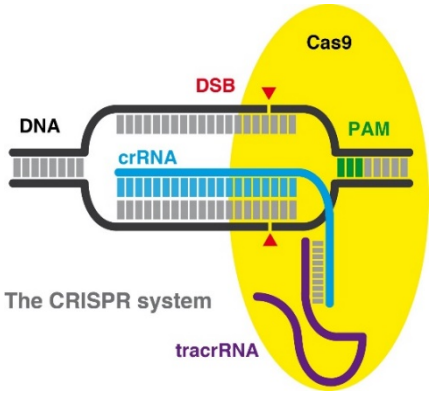
BREVE HISTORIA DE CRISPR-Cas9

Rafael Navajas Pérez

Enero 2025

Alicia Calvo-Villamañán
@AliciaPCV
I have not been able to calmly enjoy my cereal in the morning since 2015. Does anybody else relate to this? #Science #sciencecommunication #CRISPR #comics #PhD #phdlife

CRONOLOGÍA DE LOS PRINCIPALES DESCUBRIMIENTOS QUE HAN DADO LUGAR A LA DESCRIPCIÓN DEL SISTEMA CRISPR-Cas



Francisco Mojica
University of Alicante, Spain

Rodolphe Barrangou
North Carolina State Univ, Raleigh, USA

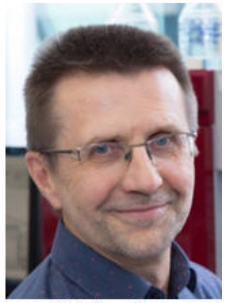
Philippe Horvath
DuPont Nutrition and Health, France

Luciano Marraffini
The Rockefeller Univ, New York, USA

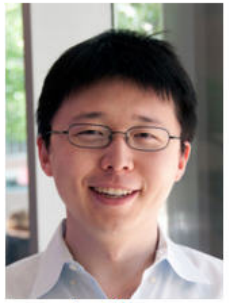
John van der Oost
Wageningen University, The Netherlands

Emmanuelle Charpentier
MPI for Infect. Biol., Berlin, Germany

Jennifer Doudna
Univ California Berkeley, CA, USA



Virginijus Siksnys
Vilnius University, Lithuania

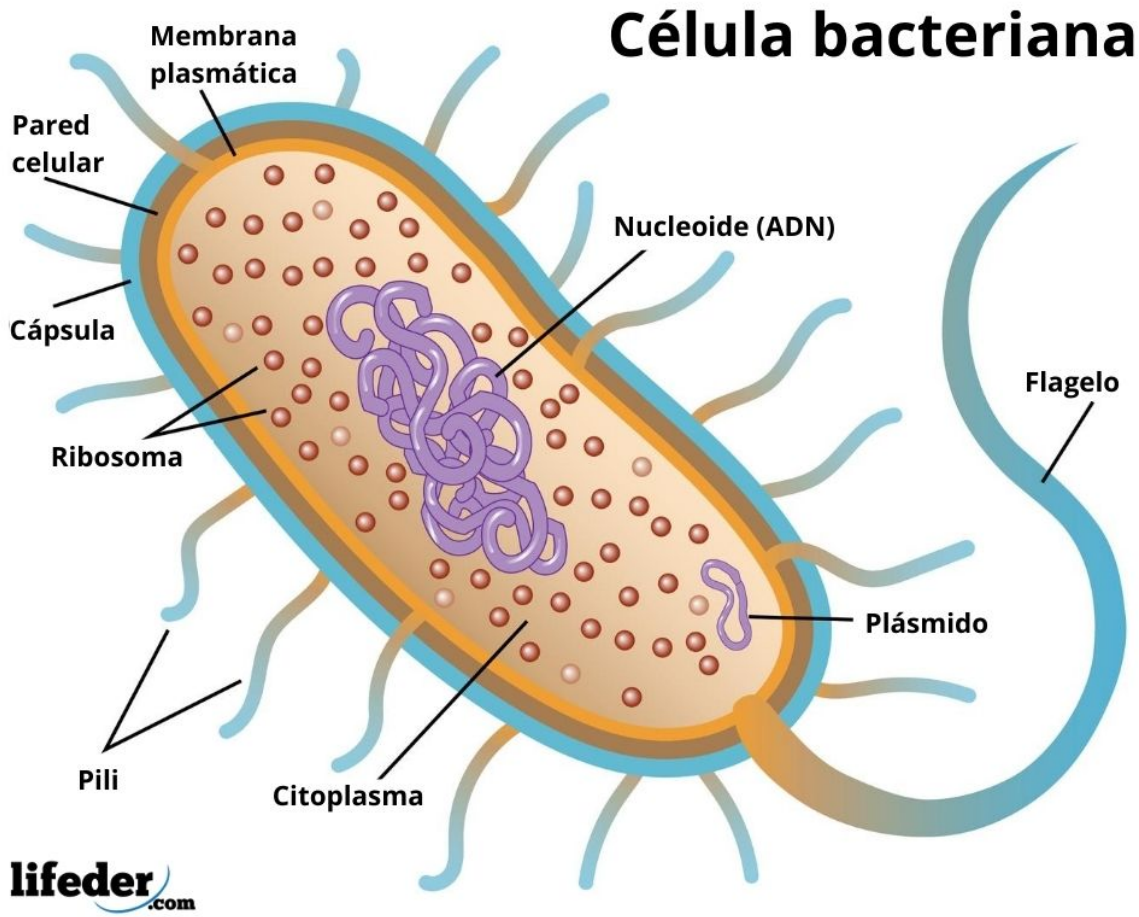


Feng Zhang
BROAD-MIT, Cambridge, MA, USA

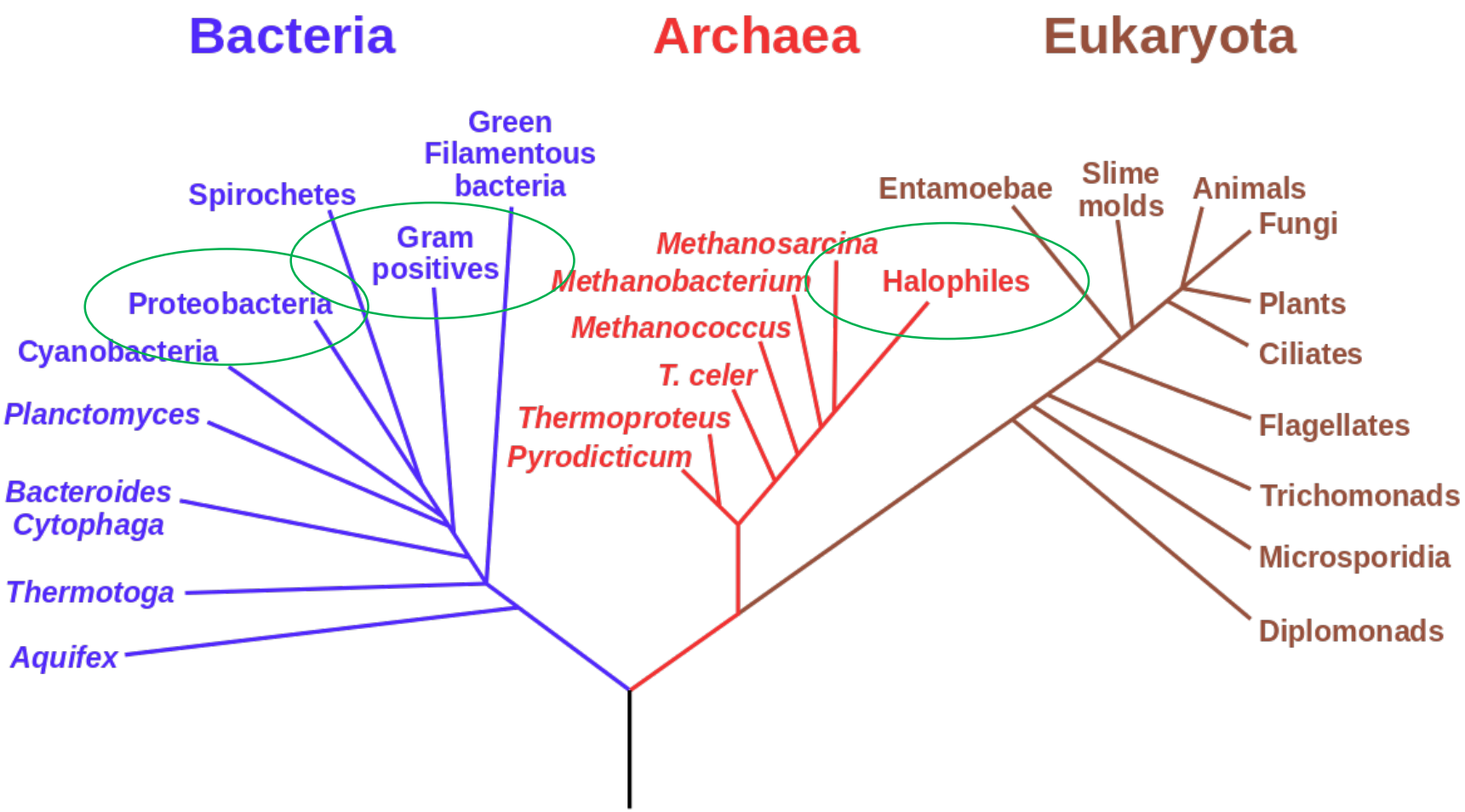
George Church
Harvard Med School, Boston, MA, USA

Rudolf Jaenisch
Whitehead Inst, Cambridge, MA, USA

J. Keith Joung
Mass Gen Hosp, Charlestown, MA, USA


Célula bacteriana
Membrana plasmática
Pared celular
Cápsula
Ribosoma
Pili
Nucleoide (ADN)
Citoplasma
Plásmido
Flagelo
lifeder.com

Phylogenetic Tree of Life



JOURNAL OF BACTERIOLOGY, Dec. 1987, p. 5429–5433
0021-9193/87/125429-05$02.00/0

Vol. 169, No. 12

Nucleotide Sequence of the *iap* Gene, Responsible for Alkaline Phosphatase Isozyme Conversion in *Escherichia coli*, and Identification of the Gene Product

YOSHIZUMI ISHINO, HIDEO SHINAGAWA, KOZO MAKINO, MITSUKO AMEMURA, AND ATSUO NAKATA*

(1987) Repeticiones regularmente espaciadas y palindrómicas

```
TGAAAATGGGAGGGAGTTCTACCGCAGAGGCGGGGGAACTCCAAGTGATATCCATCATCGCATCCAGTGCGCC (1,451)
     (1,452) CGGTTTATCCCCGCTGATGCGGGGAACACCAGCGTCAGGCGTGAAATCTCACCGTCGTTGC (1,512)
     (1,513) CGGTTTATCCCTGCTGGCGCGGGGAACTCTCGGTTCAGGCGTTGCAAACCTGGCTACCGGG (1,573)
     (1,574) CGGTTTATCCCCGCTAACGCGGGGAACTCGTAGTCCATCATTCCACCTATGTCTGAACTCC (1,634)
     (1,635) CGGTTTATCCCCGCTGGCGCGGGGAACTCG (1,664)

consensus: CGGTTTATCCCCGCT[GG/AA]CGCGGGGAACTC
```

Journal List > J Bacteriol > v.171(6); 1989 Jun > PMC210085

AMERICAN SOCIETY FOR MICROBIOLOGY | Journal of Bacteriology®

J Bacteriol. 1989 Jun; 171(6): 3553–3556. PMCID: P
PMI

Unusual nucleotide arrangement with repeated sequences in the Escherichia coli K-12 chromosome.

A Nakata, M Amemura, and K Makino

```
                                        -iap-TGAT GGGTTTGAAA ATGGGAGCTG    (1390)
GGAGTTCTAC CGCAGAGGCG GGGGAACTCC AAGTGATATC CATCATCGCA TCCAGTGCGC C (1451)
CGGTTTATCC CCGCTGATGC GGGGAACACC AGCGTCAGGC GTGAAATCTC ACCGTCGTTG C (1512)
CGGTTTATCC CTGCTGGCGC GGGGAACTCT CGGTTCAGGC GTTGCAAACC TGGCTACCGG G (1573)
CGGTTTATCC CCGCTAACGC GGGGAACTCG TAGTCCATCA TTCCACCTAT GTCTGAACTC C (1634)
CGGTTTATCC CCGCTGGCGC GGGGAACTCC CGGGGGATAA TGTTTACGGT CATGCGCCCC C (1695)
CGGTTTATCC CCGCTGGCGC GGGGAACTCT GGGCGGCTTG CCTTGCAGCC AGCTCCAGCA G (1756)
CGGTTTATCC CCGCTGGCGC GGGGAACTCA AGCTGGCTGG CAATCTCTTT CGGGGTGAGT C (1817)
CGGTTTATCC CCGCTGGCGC GGGGAACTCT AGTTTCCGTA TCTCCGGATT TATAAAGCTG A (1878)
CGGTTTATCC CCGCTGGCGC GGGGAACTCG CAGGCGGCGA CCGGCAGGGT ATGCGCGATT CG(1940)
CGGTTTATCC CCGCTGGCGC GGGGAACTCG CGACCGCTCA GAAATTCCAG ACCCGATCCA AA(2002)
CGGTTTATCC CCGCTGGCGC GGGGAACTCT CAACATTATC AATTACAACC GACAGGGAGC C (2063)
CGGTTTATCC CCGCTGGCGC GGGGAACTCA GCGTGTTCGG CATCACCTTT GGCTTCGGCT G (2124)
CGGTTTATCC CCGCTGGCGC GGGGAACTCT GCGTGAGCGT ATCGCCGCGC GTCTGCGAAA G (2185)
CGGTTTATCC CCGCTGGCGC GGGGAACTCT CTAAAAGTAT ACATTTGTTC TTAAAGCATT    (2255)
TTTTCCCATA AAAACAACCC ACCAACCTTA ATGTAACATT TCCTTATTAT TAAAGATCAG    (2315)
CTAATTCTTT GTTTTCAAAC AGGTAAAAAA GACACCAACC TTAAACCATC CAAATCTACC    (2375)
GGGGTACGCC TGTTTAACCC AAATGTCTGG AACTCAAATC CCGTTTCCGT ATTCGTTGCC    (2435)
CATGCCATCA CTACATTGCC TTCTTCCGCC AGTCCAGCTA TTTGTTCCCA GATCATTTCA    (2495)
CGAATTTTTG CGGATACATC ACCTACATAT ACCCCTGCAC GTACCTCCAA CAACCAGATG    (2555)
GCTAATCTGC CTCGTAAGCG CGGAGGTACA TTTTCAGTGA CCACGACCAA CATACTCATT    (2615)
TCAGCTACTC CGATGGCCTG CATCTCCCAG TGAAACAGGA AGCGGAATGG CAACAGGCTG    (2665)
TGCATCTTCA GGTGGGGCCG GCGGTTGTAT TTCTCCAGCG GCAAGCACGT CCTCTATAAG    (2725)
CGGAATCAAT TTGGCTAATG TTTTACTACT GCGAAAAATA TCCCTGCACG CCAAACGGAC    (2785)
TTCCCGGTCC GGCTCACCAG GGTTACGACG CGCTATCTCA AAAGCTT                  (2832)

(B)
                                        AAGCTTAAAA AATATACTGT    (  20)
TATTCTAAAG AAAAAATTAA CAGGCATTAA TTCAATATTA AAAAAATAAT AGATTAAAAT    (  80)
TTCTTAACGA TTTAAGAATC ATACAAATAA CACTTTGATT AAATTTAATT TTTTGTATCG    ( 140)
ATAATTGTGA ACCTCTCTGG CATGGAGAAC TATTTTGAAC ATGAGGTGTT ACGTGGATAT    ( 200)
GTTGCTTATT ACAAGTACTG CTAATATAAA AACTTGAGAA AGAGATAACG GGTTATATGG    ( 260)
TGGTTTATCC CCGCTGGCGC GGGGAACTCG ACAGAACGGC CTCAGTAGTC TCGTCAGGCT C ( 321)
CGGTTTATCC CCGCTGGCGC GGGGAACACC TGTTTTCGCA AATCTATGGA CTATTGCTAT T ( 382)
CGGTTTATCC CCGCTGGCGC GGGGAACACG GGCGCACGGA ATACAAAGCC GTGTATCTGC T ( 443)
CGGTTTATCC CCGCTGGCGC GGGGAACACT GGCTCTGCAA CAGCAGCACC CATGACCACG T ( 504)
CGGTTTATCC CCGCTGGCGC GGGGAACACG AAATGCTGGT GAGCGTTAAT GCCGCAAACA C ( 565)
AGGTTTATCC CCGCTGGCGC GGGGAACACA TTACGCCTTT TTGCGATTGC CCGGTTTTTG C ( 626)
CGGTTTATCC CCGCTGGCGC GGGGAACACT CTAAACATAA CCTATTATTA ATTAATGATT    ( 686)
TTTTAAGCCA GTCACAATCT ACCAACTTTA TAGTATCACA CAAACAACAC ATCCATTATG    ( 746)
TTAAAGAGCA CTTAATCCAT TGATTAAAAA GGTAAATATT TAAAATAACT CTATACAAAC    ( 806)
TAAAATCTAC CAAACTTTAC CGCAATAATT TTCACTCCAG CGAAAAATTA ATGCCACAGA    ( 866)
ATTTGTAGAG AATGCTAATG ATTAGCCCTG GATGGGTAAA ATGGAGGAGT TTTCAGAGGC    ( 926)
GACAAACAAT ATAAATGAGT AGAAGTCTTT ACAGGTTCCA CCCATTTATA ACGCTTATAA    ( 986)
ATGTTTAATC AGGCAATATT TAGATATTTA TGTGTTTGCA TCGACAAACG CCAATTACGC    (1046)
GCAATGCAGG TTTCAATGCA CAAACGTGTG GCATCATCCT TTTGGCTAAT CGGCTGCAGT    (1106)
GCAATGACTC GCGGTTTATC ATCGGTCAGC GTTGCCAGTA GTTCATCCAG TGCTTCAATA    (1166)
TCGCGTACGC GCCCCACTGG ATGCTTGATT TCGTTGGCTC GCTCCAGTGC CTGTGACAAC    (1226)
ACTTCATAGC CGCCGCGCAT GTTCAGCTTT GGCGATACGG TAACCCAGGT ATTCGGTGTG    (1286)
CAGCGTACCT CATGAGTACC ACTGGTTTCG ATCTGGCAGC TAAAACCGTT CTTTTCGAGC    (1346)
AGATCAGTCA GTGGCAGCAA ATCATGAATG CAAGGCTCAC CACCCGTAAT CACCACATGC    (1406)
CGCGCGGTGT ATCCCTGGCG ACCAATGACA GCCAGCAAAT CTTCACTGCT CGCAGCCCCC    (1466)
CACTTATCAC TCTCTTTGGT CTTCGCCAGA ATGCTGAAAA GGGAGACTTC CCGATCCTCA    (1526)
AGCTT
```

INFECTION AND IMMUNITY, Aug. 1991, p. 2695–2705
0019-9567/91/082695-11$02.00/0

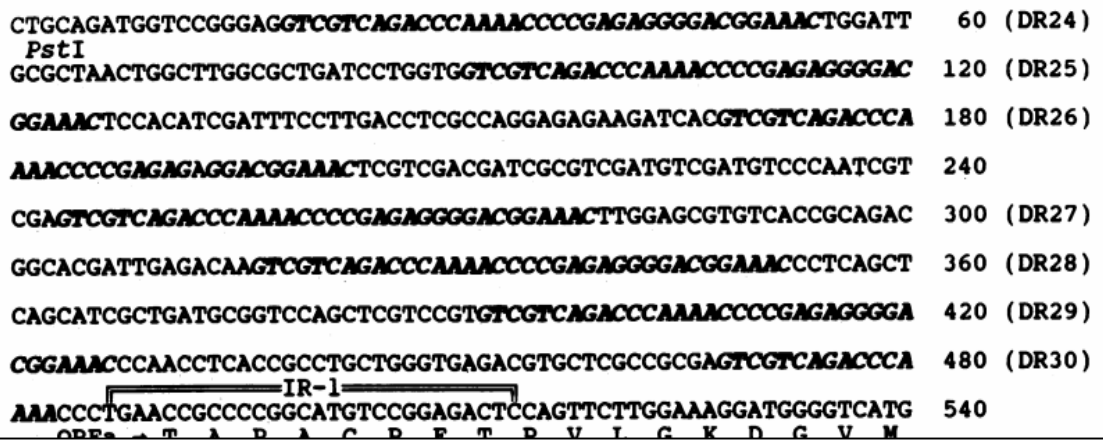
Vol. 59, No. 8

Insertion Element IS*987* from *Mycobacterium bovis* BCG Is Located in a Hot-Spot Integration Region for Insertion Elements in *Mycobacterium tuberculosis* Complex Strains

PETER W. M. HERMANS,[1]* DICK VAN SOOLINGEN,[1] ELISABETH M. BIK,[1] PETRA E. W. DE HAAS,[1] JEREMY W. DALE,[2] AND JAN D. A. VAN EMBDEN[1]

National Institute of Public Health and Environmental Protection, P.O. Box 1, 3720 BA Bilthoven, The Netherlands,[1] *and Department of Microbiology, University of Surrey, Guildford, Surrey GU2 5XH, United Kingdom*[2]

Received 18 February 1991/Accepted 20 May 1991



CTGCAGATGGTCCGGGAG*GTCGTCAGACCCAAAACCCCGAGAGGGGACGGAAAC*TGGATT 60 (DR24)

GCGCTAACTGGCTTGGCGCTGATCCTGGTG*GTCGTCAGACCCAAAACCCCGAGAGGGGAC* 120 (DR25)

*GGAAAC*TCCACATCGATTTCCTTGACCTCGCCAGGAGAGAAGATCAC*GTCGTCAGACCCA* 180 (DR26)

*AAACCCCGAGAGAGGACGGAAAC*TCGTCGACGATCGCGTCGATGTCGATGTCCCAATCGT 240

CGA*GTCGTCAGACCCAAAACCCCGAGAGGGGACGGAAAC*TTGGAGCGTGTCACCGCAGAC 300 (DR27)

GGCACGATTGAGACAA*GTCGTCAGACCCAAAACCCCGAGAGGGGACGGAAAC*CCTCAGCT 360 (DR28)

CAGCATCGCTGATGCGGTCCAGCTCGTCCGT*GTCGTCAGACCCAAAACCCCGAGAGGGGA* 420 (DR29)

*CGGAAAC*CCAACCTCACCGCCTGCTGGGTGAGACGTGCTCGCCGCGA*GTCGTCAGACCCA* 480 (DR30)

AAACCCTGAACCGCCCCGGCATGTCCGGAGACTCCAGTTCTTGGAAAGGATGGGGTCATG 540

Mol Microbiol. 1993 Dec;10(5):1057-65.

Nature of DNA polymorphism in the direct repeat cluster of Mycobacterium tuberculosis; application for strain differentiation by a novel typing method.

Groenen PM[1], Bunschoten AE, van Soolingen D, van Embden JD.

Author information

1 Unit of Molecular Microbiology, National Institute of Public Health and Environmental Protection, Bilthoven, The Netherlands.

JOURNAL OF CLINICAL MICROBIOLOGY, Nov. 1996, p. 2734–2740
0095-1137/96/$04.00+0

Vol. 34, No. 11

Spacer Oligonucleotide Typing of *Mycobacterium bovis* Strains from Cattle and Other Animals: a Tool for Studying Epidemiology of Tuberculosis

ALICIA ARANAZ,[1] ERNESTO LIÉBANA,[1] ANA MATEOS,[1] LUCAS DOMINGUEZ,[1] DOLORES VIDAL,[2] MARIANO DOMINGO,[2] OSCAR GONZOLEZ,[3] ELIAS F. RODRIGUEZ-FERRI,[3] ANNELIES E. BUNSCHOTEN,[4] JAN D. A. VAN EMBDEN,[4] AND DEBBY COUSINS[5]*

Departamento de Patología Animal I (Sanidad Animal), Facultad de Veterinaria, Universidad Complutense de Madrid, 28100 Madrid,[1] *Departamento de Anatomía Patológica, Facultad de Veterinaria, Universidad Autónoma de Bellaterra, 08193 Bellaterra, Barcelona,*[2] *and Patología Animal (Sanidad Animal), Facultad de Veterinaria, Campus de Vegazana, 24071 León,*[3] *Spain; Department of Bacteriology, Research Laboratory for Infectious Diseases, National Institute of Public Health and Environmental Protection, 3720A, Bilthoven, The Netherlands*[4]*; and Australian Reference Laboratory for Bovine Tuberculosis, Agriculture Western Australia, South Perth, Western Australia, 6151 Australia*[5]

Received 15 May 1996/Returned for modification 18 June 1996/Accepted 8 August 1996

The spacer oligonucleotide typing (spoligotyping) method was evaluated for its ability to differentiate *Mycobacterium bovis* strains. This method detects the presence or absence of spacers of the direct repeat locus of the *M. bovis* genome. The spacers in the direct repeat locus are amplified by PCR and are detected by hybridization of the biotin-labelled PCR product with a membrane containing oligonucleotides derived from spacer sequences that have previously been bound to a membrane. One hundred eighty-two *M. bovis* isolates from domestic animals (cattle, goat, sheep, and cats) and wild animals (deer and wild boar) were spoligotyped, and the results were compared with those obtained by IS*6110* restriction fragment length polymorphism analysis. Two rather homogeneous clusters of isolates containing 20 and 4 types, respectively, were identified by spoligotyping. The first cluster included isolates from cattle, cats, and feral animals. By spoligotyping, isolates from the Spanish wild boar and deer had the same pattern as some bovine isolates, suggesting transmission between these animals and cattle and highlighting the importance of the study of these reservoirs. The second cluster included all the caprine and ovine isolates. Within each cluster, the patterns of the different strains differed only slightly, suggesting that the spoligotypes may be characteristic of strains from particular animal species. Spoligotyping proved to be useful for studying the epidemiology of bovine *M. bovis* isolates, especially of those isolates containing only a single copy of IS*6110*. In view of our results, we suggest fingerprinting all *M. bovis* strains by the spoligotyping method initially and then by IS*6110* restriction fragment length polymorphism typing of the strains belonging to the most common spoligotypes.

Francisco Mojica
University of Alicante, Spain

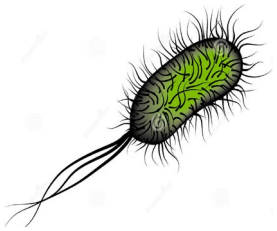
Transcription at different salinities of *Haloferax mediterranei* sequences adjacent to partially modified *Pst*I sites

F. J. M. Mojica, G. Juez and F. Rodríguez-Valera*

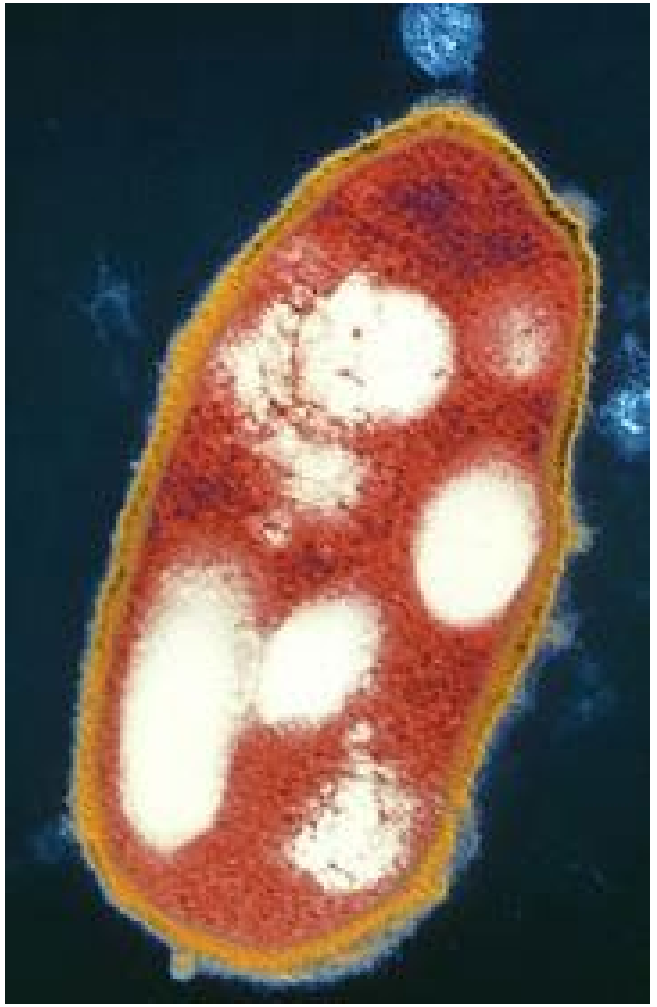
Mol Microbiol. 1993 Aug;9(3):613-21.

(1993) Repeticiones semejantes descritas en otras bacterias y arqueas.

"*Encontré unas secuencias repetidas en su genoma. Tenían que ser importantes para las células, porque muchas se morían cuando las manipulábamos […] comprendí que debían cumplir una función importante para la célula*" (**Mojica**)



Posteriormente encontradas *Mycobacterium tuberculosis*



Arquea *Haloferax mediterranei*

Francisco Mojica
University of Alicante, Spain

(1995) TREPs (Repeticiones en Tándem) que se transcriben.

(2000) Nueva familia de ADN repetido a partir del análisis de 20 especies distintas de bacterias.

SRSR, “Short Regularly Spaced Repeats”.

Molecular Microbiology (1995) **17**(1), 85–93

Long stretches of short tandem repeats are present in the largest replicons of the Archaea *Haloferax mediterranei* and *Haloferax volcanii* and could be involved in replicon partitioning

F. J. M. Mojica, C. Ferrer, G. Juez and F. Rodríguez-Valera*

```
CTGCAGTCTG CTCTCCATCC TACAGTTCTT CATATCCGCC GCAAAGCACT CGATGTGCAG              60
GGCTGCGAGT ATTCCGAGCA ACTAACTCAA CGACCTACTC GCTTCTCAAA CTGGGTTACC             120
TATAGTAGCG TTTGCAAGTC ATTGCACACT CGATCGACCG CTATCGTGCG ATTGGCTGTG             180
TCACCAGTTG CAAACGCTAC TATAGACAGT GCCAGTCTAA GAGTGTCATT GGAGCCCAGA             240
TCTGAAAAAC TGAAGAATAA TCACAGACCA AAGAAACAGA CCCAAGCCAT AGCAGATTAA             300
AATAATTCGA GTACTGTCCG TTCCAGATGT TGATGGTAAG TGAATATTCC CAACCACTCC             360
TCTGCCAATG GCTTCTTTTT CCTGGACGCC TTCACTAGTC ACATTCGTCC TTCCTGCTTG             420
ACCACCACCG AGAGCTACCA ACACGACCCC GATAATTGCG GTCAGGACGA GAATATAACC             480
CAGAGTGTGT CGTTAGATAG ATAGCACCGA CAGTAATGAT TCCCGCGAGA ATCGTATAGA             540
TGAGGACTGT TACTGCGACT ACTCGCTTGT CCATGTCATA AGTAGAACGA CAGTTAGTTT             600
AATTTTTATC ATTTTGAGGA ATTGGTGTAT CGCGCGTCCC GGTGTTCTCG GAAGTCCGTT             660
ACGTGGGTCT TGACCTGAAT TTCCGTCGAC CCCCCGGGGG GTTGGGGGGT ATTG                   714
GGGGTCGACG GAAACT GTT GAGTGGGAGT AGTGTGTAGG AGGCTGTATA CCCTCGAATC GGGCATG     780
GTTACAGACG AACCCTAGTT GGGTTGAAGC GAACAGGATG GCGAACCGGT GTCTGCACCA GTT         843
GTTACAGACG AACCCTAGTT GGGTTGAAGC CACGACAATC AAGTCTGGTT GCATGGCGAC ACGGA       908
GTTACAGACG AACCCTAGTT GGGTTGAAGC CTGTGCCTCC AGCGGCCGTC AGACAGTCGC ATCCGA      974
GTTACAGACG AACCCTAGTT GGGTTGAAGC AAGAAGCCGC TCGCCGTCCT CGATGACGGG CGGGCG     1040
GTTACAGACG AACCCTAGTT GGGTTGAAGC GACAAGACTC GCGACGAAGC CGAGTCGAAA CGCCGC     1106
GTTACAGACG AACCCTAGTT GGGTTGAAGC CTCTTTATCC CTCCTGCCCG AATGTCTACG AATATC     1172
GTTACAGACG AACCCTAGTT GGGTTGAAGC GAACCCACTG GTGAAGAAAA AGTTGTAGAG ACCCTA     1238
GTTACAGACG AATCCCTAGTTGGGTTGAAGC ACGACAATCA AGTCTGGTTA CATGGCGACA GGATGG     1305
GTTACAGACG AACCCTAGTT GGGTTGAAGC TTCCACAACG TCGGGGAGGG CGAAATTAGC CAAGCA     1371
GTTACAGACG AACCCTAGTT GGGTTGAAGC TCCCGCTGGG GATGTCGGGA GTGCCGGGCG AGCCA      1436
GTTACAGACG AACCCTAGTT GGGTTGAAGC CCCGGCCCGT TGCCCCCCAC GGCAATCGTC TGCT       1500
GTTACAGACG AACCCTAGTT GGGTTGAAGC CGTCTGTGTT ATTCTGTGCG TCTGCCGCGA CAAC      1564
GTTACAGACG AACCCTAGTT GGGTTGAAGC ATTGCCTGTA CCCGTCGTGT AATCAACTCG GAATC     1629
GTTACAGACG AACCCTAGTT GGGTTGAAGC GAGATGTGCG ACCGCGGCGA AATGAGCAGT TCGTG     1694
GTTACAGACG AACCCTAGTT GGGTTGAAGC GCGACATGGG GACCGTCGAG AACGCGCTCT ATGGGGA    1761
GTTACAGACG AACCCTAGTT GGGTTGAAGC CGAGGGTCCC GGTGTCGAGA GGACCGGGAC GGACGGA    1828
GTTACAGTCG AACCCTAGTT GGGTTGAAGC TCGGTAATCT GGGAAGGCGT CAGTCTCGGC CGAGTAATC 1897
GTTACAGACG AACCCTAGTT GGGTTGAAGC CTCGCCATCG CCGCGAACTC GGTCCTCCTC GGGGTG     1963
GTTACAGACG AACCCTAGTT GGGTTGAAGC AAGCCTTGAG AGTGTCTGTT GGTATGATGA ATGTT      2028
GTTACAGACG AACCCTAGTT GGGTTGAAGC AAGTAGACCG CGCTCAGTTA CGACAGCTGC TCGA       2092
GTTACAGACG AACCCTAGTT GGGTTGAAGC ACGATGATCT CGCCAGTCTG CAGCGTTACA TTGG       2156
GTTACAAACG AATCTTTCT CGTGAGGACT TCCGAAACTA ACCTCTTCCC GGAACTAGTC             2216
```

Fig. 1. Nucleotide sequence showing the extension of the tandem repeats (underlined). Sequence identities to the consensus repeated sequence are underlined. *Hin*dIII and *Pst*I sites are in bold type. These sequence data appear in the EMBL/GenBank/DDBJ Nucleotide Sequence Data Libraries under the Accession Number X73453.

OMICS A Journal of Integrative Biology
Volume 6, Number 1, 2002
Mary Ann Liebert, Inc.

Identification of a Novel Family of Sequence Repeats among Prokaryotes

RUND JANSEN,[1] JAM D.A. VAN EMBDEN,[2] WIM GAASTRA,[1] and LEO M. SCHOULS[2]

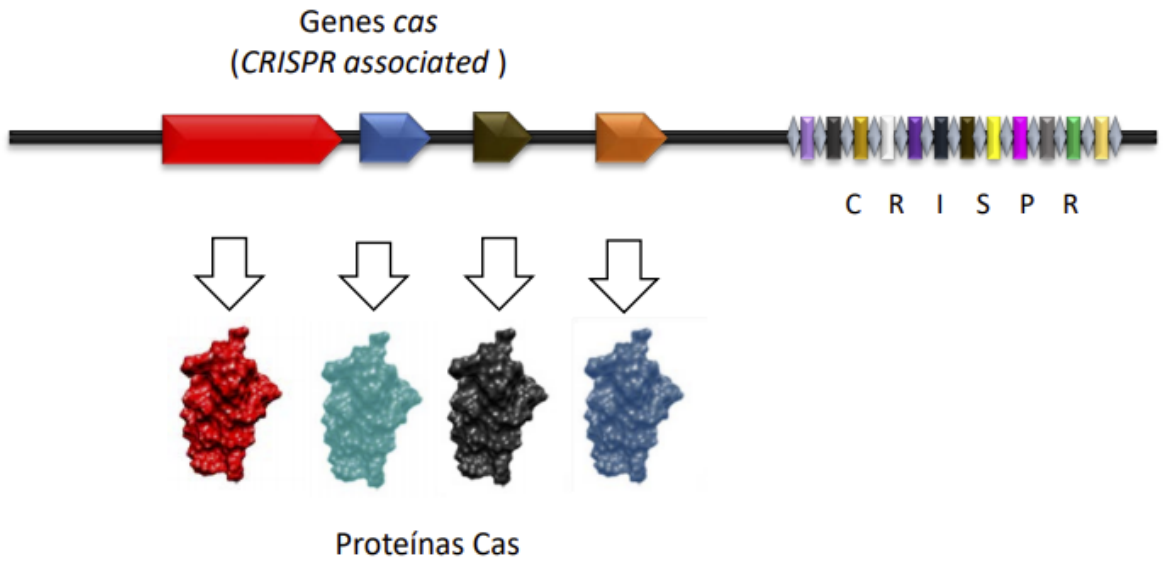
ABSTRACT

"A distinct class of interspersed SSRs was recognized in 1987 in *E. coli* K12 (Ishino et al., 1987; Nakata et al., 1989). Since then, similar interspersed SSRs were identified in *Haloferax mediterranei, Streptococ- cus pyogenes*, *Anabaena*, and *Mycobacterium tuberculosis* (Groenen et al., 1993; Hoe et al., 1999; Masepohl et al., 1996; Mojica et al., 1995). Loci containing this class of repeats will be designated as SPacer Interspersed Direct Repeat (SPIDR) loci**. The structural relationship for some of the SPIDR loci was recognized by Mojica et al. (2000) and is designated Short Regularly Spacer Repeats (SRSRs).** The SPIDR loci differs from other SSRs in their regular structure. The repeat sequences have the same orientation, and each repeat is separated from its neighbor by a spacer sequence that has a size similar to the repeat. In contrast to the repeats, no mutual sequence similarity exists between the spacer sequences."

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]



Sistemas CRISPR

Descubrimiento de genes Cas
(Asociados a CRISPR)

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]

Only recently, this class of repeats was recognized as one family with members in many prokaryotic species (Mojica *et al.*, 2000). Each member of this family of repeats was designated differently by the original authors, leading to a confusing nomenclature. To acknowledge the joining of this class of repeats as one family and to avoid confusing nomenclature, Mojica *et al.* and our research group have agreed to use in this report and future publication the acronym CRISPR, which reflects the characteristic features of this family of clustered regularly interspaced short palindromic repeats.

Acknowledgements

We enjoyed pleasant discussions with Francisco Mojica of the University of Alicante, Spain, about the renaming of CRISPRs. This work was financially supported by the Dutch Foundation for Technical Sciences and the European Union

(2002) Se acuña el término CRISPR

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>

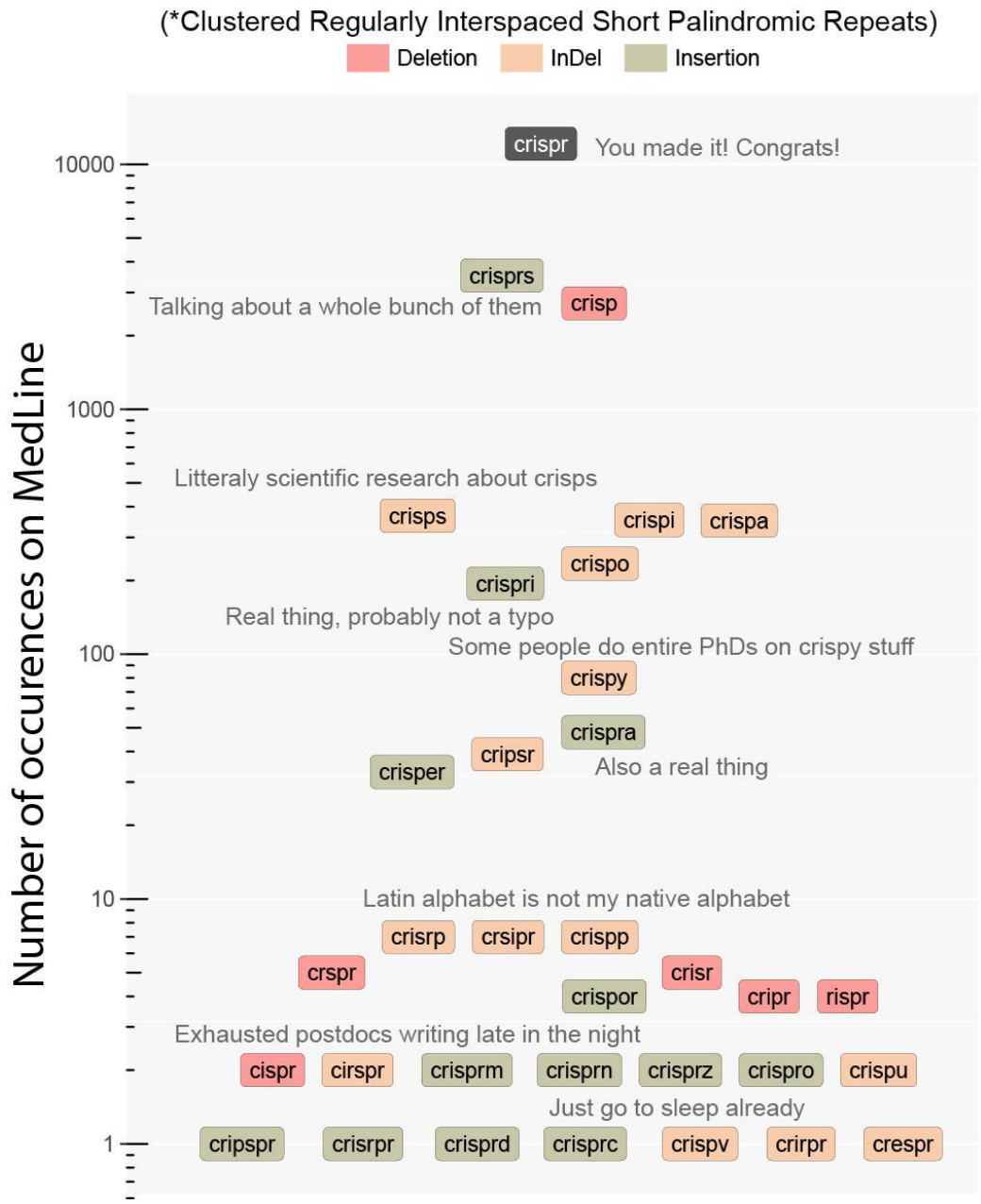
Dear Francis

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.

David Bikard

@dbikard

My PhD student Antoine Vigouroux just made this. Thought it was too funny not to share :-) How do you write #CRISPR ?



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

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]

Abstract. Prokaryotes contain short DNA repeats known as CRISPR, recognizable by the regular spacing existing between the recurring units. They represent the most widely distributed family of repeats among prokaryotic genomes, suggesting a biological function. The origin of the intervening sequences, at present unknown, could provide clues

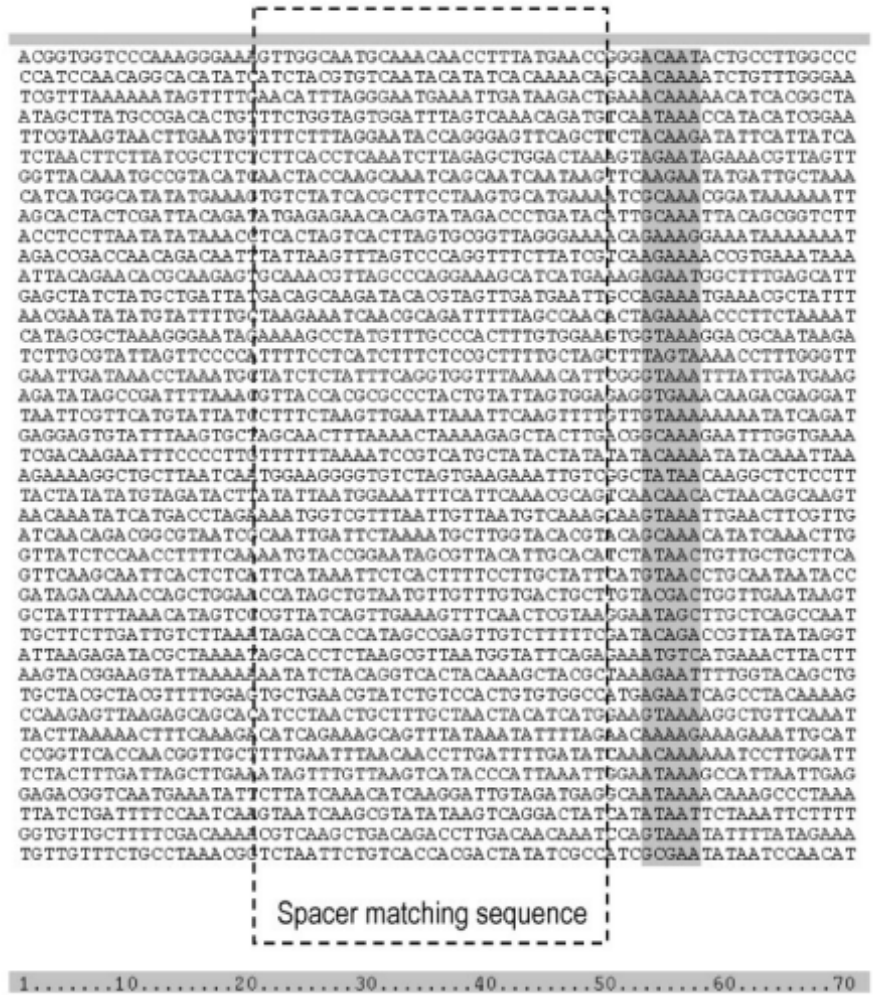
Introduction

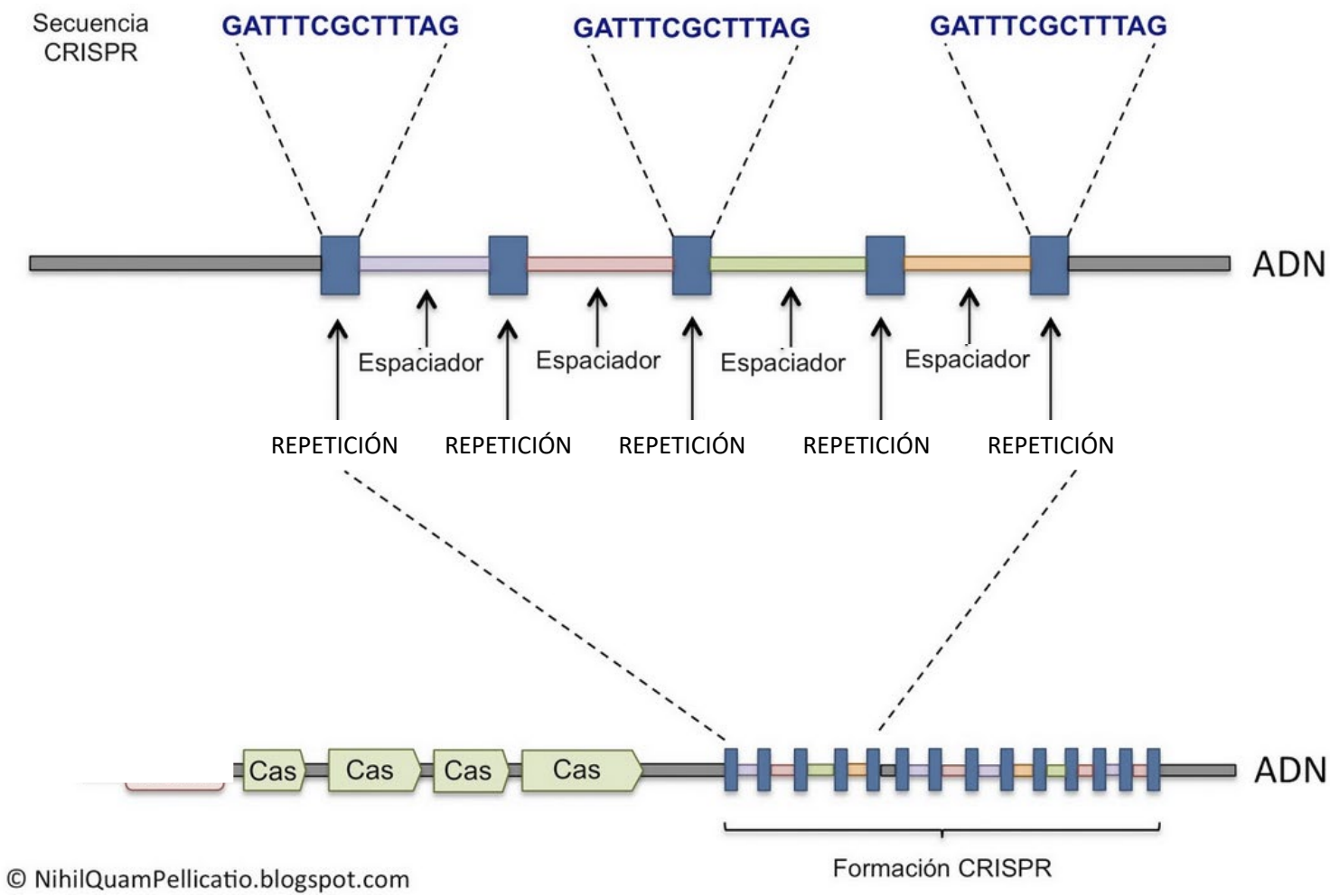
Prokaryotic genomes contain a peculiar family of repeated DNA sequences. They consist of 24- to 40-nucleotide (nt) recurrent motifs regularly spaced by intervening sequences of sizes similar to that of the repeated unit. These repetitive elements were defined

Clustered regularly interspaced short palindrome repeats (CRISPRs) have spacers of extrachromosomal origin

Alexander Bolotin, Benoit Quinquis, Alexei Sorokin and S. Dusko Ehrlich

Génétique Microbienne, Institut National de la Recherche Agronomique, Domaine de Vilvert, 78352 Jouy en Josas CEDEX, France




Secuencia CRISPR
GATTTCGCTTTAG
GATTTCGCTTTAG
GATTTCGCTTTAG
ADN
Espaciador
Espaciador
Espaciador
Espaciador
REPETICIÓN
REPETICIÓN
REPETICIÓN
REPETICIÓN
REPETICIÓN
Cas
Cas
Cas
Cas
ADN
Formación CRISPR
© NihilQuamPellicatio.blogspot.com

Rodolphe Barrangou
North Carolina State Univ, Raleigh, USA

Philippe Horvath
DuPont Nutrition and Health, France

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 23 Mar 2007:
Vol. 315, Issue 5819, pp. 1709-1712
DOI: 10.1126/science.1138140

(2007) Se demuestra el papel en el **sistema inmunitario** de procariotas de CRISPR.

DUPONT®

DANISCO®

John van der Oost
Wageningen University, The Netherlands

Small CRISPR RNAs Guide Antiviral Defense in Prokaryotes

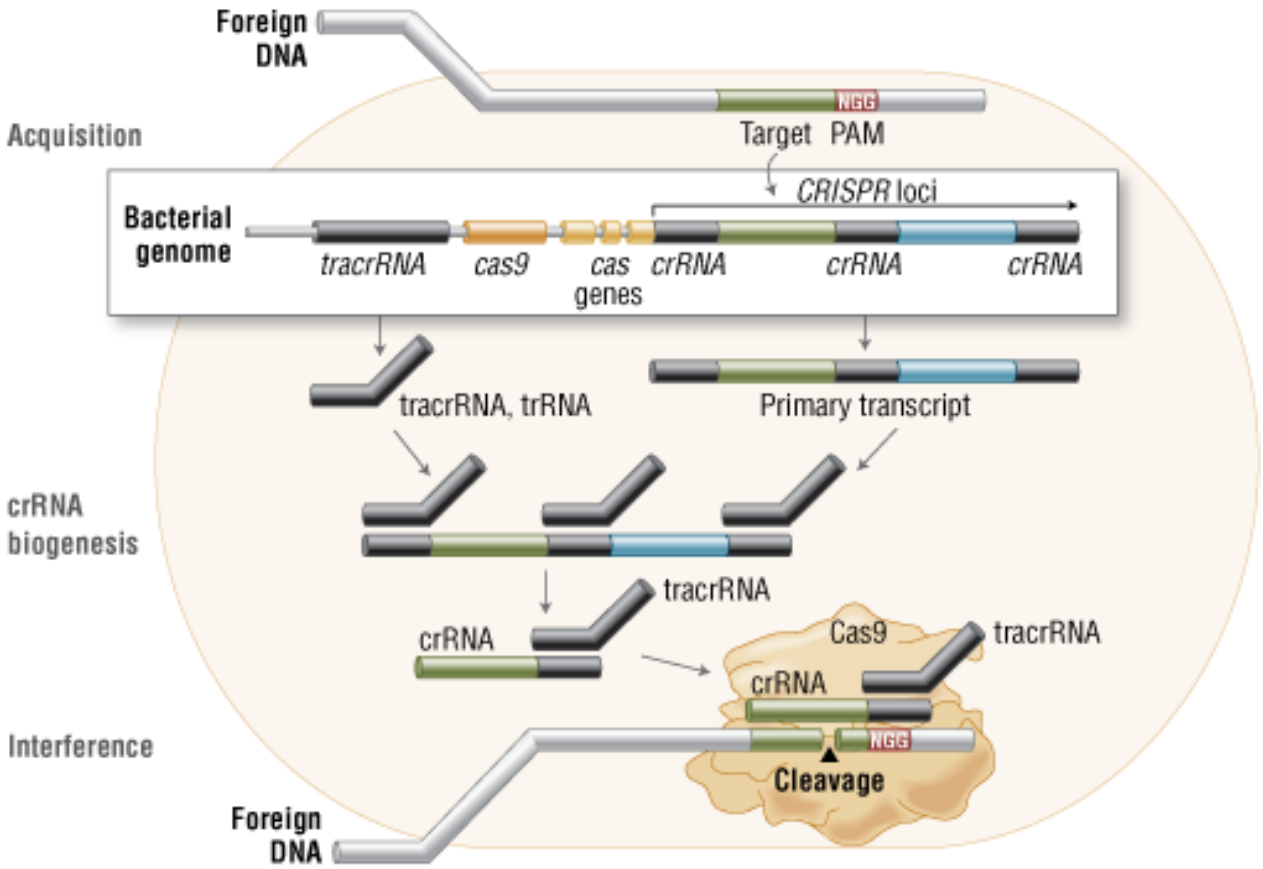
Stan J. J. Brouns,[1]* Matthijs M. Jore,[1]* Magnus Lundgren,[1] Edze R. Westra,[1] Rik J. H. Slijkhuis,[1] Ambrosius P. L. Snijders,[2] Mark J. Dickman,[2] Kira S. Makarova,[3] Eugene V. Koonin,[3] John van der Oost[1]†

Science 15 Aug 2008:
Vol. 321, Issue 5891, pp. 960-964
DOI: 10.1126/science.1159689

(2008) Función de los genes Cas y del crRNA. Además, se demuestra que el target es el ADN.

Luciano Marraffini
The Rockefeller Univ, New York, USA

CRISPR (Clustered Regularly Interspaced Short Palindormic Repeats)



Jennifer Doudna
Univ California Berkeley, CA, USA

Emmanuelle Charpentier
MPI for Infect. Biol., Berlin, Germany

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]‡

Science 17 Aug 2012:
Vol. 337, Issue 6096, pp. 816-821
DOI: 10.1126/science.1225829

(2012) Identifican los elementos mínimos de CRISPR con los que se puede cortar el ADN, abriéndose así la puerta a la **edición de genomas** (el llamado "*corta y pega genético*"). Cortan y sustituyen ADN de una bacteria por primera vez.

Virginijus Siksnys
Vilnius University, Lithuania

Proc Natl Acad Sci U S A. 2012 Sep 25;109(39):E2579-86.

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]

(2012) Reconstrucción del funcionamiento de CRISPR-Cas y propuesta de su uso en ingeniería genética

CRISPR en Ingeniería Genética

Virginijus Siksnys
Vilnius University, Lithuania

Proc Natl Acad Sci U S A. 2012 Sep 25;109(39):E2579-86.

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]

Jennifer Doudna
Univ California Berkeley, CA, USA

Emmanuelle Charpentier
MPI for Infect. Biol., Berlin, Germany

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

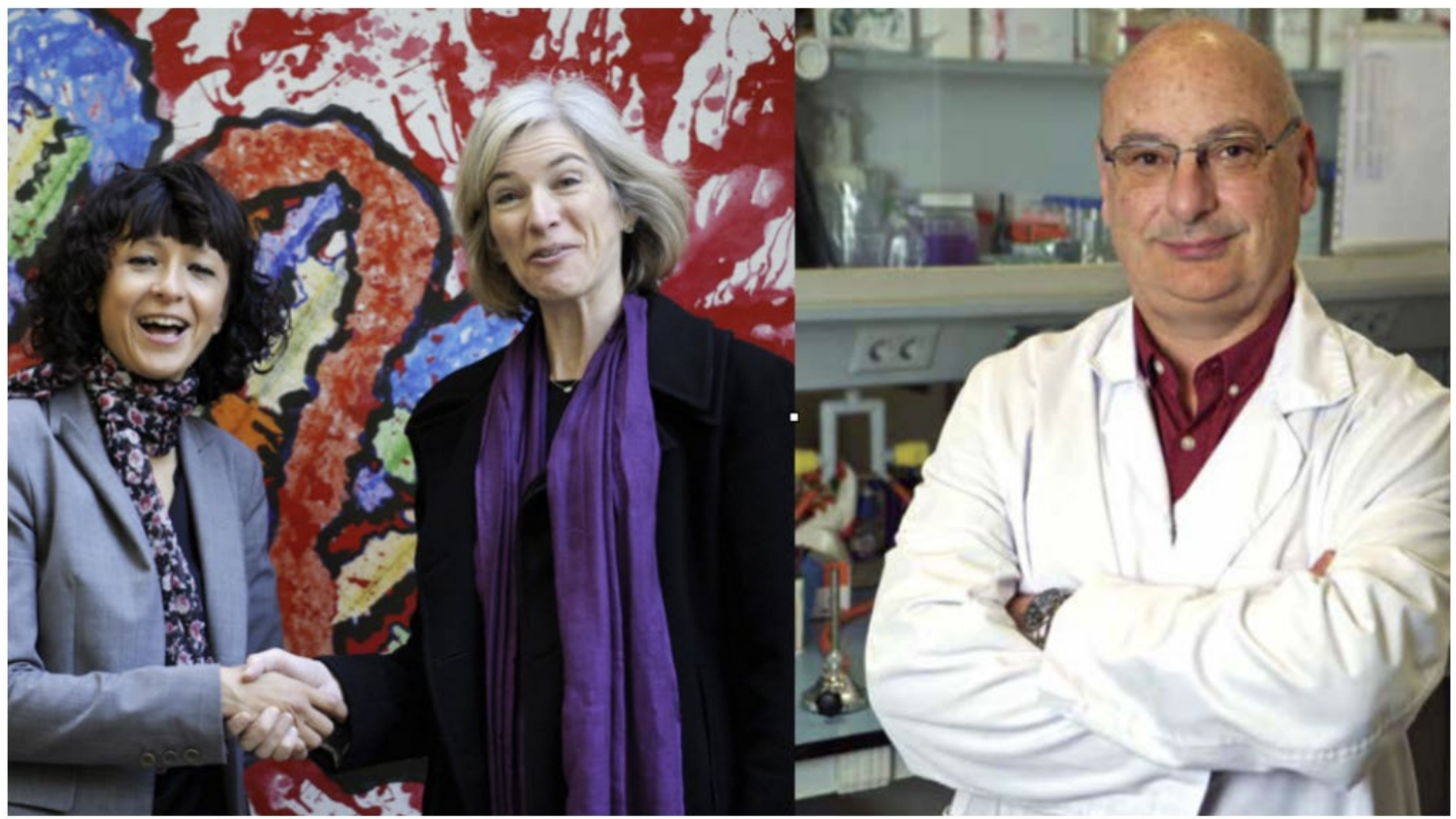
Martin Jinek,[1,2]* Krzysztof Chylinski,[3,4]* Ines Fonfara,[4] Michael Hauer,[2]†
Jennifer A. Doudna,[1,2,5,6]‡ Emmanuelle Charpentier[4]‡

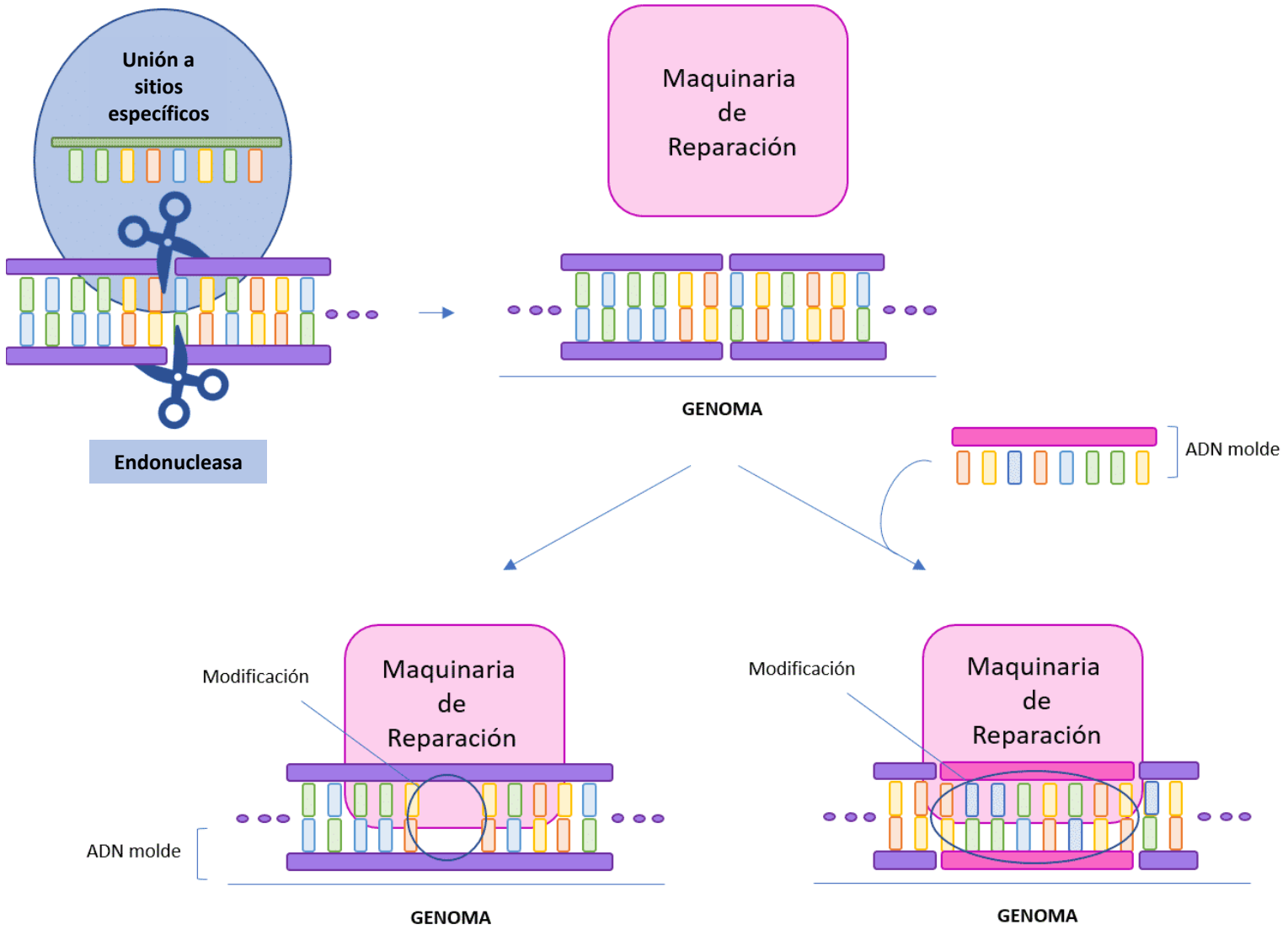
Science 17 Aug 2012:
Vol. 337, Issue 6096, pp. 816-821
DOI: 10.1126/science.1225829

Enviado: 21 de mayo | Aceptado: 25 de septiembre

Enviado: 8 de junio | Aceptado: 20 de junio

Francis Mojica se queda sin el Nobel: Emmanuelle Charpentier y Jennifer A. Doudna se llevan el premio de Química 2020 por CRISPR-Cas9



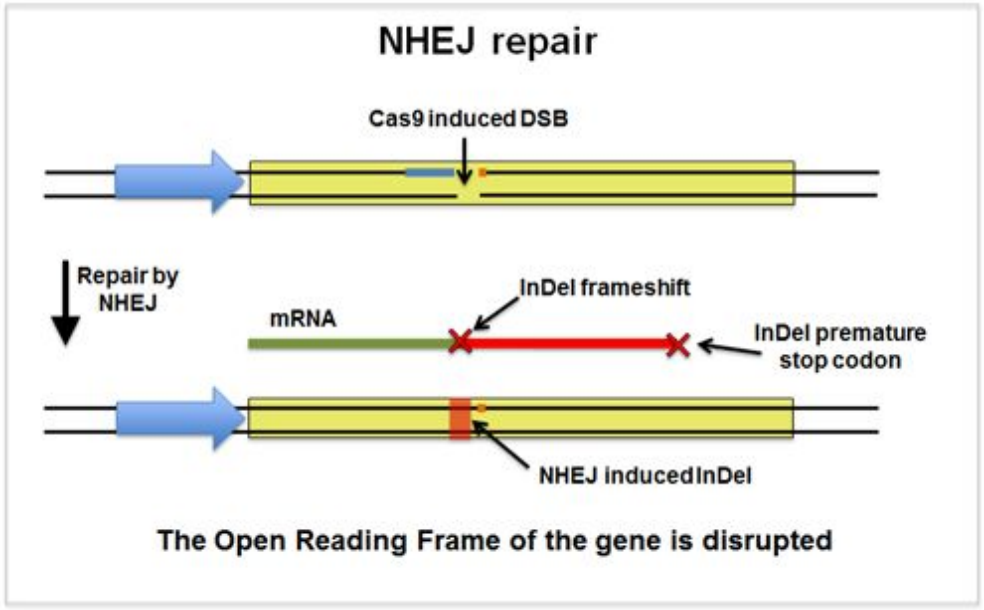

Unión a sitios específicos
Endonucleasa
Maquinaria de Reparación
GENOMA
ADN molde
Modificación
Maquinaria de Reparación
ADN molde
GENOMA
Modificación
Maquinaria de Reparación
GENOMA

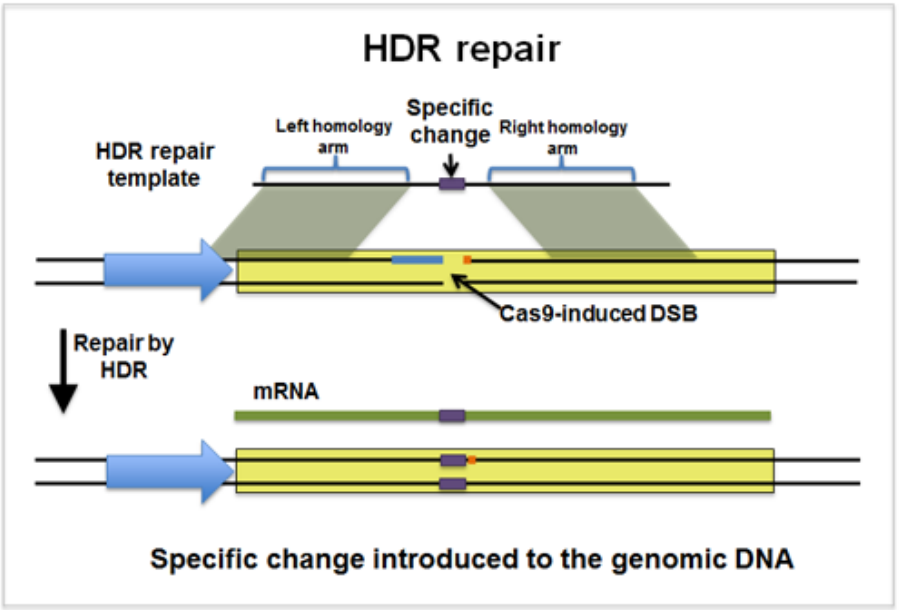
Inserciones/deleciones (Knock outs)

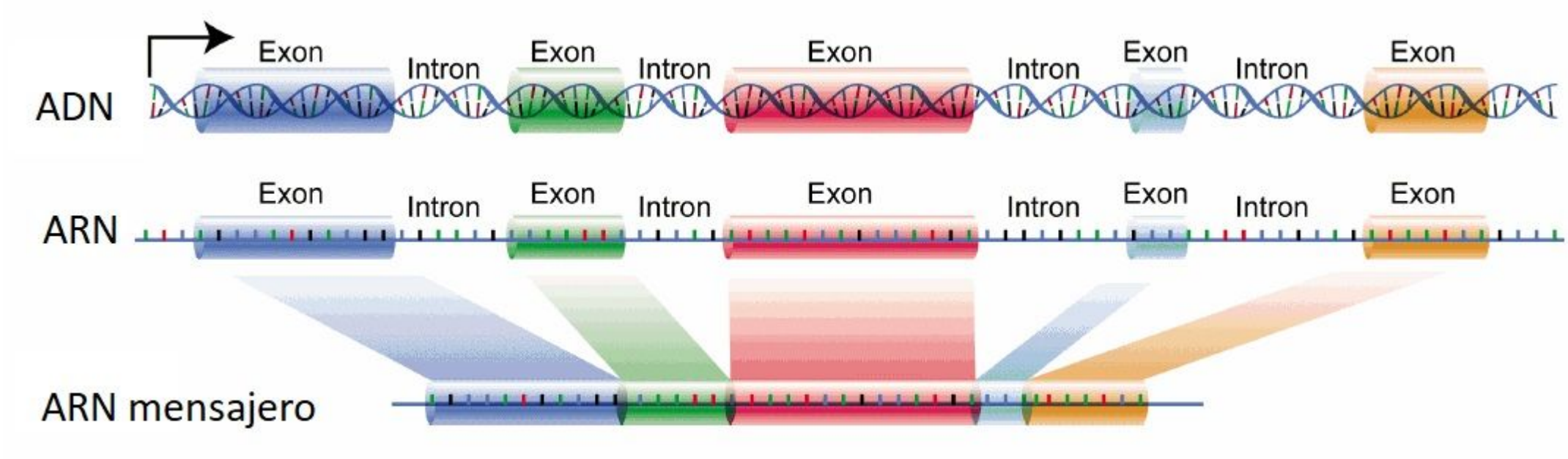
NHEJ: (Non-homologous end joining) **Recombinación No Homóloga**. Los extremos de las dobles roturas se ligan sin la intervención de un ADN molde.

Cambios precisos en el ADN

HDR: (*Homology Directed Repair*) o **Recombinación Homóloga**. Las dobles roturas se reparan utilizando un ADN homólogo como molde.

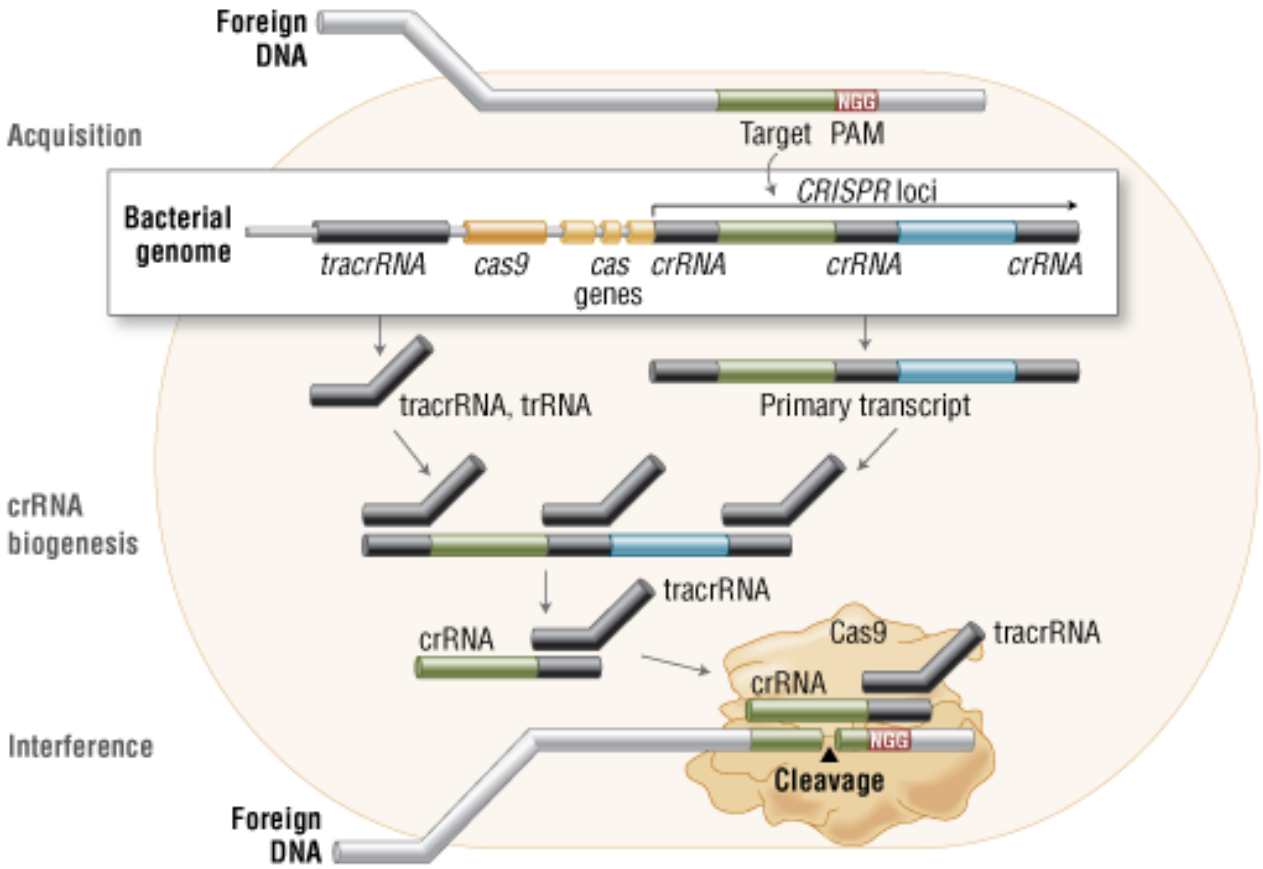




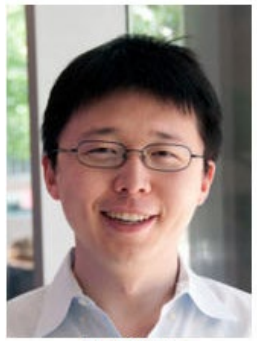


Fuente: https://genotipia.com/

CRISPR (Clustered Regularly Interspaced Short Palindormic Repeats)



Luciano Marraffini
The Rockefeller Univ, New York, USA



Feng Zhang
BROAD-MIT, Cambridge, MA, USA

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] Feng Zhang[1]†

Science 15 Feb 2013:
Vol. 339, Issue 6121, pp. 819-823
DOI: 10.1126/science.1231143

(2013) Primera vez que se usa CRISPR para cortar ADN en células animales *in vitro* (ratón y humanos).

George Church
Harvard Med School, Boston, MA, USA

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] George M. Church[1,2]*

Science 15 Feb 2013:
Vol. 339, Issue 6121, pp. 823-826
DOI: 10.1126/science.1232033

(2013) Puesta a punto de protocolos CRISPR/Cas para la modificación de distintos genomas (incluidos el humano y el de mamut).