De impact van CRISPR-Cas op onze maatschappij

Raymond H.J. Staals
Associate Professor, Laboratory of Microbiology
Wageningen University & Research

8e Nationale Docentencongres Biologie

Conflict of interest disclaimer

Co-founder, scientific advisor and shareholder of Scope Biosciences (diagnostics)

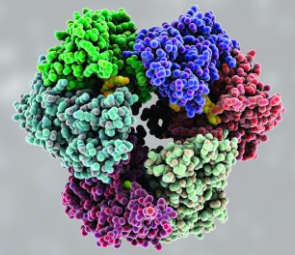
Scientific advisor for Novya Biotech

Inventor of several CRISPR-Cas-related patents/patent applications

CV Raymond Staals (1979)

2006-2011 : PhD student

Department of Biomolecular Chemistry
Radboud University Nijmegen



Human RNA Exosome

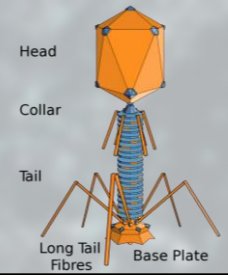
2011-2014 : Research fellow

Laboratory of Microbiology
Wageningen University & Research

Type III CRISPR-Cas

2014-2017 : Postdoc / Principal investigator

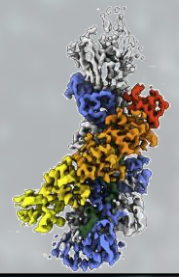
Department of Microbiology and Immunology
Otago University (New Zealand)



CRISPR-Cas & phage biology

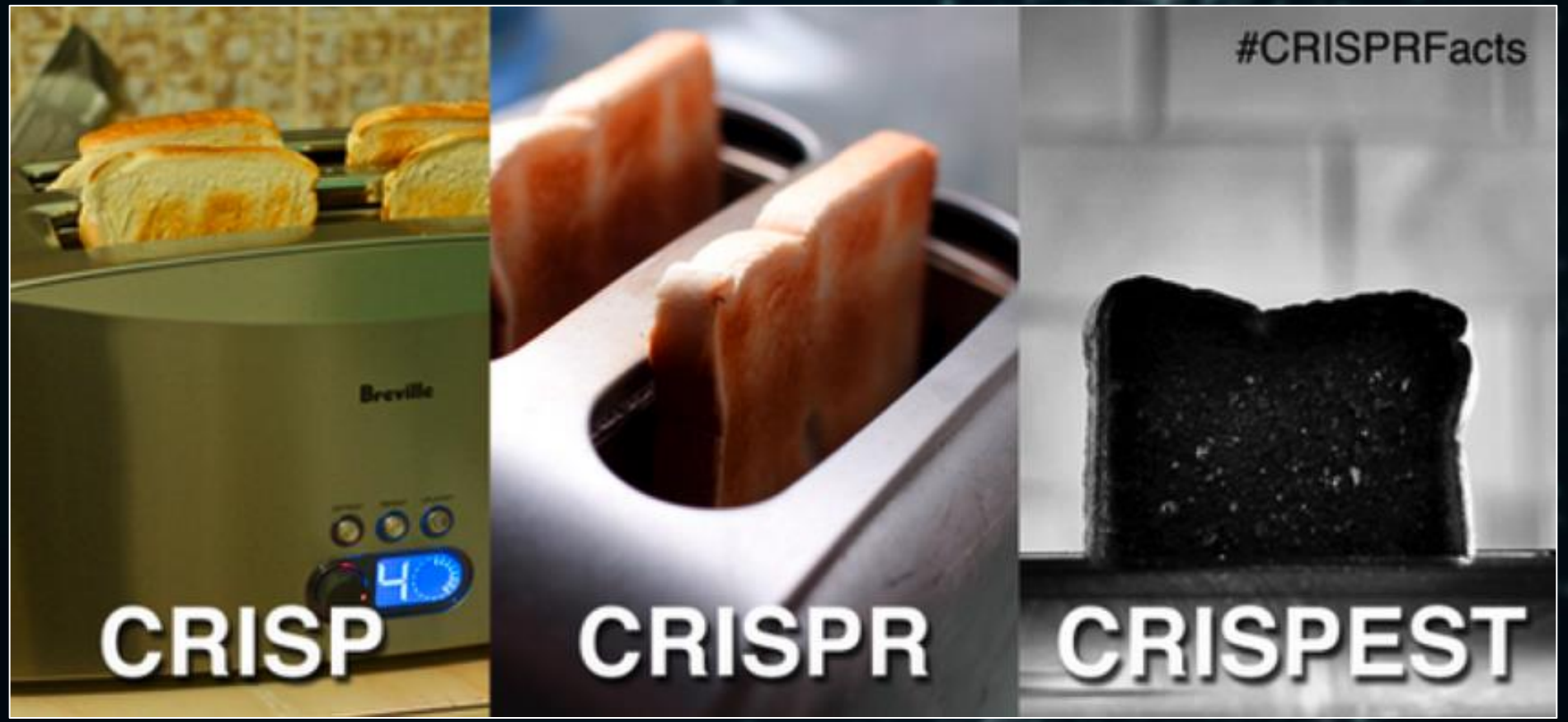
2017-present : Associate Professor

Laboratory of Microbiology
Wageningen University & Research



CRISPR-Cas & applications

CRISPR-Cas?



CRISPR-Cas?

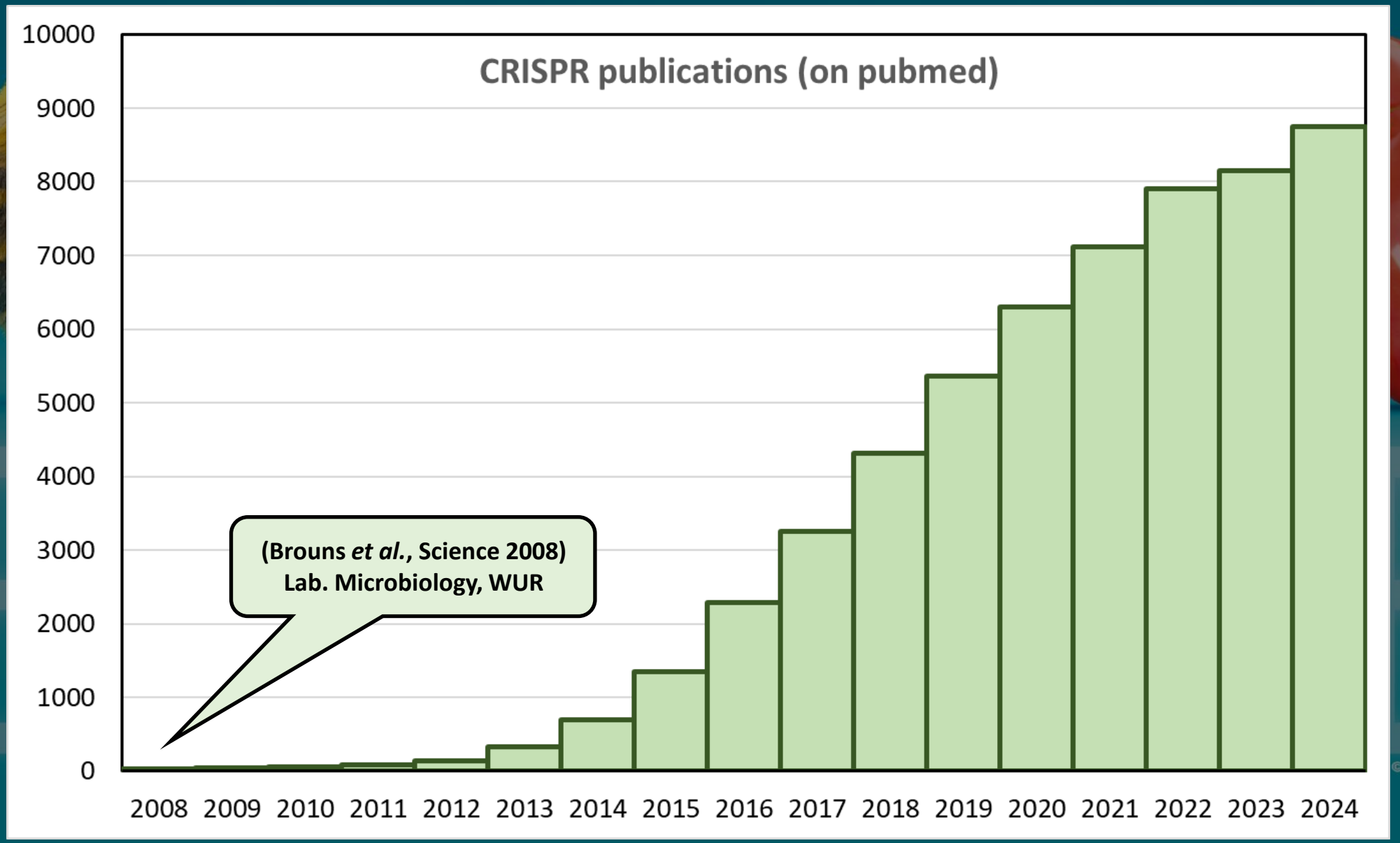
2020 Nobel Prize in Chemistry

Jennifer Doudna

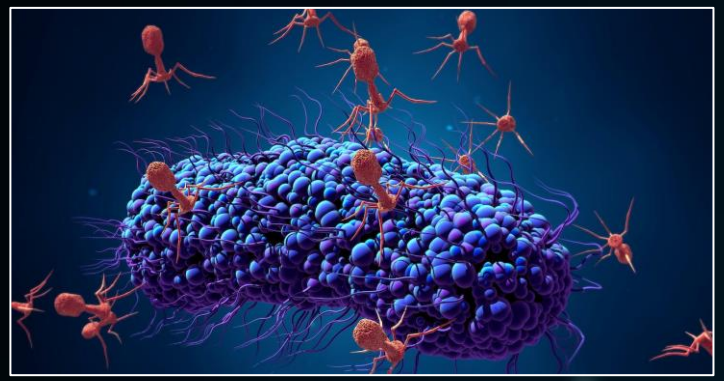
Emmanuelle Charpentier

CRISPR EVERYWHERE

Illustration by Chris Labrooy ©nature


CRISPR publications (on pubmed)
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
2018
2019
2020
2021
2022
2023
2024
(Brouns *et al.*, Science 2008)
Lab. Microbiology, WUR

Onderwerpen

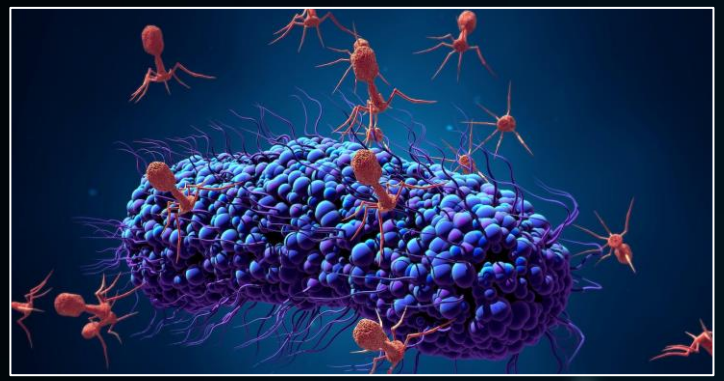


Oorsprong CRISPR-Cas

CRISPR-Cas als
genetisch gereedschap

Impact op de maatschappij

Onderwerpen



Oorsprong CRISPR-Cas

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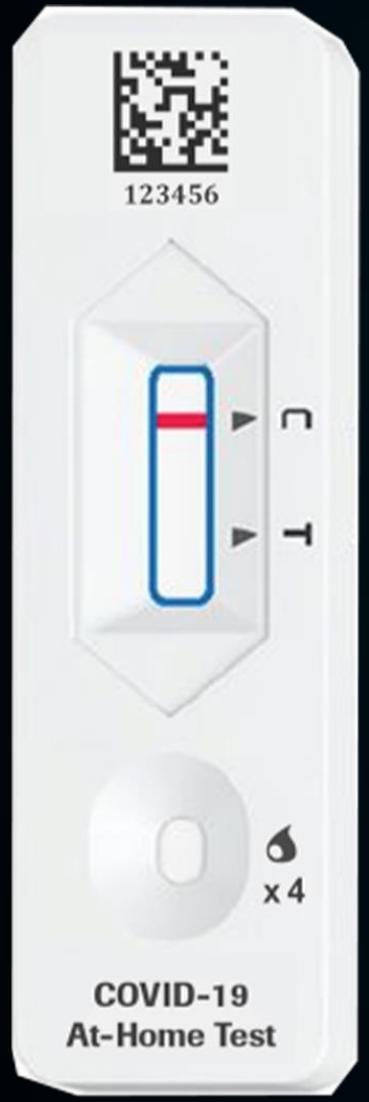
Oorsprong CRISPR-Cas

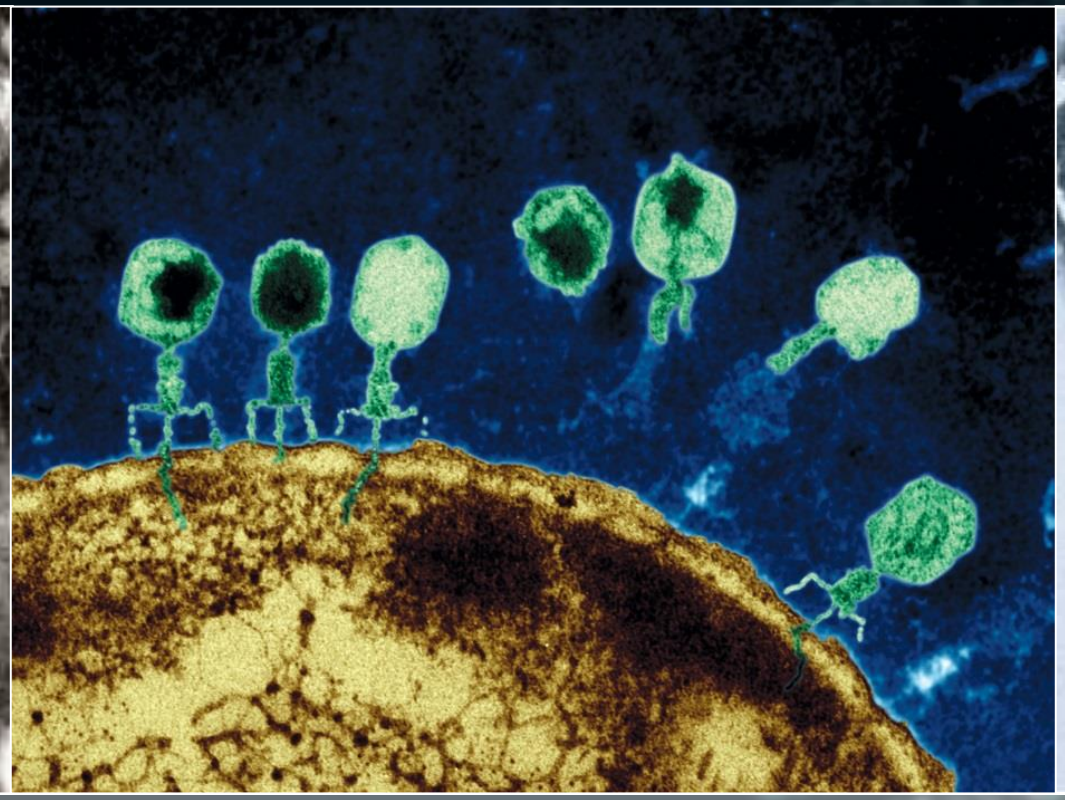


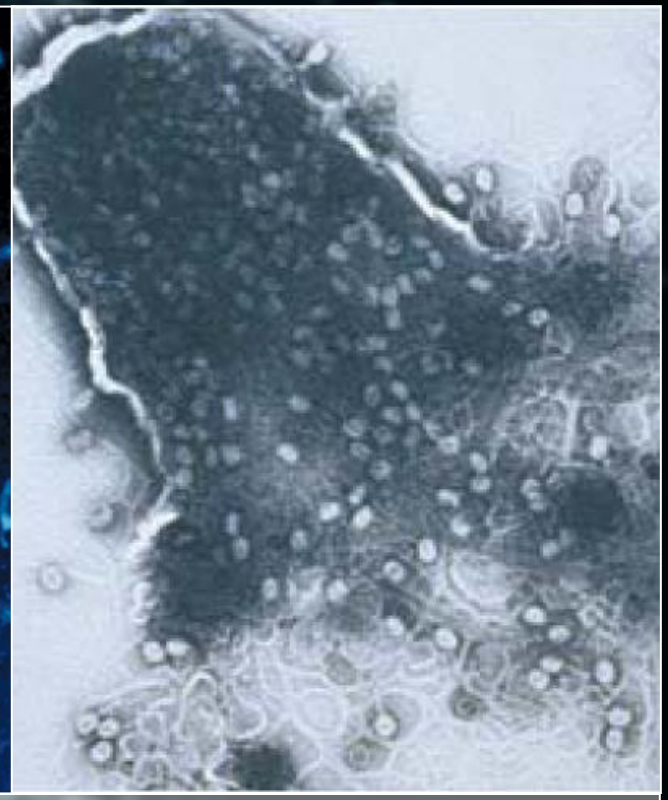
Dramatic impact of viruses on life…

COVID-19

Coronavirus Disease 2019

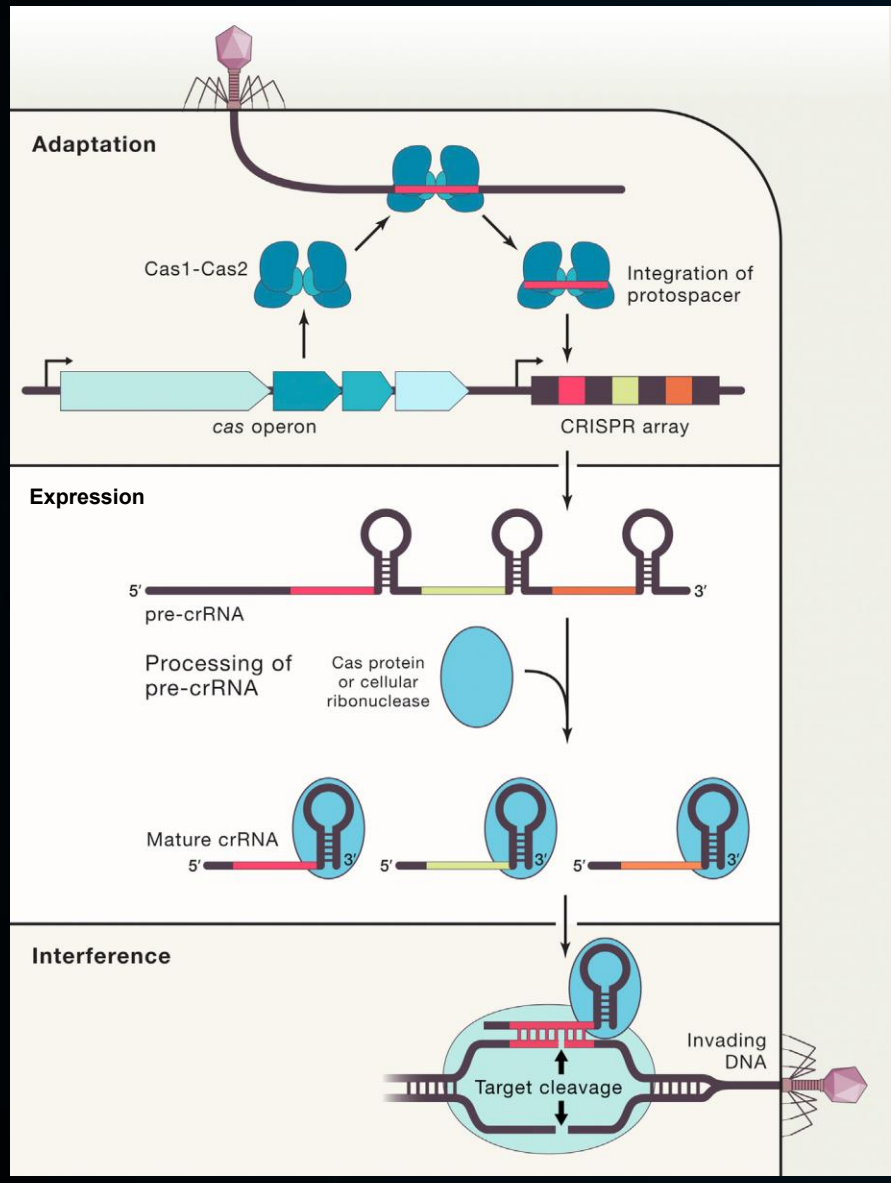
Oorsprong CRISPR-Cas





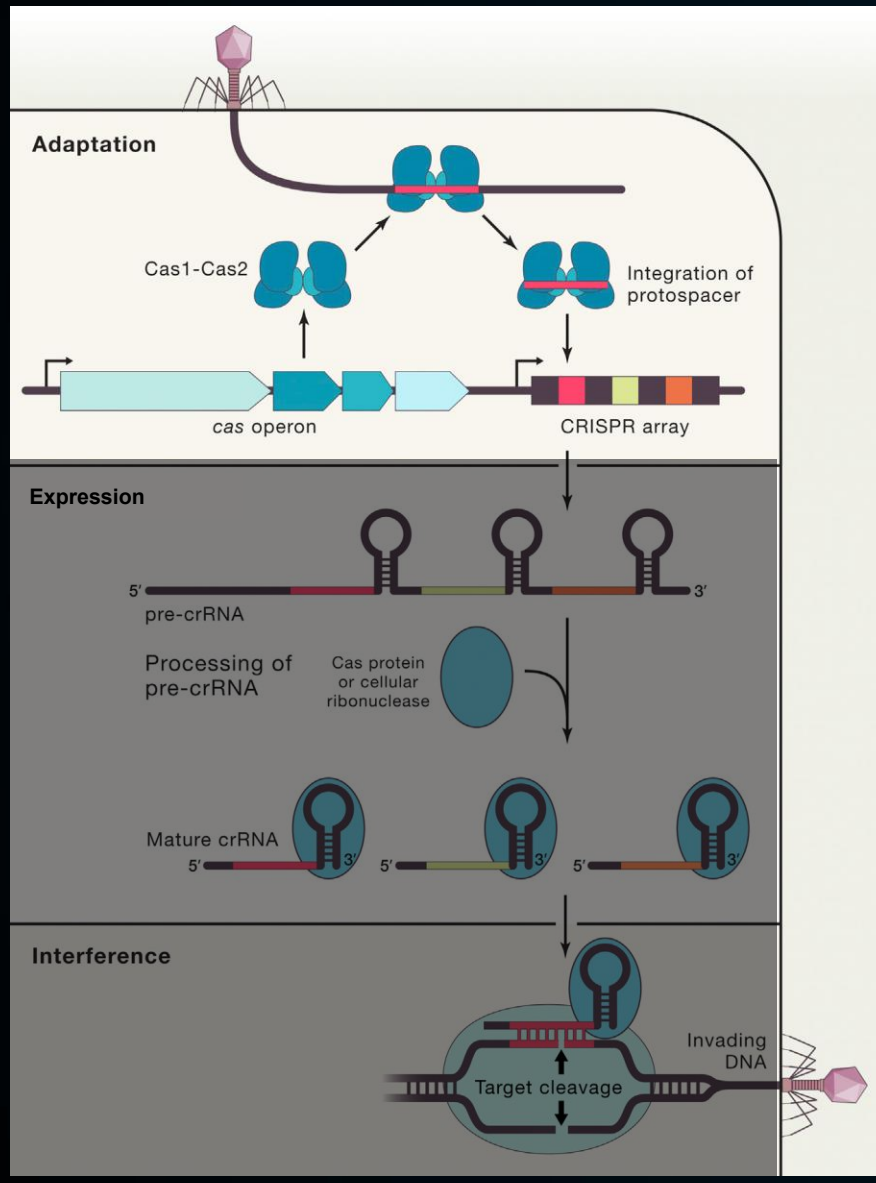
- 10^{24} infections/second!
- “If we line up all the viruses in the ocean, they would stretch across the diameter of the Milky Way galaxy one hundred times.” (Suttle 2007)

Oorsprong CRISPR-Cas



Three stages of CRISPR-Cas immunity

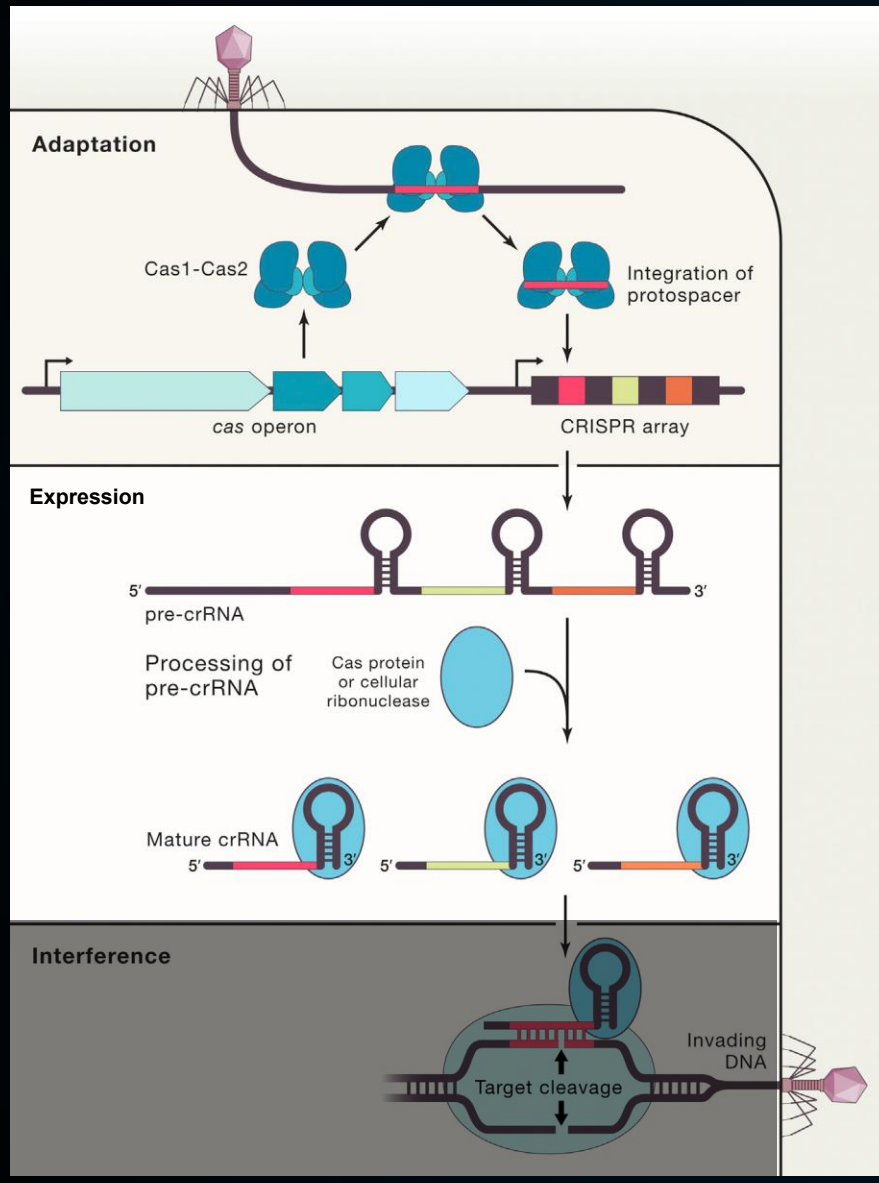
Oorsprong CRISPR-Cas



1. Adaptation

Store short DNA sequence from virus into the CRISPR array

Oorsprong CRISPR-Cas



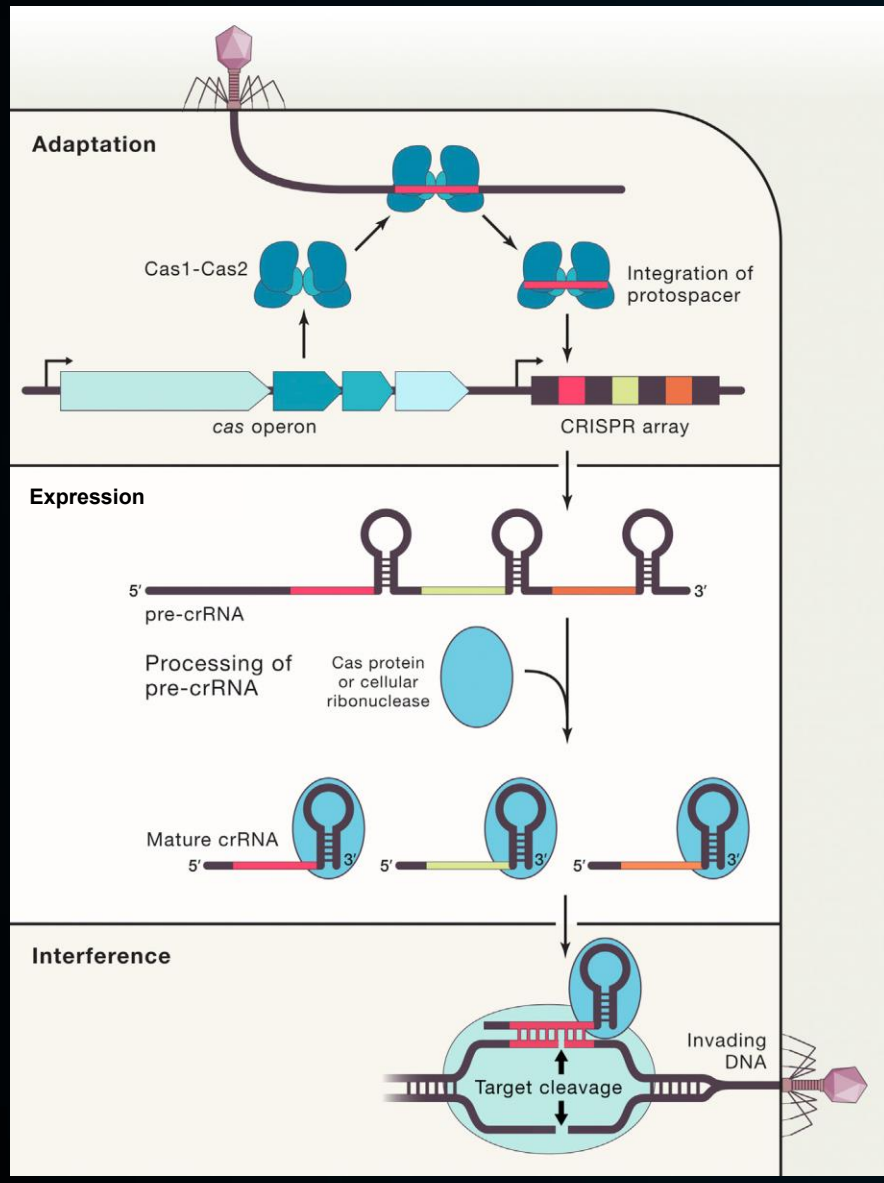
1. Adaptation

Store short DNA sequence from virus into the CRISPR array

2. Expression

Cas genes and CRISPR RNA expression
Formation of Cas-crRNA complex

Oorsprong CRISPR-Cas



1. Adaptation

Store short DNA sequence from virus into the CRISPR array

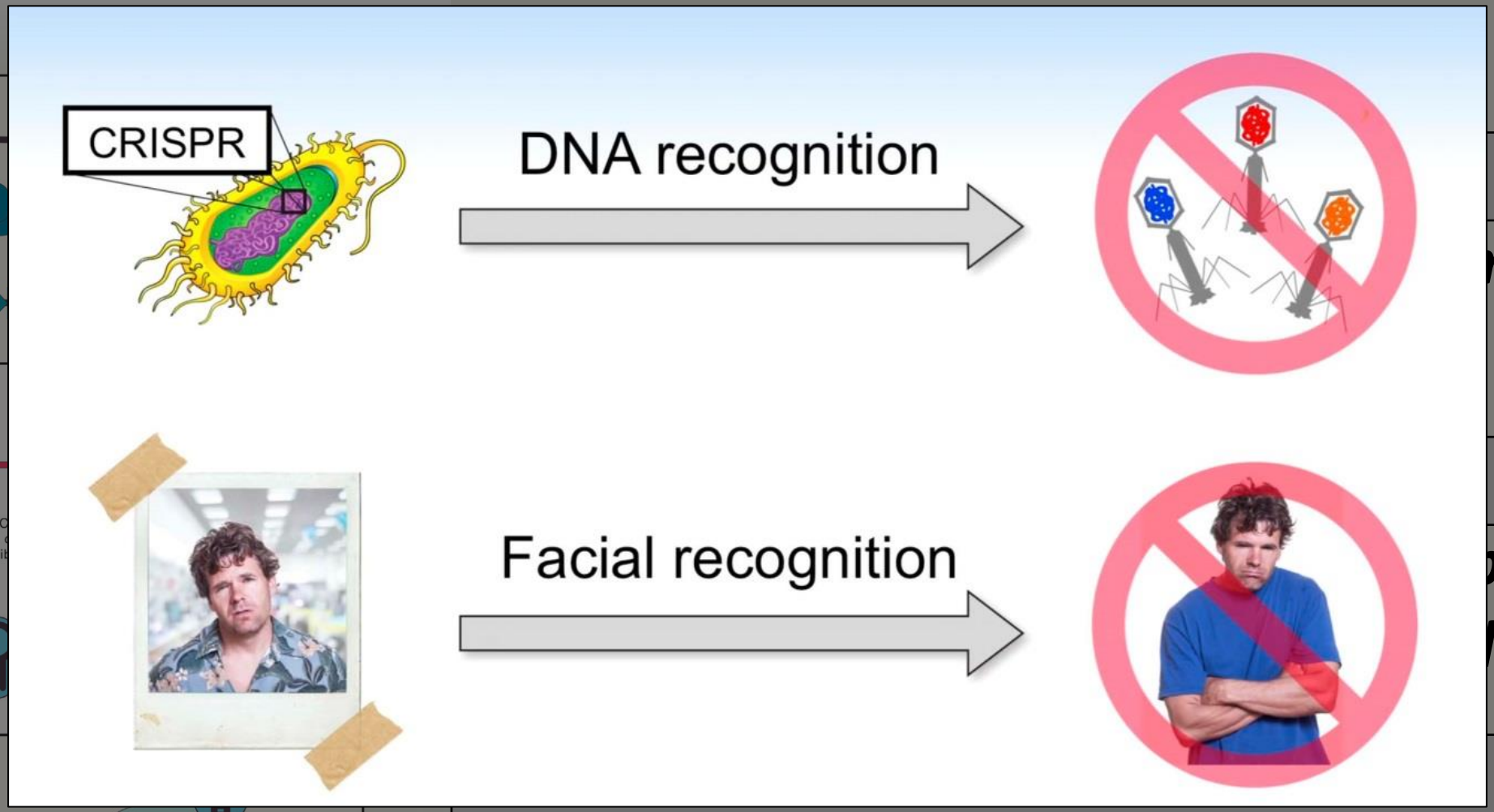
2. Expression

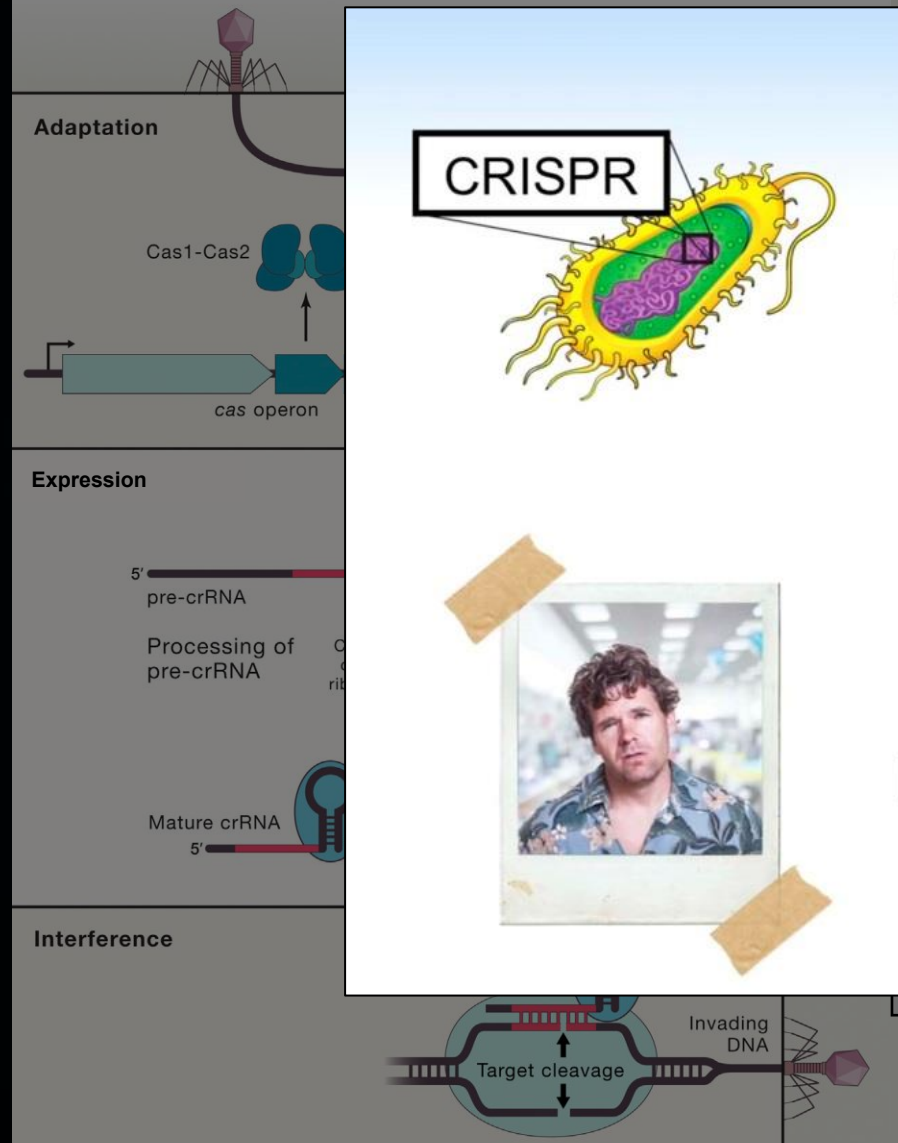
Cas genes and CRISPR RNA expression
Formation of Cas-crRNA complex

3. Interference

Cas-crRNA complex degrades virus

Oorsprong CRISPR-Cas





n virus

pression

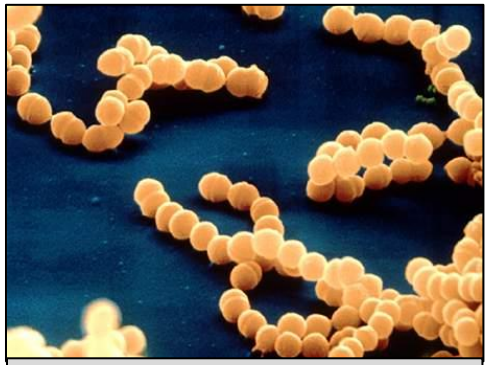
lex

Cas-crRNA complex degrades virus

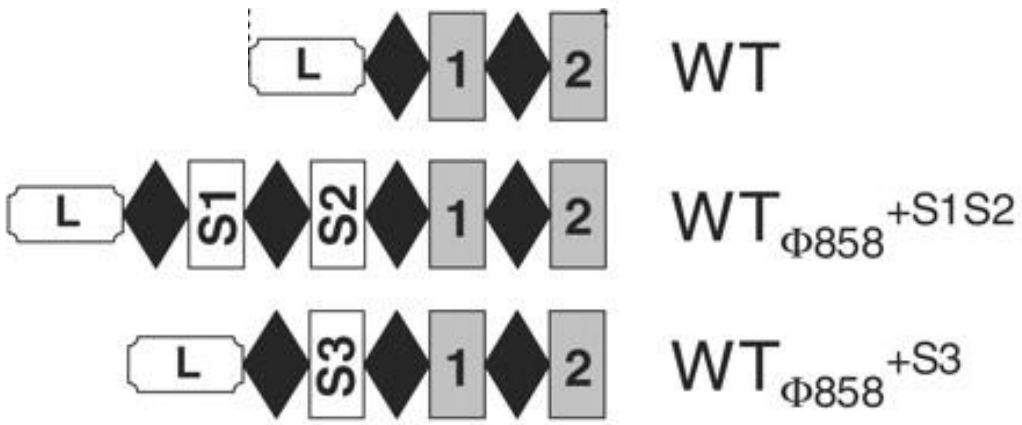
Oorsprong CRISPR-Cas

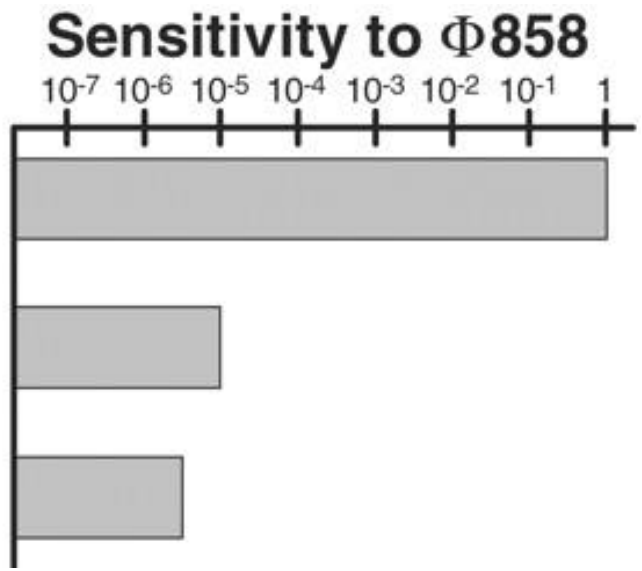
1. Bacteria
2. Bacteria + viruses
3. Bacteria (with CRISPR) + viruses

First application of CRISPR-Cas: virus-resistant bacterial production strains



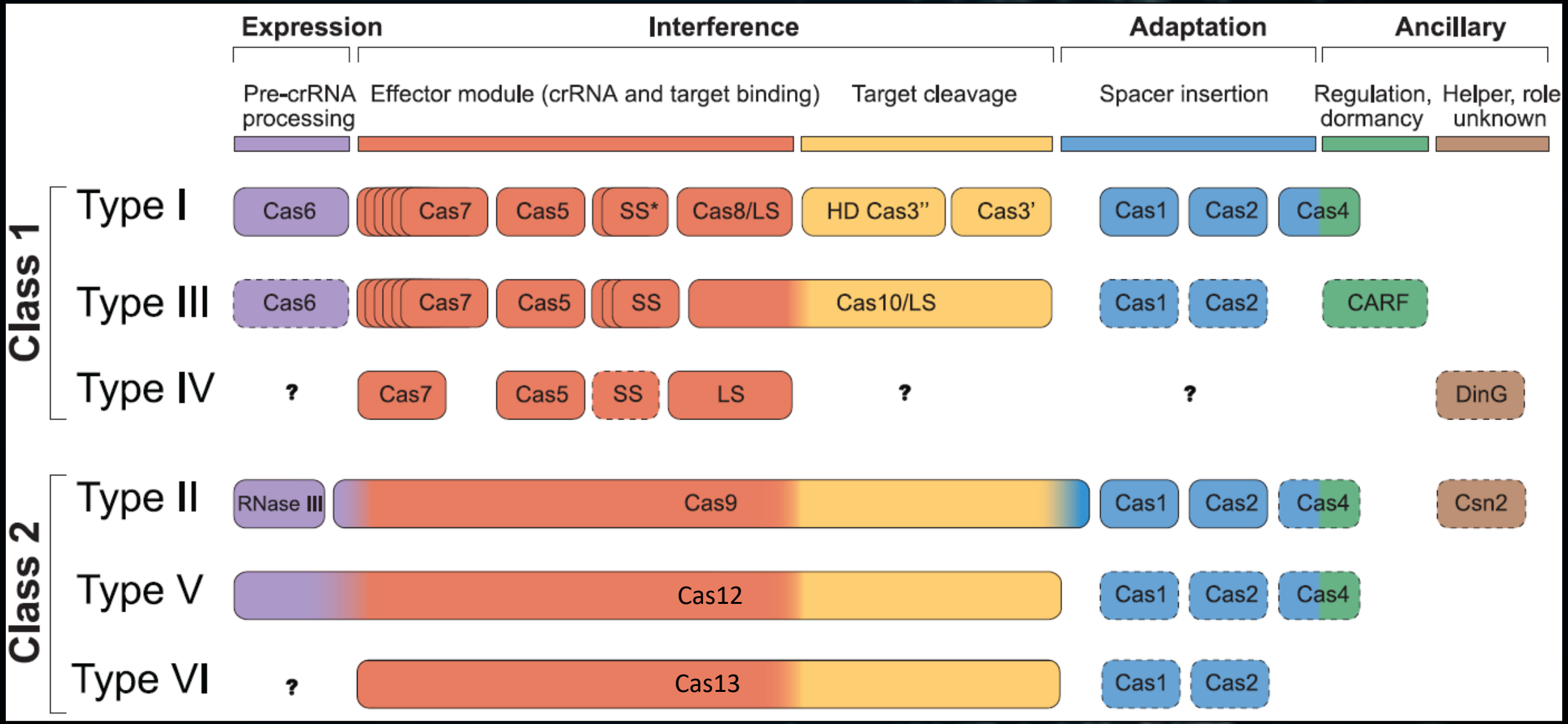
Streptococcus thermophilus





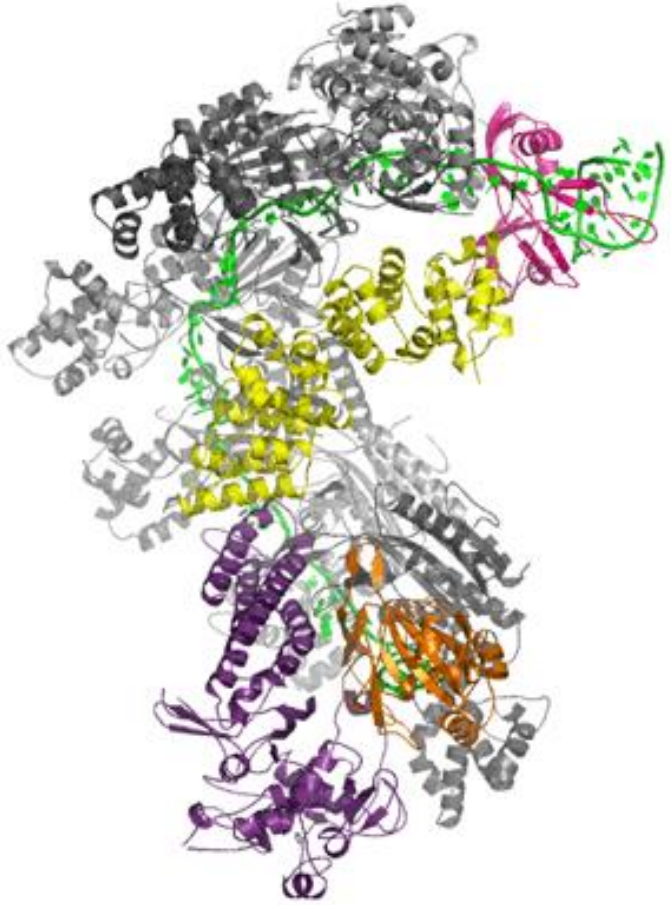
(Barrangou *et al.*, Science 2007)

Oorsprong CRISPR-Cas

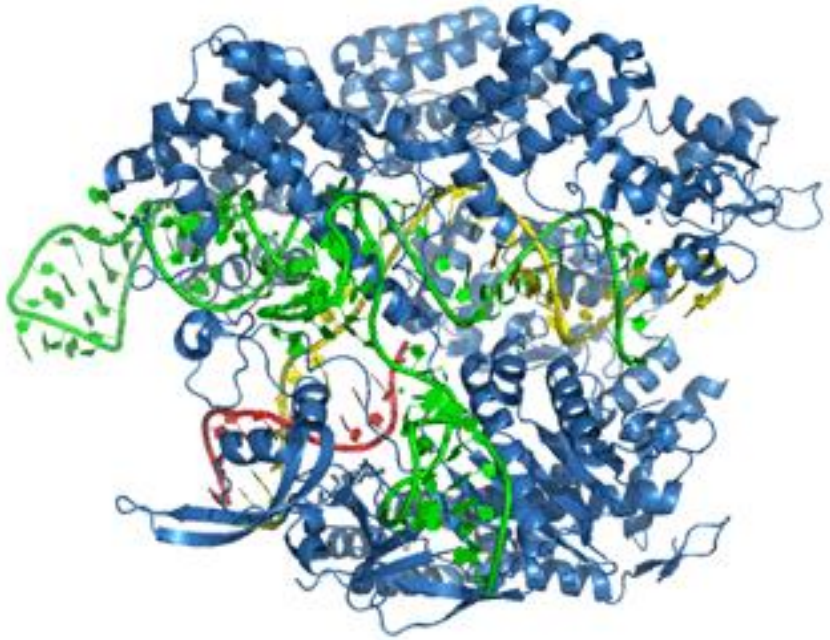


Oorsprong CRISPR-Cas

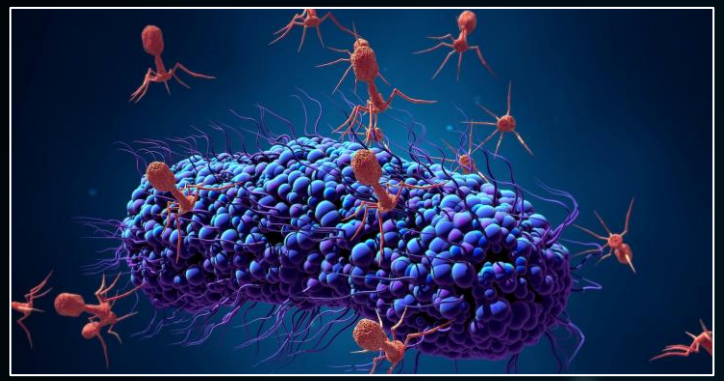
Type I: Cascade
(multi-protein complex)



Type II: Cas9
(single-protein complex)



Onderwerpen

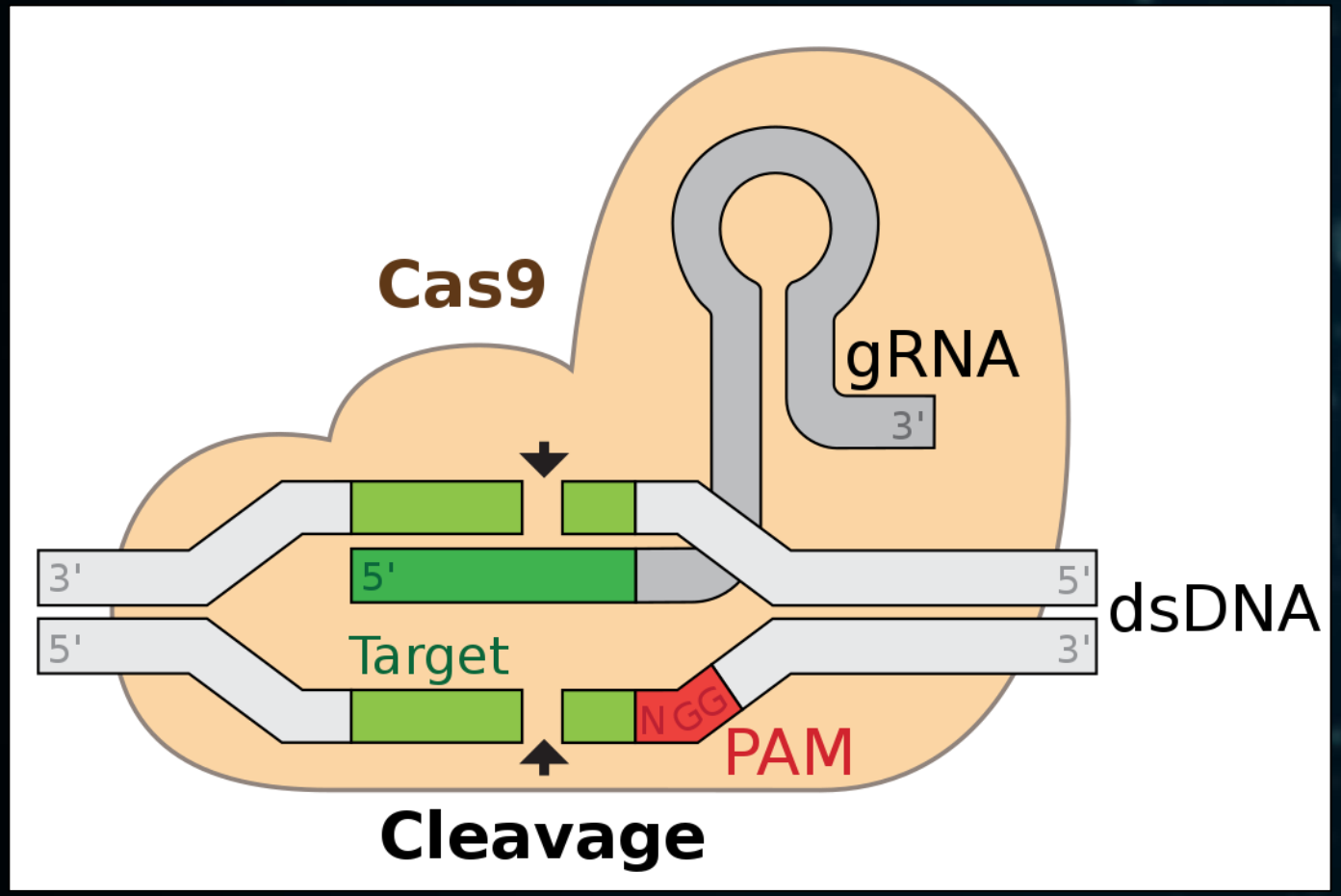


Oorsprong CRISPR-Cas

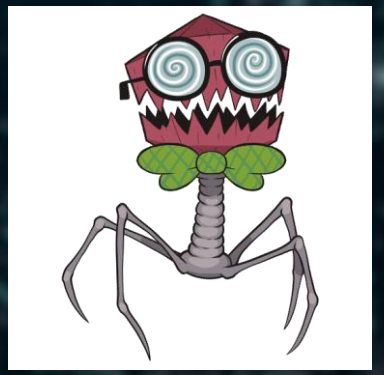
CRISPR-Cas als
genetisch gereedschap

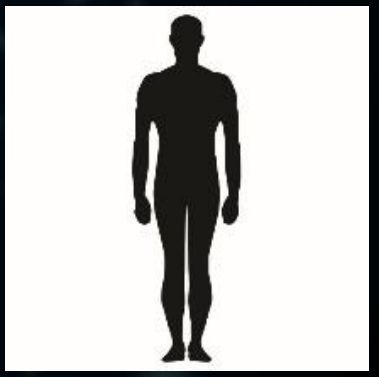
Impact op de maatschappij

CRISPR-Cas als genetisch gereedschap



You can change the gRNA to any sequence of interest!



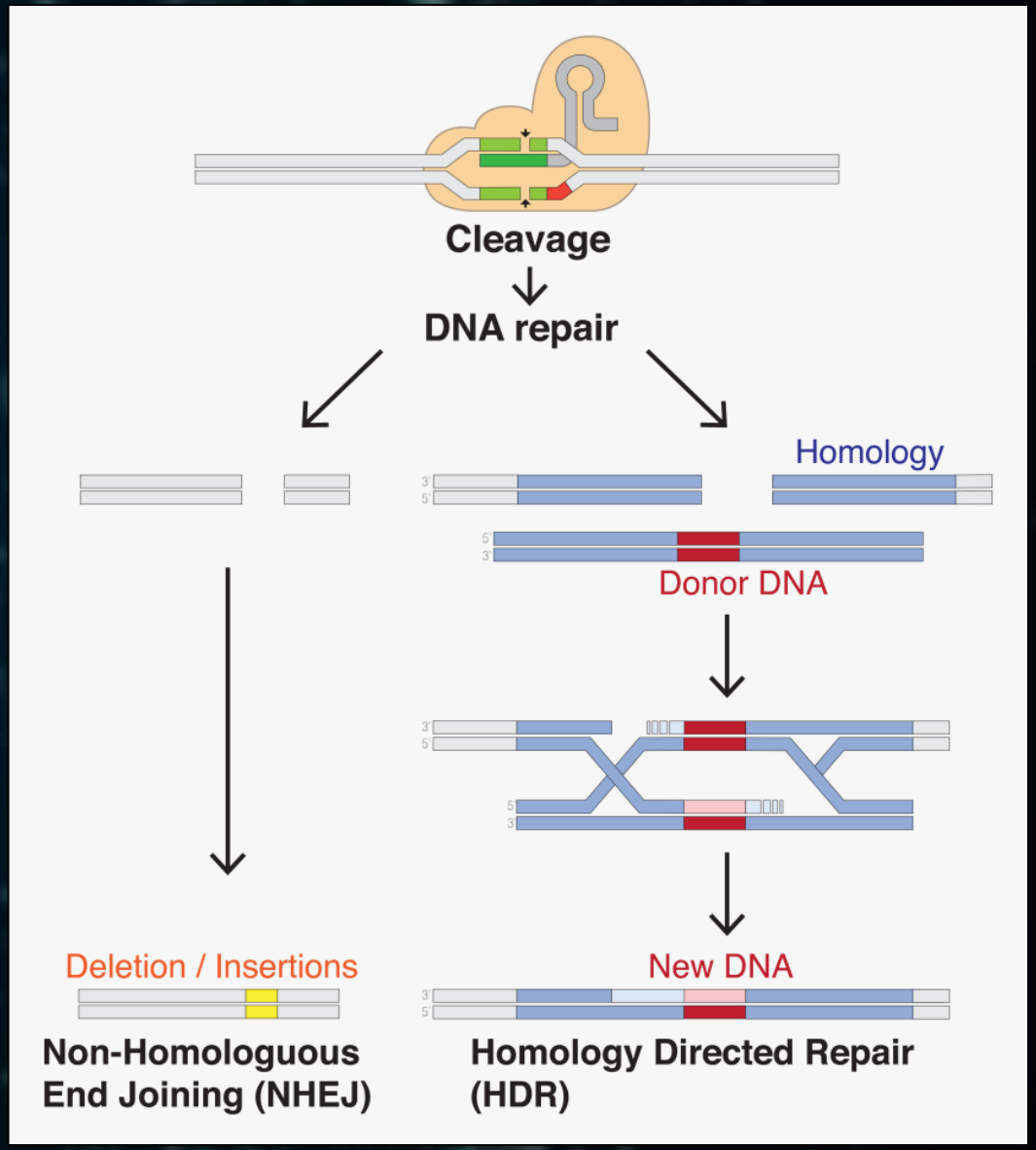


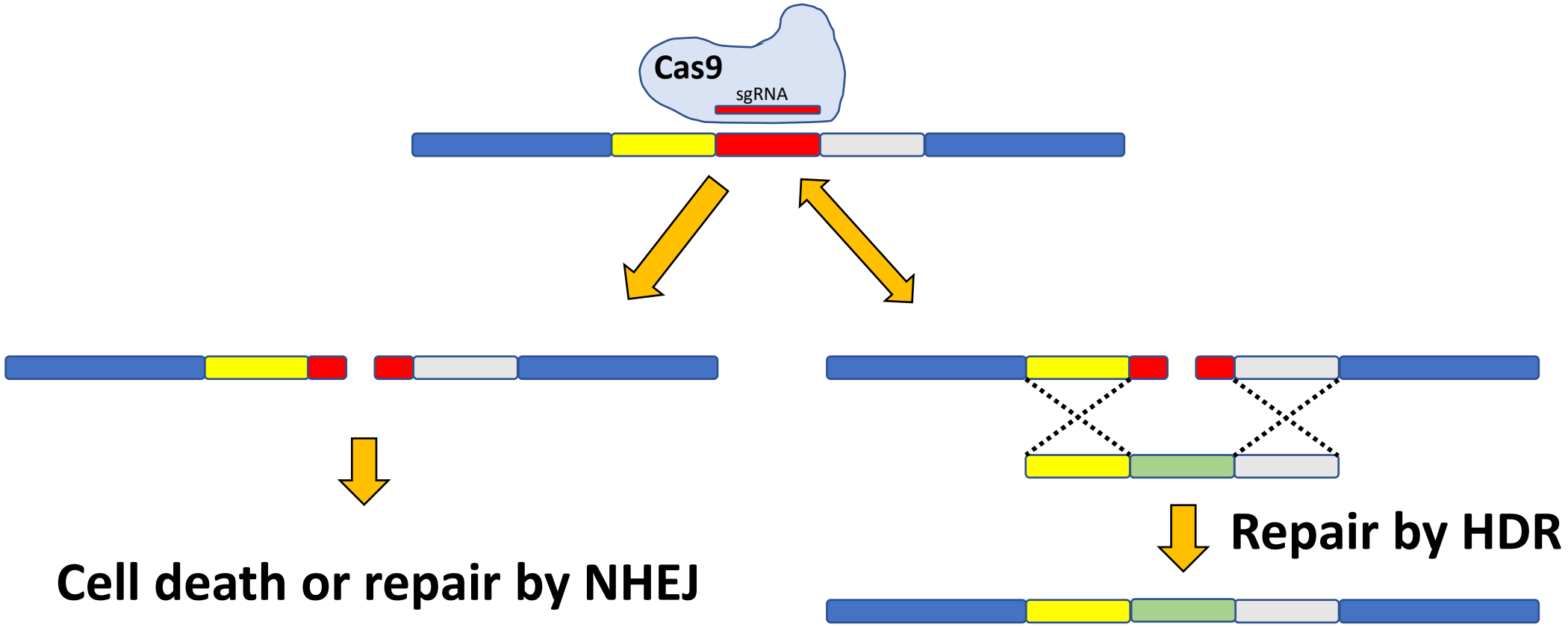
CRISPR-Cas als genetisch gereedschap

How does cleaving DNA help with editing the DNA?

CRISPR-Cas als genetisch gereedschap

CRISPR-Cas
counter-selects
against the
wild-type allele
and stimulates
DNA repair




Cas9
sgRNA
Cell death or repair by NHEJ
Repair by HDR

CRISPR-Cas als genetisch gereedschap

CRISPR-edited cells, plants & animals

June 2012
CRISPR–Cas9 invented

2013

2014

2015

?
?
?
?

CRISPR-Cas als genetisch gereedschap

Gene editing

Epigenetics

(Source: Kurzgesagt)

Other…

Diagnostics

CRISPR-Cas als genetisch gereedschap

Gene editing

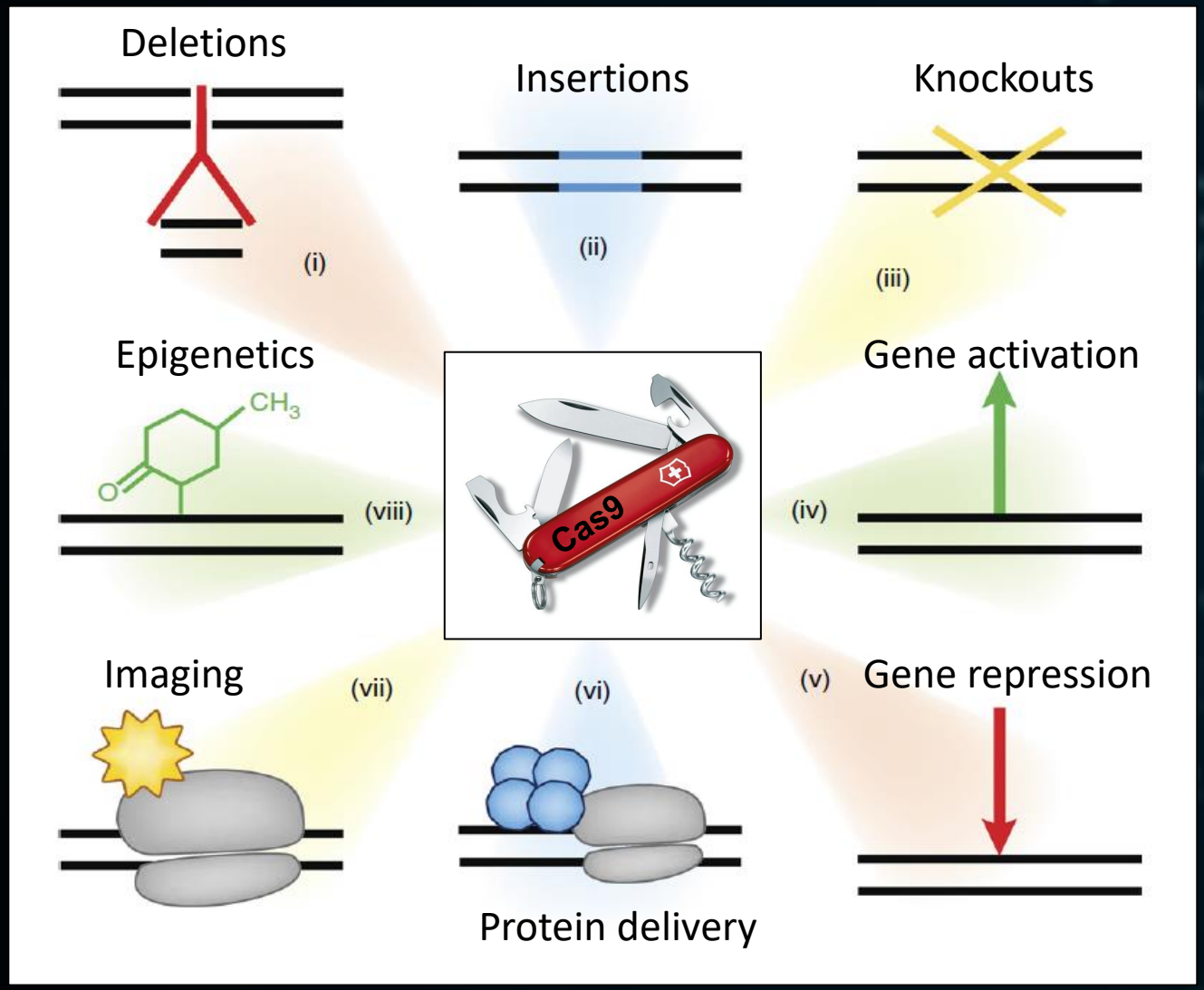
Epigenetics

(Source: Kurzgesagt)

Other…

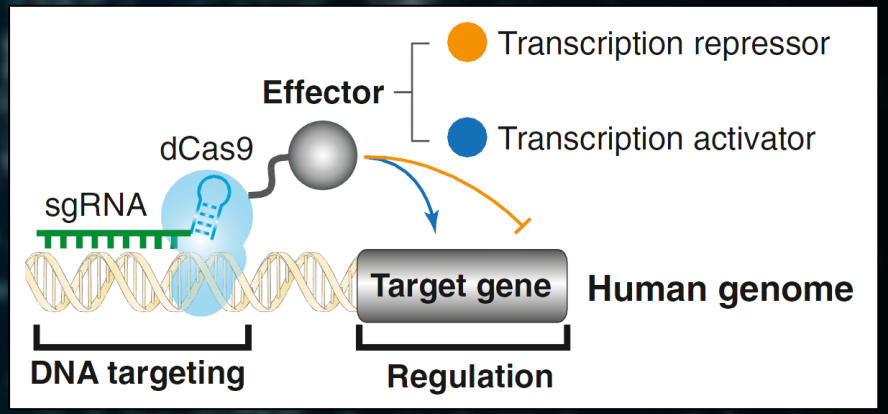
Diagnostics

CRISPR-Cas als genetisch gereedschap



(Barrangou & Doudna, Nat Biotechnol. 2016)

Epigenetics



CRISPR-Cas als genetisch gereedschap

Gene editing

Epigenetics

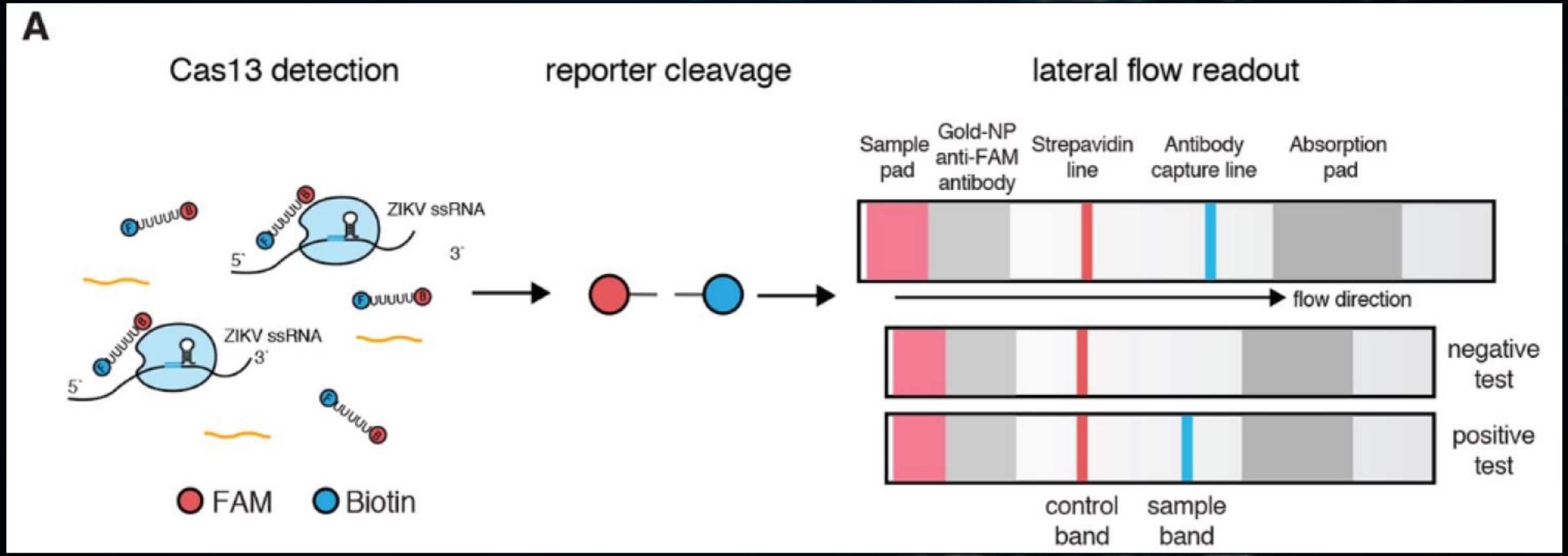
(Source: Kurzgesagt)

Other…

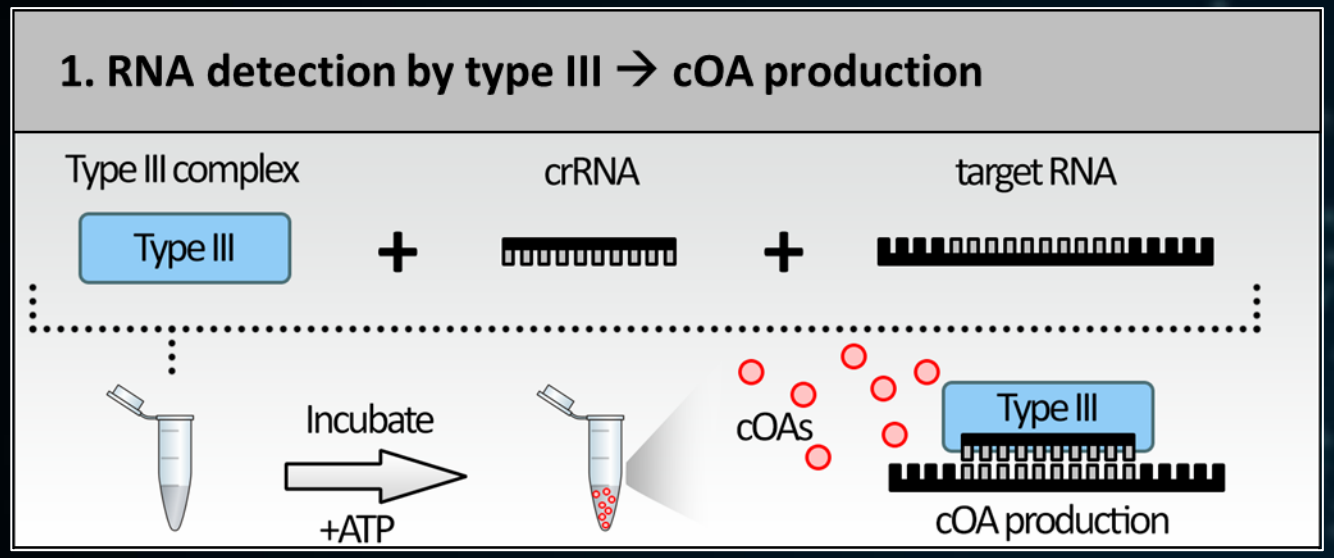
Diagnostics

CRISPR-Cas als genetisch gereedschap

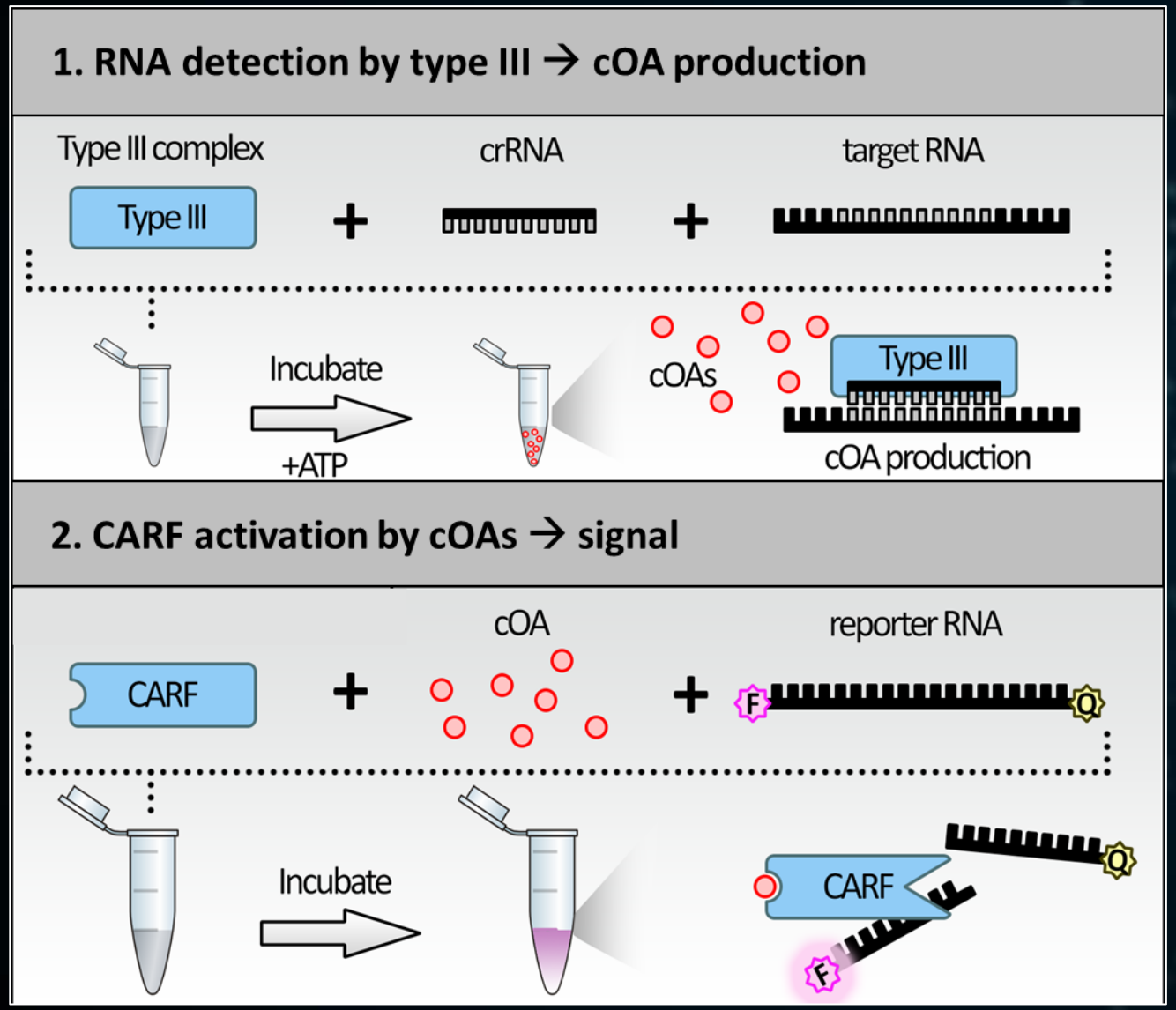
Diagnostics



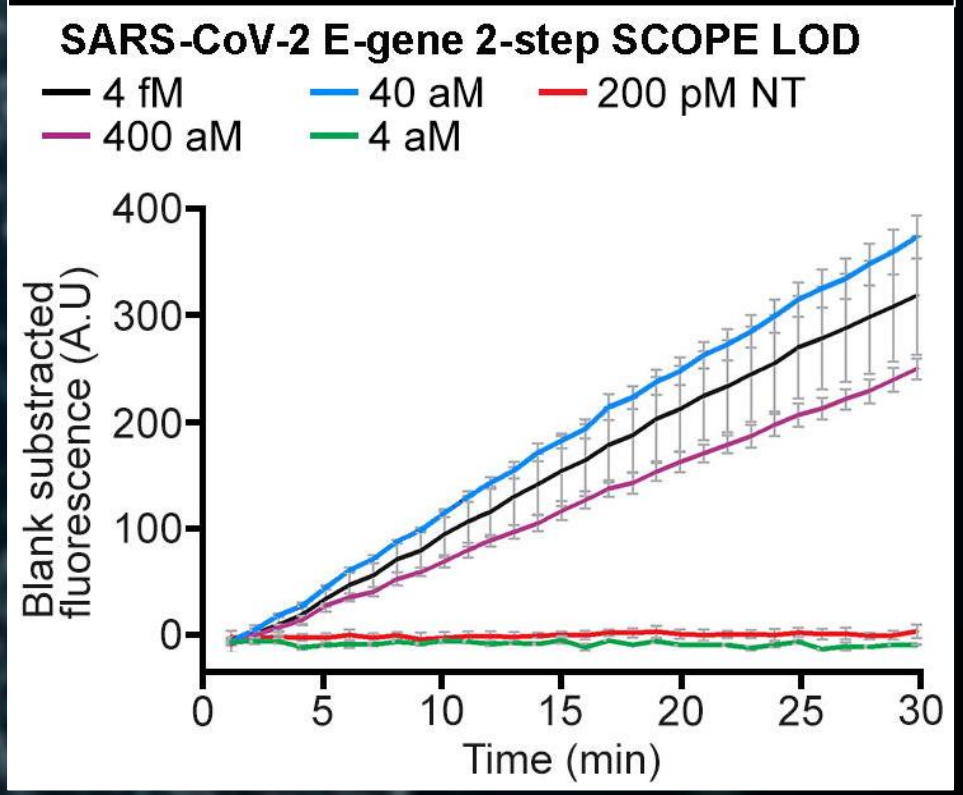
CRISPR-Cas als genetisch gereedschap



CRISPR-Cas als genetisch gereedschap



scope biosciences



(Steens *et al.*, Nature Communications 2021)

CRISPR-Cas als genetisch gereedschap

CRISPR diagnostic company Scope Biosciences raises €1M funding in a partnership with GenDx

November 5, 2021

WAGENINGEN, 29th October 2021 – Diagnostic startup company Scope Biosciences B.V. has raised €1M funding from Utrecht based GenDx, specialized in Next Generation Sequencing (NGS) products for transplant diagnostics.

1. RNA dete
Type III complex
Type III
2. CARF acti
CARF

OPE LOD
pM NT
20 25 30
Time (min)

(Steens *et al.*, Nature Communications 2021)

CRISPR-Cas als genetisch gereedschap

Gene editing

Epigenetics

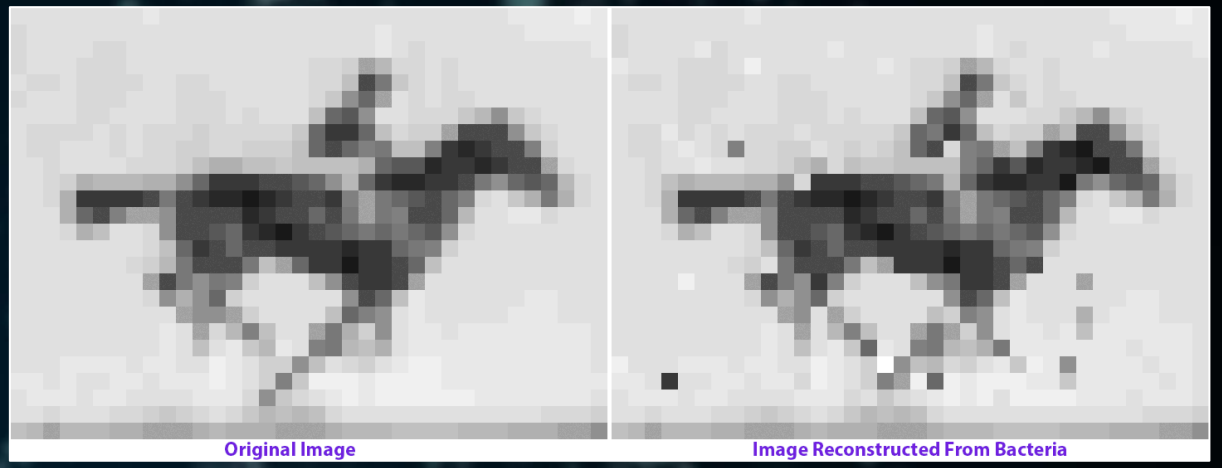
(Source: Kurzgesagt)

Other…

Diagnostics

CRISPR-Cas als genetisch gereedschap

- Molecular recording
- Reviving extinct species
- ‘Hybrid’ species
- Gene drives (!)



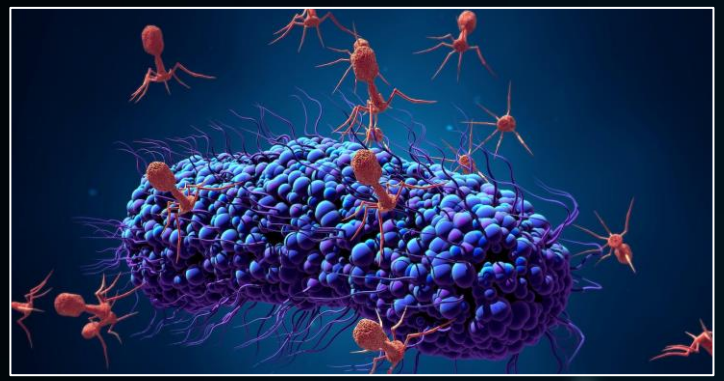
(First movie recorded on a bacterial genome using CRISPR-Cas)

(Mammoth revival project - Colossal Biosciences)

(Pyrenean ibex)

(‘Woolly Mouse’ with mammoth-like traits)

Onderwerpen



Oorsprong CRISPR-Cas

CRISPR-Cas als
genetisch gereedschap

Impact op de maatschappij

Impact op de maatschappij

Healthcare

Environment

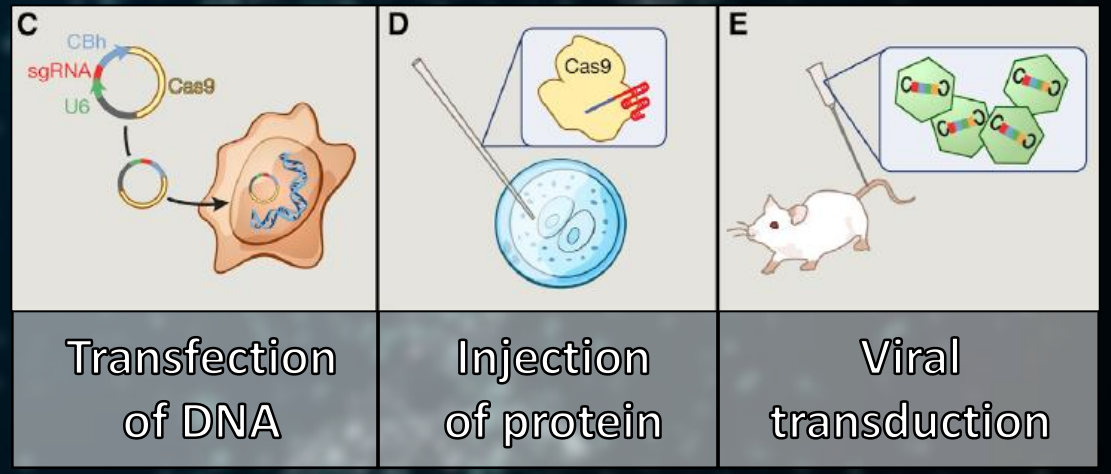
Agriculture & food

Ethics & legislation

Healthcare

- ✓ Personalized medicine
- ✓ Germline editing
- ✓ Diagnostics
- × Delivery
- × Off-targeting
- × Ethics / legislation

Delivery methods



Healthcare

BIOMEDICINE

Tweaking genes with CRISPR or viruses fixes blood disorders

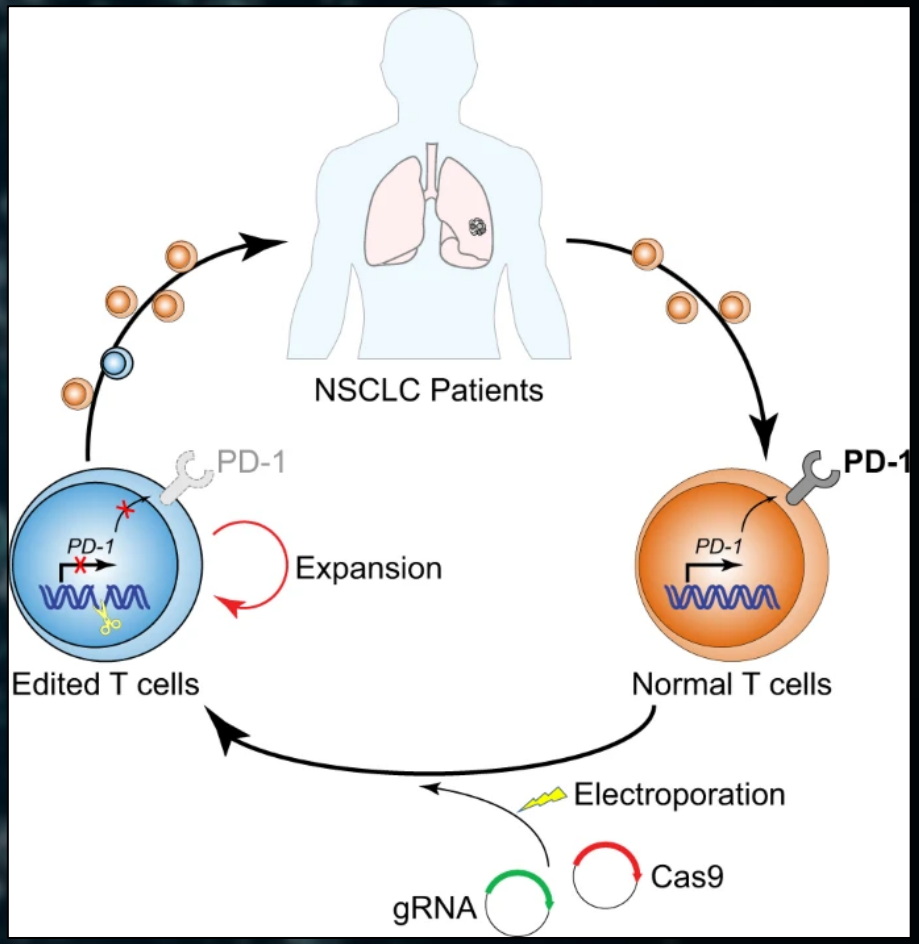
People with sickle cell disease or beta-thalassemia could be freed of debilitating symptoms for a lifetime

Dec 2020

UK first to approve CRISPR treatment for diseases: what you need to know

The landmark decision could transform the treatment of sickle-cell disease and β-thalassaemia – but the technology is expensive.

Nov 2023



Healthcare

Menu | Amsterdam UMC

Amsterdam UMC
Universitair Medische Centra

Zoek

Vandaag

24 mei 2022

Eerste Nederlandse patiënt behandeld met CRISPR-Cas9-infuus

Innovatie | Patiëntenzorg | Zeldzame ziekten | Genen

De eerste behandeling met CRISPR-Cas9-infuus in Amsterdam UMC is een feit! Na vier uur aan het infuus kon de patiënt, die een ernstige vorm heeft van het hereditair angio-oedeem (HAE), nog dezelfde dag naar huis. Wereldwijd is hij de vijfde patiënt met HAE die deze nog experimentele behandeling mocht ondergaan. Internist en onderzoeksleider Danny Cohn volgde het proces vanaf Bonaire, waar hij tijdelijk is gedetacheerd.

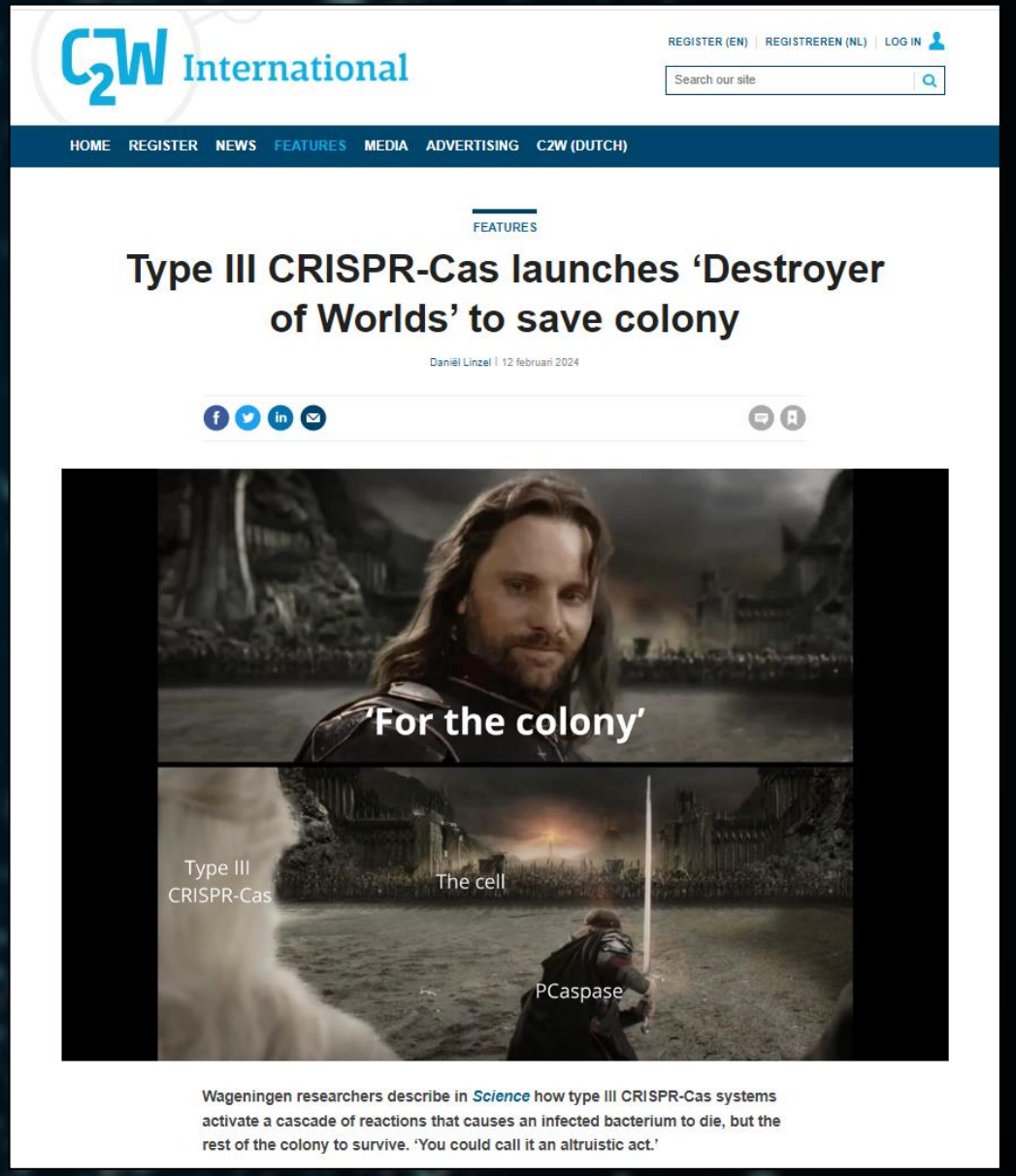
Deel dit

Onderzoeksprofiel
Danny M. Cohn

Onderzoeksinstituut

Healthcare

"Type III-B CRISPR-Cas cascade of proteolytic cleavages"
(Steens *et al.*, Science 2024)

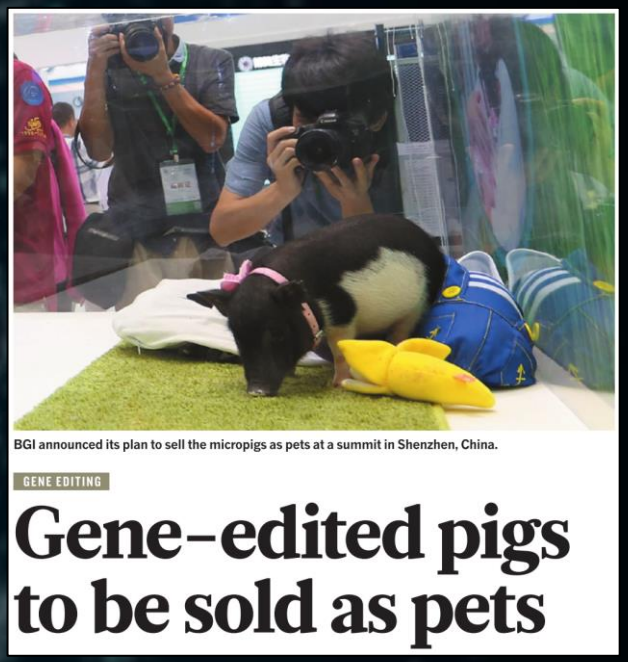


Agriculture & food

- ✓ Climate-resilient crops
- ✓ Higher yields, less pesticides
- ✓ Speed breeding
- ✓ Biotechnology / fermentation
- × GMO?
- × (European) legislations
- × Patents & malpractices

Bioreactor

Agriculture & food



SCIENCEINSIDER | EUROPE

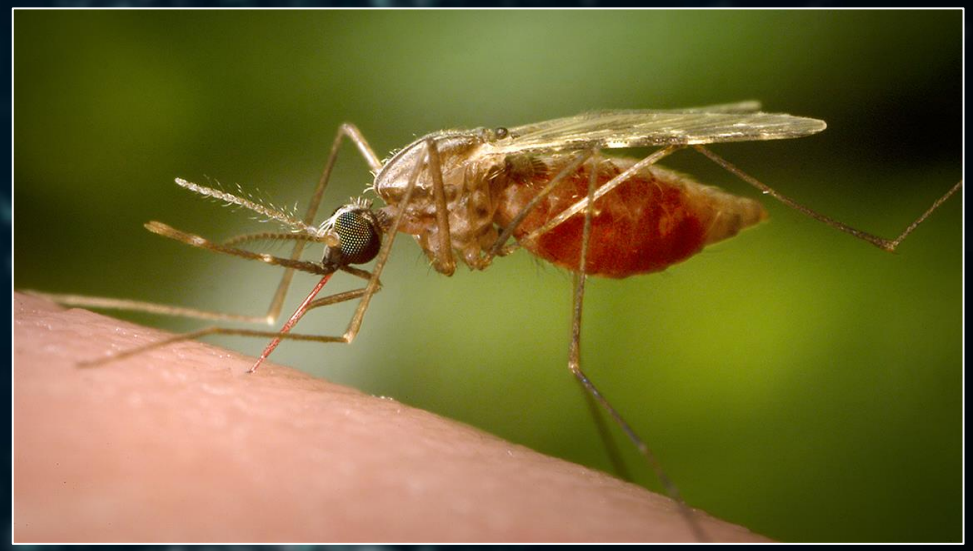
European Parliament votes to ease regulation of gene-edited crops

Move is a major victory for biotechnology, but debate remains over patents and labels

7 FEB 2024 • 6:20 PM ET • BY ERIK STOKSTAD

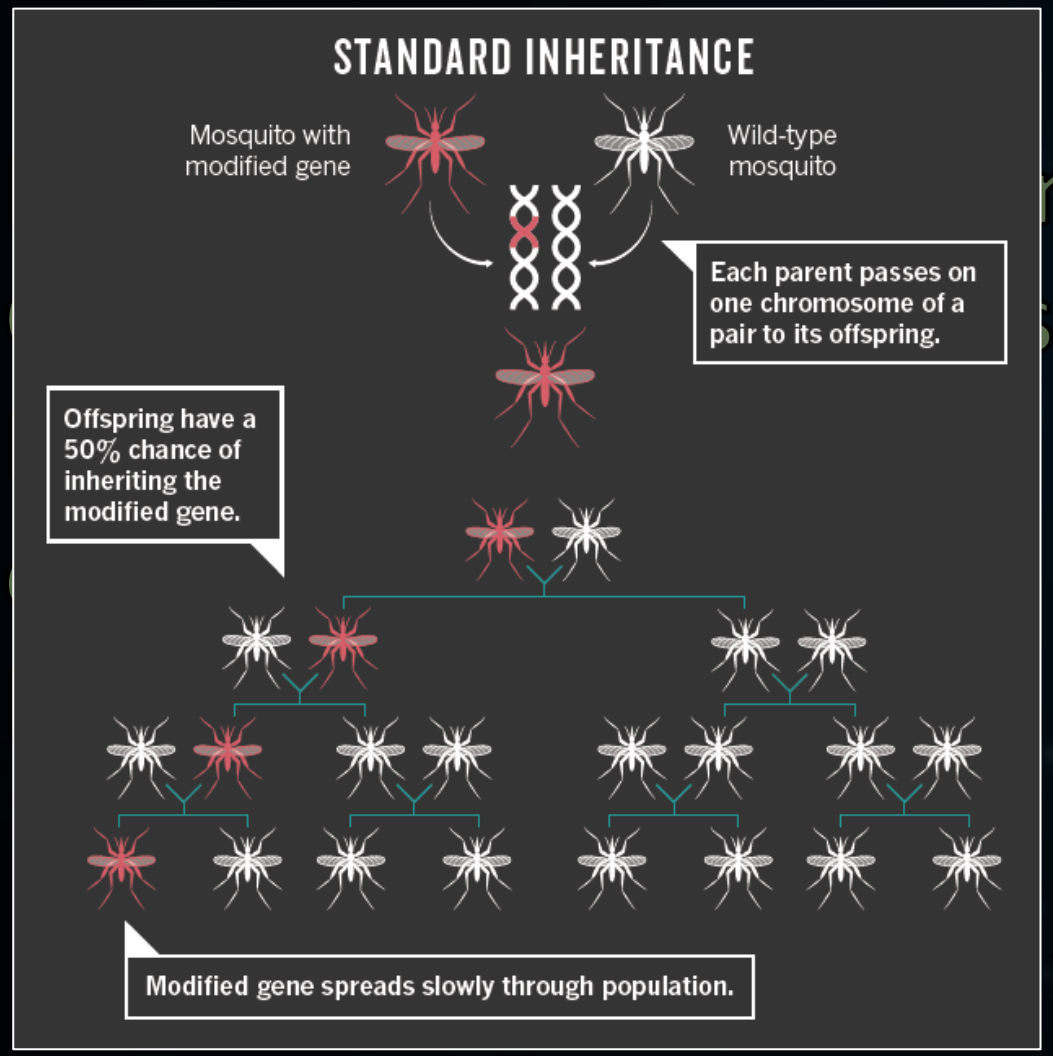
Environment

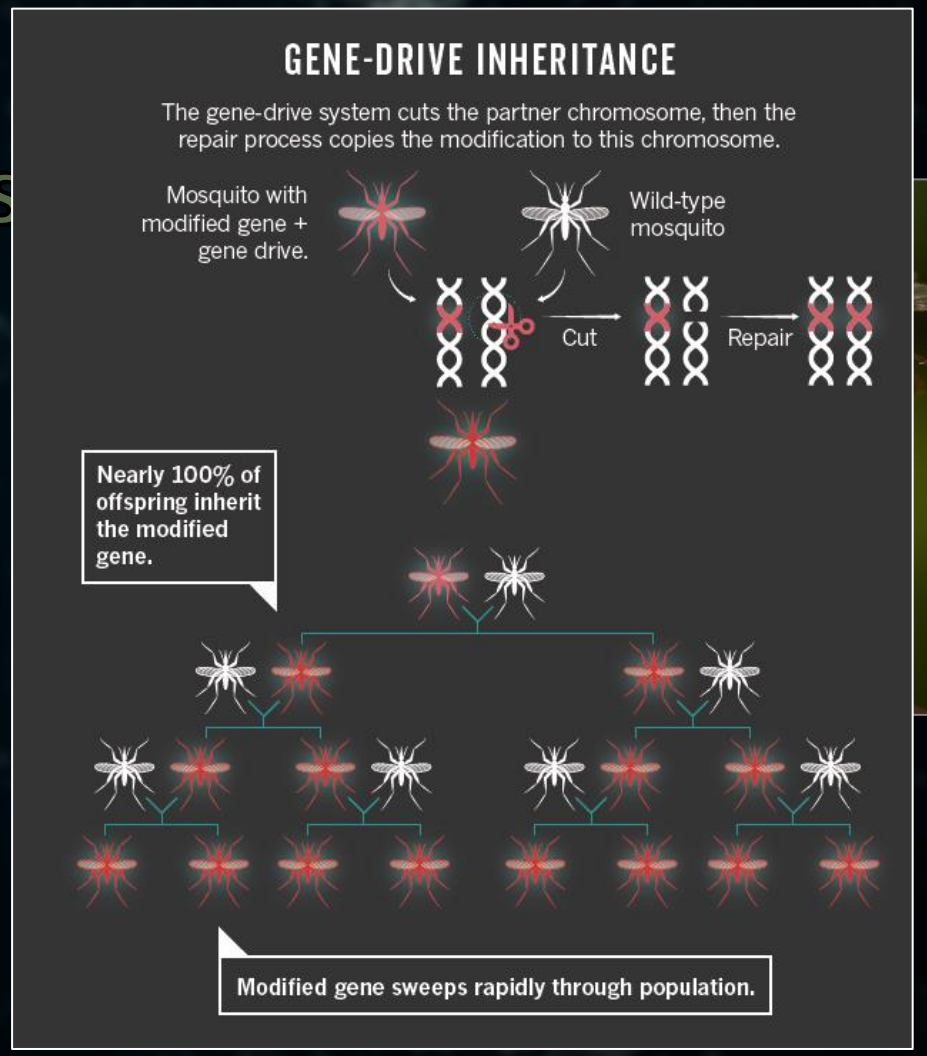
- ✓ More resilient ecosystems
- ✓ Control invasive species
- ✓ Eradication of disease-carrying pests
- × Ecological (in)balance

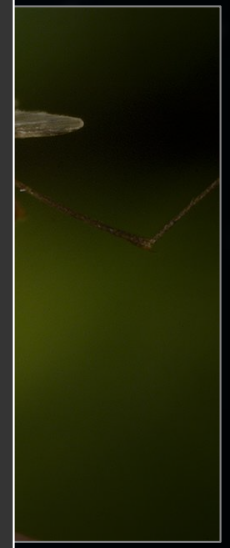


Environment

Gene Drives







Ethics & legislation

Where do we draw the line?

GENETICS

Embryo editing divides scientists

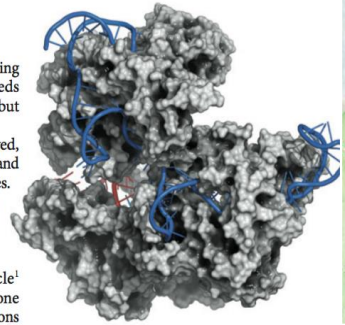
Researchers disagree over whether making heritable changes to genes crosses an ethical line.

BY DAVID CYRANOSKI

Research that uses powerful gene-editing techniques on human embryos needs to be restricted, scientists agree — but they are split over why.

Some say that if safety fears can be allayed, such applications could have a bright future, and could help to eradicate devastating diseases. Others say that modifying the DNA of embryos, which means that the changes could be passed on to future generations, is an ethical line that should not be crossed.

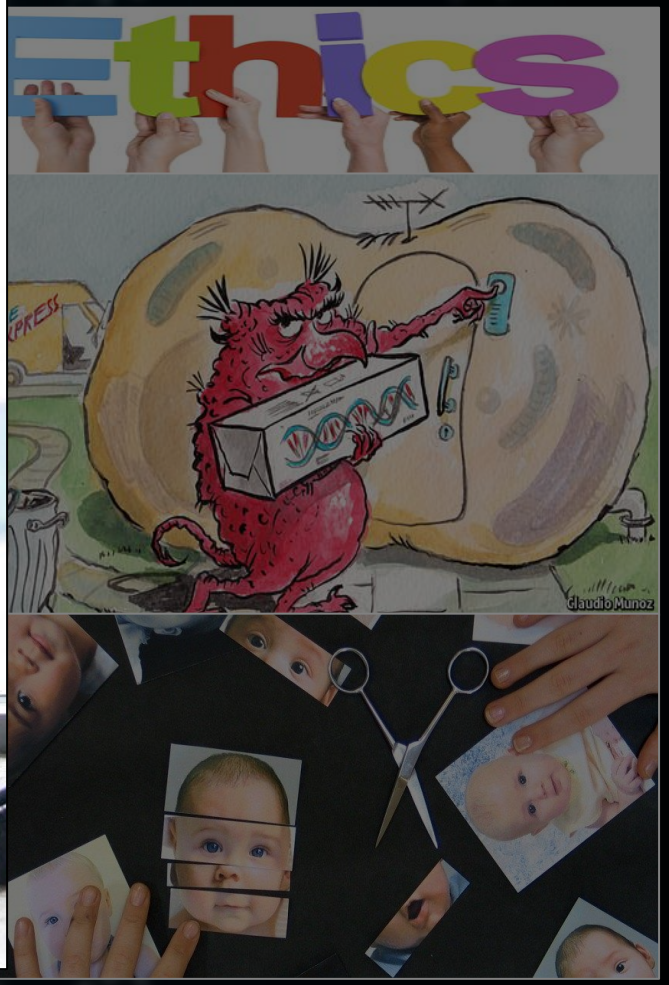
The concerns are laid out in an article[1] published in *Nature* on 12 March and in one expected to appear in *Science*, amid suspicions that scientists have already edited the genes of human embryos.



CRISPR/Cas9 makes precisely targeted gene edits.

Ethics & legislation

Where do w
draw the
line?



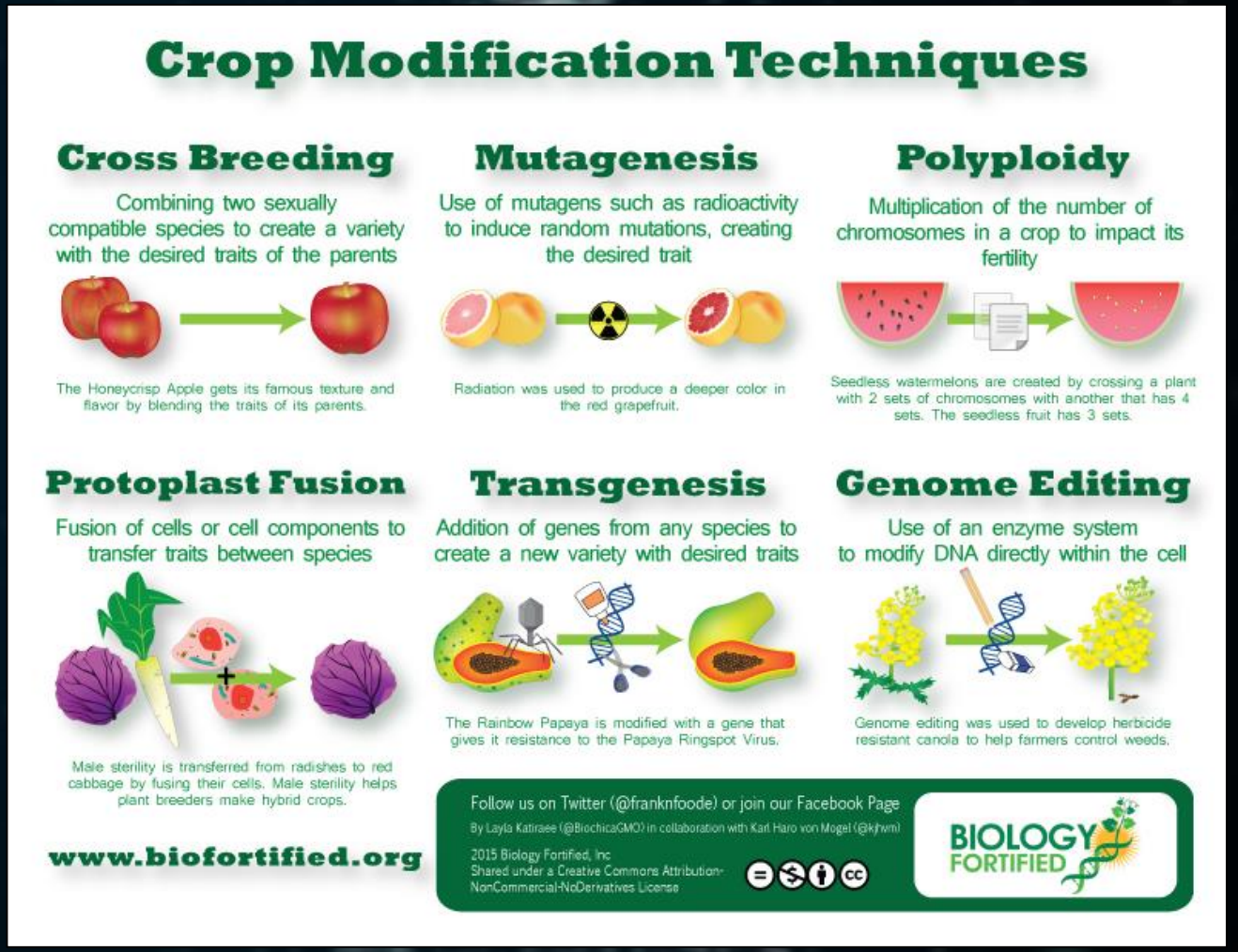
Ethics & legislation

Plant breeding

What IS a GMO?

Public perception

Accessibility



Take home messages

- CRISPR-Cas is an adaptive antiviral immune system in bacteria.
- CRISPR-Cas genome editing is a disruptive technology for many different fields
- Many technical, ethical and legislative hurdles still left to tackle

Questions?
Raymond.Staals@wur.nl

De impact van CRISPR-Cas op onze maatschappij

Raymond H.J. Staals
Associate Professor, Laboratory of Microbiology
Wageningen University & Research

8e Nationale Docentencongres Biologie