THE BCH III PROJECT

Synthetic Biology

Prof Ossama AbdelKawy

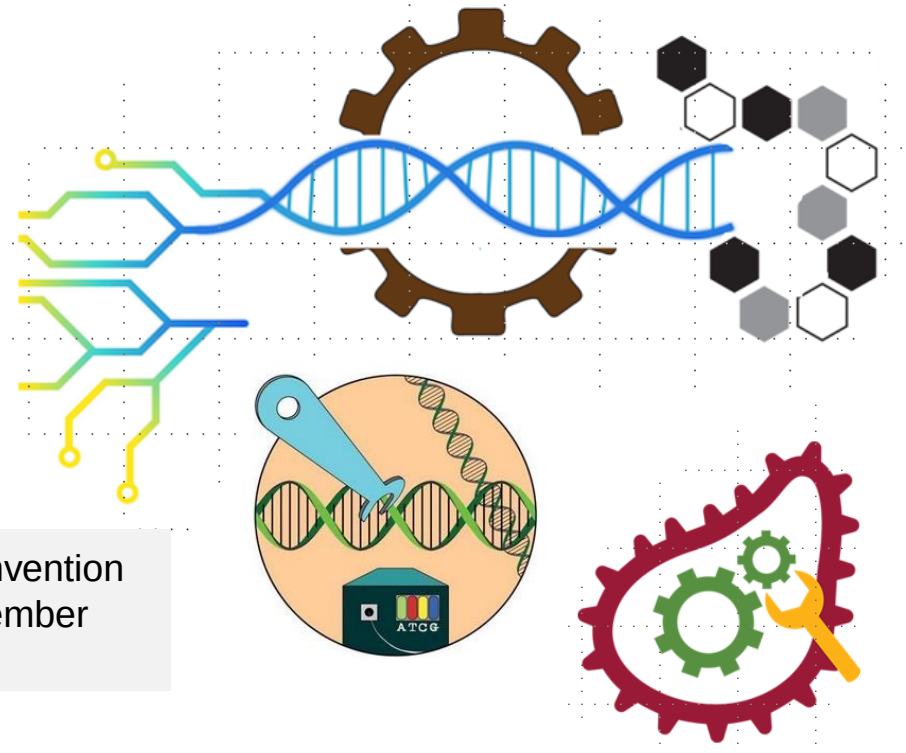
2023

GENETIC ENGINEERING – SYNTHETIC BIOLOGY

WHAT IS A SYNTHETIC BIOLOGY?

- "Synthetic Biology is 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.



GENETIC ENGINEERING – SYNTHETIC BIOLOGY

WHAT IS A SYNTHETIC BIOLOGY?

- Humans always tried to make nature more ‘engineerable

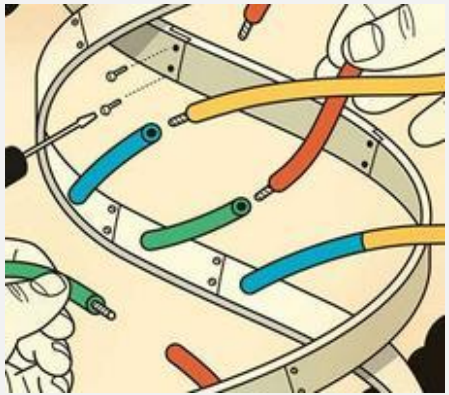


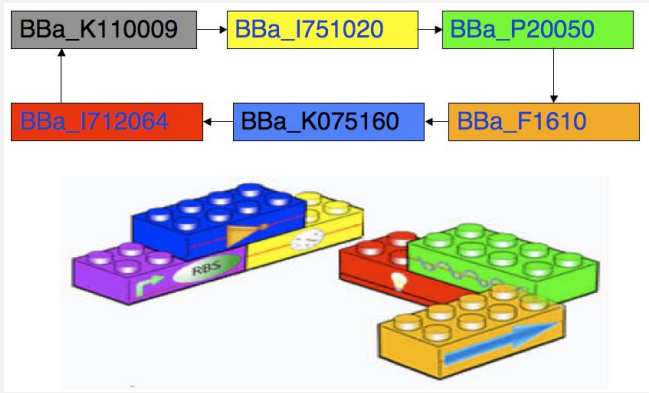


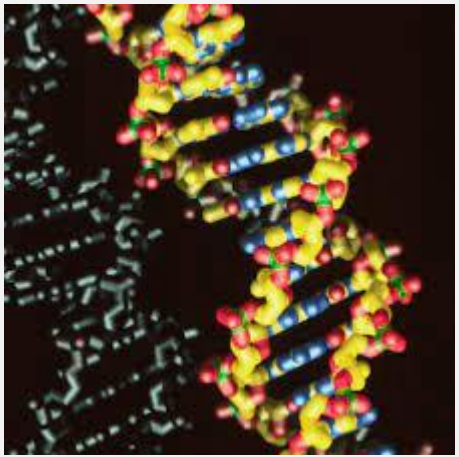

GENETIC ENGINEERING – SYNTHETIC BIOLOGY

WHAT IS A SYNTHETIC BIOLOGY?

- Making ‘engineerable’ genetic systems based standardized, predictable genetic parts (genetic circuits) to create new programmable life forms







GENETIC ENGINEERING – SYNTHETIC BIOLOGY

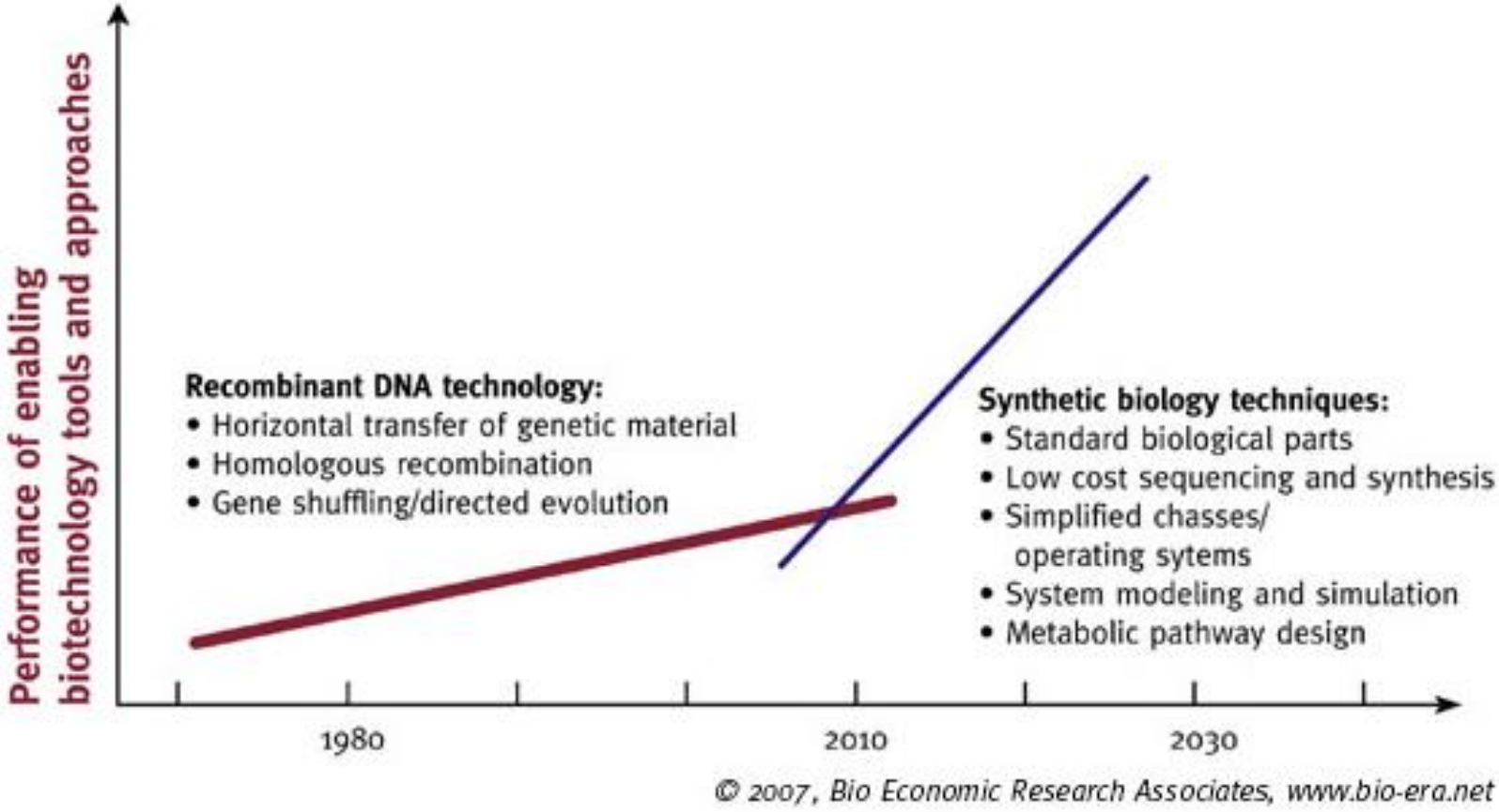
HOW IS IT DIFFERENT?

- Synthetic Biology is the next generation of genetic engineering.

	Recombinant DNA technology	Synthetic biology
Target	- Modifying existing biological systems	- Designing and fabricating new ones that are built with DNA that is partially or entirely artificial.
Level of complexity	- Focusing on expression of single genes or gene components	- Involves whole interacting genetic networks, genomes and entire organisms
What is it about?	- Introducing of naturally occurring, mutated or otherwise altered DNA into an organism with the source of DNA being an organism of a different or the same species. - Limited to the modification of natural organisms	- Introducing synthetically constructed parts - Extended to the construction of new life forms with no natural counterpart.

Both incorporate the techniques of molecular biology

Figure 1-2: *An Inflection Point for Biological Technology*



This is now…

Genome READING

2015 Study: 2,500 high-throughput instruments, located in nearly 1,000 sequencing centers in 55 countries

PLoS Biol. 2015 Jul; 13(7): Stephens et al "**Big Data: Astronomical or Genomical?"**

Annual genomic data If 1 bp was a grain of sand… New industrial raw material

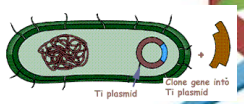
2015: 35 petabases of genome sequencing (35 thousand trillion BP)
-32,000 microbial genomes, ~5,000 plant and animal genomes, and ~250,000 individual human genomes .

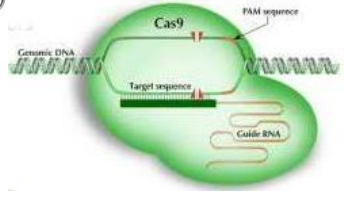
2025: 1 zetabase of genome sequencing (1 thousand million trillion BP).
Encompass All 1.2 million described species of plants and animals.
Estimated that there will be at least 2.5 million plant and animal genome sequences

PLoS Biol. 2015 Jul; 13(7): Stephens et al **"Big Data: Astronomical or Genomical?"**

This is now… new industrial tools

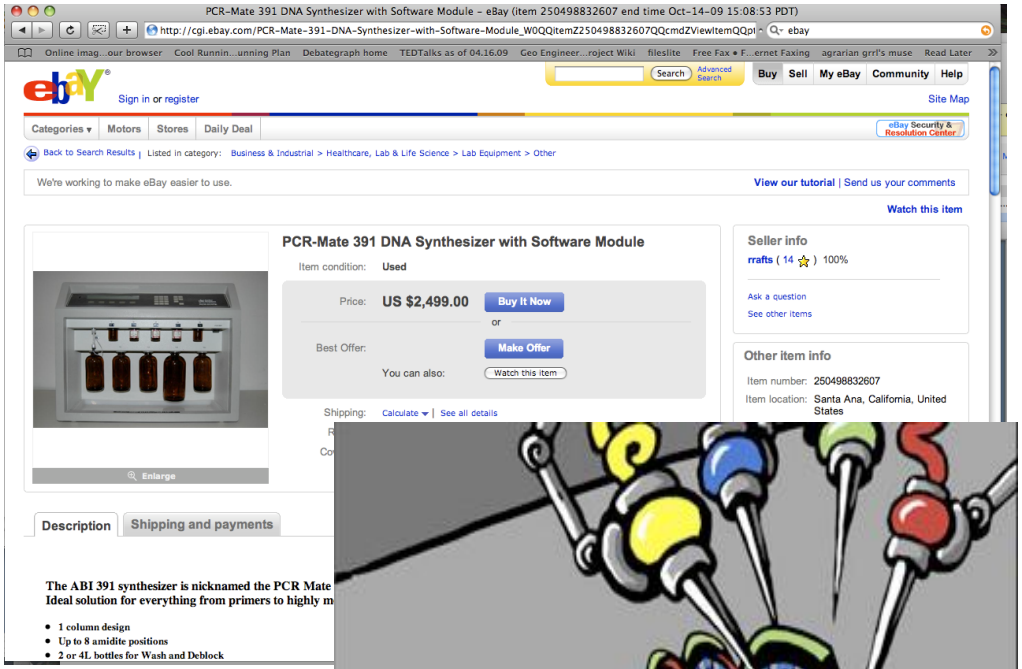
GMO’s 2.0 – Wider toolbox of techniques,

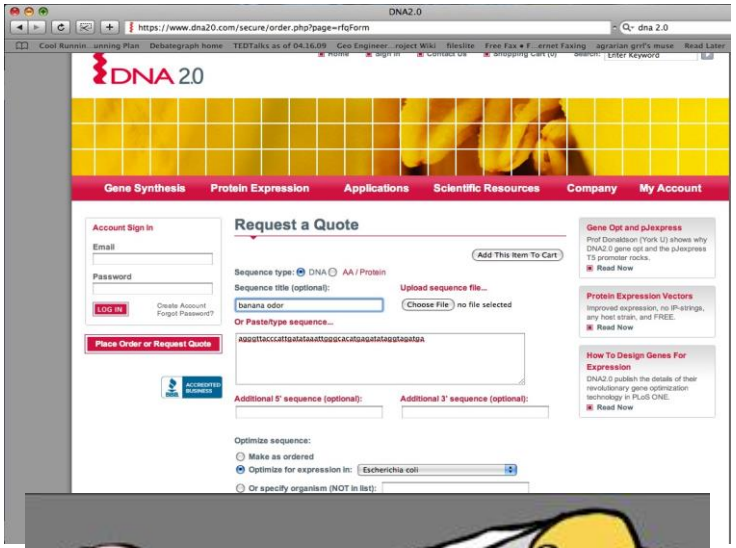




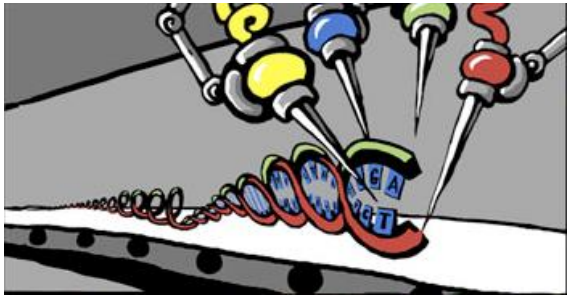
lustered Regularly Interspersed Short Palindomic Repeats (CRISPR),
Directed Evolution,
DNA-based genetic circuits,
DNA Synthesis and Assembly,
Epigenetic Modification,
Expanded Genetic Alphabets,
Genome Editing,
Genome-level Engineering,
Genome Shuffling,
Gibson Assembly,
Minimal Genomes,
Multiplex Automated Genome Engineering,
Oligonucleotide Directed Mutagenesis,
Protocell Construction,
Refactoring of Genomes,
RNA-Directed DNA Methylation (RDDM).
RNAi (RNA Interference)
Standard Modular DNA ‘parts’ or ‘Biobricks’
Synthetic Metabolic Pathway Engineering,
Synthetic Genomics,
:ription-Activator-like Effector Nucleases (TALENs),
Xenobiology,
Zinc Finger Nucleases(ZFN),

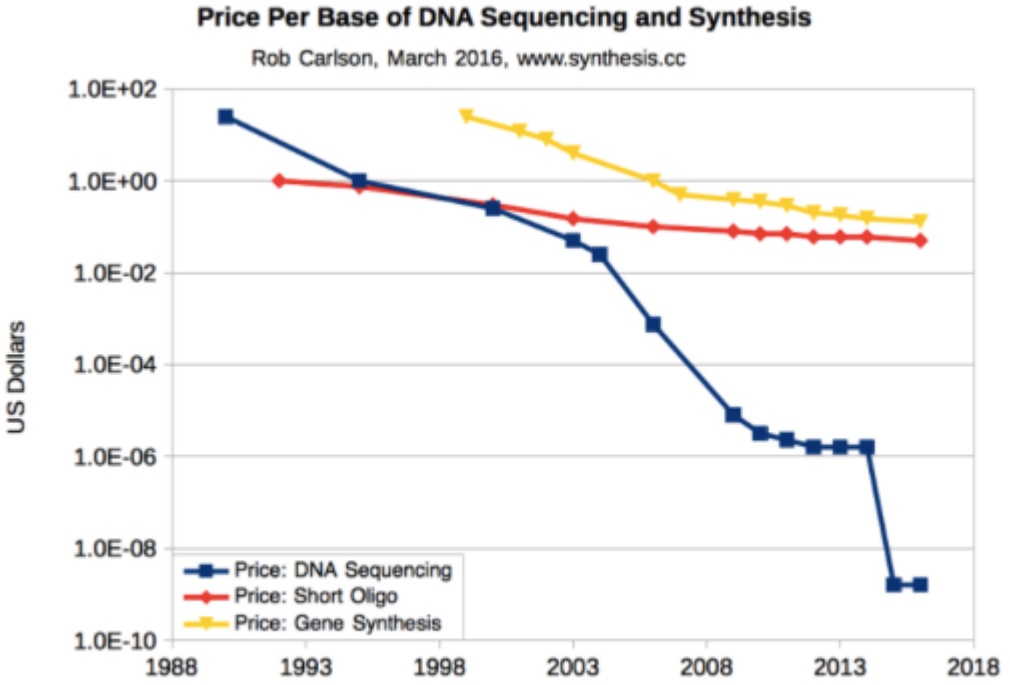
Synthesizing the parts of life





Genome WRITING



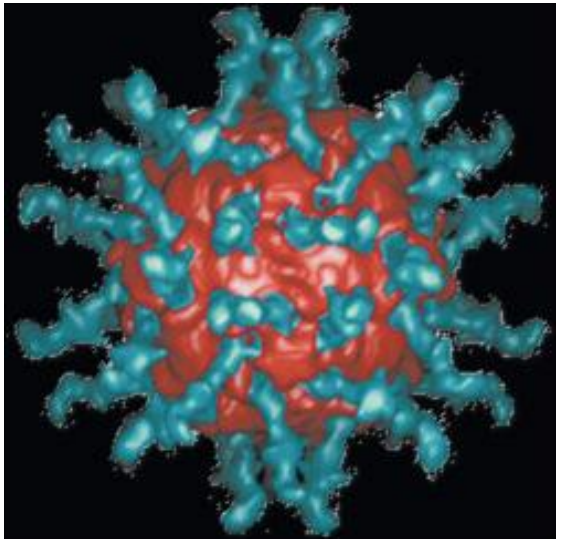


Commercial gene synthesis: 7- 17 cents per base Currently a billion base market – around a million genes.

Commercial Oligo Synthesis – 5 cents per base. Currently a 4.8 billion base market

Roughly equivalent to one human genome per year.

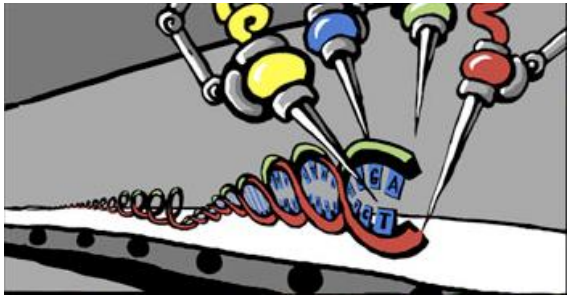
Source Rob Carlson synthesis.cc – March 2016



Polio genome =
Approx $500 to
synthesize??

7500bp

Genome WRITING



Human genome currently $21 billion

¼ Gates (approx)
1/3 Zuckerberg
1/5 Bezos
1 week US military spending

The Genome Project-write (GP-write) will be an open, international research project led by a multi-disciplinary group of scientific leaders who will oversee a reduction in the costs of engineering and testing large genomes in cell lines more than 1,000-fold within ten years.

GP-write will include whole genome engineering of human cell lines and other organisms of agricultural and public health significance. Thus, the Human Genome Project-write (HGP-write) will be a critical core activity within GP-write focused on synthesizing human genomes in whole or in part. It will also be explicitly limited to work in cells, and organoids derived from them only. Because of the special challenges surrounding human genomes, this activity will include an expanded examination of the

Download the GP-write White Paper

Learn How to Get Involved

Robotic Genome construction

“AI - POWERED BIOTECH”

“Zymergen’s algorithms suggest making

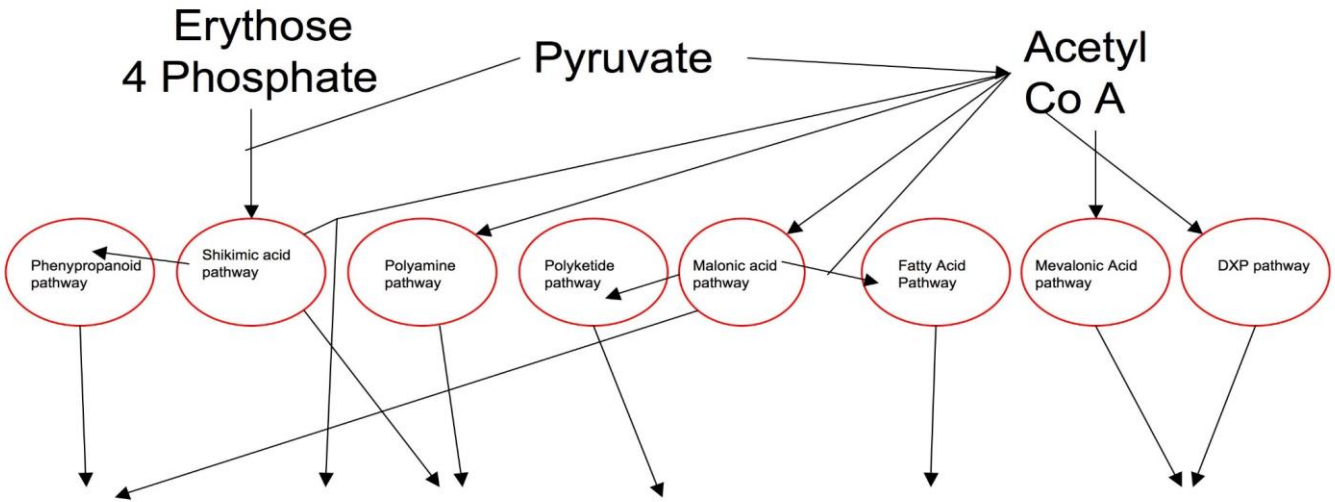
1,000 or so changes to the microbe’s genetic material . Then the robots take over, injecting the suggested DNA snippets into the specimens, testing their properties, collecting

SYNTHETIC BIOLOGY INDUSTRY

- **Rapid market growth** ($10.8 billon for 2016. $38.7 billion by 2020)
- **Govt funding rapidly growing** (US: dominated by Defence/DARPA)
- **Many deals with fortune 500** companies – food, flavour, chemicals, cosmetics, fuels, pharma, textiles.

“programming” lifeforms

Biosynthetic routes aiming to completely replace any natural sources”



Phenols
tannins
flavonoids
polyphenols
stilbenes
Cinnamates
Coumarins

Hemiterpenes
monoterpenes
sesquiterpenes
diterpenes
tetraterpenes
pyrethins
indole alkaloids
sterols

Over 200,000
natural compounds

Evolva – a yeast "metro" for valuable products

evolva

Ambergris

Pyrethrin

Caffeine

Opiates

Cocoa

Sandalwood

Stevia

Saffron

Musk

Frankincense

Caviar

Mint

Capsiate

Taxol

Vanilla

Dopamine

Resveratrol

Turmeric

Carmine

Breast Milk

Ginseng

Truffles

GMO 2.0 INDUSTRY

SECOND WAVE:

CROPS, INSECTS, ANIMALS

GENETIC ENGINEERING – SYNTHETIC BIOLOGY

GENOME EDITING TECHNIQUES

- Give 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 CRISPR-CAS9, Zinc Fingers, TALENS, Directed Mutagenesis.

GMO +

"New Plant Breeding techniques"

Genome edited crops:
- CRISPR-CAS9
- Zinc Finger Nucleases
- TALENS
- Oligo-Directed Mutagenesis

Epigenetic Enginering
- RNAi (RNA Interference)
- RDDM (RNA Directed DNA Methylation)

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SHORT SHARP SCIENCE 23 September 2016

Monsanto cuts deal to use CRISPR to engineer food

Monsanto agribusiness greenhouses on top of a research building in St Louis
Brent Stirton/Getty

MIT Technology Review

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Biomedicine

DuPont Predicts CRISPR Plants on Dinner Plates in Five Years

Powerful and possibly unregulated gene editing

Agricultural biotech giants are starting to make moves into CRISPR gene editing, saying they'll be selling seeds engineered with the technology by the end of this decade.

DuPont said today it entered an agreement with Caribou Biosciences, a spin-off from the laboratory of Jennifer Doudna at the University of California, Berkeley, who carried out key work on CRISPR-Cas9, a technology that provides something like a find-and-replace feature for DNA.

DuPont says it is already growing corn and wheat plants edited with

DUPONT FOOD SECURITY

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September 29, 2016

DuPont Pioneer & CIMMYT Form CRISPR-Cas Public/Private Partnership

DuPont Pioneer and the International Maize and Wheat Improvement Center (CIMMYT) have entered into a Master Alliance Agreement to jointly develop improved crops using CRISPR-Cas advanced plant breeding technology for characteristics that address the needs of smallholder farmers around the world. The collaboration announcement coincides with CIMMYT's 50th anniversary celebrations being held this week in El Batán, Mexico.

"Working together with CIMMYT will enable smallholder farmers to benefit from technology like CRISPR-Cas, helping them solve their challenges," said DuPont Pioneer President Paul Schickler.

Pioneer and CIMMYT collaborations span decades and have contributed significantly to the food security and livelihoods of farmers and consumers in developing countries.

"In a world of rapid technology evolution, it's essential that new approaches such as CRISPR-Cas are applied widely to benefit both poorer and wealthier farmers," said CIMMYT Director General Martin Kropff. "This collaboration with DuPont Pioneer will allow us to provide climate and disease

Paul Schickler DuPont Pioneer President, and CIMMYT Director General, Martin Kropff, sign CRISPR-Cas collaboration agreement at CIMMYT 50th anniversary celebration in Mexico.

SCIENCE

CRISPR-MODIFIED CORN MAY SOON BE READY FOR MARKET

IT WOULD BE THE FIRST CROP TO GO ON SALE THAT HAS BEEN GENETICALLY ALTERED WITH THE ENZYME

By **Alexandra Ossola** September 6, 2016

GMO +

Biotech Industry argues:

- Not GMO's according to regulations (legal argument around wording) – the techniques do not give rise to 'a GMO'
- More 'precise'/ less intervention ('editing')
- Do not use 'foreign DNA' therefore consumers will not be concerned.
- In some cases do not even involve modifying DNA.

NGO's/critics argue:

- This is genetic engineering 2.0 – therefore should be regarded as GMO's
- Genome editing has similar 'off-target' effects as 1st gen GMO's – risks.
- Techniques are new and more powerful therefore GMO risk concerns are magnified.
- Creates entirely novel sequences.
- Wrong to claim that new edited sequences are 'predictable'/well understood. Small genome changes > big changes in organism.

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THE CROPS

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CANOLA

Cibus' new ***SU Canola***™ is a non-transgenic (non-GMO) sulfonylurea (SU) herbic canola that is

1) now available in the United States;

2) on track to be available in Canada in 2017; and,

3) expected to be launched in other major global markets after 2018.

Bloomberg Technology

Markets Tech Pursuits Politics Opinion Businessweek

Americans Are Buying Gene-Edited Food That's Not Labeled GMO

by **Craig Giammona** and **Jack Kaskey**
July 14, 2016 — 5:00 AM EDT

- USDA passes on oversight of cooking oil new to store shelves
- Monsanto, DuPont, Dow developing crops with the new technology

Table 1: CRISPR-edited plants in the pipeline that USDA will not oversee

From: With a free pass, CRISPR-edited plants reach market in record time

Date of USDA response	Inquiring institution (location)	Plant trait engineered with CRISPR–Cas9
10/16/2017	USDA ARS, Plant Science Research Unit (St. Paul, Minnesota)	Soybean (*Glycine max)* with drought and salt tolerance; achieved by disrupting the *Drb2a* and *Drb2b* genes (double-stranded RNA-binding protein2 genes)
8/29/2017	Yield10 Bioscience (Woburn, Massachusetts)	Camelina with increased oil content; target genes not disclosed
4/07/2017	Donald Danforth Plant Science Center (St. Louis)	*Setaria viridis*, or green bristlegrass, with delayed flowering time; achieved by deactivating the *S. viridis* homolog of the *Zea mays* ID1 gene
4/18/2016	DuPont Pioneer (Johnston, Iowa)	Waxy corn with starch composed exclusively of amylopectin; achieved by inactivating the endogenous waxy gene *Wx1* that encodes a granule-bound start synthase catalyzing production of amylose
4/13/2016	The Pennsylvania State University (University Park, Pennsylvania)	White button mushroom *(Agaricus bisporus)* with anti-browning properties; achieved by knocking out a gene coding for polyphenol oxidase (*PPO*)
Source: USDA		

“Gene editing could, for example, be used to knock out the receptor that the fungus uses to invade cells

nature International weekly journal of science

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NATURE | NEWS

CRISPR tweak may help gene-edited crops bypass biosafety regulation

Technique deletes plant genes without adding foreign DNA.

David Cyranoski

19 October 2015

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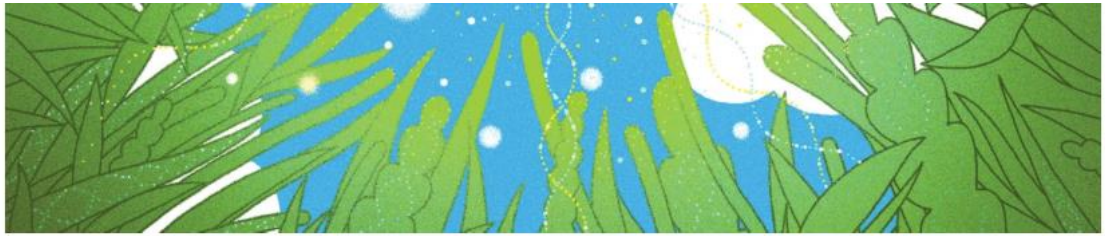
GMO +

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

Gene Drives

Fig 1a. Normal inheritance in 4 generations of flies:

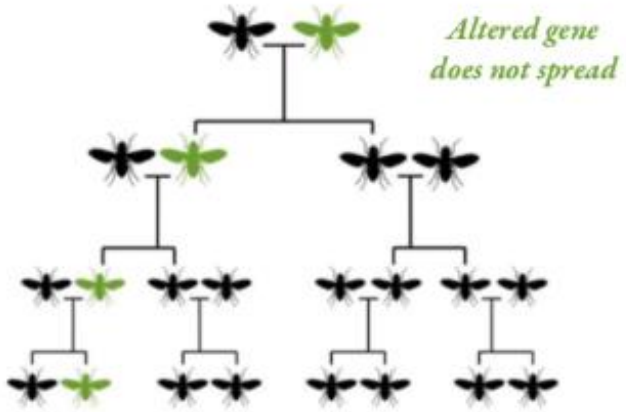
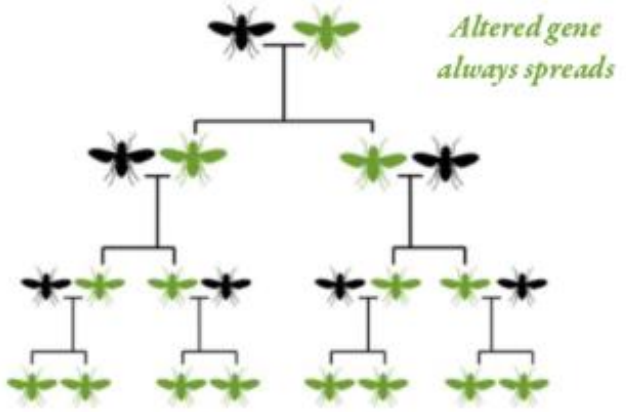


Fig 1b. Gene drive inheritance in 4 generations of flies:



GENETIC ENGINEERING – SYNTHETIC BIOLOGY

MAIN BIOSAFETY ISSUES

- The behavior of synthetic biological systems is inherently uncertain and unpredictable especially when it comes to potential ecological risks

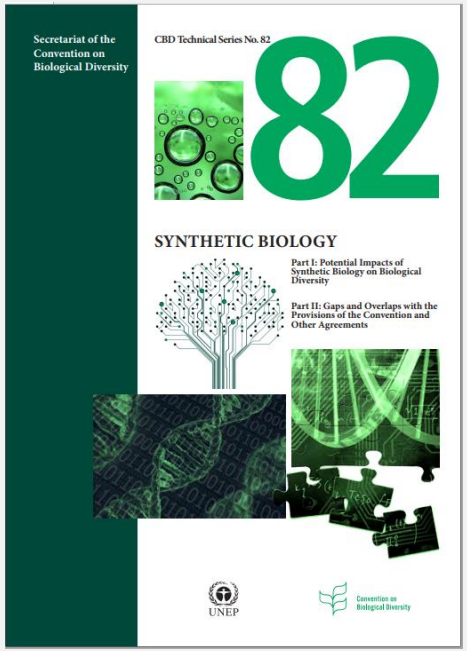
- No risk assessment protocols have been developed to assess all potential risks associated with synthetic biology

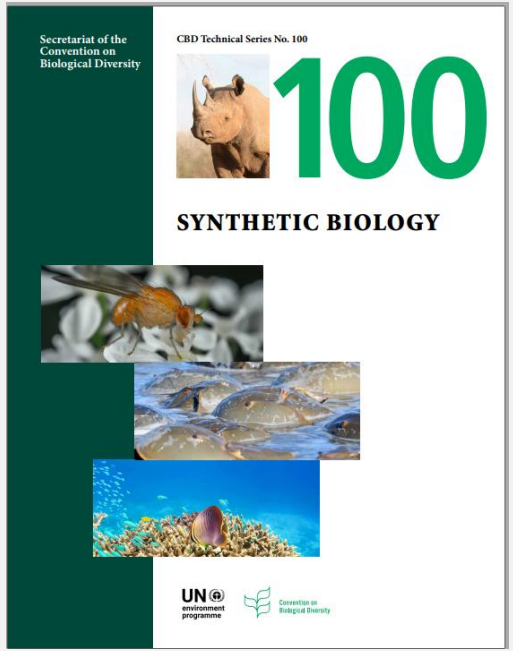
- Assured containment of organisms developed with synthetic biology is not always practical or possible. (Xenobiology does not offer safe or reliable tools to ensure confinement or biological containment)

- Synthetic biology Researchers do not necessarily have training in biological sciences or biosafety.

SYNTHETIC BIOLOGY

CBD TECHNICAL SERIES





GENETIC ENGINEERING – SYNTHETIC BIOLOGY

MAIN BIOSAFETY ISSUES

- The Cartagena Protocol does not sufficiently cover synthetic biology and its potential impacts on biodiversity.
  - i. virtual (digital) transfer of LMOs
  - ii. transfer of constituent parts of an LMO
  - iii. import of synthetic organisms for contained use.

- Currently there is no comprehensive regulatory apparatus for the oversight and governance of synthetic biology

- Synthetic biology could profoundly alter current practices related to the conservation and sustainable use of biodiversity and rules governing access and benefit sharing. It will also affect Food and Livelihood Security, especially in the developing World

Thank you !

For more information, please email

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