

# HCB views on Gene Drive Techniques

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## Disclosure

This talk is based on work made by the High Council for Biotechnology, but was not discussed as such.

It does not expose a position from the French government.

*Conflict of interest: none to declare.*

# Principle for Gene drive

The gene drive relies on a series of tool and specificities:

- At the molecular level
- At the population level

Could be, as many other biological tool, also harmful for the manipulator.

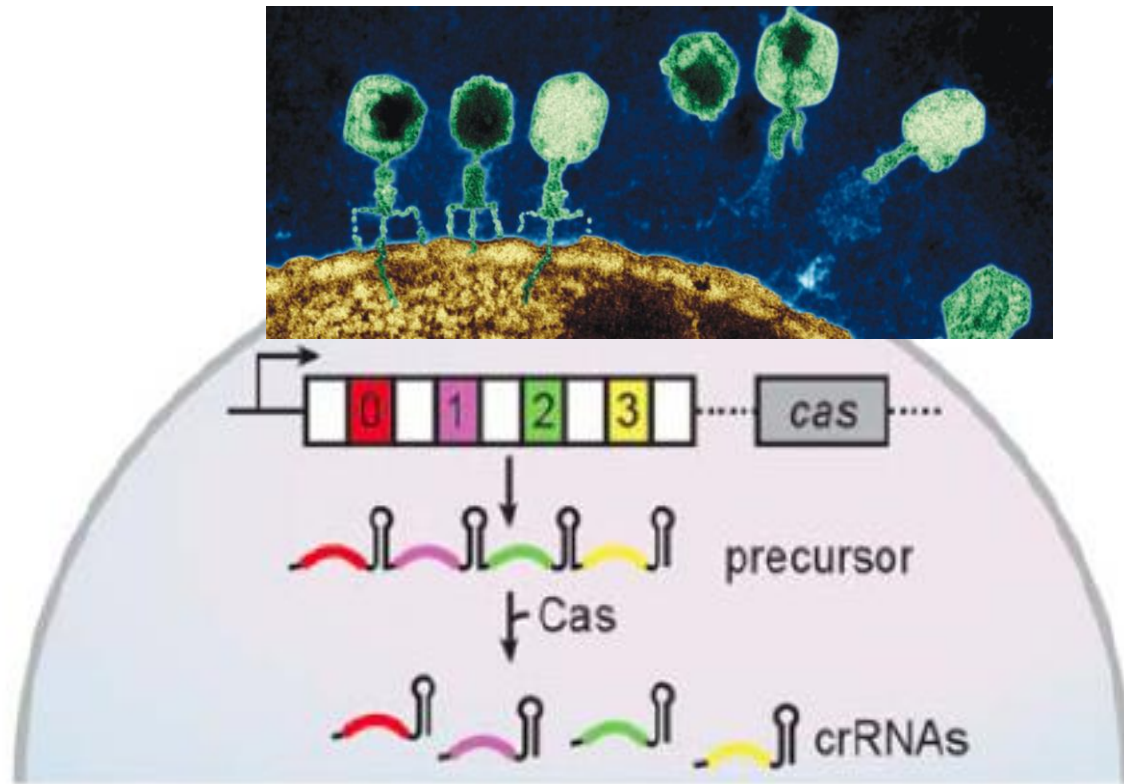
Is a sophisticated technique, perhaps not cost-effective for dual use.

Could be a hidden technique with lag mode of action: which makes it pernicious for detection.

→ However, for CRISPR-based, molecular tools exist.

# CRISPR/cas system

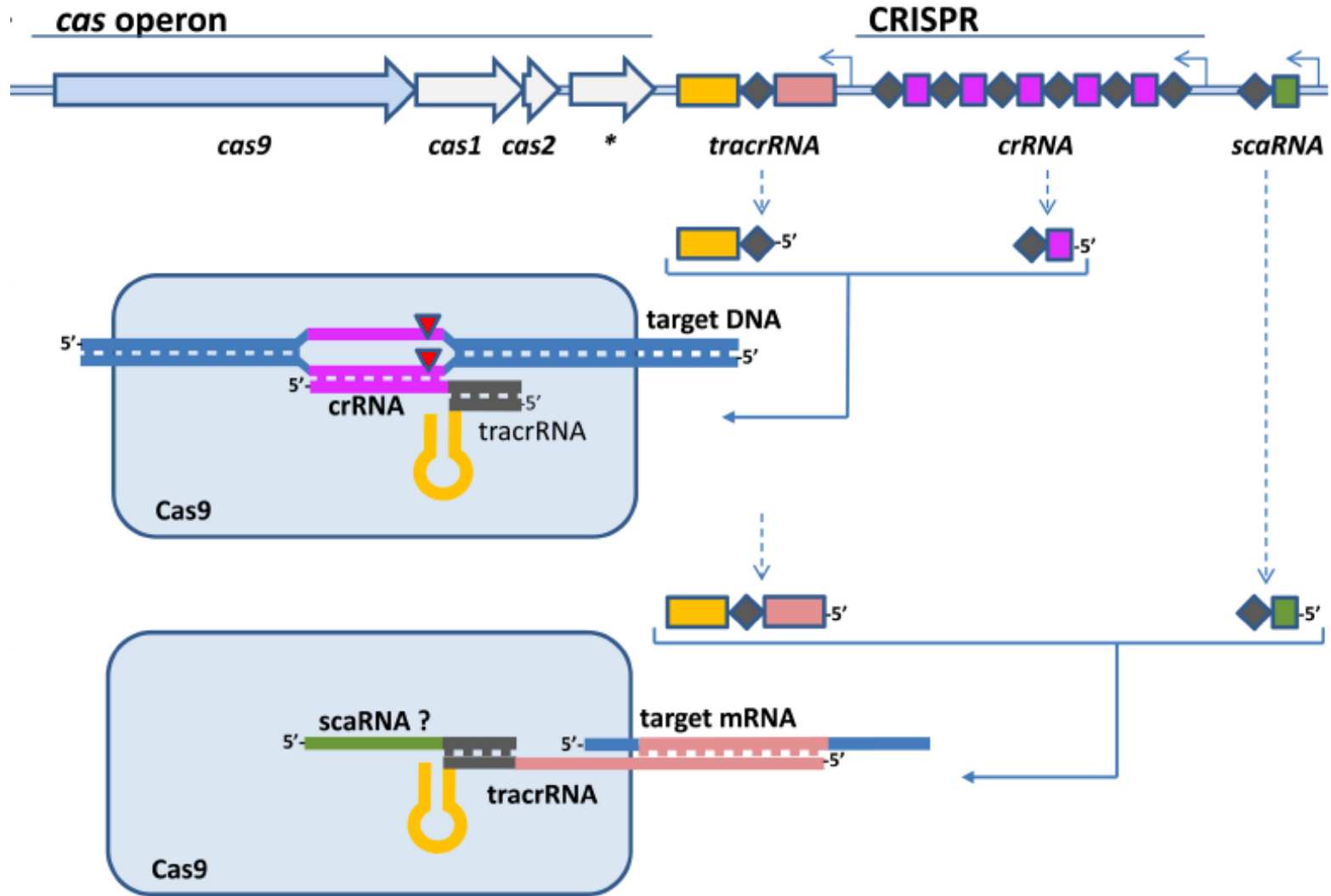
*Clustered Regularly Interspaced Short Palindromic Repeats*



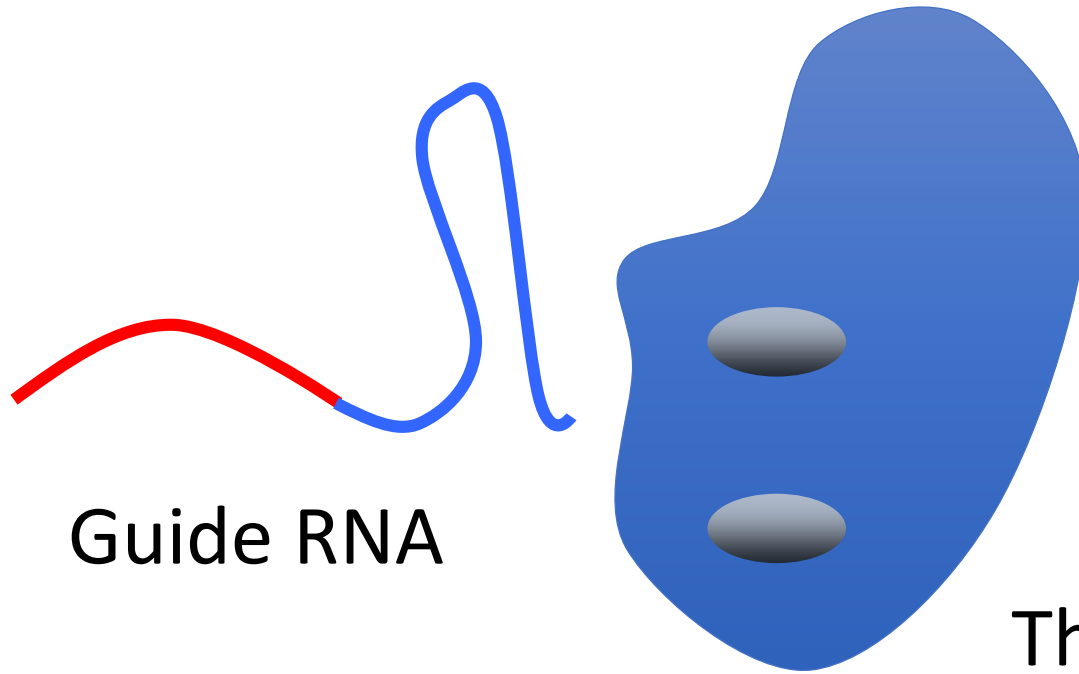
*Bacterial adaptive immunity*

# CRISPR/cas System

## Type II



# CRISPR: the players



Guide RNA

The active protein:  
Cas9

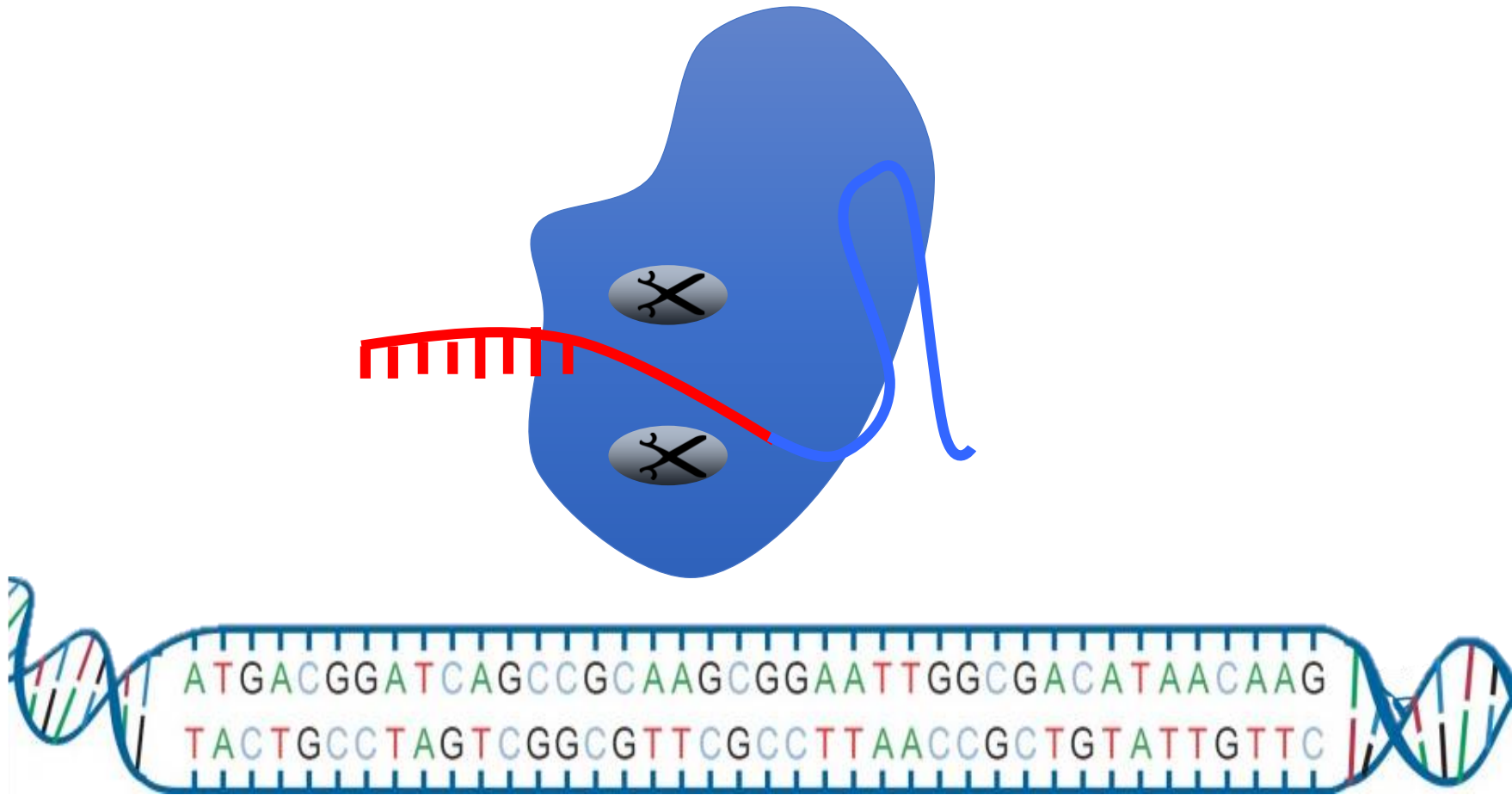
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## RNA-Guided Human Genome Engineering via Cas9

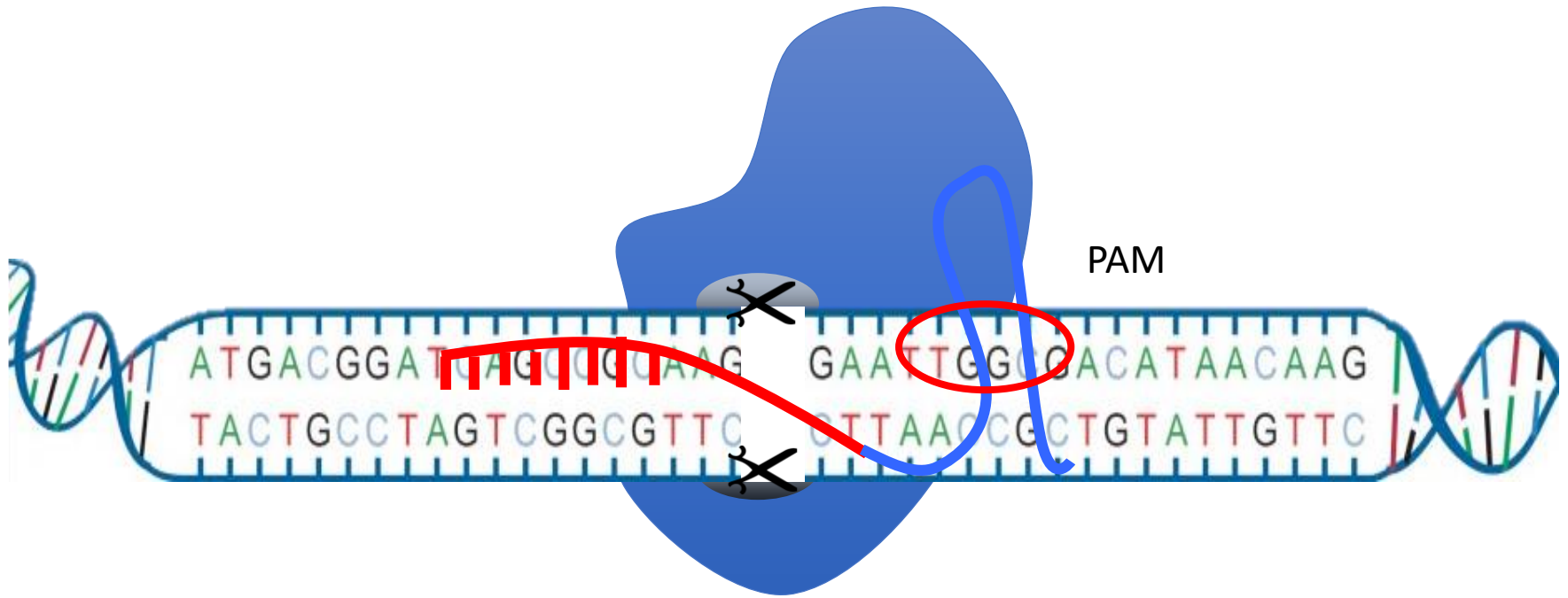
Prashant Mali,<sup>1\*</sup> Luhan Yang,<sup>1,3\*</sup> Kevin M. Esvelt,<sup>2</sup> John Aach,<sup>1</sup> Marc Guell,<sup>1</sup> James E. DiCarlo,<sup>4</sup>  
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# CRISPR: the players



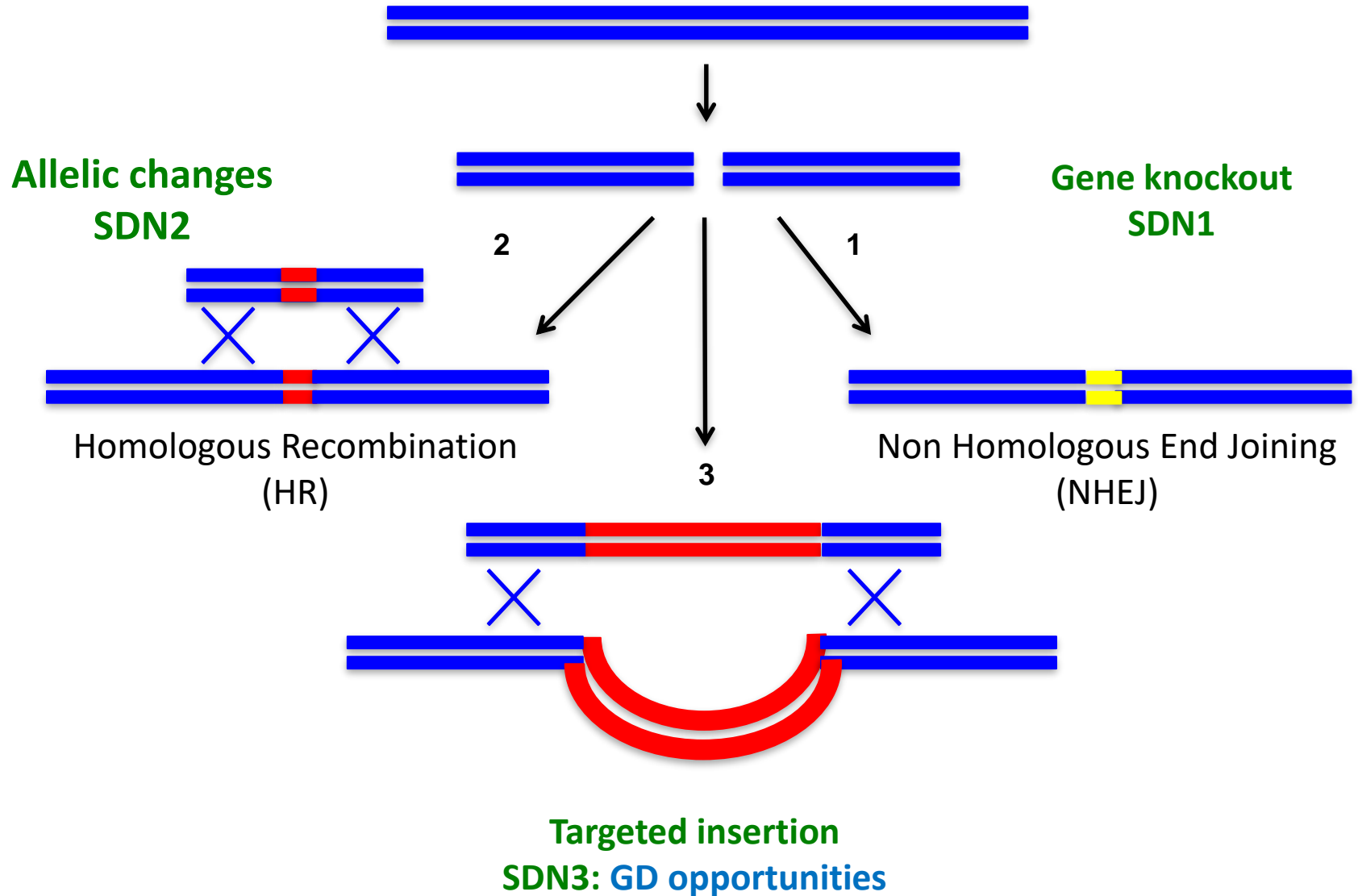
# CRISPR: mode of action



**PAM** *Protospacer adjacent motif*:  
Part of the specificity determinant.

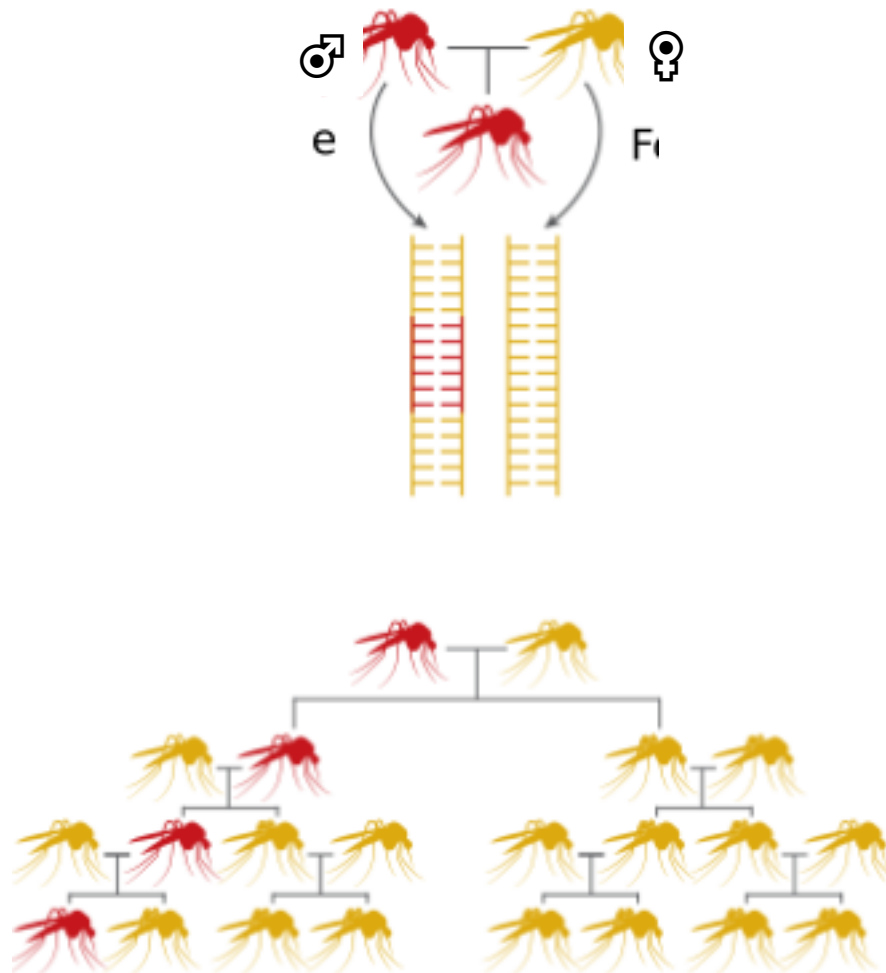


# Attenable objectives



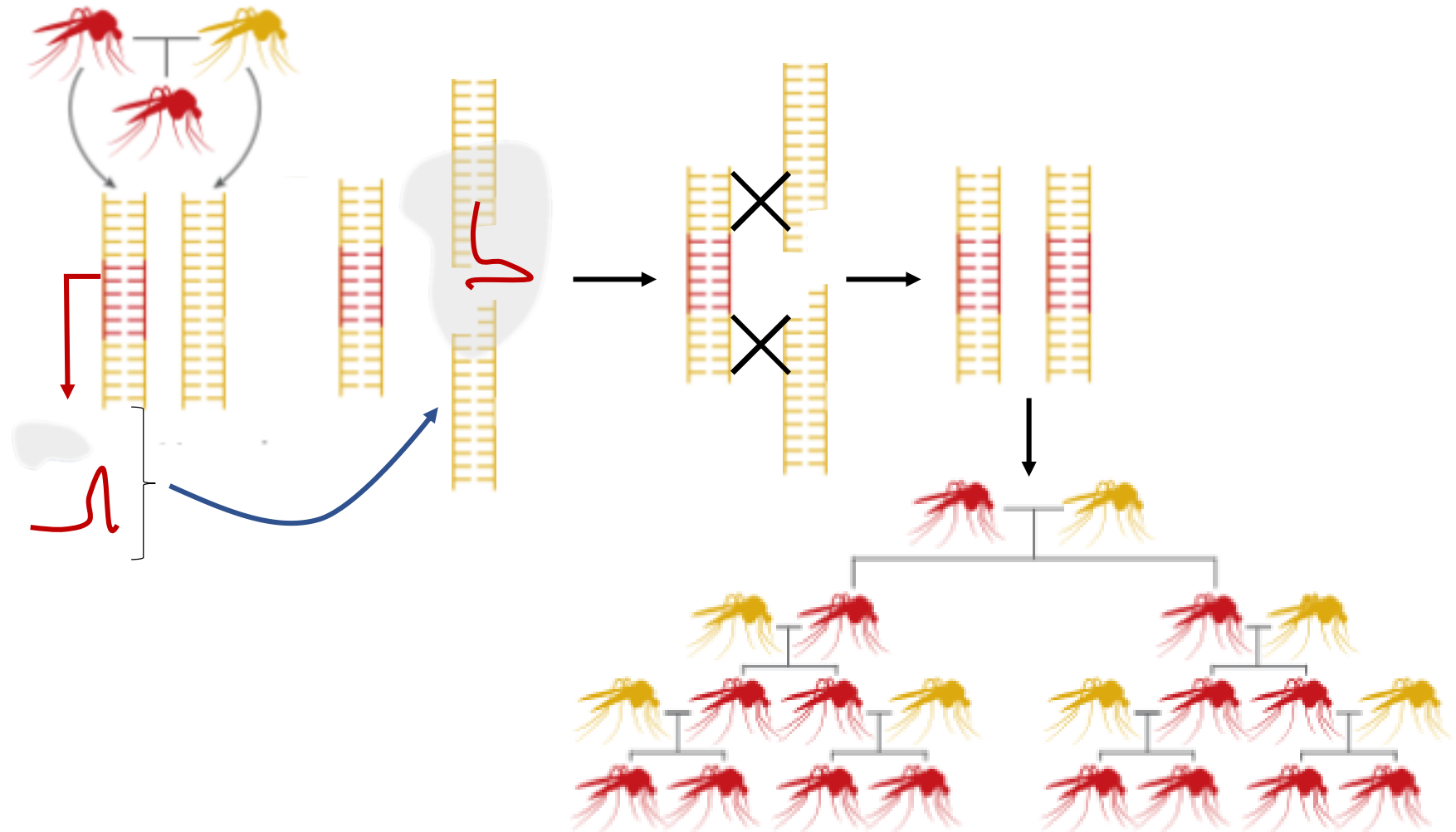
# Principle for Gene drive

Conventional breeding and spread of alleles



# Principle for Gene drive

Gene Drive spread of alleles



# Gene drive possible interests

Single-cut CRISPR gene drive systems:

- Are envisioned to fight against:
  - The rapid spread of invasive species
  - Vector born diseases

However there is a mandatory need for:

- Ethical, societal involvement of the population. As quoted by K Esvelts: “Closed-door science is morally and practically unacceptable in the era of gene drive”, and “...those who are to be bound by laws, ought to have a voice in making them”- James Madison.
- Specific regulation and tools as models and for pre-open-field utilization.

# Gene drive limits

Single-cut CRISPR gene drive systems:

- Relies on systems with sex specific target-gene for eradication strategies
- Won't affect every organism on earth
- Can still invade every population of inter-fertile species
- Is affected, by the genetic cost of the targeted gene
- Is limited by target-population genetic polymorphism constrains, which could be overcome by multiple targets or cassettes
- Its efficacy relies on the mode of reproduction:
  - Rapid spread for species with multiple offspring per generation
  - Almost impossible for isolated reproduction

# Gene drive as a potential weapon

- As a tool to invade, there is a need for a vector:
  - The target species itself:
    - To spread a harming gene
    - To eliminate a species
  - A vector to target a species
- As a tool to impair:
- To block the ability to take part to the market: disease marker p.e.
- Spread a weakening gene: reducing agricultural yields p.e.

## Limits:

- Won't affect every organism of the species in a short period of time
- Is, as most biological tool, also dangerous to it's producer

# Gene drive as a weapon: survey and prevention

To prevent:

- Public awareness
- Ability to identify situation at risk:
  - A new focus for existing security services.
  - Adapted facilities to test for harmfulness: not easy to preset.

To detect:

- A general survey for plant, animal and human health, and wildness
- Need for molecular tools:
  - To detect the Gene Drive cassette
  - To eliminate a species (Counter measures)

Counter measures:

- Develop resistant target species (using GD.... for spreading!)

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