What's Happening in the World of Synthetic Biology: A Report From A Global Conference

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What is Synthetic Biology?

Synthetic biology is a field of science that involves redesigning organisms for useful purposes by engineering them to have new abilities. Synthetic biology researchers and companies around the world are harnessing the power of nature to solve problems in medicine, manufacturing and agriculture. – NHGRI

Redesigning organisms [or cell free extracts] so that they produce a substance, such as a medicine or fuel, or gain a new ability, such as sensing something in the environment, are common goals of synthetic biology projects.

Sustainability!

Novelty!

Historic Landmarks of Synthetic Biology

1973: First molecular cloning and amplification of DNA in a plasmid is published in *P.N.A.S.* by Cohen, Boyer et al. constituting the dawn of synthetic biology.

1988: First DNA amplification by the polymerase chain reaction (PCR) using a thermostable DNA polymerase is published in *Science* by Mullis et al.

1993: Arnold publishes her work on the "evolution" of subtilisin E for increased activity in DMF

2000: Two papers in *Nature* report synthetic biological circuits, a genetic toggle switch and a biological clock, by combining genes within *E. coli* cells.

2010: Researchers publish in Science the first synthetic bacterial genome, called *M. mycoides* JCVI-syn1.0. The genome is made from chemically-synthesized DNA using yeast recombination.

2011: Functional synthetic chromosome arms are engineered in yeast.

2012: Charpentier and Doudna labs publish in *Science* the programming of CRISPR-Cas9 bacterial immunity for targeting DNA cleavage. This technology greatly simplified and expanded eukaryotic gene editing.

Nobel Prizes of Synthetic Biology

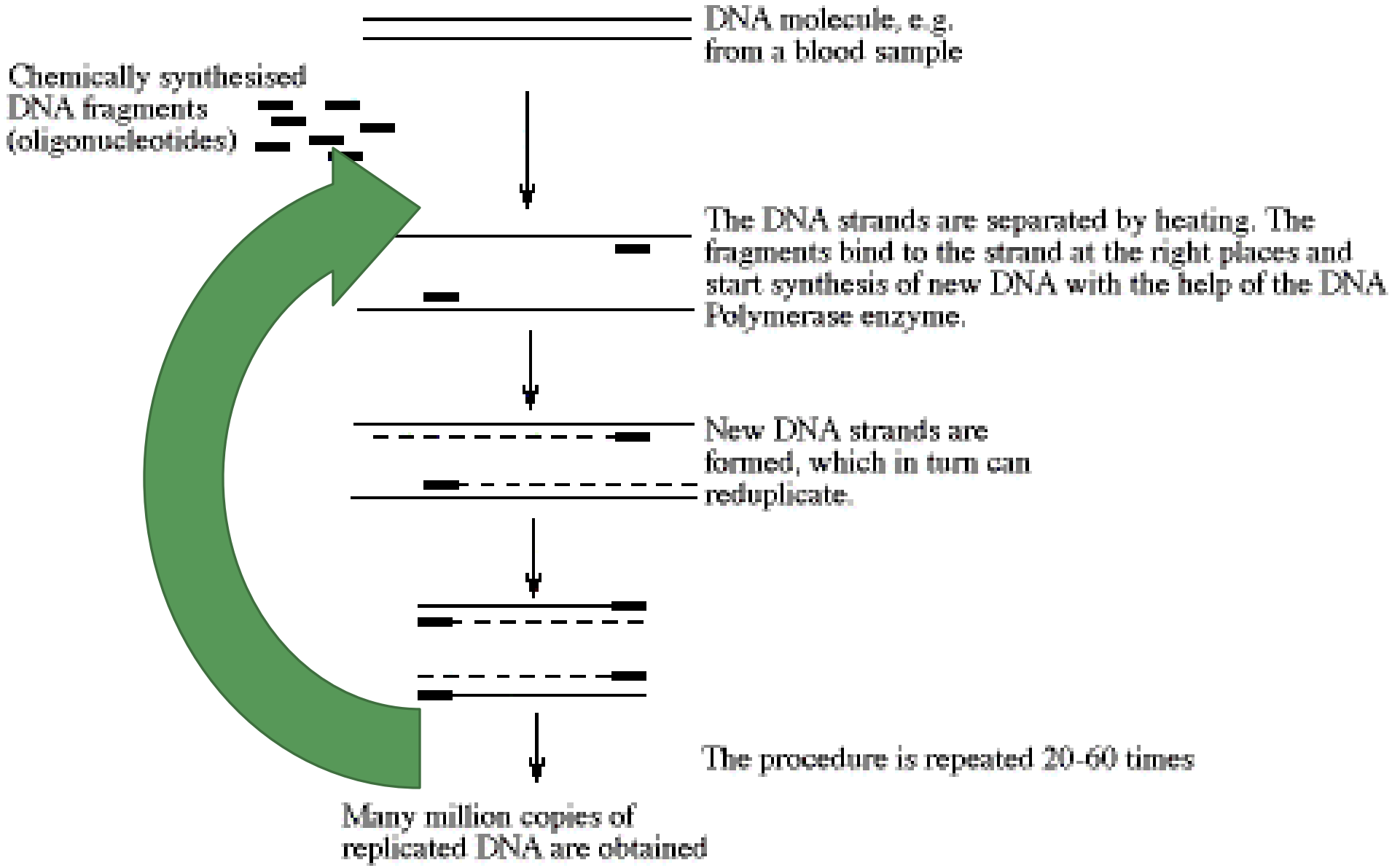
1978: Arber, Nathans and Smith win the Nobel Prize in Physiology or Medicine for the discovery of restriction enzymes

1993: The Nobel Prize in Chemistry 1993 was awarded "for contributions to the developments of methods within DNA-based chemistry" jointly with one half to Kary B. Mullis "for his invention of the polymerase chain reaction (PCR) method" and with one half to Michael Smith "for his fundamental contributions to the establishment of oligonucleotide-based, site-directed mutagenesis and its development for protein studies."

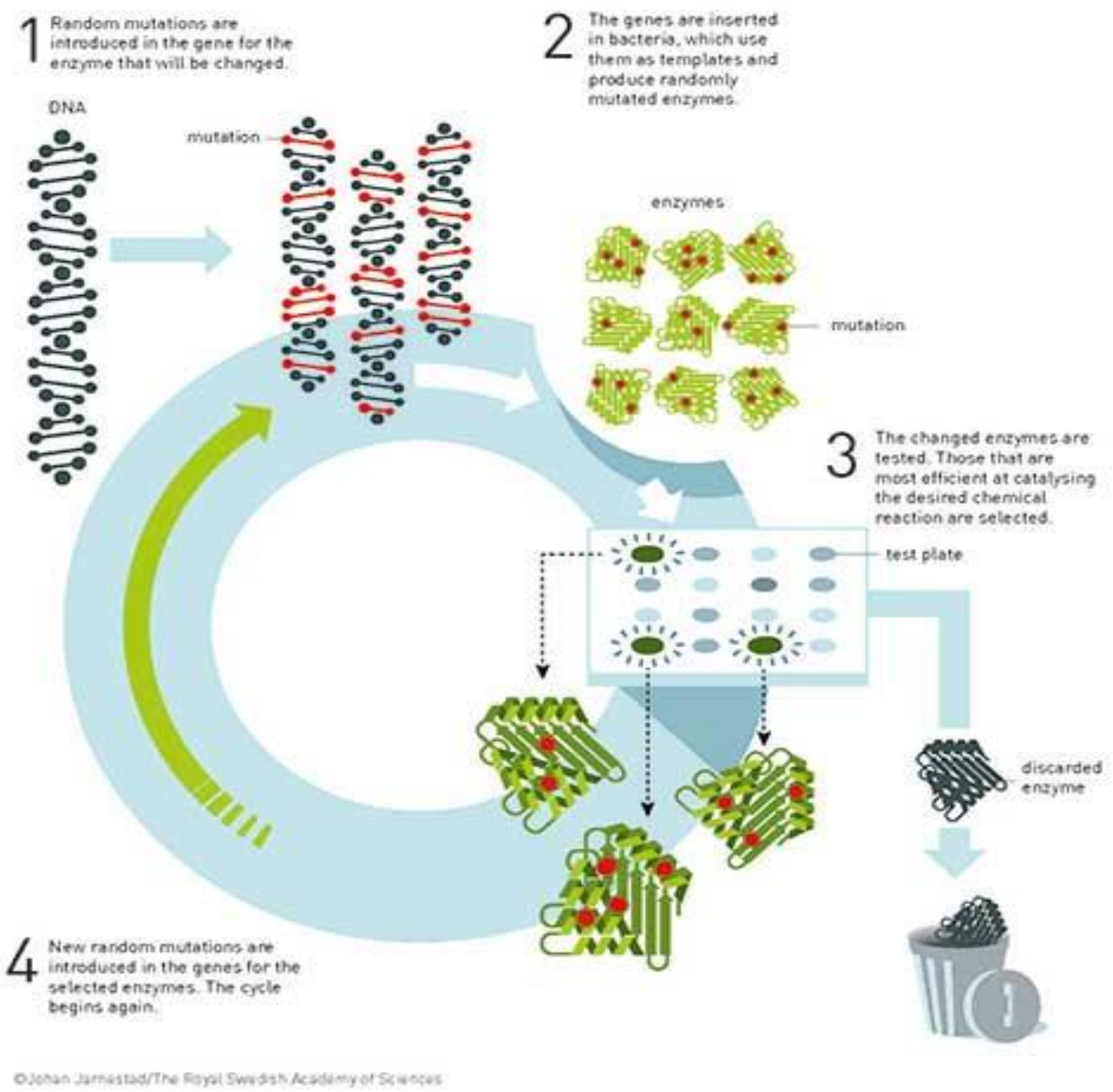
2018 Nobel Prize in Chemistry is awarded to Frances H. Arnold, George P. Smith and Sir Gregory P. Winter, because they have revolutionised both chemistry and the development of new pharmaceuticals through directed evolution.

2020: the Nobel Prize in Chemistry 2020 to Emmanuelle Charpentier and Jennifer A. Doudna "for the development of a method for genome editing"

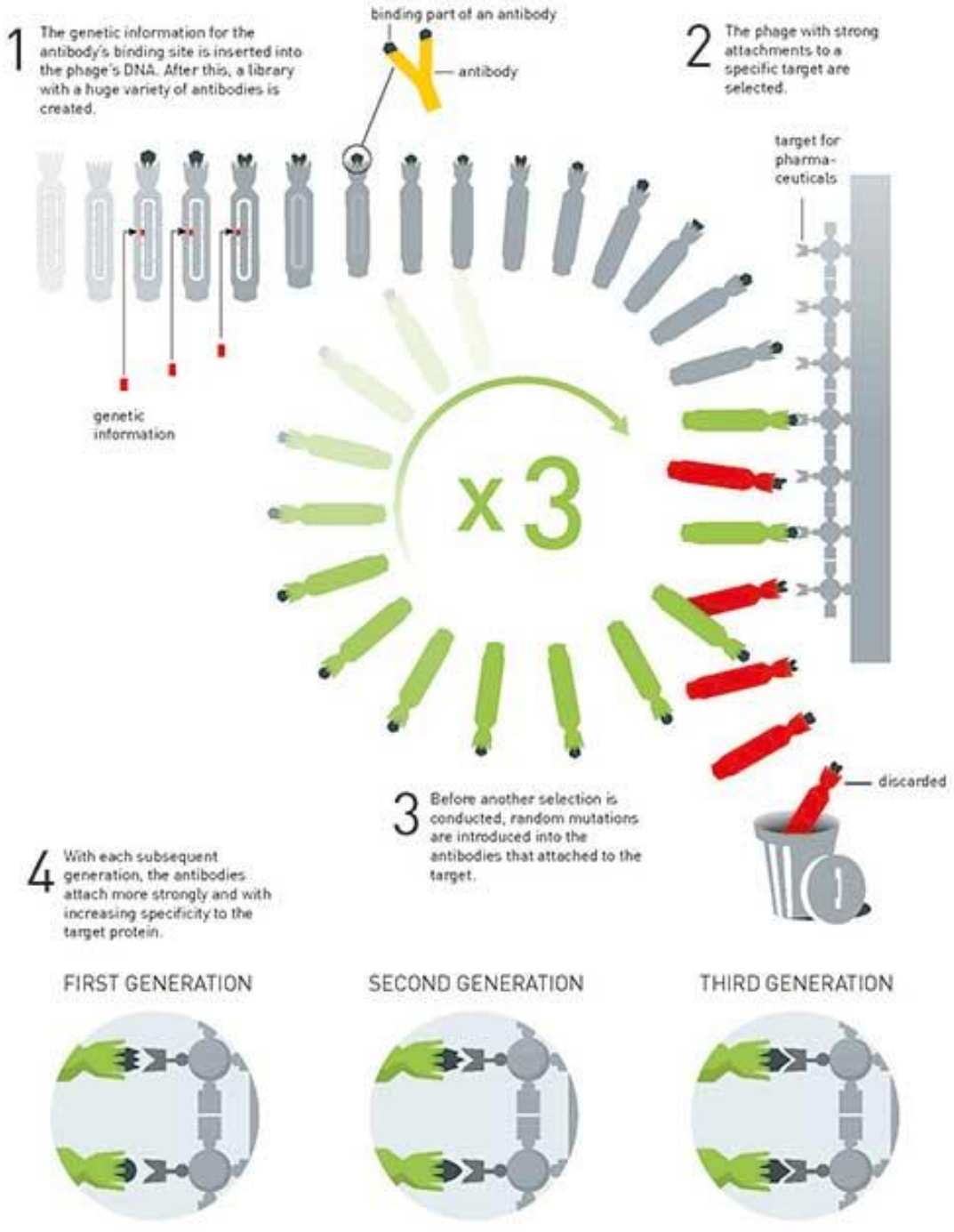
Amplifying DNA with PCR



The underlying principle for the directed evolution of enzymes.



The principle for the directed evolution of antibodies using phage display



Historic Products of Synthetic Biology

1978-1982: Genes encoding human insulin and growth hormone were cloned and expressed in *E. coli.* The first licensed drug produced using recombinant DNA technology was human insulin, which was developed by Genentech and licensed as well as marketed by Eli Lilly in 1982.

1990s [Nobel Prize work] Greg Winter and his colleagues founded a company based on the phage display of antibodies. It developed a pharmaceutical entirely based on a human antibody: adalimumab. 2002 approved for the treatment of rheumatoid arthritis

1996/1998: *Roundup Ready* soybeans/corn become commercially available from Monsanto

2003: Researchers engineer an artemisinin precursor pathway [from plant] in *E. coli.*

2020-2030: six commercially-available products that are changing our world -- leghemoglobin, sitgaliptin, diamines, engineered bacteria, CAR-Ts, genome edited soy

SynBioBeta

SynBioBeta was founded in 2012 by John Cumbers and is located in Beverly Hills, California. It is an organization seeking to help scientists, investors, entrepreneurs, and policy makers create sustainable products and services using synthetic biology. Current CEO Frank Tate.

DNA synthesis/Cloning

Strain engineering

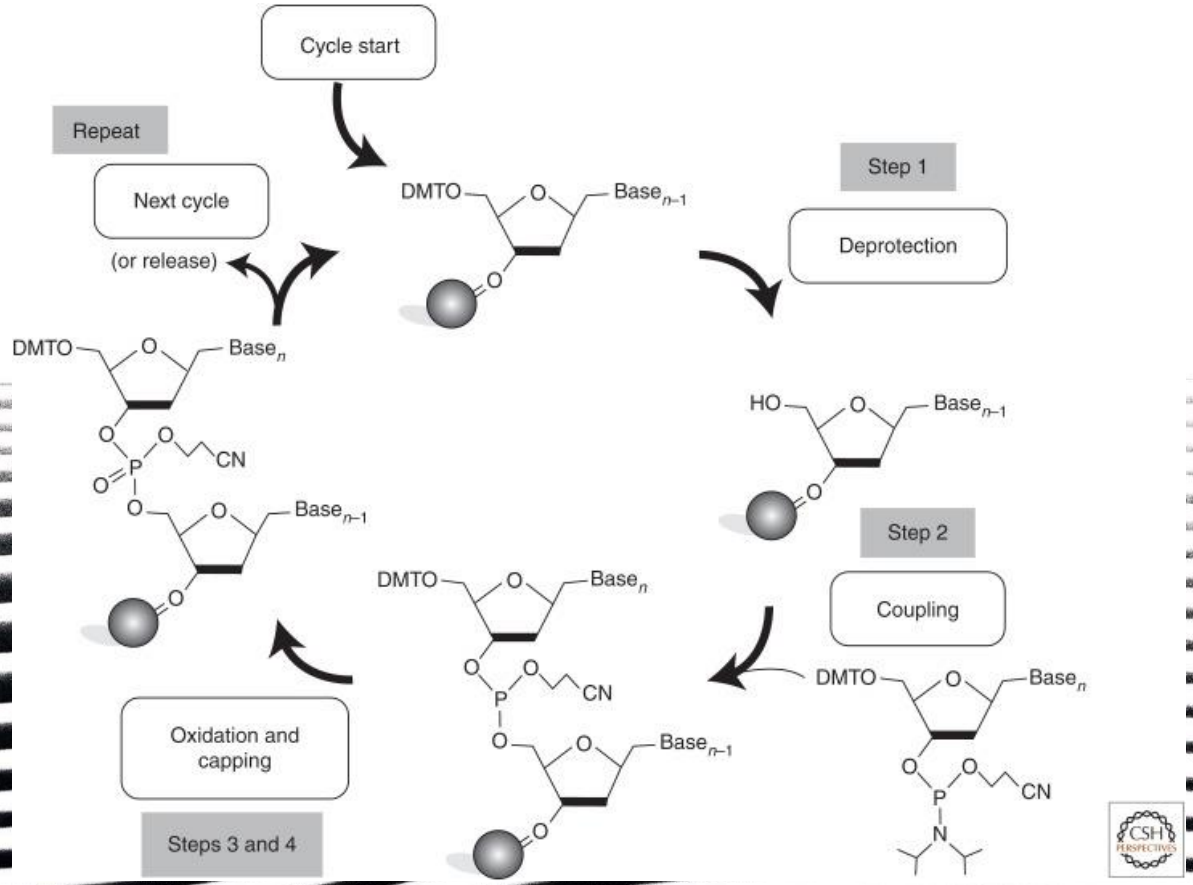
BioFoundry Services

Alternate Food

DNA SYNTHESIS CLONING

Write whatever you want

Phosphoramidite-based synthesis of oligonucleotide
Efficient up to 60 bases



DNA Synthesis/Cloning

TWIST BIOSCIENCE

- Genes
- Oligo Pools
- NGS
- Variant Libraries
- Synthetic Controls
- Antibodies
- SARS-CoV-2 Tools
- DNA Data Storage

DNASCRIPT

SYNTAX System

On-demand, in-house oligo production

GenScript®
Make Research Easy

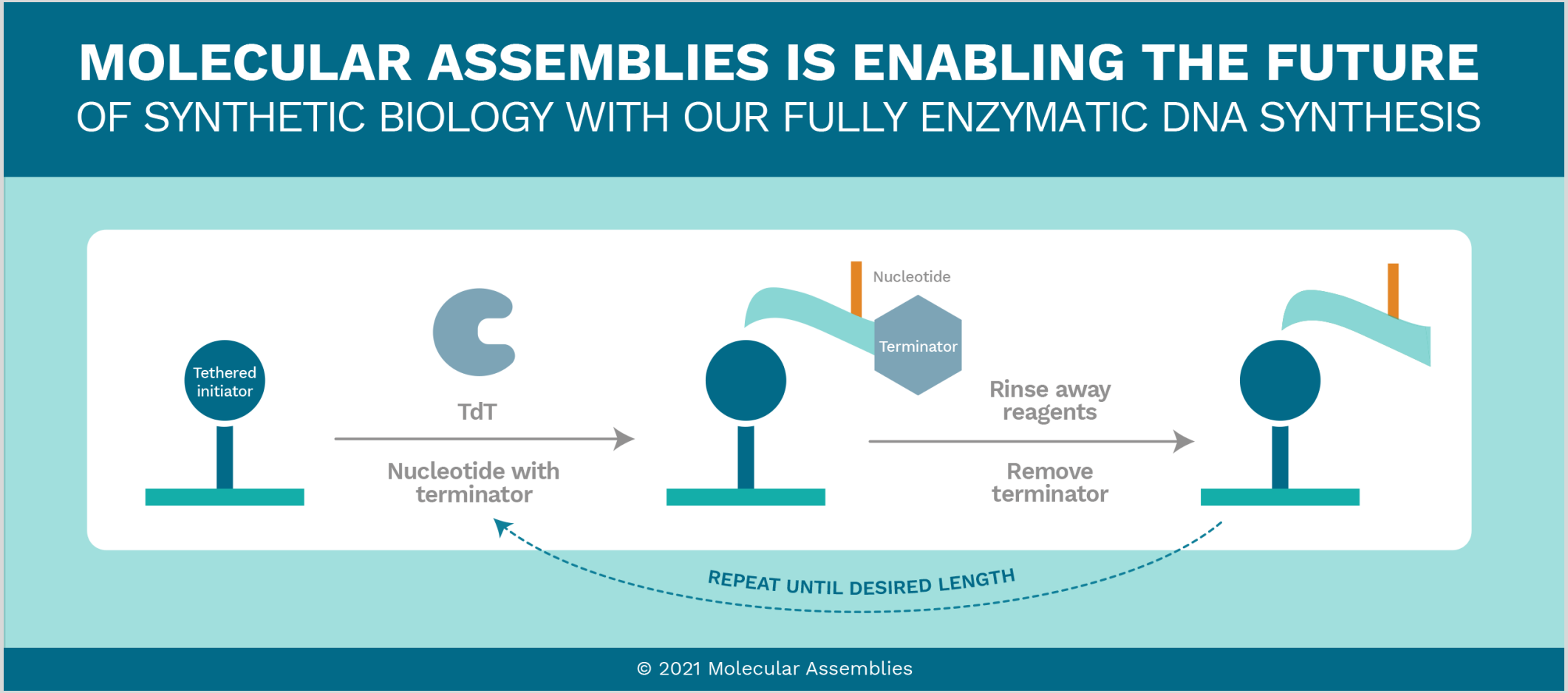
- Gene Services
- Peptide Services
- Protein Services
- Reagent Antibody Services
- Biologics Services
- CRISPR Services
- Catalog Products
- Hot New Products

CODEX DNA

Bio XP

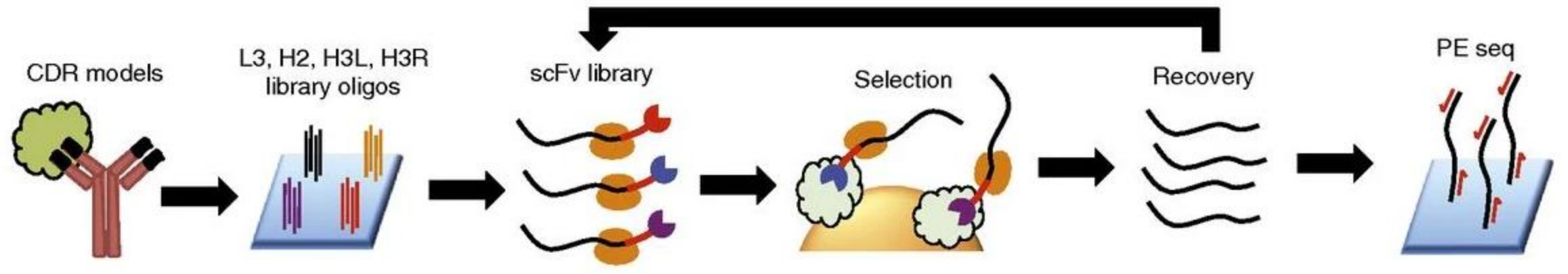
In-house fragment synthesis and cloning

DNA Synthesis/Cloning



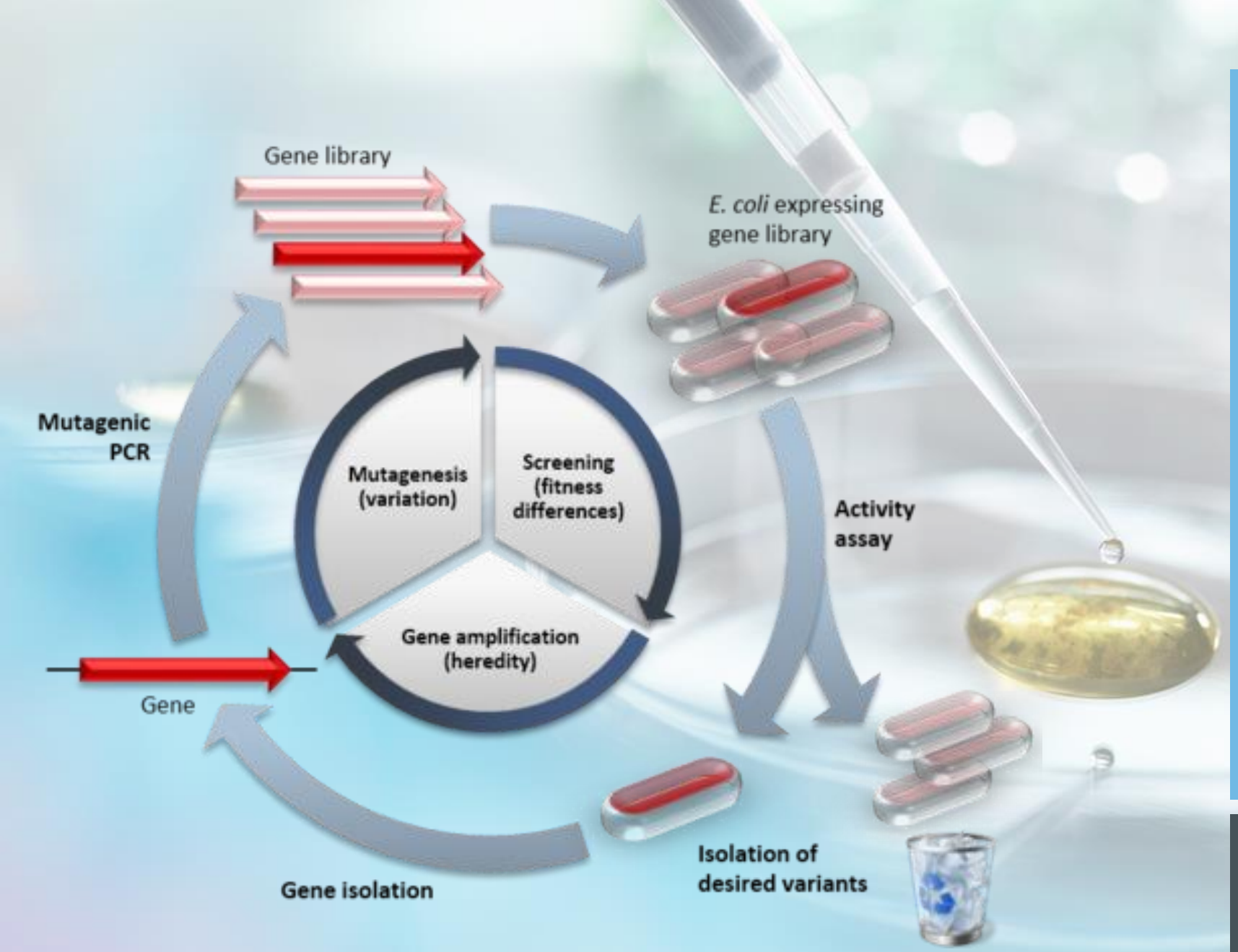
Evolved Enzyme to replace chemical synthesis

Phage Display Libraries by Design



No longer relying on random mutagenesis

Larman, H. Benjamin, et al. "Construction of a rationally designed antibody platform for sequencing-assisted selection." *Proceedings of the National Academy of Sciences* 109.45 (2012): 18523-18528.

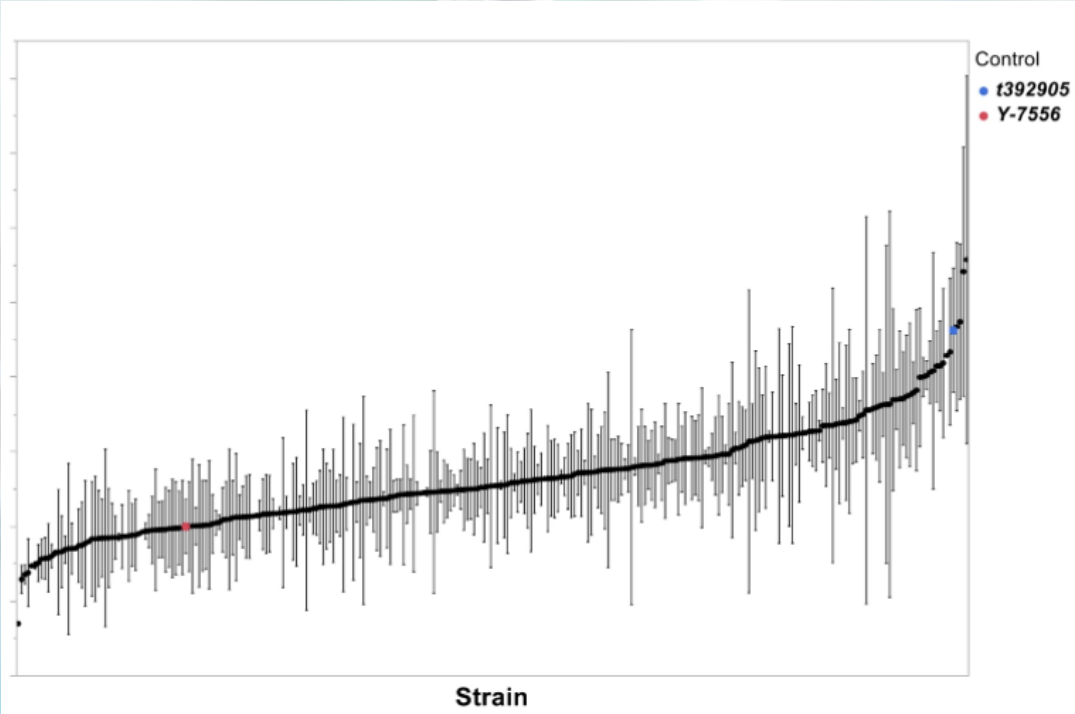


STRAIN ENGINEERING

RAPID EVOLUTION OF MICROBES

Biology by design.

Our partnership with Motif centers on developing commercial yeast strains and processes for protein production at kilogram scale.



GINKGO BIOWORKS

STRAIN ENGINEERING

RAPID EVOLUTION OF MICROBES

Biology by design.

By transferring the DNA sequences for cannabinoid production into organisms such as yeast and *E. coli*, and using the foundry and our existing high-throughput fermentation processes, Ginkgo is building strains that produce these cannabinoids at high quality and purity, starting with eight target cannabinoids.

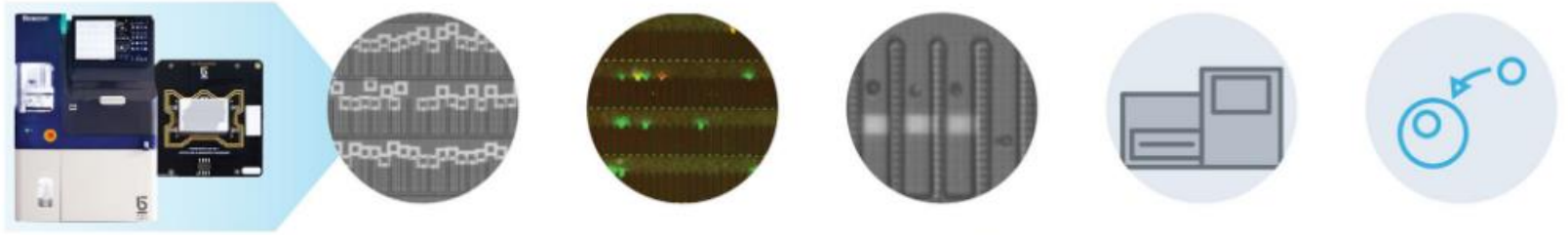
To date, we have run 8 million tests of more than 10,000 engineered strains, leveraging 30,000 different gene constructs

GINKGO BIOWORKS

STRAIN ENGINEERING

RAPID EVOLUTION OF MICROBES

RAPIDLY DOWNSELECT LEAD MOLECULES AND PREPARE LIBRARIES FOR NGS SEQUENCING



Beacon system and OptoSelect™ chip

Clone 10,000s of single B cells into NanoPen™ chambers

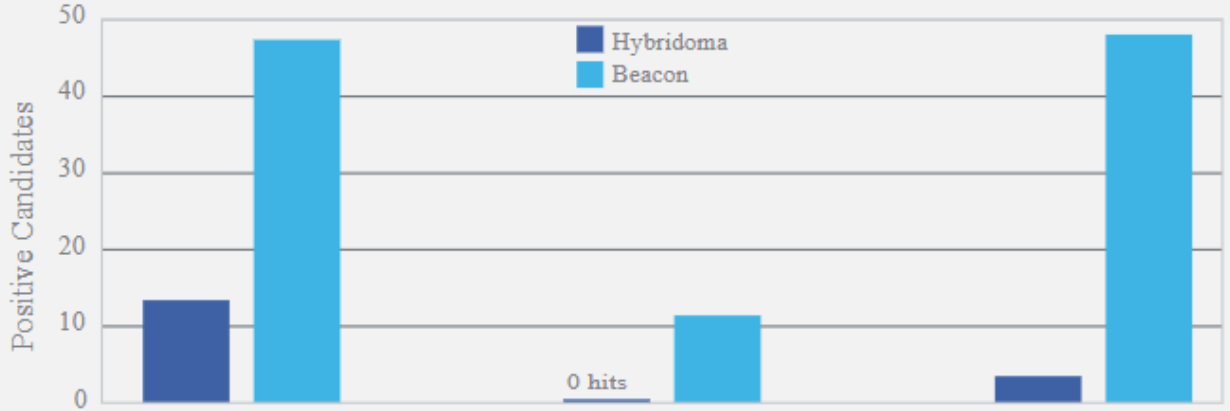
Characterize function within minutes using multiple assays

Automate cDNA synthesis and sequence recovery with the OptoSeq™ BCR kit

Prepare barcoded libraries for accurate next generation sequencing with the OptoSeq™ BCR NGS kit

Rapidly re-express antibodies without gene synthesis and cloning using the Opto BRC Re-expression kit

Direct functional profiling of B cells enables discovery of 10-fold more antibodies against GPCRs and other high-value targets.



- Adequate cell-surface expression
- Small extracellular region
- Low sequence homology

- Poor cell-surface expression
- Small extracellular region
- Very high sequence homology

- Poor cell-surface expression
- Large extracellular region
- Very high sequence homology

BERKELEY LIGHTS

STRAIN ENGINEERING

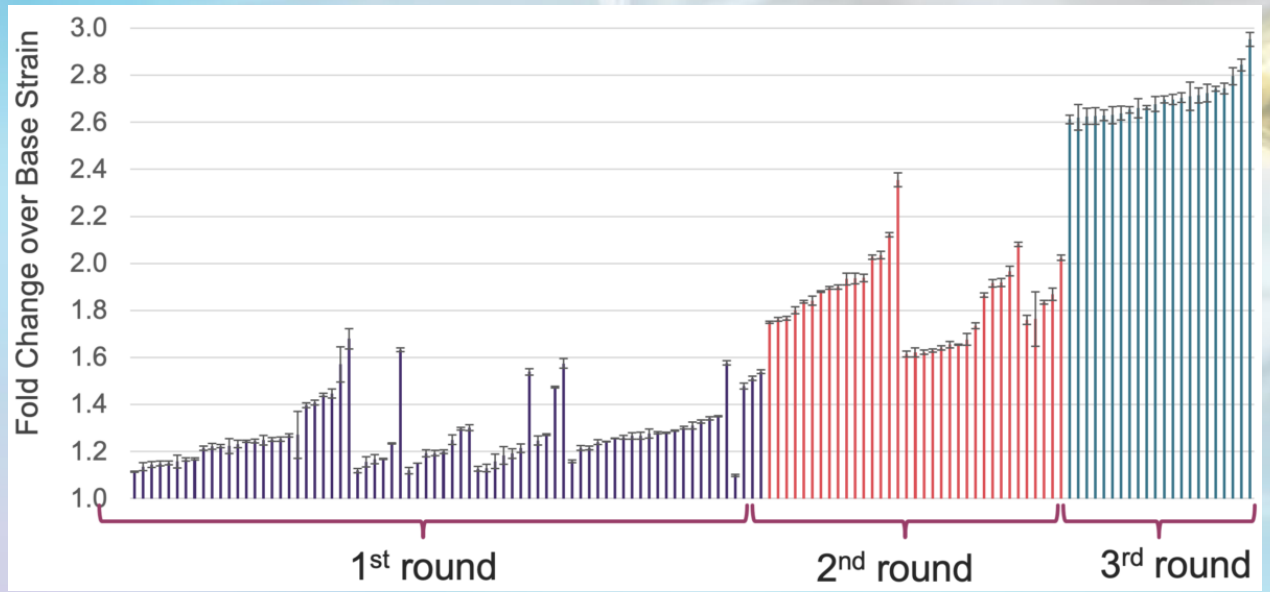
RAPID EVOLUTION OF MICROBES

Rational CRISPR editing on benchtop

INSCRIPTA®
The Digital Genome Engineering Company

STRAIN ENGINEERING

RAPID EVOLUTION OF MICROBES



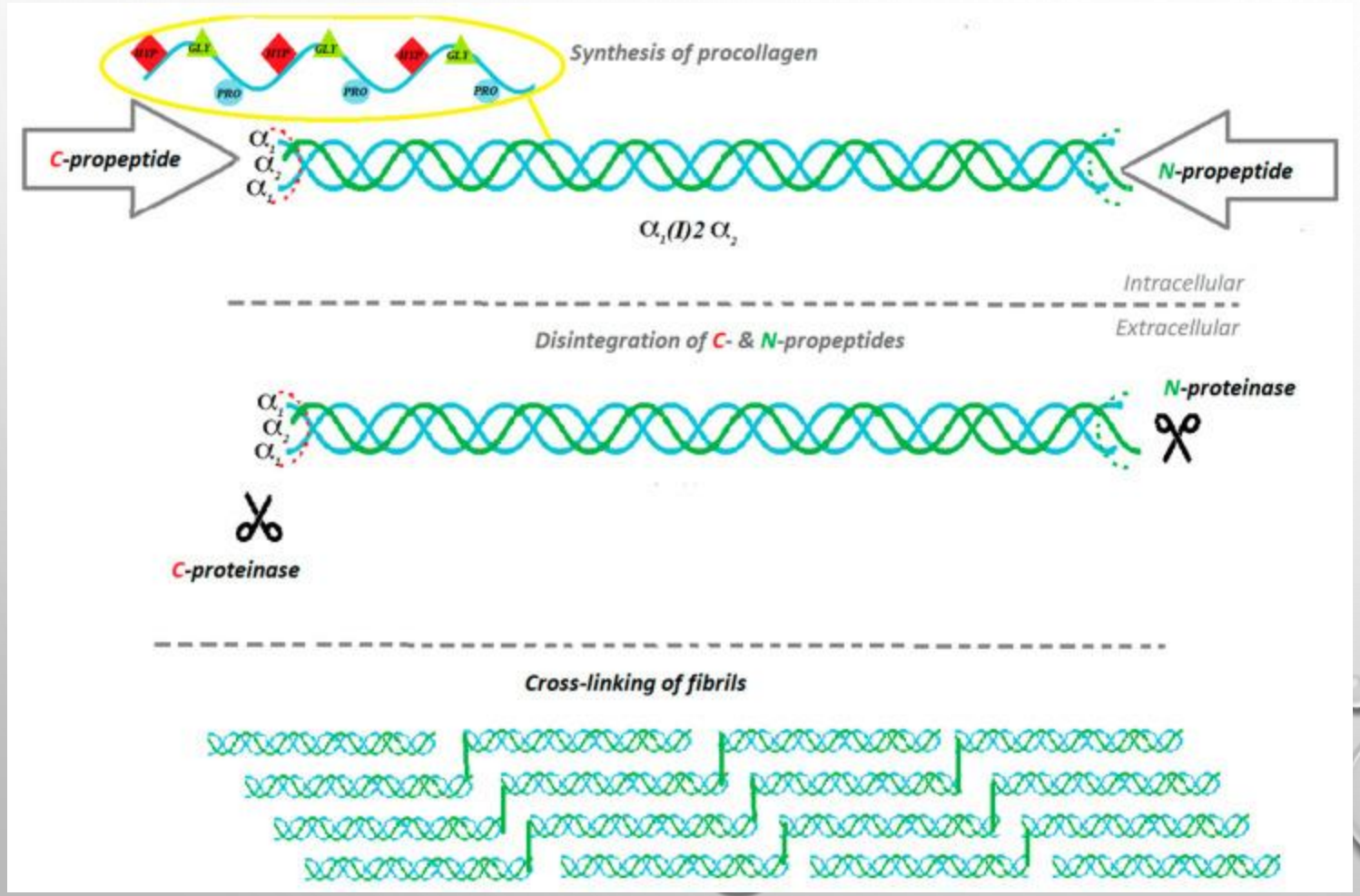
FOLD-IMPROVEMENT IN CBH1 ACTIVITY OVER 3 CYCLES OF ITERATIVE GENOME ENGINEERING (PLATE-BASED SCREENING)

BIOFOUNDRIES

FROM CHEMISTRY TO BIOLOGICAL FERMENTERS

BIOFOUNDRIES

COLLAGEN



TRADITIONAL SOURCES

LIVESTOCK

MARINE – SPONGES AND JELLYFISH AND OCTOPUSES AND FISH

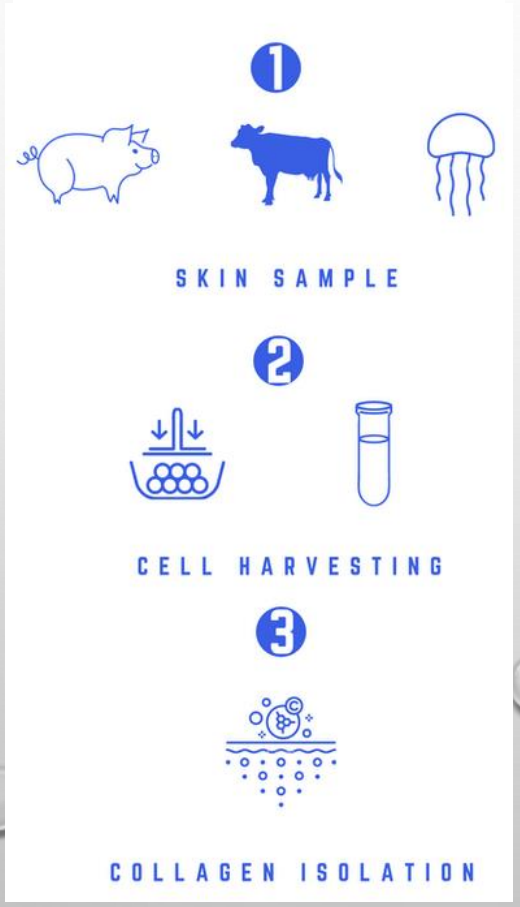
BIOFOUNDRIES

COLLAGEN

GELTOR

100% plant-based fermentation process using zero human or animal inputs.

JELLATECH



BIOFOUNDRIES

FROM CHEMISTRY TO BIOLOGICAL FERMENTERS

amyris

BIOFOUNDRIES

FROM CHEMISTRY TO BIOLOGICAL FERMENTERS

Solugen

AcquaCore™ 50 & AcquaCore™ 60
Water treatment

CEMVITA FACTORY

BIOETHYLENE FROM CO2

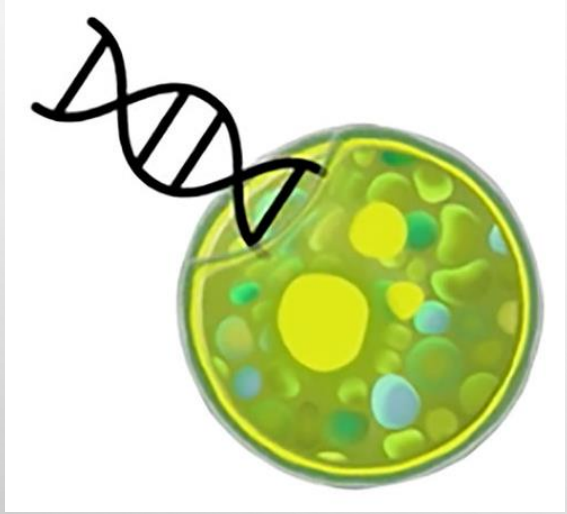
CONAGEN®

Phytolon
Natural Food Colors

BIOFOUNDRIES

FROM CHEMISTRY TO BIOLOGICAL FERMENTERS

ALGAE-C



Using our technology, we take the DNA from plants and insert it into microalgae

Platform Advantage

- 95% reduction in production cost (avg.)
- Consistent, high quality yields
- Faster development of new molecules
- 90% lower environmental footprint

MyFOREST FOODS

ALTERNATE FOODS

BUT DOES IT MEAT?

motif

ALTERNATE FOODS

BUT DOES IT MEAT?

HEMAMI™

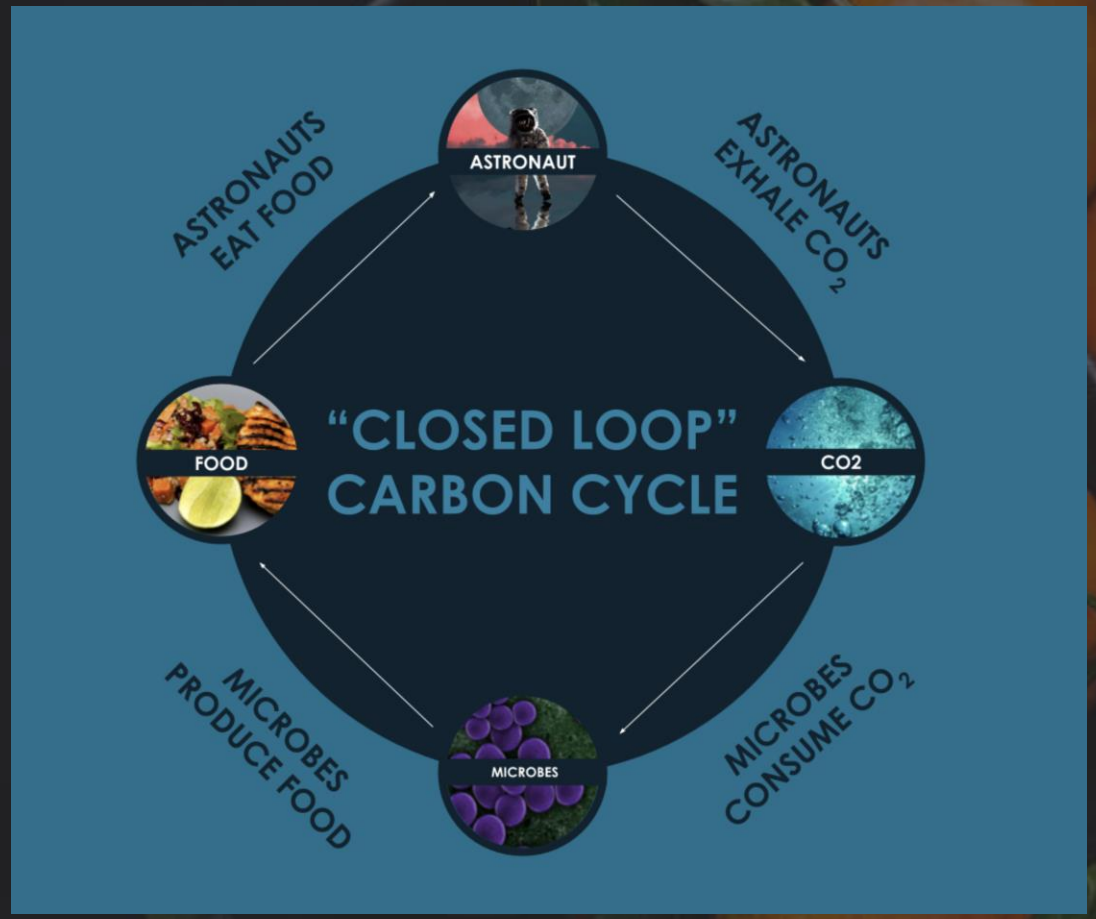
The real umami flavors, appearance and aromas of meat

APPETEX™

We literally recreated the texture of animal tissue

air protein.

ALTERNATE FOODS



Hydrogenotroph

$CO_2 + 4H_2 \rightarrow CH_4 + 2H_2O$

Methylotroph