

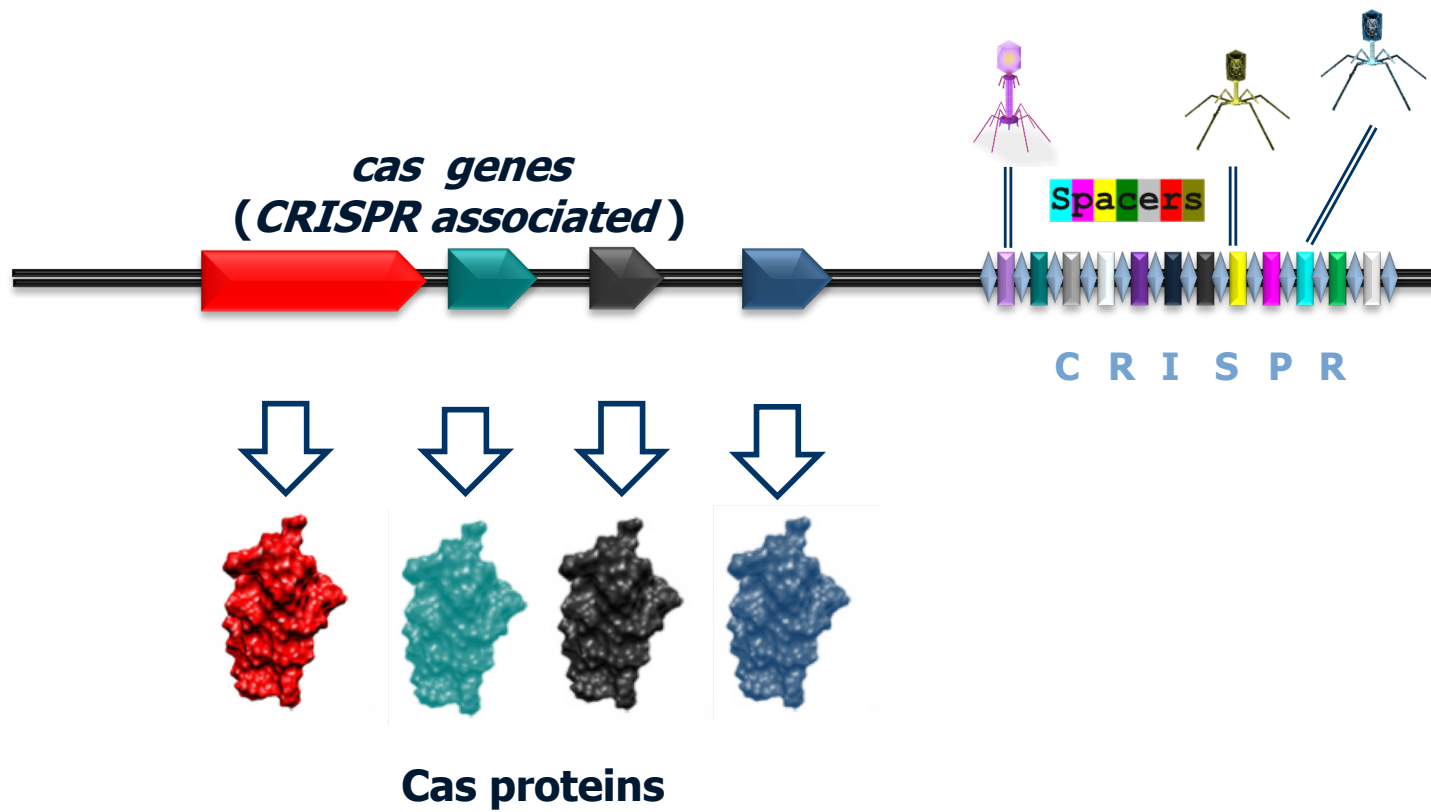
JORNADA NUEVAS  
TÉCNICAS DE  
MEJORA GENÉTICA



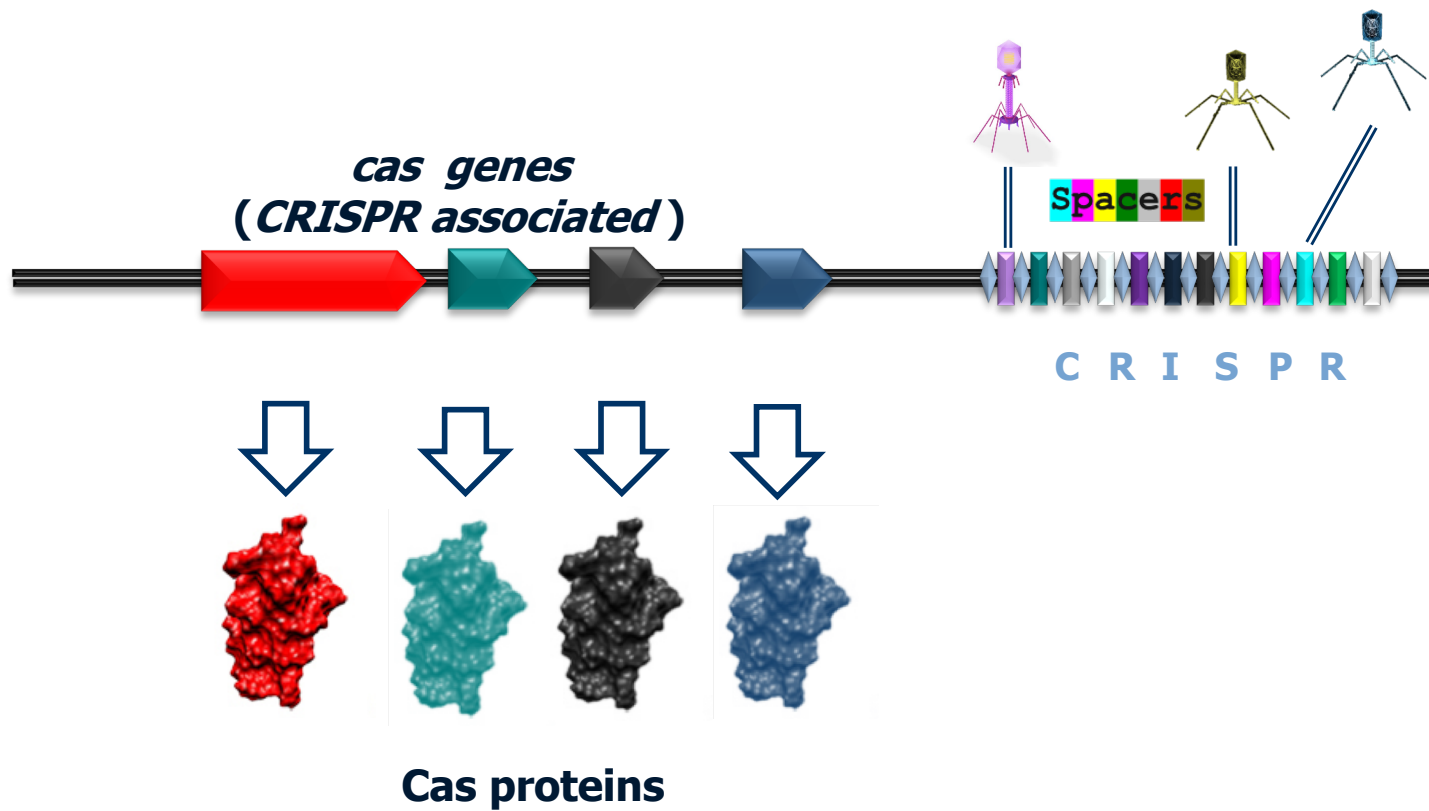
# The CRISPR-Cas system

Francisco J. M. Mojica

 Universitat d'Alacant  
Universidad de Alicante



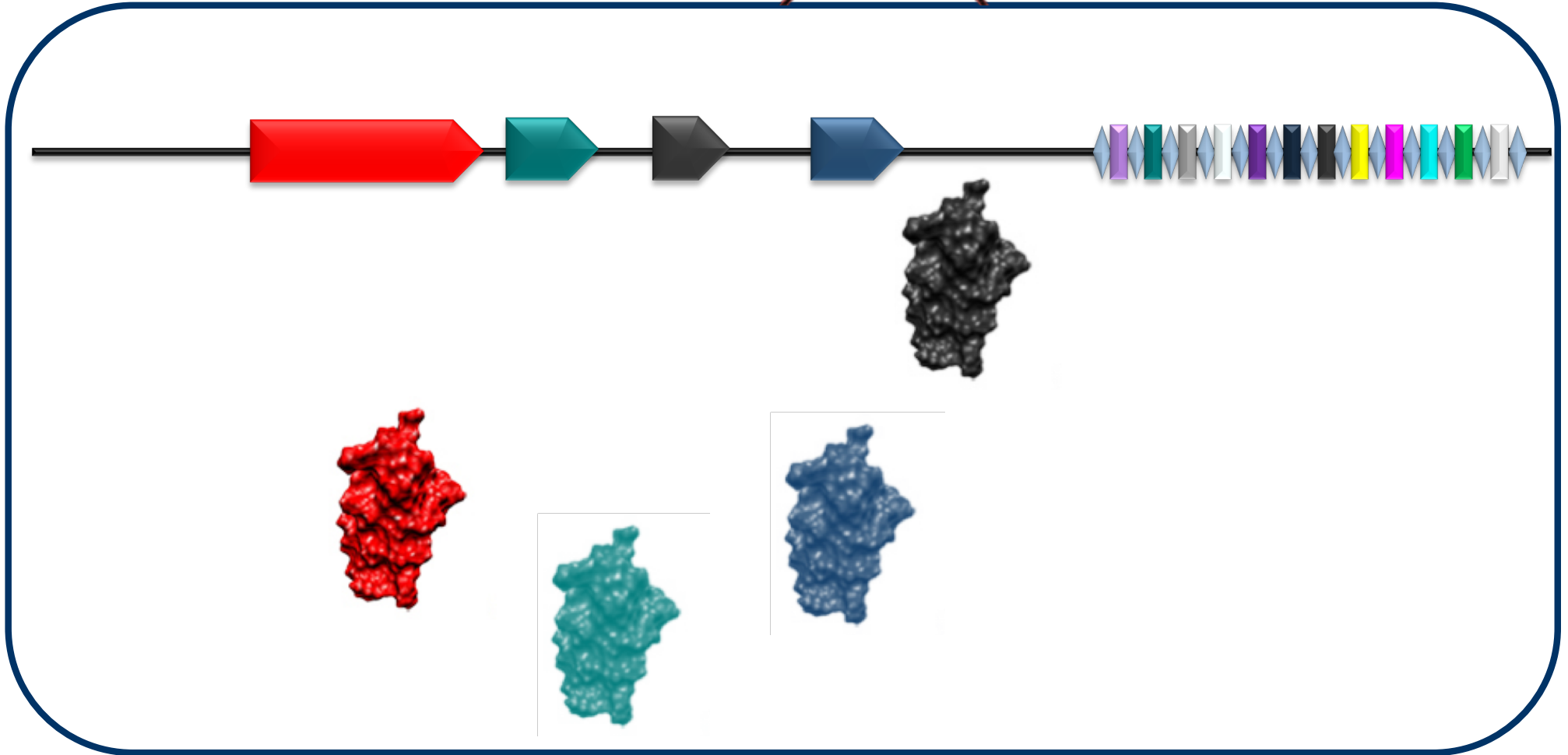
# CRISPR-Cas System



# CRISPR-Cas System

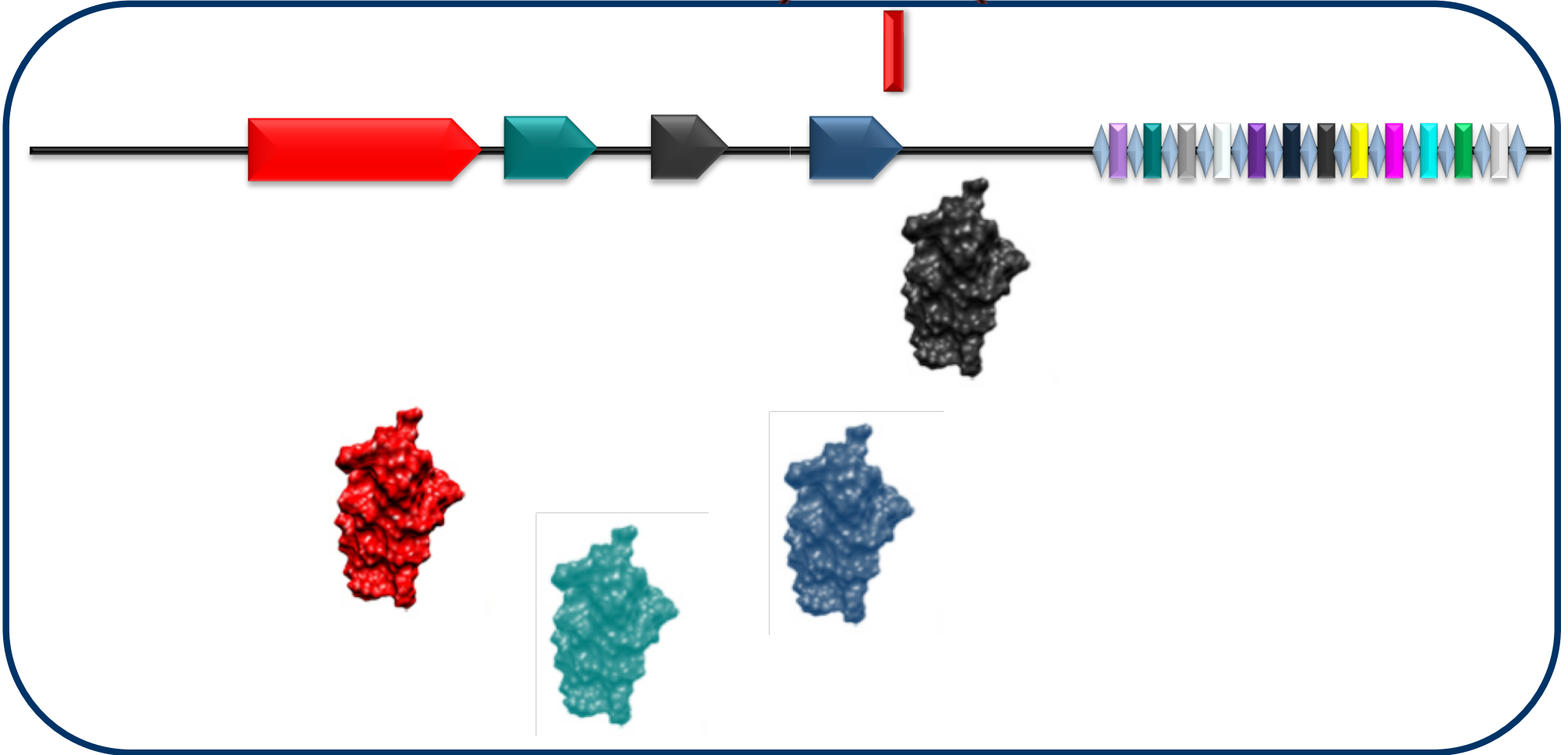
## Immunity

# Infection

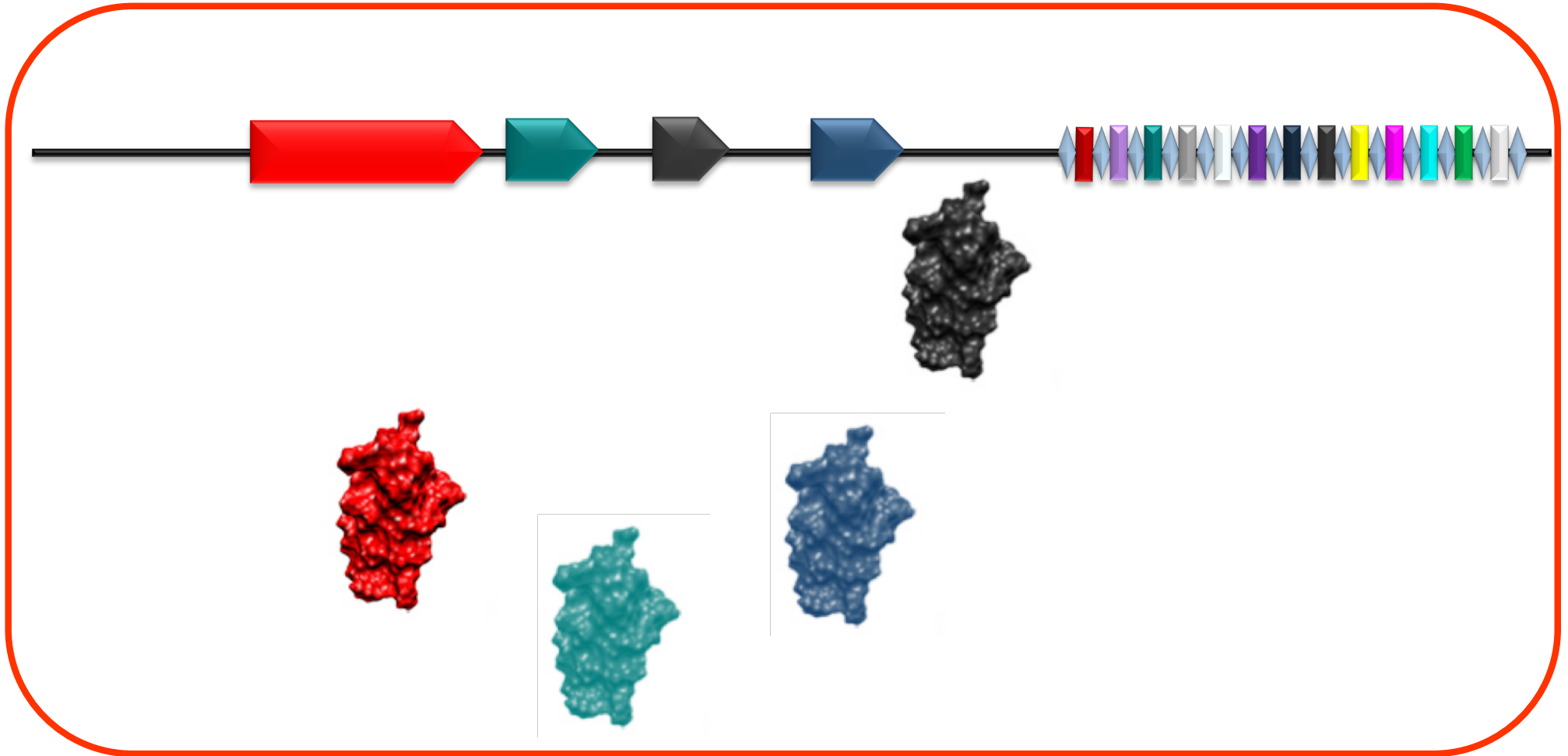




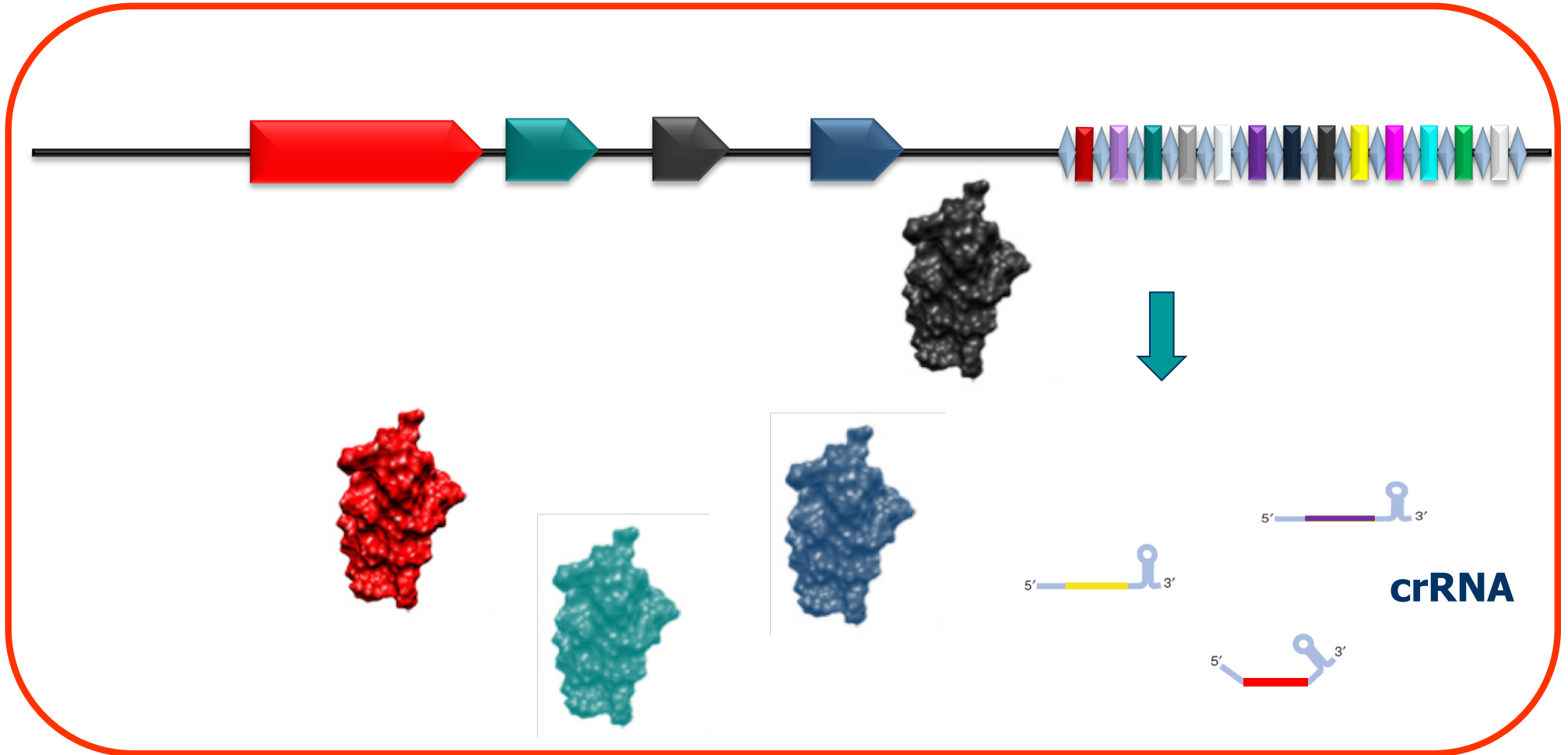
# Immunization



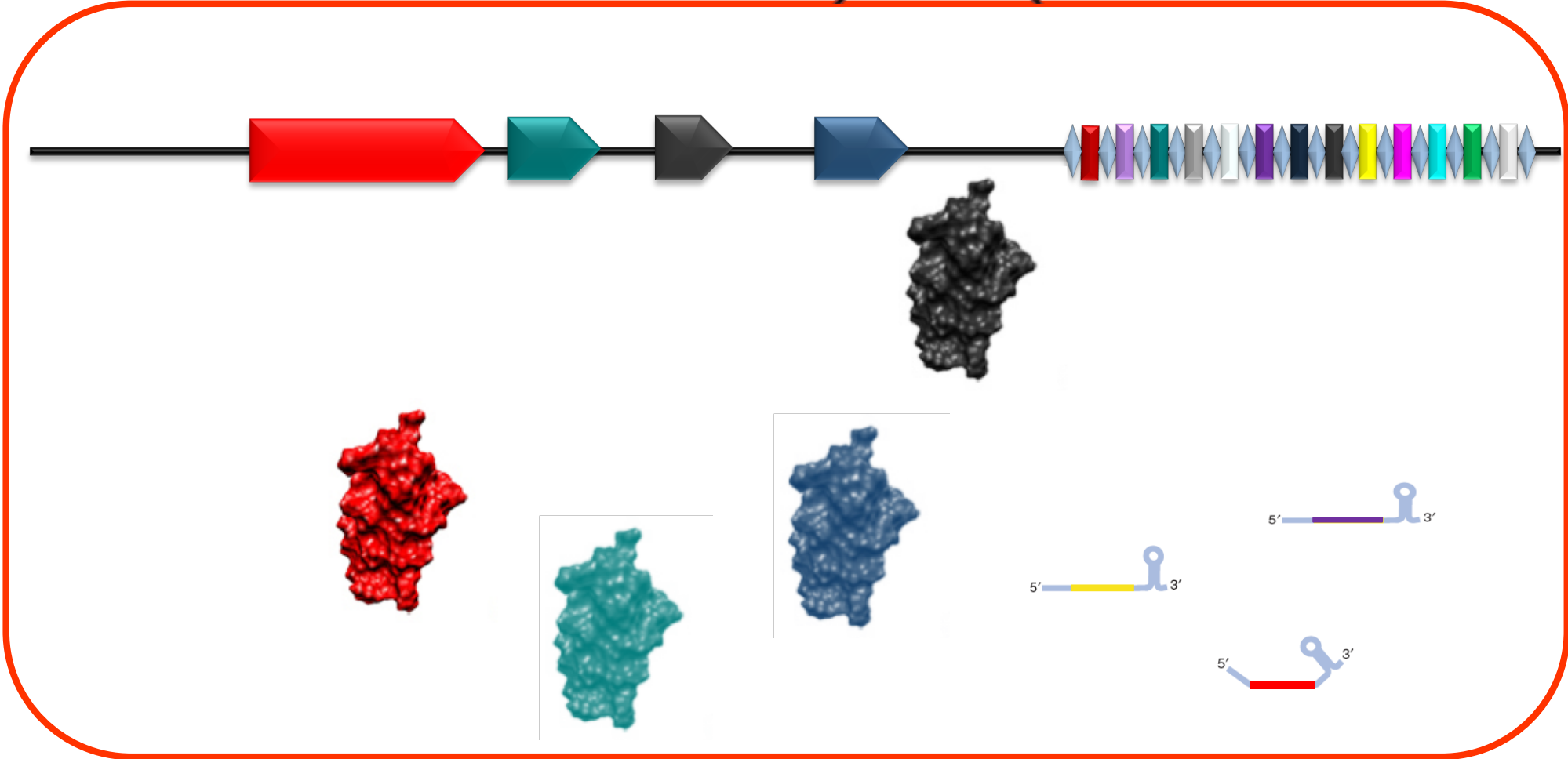
# Immunized Bacterium



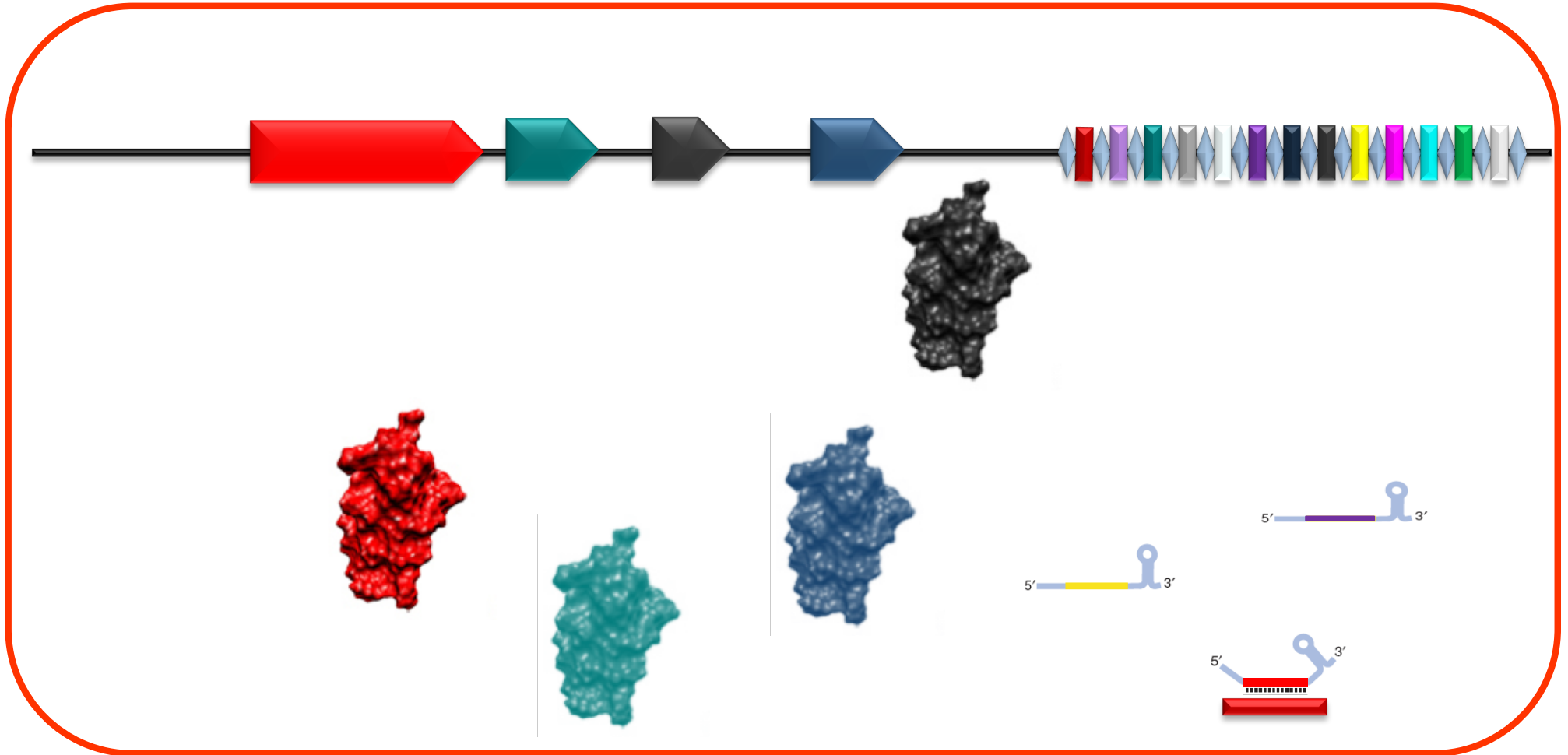
# Guides Production



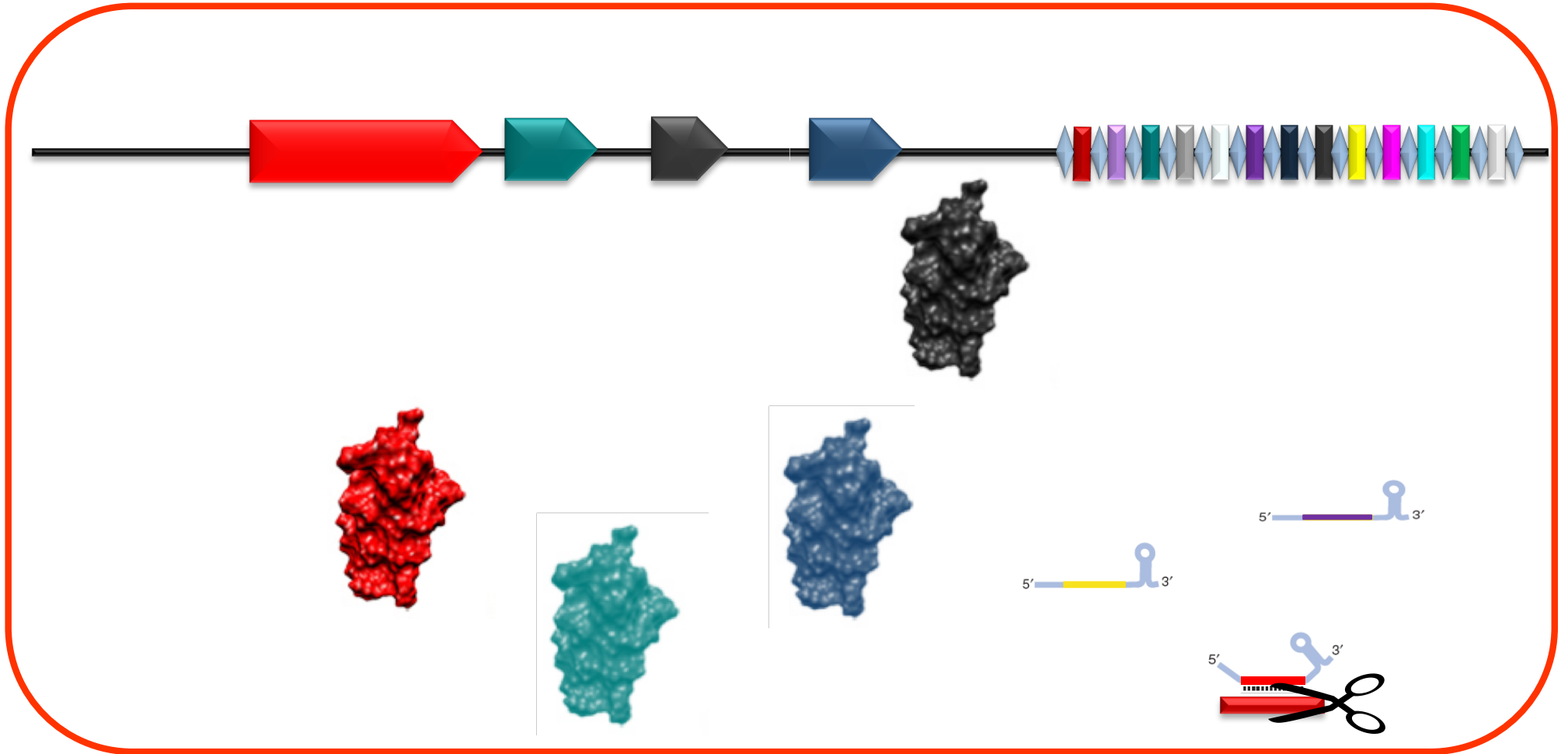
# Reinfection



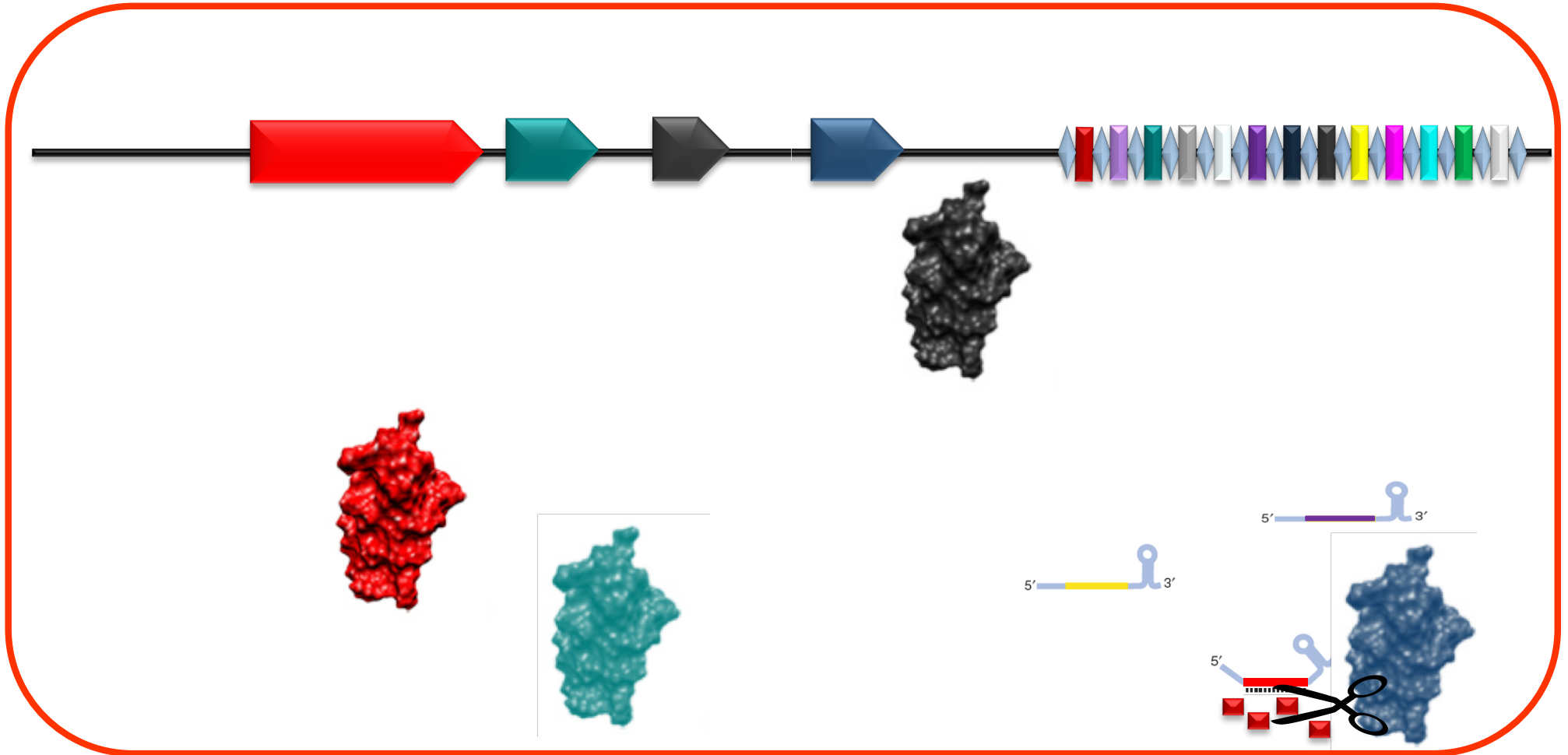
# Target Recognition



# Target Cleavage

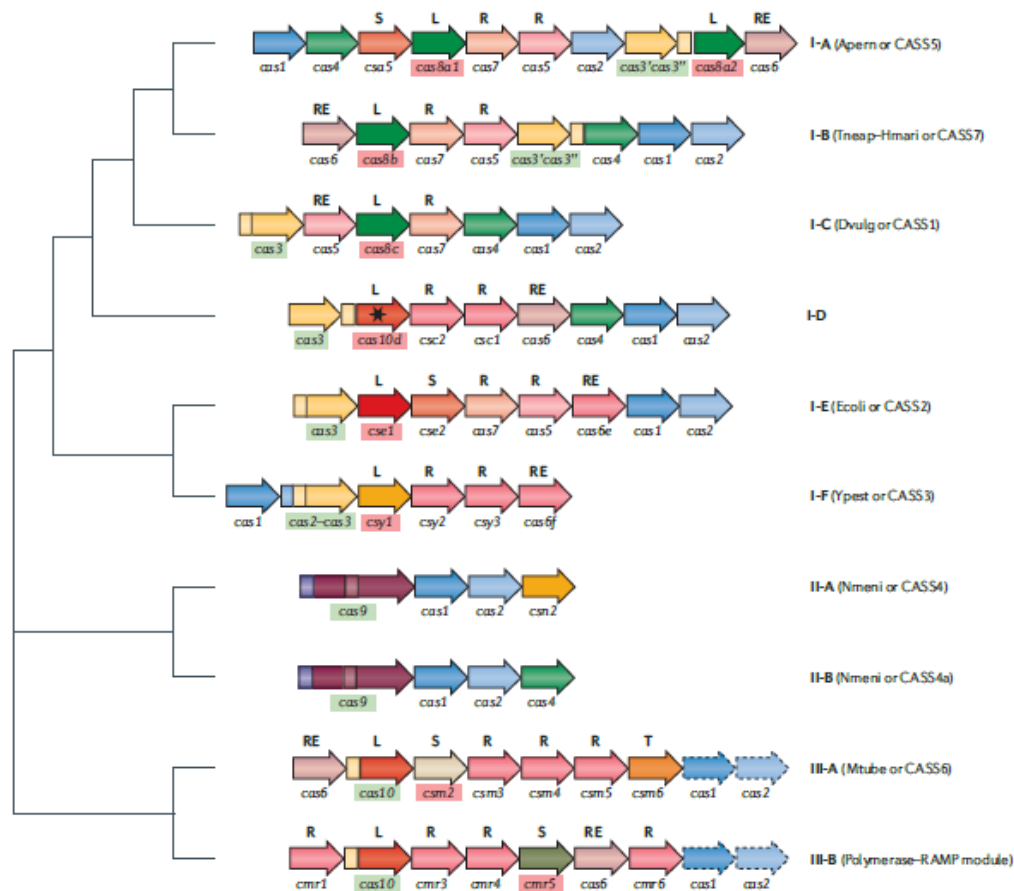


# Target Inactivation



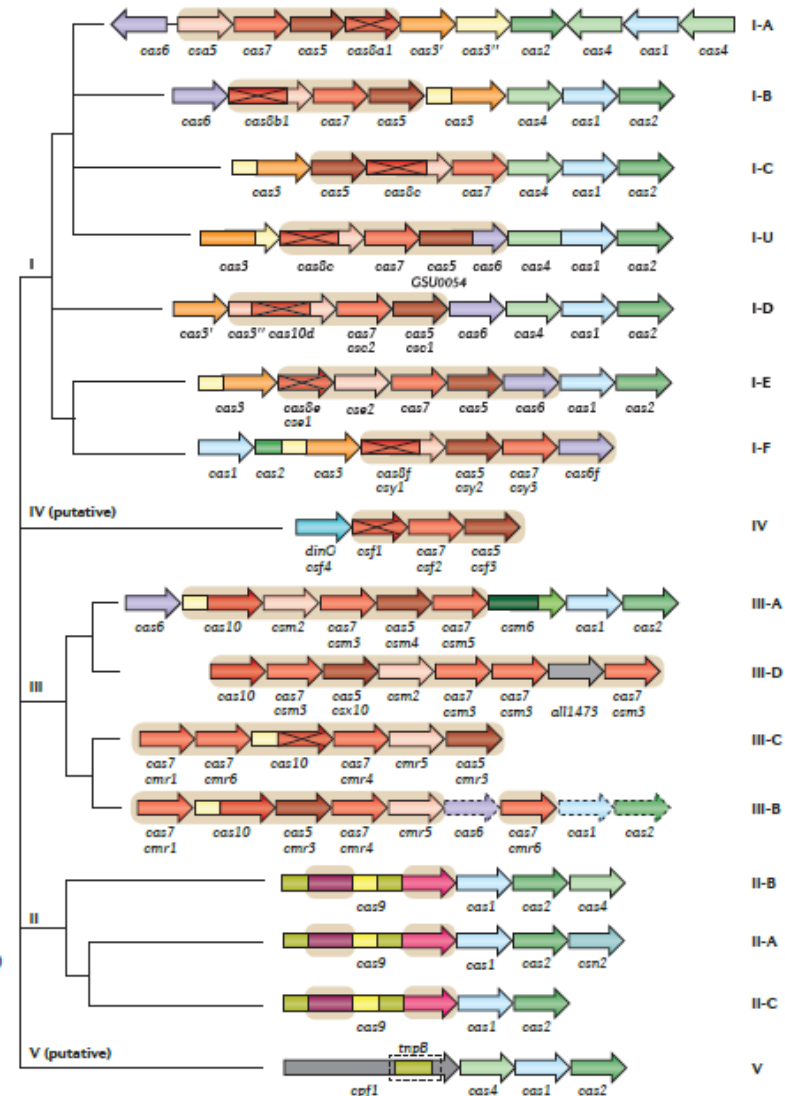
# Diversity of CRISPR-Cas

## 3 Types; 10 Subtypes



Makarova et al. Nat. Rev. Microbiol. 2011

## 5 Types; 16 Subtypes



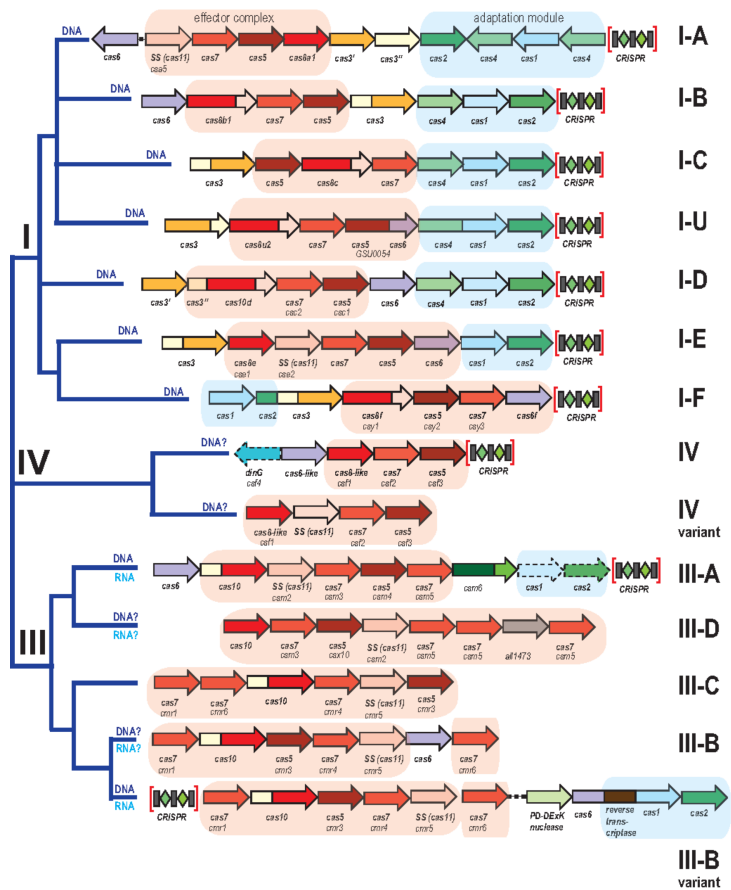
Makarova et al. Nat. Rev. Microbiol. 2015



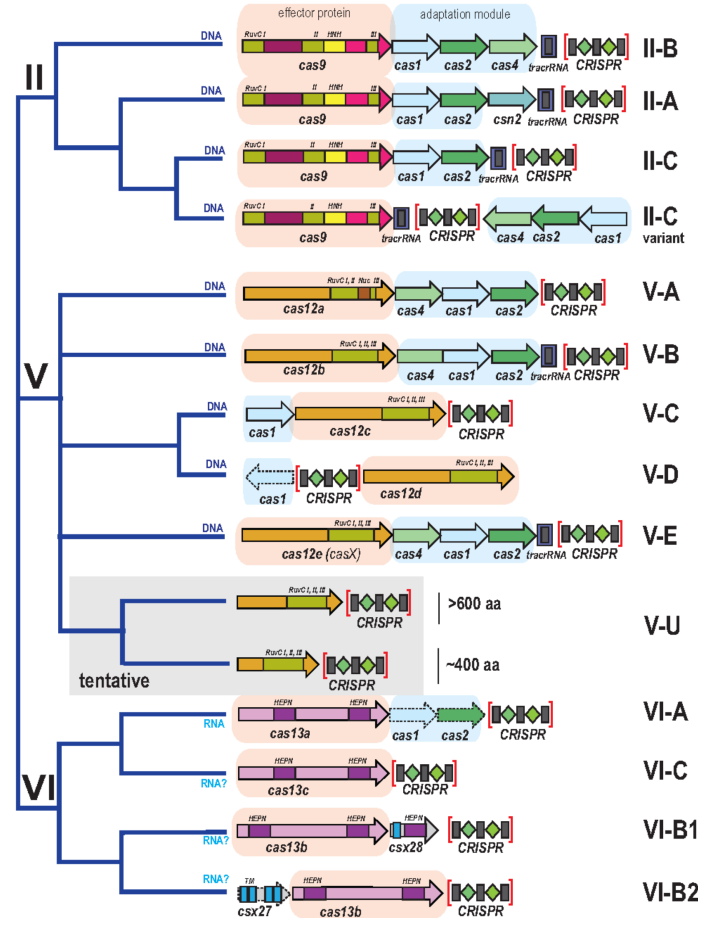
# Diversity of CRISPR-Cas

2 Classes; 6 Types; 30 Subtypes

## Class 1



## Class 2



# Applications of CRISPR-Cas in prokaryotes

# 1<sup>st</sup> Application (typing of pathogenic bacteria)

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**Isolate 1**



**Isolate 2**



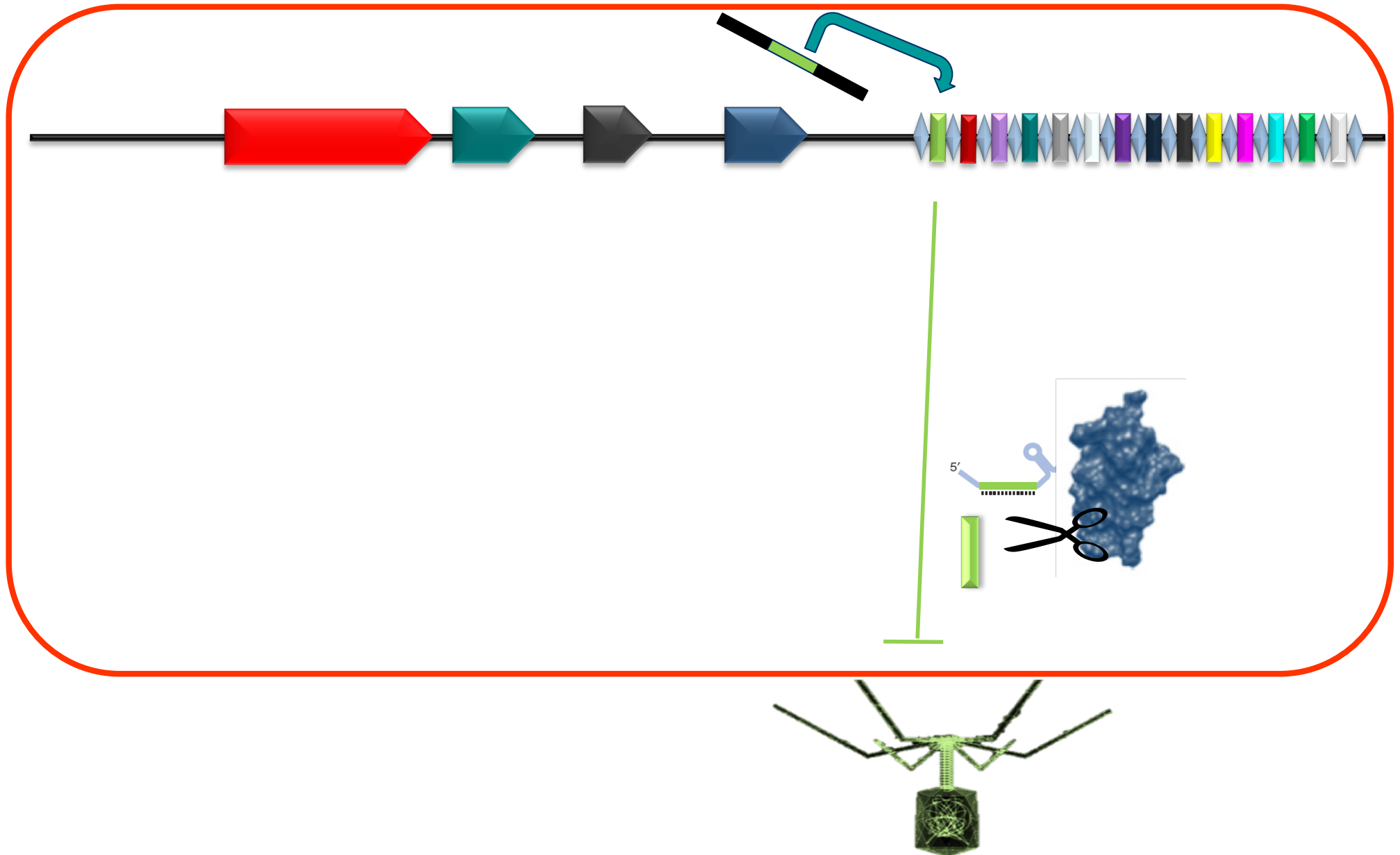
**Isolate 3**



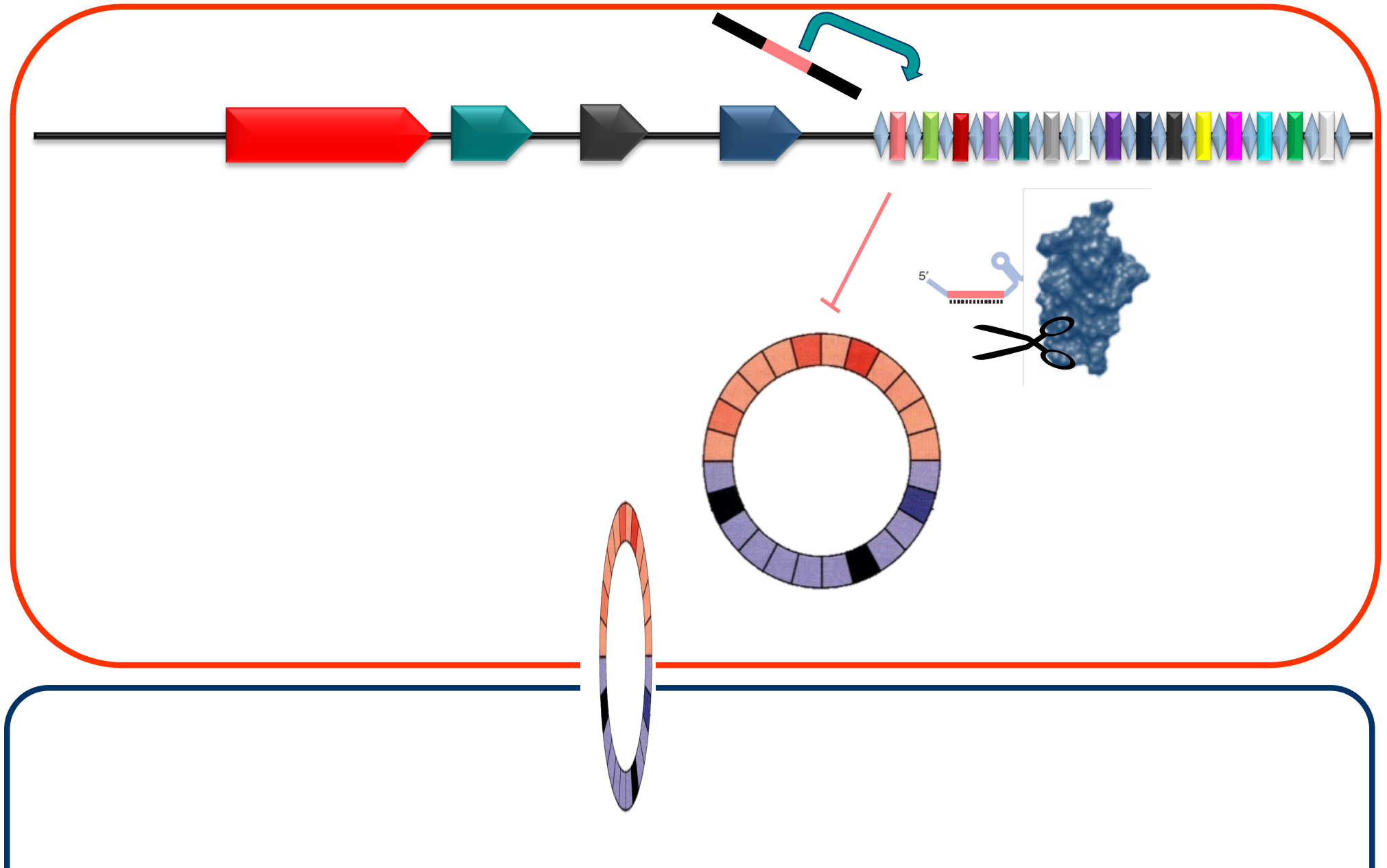
**Isolate 4**



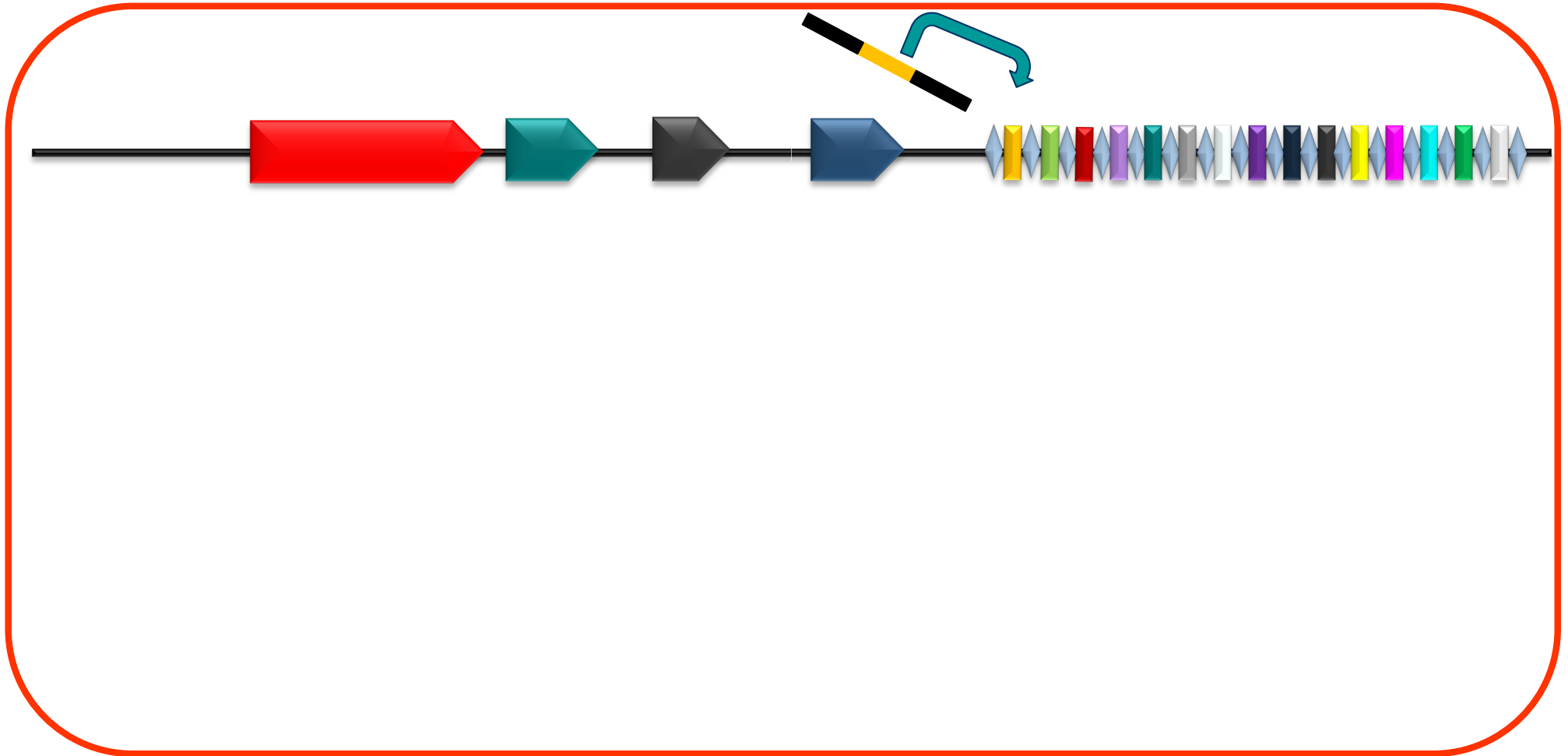
# Protection

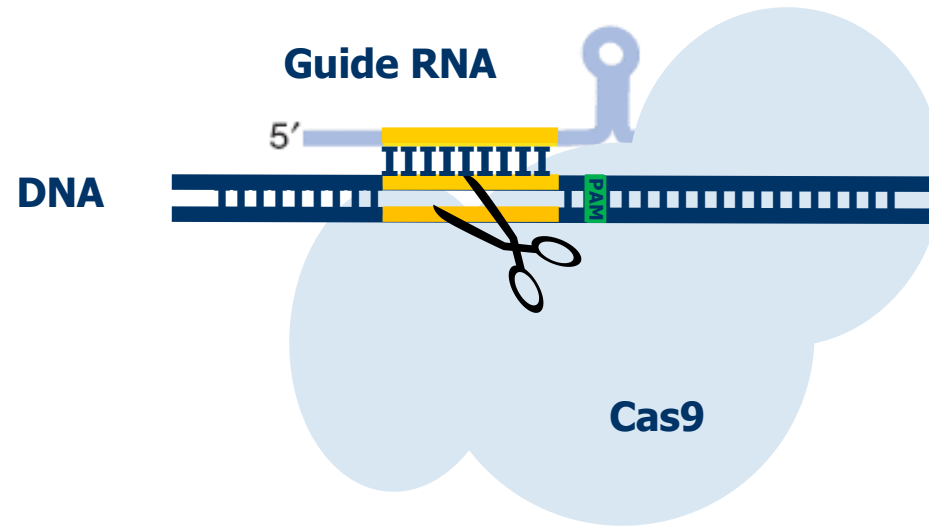
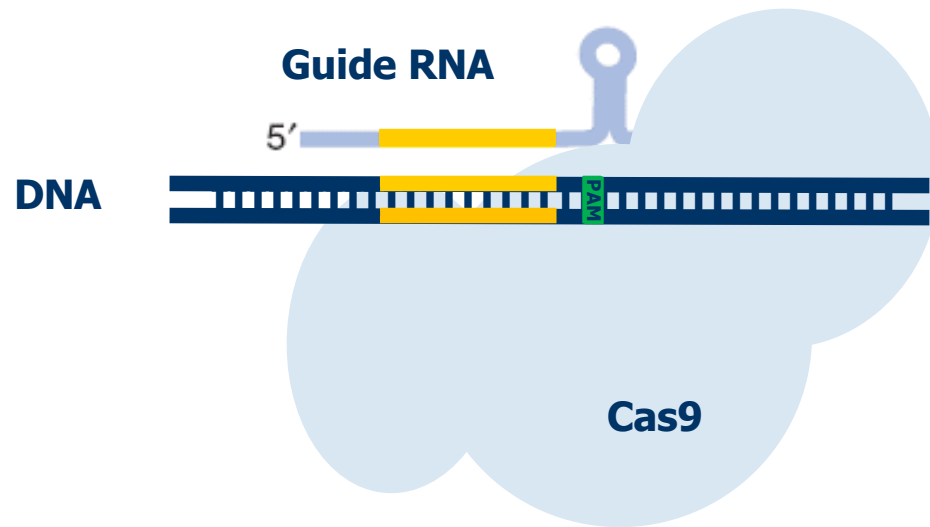


# Genetic Barrier

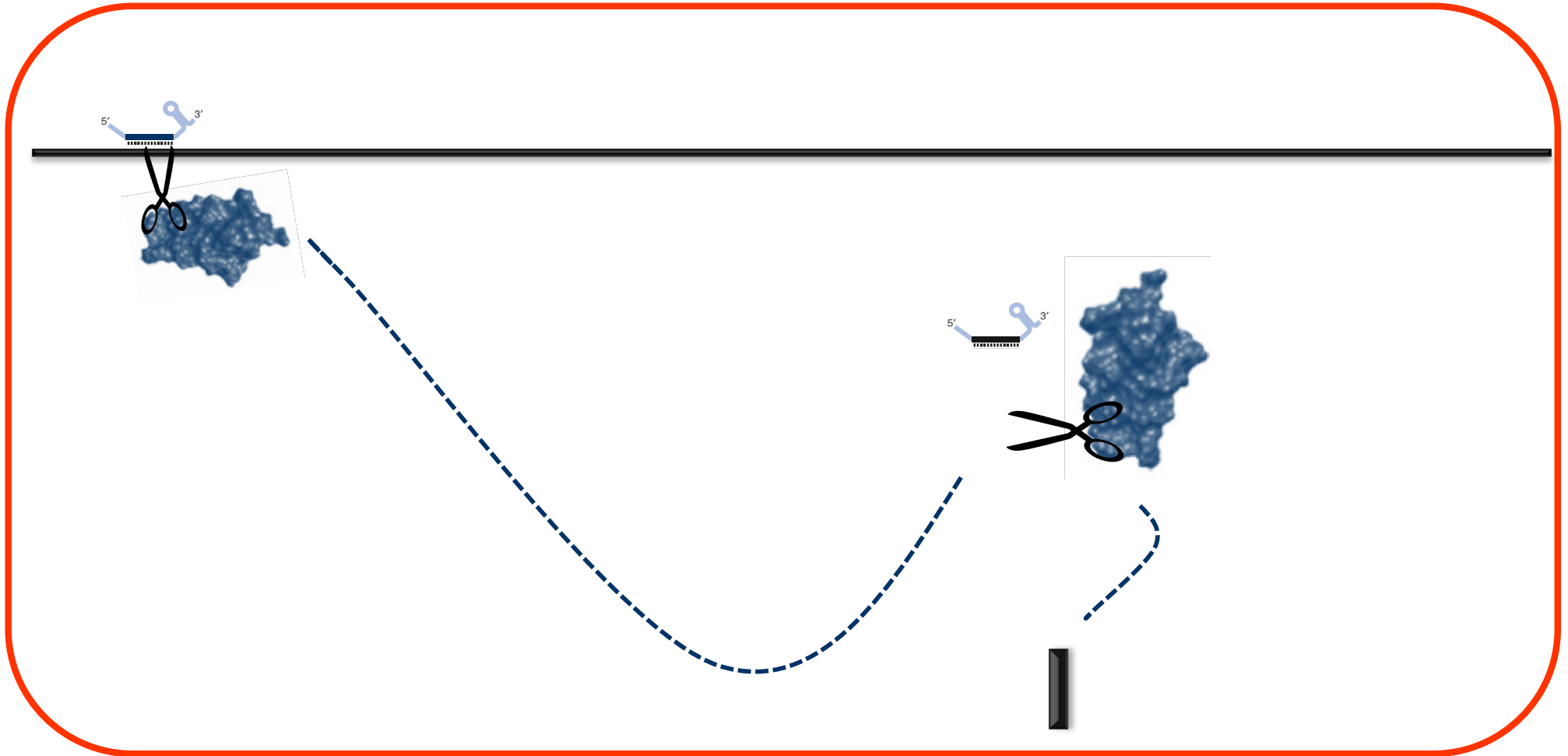


# Data storage/recording





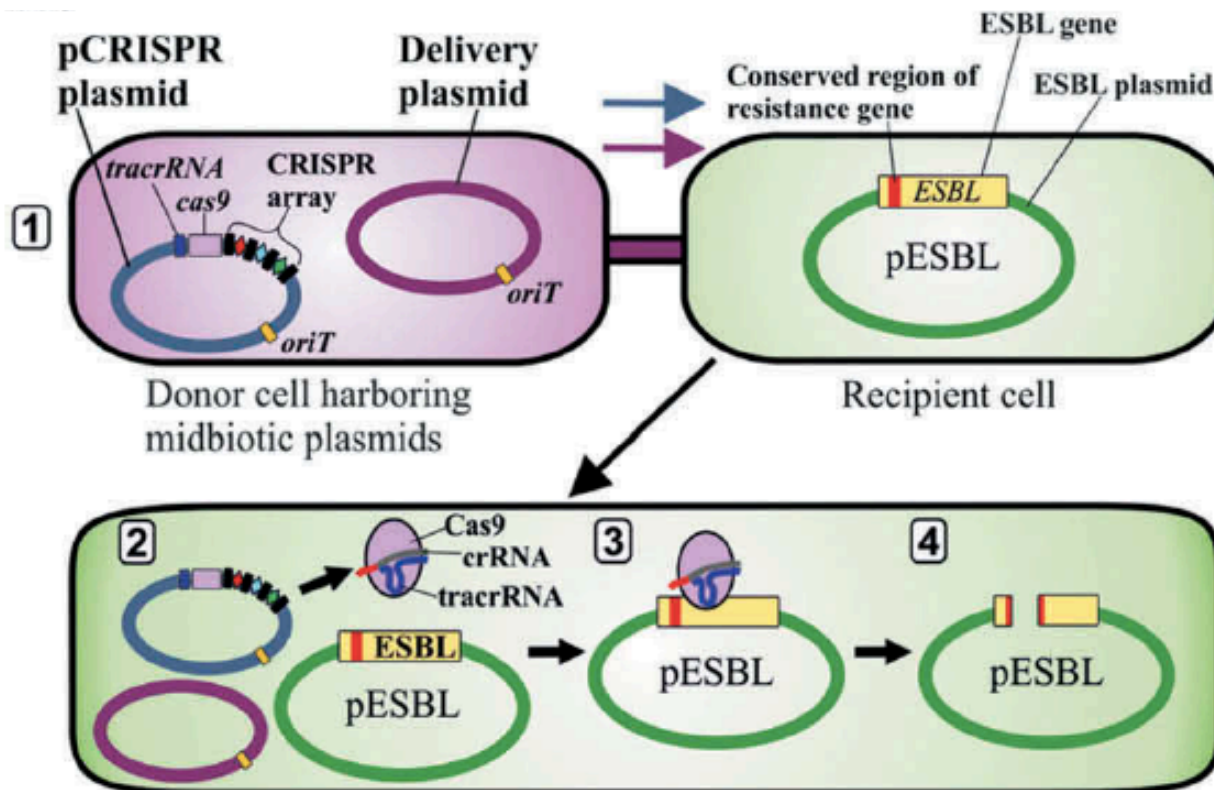
# Antimicrobials





## Midbiotics: conjugative plasmids for genetic engineering of natural gut flora

Pilvi Ruotsalainen<sup>a</sup>, Reetta Penttinen <sup>a</sup>, Sari Mattila<sup>b</sup>, and Matti Jalasvuori<sup>a,c</sup>

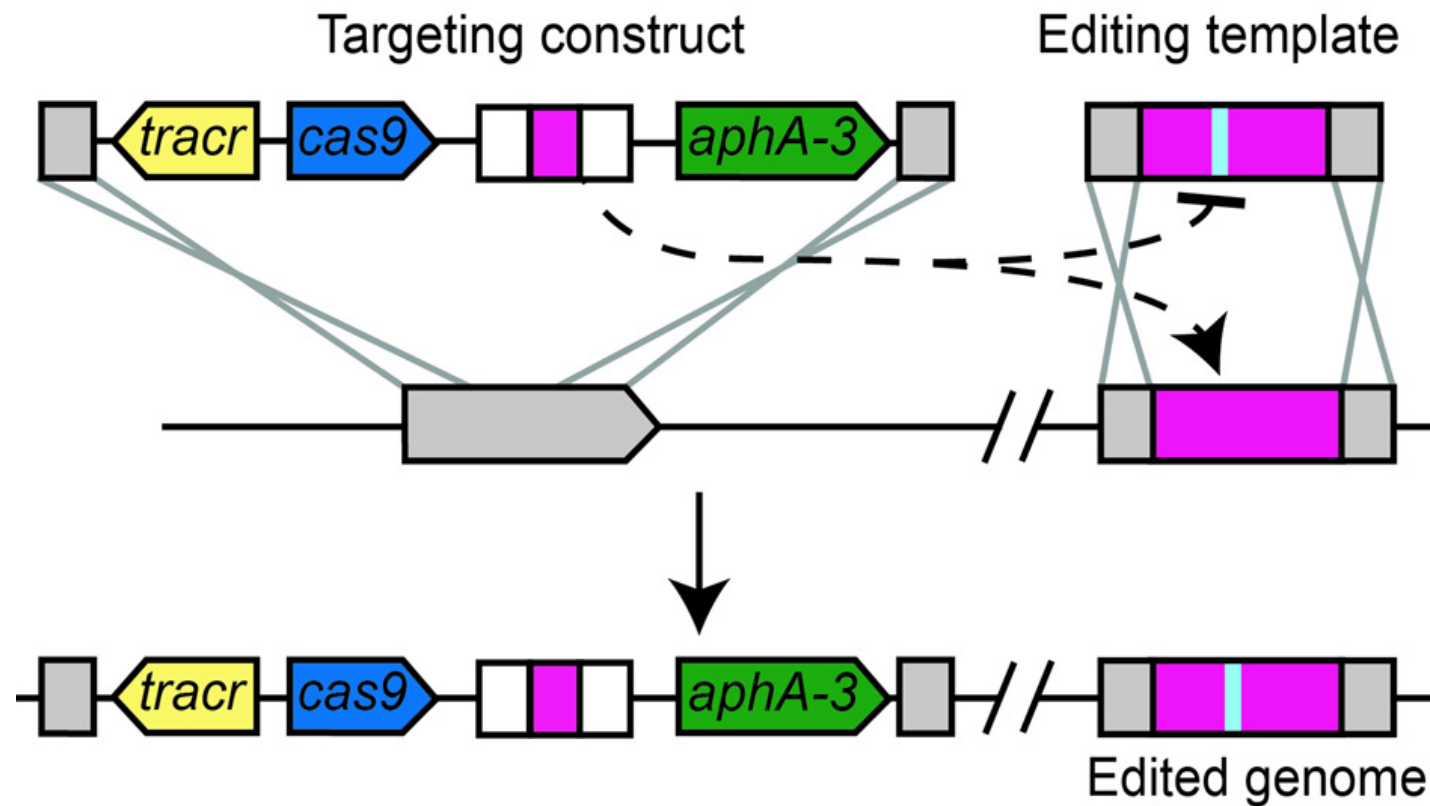


TREATMENTS

# Scientists Modify Viruses With CRISPR To Create New Weapon Against Superbugs

May 22, 2019 · 5:01 AM ET  
Heard on [Morning Edition](#)

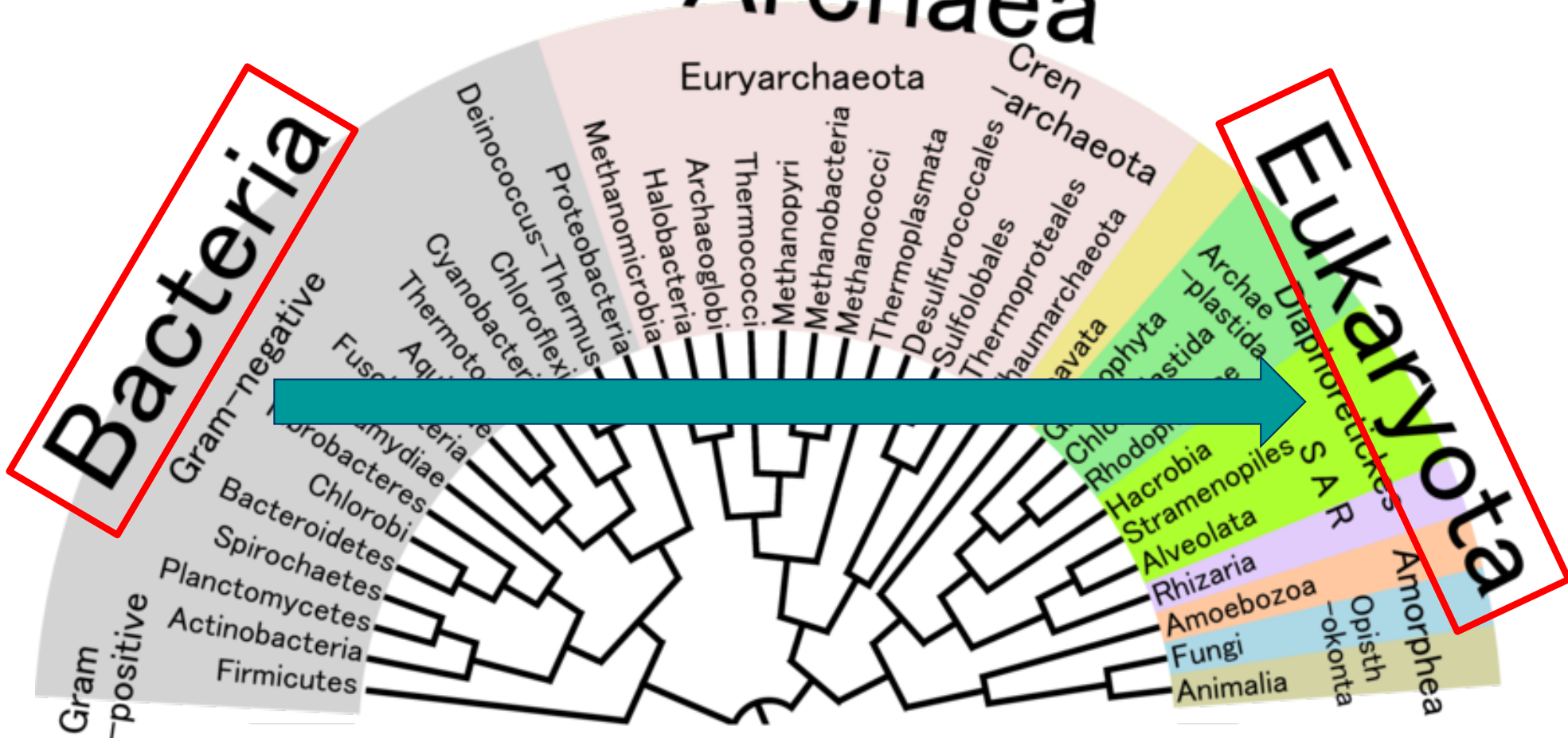
# Selection of recombinant Bacteria



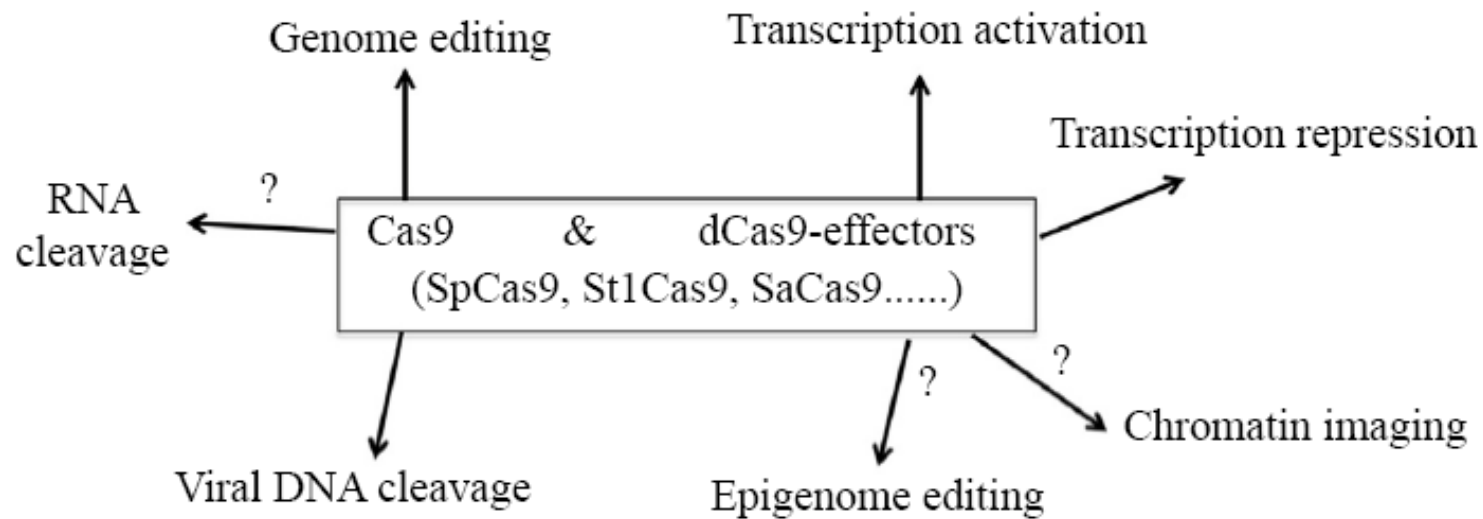
# Archaea

**Bacteria**

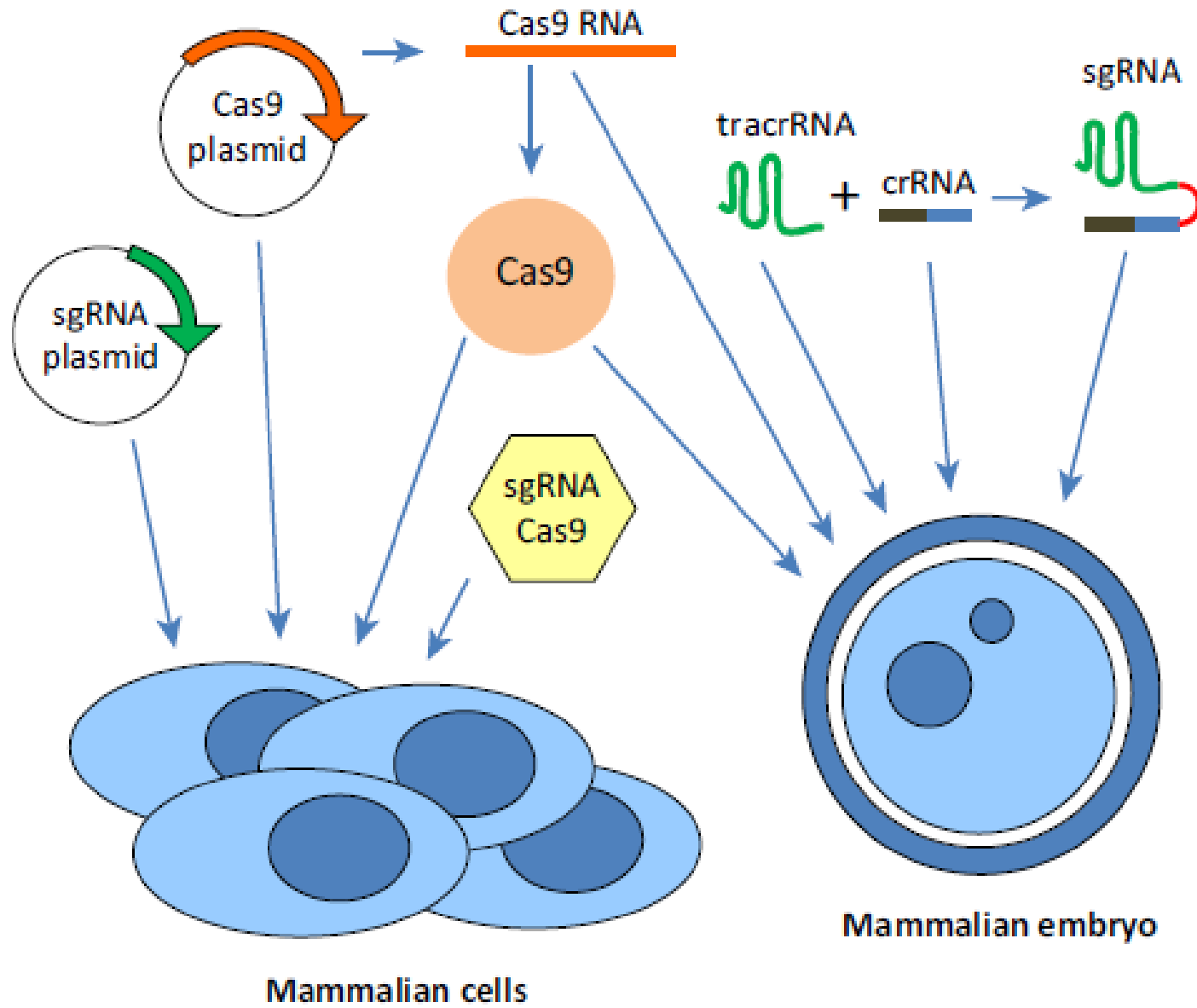
**Eukaryota**



# Applicable to Plants

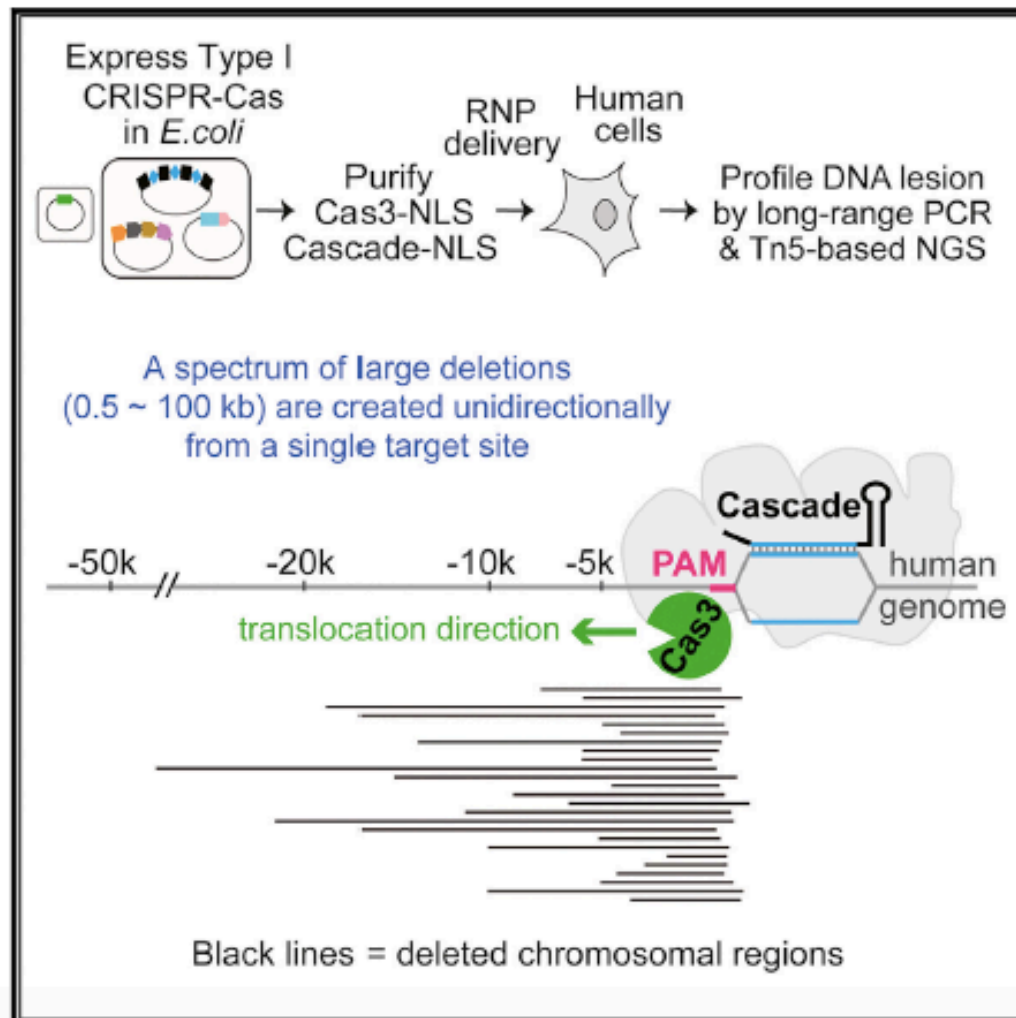


Zhang, D., et al., Targeted Gene Manipulation in Plants Using the CRISPR/Cas Technology, Journal of Genetics and Genomics (2016), <http://dx.doi.org/10.1016/j.jgg.2016.03.001>



## Introducing a Spectrum of Long-Range Genomic Deletions in Human Embryonic Stem Cells Using Type I CRISPR-Cas

### Graphical Abstract



### Authors

Adam E. Dolan, Zhonggang Hou, Yibei Xiao, ..., Peter L. Freddolino, Ailong Ke, Yan Zhang

### Correspondence

ailong.ke@cornell.edu (A.K.),  
yzhangbc@med.umich.edu (Y.Z.)

### In Brief

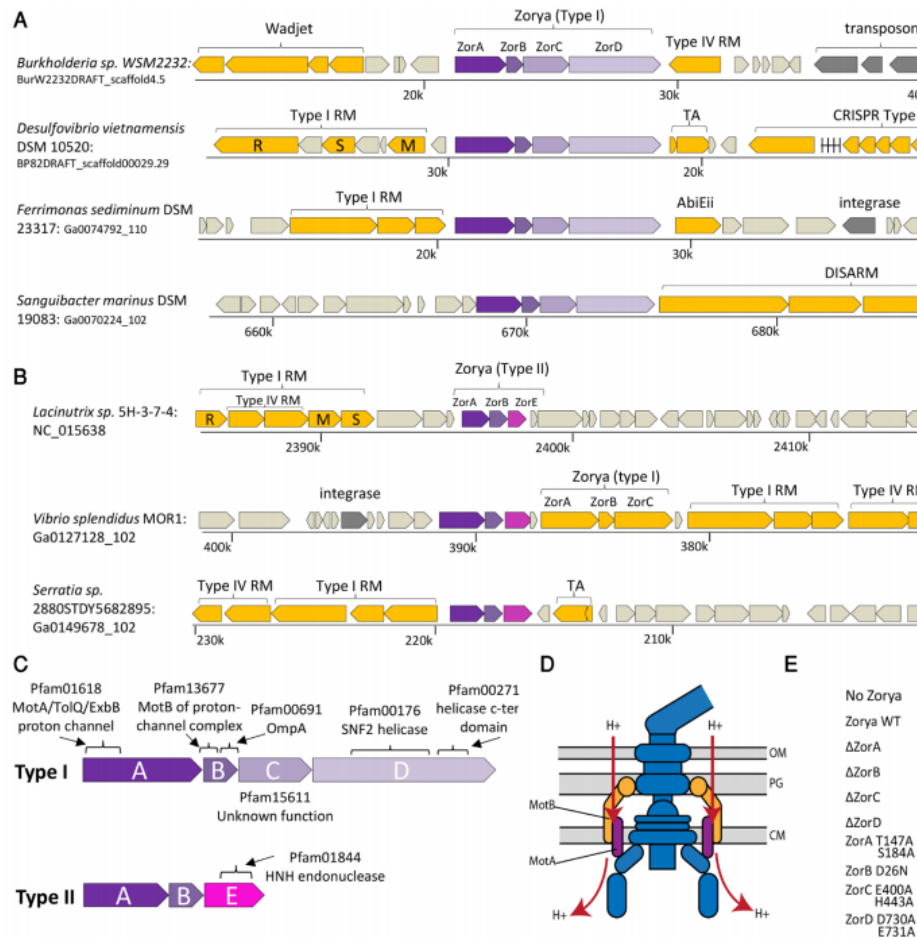
Dolan et al. demonstrate that *T. fusca* type I CRISPR-Cas can generate a spectrum of large genome deletions in human cells. Cascade and Cas3 together induce heterogeneous DNA lesions upstream of a single CRISPR-targeted site, highlighting their potential utilities for long-range genome manipulation and deletion screen.



Cite as: S. Doron *et al.*, *Science* 10.1126/science.aar4120 (2018).

# Systematic discovery of antiphage defense systems in the microbial pangenome

Shany Doron,\* Sarah Melamed,\* Gal Ofir, Azita Leavitt, Anna Lopatina, Mai Keren, Gil Amitai, Rotem Sorek†



**Table I. Composition of defense systems reported in this study.**

System	Operon	Associated domains*	Domain annotations	No. of instances detected within microbes	No.(%) of genomes in which system is found	Comments
<b>Thoeris</b>	ThsAB	pfam13289, pfam14519, pfam08937, pfam13676	SIR2, Macro domain, TIR domain	2099	2070 (4.0%)	Membrane associated (sometime)
<b>Ha-chiman</b>	HamAB	pfam08878, COG1204, pfam00270, pfam00271	Helicase	1781	1742 (3.4%)	
<b>Shedu</b>	SduA	pfam14082	Nuclease	1246	1191 (2.3%)	
<b>Gabija</b>	GajAB	pfam13175, COG3593, pfam00580, pfam13361, COG0210, pfam13245	ATPase, nuclease, helicase,	4598	4360 (8.5%)	
<b>Septu</b>	PtuAB	pfam13304, COG3950, pfam13395, pfam01844	ATPase, HNH nuclease	2506	2117 (4.1%)	
<b>Lamassu</b>	LmuAB	pfam14130, pfam02463	SMC ATPase N-terminal domain	697	682 (1.3%)	
<b>Zorya (type I)</b>	ZorABCD	pfam01618, pfam13677, pfam00691, COG1360, pfam15611, pfam00176, pfam00271, COG0553, pfam04471	MotA/ExbB, MotB, helicase, Mrr-like nuclease	1173	1055 (2.1%)	Membrane associated
<b>Zorya (type II)</b>	ZorABE	pfam01618, pfam13677, pfam00691, COG1360, COG3183, pfam01844	MotA/ExbB, MotB, HNH nuclease	656	655 (1.3%)	Membrane associated
<b>Kiwa</b>	KwaAB	pfam16162	No annotated domain	934	924 (1.8%)	Membrane associated
<b>Druantia</b>	DruA-BCDE (type I) DruMFGE (type II) DruHE (III)	pfam14236, pfam00270, pfam00271, pfam09369, COG1205, pfam00145, COG0270	Helicase, methylase	1342	1321 (2.6%)	
<b>Wadjet</b>	JetABCD	pfam11855, pfam09660, pfam13835, pfam09661, pfam13555, pfam13558, COG4913, COG1196, pfam11795, pfam09983, pfam11796, pfam09664, COG4924	MukBEF condensin, topoisomerase VI	3173	2880 (5.6%)	

\*Pfam and COG domains were assigned according to the information in the IMG database (48) and supplemented using HHpred (52).

Fig. 3. The Zorya system. (A) Representative instances of the Type I Zorya system and their defense island context.