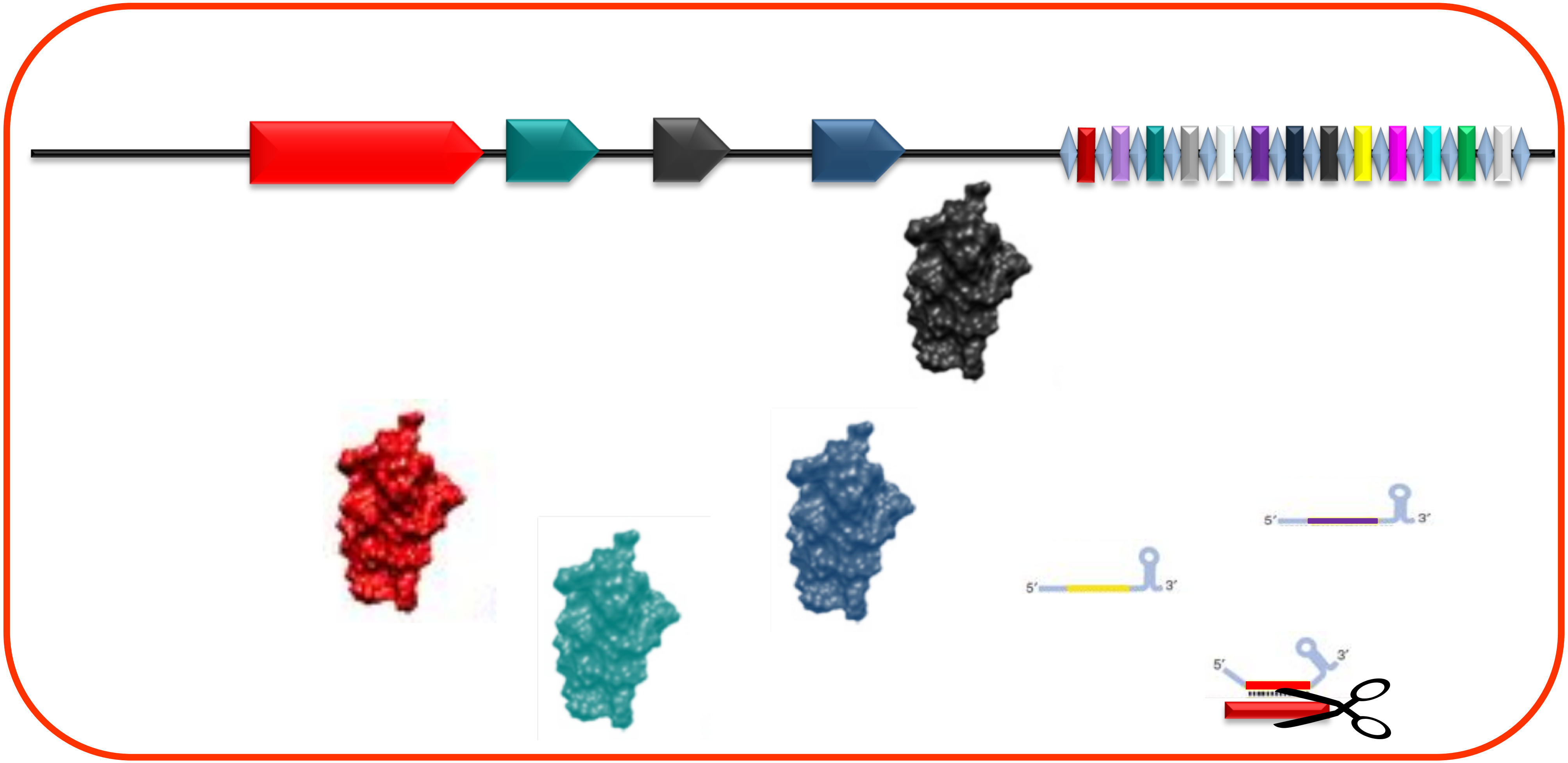
Reinfection



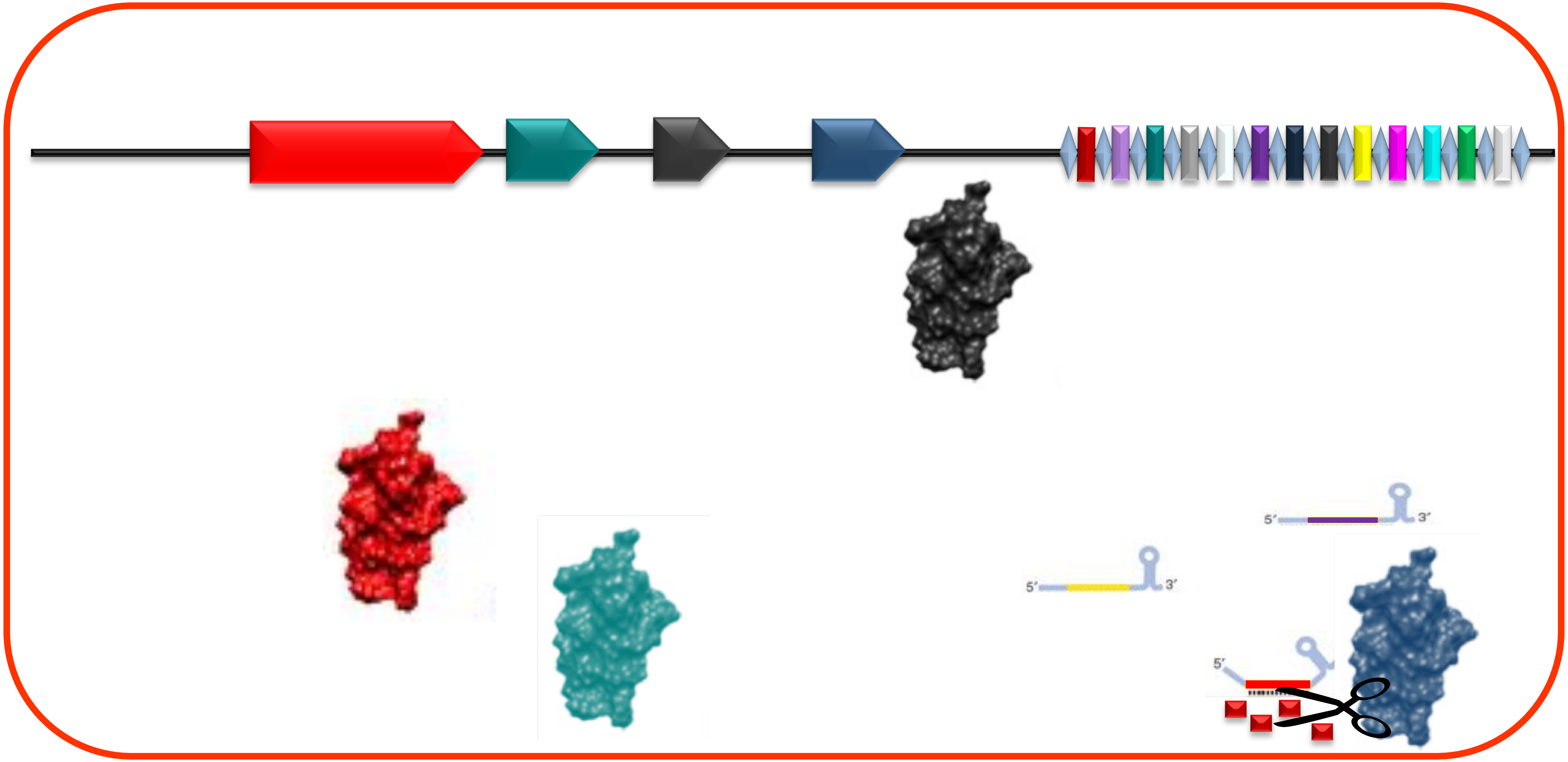
Targeting



Cleavage



Inactivation



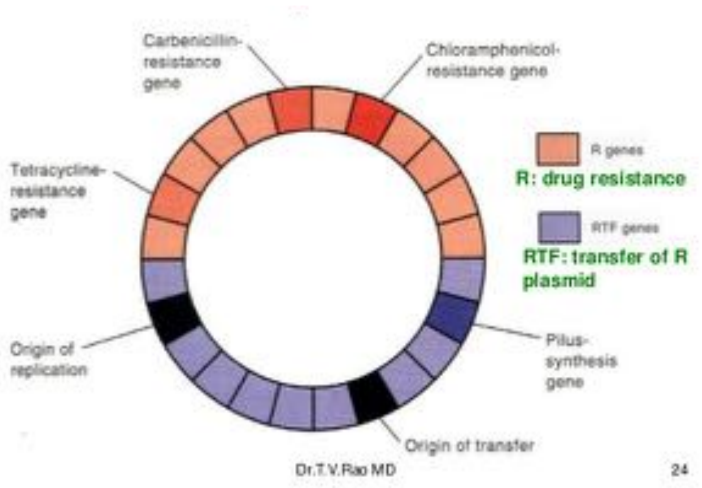
Applications of CRISPR

…in the natural host

Programmable Immunity

- Viruses
  - Resistant strains

- Plasmids
  - Prevention of antibiotic-resistance dissemination

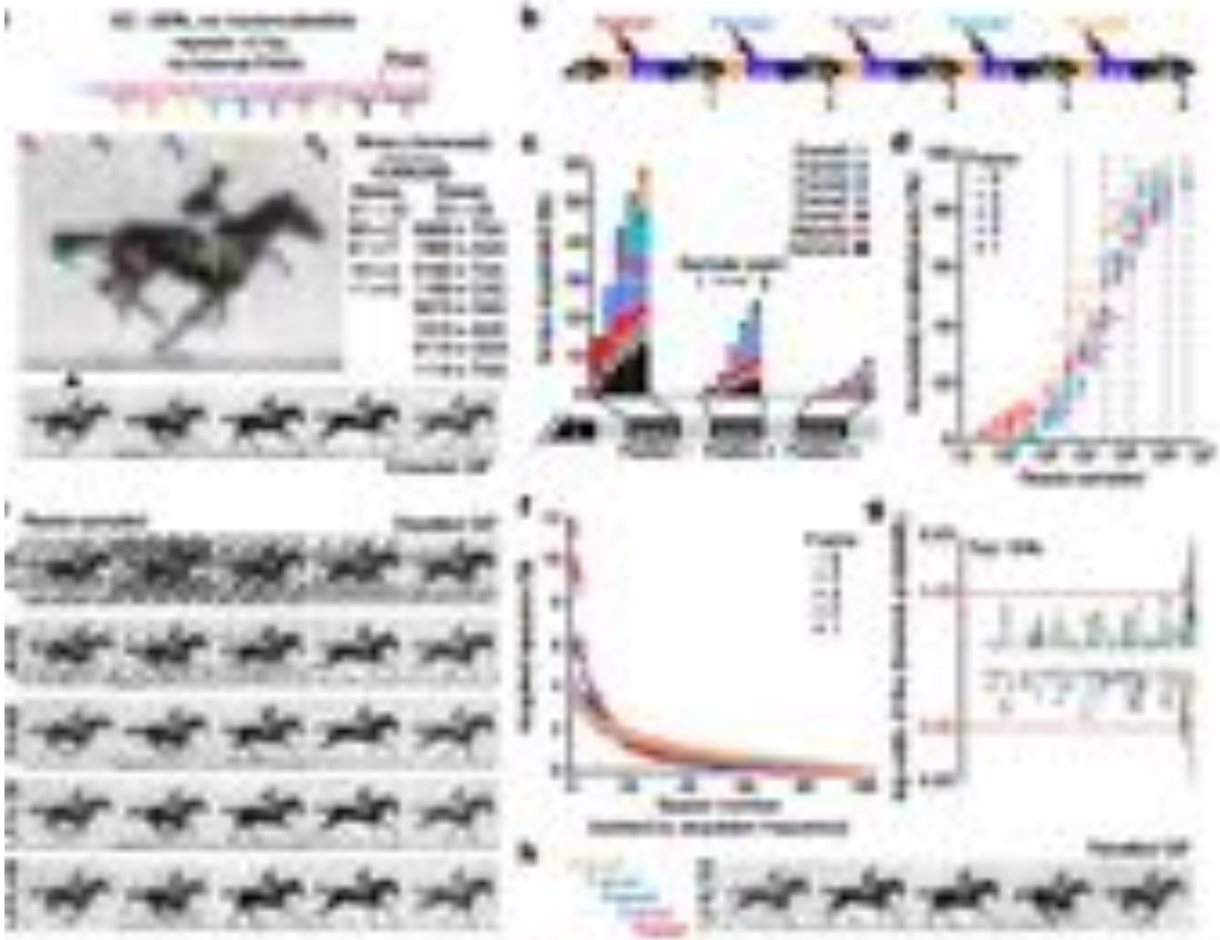


LETTER

doi:10.1038/nature23017

CRISPR–Cas encoding of a digital movie into the genomes of a population of living bacteria

Seth L. Shipman, Jeff Nivala, Jeffrey D. Macklis & George M. Church



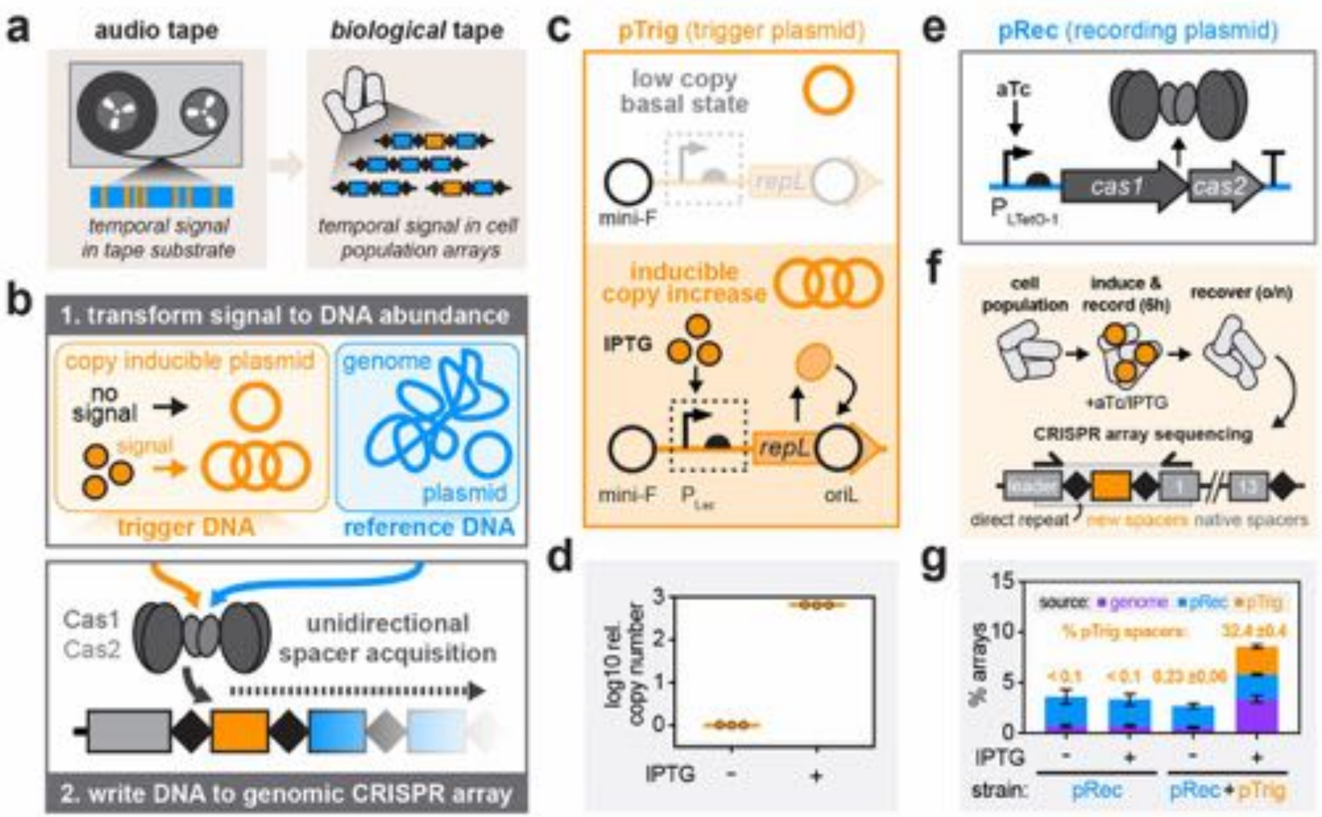
Science

REPORTS

Cite as: R. U. Sheth *et al.*, *Science*
10.1126/science.aao0958 (2017).

Multiplex recording of cellular events over time on CRISPR biological tape

Ravi U. Sheth,[1,2] Sung Sun Yim,[1] Felix L. Wu,[1,2] Harris H. Wang[1,3]*



…in heterologous hosts

Programmable DNA cleavage

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 53716; and [c]DuPont Nutrition 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, 2012)

R. Barrangou

P. Horvath

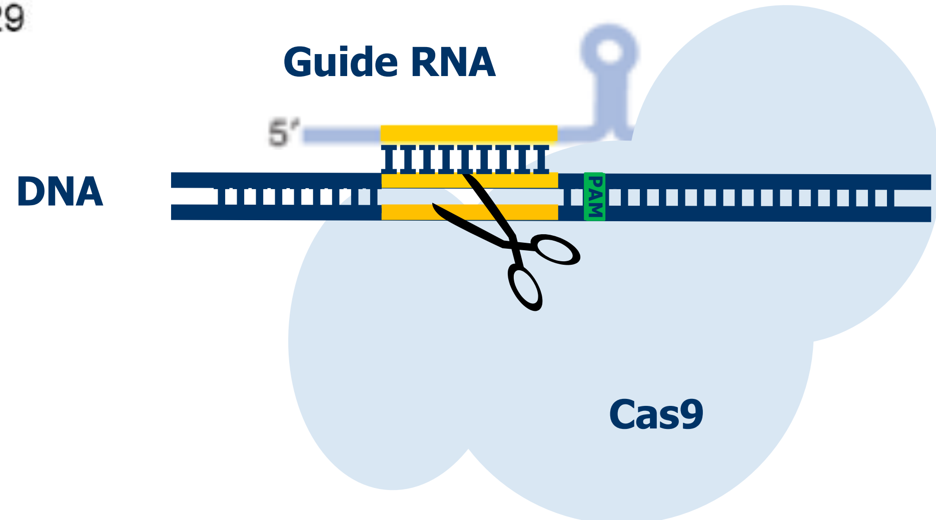
V. Siksnys

Science AAAS

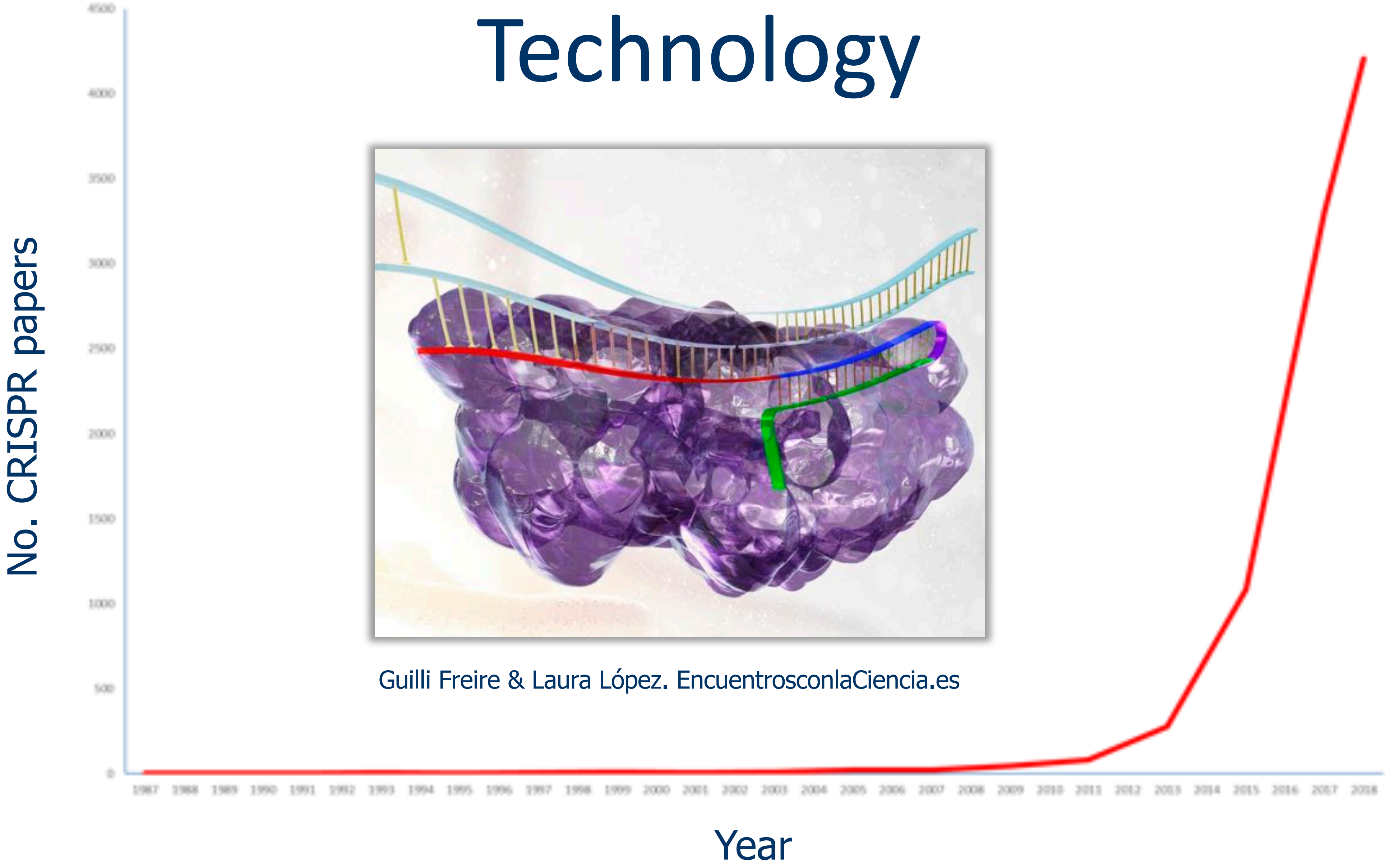
A Programmable Dual-RNA–Guided DNA Endonuclease in Adaptive Bacterial Immunity
Martin Jinek *et al.*
Science **337**, 816 (2012);
DOI: 10.1126/science.1225829

E. Charpentier

J. Doudna



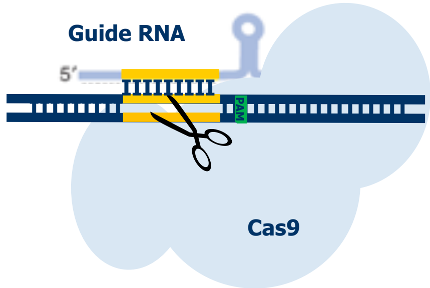
CRISPR-Cas9 Technology



Guilli Freire & Laura López. EncuentrosconlaCiencia.es

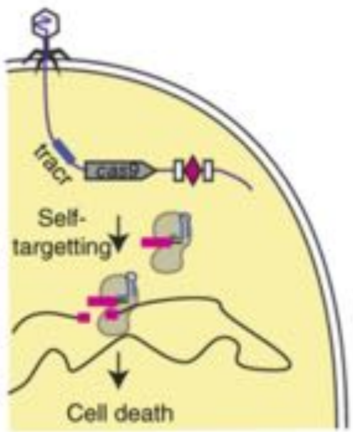
Prokaryotic chromosome targeting

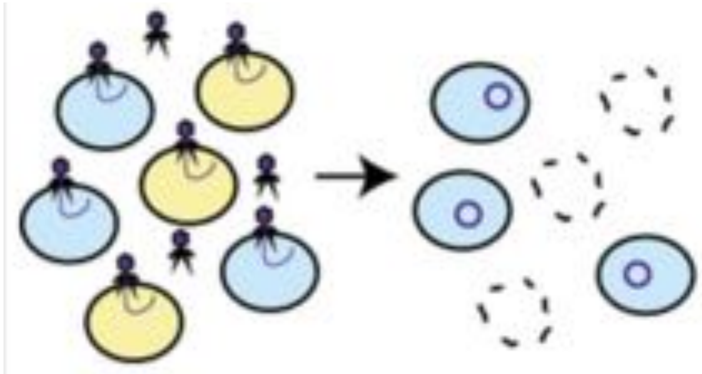
D. Bikard



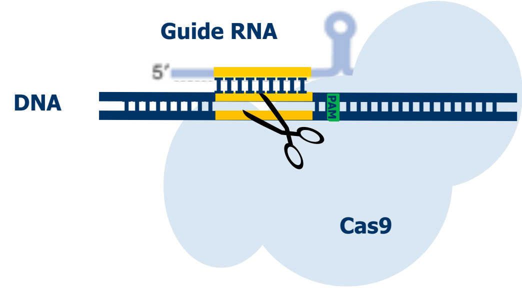
L. Marraffini

Bikard *et al*. (2014). **Exploiting CRISPR-Cas nucleases to produce sequence-specific antimicrobials.** *Nature Biotechnology*





Eukaryotic chromosome targeting



L. Marraffini

Science. 2013 February 15; 339(6121): 819–823. doi:10.1126/science.1231143.

Multiplex Genome Engineering Using CRISPR/Cas Systems

Le Cong[1,2,*], F. Ann Ran[1,4,*], David Cox[1,3], Shuailiang Lin[1,5], Robert Barretto[6], Naomi Habib[1], Patrick D. Hsu[1,4], Xuebing Wu[7], Wenyan Jiang[8], Luciano A. Marraffini[8], and Feng Zhang[1,†]

F. Zhang

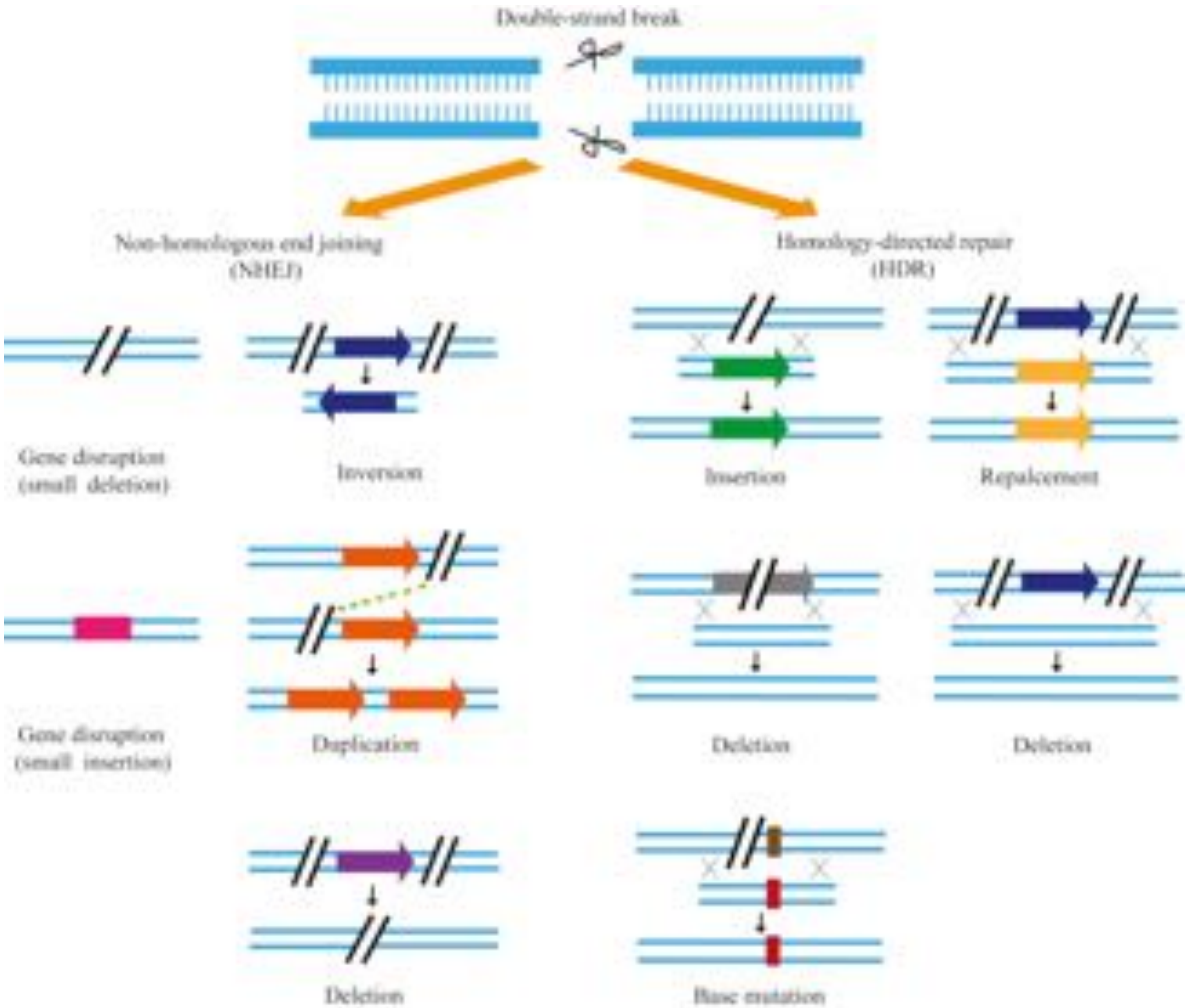
G. Church

Science. 2013 February 15; 339(6121): 823–826. doi:10.1126/science.1232033.

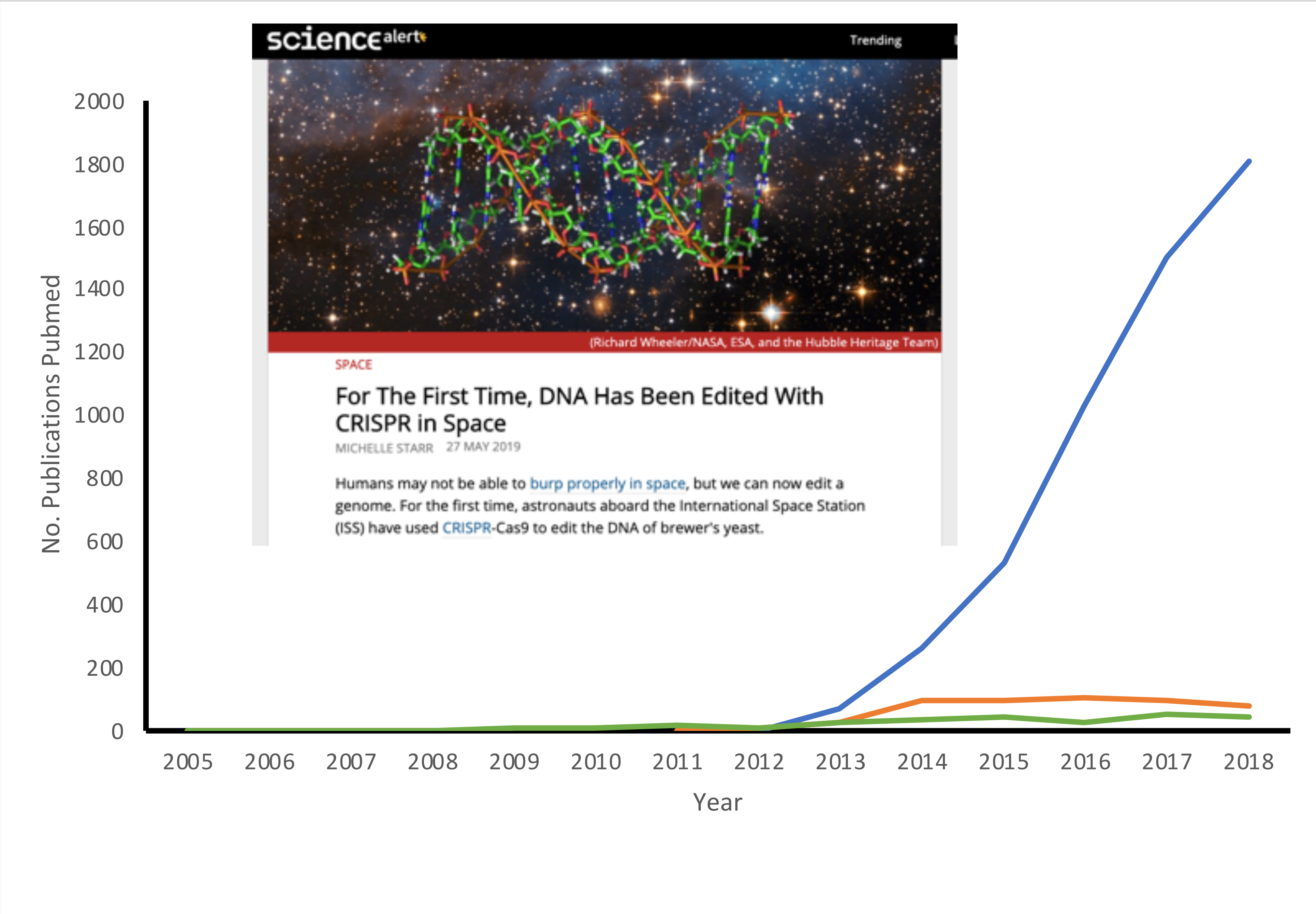
RNA-Guided Human Genome Engineering via Cas9

Prashant Mali[1,5], Luhan Yang[1,3,5], Kevin M. Esvelt[2], John Aach[1], Marc Guell[1], James E. DiCarlo[4], Julie E. Norville[1], and George M. Church[1,2,*]

Genome Editing



Yue Mei, et al. Journal of Genetics and Genomics, Volume 43, Issue 2, 2016



sciencealert
Trending
(Richard Wheeler/NASA, ESA, and the Hubble Heritage Team)
SPACE
For The First Time, DNA Has Been Edited With CRISPR in Space
MICHELLE STARR 27 MAY 2019
Humans may not be able to burp properly in space, but we can now edit a genome. For the first time, astronauts aboard the International Space Station (ISS) have used CRISPR-Cas9 to edit the DNA of brewer's yeast.
No. Publications Pubmed
2000
1800
1600
1400
1200
1000
800
600
400
200
0
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
2018
Year

CRISPR-edited organisms

- **Bacteria**
- **Protozoa***: Leishmania, Toxoplasma, Plasmodium, Trypanosoma*…
- **Fungi:** yeasts, molds, mushroom
- **Plants**:

Rice	Orange	Wheat
Soybean	Corn	Potato
Tomato	Tobacco	*Arabidopsis*
Grapefruit	Petunia	Cotton
Lettuce	Cucumber	Sorghum

- Tastier
- Stress tolerant
- Promote productivity
- Composition (oil content, gluten free..
- Resistant to diseases, herbicides…

Mutations in a subfamily of abscisic acid receptor genes promote rice growth and productivity

Chunbo Miao[a], Lihong Xiao[a], Kai Hua[a], Changsong Zou[a], Yang Zhao[a], Ray A. Bressan[b], and Jian-Kang Zhu[a,b,1]

www.pnas.org/cgi/doi/10.1073/pnas.1804774115

frontiers in Plant Science
OPINION
published: 27 May 2015
doi: 10.3389/fpls.2015.00375

Function genomics of abiotic stress tolerance in plants: a CRISPR approach

Mukesh Jain *

CRISPR-edited 'super plants' might be our best chance to slow climat..
Genetic Literacy Project - Hace 2 horas
If this were a film about humanity's last hope before climate change wiped us out, Hollywood would be accused of flagrant typecasting. That's because Dr ...

Non-addictive CRISPR-edited tobacco could help eliminate smoking
New Scientist - 25 jun. 2019
A gene-edited tobacco plant created using the **CRISPR** technique has the lowest ever amount of nicotine. It could boost efforts to reduce ...

Gene-Edited, Less Addictive Tobacco Could Help You Quit Smoking

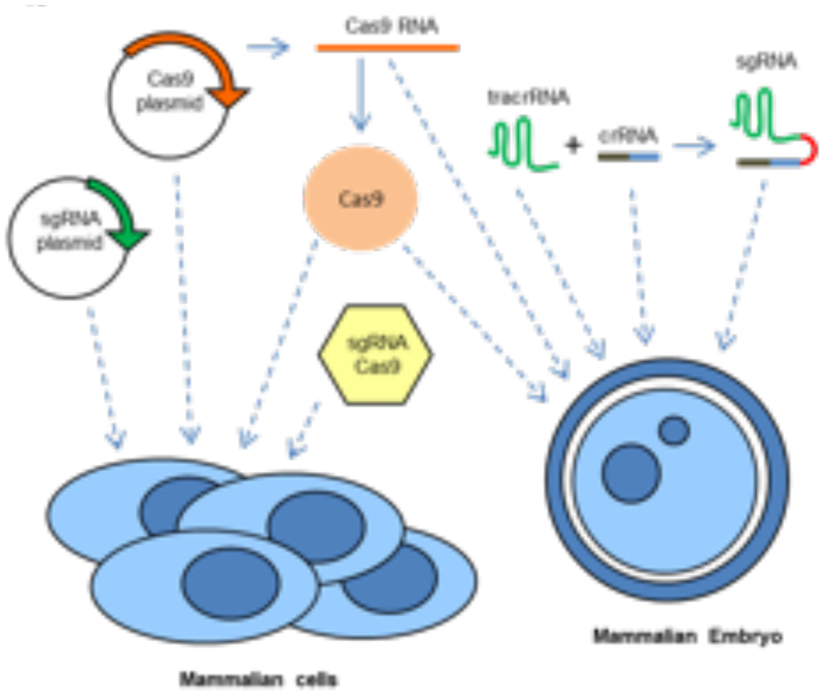
CRISPR immunizes potato against plant viruses, cutting production costs of globally important food crop
ISAAA | July 12, 2019

CRISPR-edited organisms

- **Worms**
- **Insects**
- **Reptiles**
- **Amphibians**
- **Molluscs**
- **Fish**
- **Birds**

- **Mammals**: mouse, rabbit, goat, rat, dog, pig, primate…

CRISPR-editing in animals



Mojica & Montoliu, Trends Microbiol. 2016

Science News *from research organizations*

Novel nanoparticles deliver CRISPR gene editing tools into the cell with much higher efficiency

Researchers used lipid nanoparticles to deliver CRISPR/Cas9 gene editing tools for potential treatment of hyperlipidemia.

Date: July 12, 2019

Source: Tufts University

Summary: Researchers have developed a significantly improved delivery mechanism for the CRISPR/Cas9 gene editing method in the liver. The delivery uses biodegradable synthetic lipid nanoparticles that carry the molecular editing tools into the cell to precisely alter the cells' genetic code with as much as 90 percent efficiency. The nanoparticles could help overcome technical hurdles to enable gene editing in a broad range of clinical therapeutic applications.

nature medicine — LETTERS

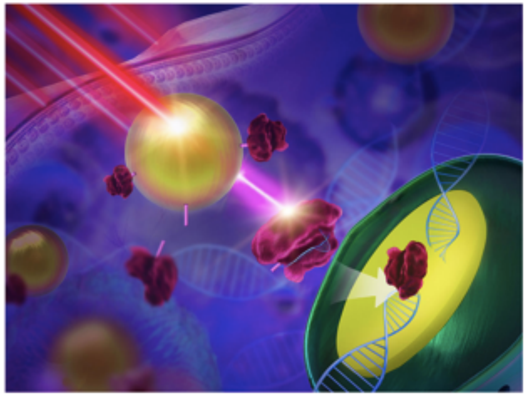
In utero CRISPR-mediated therapeutic editing of metabolic genes

Avery C. Rossidis, John D. Stratigis, Alexandra C. Chadwick, Heather A. Hartman, Nicholas J. Ahn, Haiying Li, Kshitiz Singh, Barbara E. Coons, Li Li, Wenjian Lv, Philip W. Zoltick, Deepthi Alapati, William Zacharias, Rajan Jain, Edward E. Morrisey, Kiran Musunuru and William H. Peranteau

Scientists Control CRISPR With Light

Engineers show that near-infrared light can trigger the release of CRISPR-Cas9 to slow tumor growth

By Emily Waltz



Tuberculosis-resistant **cows** developed for the first time using **CRISPR** ...

Phys.Org - 31 ene. 2017

CRISPR/Cas9 gene-editing technology has been used for the first time to successfully produce live **cows** with increased resistance to **bovine** ...

'Tuberculosis-resistant' **cattle** developed in China

Gene-edited chicken cells may stop the spread of bird flu

Food Dive - 19 jun. 2019

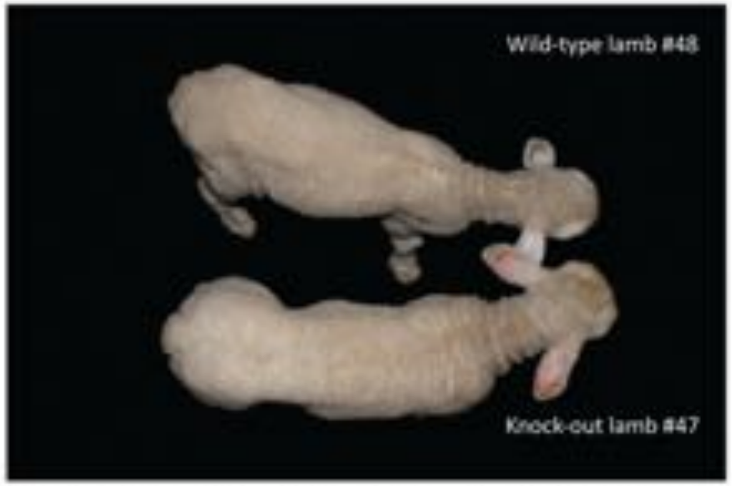
... DNA within lab-grown cells using **CRISPR** gene-editing technology. ... The Washington Post reported last year more than 300 pigs, **cows**, ...

Making **Pigs** Leaner Through **CRISPR**

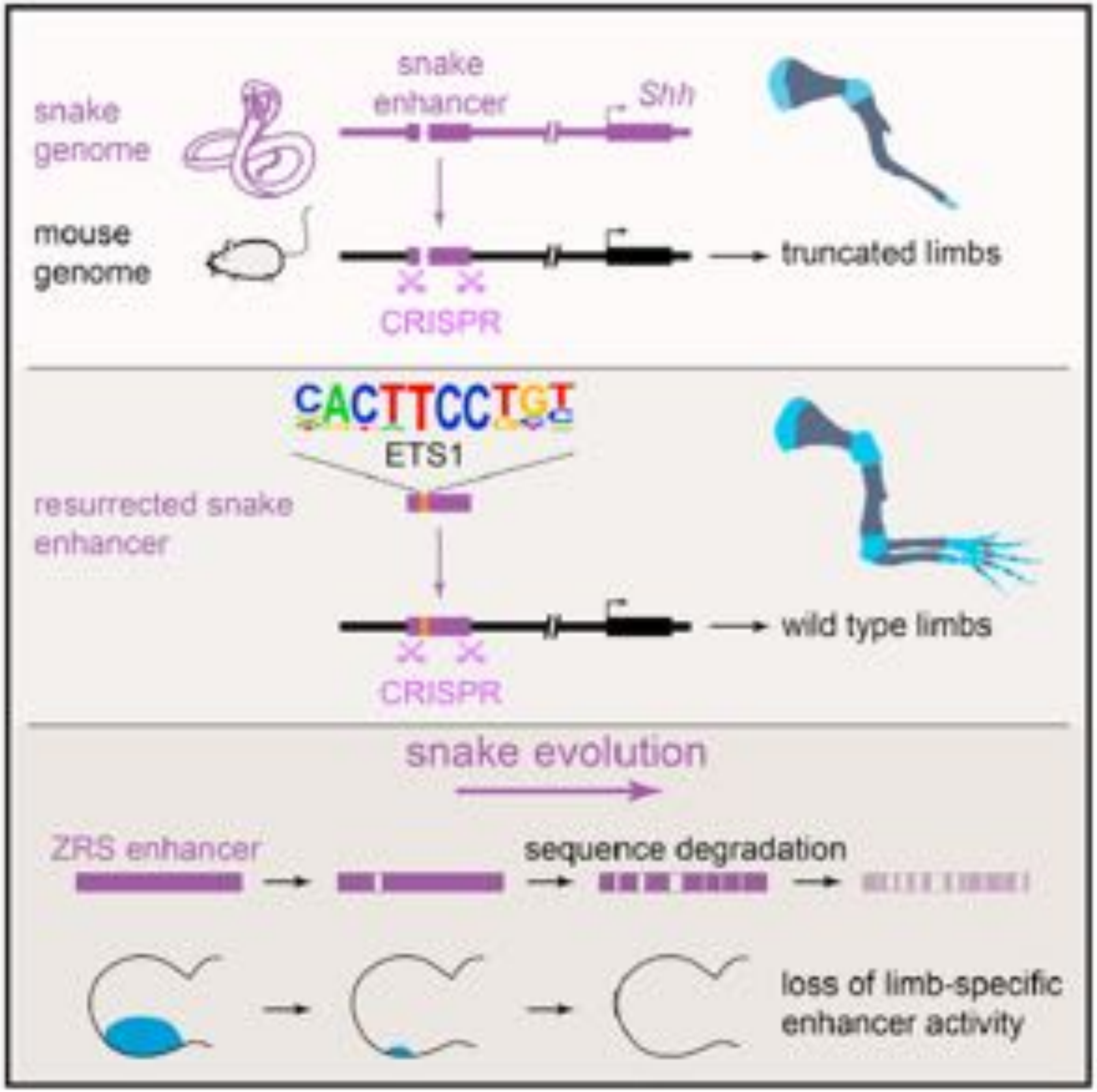
Asian Scientist Magazine - 31 oct. 2017

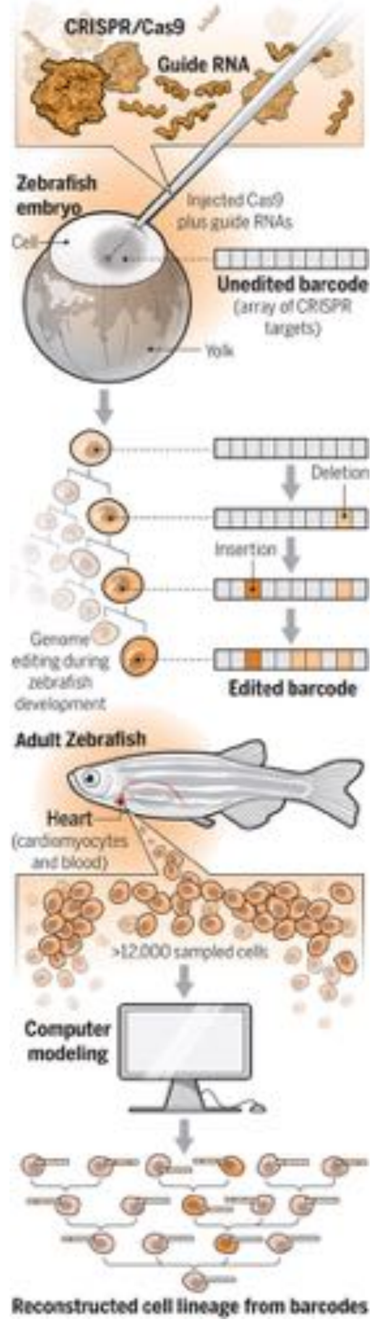
Using **CRISPR**/Cas gene-editing, scientists in China have introduced a gene into **pigs** that makes them lean and cold-resistant.

Fig 6. Phenotype of lambs 30 days after birth.



Crispo M, Mulet AP, Tesson L, Barrera N, Cuadro F, et al. (2015) Efficient Generation of Myostatin Knock-Out Sheep Using CRISPR/Cas9 Technology and Microinjection into Zygotes. PLOS ONE 10(8): e0136690. doi:10.1371/journal.pone.0136690


snake genome
snake enhancer
Shh
mouse genome
truncated limbs
CRISPR
CACTTCCTGT
ETS1
resurrected snake enhancer
wild type limbs
CRISPR
snake evolution
ZRS enhancer
sequence degradation
loss of limb-specific enhancer activity

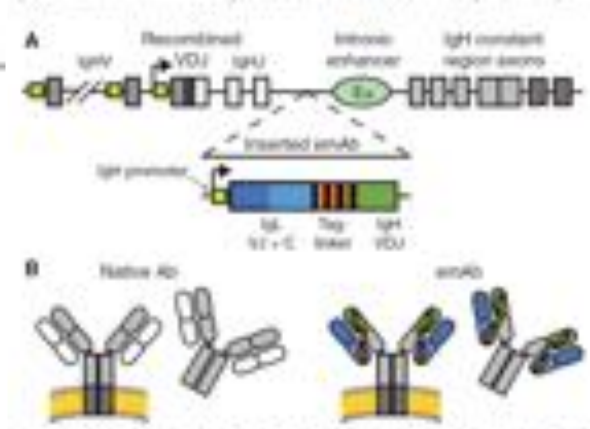

CRISPR/Cas9
Guide RNA
Zebrafish embryo
Injected Cas9 plus guide RNAs
Cell
Unedited barcode
(array of CRISPR targets)
Yolk
Deletion
Insertion
Genome editing during zebrafish development
Edited barcode
Adult Zebrafish
Heart
(cardiomyocytes and blood)
>12,000 sampled cells
Computer modeling
Reconstructed cell lineage from barcodes

SCIENCE IMMUNOLOGY | RESEARCH ARTICLE

ANTIBODIES

B cells engineered to express pathogen-specific antibodies protect against infection

Howell F. Moffett[1], Carson K. Harms[1], Kristin S. Fitzpatrick[1], Marti R. Tooley[1], Jim Boonyaratanakornkit[1], Justin J. Taylor[1,2,3]*

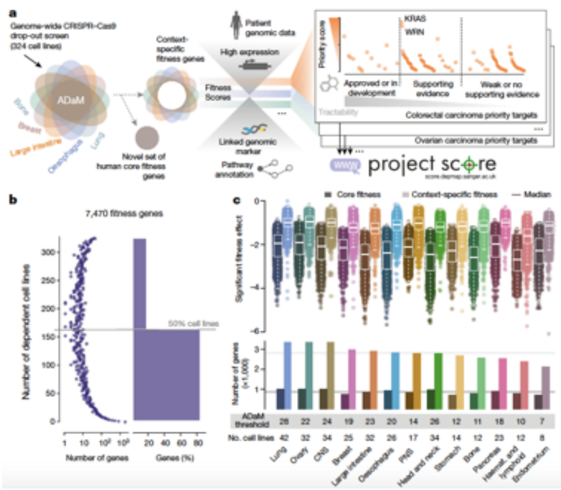


ARTICLE

https://doi.org/10.1038/s41586-019-1103-9

Prioritization of cancer therapeutic targets using CRISPR–Cas9 screens

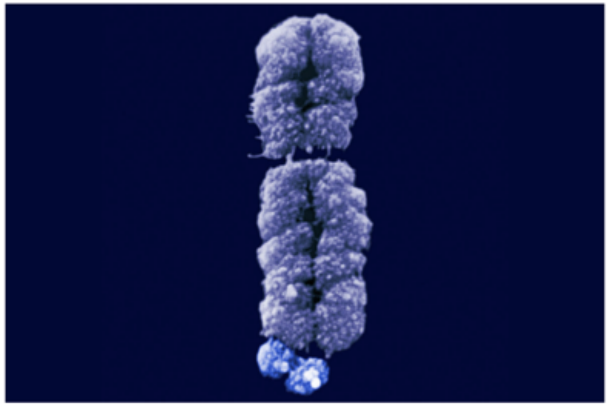
Fiona M. Behan[1,2,12], Francesco Iorio[1,2,3,12], Gabriele Picco[1,12], Emanuel Gonçalves[1], Charlotte M. Beaver[1], Giorgia Migliardi[4,5], Rita Santos[6], Yanhua Rao[7], Francesco Sassi[4], Marika Pinnelli[4,5], Rizwan Ansari[1], Sarah Harper[1], David Adam Jackson[1], Rebecca McRae[1], Rachel Pooley[1], Piers Wilkinson[1], Dieudonne van der Meer[1], David Dow[2,6], Carolyn Buser-Doepner[2,7], Andrea Bertotti[4,5], Livio Trusolino[4,5], Euan A. Stronach[2,6], Julio Saez-Rodriguez[2,3,8,9,10], Kosuke Yusa[1,2,11,13]* & Mathew J. Garnett[1,2,13]*



Targeting Genetic Diseases

DAILY NEWS 15 February 2018

CRISPR has fixed the genetic cause of a learning disability



Fragile X syndrome is the most common genetic cause of intellectual disability
Christine Harrison/Visuals Unlimited, Inc. /SCIENCE PHOTO LIBRARY

Cancer
Malaria
Albinism
Cataracts
Hemophilia
Cystic fibrosis
β-thalassemia
Retinitis Pigmentosa
Hypercholestorolemia
Neurodegenerative disorders
Amyotrophic Lateral Sclerosis
Duchenne Muscular Dystrophy

GENETICS

Correction of diverse muscular dystrophy mutations in human engineered heart muscle by single-site genome editing

Towards Gene Therapy

LETTER

Treatment of autosomal dominant hearing loss by in vivo delivery of genome editing agents

Gene Ther. 2016 May 19. doi: 10.1038/gt.2016.41. [Epub ahead of print]

Excision of HIV-1 DNA by gene editing: a proof-of-concept in vivo study.

EMBO Molecular Medicine

Sci Adv. 2017 Dec 20;3(12):eaar3952. doi: 10.1126/sciadv.aar3952. eCollection 2017 Dec.

In vivo genome editing improves motor function and extends survival in a mouse model of ALS.

Gaj T[1], Ojala DS[2], Ekman FK[3], Byrne LC[4], Limsirichai P[5], Schaffer DV[1,2,4].

CRISPR/Cas9-mediated somatic correction of a novel coagulator factor IX gene mutation ameliorates hemophilia in mouse

Yuting Guan[1,†], Yanlin Ma[2,3,†,*], Qi Li[2], Zhenliang Sun[4], Lie Ma[1], Lijuan Wu[1], Liren Wang[1], Li Zeng[1], Yanjiao Shao[1], Yuting Chen ...

Science News

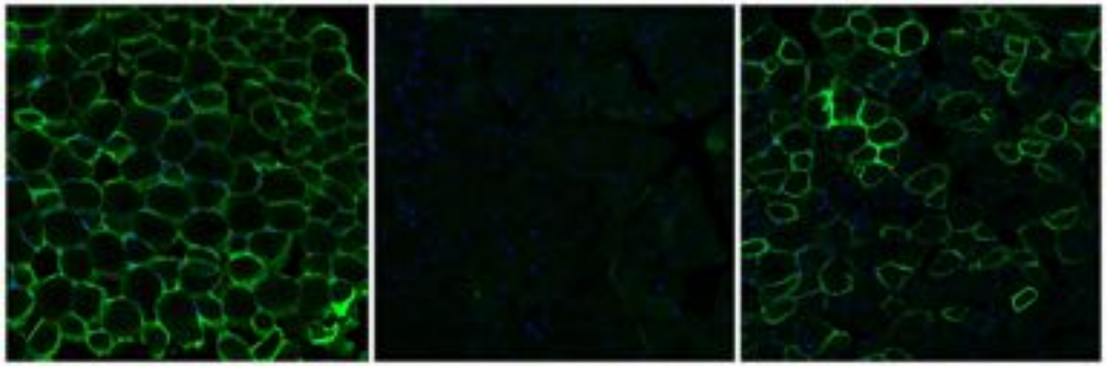
New gene-editing technology partially restores vision in blind animals

Date: November 16, 2016

Source: Salk Institute

Summary: Researchers have discovered a holy grail of gene editing -- the ability to, for the first time, insert DNA at a target location into the non-dividing cells that make up the majority of adult organs and tissues. The technique, which the team showed was able to partially restore visual responses in blind rodents, will open new avenues for basic research and a variety of treatments, such as for retinal, heart and neurological diseases.

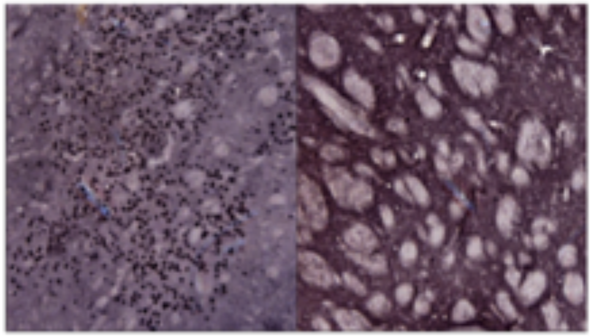
CRISPR GENE EDITING SUCCESSFULLY STOPS MUSCULAR DYSTROPHY IN LIVING MICE



Science AAAS

NEWS | SCIENCE JOURNALS | CAREERS | MULTIMEDIA | COLLECTIONS

LATEST NEWS



NICOLE DÉGLON

The brain of an untreated mouse on the left, showing huntingtin protein aggregation (a hallmark of Huntington's disease) and on the right, the brain of a mouse treated with CRISPR-Cas9 editing, showing the lack of protein aggregation.

Gene-editing method halts production of brain-destroying proteins

Editing Human Embryos

Protein Cell
DOI 10.1007/s13238-015-0153-5
Protein & Cell

RESEARCH ARTICLE

CRISPR/Cas9-mediated gene editing in human tripronuclear zygotes

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

Mol Genet Genomics (2017) 292:525–533
DOI 10.1007/s00438-017-1299-z

ORIGINAL ARTICLE

CRISPR/Cas9-mediated gene editing in human zygotes using Cas9 protein

Lichun Tang[1,2] · Yanting Zeng[3] · Hongzi Du[3] · Mengmeng Gong[1] · Jin Peng[1] · Buxi Zhang[1] · Ming Lei[3] · Fang Zhao[4] · Weihua Wang[5] · Xiaowei Li[6] · Jianqiao Liu[3]

TECHNOLOGICAL INNOVATIONS

Introducing precise genetic modifications into human 3PN embryos by CRISPR/Cas-mediated genome editing

ARTICLE

Genome editing reveals a role for OCT4 in human embryogenesis

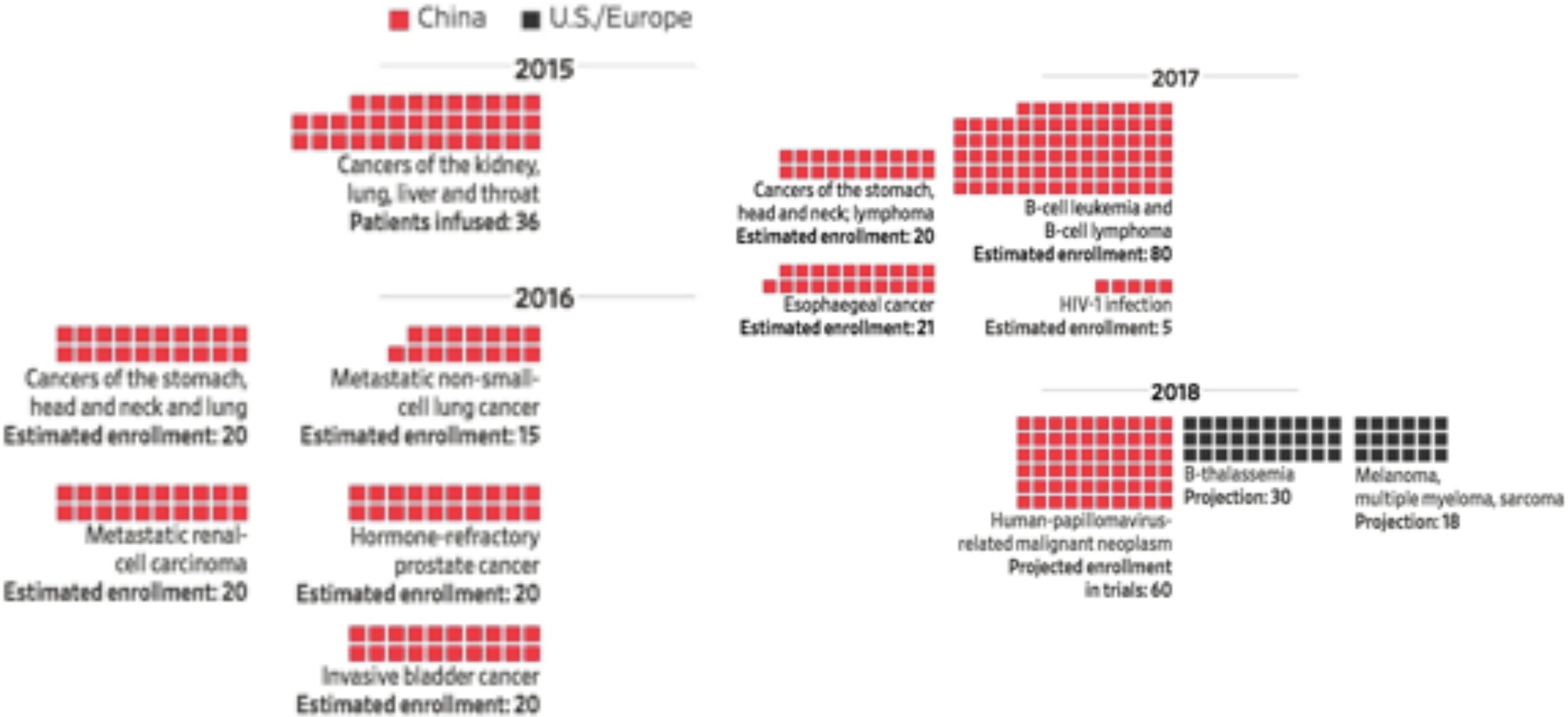
ARTICLE

doi:10.1038/nature23305

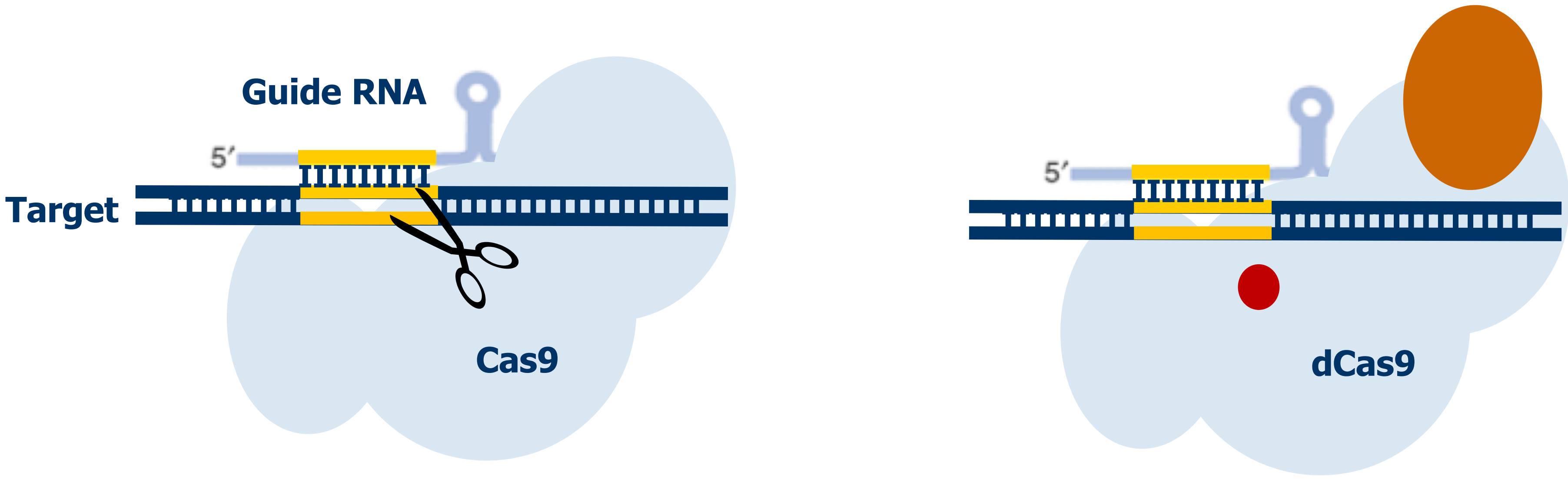
Correction of a pathogenic gene mutation in human embryos

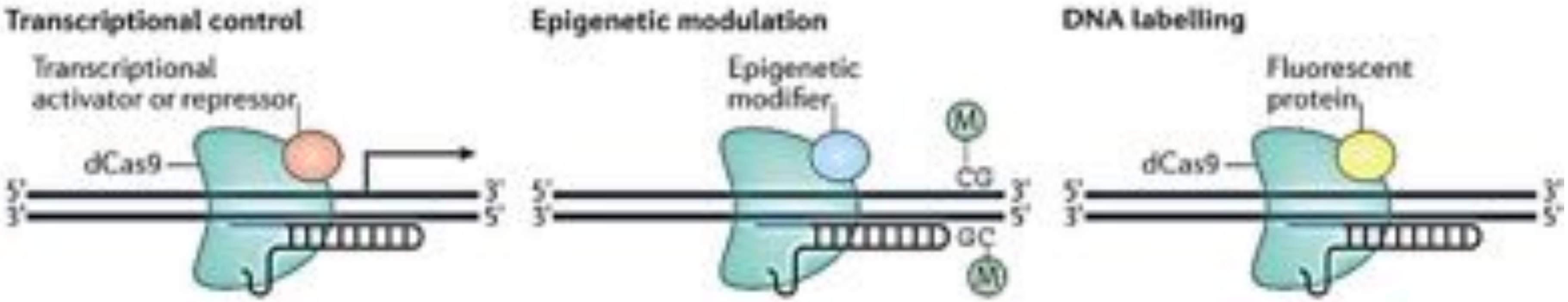
Hong Ma[1]*, Nuria Marti-Gutierrez[1]*, Sang-Wook Park[2]*, Jun Wu[3]*, Yeonmi Lee[1], Keiichiro Suzuki[3], Amy Koski[1], Dongmei Ji[1], Tomonari Hayama[1], Riffat Ahmed[1], Hayley Darby[1], Crystal Van Dyken[1], Ying Li[1], Eunju Kang[1], A.-Reum Park[2], Daesik Kim[4], Sang-Tae Kim[2], Jianhui Gong[5,6,7,8],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

Clinical Trials in Humans



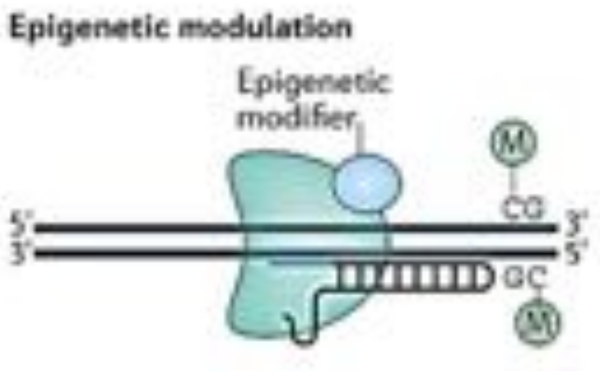
Much more than an editing tool

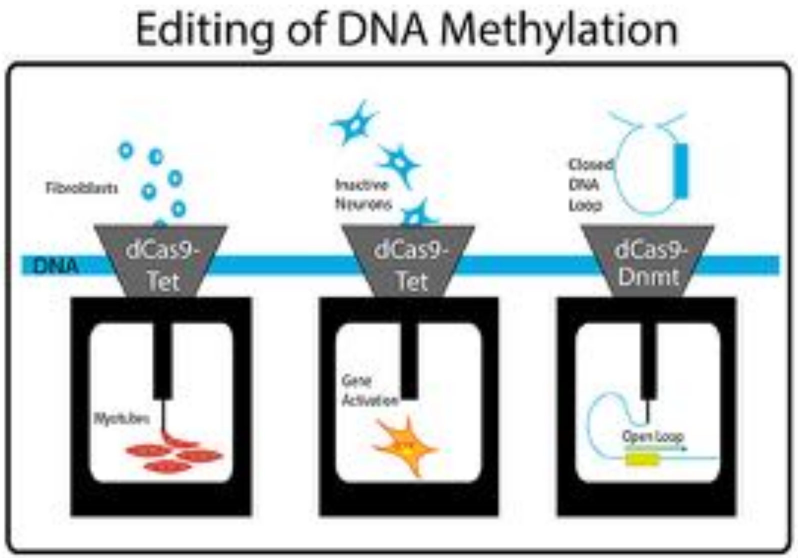


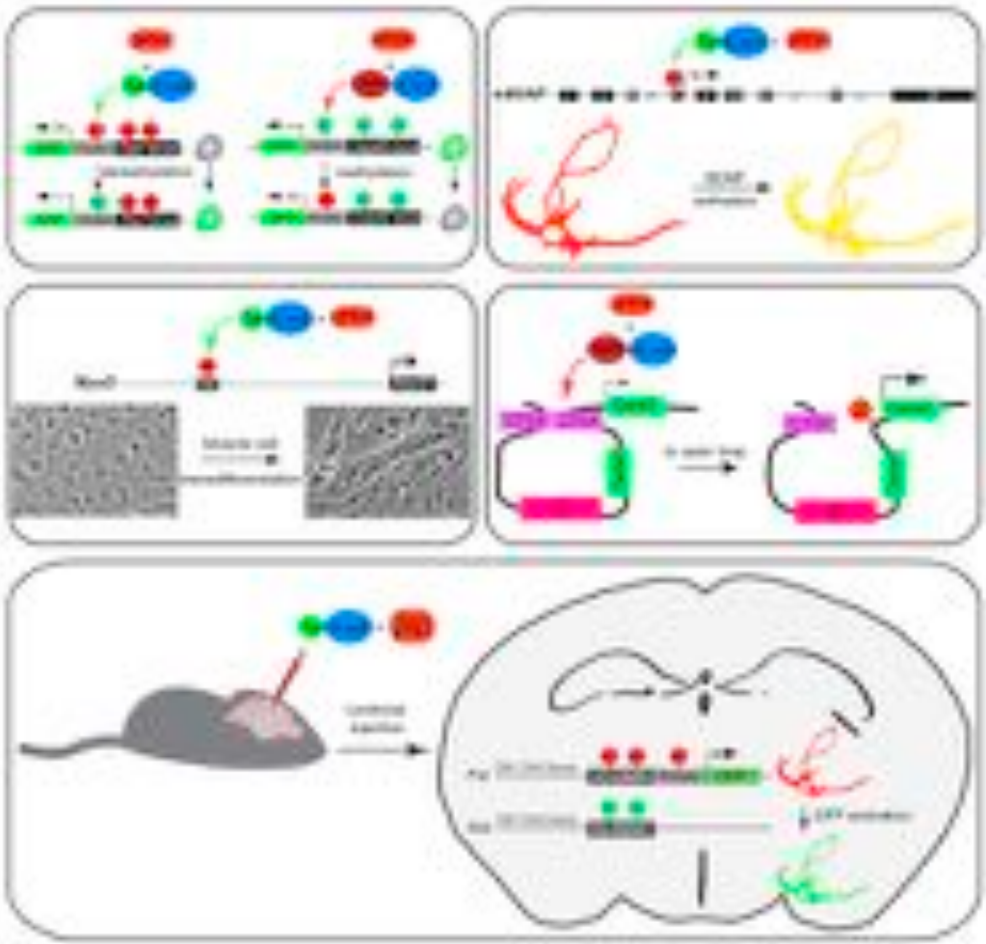


Reprinted by permission from Macmillan Publishers Ltd: *Nature Reviews Neuroscience*, advance online publication, 10 Dec 2015 (doi: 10.1038/nrn.2015.2)

dCas9





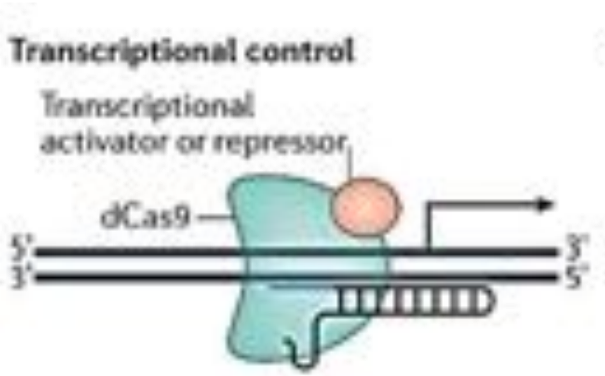


Cell

Editing DNA Methylation in the Mammalian Genome

X. Shawn Liu[4], Hao Wu[4], Xiong Ji[5], Yonatan Stelzer, Xuebing Wu, Szymon Czauderna, Jian Shu, Daniel Dadon, Richard A. Young, Rudolf Jaenisch[6]

dCas9



Highlights

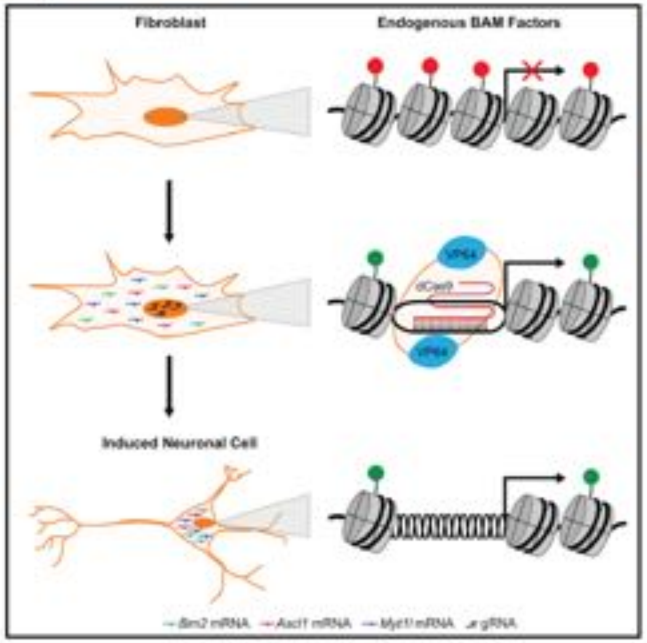
- Multiplexed CRISPR/Cas9 activators induce expression of endogenous neurogenic genes
- Induced endogenous gene expression directly converts fibroblasts to neuronal cells
- Targeted activation of endogenous genes rapidly remodels chromatin at target loci
- High expression from the endogenous genes is sustained throughout reprogramming

Short Article

Cell Stem Cell

Targeted Epigenetic Remodeling of Endogenous Loci by CRISPR/Cas9-Based Transcriptional Activators Directly Converts Fibroblasts to Neuronal Cells

Graphical Abstract



Authors

Joshua B. Black, Andrew F. Adler, Hong-Gang Wang, ..., Geoffrey S. Pitt, Kam W. Leong, Charles A. Gersbach

Correspondence

charles.gersbach@duke.edu

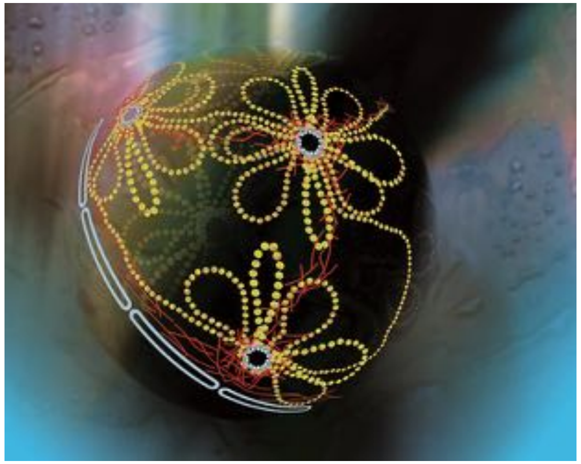
In Brief

Black et al. show that reprogramming of fibroblasts to induced neurons via CRISPR/Cas9-based activation of endogenous neurogenic genes leads to rapid epigenetic remodeling at the targeted endogenous loci and sustained gene expression throughout the reprogramming process.

dCas9


ARTICLE

Manipulation of nuclear architecture through CRISPR-mediated chromosomal looping



http://www.biology.emory.edu/research/Corces/Research2.html

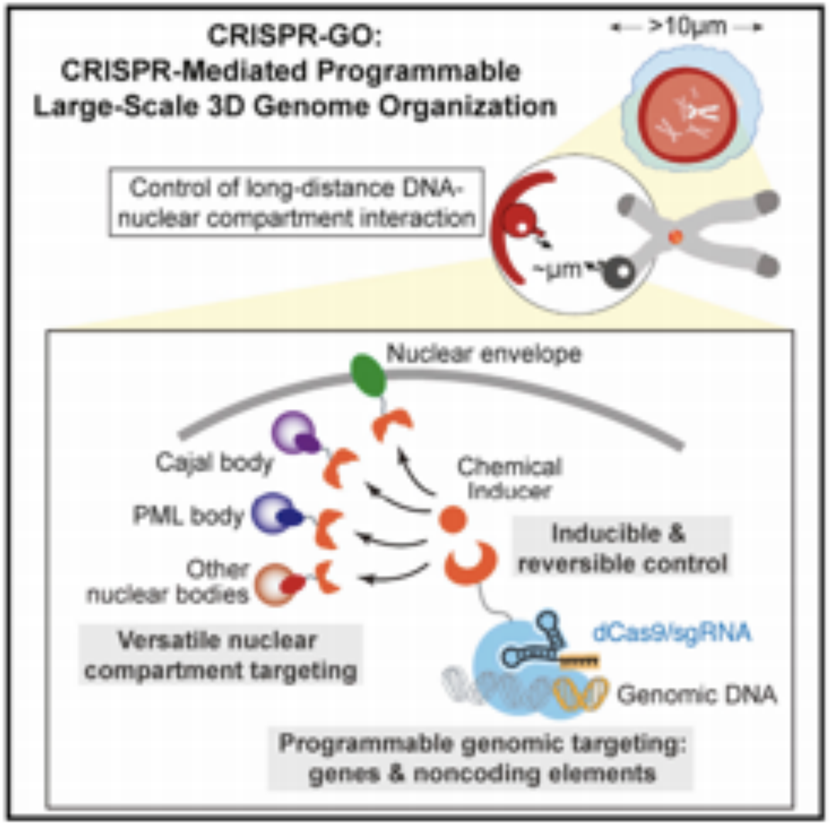
dCas9

Resource

Cell

CRISPR-Mediated Programmable 3D Genome Positioning and Nuclear Organization

Graphical Abstract



Authors

Haifeng Wang, Xiaoshu Xu,
Cindy M. Nguyen, ..., Nathan H. Kipniss,
Marie La Russa, Lei S. Qi

Correspondence

stanley.qi@stanford.edu

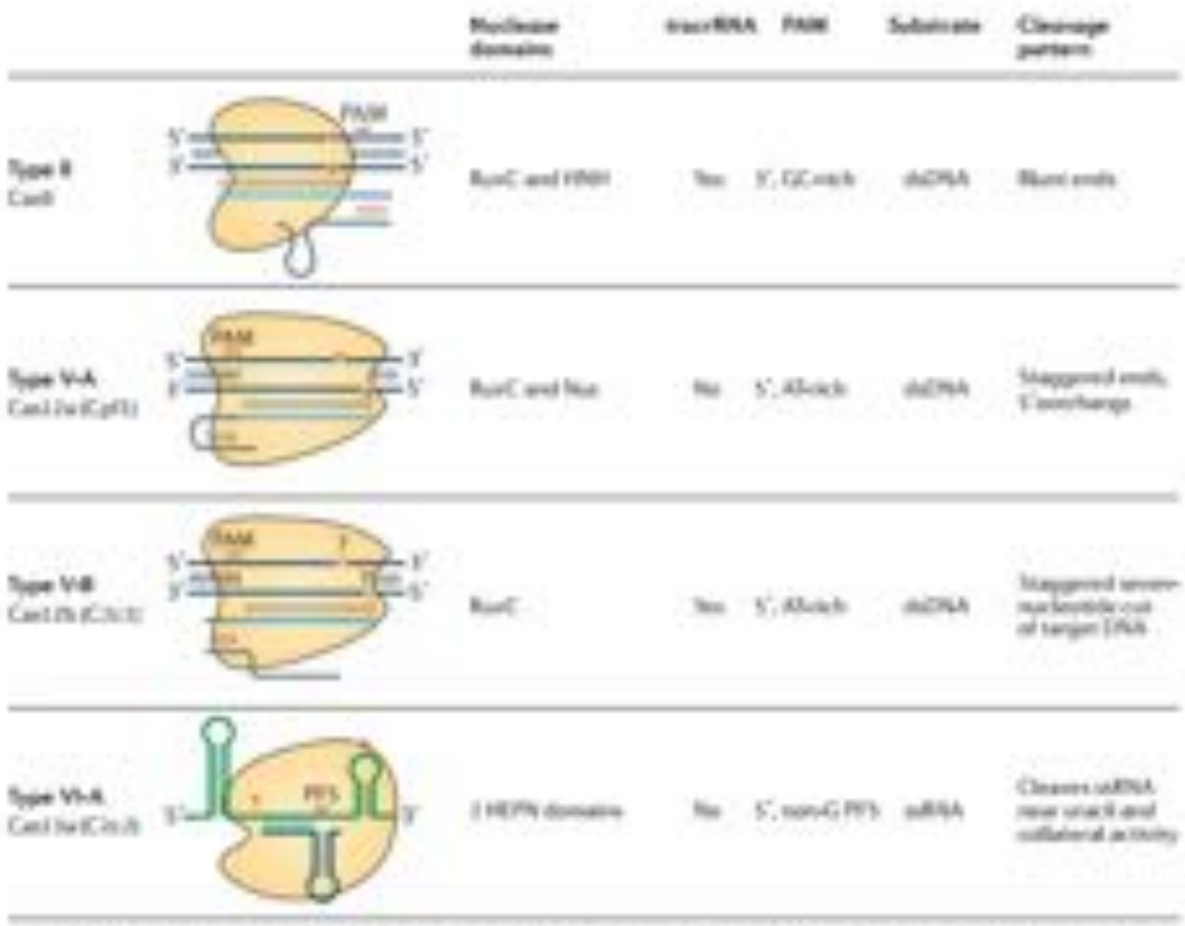
In Brief

An engineered CRISPR-based platform for inducible recruitment of specific genomic loci to distinct nuclear compartments reveals positional effects on gene expression and cellular function.

Wang et al., 2018, Cell *175*, 1–13
November 15, 2018 © 2018 Elsevier Inc.
https://doi.org/10.1016/j.cell.2018.09.013

Diversity and evolution of class 2 CRISPR–Cas systems

Sergey Shmakov[1,2], Aaron Smargon[3,4], David Scott[3], David Cox[3], Neena Pyzocha[3,5], Winston Yan[3], Omar O. Abudayyeh[3,6], Jonathan S. Gootenberg[3,7], Kira S. Makarova[2], Yuri I. Wolf[2], Konstantin Severinov[1,8,9], Feng Zhang[3,6,7,10,11] and Eugene V. Koonin[2]



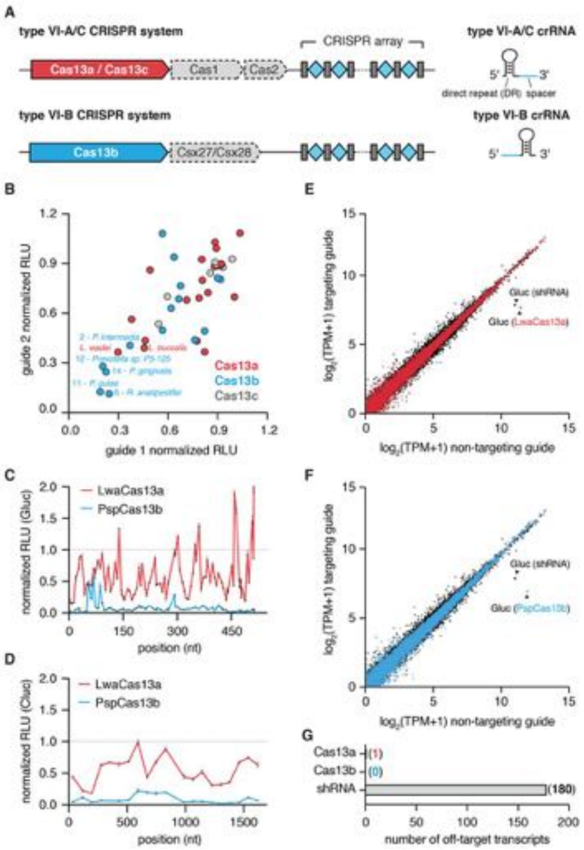
Nature Rev. Microbiol. 2017

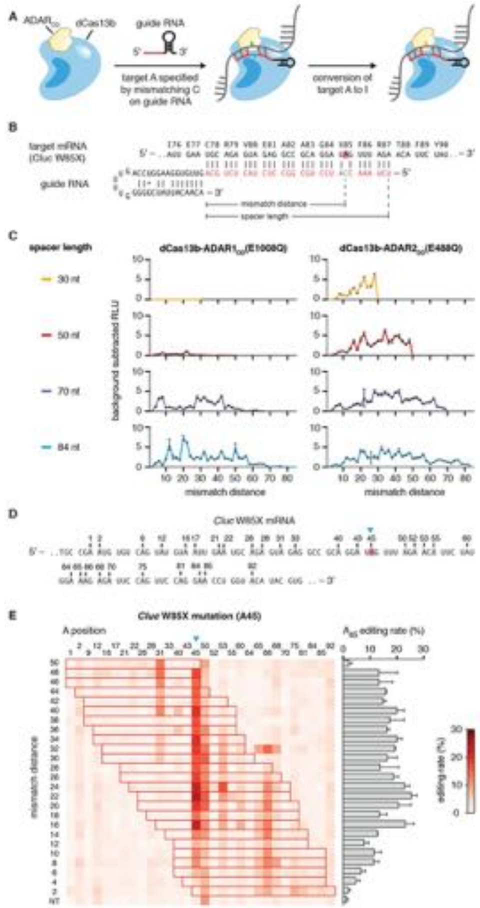
Science RESEARCH ARTICLES

Cite as: D. B. T. Cox et al., Science 10.1126/science.aaq0180 (2017).

RNA editing with CRISPR-Cas13

David B.T. Cox, Jonathan S. Gootenberg, Omar O. Abudayyeh, Brian Franklin, Max J. Kellner, Julia Joung, Feng Zhang





Feng Zhang

Molecular diagnostics

Science *REPORTS*

Cite as: J. S. Gootenberg *et al.*, *Science* 10.1126/science.aaq0179 (2018).

Multiplexed and portable nucleic acid detection platform with Cas13, Cas12a, and Csm6

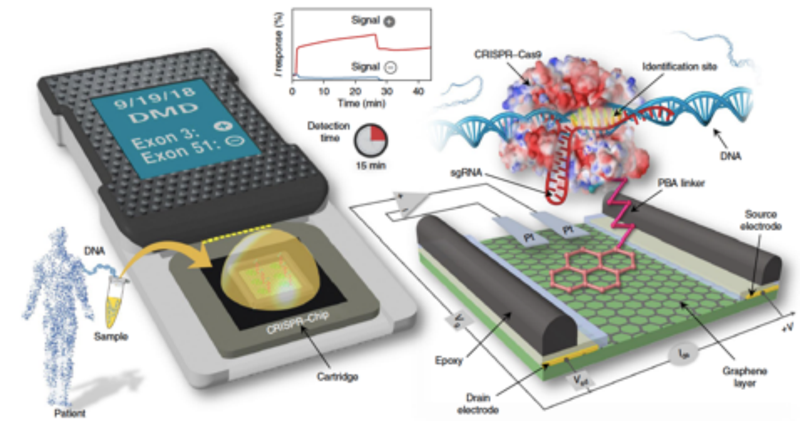
Jonathan S. Gootenberg,[1,2,3,4,7*] Omar O. Abudayyeh,[1,2,3,4,5*] Max J. Kellner,[1] Julia Joung,[1,2,3,4] James J. Collins,[1,4,5,6,8] Feng Zhang[1,2,3,4†]

nature biomedical engineering ARTICLES

https://doi.org/10.1038/s41551-019-0371-x

Detection of unamplified target genes via CRISPR–Cas9 immobilized on a graphene field-effect transistor

Reza Hajian[1], Sarah Balderston[1], Thanhtra Tran[1], Tara deBoer[2], Jessy Etienne[2], Mandeep Sandhu[1], Noreen A. Wauford[2], Jing-Yi Chung[2], Jolie Nokes[3], Mitre Athaiya[1], Jacobo Paredes[4], Regis Peytavi[5], Brett Goldsmith[3], Niren Murthy[2], Irina M. Conboy[2] and Kiana Aran[1,2,5*]

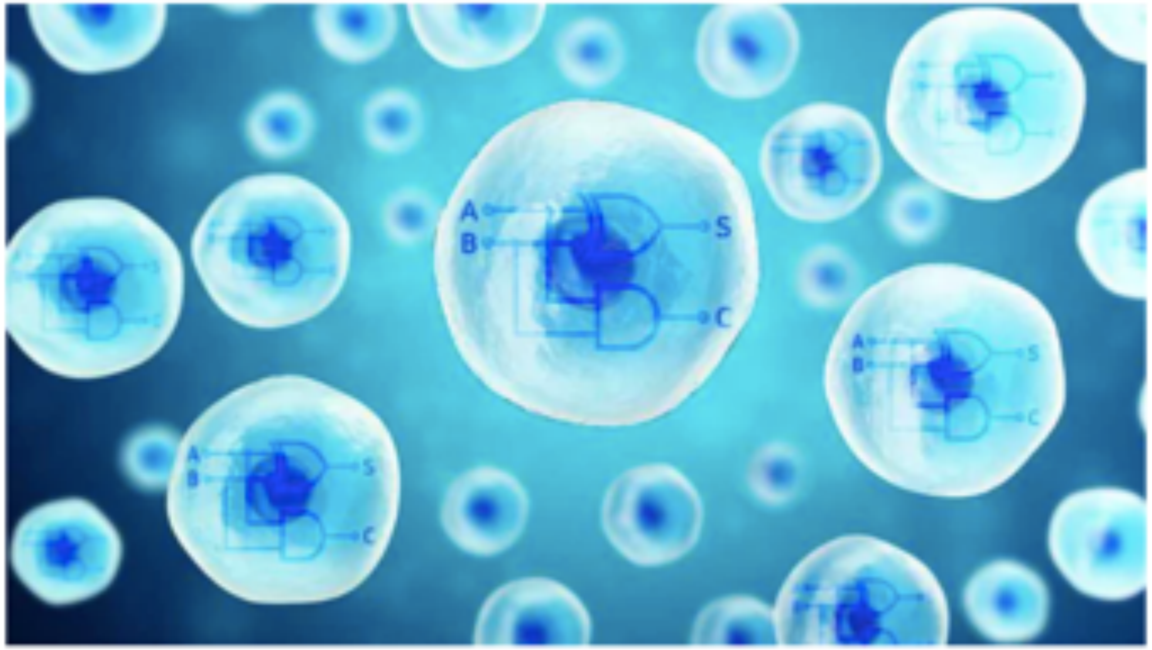


SCIENCE

CRISPR used to build dual-core computers inside human cells

Michael Irving | April 17th, 2019

An audio version of this article is available to **New Atlas Plus subscribers**. **More audio articles**



CRISPR has been used to insert biological computer processors into human cells (Credit: Colourbox/Steven Emmett, ETH Zurich)

N. M. Guzmán A. Peña J. García-Martínez R. Ruiz R. Maldonado

Enrique Viguera

UNIVERSIDAD DE MÁLAGA

Konstantin Severinov

Sckolthech Center of Life Sciences

Andrea Quiberoni

UNIVERSIDAD NACIONAL DEL LITORAL
SANTA FE, ARGENTINA

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SEVENTH FRAMEWORK PROGRAMME

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AGENCIA NACIONAL DE PROMOCION CIENTIFICA Y TECNOLOGICA

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