UN environment programme

BCH Project

gef

Regional Joint BCH and ABSCH Training of Trainers Workshop for Africa Region

Nairobi, 7-11 October 2024

Synthetic Biology

Prof. Ossama Abdelkawy

Engineering

Logs

Rocks

Humans always try to make nature more engineerable.

Engineering

Logs

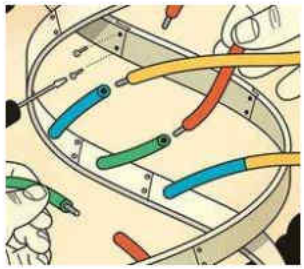
Planks

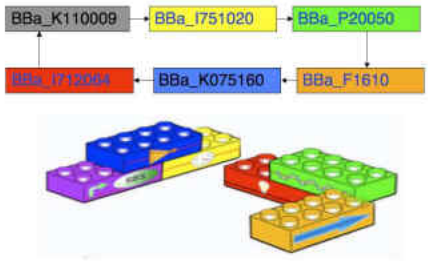
Rocks

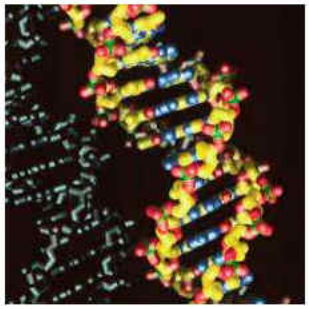
Bricks

Developing a standardized building units improve efficiency, quality, and sustainability.

Engineering Biological Sysiems



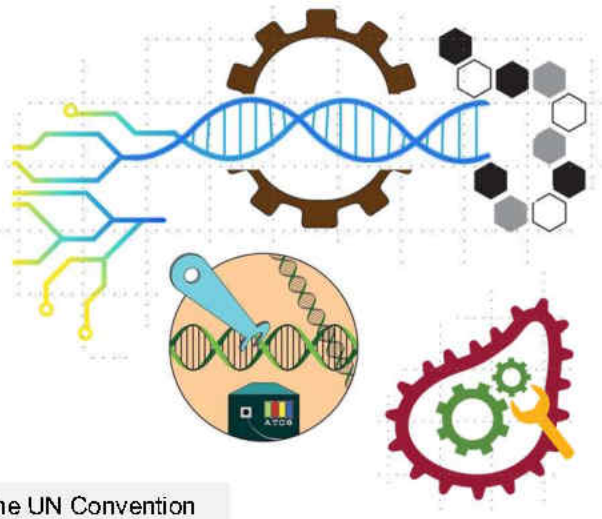




Make 'engineerable' genetic systems based on standardized, predictable genetic parts (biobricks) and simplifying complex biological processes into manageable units (genetic circuits) to create new programmable life forms.

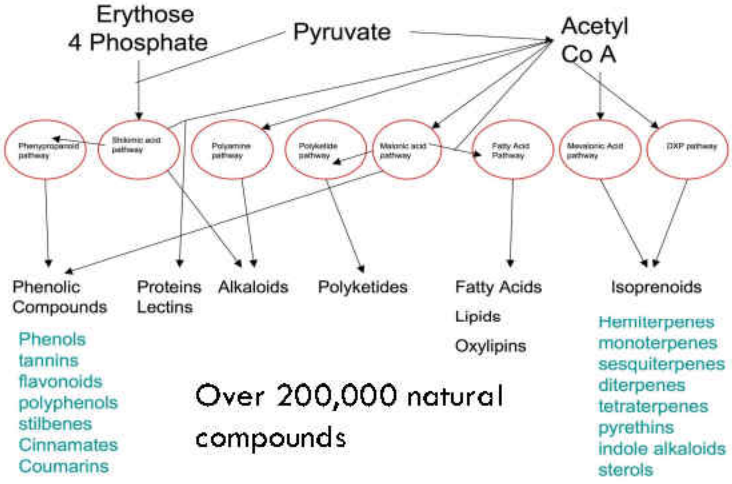
Synthetic Biology

A further development and new dimension of modern biotechnology that combines science, technology and engineering to facilitate and accelerate the understanding, design, redesign, manufacture and/or modification of genetic materials, living organisms and biological systems.



- Operational definition adopted by the UN Convention on Biological Diversity COP13, Cancun - December 2016.

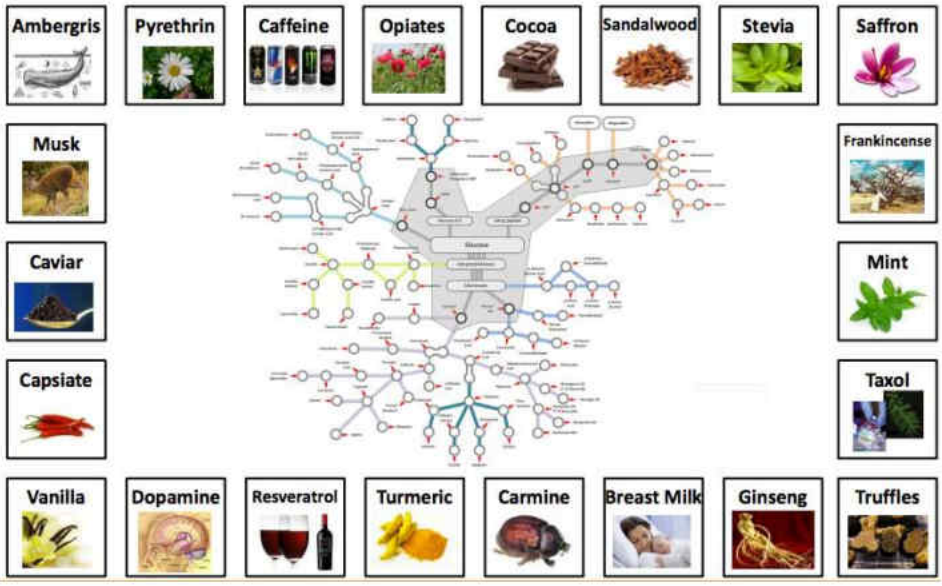
Bio-production



Over 200,000 natural compounds

'Biosynthetic routes aiming to replace natural sources'

Bio-Production



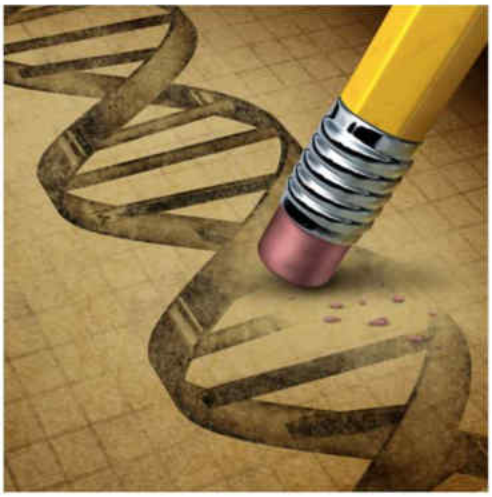
GMOs 2.0

SECOND WAVE:

CROPS, INSECTS, ANIMALS

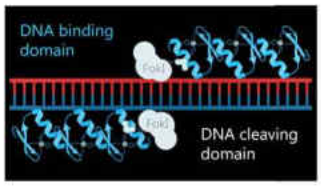
Gene Editing

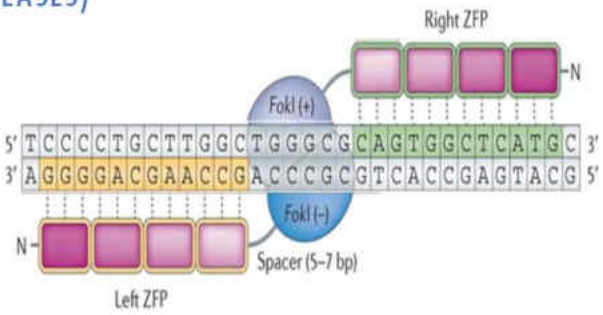
- Gives scientists the ability to change an organism's DNA.
- These technologies allow genetic material to be added, removed, or altered at particular locations in the genome.
- Include Zinc Fingers, TALENS and CRISPR-CAS9.

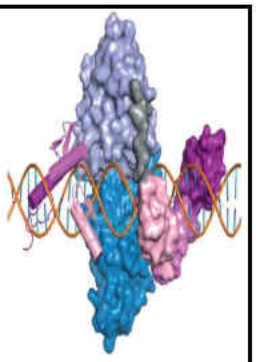


Gene Editing Tools

ZFNs (ZINC FINGER NUCLEASES)



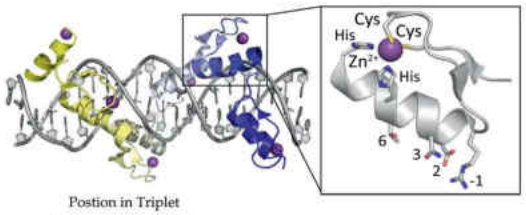




- DNA Binding: Zinc fingers recognize and bind to specific 3-4 base pair DNA sequences.
- DNA Cutting: FokI nuclease dimerizes to cut the DNA at the targeted site.
- Gene Editing: The resulting DSB is repaired by the cell, allowing gene modification.

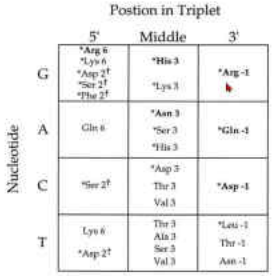
Gene Editing Tools

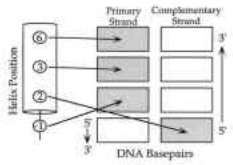
ZFNs (ZINC FINGER NUCLEASES)



Limitation:

- Designing functional ZFNs is complex and time-consuming.
- Potential off-target effects as specificities of individual zinc fingers can overlap and depend on the context of the surrounding zinc fingers and DNA.





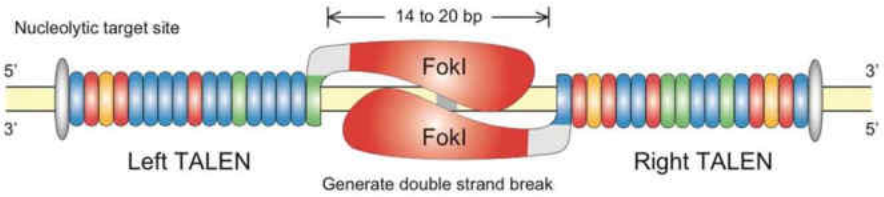
⑤ ⑥ ⑦

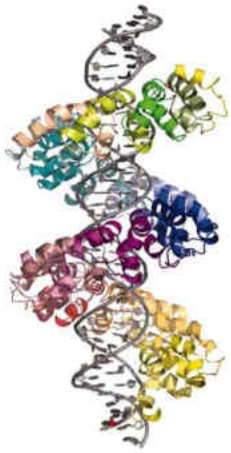
Applications:

- Functional Genomics: Studying gene function through targeted knockout.
- Biotechnology: Developing disease-resistant plants.

Gene Editing Tools

TALENS (TRANSCRIPTION ACTIVATOR-LIKE EFFECTOR NUCLEASES)





- TAL Effectors: Proteins derived from Xanthomonas bacteria, which bind to specific DNA sequences.
- Nuclease Domain: FokI enzyme that cuts the DNA at the targeted site.

Gene Editing Tools

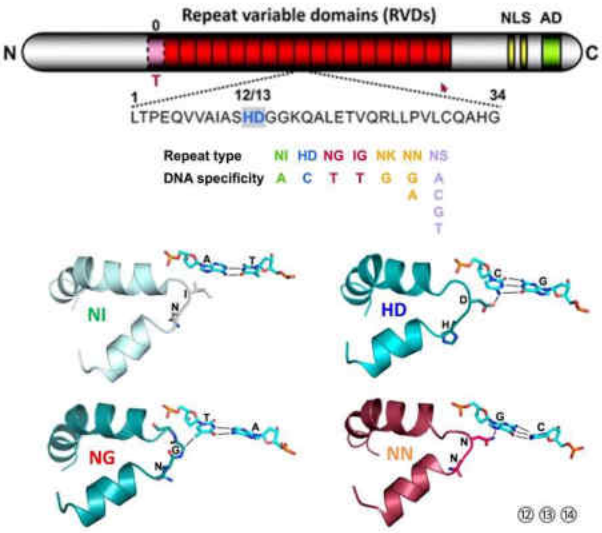
TALENS (TRANSCRIPTION ACTIVATOR-LIKE EFFECTOR NUCLEASES)

Applications:

- Gene Knockout: Disrupting specific genes to study their function.
- Gene Correction: Repairing mutations in diseases (e.g., muscular dystrophy).
- Agricultural Improvements: Creating crops with enhanced traits.

Limitation:

- Complex design and large size, making delivery into cells challenging.



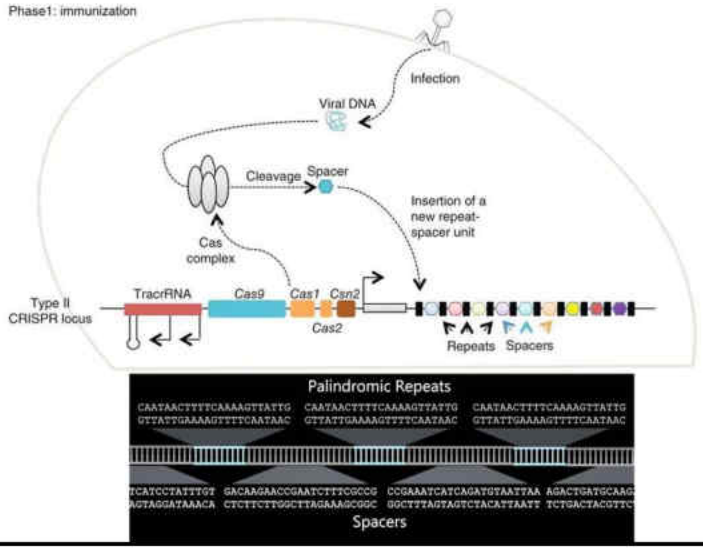
Gene Editing Tools

CRISPER (CLUSTERED REGULARLY INTERSPACED SHORT PALINDROMIC REPEAT)

CRISPR-Cas9 is a bacterial immune system that protects bacteria from invading viruses, particularly bacteriophages.

1. Viral DNA Acquisition

- When a virus (bacteriophage) infects a bacterium, the bacterial defense system captures a small piece of the viral DNA.
- This viral DNA is integrated into the **CRISPR array** in the bacterium's genome as a **spacer** between repeated sequences.

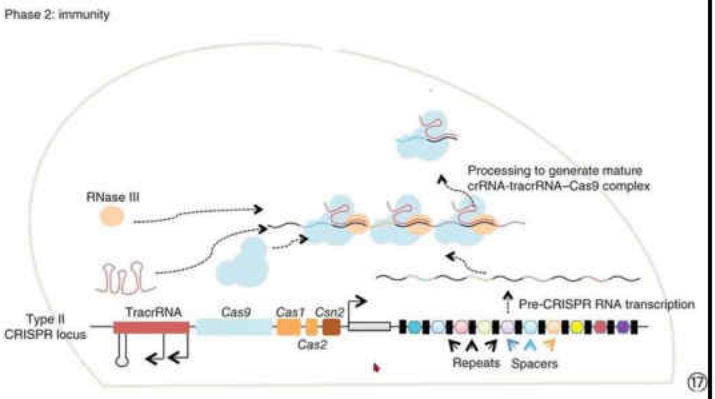


Gene Editing Tools

CRISPER (CLUSTERED REGULARLY INTERSPACED SHORT PALINDROMIC REPEAT)

2. crRNA Formation

- The CRISPR array is transcribed into a long RNA molecule which is processed into smaller segments called CRISPR RNAs (crRNAs), each containing a viral DNA sequence.
- The crRNA binds to the Cas protein (e.g., Cas9), forming an RNA-protein complex.

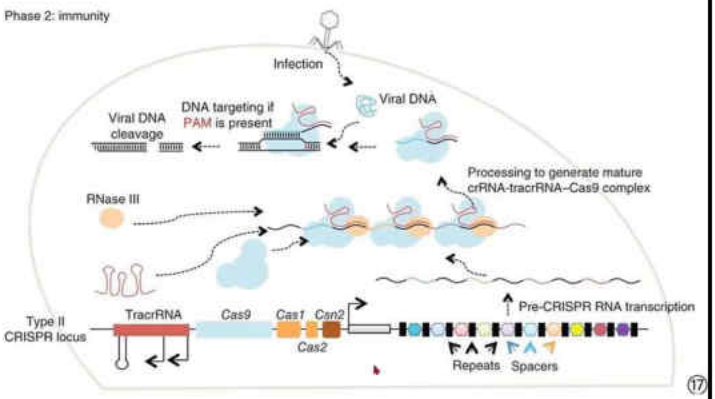


Gene Editing Tools

CRISPER (CLUSTERED REGULARLY INTERSPACED SHORT PALINDROMIC REPEAT)

3. Targeting & Cutting

- When the same virus re-infects the bacterium, The crRNA binds to the matching viral DNA and guides the Cas9 protein.
- Cas9 cleaves the viral DNA, cutting it and preventing the virus from replicating, neutralizing the infection.



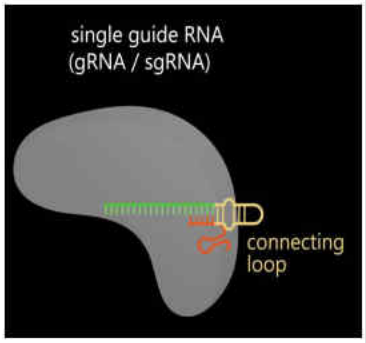
Gene Editing Tools

CRISPR-Cas9

- A revolutionary gene-editing technology adapted from bacterial defense systems against viruses.

How does it work?

- Guide RNA (gRNA): A synthetic RNA molecule designed to match a target DNA sequence.
- DNA Targeting: The gRNA directs the Cas9 enzyme to the specific DNA sequence.
- DNA Cutting: Cas9 introduces a double-strand break (DSB) at the target site.
- Gene Editing: The cell's natural repair mechanisms either disable the gene (via NHEJ) or correct it using a template (via HDR).



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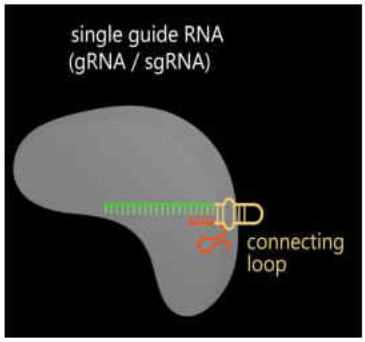
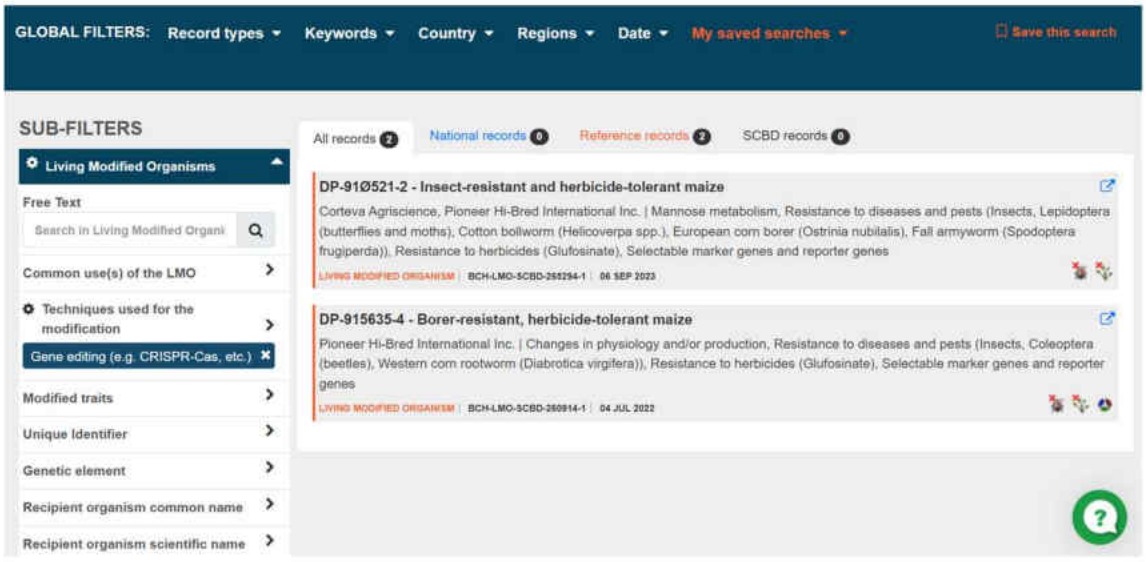


Gene Editing

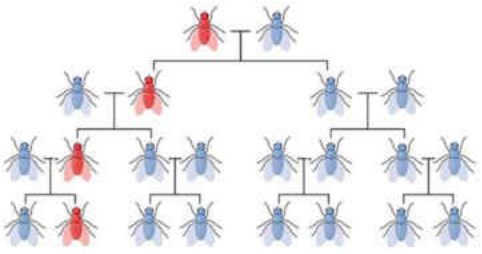


Gene Drives

In traditional Mendelian inheritance, there is a 50% chance of an allele being passed to offspring.

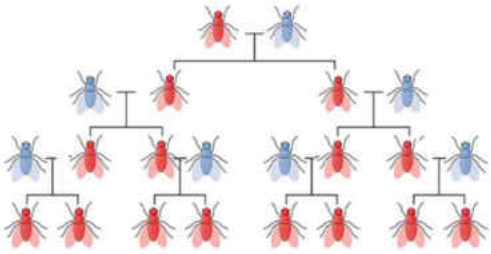
Gene drive alters this probability, allowing certain genes to propagate through a population more rapidly.

Normal inheritance



Altered gene does not spread

Gene drive inheritance



Altered gene is always inherited

Gene Drives

Gene drives aim to modify specific populations and entire species effectively.

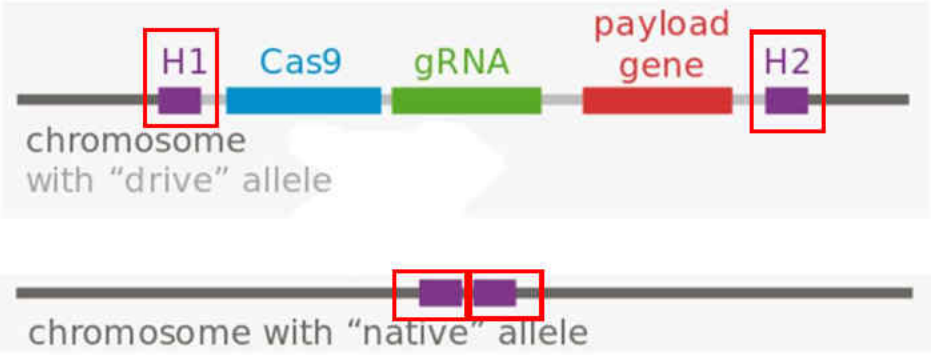
Proposed Applications:

- Exterminating insects that carry pathogens.
- Controlling invasive species.
- Eliminating herbicide or pesticide resistance.

Potential Risks:

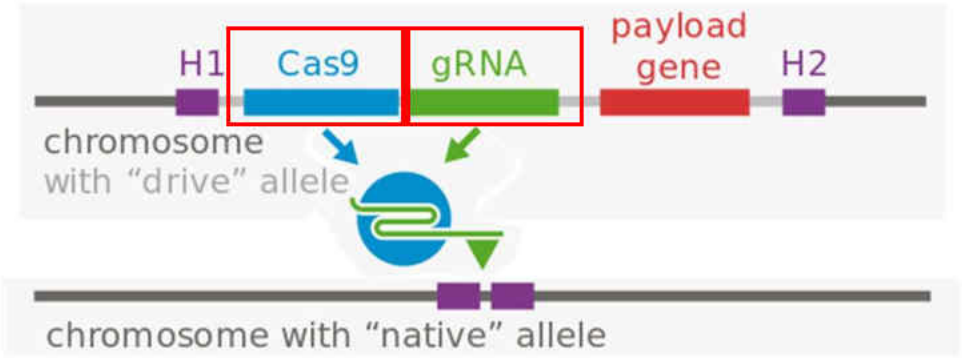
- Powerful techniques can be misused.
- Eradicating species can have broader ecological consequences.
- Relocation or accidental return of individuals carrying harmful gene drives could unintentionally lead to extinction of the species.

Self Propagating Gene Drive



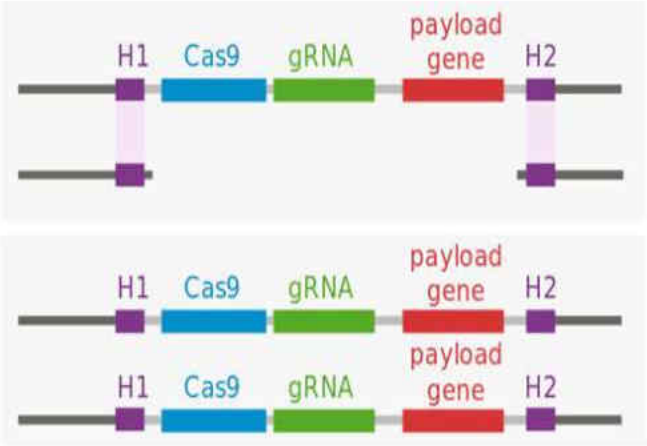
Sides homologous to the sequences that are adjacent to the cutting site in the host genome

Self Propagating Gene Drive



An RNA-guided endonuclease (e.g., Cas9 or Cas12a) and its guide RNA that cut the chromosome at a specific site

Self Propagating Gene Drive



- As a result, the gene drive insertion in the genome will re-occur in each organism that inherits one copy of the modification and one copy of the wild-type gene.

GMO +

RNAi
(RNA Interference)

Spraying synthetic RNA on crops to interfere with DNA functioning.

Big Ag very invested: Monsanto, Syngenta

"non-GMO"

Biomedicine

The Next Great GMO Debate

Deep inside its labs, Monsanto is learning how to modify crops by spraying them with RNA rather than tinkering with their genes.

by Antonio Regalado August 11, 2015

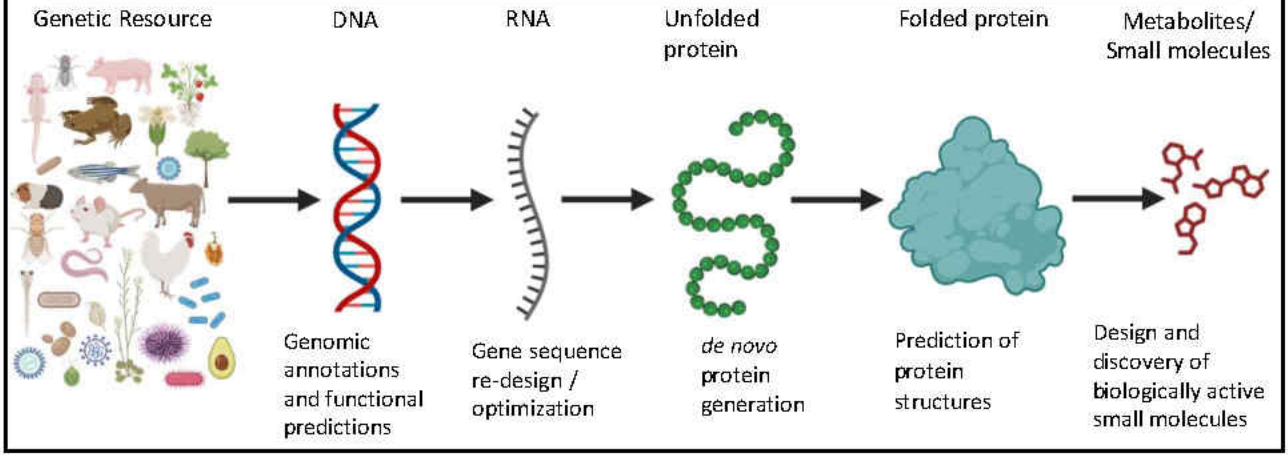
The Colorado potato beetle is a voracious eater. The insect can chew through 10 square centimeters of leaf a day, and left unchecked it will strip a plant bare. But the beetles I was looking at were doomed. The plant they were feeding on—bright green and carefully netted in Monsanto's labs outside St. Louis—had been doused with a spray of RNA.

The experiment took advantage of a mechanism called RNA interference. It's a way to temporarily turn off the activity of any gene. In this case, the gene being shut down was one vital to the insect's survival. "I am pretty sure 99 percent of them will be dead soon," said Jodi Beattie, a Monsanto scientist who showed me her experiment.

The discovery of RNA interference earned two academics a Nobel Prize

Generative Biology

- The intersection of biology and AI, where machine learning models are used to design, predict, and generate novel biological entities, such as proteins, DNA sequences, or even entire organisms.



Robotic Genome construction

"AI - POWERED BIOTECH"

- "Zymergen's algorithms suggest making 1,000 or so changes to the microbe's genetic material.
- Then the robots take over, injecting the suggested DNA snippets into the specimens, testing their properties, collecting data and feeding that information back into the data trove."

  - Bloomberg

Generative Biology

Challenges:

- AI simplifies synthetic biology techniques, making advanced tools and knowledge more accessible.
- Lowers the barrier for potential misuse by less experienced actors, escalating the risks.
- Need for robust governance and risk assessment frameworks able manage and regulate these emerging technologies and cope with their speed of development.

Development

	Modern Biotechnology	Synthetic Biology	Generative Biology
Def.	Techniques to combine DNA from different organisms to create new genetic sequences.	Techniques to design, redesign, manufacture and/or modification of genetic materials, living organisms and biological systems.	Employing artificial intelligence and deep learning models to predict and design biological systems such as new protein structures, metabolic pathways, or entire genomes
Tech.	Gene splicing, and plasmid insertion.	Gene editing (e.g., CRISPR), pathway engineering, and synthetic genome construction.	Computational modeling, machine learning algorithms, and design of new biological processes.
App.	Primarily focuses on the manipulation of existing genetic material.	Emphasizes engineering new biological systems and functions beyond natural organisms.	Focuses on the principles of biological generation, including natural processes and synthetic systems.

Thank you !

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