



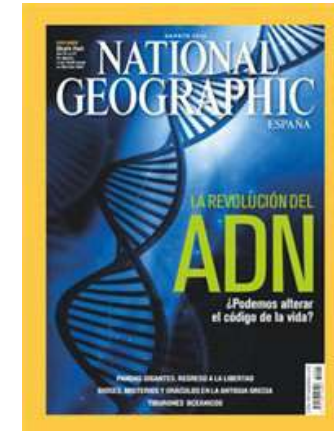
Historia del campo de investigación CRISPR y su traslación a la medicina

Francisco J. Martínez Mojica

24 de octubre de 2017

Evolución del campo de investigación CRISPR

Publicaciones CRISPR



The New York Times

HEALTH

A Powerful New Way to Edit DNA

By ANDREW POLLACK MARCH 3, 2014



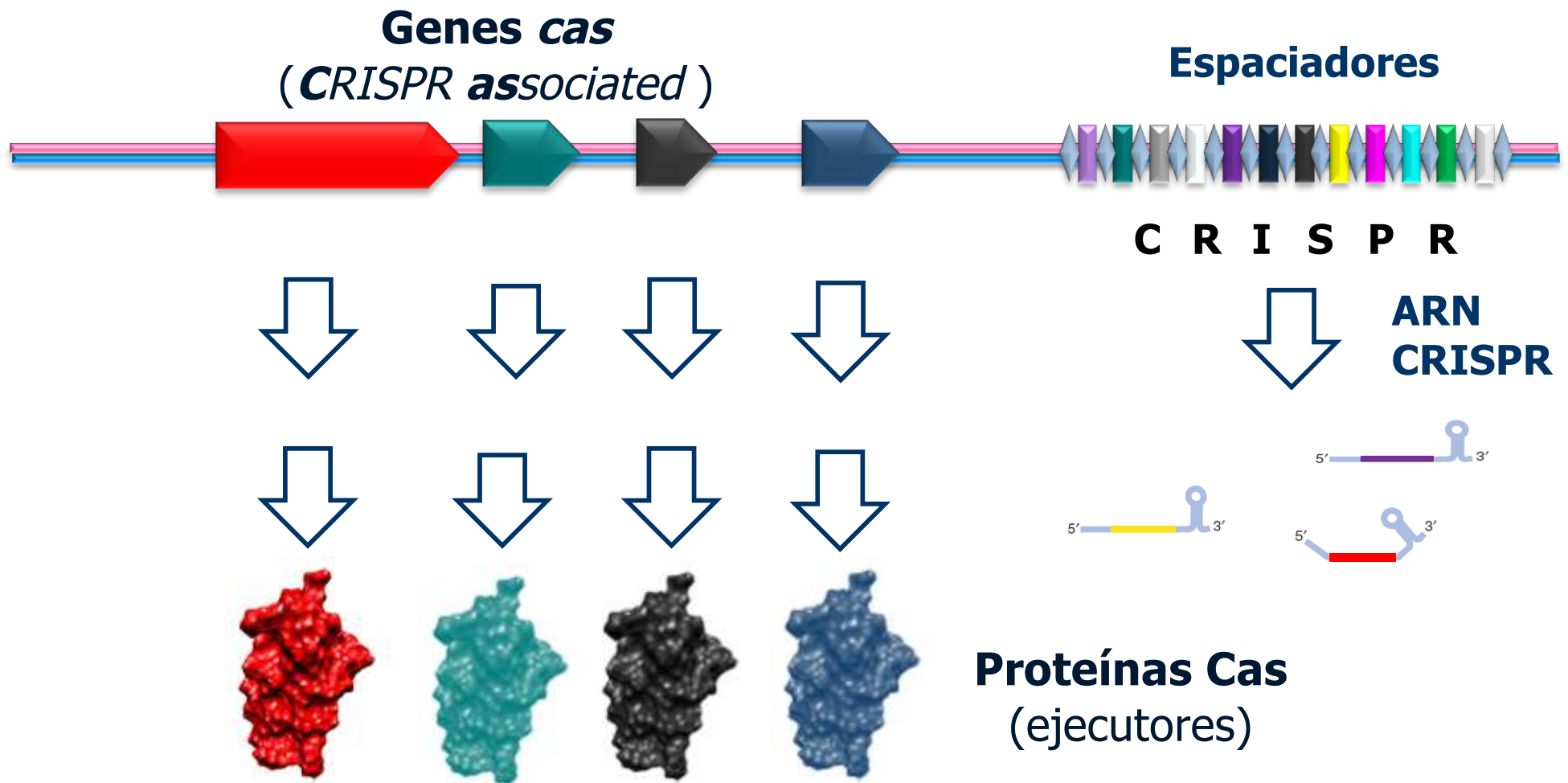
Año

¿Qué son
los sistemas CRISPR?

Genoma



◆ **C R I S P R**
l e n h a e
u g t o l p
s u e r i e
t l r t n a
e a s d t
r r p r s
e l a o
d y c m
e i
d c



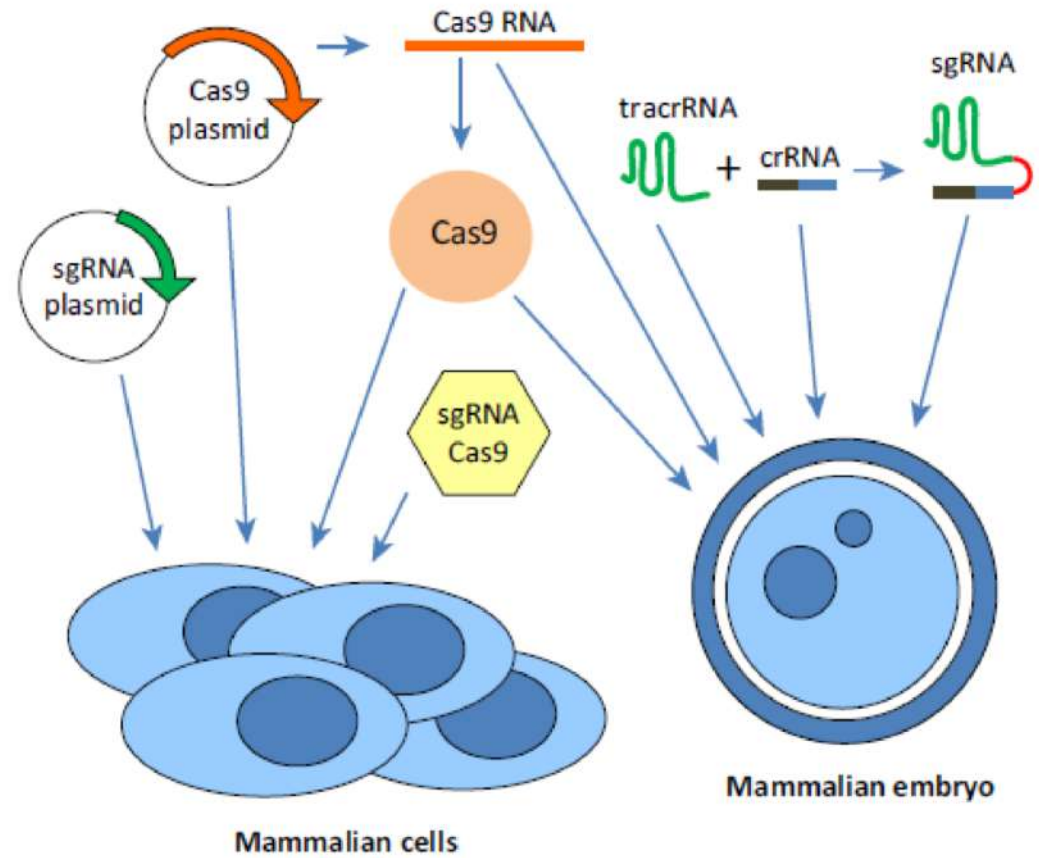
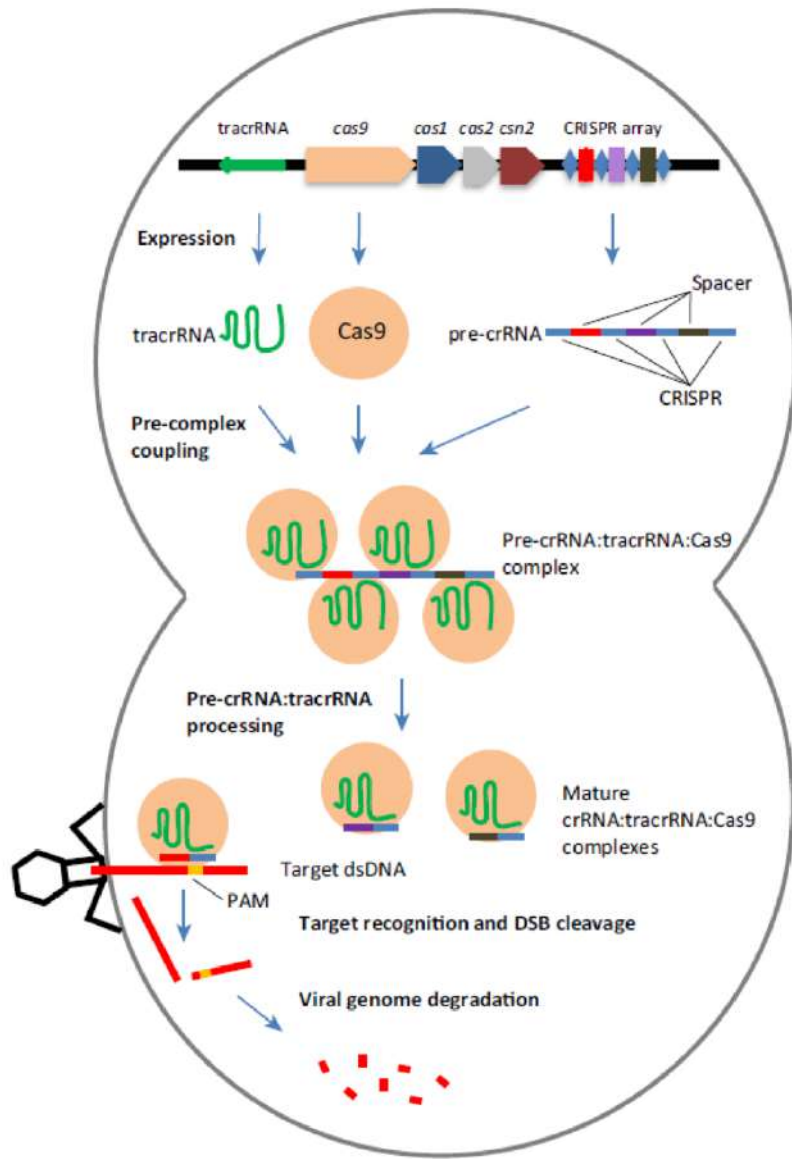
Sistema CRISPR

– Defensa *et al.* –

Inmunidad CRISPR



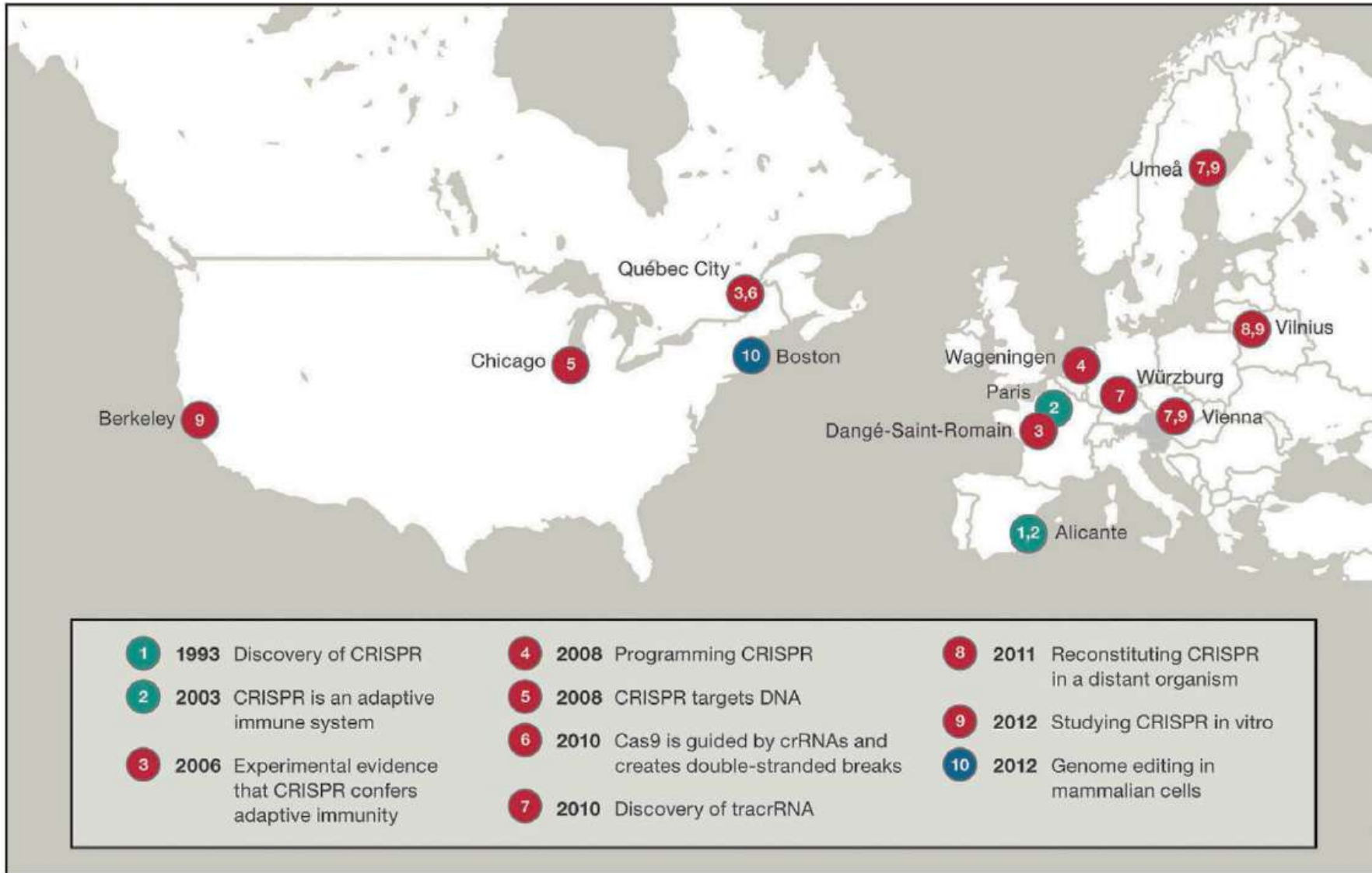
Tecnología CRISPR



Descubrimiento de los sistemas CRISPR

The Heroes of CRISPR

Eric S. Lander^{1,2,3,*}





ZB. Alicante, Spain: Francisco Mojca characterised the CRISPR locus

AROUND THE WORLD IN 80 MICROBES

Tick off the sites on your travels!

This list was in part crowd-sourced from our Twitter followers but is by no means exhaustive, please add your own and let us know @NatureMicrobiol

AFRICA

- 1. Trieste, Austria: *E. coli*. Tuberculosis infection in mummy from 600BC
- 2. Ziba Forest, Uganda: Ziba Virus first identified from Rhinopithecus here, 1947
- 3. Semliki forest, Uganda: Semliki forest virus first isolated from mosquitoes here, 1947
- 4. Ebola River, Congo: Ebola virus named after an outbreak near here, 1976
- 5. Mogadishu, Somalia: Last natural case of smallpox before eradication
- 6. Western Sahara: Saharan desert is a source of iron for Atlantic primary producers
- 7. Mponeng mine, S. Africa: Desulfohalobium amalyanum found in cavern 7.8 km below ground

ANTARCTICA

- 8. McMurdo Dry Valleys, Antarctica: Permafrost soil microbial communities
- 9. Lake Vostok, Antarctica: Microbial life thrives in lakes under the Antarctic ice

ASIA

- 10. Tokyo, Japan: Meguro Parasitology Museum
- 11. Mollath, Bangladesh: Cholera vaccine trials led by ICDDR,B
- 12. Beijing, China: Purification of artemisinin for malaria treatment (2015 Nobel Prize)
- 13. Seoul, South Korea: Museum Kimchiikan
- 14. Mishima, Japan: Japanese Microbial Memorial
- 15. Hwa Tsung, Vietnam: Yenisei Museum
- 16. Chersky, Russia: Permafrost soil microbial communities
- 17. Eilat, Israel: *Epilobium* *salicoides*, one of the largest bacteria, in reef sponges
- 18. Dead Sea: Microbial mats are found here, one of the world's saltiest water bodies
- 20. Chukotka, Russia: Soil amoeba contains huge viruses such as *Mollivirus subterraneus*
- 21. Al Ahsa, Saudi Arabia: The first reported case of MERS in 2012

EUROPE

- 22. London, England: Gai's Pathology Museum
- 23. Delft, Netherlands: Beijerinck Museum & Oude Kerk, resting place of Van Leeuwenhoek
- 24. Amsterdam, Netherlands: Microtop Museum
- 25. Aix, France: Hippocrate Museum

- 26. Alkmaar, Netherlands: Dutch Cheese Museum
- 27. Lascaux, France: Palaeolithic cave paintings are under threat by an invasive black mould
- 28. Alicante, Spain: Francisco Mojca characterised the CRISPR locus
- 29. Sheffield, England: Caves Museum
- 30. Vienna, Austria: Pestisole plague monument
- 31. Berlin, Germany: Robert Koch Institute museum
- 32. Epsom, England: Plague infection control in 1665-66
- 33. Grimland Island, Scotland: Anthrax testing during WWII
- 34. London, England: Alexander Fleming Laboratory Museum
- 35. London-England: Broad Street pump identified as source of cholera outbreak by John Snow, 1854
- 36. Bath, England: *Methylobacillus capsulatus* isolated from Roman Bath Thermal springs
- 37. Motra, Slovakia: Saclatonyces sculpture
- 38. Paris, France: Pasteur Museum
- 39. Glasgow, Scotland: Hunterian Museum
- 40. Copenhagen, Denmark: Carlsberg Laboratory & Brewery
- 41. Svalbard, Norway & Greenland: Glacial snow algae give colour to ice and snow
- 42. Isle of Rhé, Germany: Fischer-Loeffler Institut - discovery of foot & mouth disease
- 43. Berkeley, England: Edward Jenner's house
- 44. Valletta, Malta: Depositioned milk identified as the source of Malta Fever (*Breitschia malteseensis*)
- 45. Geneva, Switzerland: home of the World Health Organization
- 46. Prague, France: Proposed first outbreak that led to the 1918 Spanish influenza pandemic

- 47. Dolni Věstonky, Czechia: The first human was found to harbor *Helicobacter pylori* in his stomach
- 48. Paris, France: HIV reported to be the causative agent of AIDS
- 49. Tokaj, Hungary: Botrytised wines are made from grapes infected with *Botrytis cinerea*
- 50. London, UK: Home of the Nature Microbiology office!

LATH AMERICA

- 51. Gamboa, Panama: Leaf-cutter ants feed to fungal gardens
- 52. Bismarck Bay, Papua New Guinea: *Bismarckia* *stratfordi* - first Legionnaires outbreak
- 53. Havana, Cuba: Carlos Finlay helps eradicate yellow fever in Cuba through mosquito control

NORTH AMERICA

- 48. Bethesda, USA: HIV was reported to be the causative agent of AIDS
- 54. Seattle, USA: Home of the Bill and Melinda Gates Foundation
- 55. Yellowstone National Park, USA: Thermophilic bacteria in hot springs & geysers
- 56. Urbana, USA: Carl Woese & George Fox characterise Archaea as a 3rd domain of life
- 57. Washington, USA: Home of the American Society of Microbiology
- 58. Philadelphia, USA: Bellevue-Stratford Hotel Philadelphia - first Legionnaires outbreak
- 59. Saguenay Sea, Atlantic Ocean: First identification of SAR11
- 60. San Francisco, USA: Salt ponds in San Francisco bay
- 61. San Francisco, USA: Winogradsky column of Escherichia coli
- 62. Atlanta, USA: Home of the Carter Center
- 63. Foster City, California: First effective drug cure for Hepatitis C virus - ledipasvir/sofosbuvir
- 64. Mid-west USA: Synthetic N-fixing bacteria in cyanogen agriculture

- 65. Texas, USA: The first metallic ossuary was Texas fever (*Babesia microti*)
- 66. Newville, USA: Max Perutz's lab (1950s Nobel Prize) - bacterial resistance to viral restriction
- 67. Hayward, USA: First development of massively parallel DNA sequencing
- 68. O'ahu, New Zealand: ALOHA long-term monitoring site set up in 1980
- 69. Madison, USA: James Watson's lab (1958 Nobel Prize - transcription)
- 70. Corvallis, USA: Arthur Andersen discovered calcium-resistant bacterium, *Deinococcus radiodurans*, 1946
- 71. Winlow, USA: Impact crater beltline - can microorganisms survive in space?

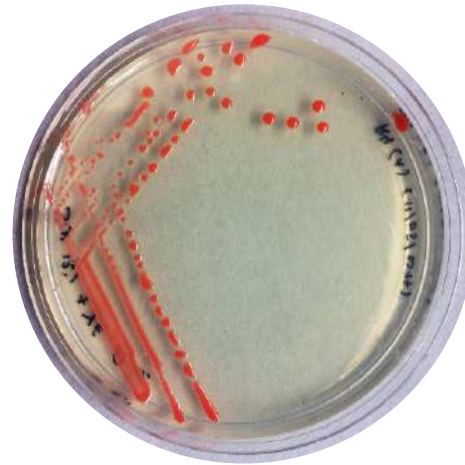
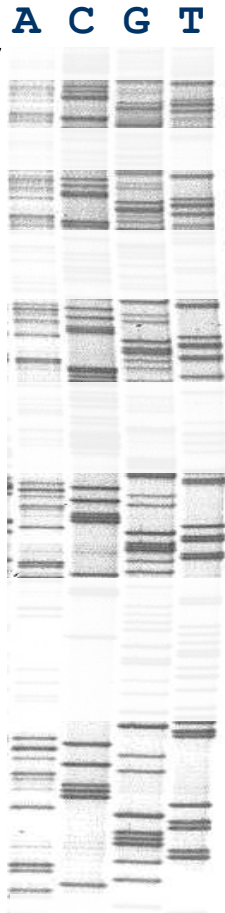
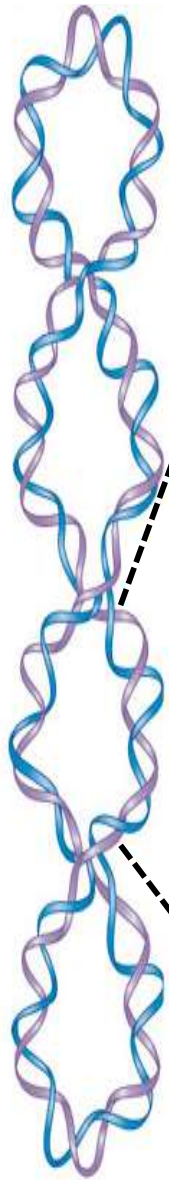
OCEANIA

- 72. Shark Bay, Australia: Stromatolite colonies of cyanobacteria with a laminated structure
- 73. Great Barrier Reef, Australia: *Symbiodinium* coral colonies form the world's largest coral reef system
- 74. Rotarua, New Zealand: *Streptomyces* thrive in geothermal pools
- 75. Lake Conlin, Australia: Truncatella colonies of cyanobacteria with a chitinous structure

SOUTH AMERICA

- 76. Olvera, Brazil: Carlos Chagas described the *Trypanosoma cruzi* infection
- 77. Easter Island (Rapa Nui), Chile: Rapamycin discovered in *Streptomyces* *Agospospices*
- 78. Andes, Quechua people first used quinine from *Cinchona* tree bark to treat malaria
- 79. Atacama desert, Chile: Microorganisms even thrive here, one of the driest places on earth
- 80. Galapagos Islands, Ecuador: The inspiration behind Charles Darwin's work on evolution

Procariotas "Amantes de la Sal"



Mojica, FJM
Tesis Doctoral (1993)

GTTACAGACGAACCCTAGTTGGGTTGAAGCGAACAGGATGGCGAACCGGTGTCTGCACCAGTT
GTTACAGACGAACCCTAGTTGGGTTGAAGCCACGACAATCAAGTCTGGTTGCATGGCGACACG
GAGTTACAGACGAACCCTAGTTGGGTTGAAGCCTGTGCCTCCAGCGGCCGTCAGACAGTCGCA
TCCGAGTTACAGACGAACCCTAGTTGGGTTGAAGCAAGAAGCCGCTCGCCGTCTCGATGACG
GGCGGGCGGTTACAGACGAACCCTAGTTGGGTTGAAGCGACAAGACTCGCGACGAAGCCGAGT
CGAAACGCCGCGTTACAGACGAACCCTAGTTGGGTTGAAGCCTCTTTATCCCTCCTGCCCGAA
TGTCTACGAATATCGTTACAGACGAACCCTAGTTGGGTTGAAGCGAACCCACTGGTGAAGAAA
AAGTTGTAGAGACCCTAGTTACAGACGAATCCCTAGTTGGGTTGAAGCACGACAATCAAGTCT
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GGGGAGGGCGAAATTAGCCAAGCAGTTACAGACGAACCCTAGTTGGGTTGAAGC

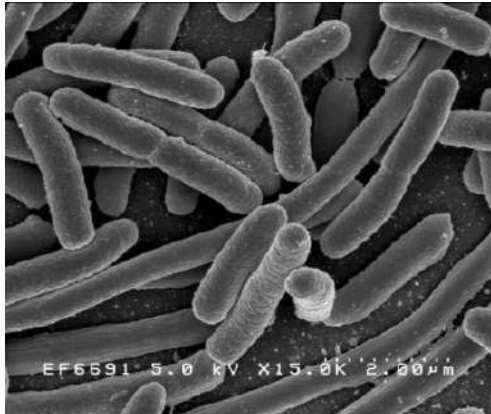
1987

Escherichia coli

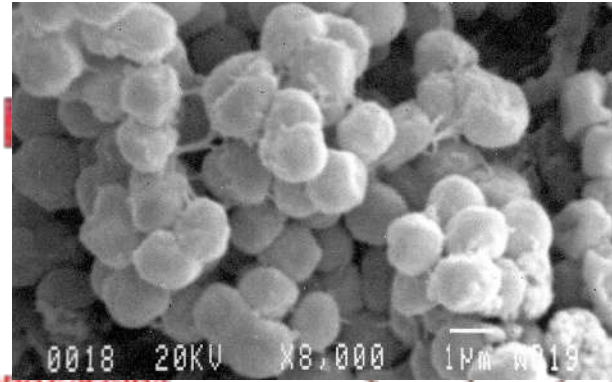
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CGGTTTATCCCTGCTGGCGCGGGGAACTC TCGGTTTCAGGCGTTGCAAACCTGGCTACCGGG
CGGTTTATCCCCGCTAACGCGGGGAACTC GTAGTCCATCATTCCACCTATGTCTGAACTCC
CGGTTTATCCCCGCTGGCGCGGGGAACTC CCGGGGGATAATGTTTACGGTCATGCGCCCC
CGGTTTATCCCCGCTGGCGCGGGGAACTC TGGGCGGCTTGCCTTGCAGCCAGCTCCAGCAG
CGGTTTATCCCCGCTGGCGCGGGGAACTC AAGCTGGCTGGCAATCTCTTTCGGGGTGAGTC
CGGTTTATCCCCGCTGGCGCGGGGAACTC TAGTTTCCGTATCTCCGGATTTATAAAGCTGA
CGGTTTATCCCCGCTGGCGCGGGGAACTC GCAGGCGGGCGACGCGCAGGGTATGCGCGATTTC

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

PROCARIOTAS



Green filamentous bacteria



Archa

ota

Proteobacteria

am positives

Methanosarcina

Methanobacterium

Halophiles

mals

Fungi

Plants



T. thermoprote
pyrodicticum



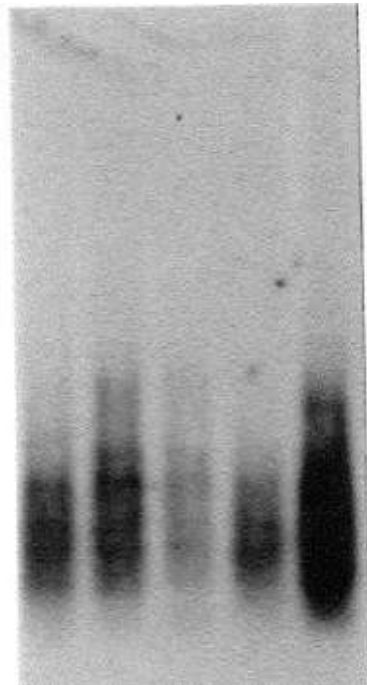
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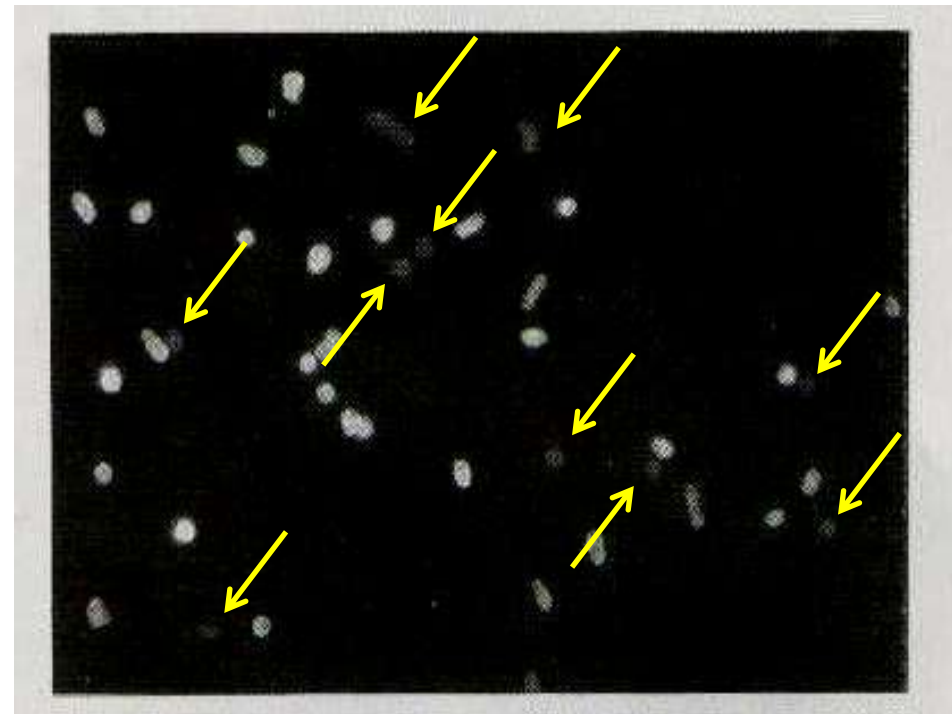
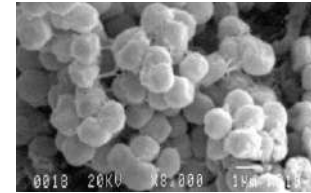
ads

1993-1995: Evidencias de actividad

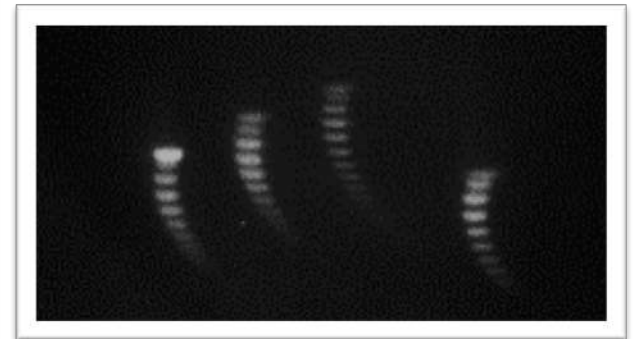
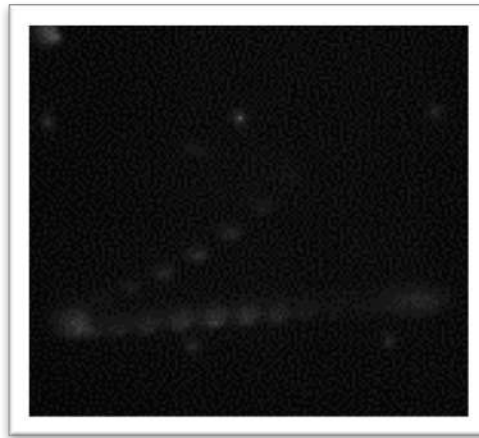
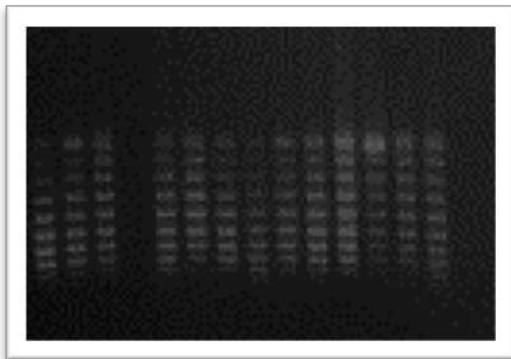
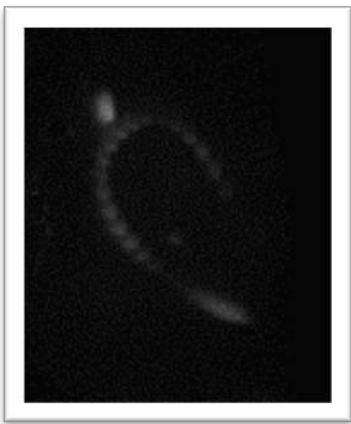
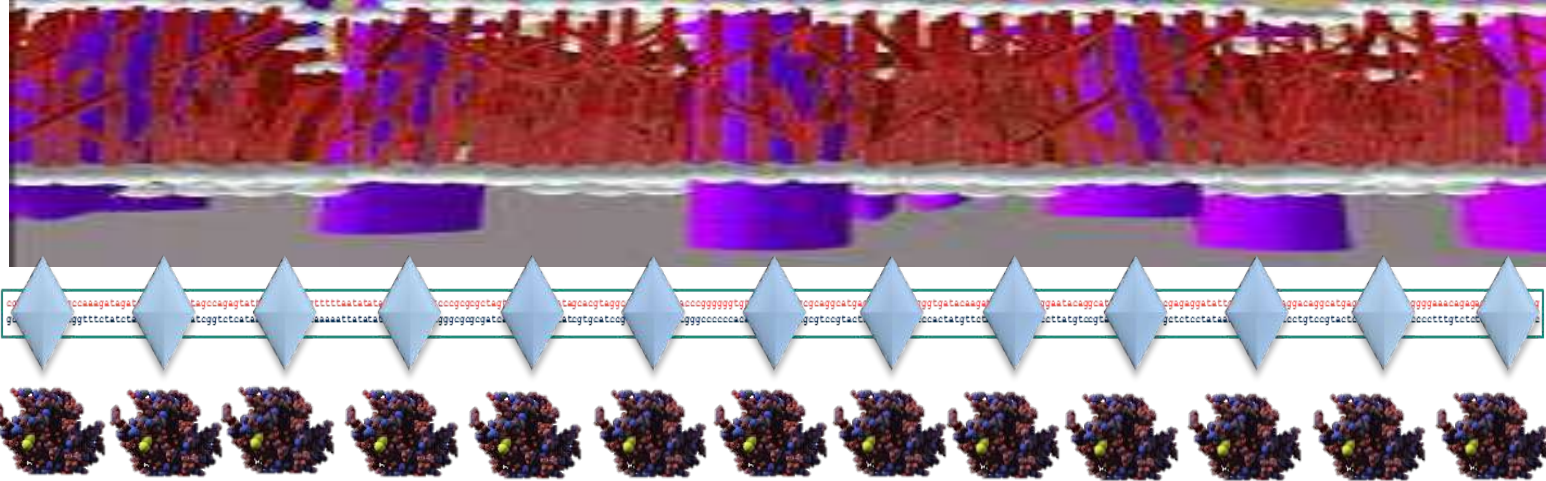


ARN CRISPR

Mojica, FJM
Tesis Doctoral (1993)

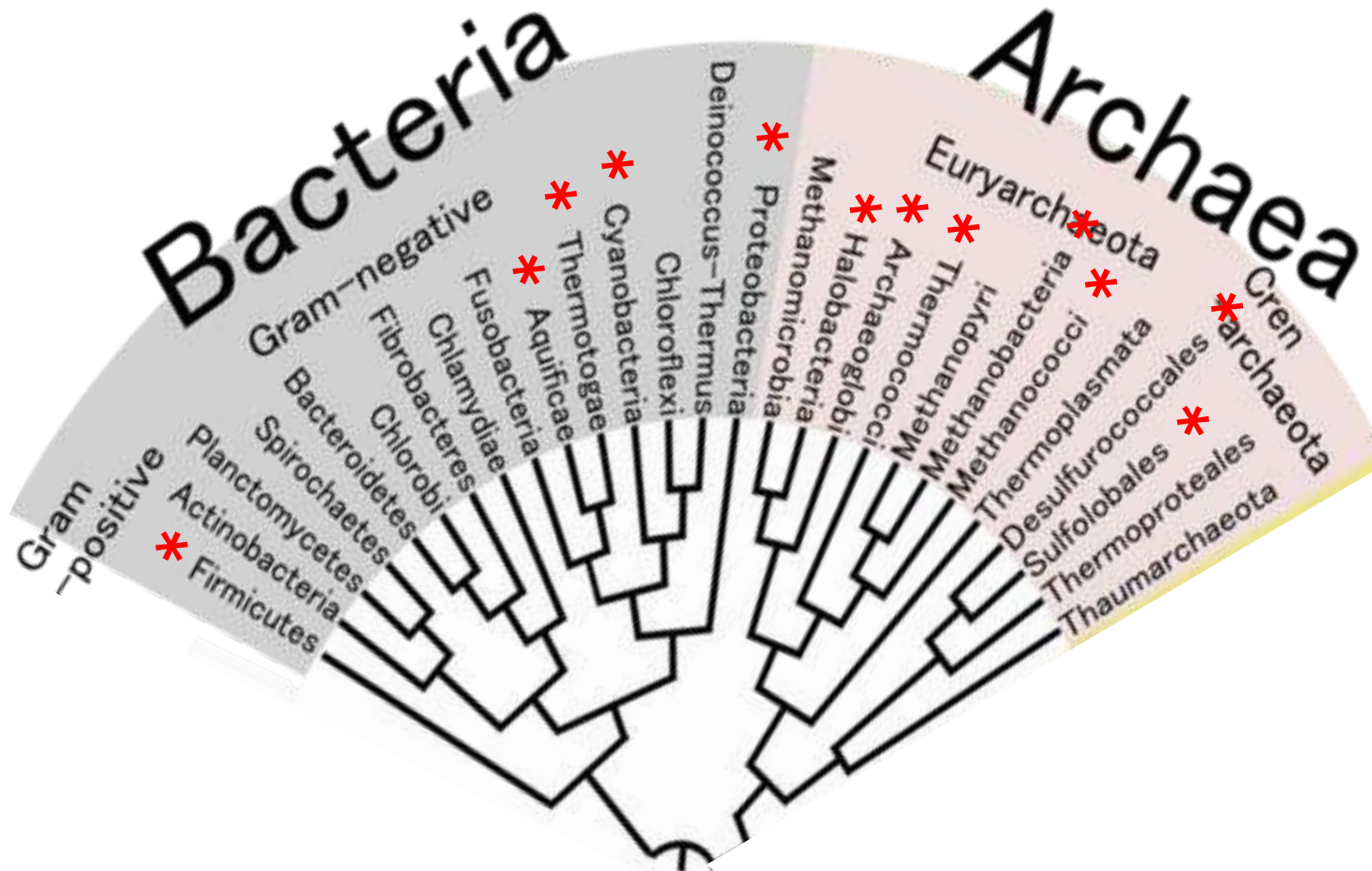


¿Qué función desempeñan?



2000: Una nueva familia de repeticiones

Short Regularly Spaced 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.

CRISPR-Cas systems, Barrangou and van der Oost (Springer-Verlag Berlin Heidelberg 2013)
With permission of Springer.

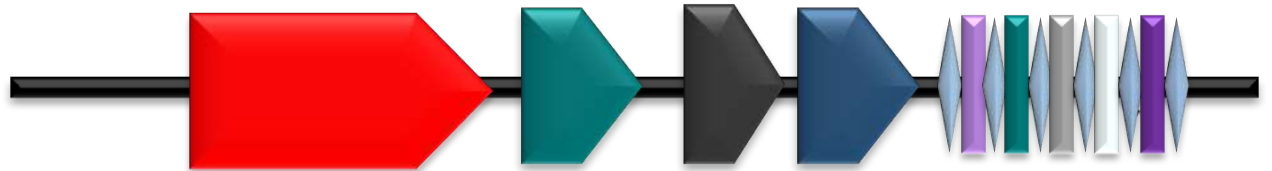
Clustered
Regularly
Interspaced
Short
Palindromic
Repeats

2002: Los genes *cas*

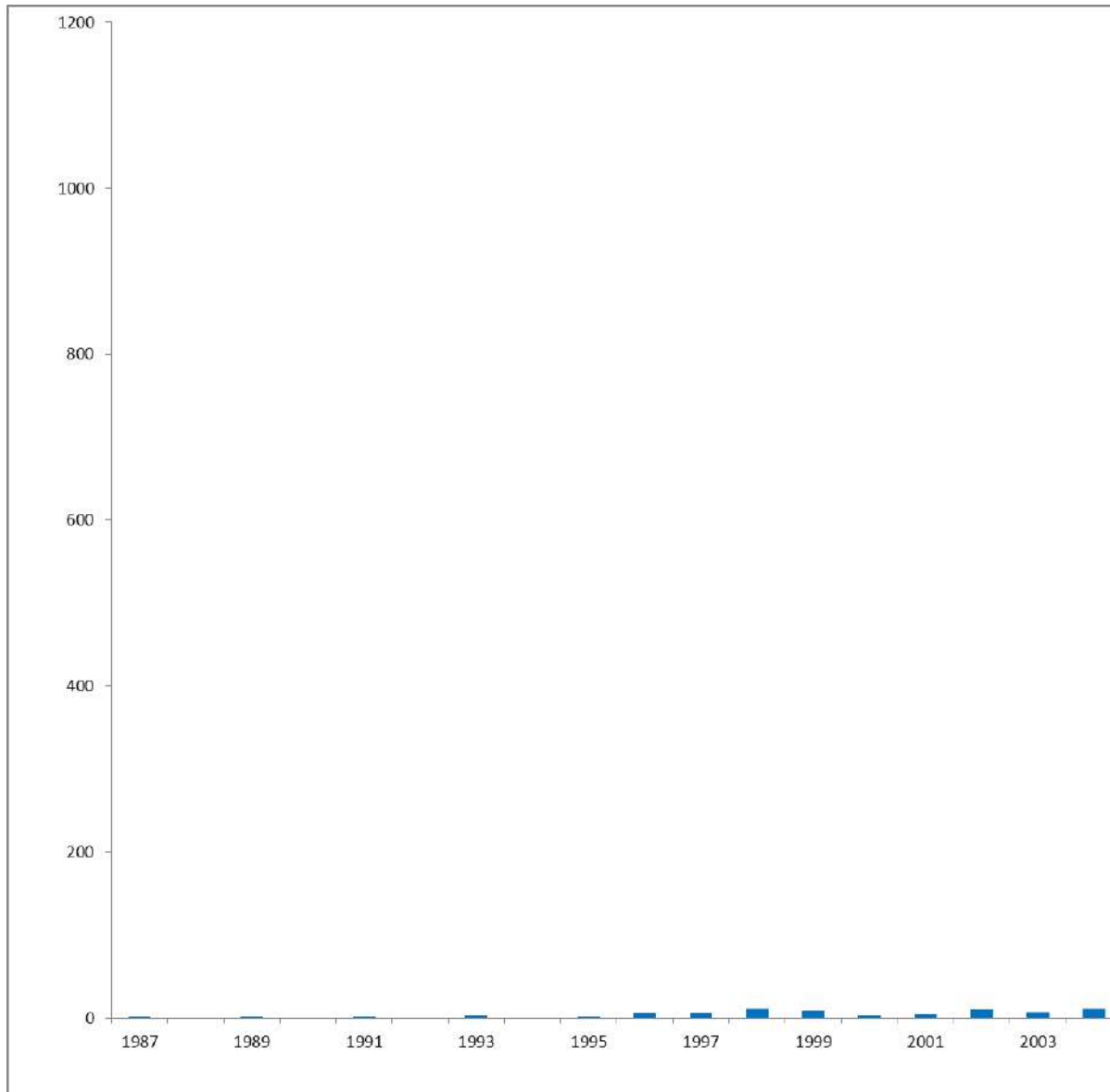
Molecular Microbiology (2002) 43(6), 1565–1575

Identification of genes that are associated with DNA repeats in prokaryotes

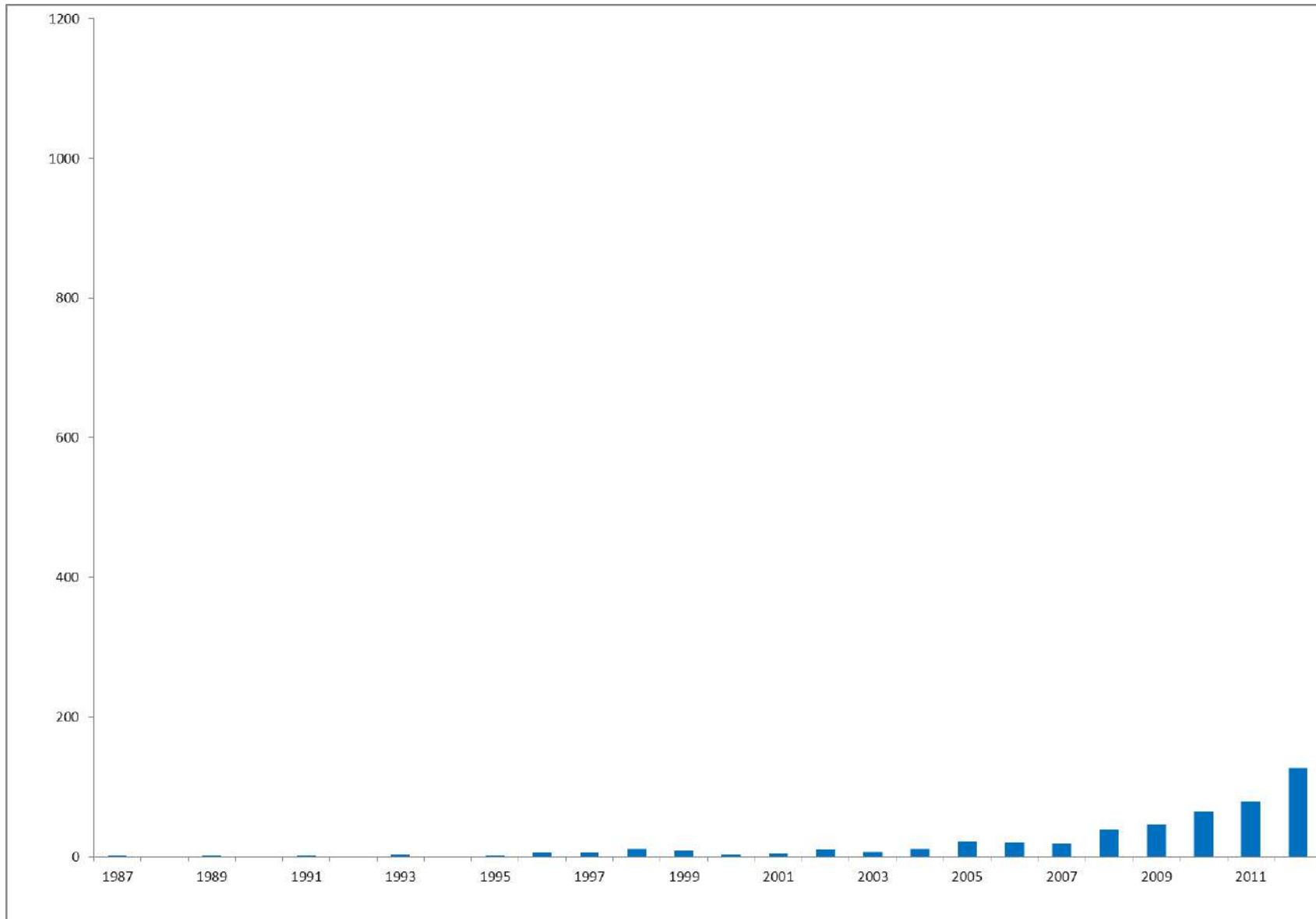
Ruud. Jansen,^{1*} Jan. D. A. van Embden,²
Wim. Gaastra¹ and Leo. M. Schouls²



Publicaciones CRISPR



Publicaciones CRISPR



2005:El origen de los espaciadores

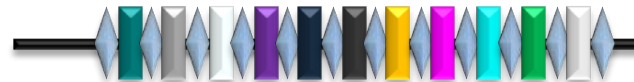
J Mol Evol (2005) 60:174–182
DOI: 10.1007/s00239-004-0046-3

JOURNAL OF **MOLECULAR
EVOLUTION**

© Springer Science+Business Media, Inc. 2005

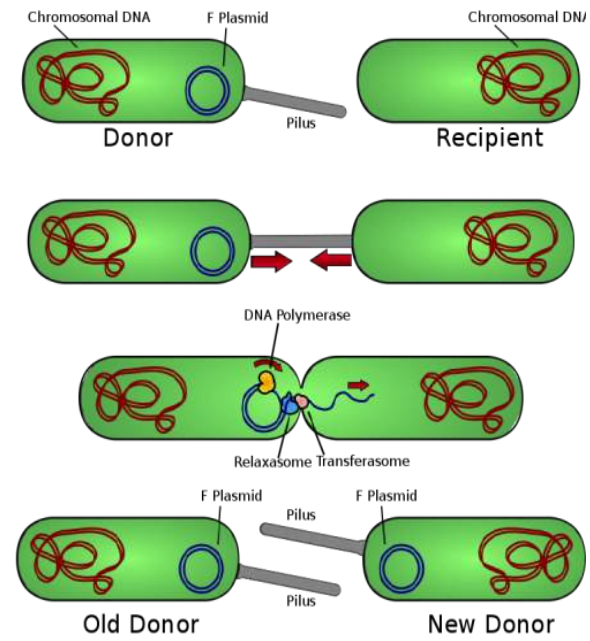
Intervening Sequences of Regularly Spaced Prokaryotic Repeats Derive from Foreign Genetic Elements

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

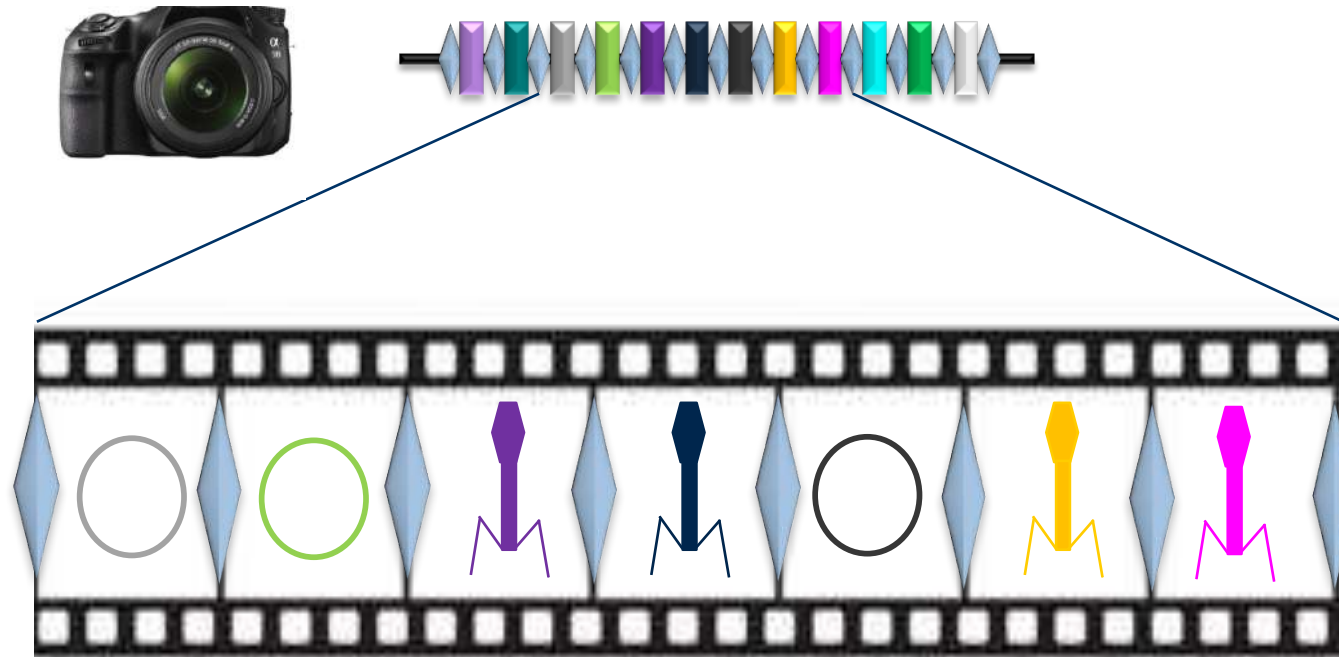




"Phage" by Dr Graham Beards - en:Image:Phage.jpg.
 Licensed under CC BY-SA 3.0 via Commons -
<https://commons.wikimedia.org/wiki/File:Phage.jpg#/media/File:Phage.jpg>



"Conjugation" by Adenosine - Own work. Licensed under CC BY-SA 3.0 via Commons-
<https://commons.wikimedia.org/wiki/File:Conjugation.svg#/media/File:Conjugation.svg>

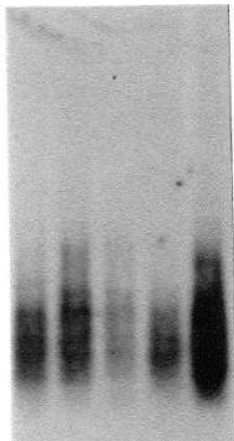


Proposición de una función

- Inmunidad

Control of both mobility and maintenance of extrachromosomal genetic elements could be a relevant task of CRISPR loci, but the homologies found

- Mediada por ARN



activity could be executed by CRISPR-RNA molecules, acting as regulatory RNA that specifically

CRISPR research mini-meeting, Berkeley, CA, July 24, 25 2008

Sponsored by NASA NAI Microbial Systems Biology and Virus working groups

Thursday July 24, 2008

1:30 – 2:30: Kira Makarova *"Comparative genomics, protein sequence analysis and evolution of the Cas system"*

2:30 – 3:30: Francis Mojica *"CRISPR PAMs: the proto-spacer adjoining motifs"*

3:45 – 5:45: Rodolphe Barrangou *"Function and Evolution of CRISPR in Lactic Acid Bacteria"*

Friday July 25, 2008

9:00 – 10:00: Alexander Yakunin *"Biochemical and structural characterization of CRISPR-associated ribonucleases"*

10:00 – 10:30: Virgis Siksnys *"Restriction modification systems: an overview, recent work on CRISPR systems"*

11:00 – 12:00 John van der Oost *"A flu shot for bacteria - the CRISPR anti-virus system of E. coli"*

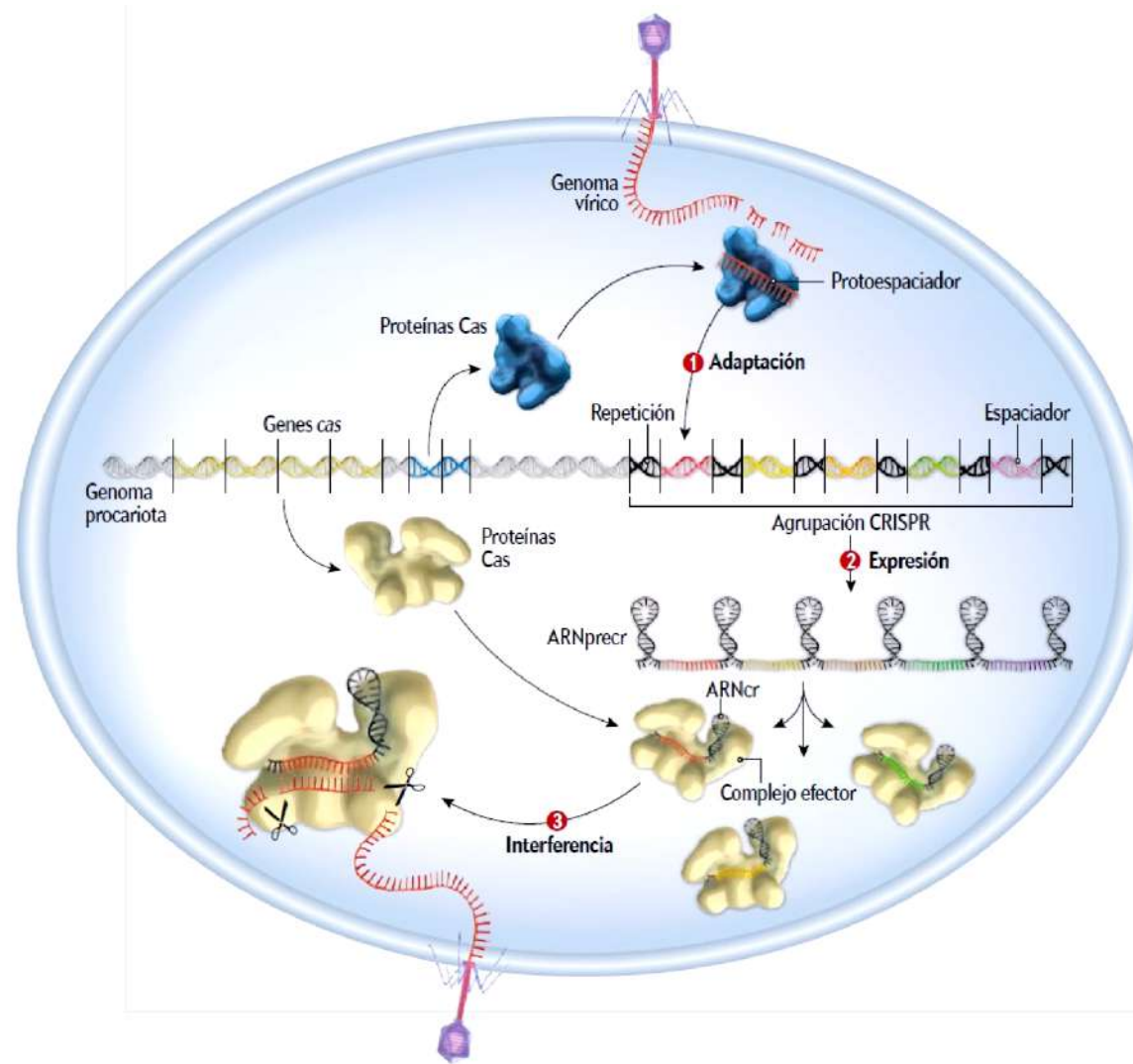
1:30 – 2:30: Blake Wiedenheft *"Biochemical characterization of the CRISPR associated immune response in P. aeruginosa"*

2:30 – 3:30 Ekaterina Semenova

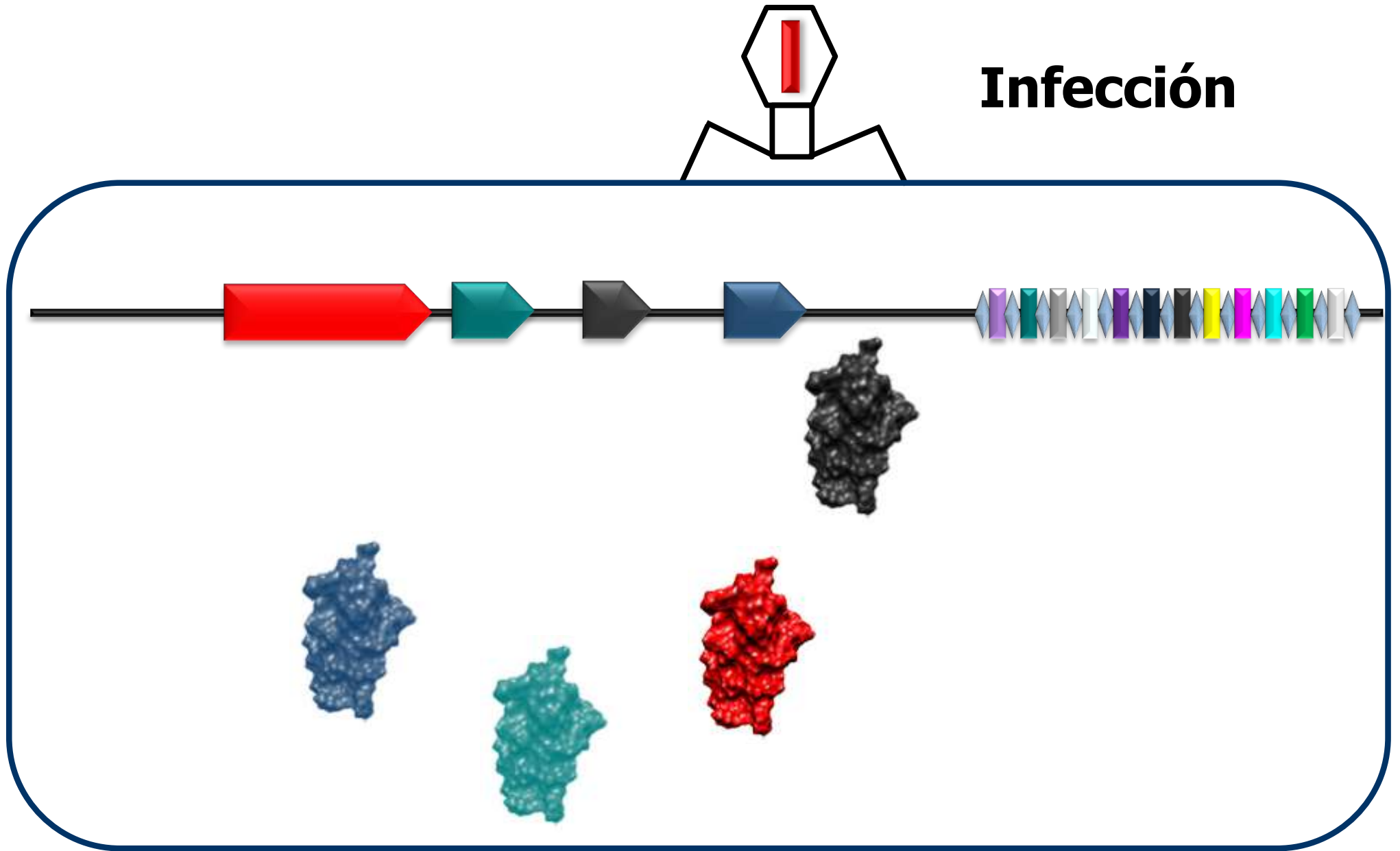
3:30 – 4:30: Jill Banfield *"The population genomics view of virus-host interactions"*

4:30 – 5:30: Mark Young *"CRISPR analysis of Yellowstone's high temperature environments"*

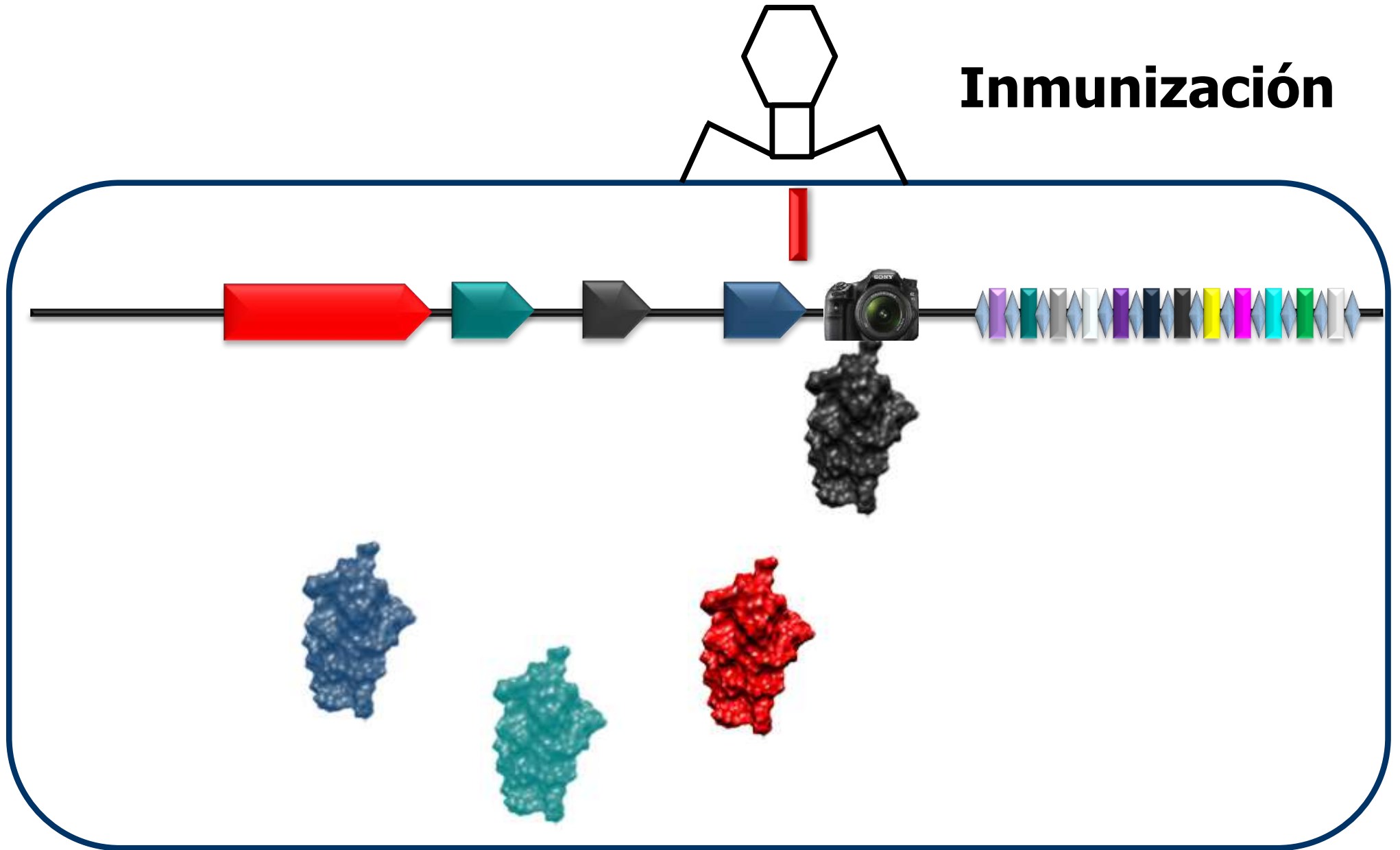
El Mecanismo CRISPR



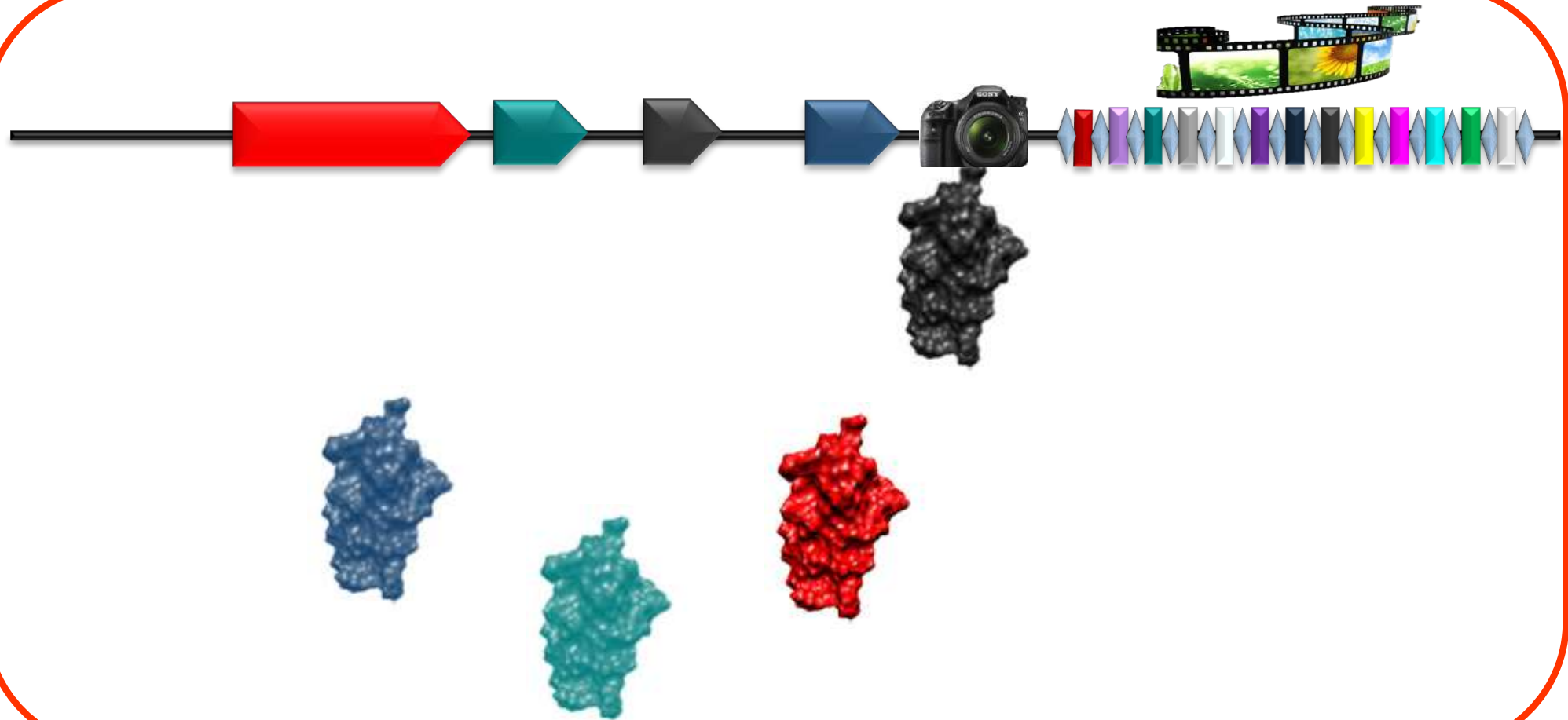
Infección



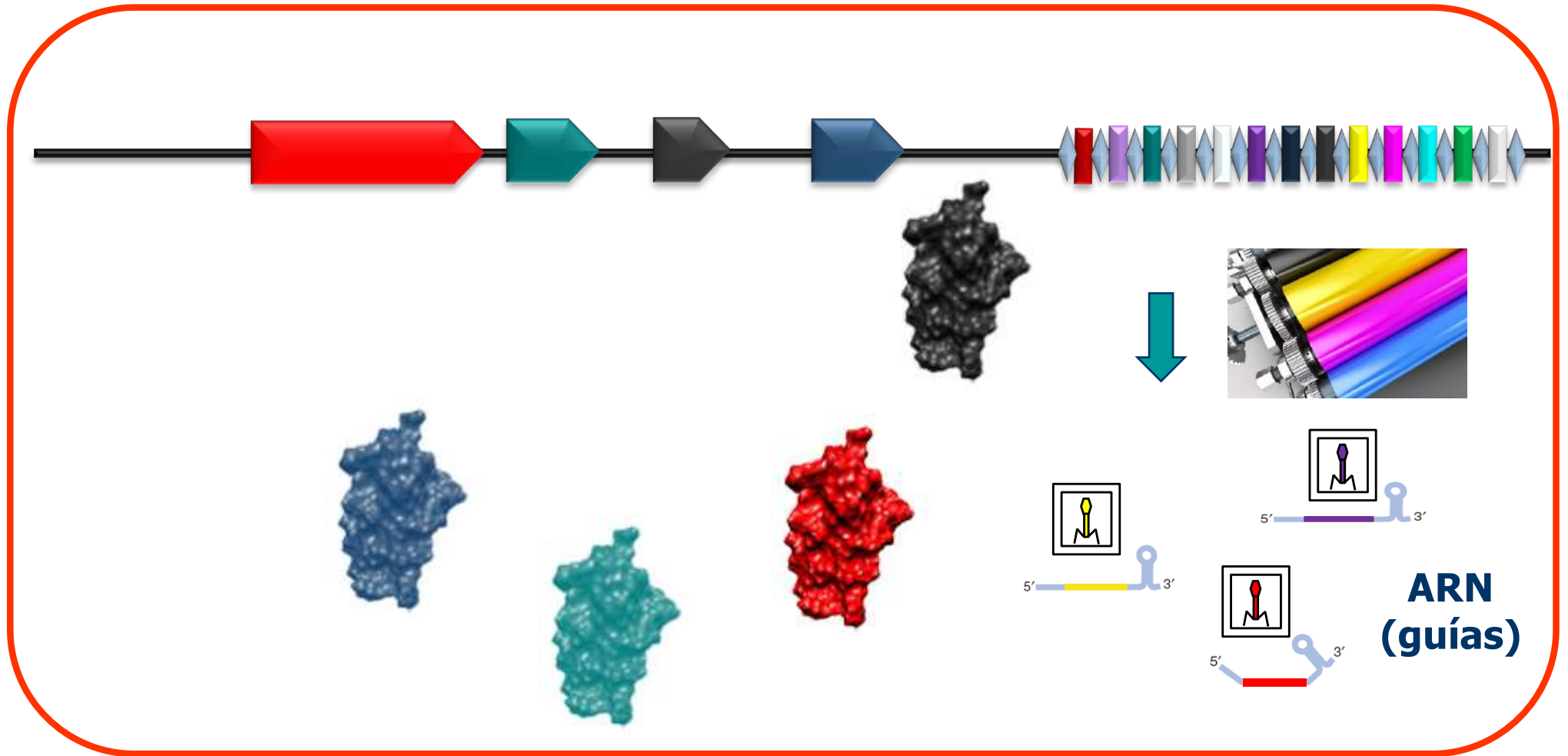
Inmunización



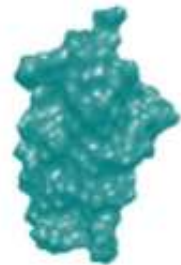
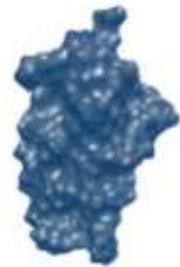
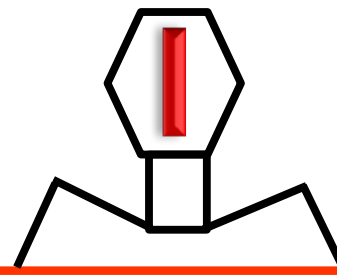
Bacteria Inmunizada



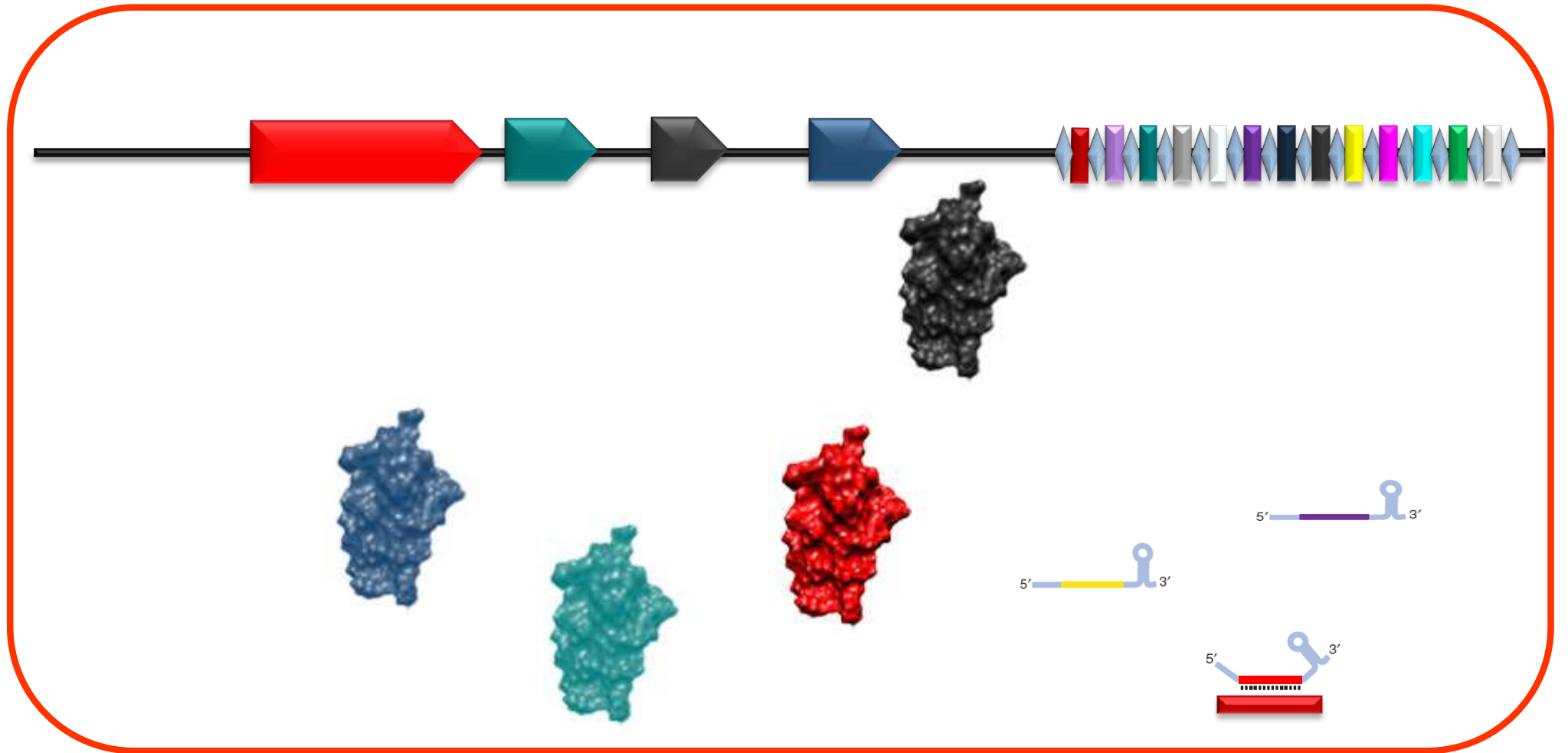
Producción de defensas



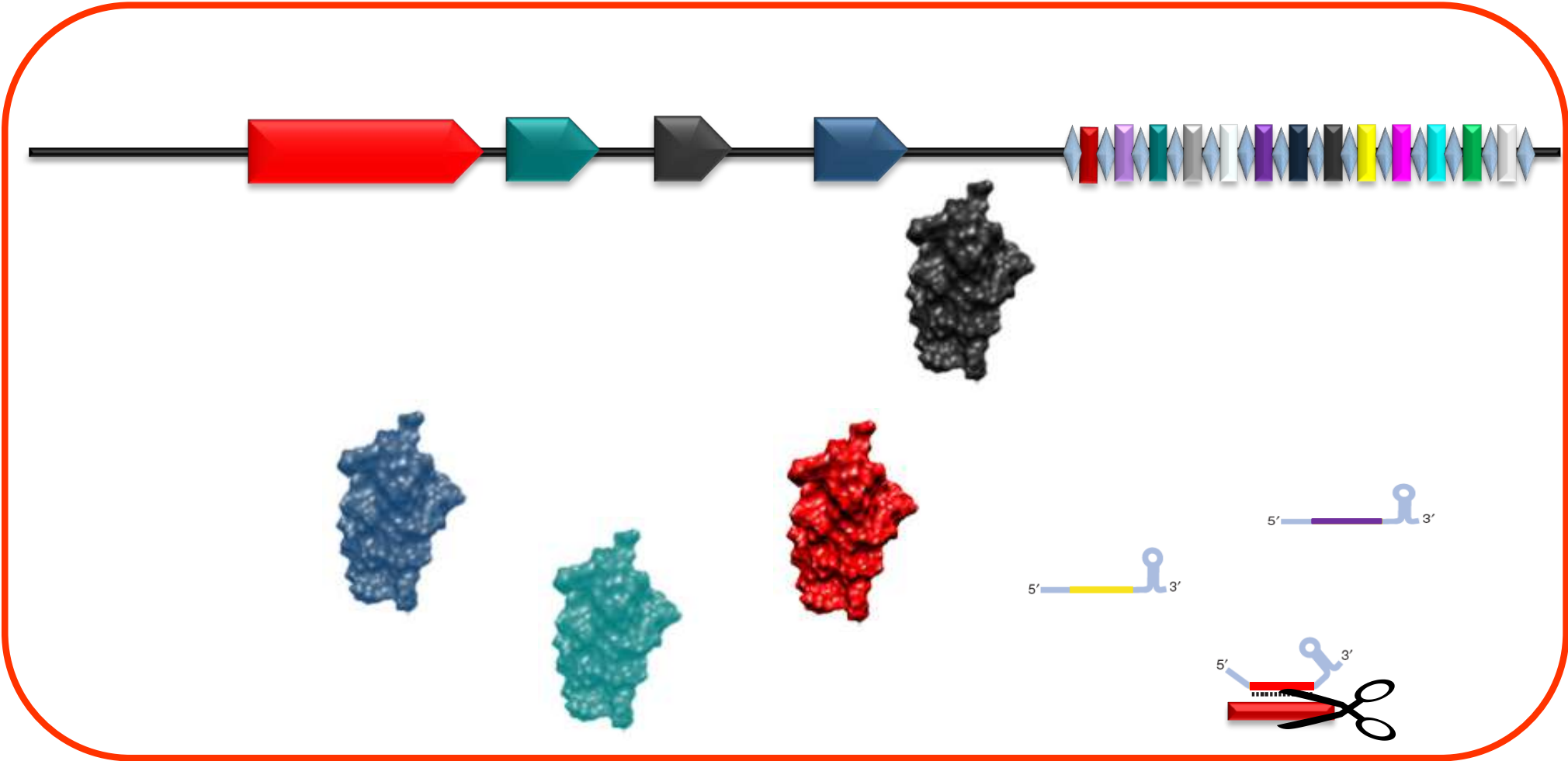
Reinfección



Reconocimiento



Destrucción



Aplicaciones de los sistemas CRISPR...

**...en sus
hospedadores**

Identificación individual

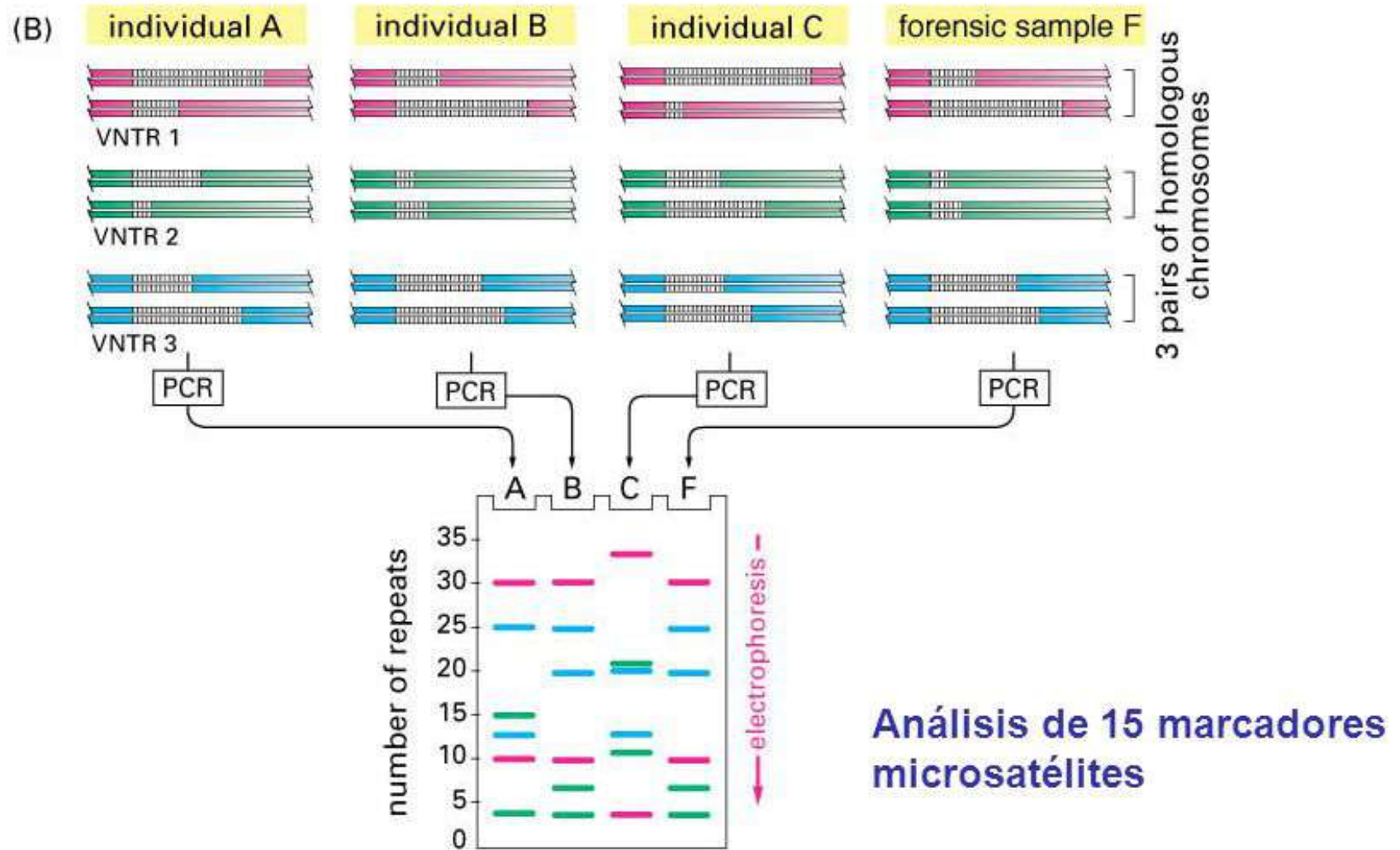
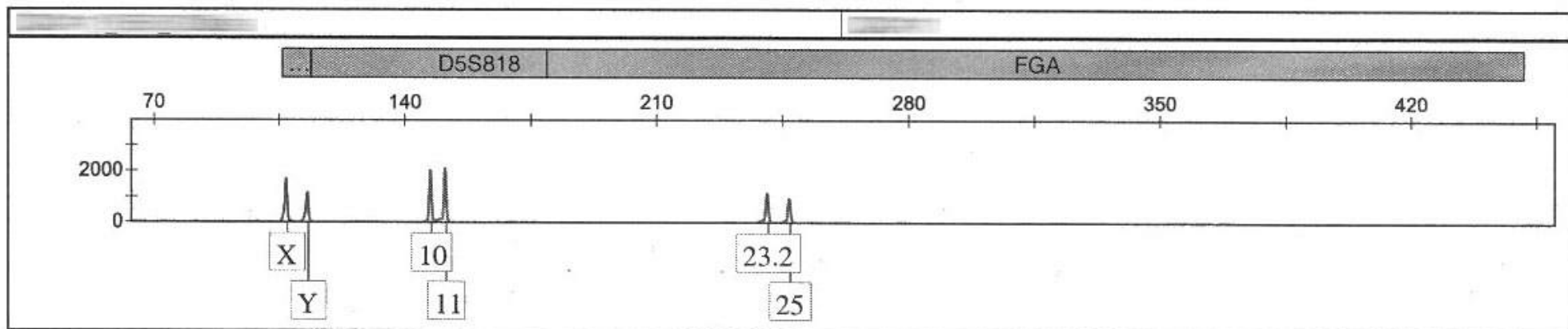
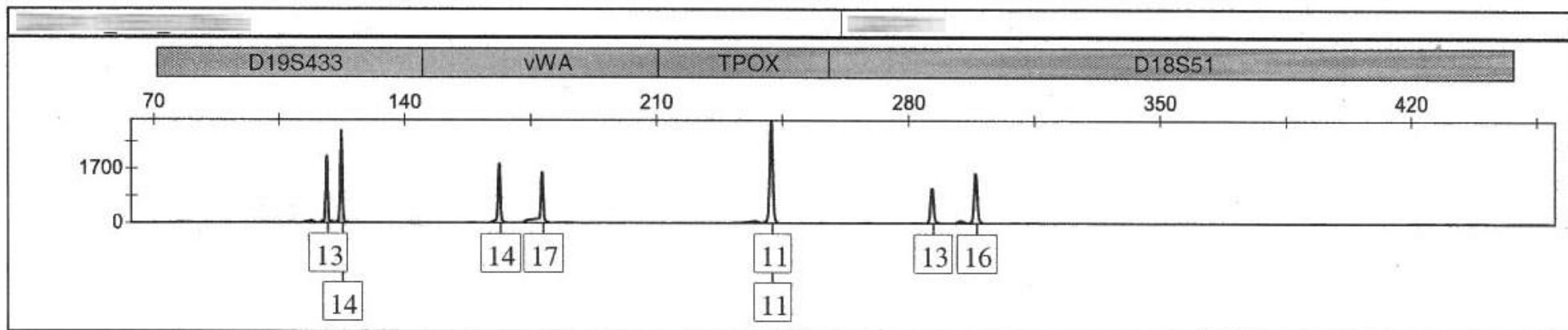


Figure 10-30 part 2 of 2 Essential Cell Biology, 2/e. (© 2004 Garland Science)



Identificación de aislados

Mycobacterium tuberculosis

Escherichia coli / *Shigella* spp.

Salmonella spp.

Corynebacterium diphtheriae

Campylobacter jejuni

Legionella pneumophila

Streptococcus spp.

Yersinia pestis

Erwinia amylovora

Vacunar bacterias

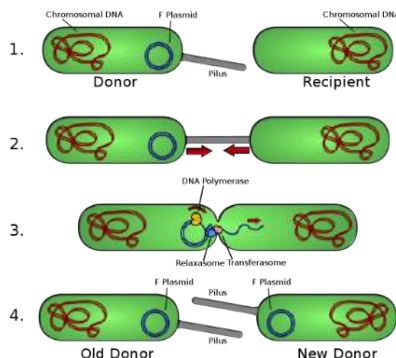
- Frente a virus



- Elaboración de alimentos fermentados
- Prevención de enfermedades

"Phage" by Dr Graham Beards - en:Image:Phage.jpg. Licensed under CC BY-SA 3.0 via Commons - <https://commons.wikimedia.org/wiki/File:Phage.jpg#/media/File:Phage.jpg>

- Frente a plásmidos

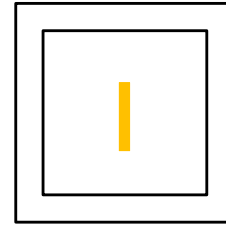
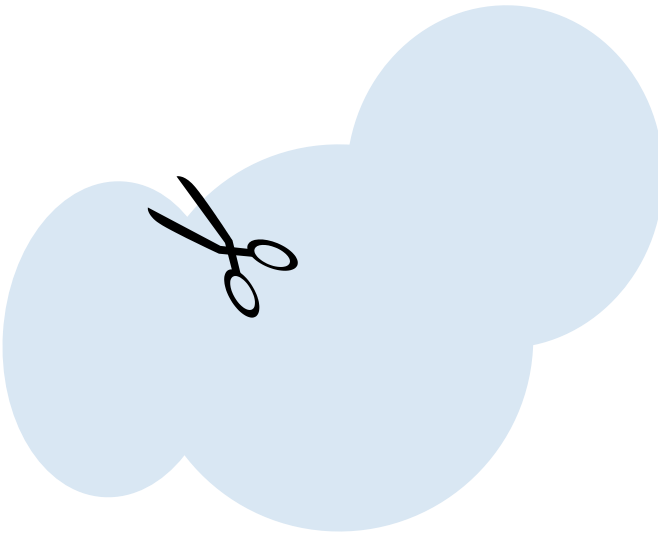


- Resistencias a antibióticos
- Prevención de enfermedades

"Conjugation" by Adenosine - Own work. Licensed under CC BY-SA 3.0 via Commons. <https://commons.wikimedia.org/wiki/File:Conjugation.svg#/media/File:Conjugation.svg>

**...en cualquier ser
vivo**

**Cas9
(Tijeras)**

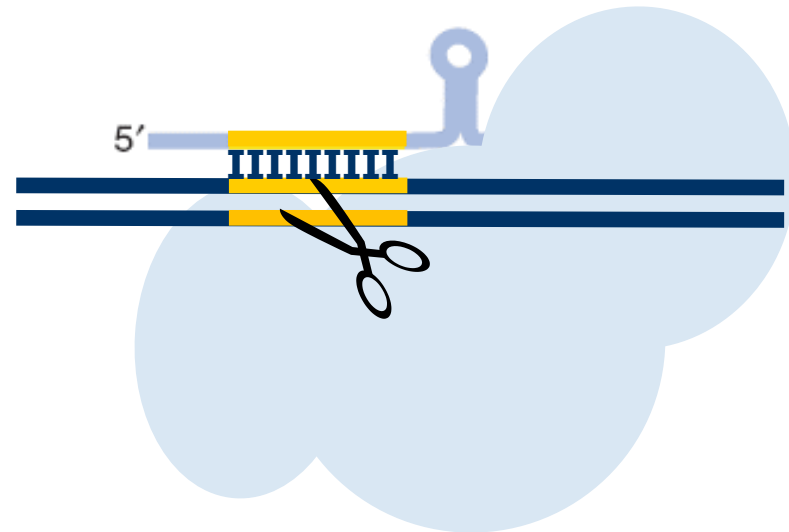


**ARN CRISPR
(Guía)**

J. Doudna E. Charpentier



**ADN
Diana**



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 Barretto⁶, Naomi Habib¹, Patrick D. Hsu^{1,4}, Xuebing Wu⁷, Wenyan Jiang⁸, Luciano A. Marraffini⁸, and Feng Zhang^{1,†}



Feng Zhang

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

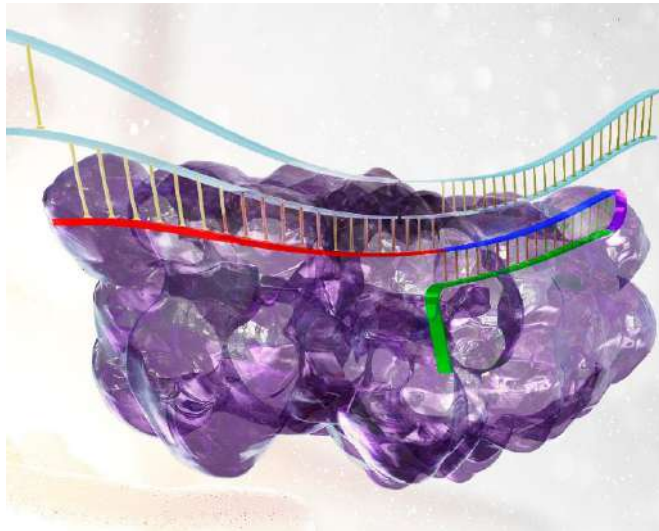
RNA-Guided Human Genome Engineering via Cas9

Prashant Mali^{1,5}, Luhan Yang^{1,3,5}, Kevin M. Esvelt², John Aach¹, Marc Guell¹, James E. DiCarlo⁴, Julie E. Norville¹, and George M. Church^{1,2,*}

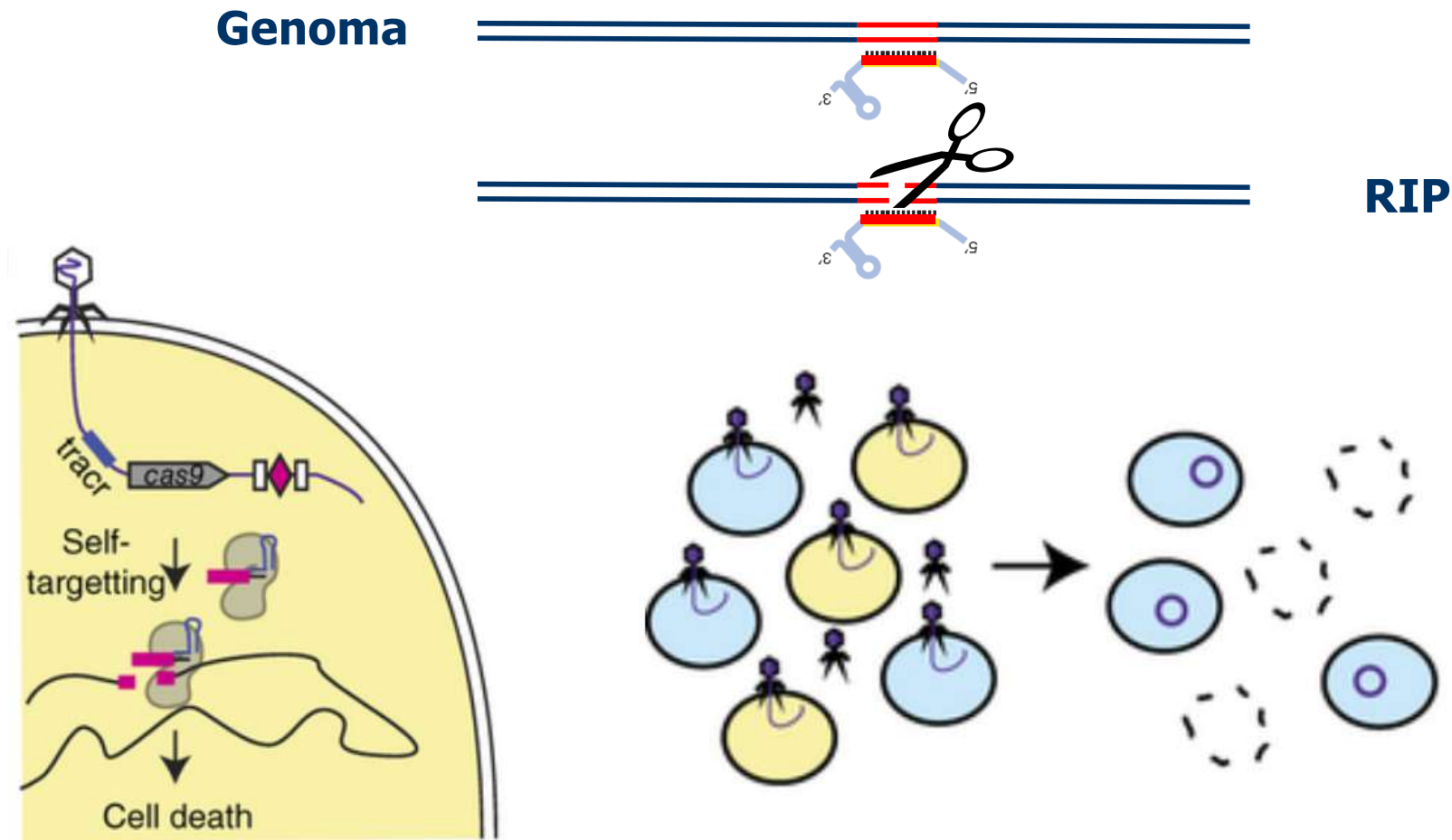


George Church

Tecnología CRISPR



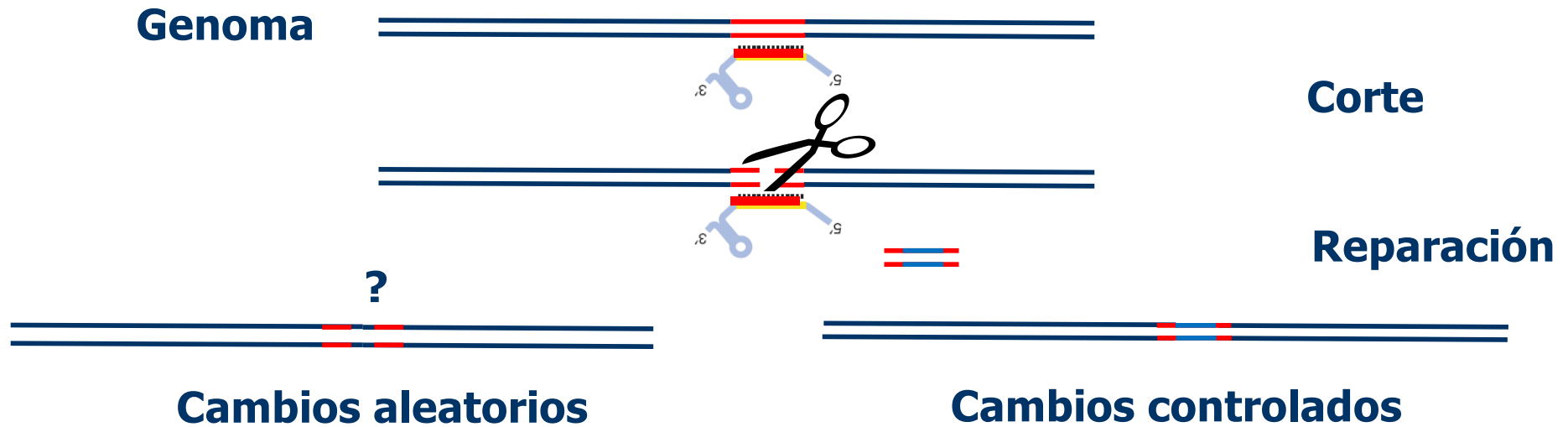
Antimicrobianos selectivos



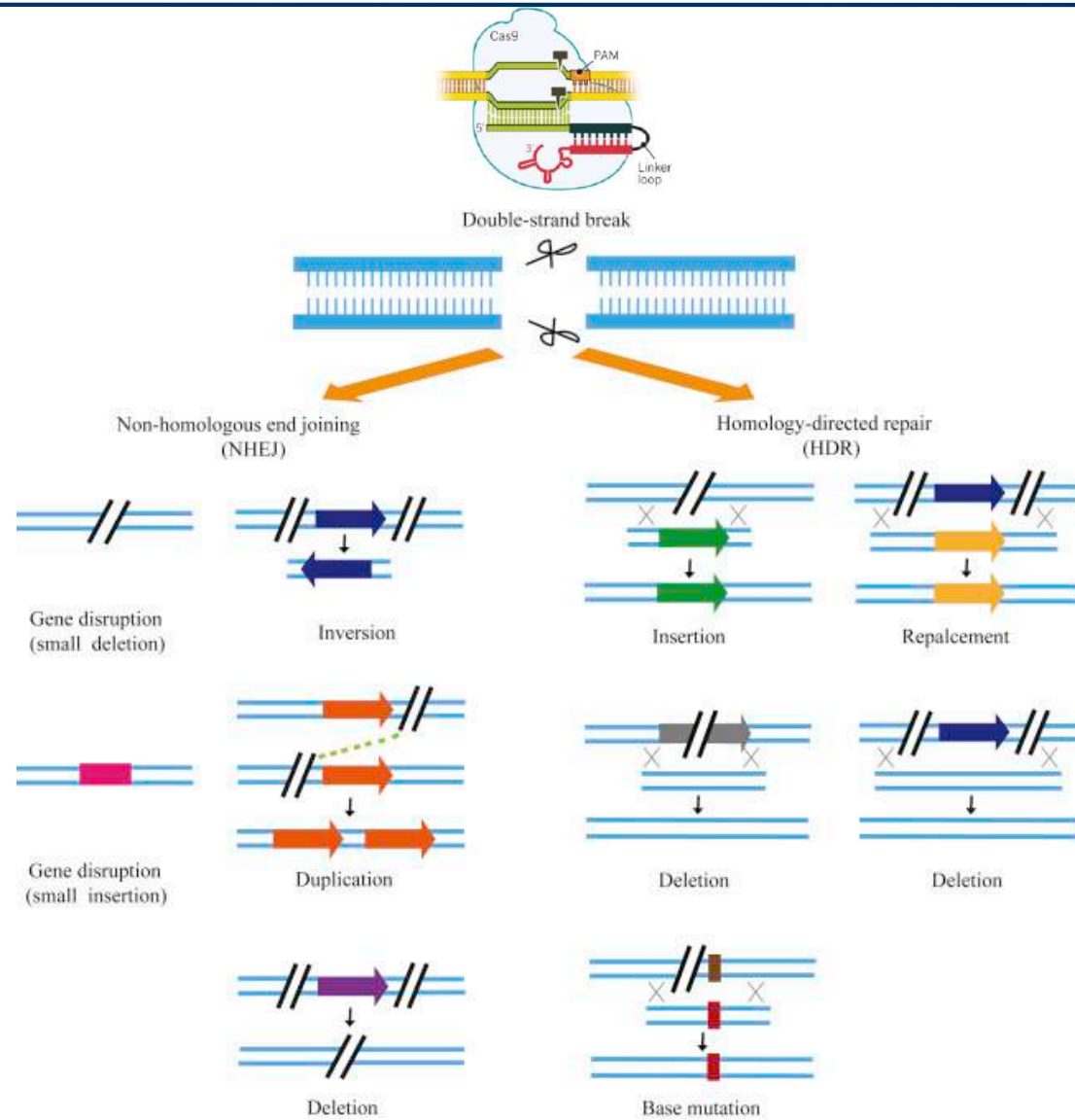
Adapted by permission from Macmillan Publishers Ltd: *Nature Biotechnology*
(Bikard *et al.*, Exploiting CRISPR-Cas nucleases to produce sequence-specific antimicrobials 32, 1146–1150) copyright (2014)

EDICIÓN DE GENOMAS

Editar Genomas



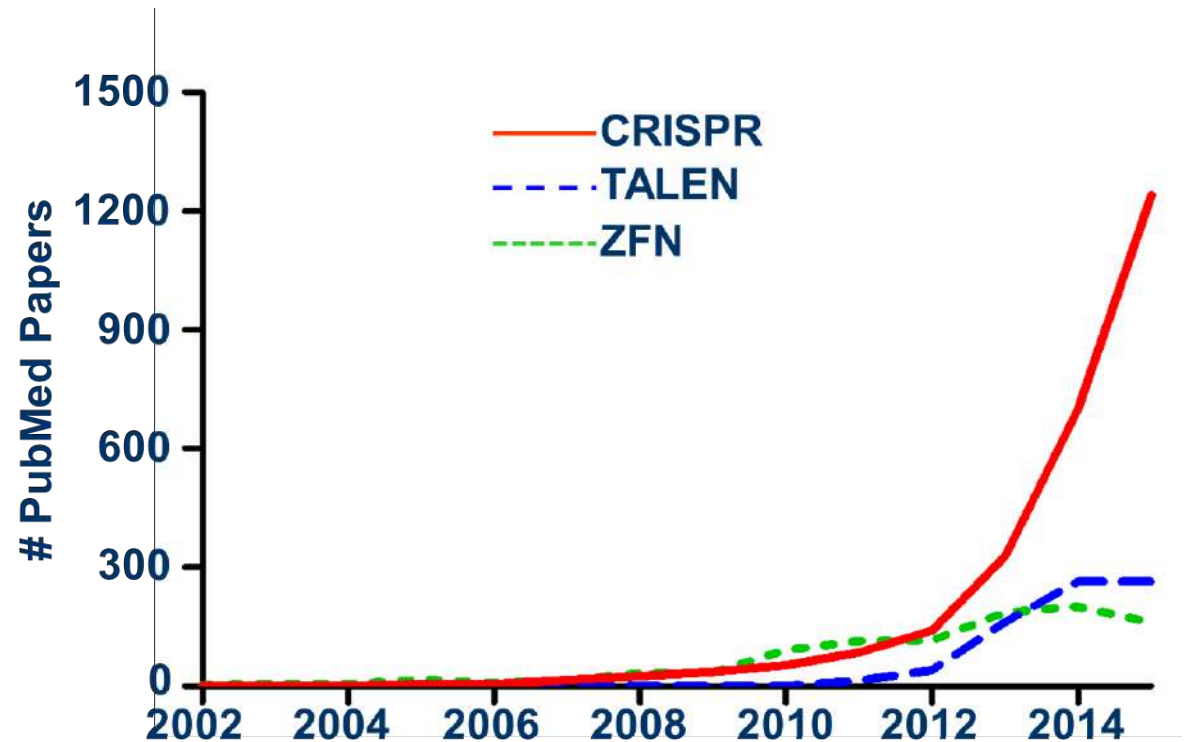
Editor Genomas



✓ **Eficaz**

✓ **Precisa**

✓ **Barata**



Joseph M. Miano. University of Rochester. USA.

✓ **Fácil de programar**

✓ **Varios cambios simultáneos**

✓ **“Cualquier” tipo celular y organismo**

- **Hongos**
- **Protozoos : leishmaniosis, toxoplasmosis, malaria...**
- **Plantas**

arroz, naranjo, trigo, soja, maíz, melón, patata, tomate, lechuga, tabaco...

- **Gusanos**
- **Insectos**
- **Moluscos**
- **Reptiles**
- **Anfibios**
- **Peces**
- **Aves**
- **Mamíferos**



ratón, conejo, cabra, oveja, rata, cerdo, perro, primates...

- Retardar el deterioro de alimentos

- Acelerar la fructificación

- Cultivos tolerantes a:

- Sequía
- Hongos
- Virus
- Herbicidas
- Plaguicidas



Los cultivos modificados genéticamente mediante **CRISPR**...
Technology Review en español - 12 oct. 2015

Los gigantes de la biotecnología están empezando a adentrarse en la técnica de edición genética **CRISPR**. Afirman que comercializarán ...

Cultivos modificados genéticamente mediante **CRISPR** llegarán al ...
AlianzaTex - 13 oct. 2015

- Ganado con mayor masa muscular

Gene-edited CRISPR mushroom escapes US regulation

A fungus engineered using CRISPR-Cas9 can be cultivated and sold without oversight.

BY EMILY WALTZ

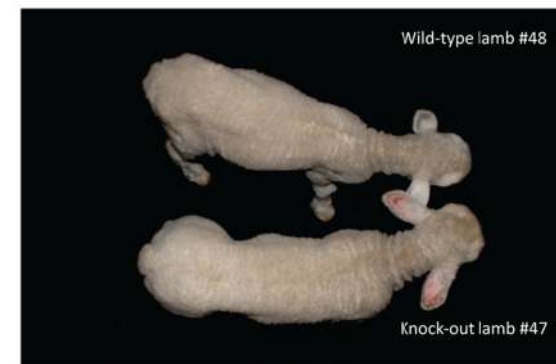
The US Department of Agriculture (USDA) will not regulate a mushroom that has been genetically modified with the gene-editing tool CRISPR-Cas9, the agency has confirmed. The long-awaited decision means that the mushrooms can be cultivated and sold without passing through the agency's regulatory process — making it the first CRISPR-edited organism to receive a green light from the US government.

"The research community will be very happy with the news," says Caixia Guo, a plant biologist at the Chinese Academy of Sciences Institute of Genetics and Developmental Biology in Beijing, who was not involved in developing the mushroom. "I am confident we'll see more gene-edited crops falling outside of regulatory authority."

Yinong Yang, a plant pathologist at Pennsylvania State University (Penn State) in University Park, engineered the fungus — the common white button mushroom (*Agaricus bisporus*) — to resist browning. The effect is achieved by targeting the family of genes that encodes polyphenol oxidase (PPO), an enzyme



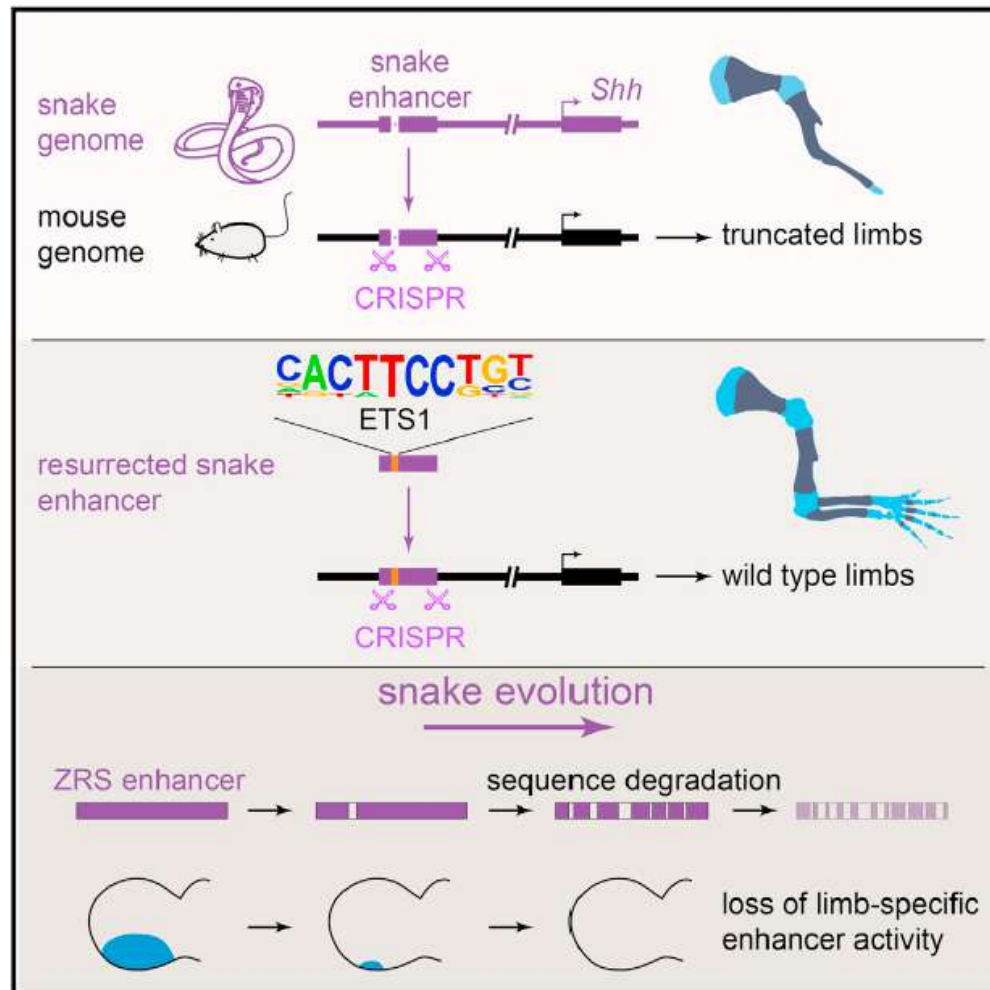
Fig 6. Phenotype of lambs 30 days after birth.



Orjino M, Mukit AP, Tessari L, Beretta N, Quidro F, et al. (2015) Efficient Generation of Myostatin Knock-Out Sheep Using CRISPR/Cas9 Technology and Microinjection into Zygotes. PLOS ONE 10(10): e0136690. doi:10.1371/journal.pone.0136690
<http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0136690>

Progressive Loss of Function in a Limb Enhancer during Snake Evolution

Graphical Abstract



Authors

Evgeny Z. Kvon, Olga K. Kamneva, Uirá S. Melo, ..., Diane E. Dickel, Len A. Pennacchio, Axel Visel

Correspondence

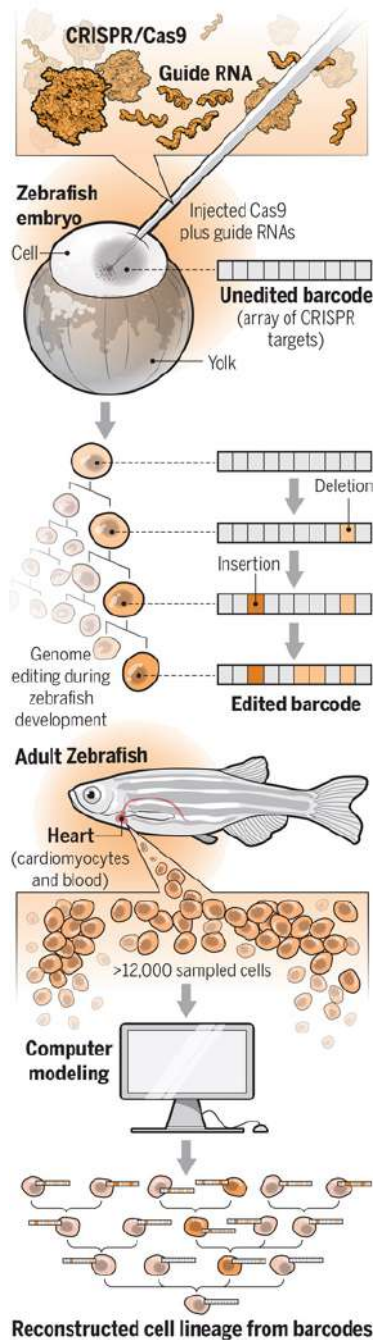
lapennacchio@lbl.gov (L.A.P.),
avisel@lbl.gov (A.V.)

In Brief

Morphological disappearance of limbs in snakes is associated with sequence changes disrupting the function of a critical limb enhancer.

Highlights

- Activity of the critical ZRS limb enhancer is highly conserved across vertebrates
- ZRS enhancer has progressively lost its function during snake evolution
- Snake-specific nucleotide changes contributed to the loss of ZRS enhancer function
- Resurrection of snake enhancer function in vivo



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Three-day-old zebrafish embryos.

Steven J. Basikauf
<http://bioimages.vanderbilt.edu/>

Genome editor CRISPR helps trace growth of embryos—and maybe cancer next

By Kai Kupferschmidt | May. 26, 2016, 2:00 PM

McKenna, G. M. Findlay, J. A. Gagnon, M. S. Horwitz, A. F. Schier, J. Shendure.

Whole organism lineage tracing by combinatorial and cumulative genome editing. *Science*, 2016

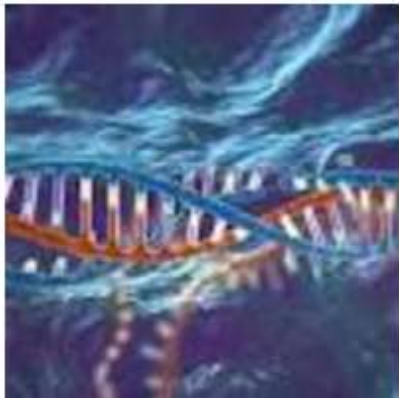
Estudiar, prevenir y curar **enfermedades infecciosas**



La tecnología **CRISPR/Cas9** vencerá a la malaria

IM Médico Hospitalario - 11 dic. 2015

Ésta se basa en la interrupción del gen mediante la endonucleasa **CRISPR/Cas9**, un enzima que puede ser diseñado para cortar secuencias ...



Logran eliminar el VIH utilizando **CRISPR**

Quo.es - 23 mar. 2016

Utilizando el tan de moda método de edición genética **CRISPR**, un equipo de científicos ha demostrado cómo eliminar el VIH del ADN de ...

Consiguen eliminar el VIH de las células del sistema inmune



La técnica **Crispr/Cas9** limpia los virus porcinos para un p...

Diario Médico (Comunicado de prensa) - 15 oct. 2015

Un equipo multicéntrico de científicos ha empleado la técnica de edición genética **Crispr/Cas9** para inactivar las 62 copias de un retrovirus en ...

Estudiar, prevenir y curar **trastornos genéticos**

- ✓ Hipercolesterolemia
- ✓ Diabetes
- ✓ Enfermedades hepáticas
- ✓ Trastornos neurodegenerativos
- ✓ Autismo
- ✓ Ceguera
- ✓ Albinismo
- ✓ Fibrosis quística
- ✓ Distrofia muscular
- ✓ Envejecimiento

Published online: March 10, 2016

Research Article



EMBO
Molecular Medicine

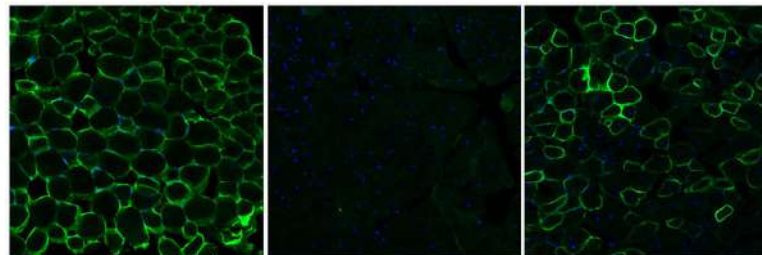
CRISPR/Cas9-mediated somatic correction of a novel coagulator factor IX gene mutation ameliorates hemophilia in mouse

Yuting Guan^{1,†}, Yanlin Ma^{2,3,†,*}, Qi Li², Zhenliang Sun⁴, Lie Ma¹, Lijuan Wu¹, Liren Wang¹, Li Zeng¹, Yanjiao Shao¹, Yuting Chen¹, Ning Ma², Wenqing Lu¹, Kewen Hu¹, Honghui Han⁵, Yanhong Yu³, Yuanhua Huang², Mingyao Liu^{1,6,**} & Dali Li^{1,***}

La superedición genética restaura la visión en animales ciegos

Cadena SER - 16 nov. 2016

Una nueva técnica que mejora el **CRISPR** ha logrado que parcialmente. Esta investigación internacional ha sido lide



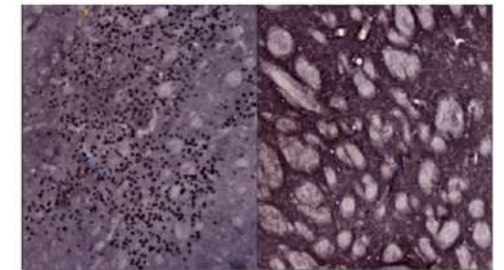
Sano

DMD

Tratado

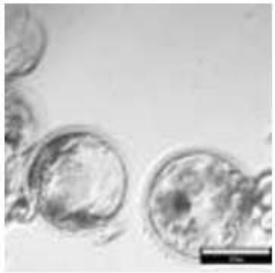


LATEST NEWS



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



Logran por primera vez modificar el ADN de **embriones humanos**

[unocero](#) - 26 abr. 2015

Logran por primera vez modificar el ADN de **embriones humanos**. El día de ... Ahora científicos de la Universidad SunYat-sen de Guangzhou en **China** han ... ello, se ha empleado una técnica de edición genética llamada **CRISPR/Cas9**, ...



Científicos de **China** crean **embriones** inmunes al **VIH-SIDA**

[EIPeriodico.com.do](#) - 14 abr. 2016

Científicos de **China** crean **embriones** inmunes al **VIH-SIDA** ... que todos los embr modificación se realizó mediante una nueva técnica llamada **CRISPR-Cas9**, ...



Investigadores de EE.UU. logran modificar genéticamente ...

[Efesalud - Noticias \(Comunicado de prensa\)](#) - 28 jul. 2017

UU. logran modificar genéticamente **embriones humanos** ... número de embriones unicelulares con la técnica de edición de genes **CRISPR**.



Modifican genoma de 41 **embriones humanos** en GB

[La Jornada en línea](#) - 21 sept. 2017

Modifican genoma de 41 **embriones humanos** en GB ... Con ayuda de la tecnología de edición genética **CRISPR/Cas9**, los científicos ... el gen que provoca la enfermedad sanguínea beta **talasemia** (o anemia mediterránea) y ...



China corrige grave enfermedad de la sangre en **embriones**

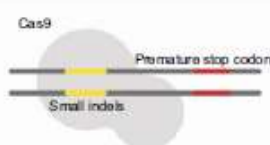

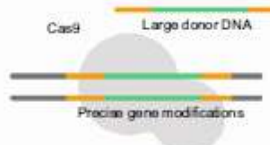
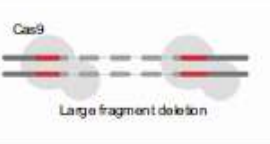
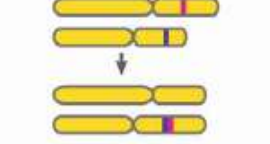

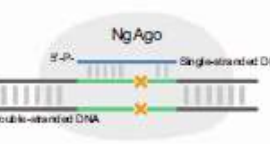
[La Jornada de Oriente](#) - 28 sept. 2017

La **talasemia** es una enfermedad genética que impide la producción ... Utilizando una nueva técnica de edición genética, que **modifica** de forma química el ... una de las variantes de esta mutación en **embriones humanos** no viables. La técnica utilizada está adaptada del método **CRISPR/Cas9** (o "tijeras ...



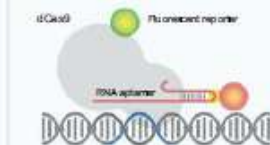
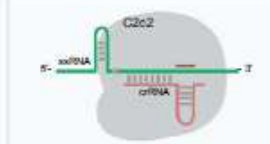
Ensayos clínicos en humanos

	Title	Recruitment	Study Results	Conditions	Interventions
1	A Safety and Efficacy Study of TALEN and CRISPR/Cas9 in the Treatment of HPV-related Cervical Intraepithelial Neoplasia#	Not yet recruiting	No Results Available	•Human Papillomavirus-Related Malignant Neoplasm	•Biological: TALEN •Biological: CRISPR/Cas9
2	Safety of Transplantation of CRISPR CCR5 Modified CD34+ Cells in HIV-infected Subjects With Hematological Malignances	Recruiting	No Results Available	•HIV-1-infection	•Genetic: CCR5 gene modification
3	Examining the Knowledge, Attitudes, and Beliefs of Sickle Cell Disease Patients, Parents of Patients With Sickle Cell Disease, and Providers Towards the Integration of CRISPR in Clinical Care	Not yet recruiting	No Results Available	•Sickle Cell Disease	
4	A Study Evaluating UCART019 in Patients With Relapsed or Refractory CD19+ Leukemia and Lymphoma	Recruiting	No Results Available	•B Cell Leukemia •B Cell Lymphoma	•Biological: UCART019
5	PD-1 Knockout Engineered T Cells for Advanced Esophageal Cancer	Recruiting	No Results Available	•Esophageal Cancer	•Drug: Cyclophosphamide •Drug: Interleukin-2 •Other: PD-1 Knockout T Cells
6	PD-1 Knockout Engineered T Cells for Muscle-invasive Bladder Cancer	Not yet recruiting	No Results Available	•Invasive Bladder Cancer Stage IV	•Biological: PD-1 Knockout T Cells •Drug: Cyclophosphamide •Drug: IL-2
7	PD-1 Knockout Engineered T Cells for Castration Resistant Prostate Cancer	Not yet recruiting	No Results Available	•Hormone Refractory Prostate Cancer	•Biological: PD-1 Knockout T Cells •Drug: Cyclophosphamide •Drug: IL-2
8	PD-1 Knockout Engineered T Cells for Metastatic Renal Cell Carcinoma	Not yet recruiting	No Results Available	•Metastatic Renal Cell Carcinoma	•Biological: PD-1 Knockout T Cells •Drug: Cyclophosphamide •Drug: IL-2
9	PD-1 Knockout Engineered T Cells for Metastatic Non-small Cell Lung Cancer	Recruiting	No Results Available	•Metastatic Non-small Cell Lung Cancer	•Drug: Cyclophosphamide •Other: PD-1 Knockout T Cells •Drug: Interleukin-2

Gene editing applications of CRISPR technology

	Schematic	Applications	Reference
Generation of small indels		<ul style="list-style-type: none"> Gene inactivation Modeling loss-of-function mutation 	Cong et al., 2013 Wang et al. 2013
Point mutations		<ul style="list-style-type: none"> Precise mutagenesis Modeling gain-of-function mutation 	Mali et al., 2013 Xue et al., 2014
Tag/large fragment insertions		<ul style="list-style-type: none"> Protein/lncRNA tag labeling Fluorescence reporter insertion Recombination signal (LoxP/Frt) insertion Insertion of transcriptional STOP signal 	Yang et al., 2013 Yang et al., 2014 Lee et al., 2016
Large fragment deletions		<ul style="list-style-type: none"> Gene Deletion Investigating higher-order chromatin structure 	Yang et al., 2014 Gröschel et al., 2014
Chromosomal rearrangements		<ul style="list-style-type: none"> Chromosomal rearrangement 	Choi et al., 2014 Maddalo et al., 2014 Blasco et al., 2014
Manipulation of cis-regulatory elements		<ul style="list-style-type: none"> Regulation of gene expression by cis-regulatory element 	Guo et al., 2015 Gröschel et al., 2014 Canver et al., 2015
DNA-guided genome editing		<ul style="list-style-type: none"> DNA-guided DNA editing Multiplexed gene targeting 	Gao et al., 2016


Non-editing applications of CRISPR technology

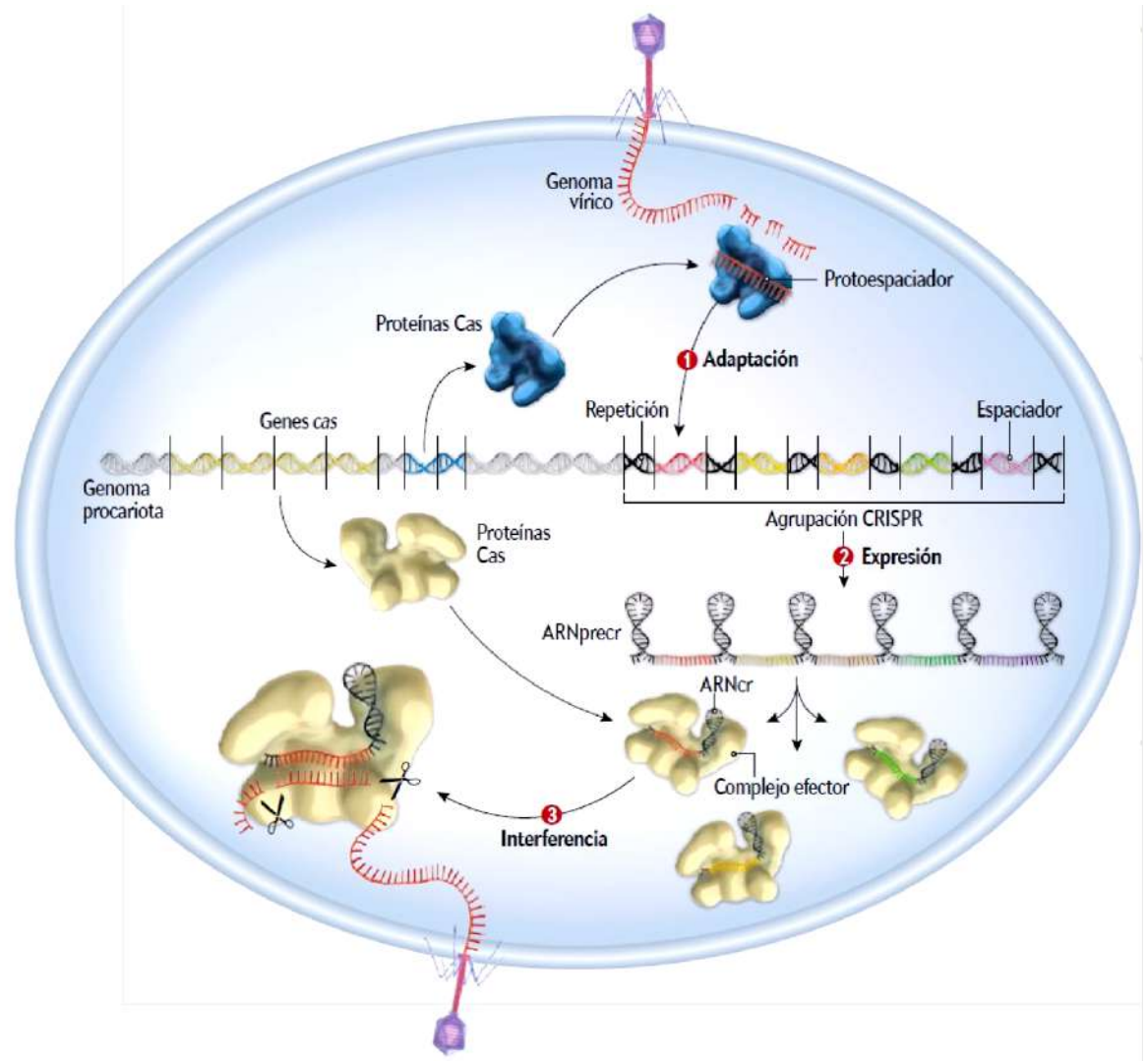
	Schematic	Applications	Reference
Transcriptional regulation		<ul style="list-style-type: none"> Precise regulation of gene expression Genome-wide gene activation/repression screens 	Gilbert et al., 2013 Gilbert et al., 2014 Konemann et al., 2015 Dominguez et al., 2016
Chromatin modification		<ul style="list-style-type: none"> Epigenetic regulation on cis-regulatory elements DNA methylation 	Keams et al., 2015 Hilton et al., 2015 Dominguez et al., 2016 Vojta et al., 2016
Visualizing genomic loci		<ul style="list-style-type: none"> Visualizing repetitive and non-repetitive genetic elements Revealing chromatin dynamics by live-cell imaging 	Chen et al., 2013 Fu et al., 2016
Targeting ssRNA		<ul style="list-style-type: none"> Targeting specific RNA Modulating non-coding RNAs 	Abudayyeh et al., 2016

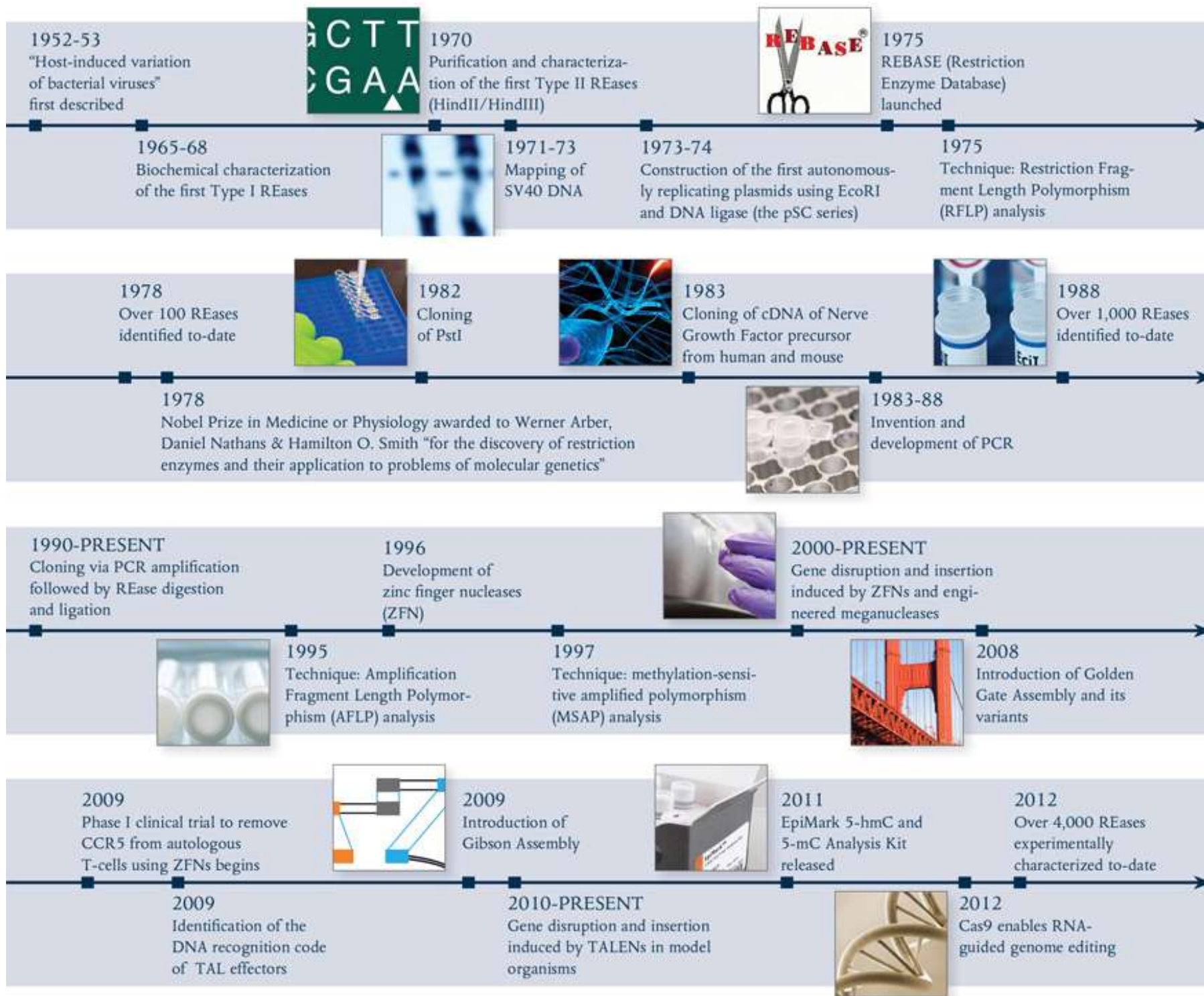
Hum Genet
DOI 10.1007/s00439-016-1713-3

REVIEW

The present and future of genome editing in cancer research

Xiaoyi Li^{1,2} · Raymond Wu^{1,2} · Andrea Ventura¹ 





TRATAMIENTOS
PERSONALIZADOS

EL FUTURO DE LA MEDICINA

TERAPIA GENICA

MEDICINA de PRECISIÓN