HC70A & SAS70A
Winter 2023
Genetic Engineering in Medicine, Agriculture, and Law

Professors Bob Goldberg & John Harada

Lecture 7
21st Century Genetic Engineering Applications - Part Two

UCLA

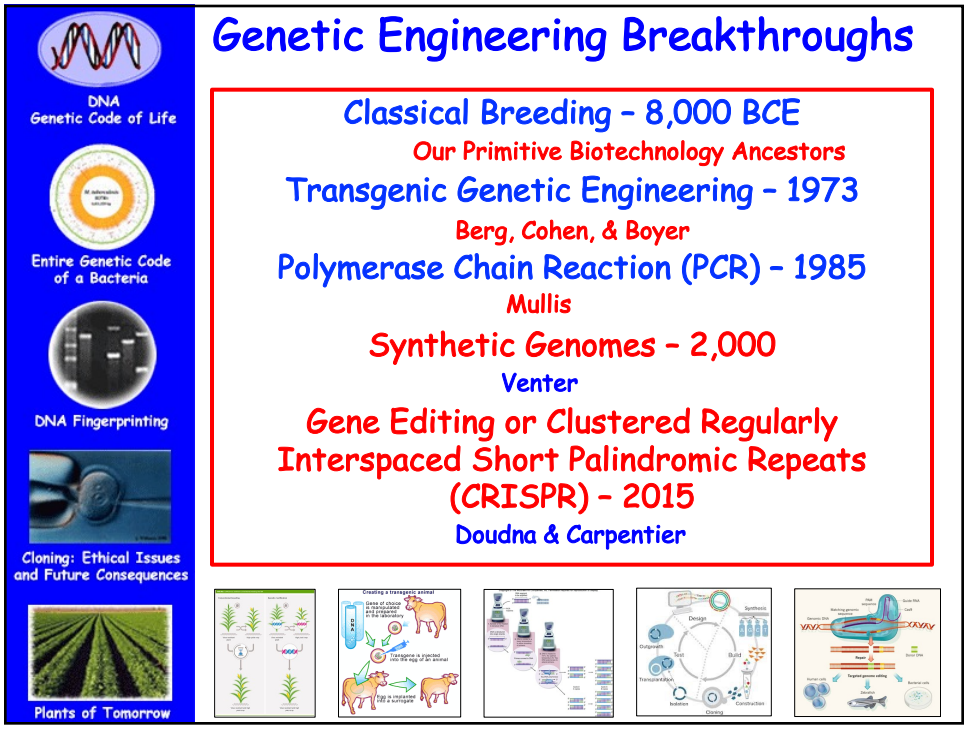
UCDAVIS
UNIVERSITY OF CALIFORNIA

1

Themes

1. What is the CRISPR-Cas Bacterial Immunity System?
2. What Are the Individual Components of the CRISPR-Cas Immunity System?
3. How Can CRISPER-Cas9 be Used For Gene Editing?
4. How Can Genetic Engineering Be Used To Eliminate or Reduce Mosquito Populations?
5. What is Gene Drive and How Can it Be Used To Fight Malaria?
6. What Are the Ethical and Regulatory Concerns of Using Gene Drive Systems?
7. What Are Other Applications of CRISPR-Cas9 Editing?

2


DNA
Genetic Code of Life
Entire Genetic Code of a Bacteria
DNA Fingerprinting
Cloning: Ethical Issues and Future Consequences
Plants of Tomorrow
Genetic Engineering Breakthroughs
Classical Breeding – 8,000 BCE
Our Primitive Biotechnology Ancestors
Transgenic Genetic Engineering – 1973
Berg, Cohen, & Boyer
Polymerase Chain Reaction (PCR) – 1985
Mullis
Synthetic Genomes – 2,000
Venter
Gene Editing or Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) – 2015
Doudna & Carpentier

3


DNA
Genetic Code of Life
Entire Genetic Code of a Bacteria
DNA Fingerprinting
Cloning: Ethical Issues and Future Consequences
Plants of Tomorrow
Genetic Engineering is the TECHNIQUE! That Generates GMOs
1. Classical Breeding By Selective Mating (Thousands of Years)
2. Insertion of a New Gene Into An Organism's Chromosomes (50 Years) – Transgenic Organism
3. Editing Existing Genes Like A "Word Program" (5 Years) – CRISPR Gene Editing
4. DNA Synthesis – Synthetic Genomes (5 Years)
Breeding or DNA Manipulation – They Are the SAME
&
Called Gene Engineering
So…….WHAT IS A GMO??

4

DNA
Genetic Code of Life

Entire Genetic Code of a Bacteria

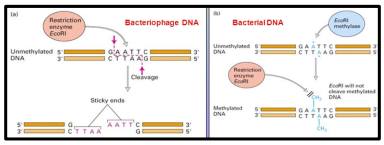
DNA Fingerprinting

Cloning: Ethical Issues and Future Consequences

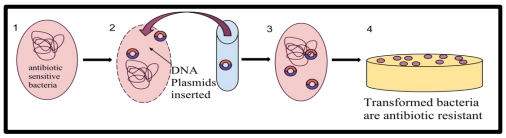
Plants of Tomorrow

Bacterial Defense Mechanisms Used For Genetic Engineering

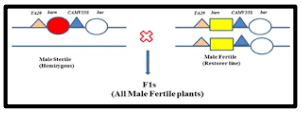
Restriction-Modification



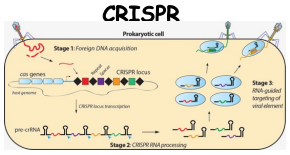
Antibiotic Resistance



Barnase & Barstar



CRISPR



5

DNA
Genetic Code of Life

Entire Genetic Code of a Bacteria

DNA Fingerprinting

Cloning: Ethical Issues and Future Consequences

Plants of Tomorrow

The CRISPR-Cas Bacterial Immunity System

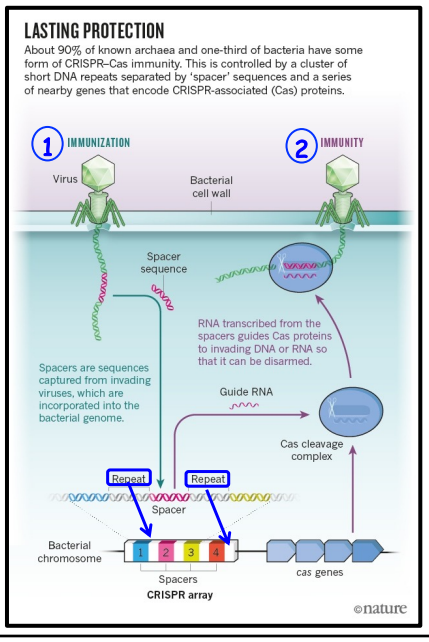
CRISPR LOCUS

Clustered
Regular
Interspaced
Short
Palindromic
Repeats

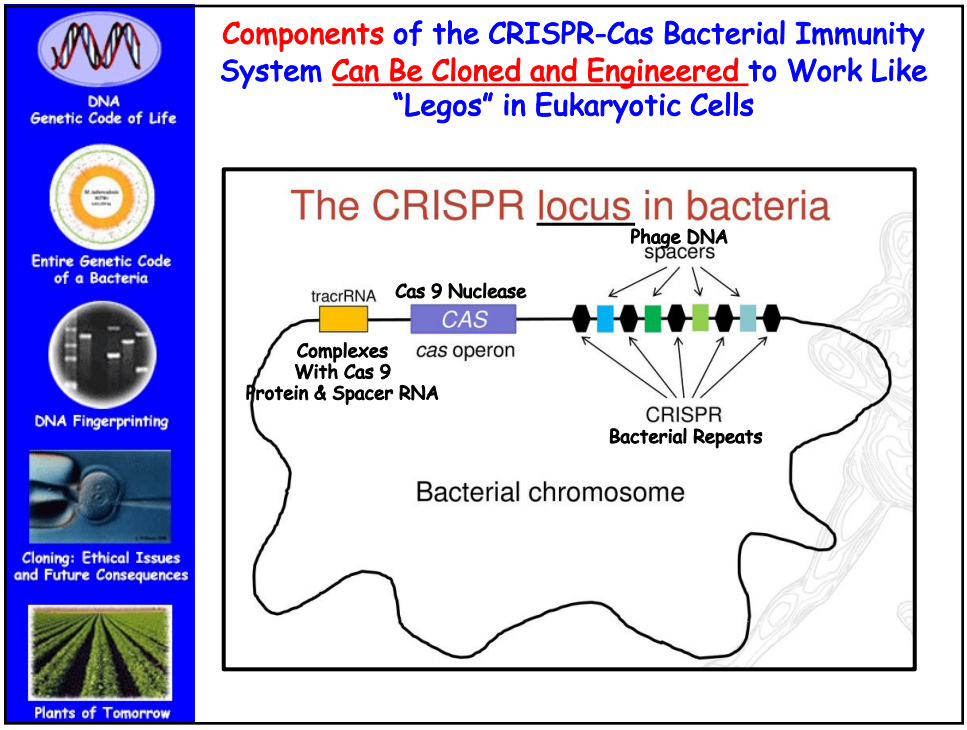
CRISPR
Associated
System

CAS is an Endonuclease That Cleaves dsDNA

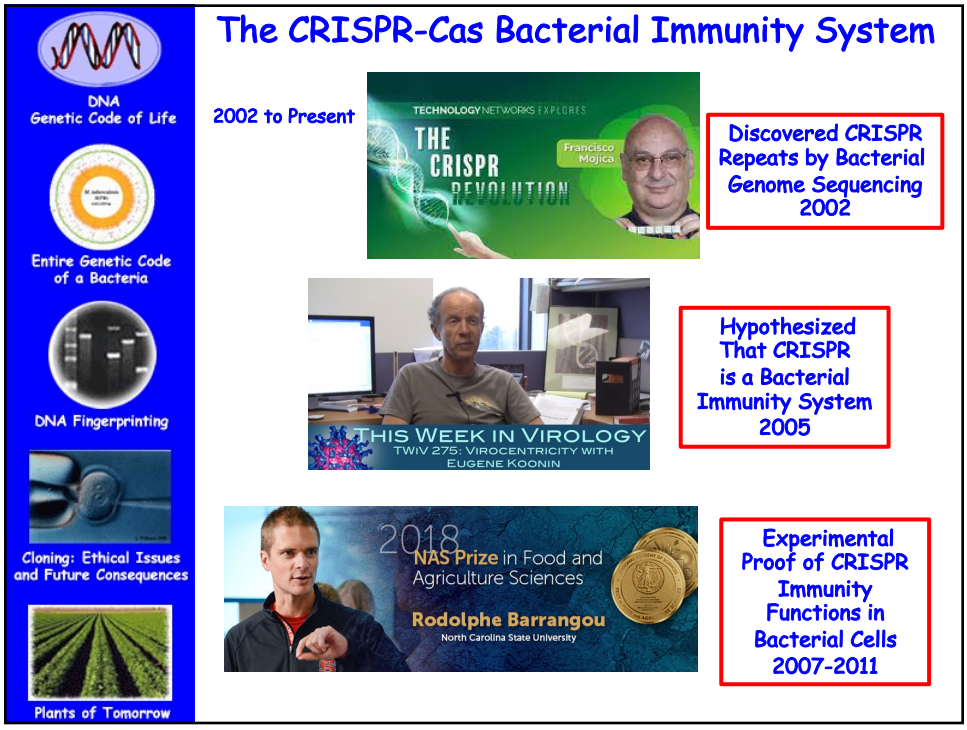
Spacer = Phage DNA



6


DNA
Genetic Code of Life
Entire Genetic Code of a Bacteria
DNA Fingerprinting
Cloning: Ethical Issues and Future Consequences
Plants of Tomorrow
Components of the CRISPR-Cas Bacterial Immunity System Can Be Cloned and Engineered to Work Like "Legos" in Eukaryotic Cells
The CRISPR locus in bacteria
Phage DNA spacers
tracrRNA
Cas 9 Nuclease
CAS
cas operon
Complexes With Cas 9 Protein & Spacer RNA
CRISPR Bacterial Repeats
Bacterial chromosome

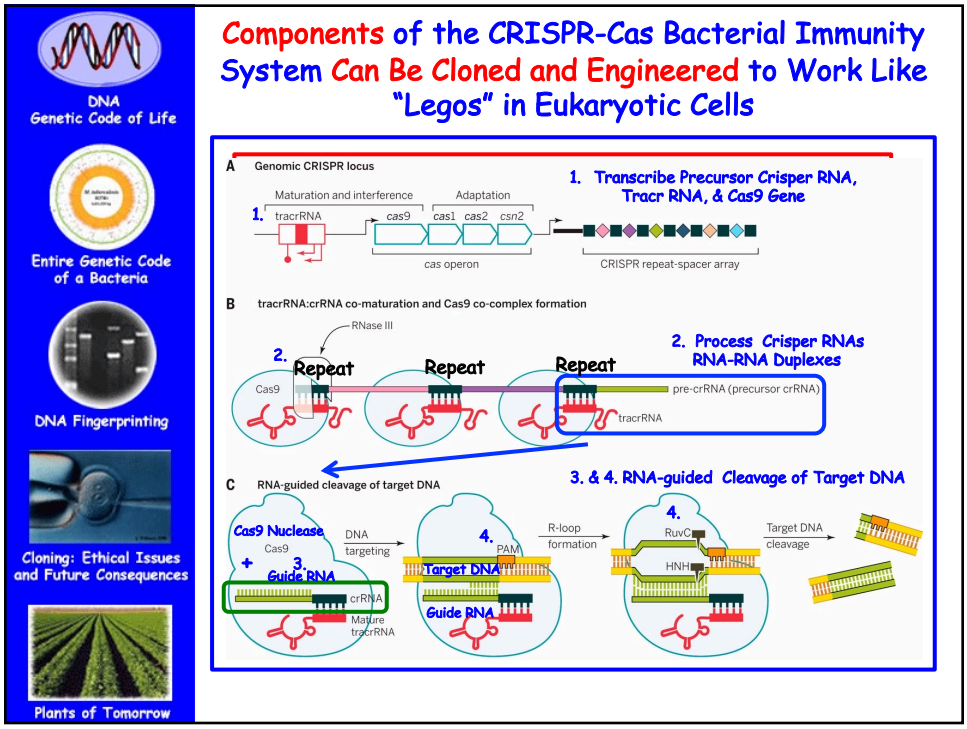
7


DNA
Genetic Code of Life
Entire Genetic Code of a Bacteria
DNA Fingerprinting
Cloning: Ethical Issues and Future Consequences
Plants of Tomorrow
The CRISPR-Cas Bacterial Immunity System
2002 to Present
TECHNOLOGY NETWORKS EXPLORES
THE CRISPR REVOLUTION
Francisco Mojica
Discovered CRISPR Repeats by Bacterial Genome Sequencing 2002
THIS WEEK IN VIROLOGY
TWiV 275: Virocentricity with Eugene Koonin
Hypothesized That CRISPR is a Bacterial Immunity System 2005
2018
NAS Prize in Food and Agriculture Sciences
Rodolphe Barrangou
North Carolina State University
Experimental Proof of CRISPR Immunity Functions in Bacterial Cells 2007-2011

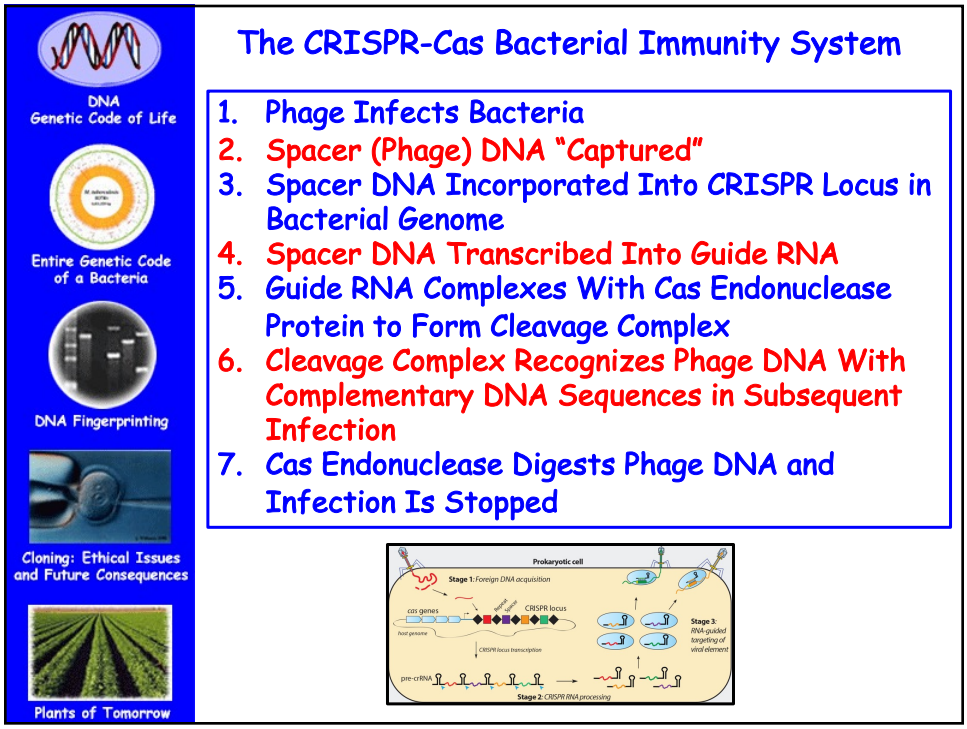
8


DNA
Genetic Code of Life
Entire Genetic Code of a Bacteria
DNA Fingerprinting
Cloning: Ethical Issues and Future Consequences
Plants of Tomorrow
The CRISPR-Cas Bacterial Immunity & Gene Editing System
XBio

9


DNA
Genetic Code of Life
Entire Genetic Code of a Bacteria
DNA Fingerprinting
Cloning: Ethical Issues and Future Consequences
Plants of Tomorrow
Components of the CRISPR-Cas Bacterial Immunity System Can Be Cloned and Engineered to Work Like "Legos" in Eukaryotic Cells
A Genomic CRISPR locus
1. Transcribe Precursor Crisper RNA, Tracr RNA, & Cas9 Gene
Maturation and interference
Adaptation
tracrRNA
cas9
cas1 cas2 csn2
cas operon
CRISPR repeat-spacer array
B tracrRNA:crRNA co-maturation and Cas9 co-complex formation
RNase III
2. Process Crisper RNAs RNA-RNA Duplexes
Repeat
Repeat
Repeat
Cas9
pre-crRNA (precursor crRNA)
tracrRNA
C RNA-guided cleavage of target DNA
3. & 4. RNA-guided Cleavage of Target DNA
Cas9 Nuclease
Cas9
3. Guide RNA
crRNA
Mature tracrRNA
DNA targeting
4.
PAM
Target DNA
Guide RNA
R-loop formation
RuvC
HNH
Target DNA cleavage

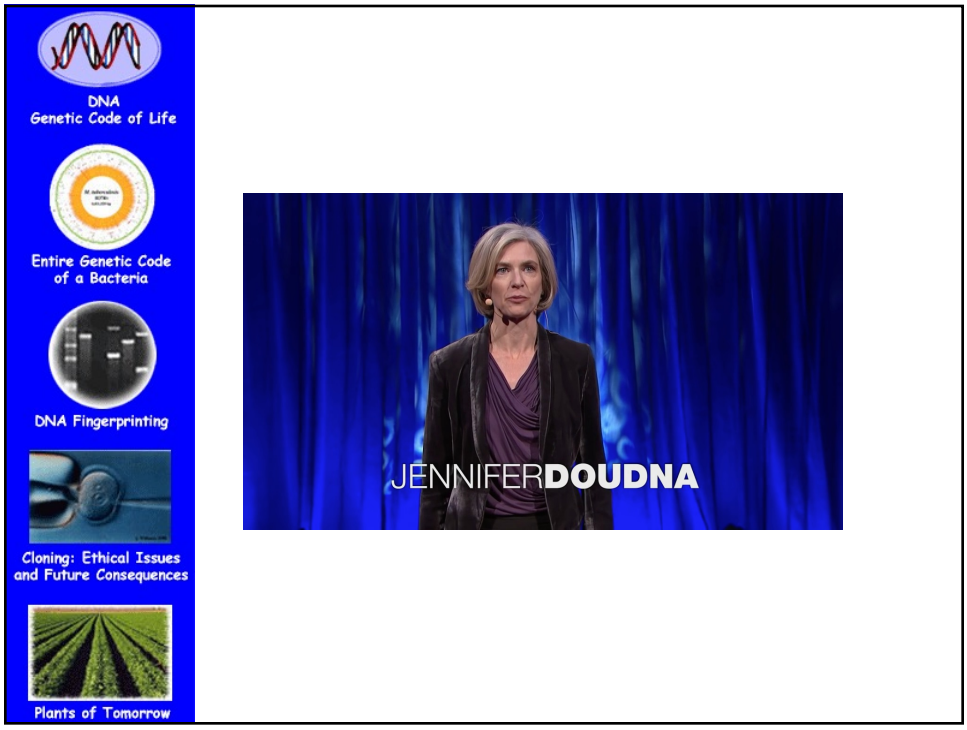
10


DNA
Genetic Code of Life
Entire Genetic Code of a Bacteria
DNA Fingerprinting
Cloning: Ethical Issues and Future Consequences
Plants of Tomorrow
The CRISPR-Cas Bacterial Immunity System
1. Phage Infects Bacteria
2. Spacer (Phage) DNA "Captured"
3. Spacer DNA Incorporated Into CRISPR Locus in Bacterial Genome
4. Spacer DNA Transcribed Into Guide RNA
5. Guide RNA Complexes With Cas Endonuclease Protein to Form Cleavage Complex
6. Cleavage Complex Recognizes Phage DNA With Complementary DNA Sequences in Subsequent Infection
7. Cas Endonuclease Digests Phage DNA and Infection Is Stopped
Prokaryotic cell
Stage 1: Foreign DNA acquisition
cas genes
CRISPR locus
Stage 3: RNA-guided targeting of viral element
pre-crRNA
Stage 2: CRISPR RNA processing

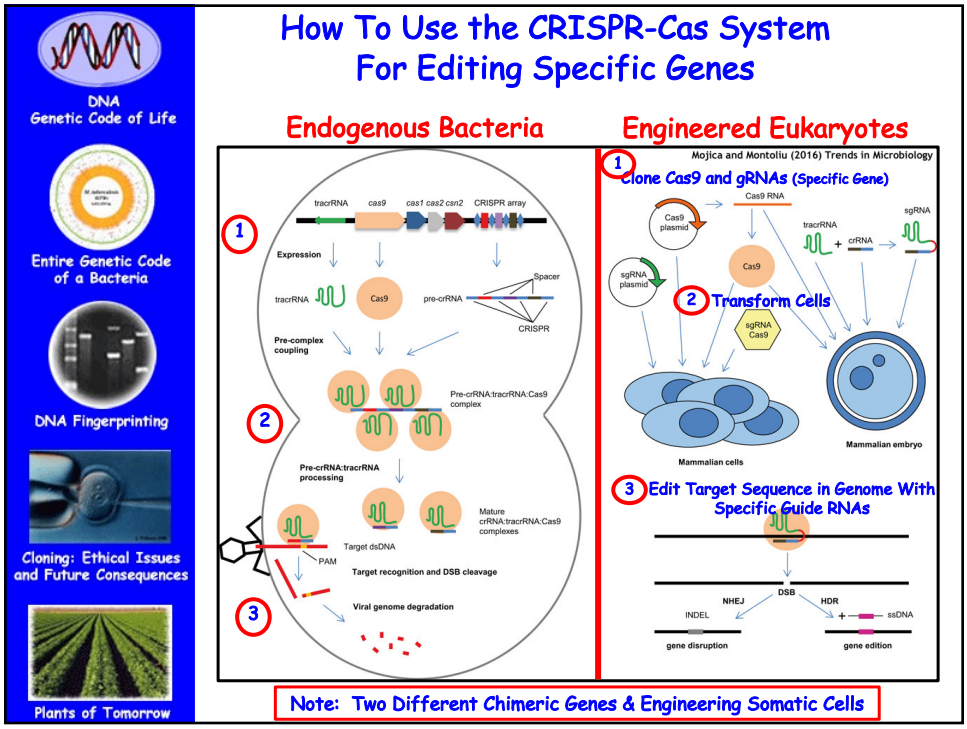
11


DNA
Genetic Code of Life
Entire Genetic Code of a Bacteria
DNA Fingerprinting
Cloning: Ethical Issues and Future Consequences
Plants of Tomorrow
Jennifer Doudna, Emmanuelle Charpentier, and Feng Zhang
CRISPR-Cas9 Editing (Molecular Typewriter)
PATENTED
Genomic DNA
Cas9
PAM
Target Sequence
Guide RNA
crRNA
tracrRNA
CRISPR Technology Editing Human Cells 2012
PATENTED

12


DNA
Genetic Code of Life
Entire Genetic Code of a Bacteria
DNA Fingerprinting
Cloning: Ethical Issues and Future Consequences
Plants of Tomorrow
JENNIFERDOUDNA

13


DNA
Genetic Code of Life
Entire Genetic Code of a Bacteria
DNA Fingerprinting
Cloning: Ethical Issues and Future Consequences
Plants of Tomorrow
How To Use the CRISPR-Cas System For Editing Specific Genes
Endogenous Bacteria
Engineered Eukaryotes
tracrRNA
cas9
cas1 cas2 csn2
CRISPR array
Expression
pre-crRNA
Spacer
CRISPR
Pre-complex coupling
Pre-crRNA:tracrRNA:Cas9 complex
Pre-crRNA:tracrRNA processing
Mature crRNA:tracrRNA:Cas9 complexes
Target dsDNA
PAM
Target recognition and DSB cleavage
Viral genome degradation
Mojica and Montoliu (2016) Trends in Microbiology
Clone Cas9 and gRNAs (Specific Gene)
Cas9 RNA
Cas9 plasmid
sgRNA
crRNA
sgRNA plasmid
Transform Cells
sgRNA Cas9
Mammalian cells
Mammalian embryo
Edit Target Sequence in Genome With Specific Guide RNAs
DSB
NHEJ
HDR
INDEL
ssDNA
gene disruption
gene edition
Note: Two Different Chimeric Genes & Engineering Somatic Cells

14

Advantages of Gene Editing Over "Cohen-Boyer" Transgenic Genetic Engineering

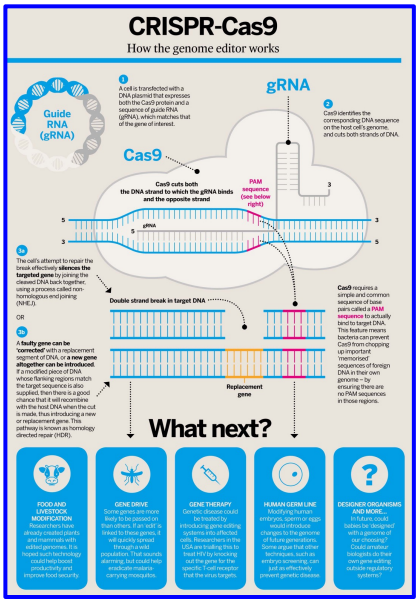
- Simple Method to Edit, Correct, or Modify Any Endogenous Gene
- Multiple Genes Can Be Corrected at Once
- Dominant Alleles Can Be Mutated & Turned Off

Disadvantages of Gene Editing Over "Cohen-Boyer" Genetic Engineering

- Cannot Add Foreign Genes (e.g., GFP)
- Limited to Species-Specific Gene Corrections

15

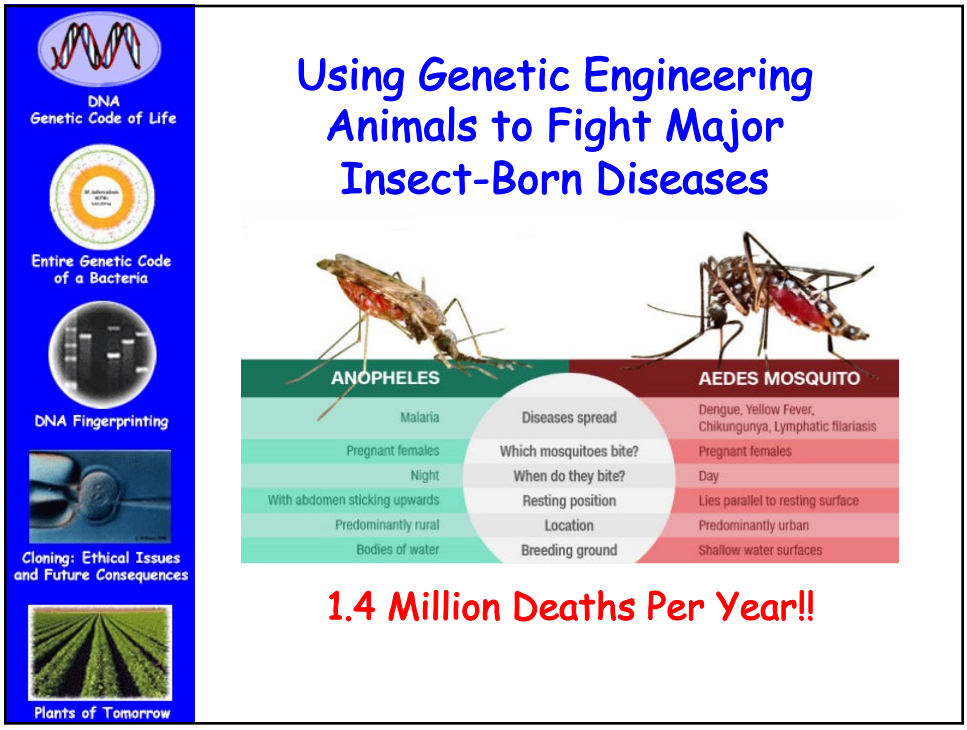
How Can Gene Editing Be Used in Genetic Engineering?



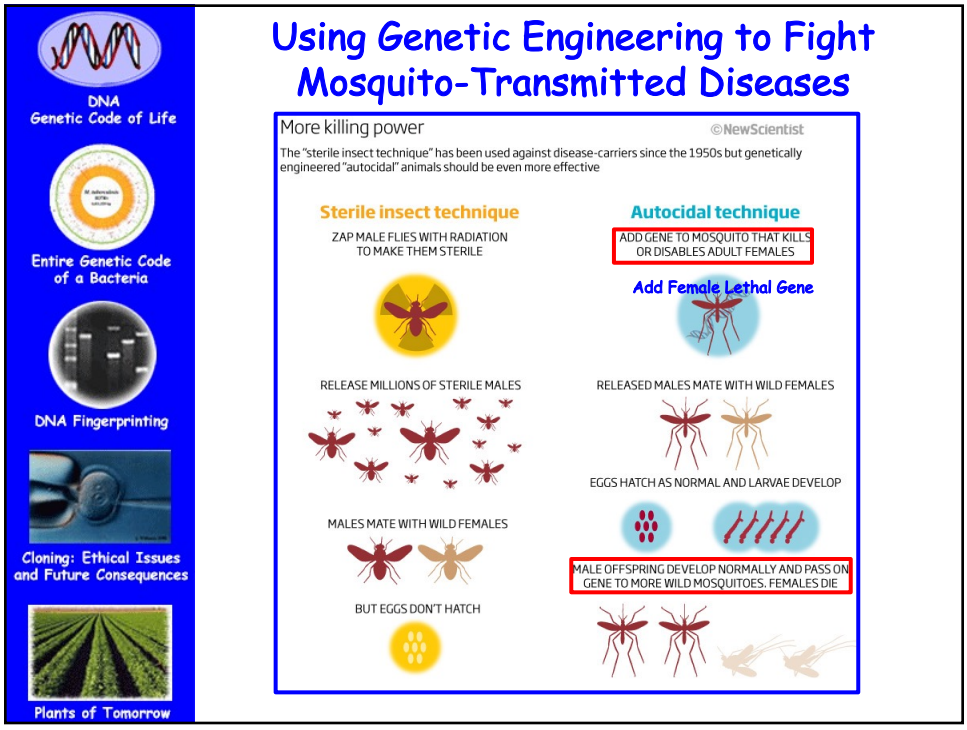
- Editing Crop Gene Genomes (e.g., drought resistance)
- Editing Farm Animals (e.g., pathogen resistance)
- Eliminating Mosquito Borne Diseases
- Correcting Human Genetic Defects – Gene Therapy
- Human Trait Enhancement

- Editing Alters Endogenous Genes Because Specific Targets Are Needed!
- Foreign Genes Are Not Added to the Genome!

16


DNA
Genetic Code of Life
Entire Genetic Code of a Bacteria
DNA Fingerprinting
Cloning: Ethical Issues and Future Consequences
Plants of Tomorrow
Using Genetic Engineering Animals to Fight Major Insect-Born Diseases
ANOPHELES
AEDES MOSQUITO
Malaria
Diseases spread
Dengue, Yellow Fever, Chikungunya, Lymphatic filariasis
Pregnant females
Which mosquitoes bite?
Pregnant females
Night
When do they bite?
Day
With abdomen sticking upwards
Resting position
Lies parallel to resting surface
Predominantly rural
Location
Predominantly urban
Bodies of water
Breeding ground
Shallow water surfaces
1.4 Million Deaths Per Year!!

17


DNA
Genetic Code of Life
Entire Genetic Code of a Bacteria
DNA Fingerprinting
Cloning: Ethical Issues and Future Consequences
Plants of Tomorrow
Using Genetic Engineering to Fight Mosquito-Transmitted Diseases
More killing power
©NewScientist
The "sterile insect technique" has been used against disease-carriers since the 1950s but genetically engineered "autocidal" animals should be even more effective
Sterile insect technique
ZAP MALE FLIES WITH RADIATION TO MAKE THEM STERILE
RELEASE MILLIONS OF STERILE MALES
MALES MATE WITH WILD FEMALES
BUT EGGS DON'T HATCH
Autocidal technique
ADD GENE TO MOSQUITO THAT KILLS OR DISABLES ADULT FEMALES
Add Female Lethal Gene
RELEASED MALES MATE WITH WILD FEMALES
EGGS HATCH AS NORMAL AND LARVAE DEVELOP
MALE OFFSPRING DEVELOP NORMALLY AND PASS ON GENE TO MORE WILD MOSQUITOES. FEMALES DIE

18

DNA
Genetic Code of Life

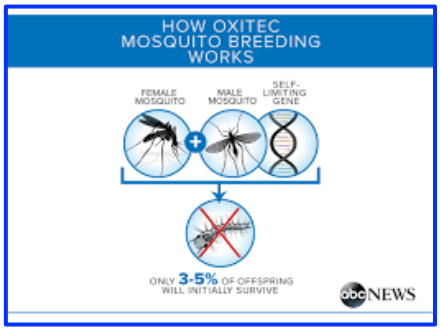
Entire Genetic Code of a Bacteria

DNA Fingerprinting

Cloning: Ethical Issues and Future Consequences

Plants of Tomorrow

Using Genetic Engineering to Fight Mosquito-Transmitted Diseases



Releases of the genetically engineered Oxitec mosquito, commonly known as 'Friendly *Aedes aegypti*', reduced the dengue mosquito population in an area of Juazeiro, Brazil by 95%, well below the modelled threshold for epidemic disease transmission.

Genetically engineered moths can knock down crop pests, but will they take off?

Genetically Modified Mosquitoes Stunt Malaria Parasite Growth, Prevent Transmission

September 23, 2022

19

DNA
Genetic Code of Life

Entire Genetic Code of a Bacteria

DNA Fingerprinting

Cloning: Ethical Issues and Future Consequences

Plants of Tomorrow

FDA approves releasing GMO mosquitoes to fight Zika in Florida

The Florida Keys approve a trial release of genetically modified mosquitoes to combat Zika

Other tests have reduced mosquito populations by 90 percent

EPA **Guidance for Industry** FDA

Regulation of Mosquito-Related Products

1. **Examples of New Animal Drugs – Regulated by FDA**

   a. Products intended to reduce the virus/pathogen load within a mosquito, including reduction in virus/pathogen replication and spread within the mosquito and/or reduction in virus/pathogen transmissibility from mosquitoes to humans.

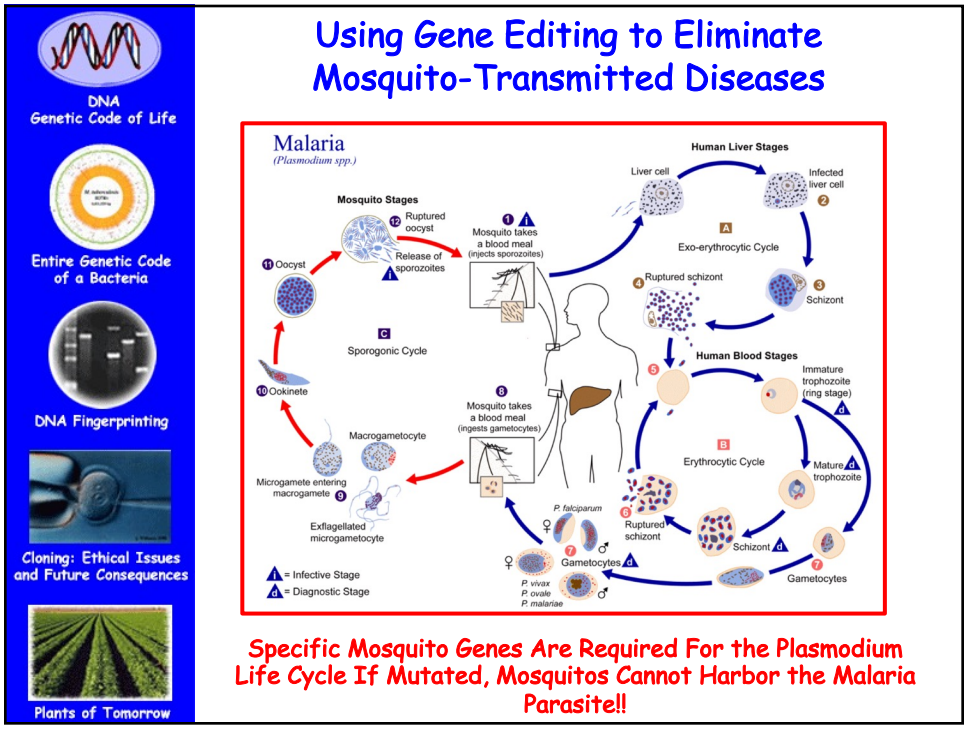
   b. Products intended to prevent mosquito-borne disease in humans or animals.

2. **Example of Pesticide Products – Regulated by EPA**

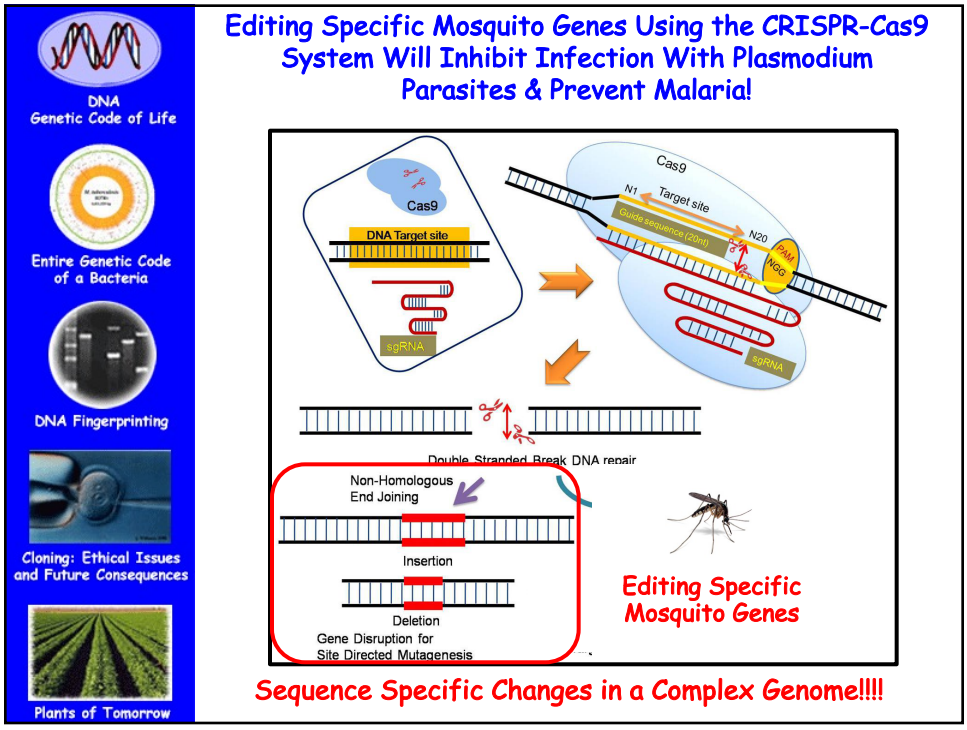
   Products intended to reduce the population of mosquitoes (for example, by killing them at some point in their life cycle, or by interfering with their reproduction or development).[3]

Self-limiting fall armyworm: a new approach in development for sustainable crop protection and resistance management

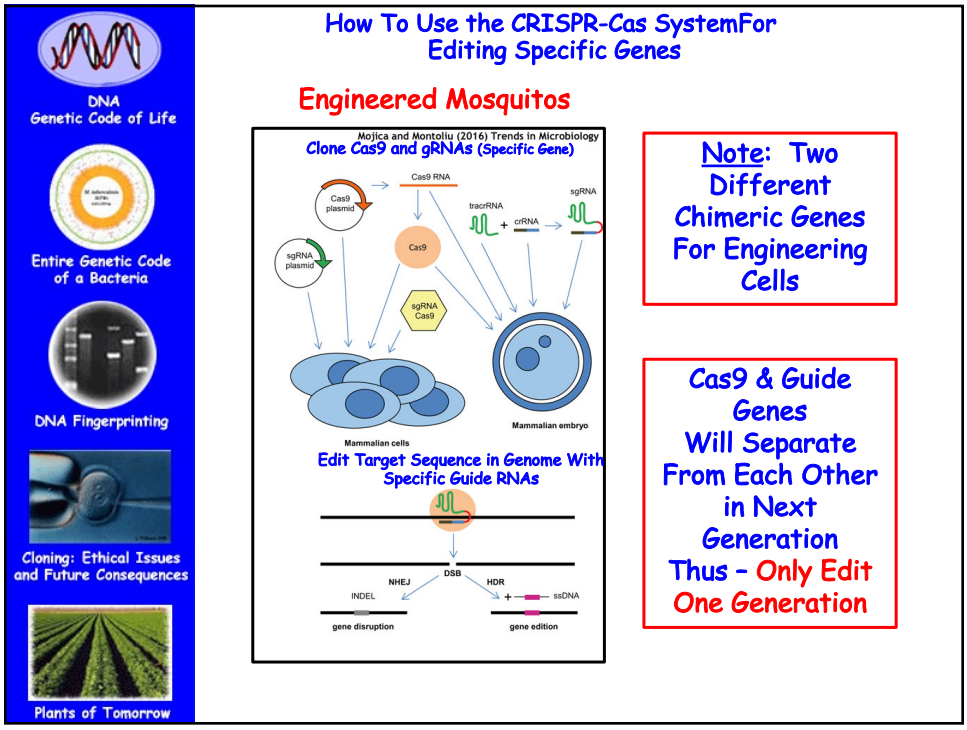
20


DNA
Genetic Code of Life
Entire Genetic Code of a Bacteria
DNA Fingerprinting
Cloning: Ethical Issues and Future Consequences
Plants of Tomorrow
Using Gene Editing to Eliminate Mosquito-Transmitted Diseases
Malaria
(Plasmodium spp.)
Human Liver Stages
Liver cell
Infected liver cell
Exo-erythrocytic Cycle
Ruptured schizont
Schizont
Human Blood Stages
Immature trophozoite (ring stage)
Mature trophozoite
Erythrocytic Cycle
Ruptured schizont
Schizont
Gametocytes
Gametocytes
P. falciparum
P. vivax
P. ovale
P. malariae
Mosquito Stages
Ruptured oocyst
Release of sporozoites
Oocyst
Sporogonic Cycle
Ookinete
Mosquito takes a blood meal (injects sporozoites)
Mosquito takes a blood meal (ingests gametocytes)
Macrogametocyte
Microgamete entering macrogamete
Exflagellated microgametocyte
= Infective Stage
= Diagnostic Stage
Specific Mosquito Genes Are Required For the Plasmodium Life Cycle If Mutated, Mosquitos Cannot Harbor the Malaria Parasite!!

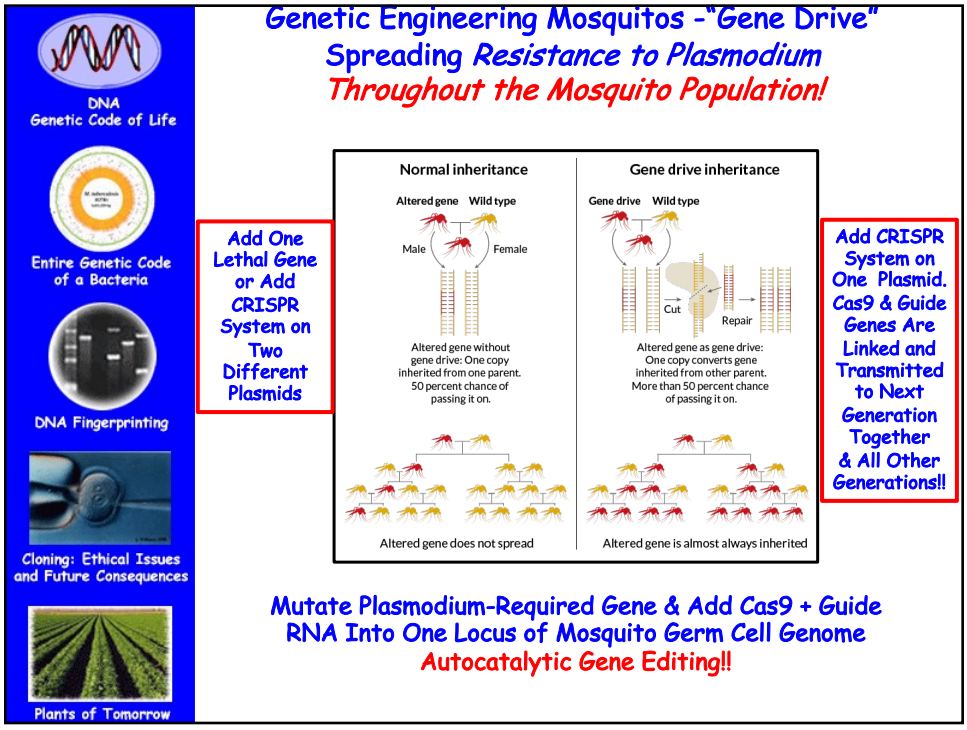
21


DNA
Genetic Code of Life
Entire Genetic Code of a Bacteria
DNA Fingerprinting
Cloning: Ethical Issues and Future Consequences
Plants of Tomorrow
Editing Specific Mosquito Genes Using the CRISPR-Cas9 System Will Inhibit Infection With Plasmodium Parasites & Prevent Malaria!
Cas9
DNA Target site
sgRNA
Cas9
N1
Target site
Guide sequence (20nt)
N20
PAM
NGG
sgRNA
Double Stranded Break DNA repair
Non-Homologous End Joining
Insertion
Deletion
Gene Disruption for Site Directed Mutagenesis
Editing Specific Mosquito Genes
Sequence Specific Changes in a Complex Genome!!!!

22


DNA
Genetic Code of Life
Entire Genetic Code of a Bacteria
DNA Fingerprinting
Cloning: Ethical Issues and Future Consequences
Plants of Tomorrow
How To Use the CRISPR-Cas SystemFor Editing Specific Genes
Engineered Mosquitos
Mojica and Montoliu (2016) Trends in Microbiology
Clone Cas9 and gRNAs (Specific Gene)
Cas9 RNA
Cas9 plasmid
tracrRNA
crRNA
sgRNA
sgRNA plasmid
Cas9
sgRNA Cas9
Mammalian cells
Mammalian embryo
Edit Target Sequence in Genome With Specific Guide RNAs
DSB
NHEJ
HDR
INDEL
ssDNA
gene disruption
gene edition
Note: Two Different Chimeric Genes For Engineering Cells
Cas9 & Guide Genes Will Separate From Each Other in Next Generation Thus – Only Edit One Generation

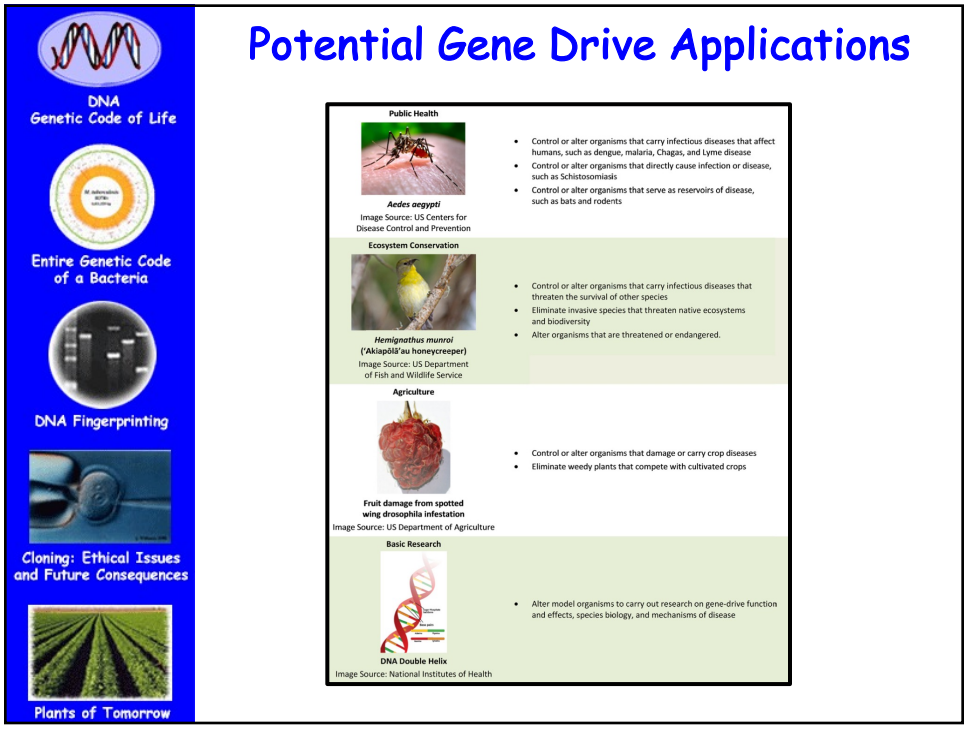
23


DNA
Genetic Code of Life
Entire Genetic Code of a Bacteria
DNA Fingerprinting
Cloning: Ethical Issues and Future Consequences
Plants of Tomorrow
Genetic Engineering Mosquitos -"Gene Drive"
Spreading Resistance to Plasmodium
Throughout the Mosquito Population!
Add One Lethal Gene or Add CRISPR System on Two Different Plasmids
Normal inheritance
Gene drive inheritance
Altered gene
Wild type
Gene drive
Male
Female
Cut
Repair
Altered gene without gene drive: One copy inherited from one parent. 50 percent chance of passing it on.
Altered gene as gene drive: One copy converts gene inherited from other parent. More than 50 percent chance of passing it on.
Altered gene does not spread
Altered gene is almost always inherited
Add CRISPR System on One Plasmid. Cas9 & Guide Genes Are Linked and Transmitted to Next Generation Together & All Other Generations!!
Mutate Plasmodium-Required Gene & Add Cas9 + Guide RNA Into One Locus of Mosquito Germ Cell Genome
Autocatalytic Gene Editing!!

24

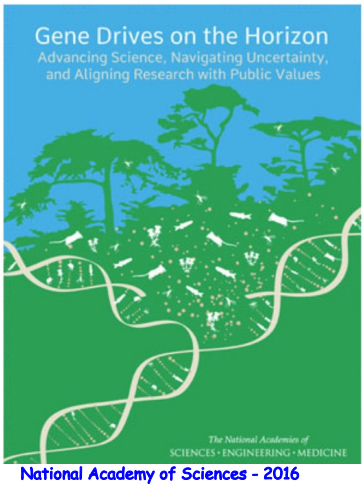

DNA
Genetic Code of Life
Entire Genetic Code of a Bacteria
DNA Fingerprinting
Cloning: Ethical Issues and Future Consequences
Plants of Tomorrow
What Are Gene Drives?

25


DNA
Genetic Code of Life
Entire Genetic Code of a Bacteria
DNA Fingerprinting
Cloning: Ethical Issues and Future Consequences
Plants of Tomorrow
Potential Gene Drive Applications
Public Health
Aedes aegypti
Image Source: US Centers for Disease Control and Prevention
Control or alter organisms that carry infectious diseases that affect humans, such as dengue, malaria, Chagas, and Lyme disease
Control or alter organisms that directly cause infection or disease, such as Schistosomiasis
Control or alter organisms that serve as reservoirs of disease, such as bats and rodents
Ecosystem Conservation
Hemignathus munroi ('Akiapōlā'au honeycreeper)
Image Source: US Department of Fish and Wildlife Service
Control or alter organisms that carry infectious diseases that threaten the survival of other species
Eliminate invasive species that threaten native ecosystems and biodiversity
Alter organisms that are threatened or endangered.
Agriculture
Fruit damage from spotted wing drosophila infestation
Image Source: US Department of Agriculture
Control or alter organisms that damage or carry crop diseases
Eliminate weedy plants that compete with cultivated crops
Basic Research
DNA Double Helix
Image Source: National Institutes of Health
Alter model organisms to carry out research on gene-drive function and effects, species biology, and mechanisms of disease

26

Potential Gene Risks & Benefits



National Academy of Sciences - 2016

- Resistance
- Escape to Non-Target Organism
- Altering Ecological Balances
- Unforeseen Consequences in the Wild

- Eliminating Mosquito Borne Diseases & Saving Millions of Lives
- Reducing Ecological Impacts of Invasive Species
- Preventing Lyme Disease By Eliminating Animal Vectors

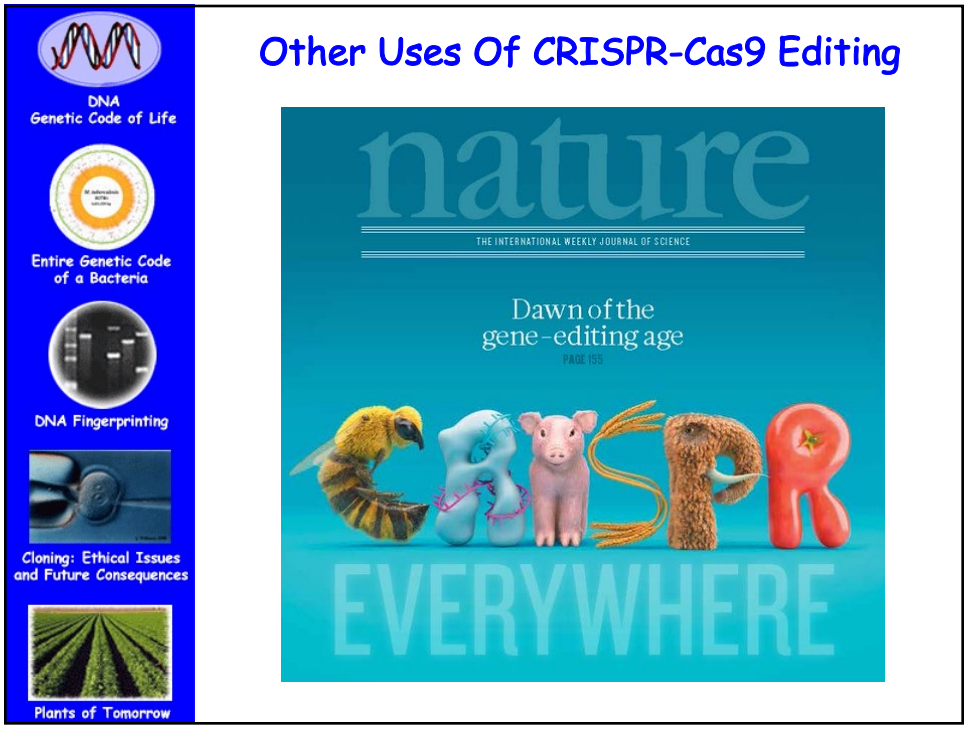
27

Recommendations For Using Gene Drive Systems

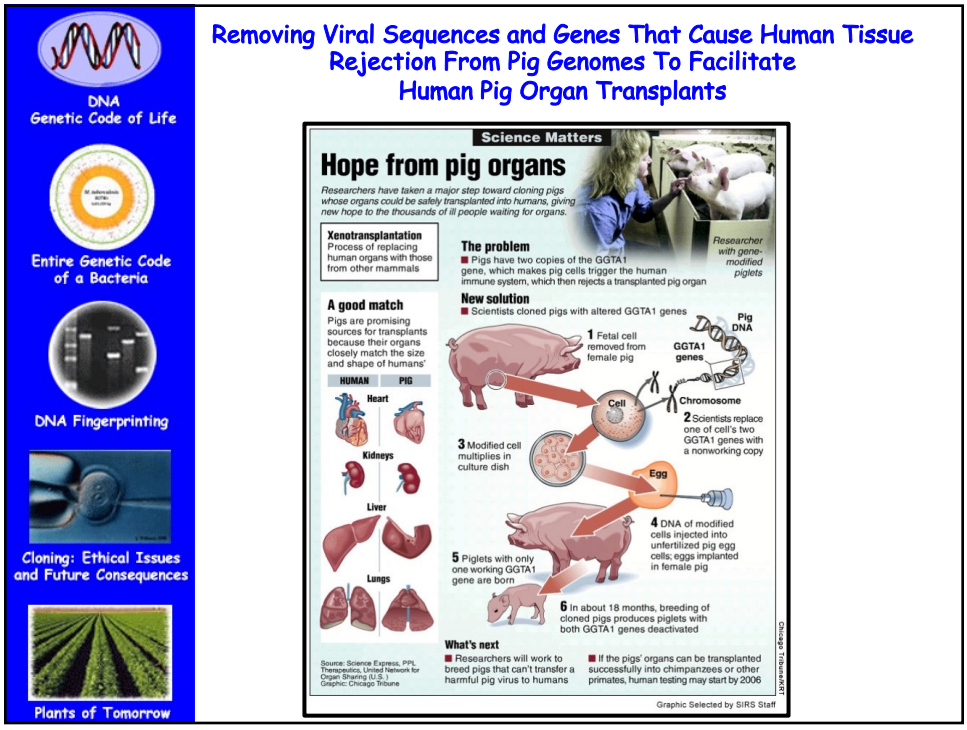
- More Research Needs To Be Performed Before Gene Drive Modified Organisms Are Released Into The Environment
- Phased Testing of Gene Drive Modified Organisms From Laboratory to the Field Should Be Carried Out Under the Relevant Regulatory Oversight
- Robust Ecological Assessment Needs to be Carried Out Before Each Gene Drive Test Should Be Approved
- Public Engagement Must Be Built Into the Risk Assessment, and Policies Should Be Developed For How Public Engagement Will Factor Into Research sand Policy Decisions
- Current Regulatory Framework For Assessing Risks and Potential Environmental Impacts of Releasing Gene Drive Modified Organisms Are Inadequate. Regulations Does Not Fit Within Purview of USDA, EPA, or FDA
- There Are Regulatory Concerns About Biosafety,
- Biosecurity, and Potential for Misuse For Harmful Purposes

Gene Drives on the Horizon – National Academy of Sciences - 2016

28


DNA
Genetic Code of Life
Entire Genetic Code of a Bacteria
DNA Fingerprinting
Cloning: Ethical Issues and Future Consequences
Plants of Tomorrow
Other Uses Of CRISPR-Cas9 Editing
nature
THE INTERNATIONAL WEEKLY JOURNAL OF SCIENCE
Dawn of the gene-editing age
PAGE 155
CRISPR
EVERYWHERE

29


DNA
Genetic Code of Life
Entire Genetic Code of a Bacteria
DNA Fingerprinting
Cloning: Ethical Issues and Future Consequences
Plants of Tomorrow
Removing Viral Sequences and Genes That Cause Human Tissue Rejection From Pig Genomes To Facilitate Human Pig Organ Transplants
Science Matters
Hope from pig organs
Researchers have taken a major step toward cloning pigs whose organs could be safely transplanted into humans, giving new hope to the thousands of ill people waiting for organs.
Xenotransplantation
Process of replacing human organs with those from other mammals
Researcher with gene-modified piglets
The problem
Pigs have two copies of the GGTA1 gene, which makes pig cells trigger the human immune system, which then rejects a transplanted pig organ
A good match
Pigs are promising sources for transplants because their organs closely match the size and shape of humans'
HUMAN
PIG
Heart
Kidneys
Liver
Lungs
New solution
Scientists cloned pigs with altered GGTA1 genes
Pig DNA
GGTA1 genes
1 Fetal cell removed from female pig
Cell
Chromosome
2 Scientists replace one of cell's two GGTA1 genes with a nonworking copy
3 Modified cell multiplies in culture dish
Egg
4 DNA of modified cells injected into unfertilized pig egg cells; eggs implanted in female pig
5 Piglets with only one working GGTA1 gene are born
6 In about 18 months, breeding of cloned pigs produces piglets with both GGTA1 genes deactivated
What's next
Researchers will work to breed pigs that can't transfer a harmful pig virus to humans
If the pigs' organs can be transplanted successfully into chimpanzees or other primates, human testing may start by 2006
Source: Science Express, PPL Therapeutics, United Network for Organ Sharing (U.S.)
Graphic: Chicago Tribune
Graphic Selected by SIRS Staff

30

DNA
Genetic Code of Life

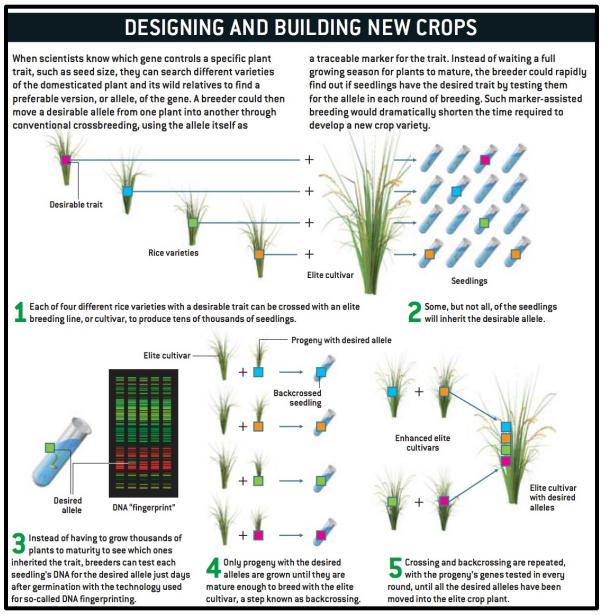
Entire Genetic Code of a Bacteria

DNA Fingerprinting

Cloning: Ethical Issues and Future Consequences

Plants of Tomorrow

Using CRISPR-Cas9 Editing For Crop Improvement



31

DNA
Genetic Code of Life

Entire Genetic Code of a Bacteria

DNA Fingerprinting

Cloning: Ethical Issues and Future Consequences

Plants of Tomorrow

Using Gene Editing to Improve Crop Plants

Geneticists Have Used CRISPR Gene Editing to Create Crops That Grow More Food

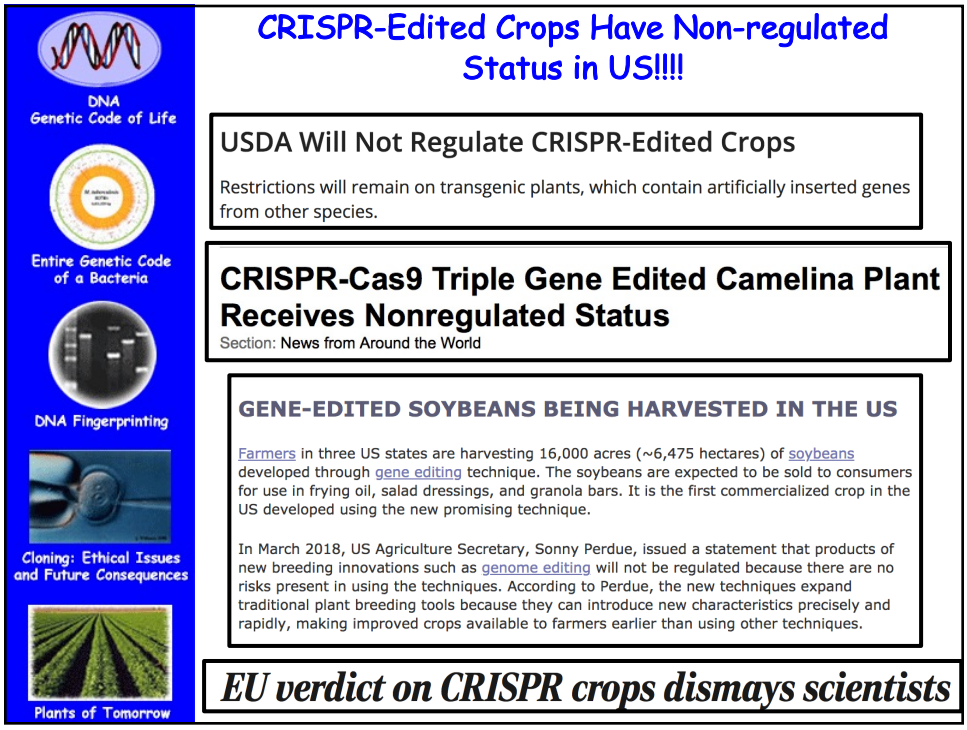
We're editing our way through global food shortage

SCIENTISTS USE CRISPR-CAS9 TECHNOLOGY TO IMPROVE DROUGHT AND SALT TOLERANCE IN RICE

GM Wheat Used to Make Bread with Less Gluten

Researchers Engineer Potyvirus Resistance Using CRISPR/Cas9

32


DNA
Genetic Code of Life
Entire Genetic Code of a Bacteria
DNA Fingerprinting
Cloning: Ethical Issues and Future Consequences
Plants of Tomorrow
CRISPR-Edited Crops Have Non-regulated Status in US!!!!
USDA Will Not Regulate CRISPR-Edited Crops
Restrictions will remain on transgenic plants, which contain artificially inserted genes from other species.
CRISPR-Cas9 Triple Gene Edited Camelina Plant Receives Nonregulated Status
Section: News from Around the World
GENE-EDITED SOYBEANS BEING HARVESTED IN THE US
Farmers in three US states are harvesting 16,000 acres (~6,475 hectares) of soybeans developed through gene editing technique. The soybeans are expected to be sold to consumers for use in frying oil, salad dressings, and granola bars. It is the first commercialized crop in the US developed using the new promising technique.
In March 2018, US Agriculture Secretary, Sonny Perdue, issued a statement that products of new breeding innovations such as genome editing will not be regulated because there are no risks present in using the techniques. According to Perdue, the new techniques expand traditional plant breeding tools because they can introduce new characteristics precisely and rapidly, making improved crops available to farmers earlier than using other techniques.
EU verdict on CRISPR crops dismays scientists

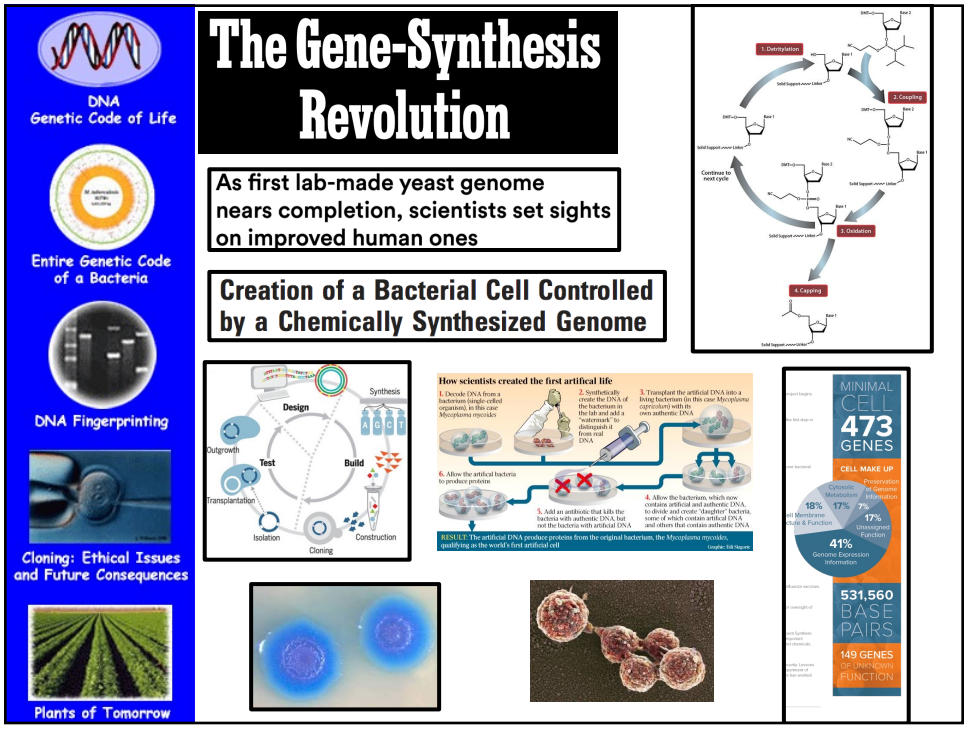
33


DNA
Genetic Code of Life
Entire Genetic Code of a Bacteria
DNA Fingerprinting
Cloning: Ethical Issues and Future Consequences
Plants of Tomorrow
Using CRISPR-Cas9 Editing For Correcting Human Genetic Disorders
Somatic Cell Gene Therapy
Ex Vivo
In Vivo
Germline Gene Therapy + Gene Enhancement
Editing humanity
The prospect of genetic enhancement

34


DNA
Genetic Code of Life
Entire Genetic Code of a Bacteria
DNA Fingerprinting
Cloning: Ethical Issues and Future Consequences
Plants of Tomorrow
Genetic Engineering is the TECHNIQUE!
That Generates GMOs
1. Classical Breeding By Selective Mating (Thousands of Years)
2. Insertion of a New Gene Into An Organism's Chromosomes (50 Years) – Transgenic Organism
3. Editing Existing Genes Like A "Word Program" (5 Years) – CRISPR Gene Editing
4. DNA Synthesis – Synthetic Genomes (5 Years)
Breeding or DNA Manipulation – They Are the SAME
&
Called Gene Engineering
So…….WHAT IS A GMO??

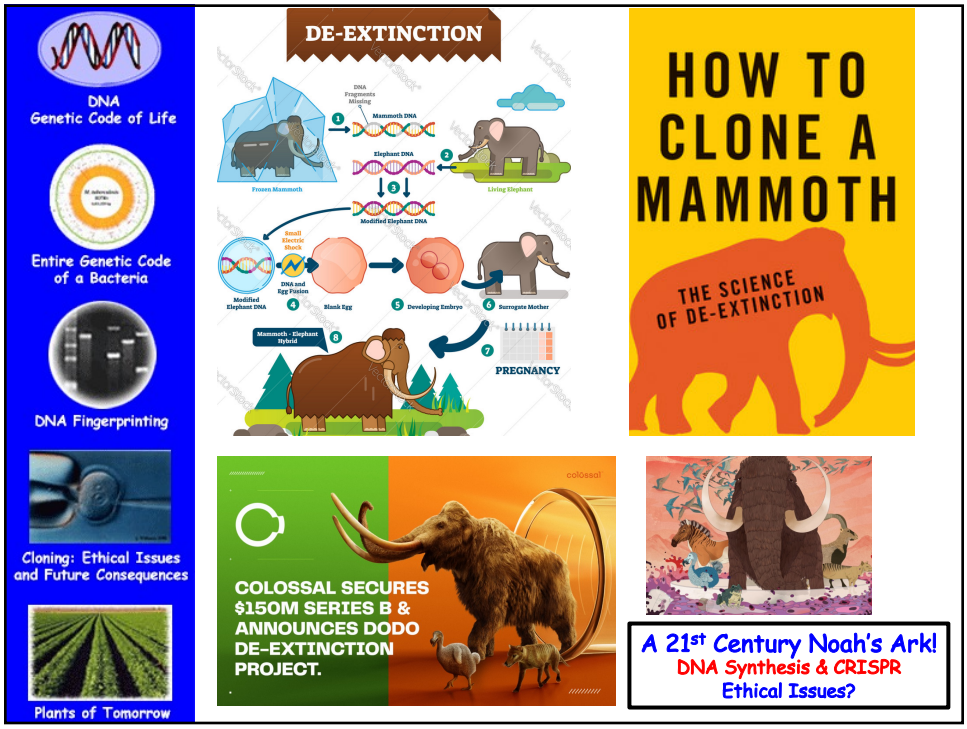
35


DNA
Genetic Code of Life
Entire Genetic Code of a Bacteria
DNA Fingerprinting
Cloning: Ethical Issues and Future Consequences
Plants of Tomorrow
The Gene-Synthesis Revolution
As first lab-made yeast genome nears completion, scientists set sights on improved human ones
Creation of a Bacterial Cell Controlled by a Chemically Synthesized Genome
Design
Synthesis
Build
Test
Outgrowth
Transplantation
Isolation
Cloning
How scientists created the first artifical life
MINIMAL CELL
473 GENES
CELL MAKE UP
531,560 BASE PAIRS
149 GENES OF UNKNOWN FUNCTION

36


DNA
Genetic Code of Life
Entire Genetic Code of a Bacteria
DNA Fingerprinting
Cloning: Ethical Issues and Future Consequences
Plants of Tomorrow
Produced By Andy Court
Designing Life

37


DNA
Genetic Code of Life
Entire Genetic Code of a Bacteria
DNA Fingerprinting
Cloning: Ethical Issues and Future Consequences
Plants of Tomorrow
DE-EXTINCTION
Frozen Mammoth
Mammoth DNA
Elephant DNA
Living Elephant
Modified Elephant DNA
Modified Elephant DNA
DNA and Egg Fusion
Blank Egg
Developing Embryo
Surrogate Mother
Mammoth - Elephant Hybrid
PREGNANCY
HOW TO CLONE A MAMMOTH
THE SCIENCE OF DE-EXTINCTION
COLOSSAL SECURES $150M SERIES B & ANNOUNCES DODO DE-EXTINCTION PROJECT.
A 21st Century Noah's Ark!
DNA Synthesis & CRISPR
Ethical Issues?

38


DNA
Genetic Code of Life
Entire Genetic Code of a Bacteria
DNA Fingerprinting
Cloning: Ethical Issues and Future Consequences
Plants of Tomorrow
60 MINUTES
PRODUCED BY
HENRY SCHUSTER
Genetic Information Age

39