

# Engineering, Ethics and Society: Bioengineering Ethics

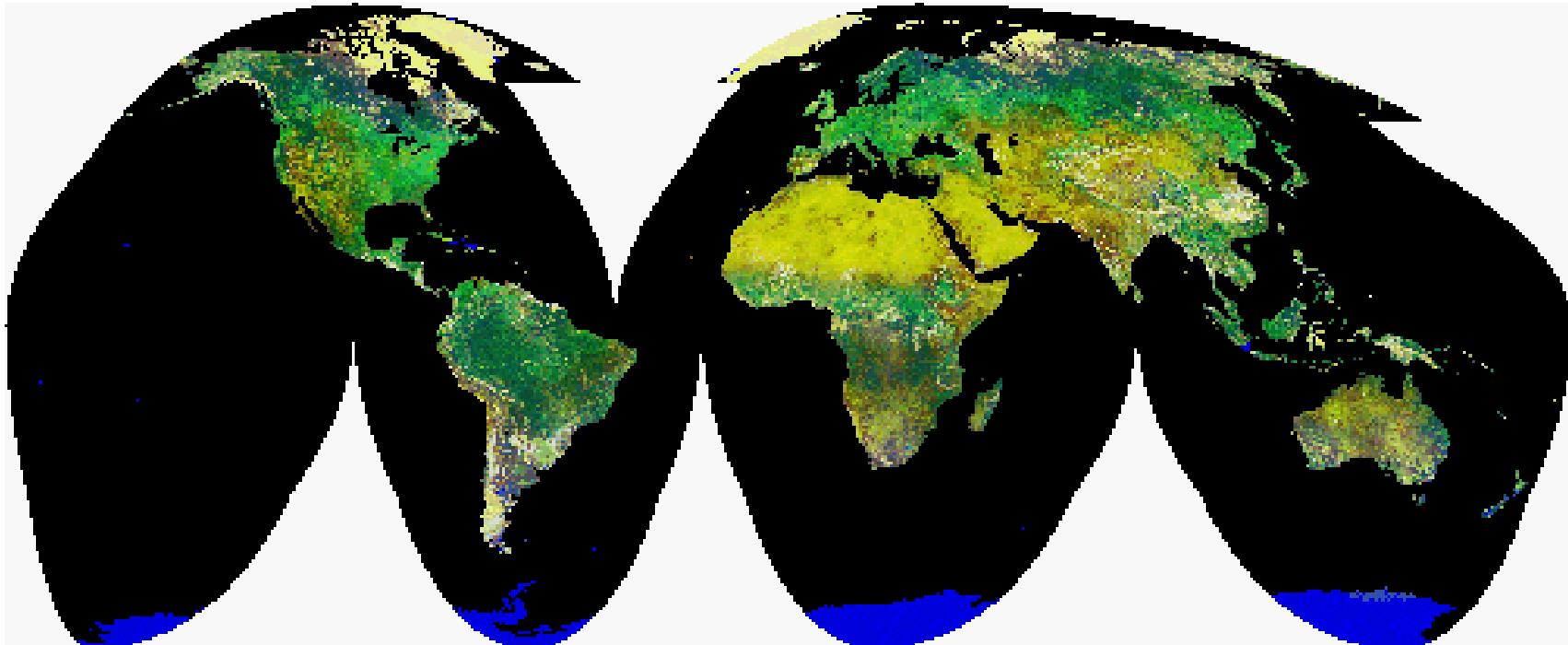
- Log on to UCLA\_WIFI
- Go to <https://onlinepoll.ucla.edu>
- Wait for further instructions

Dr. Gershon Weltman  
Engineering 183EW, UCLA SEAS  
Lecture 10

# Lecture Contents

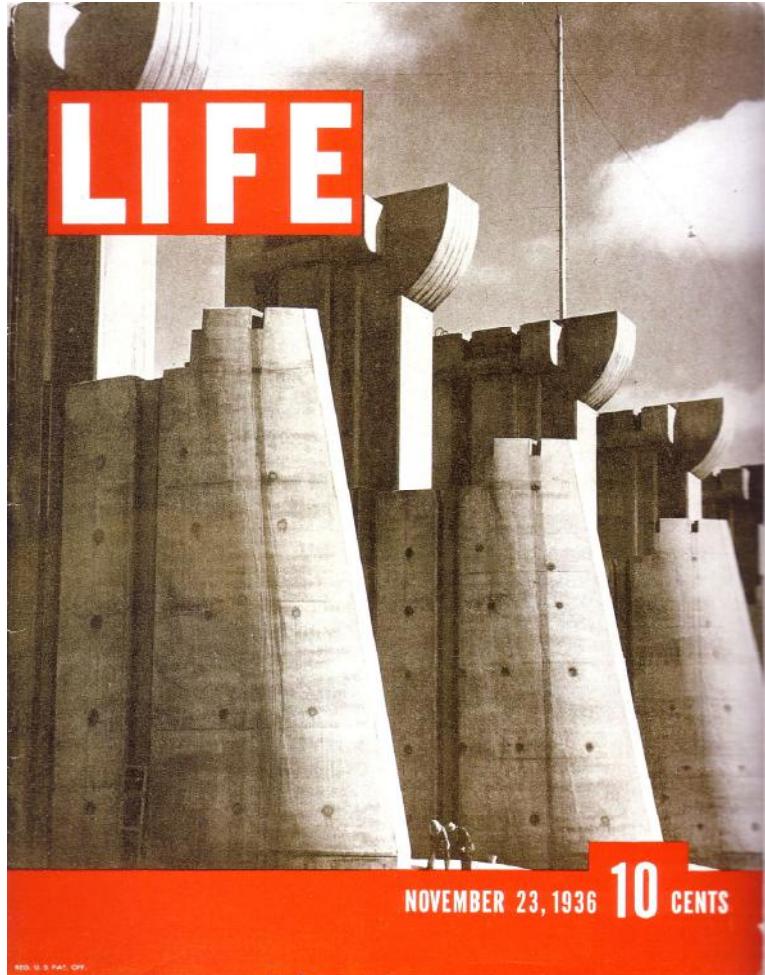
- DNA Bioengineering
  - History and objectives
  - Recombinant DNA technology
- Case I: GMO Applications
  - Objectives
  - Plants and Animals
  - Ethical Considerations
- Case 2: Hybrid Systems
  - Objectives
  - Materials and Mechanisms
  - Ethical Considerations
- Case 3: Embryonic Bioengineering
  - Objectives
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  - Applications and Frontiers
  - Ethical Considerations

# The Biosphere



The term "**Biosphere**" was coined by Russian scientist Vladimir Vernadsky in 1929. The biosphere is the life zone of the Earth and includes all living organisms, including man. In the last half century we have gained the ability to seriously modify key elements of the biosphere, including us.

# Our Focus: BioEngineering



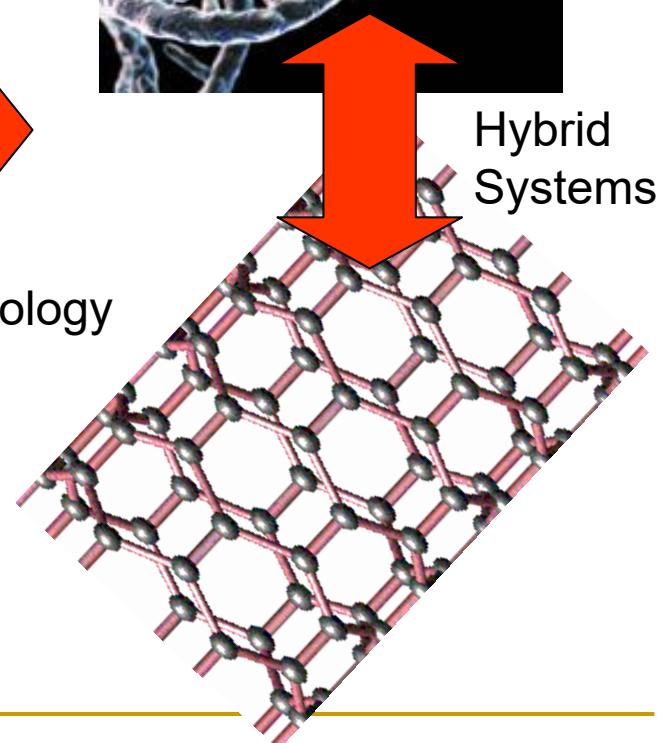
DNA-Based  
Biotechnology

$\times 10^{-12}$

Nanotechnology



Hybrid  
Systems



# Bioengineering and Genetics

- Early Technology and Science
  - Antiquity: Breeding for desired characteristics
  - 1859: Charles Darwin's "Origin of Species"
    - Changes in populations due to natural mutation
    - Survival of beneficial traits

- 
1. Random Variation
  2. Inheritance
  3. Natural Selection

# Bioengineering and Genetics

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    - Application of science and statistics
    - Dominant and recessive traits are coded particularly – by "genes"
    - Can predict occurrence of traits in successive generations

1. Dominant/Recessive Traits
2. Interdependent Appearance
3. "Mendelian Inheritance"

# Bioengineering and Genetics

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- 1900s -- Genetic material located on chromosomes
- 1940s – Practical genetic manipulation in plants and animals
- 1950s -- DNA molecule structure and function
  - Several groups of scientists compete to determine
  - 1953: James Watson, Francis Crick and Maurice Wilkins report on *Double Helix* with help from Rosalind Franklin's Photo 51

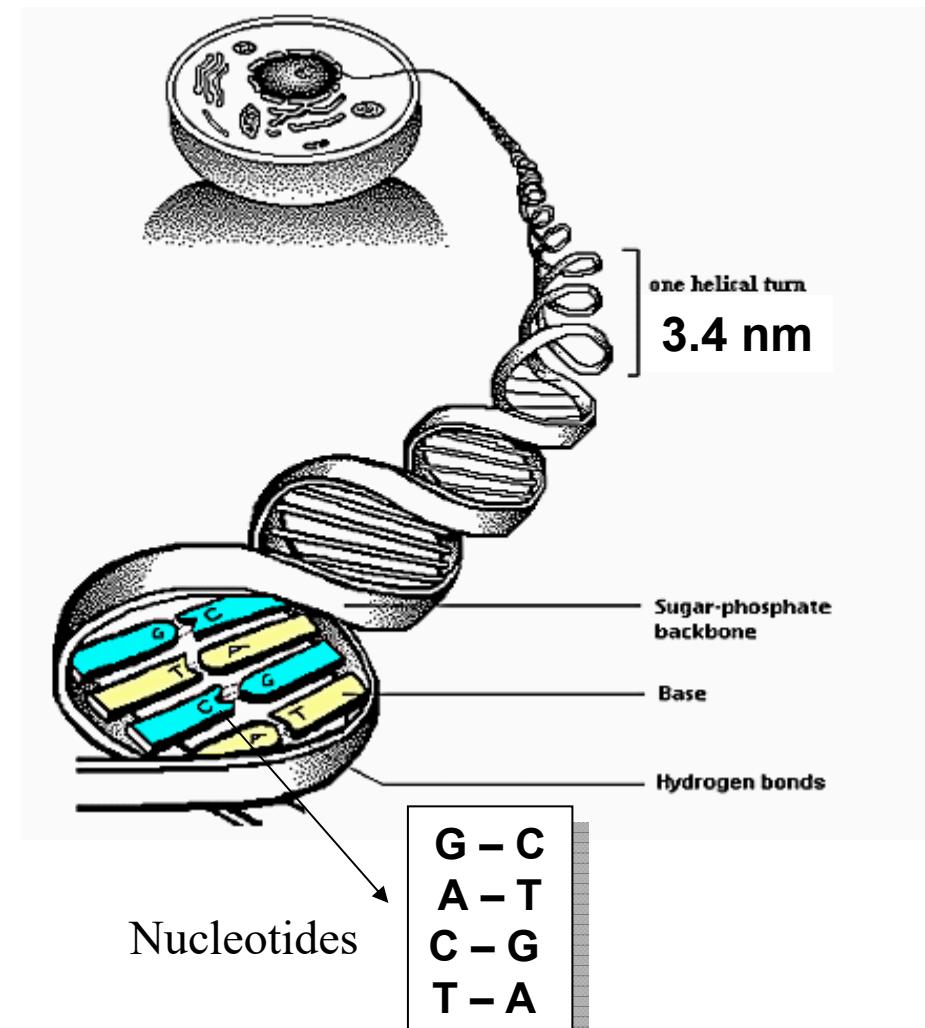
# Bioengineering and Genetics

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"Back in 1953, all we wanted to do was find out how DNA provided the information and what the cellular machinery was for making proteins."

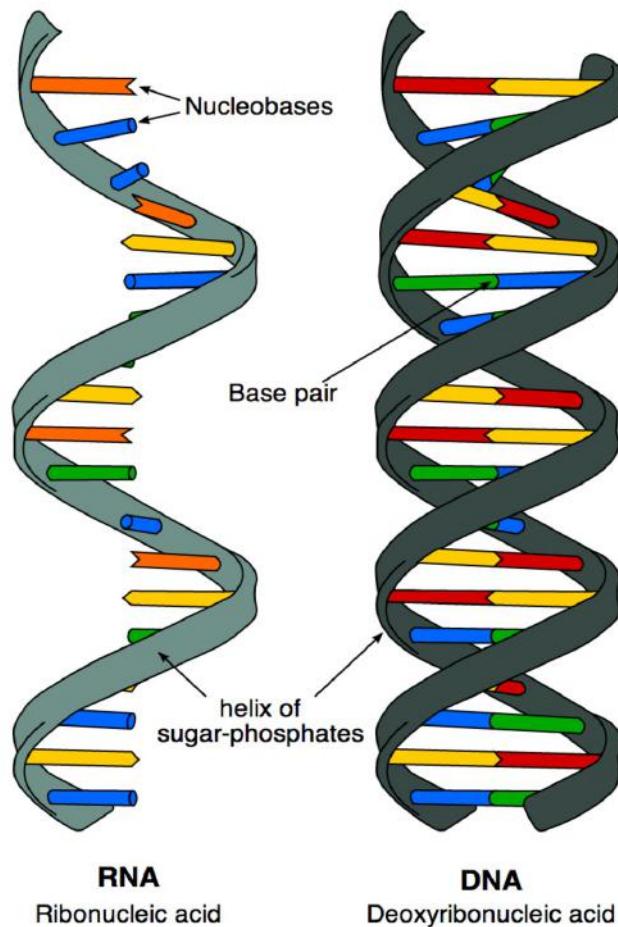
James Watson, 2003

# Structure of DNA



The Double Helix

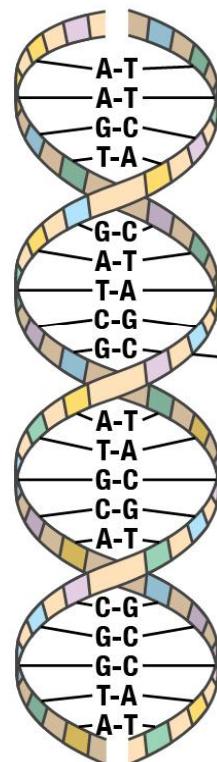
# DNA and RNA



<https://theconversation.com/explainer-what-is-rna-15169>

# DNA, RNA and Protein Formation

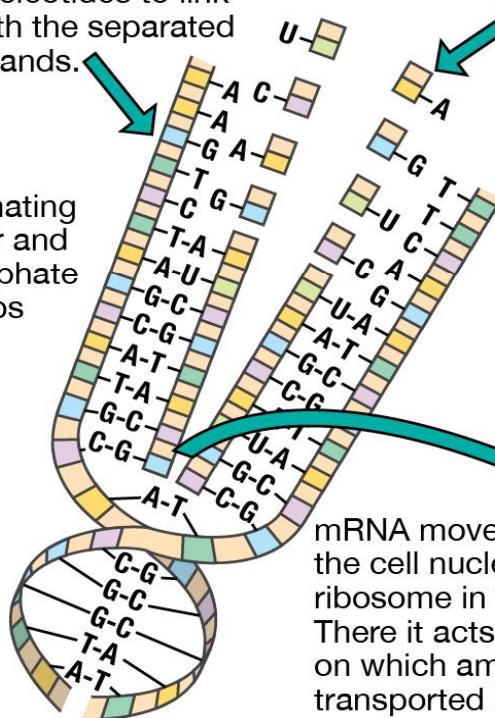
## 1. Double-stranded DNA in the cell nucleus



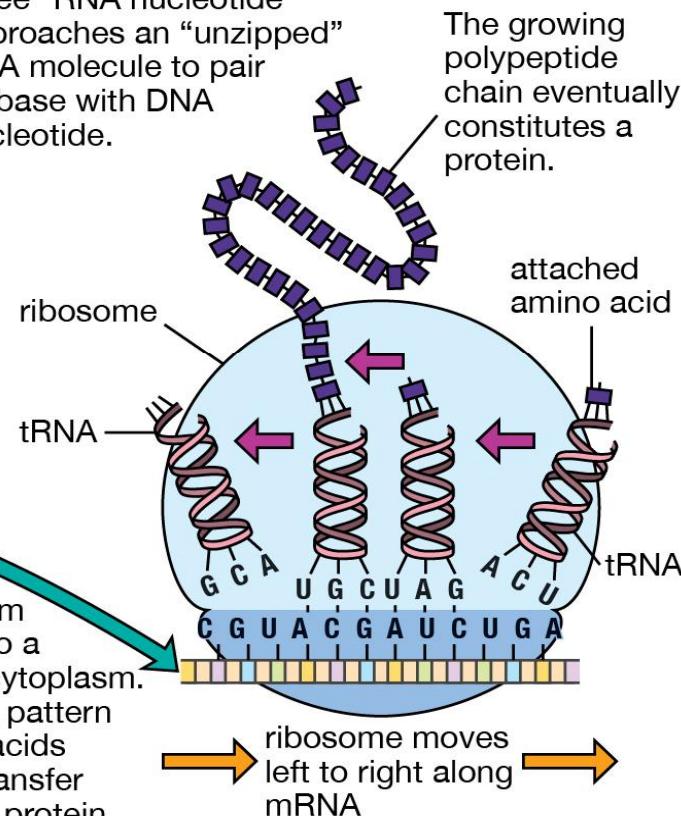
## 2. Messenger RNA (mRNA) forming on DNA strands

Strands of DNA "unzip" and allow "free" RNA nucleotides to link with the separated strands.

alternating sugar and phosphate groups



"Free" RNA nucleotide approaches an "unzipped" DNA molecule to pair its base with DNA nucleotide.



## 3. Formation of protein on ribosome

The growing polypeptide chain eventually constitutes a protein.

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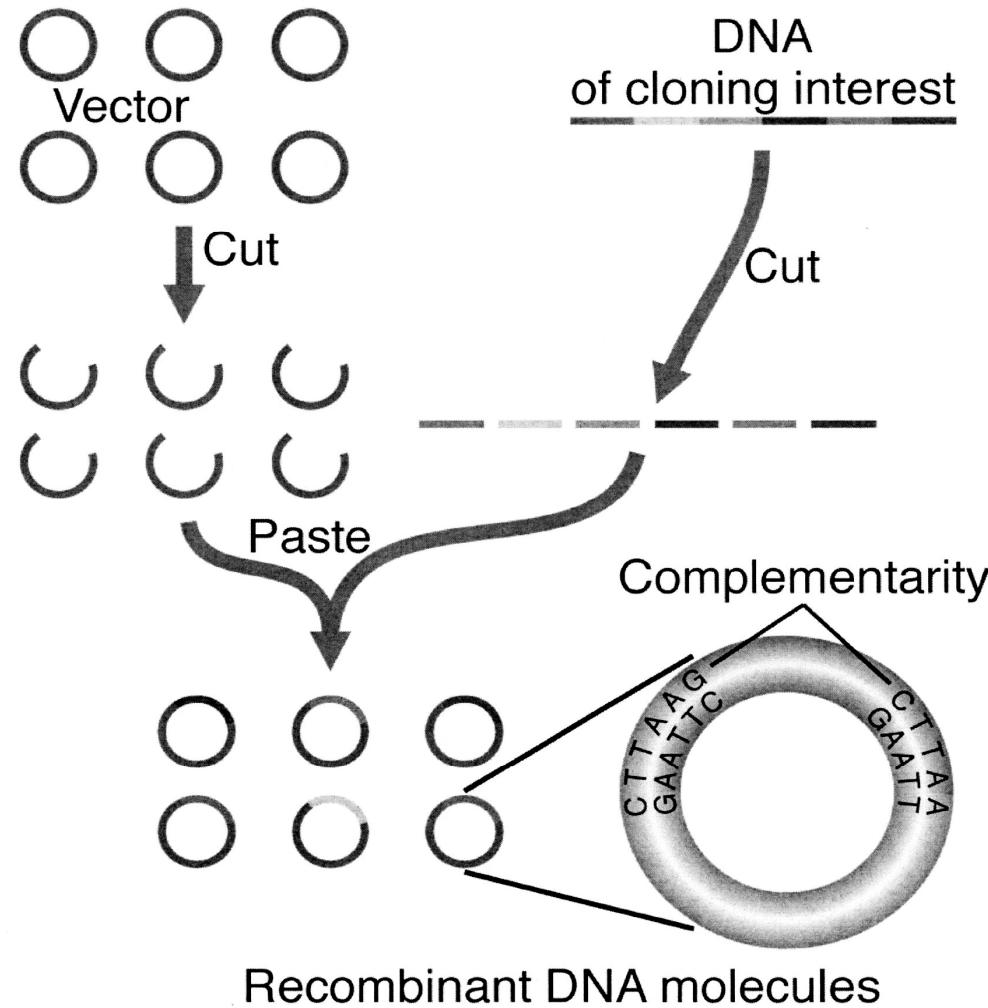
<https://www.idtdna.com/Oligos>

Copyright Gershon Weltman, 2022

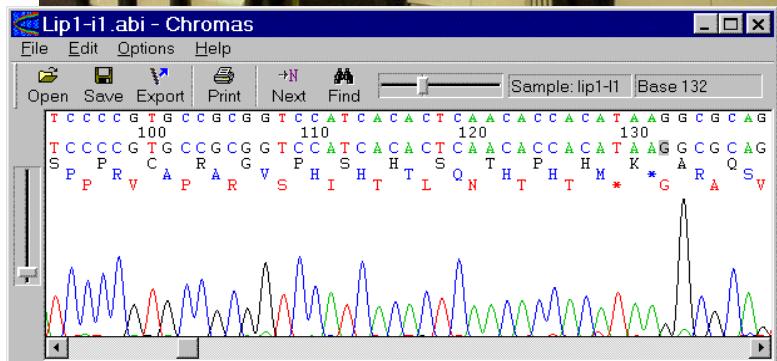
# Recombinant DNA Technology

A body of techniques for cutting apart and splicing together different pieces of DNA. When segments of foreign DNA are transferred into another cell or organism, the substance for which they code may be produced along with substances coded for by the native genetic material of the cell or organism. Thus, these cells become "factories" for the production of the protein coded for by the inserted DNA.

# Basic Recombinant Approach

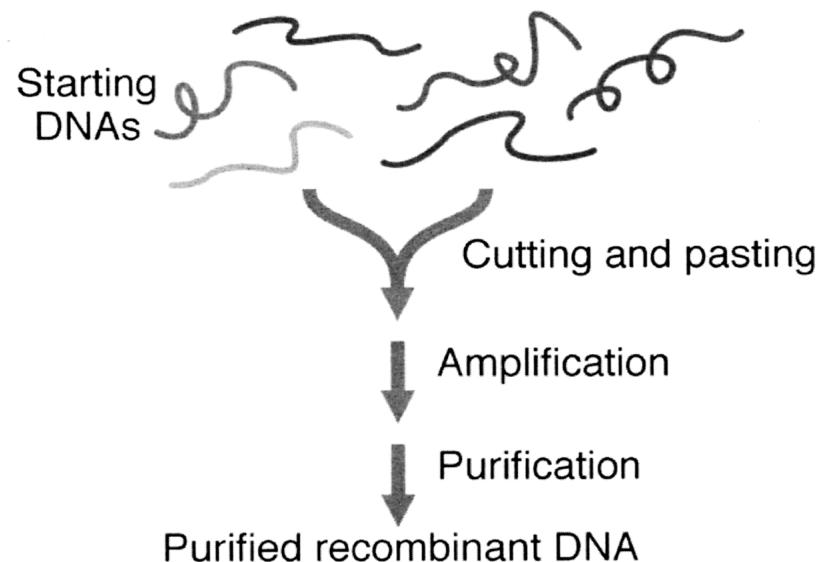


# Key Objectives of Recombinant DNA



DNA Sequencing Computer

Scientists and engineers locate 30,000 genes within the 3 billion letters of the human genome.



Analysis of genomic DNA

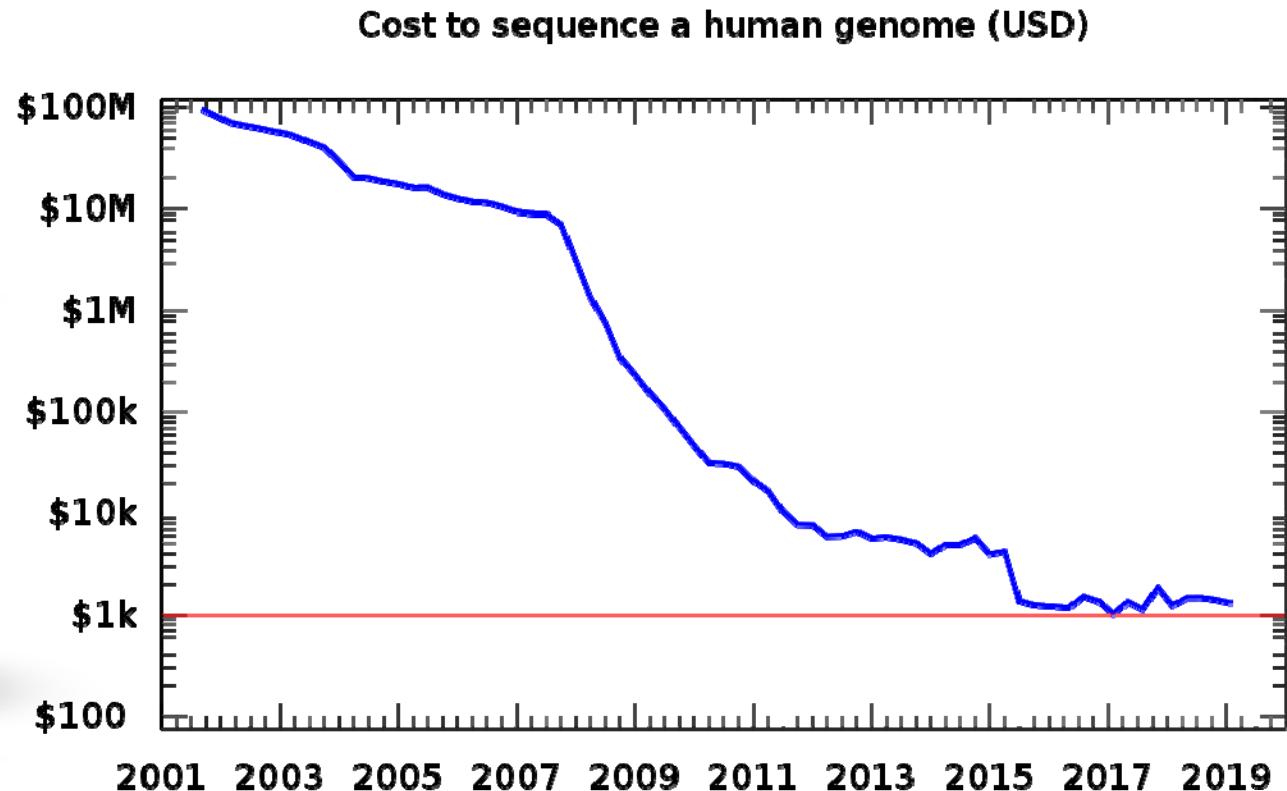
Analysis of mRNA structure and expression

Read DNA sequence and predict protein sequence.

Make protein in bacteria.

Put engineered gene into target species.

# Declining Cost of DNA Sequencing



Illumina NovaSeq6000

"The cost of sequencing an entire human DNA code has fallen from close to \$100M at the beginning of the century to near \$1K today according to the National Human Genome Research Institute (NHGRI).

# Completion of the Human Genome

THE CONVERSATION

Academic rigor, journalistic flair



Over half of the human genome contains repetitive DNA sequences whose functions are still not fully understood. Malte Mueller/fStop via Getty Images

**The Human Genome Project pieced together only 92% of the DNA – now scientists have finally filled in the remaining 8%**

Published: March 31, 2022 2.17pm EDT

Gabrielle Hartley

PhD Candidate in Molecular and Cell Biology, University of Connecticut

This is allowing investigation of previously unexamined repetitive sequences

# Current R&D Frontiers

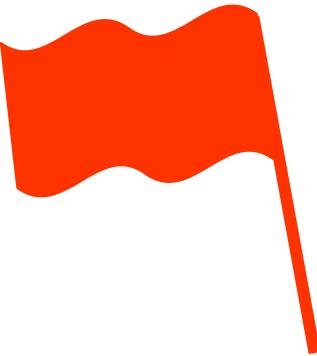
- Interactions among DNA, RNA, Ribosomes and Proteins
  - How do genes control protein formation?
  - What determines whether a given piece of DNA is functioning or is not functioning in the cell?
- Connection between DNA and Brain Function
  - How is information stored, retrieved and used?
  - How do genes influence cognition and behavior?
- Mechanisms of Development and Evolution
  - What genetic mechanisms control development?
  - How do genetic mechanisms and evolution interact

“Through development an organism’s *genotype* is expressed as a *phenotype*, exposing genes to the action of natural selection.”

<http://evolution.berkeley.edu>

# Genetic Engineering Targets

- Genetically Modified Plants
  - Increased Yields
  - Resistance to Pests and Disease
  - New Characteristics
- Genetically Modified Animals
  - Improved Growth and Size
  - New Characteristics
  - Exact Reproduction
  - Revival of Old Species
- Human Health and Reproduction
  - **Genetically Targeted Drugs**
  - **Genetic Testing and Prediction**
  - **Genetic Selection**
  - **Gene Repair**
  - **Replacement Organs**
  - **Improved Characteristics**



# Case 1: GMOs (Genetically Modified Organisms)



## For Plants

- Cisgenic -- New plants using:
  - Genes *within the same or related species*
- Transgenic -- New plants using:
  - Genes derived from *another species*.
- Subgenic -- New plants using:
  - *Gene knockdown or knockout*
  - Gene editing
  - Altering the genetic makeup without using genes from other plants

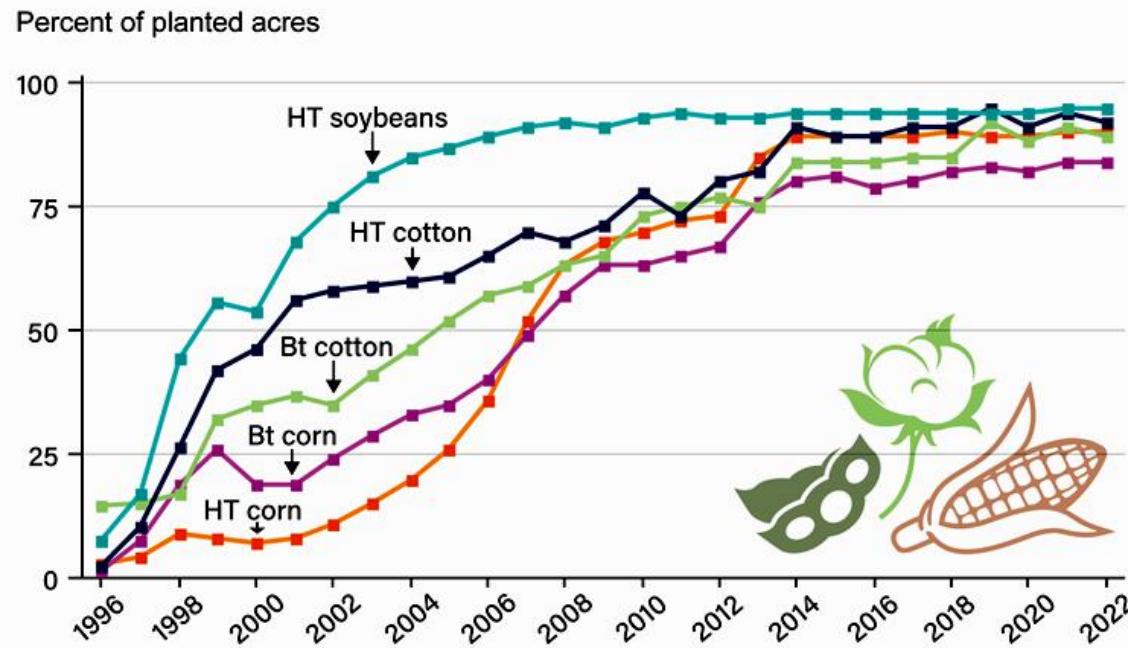
[https://en.wikipedia.org/wiki/Genetically\\_modified\\_crops](https://en.wikipedia.org/wiki/Genetically_modified_crops)

# Genetically Modified Crops in the US

Adoption of genetically engineered crops  
in the United States, 1996-2022



Economic Research Service  
U.S. DEPARTMENT OF AGRICULTURE



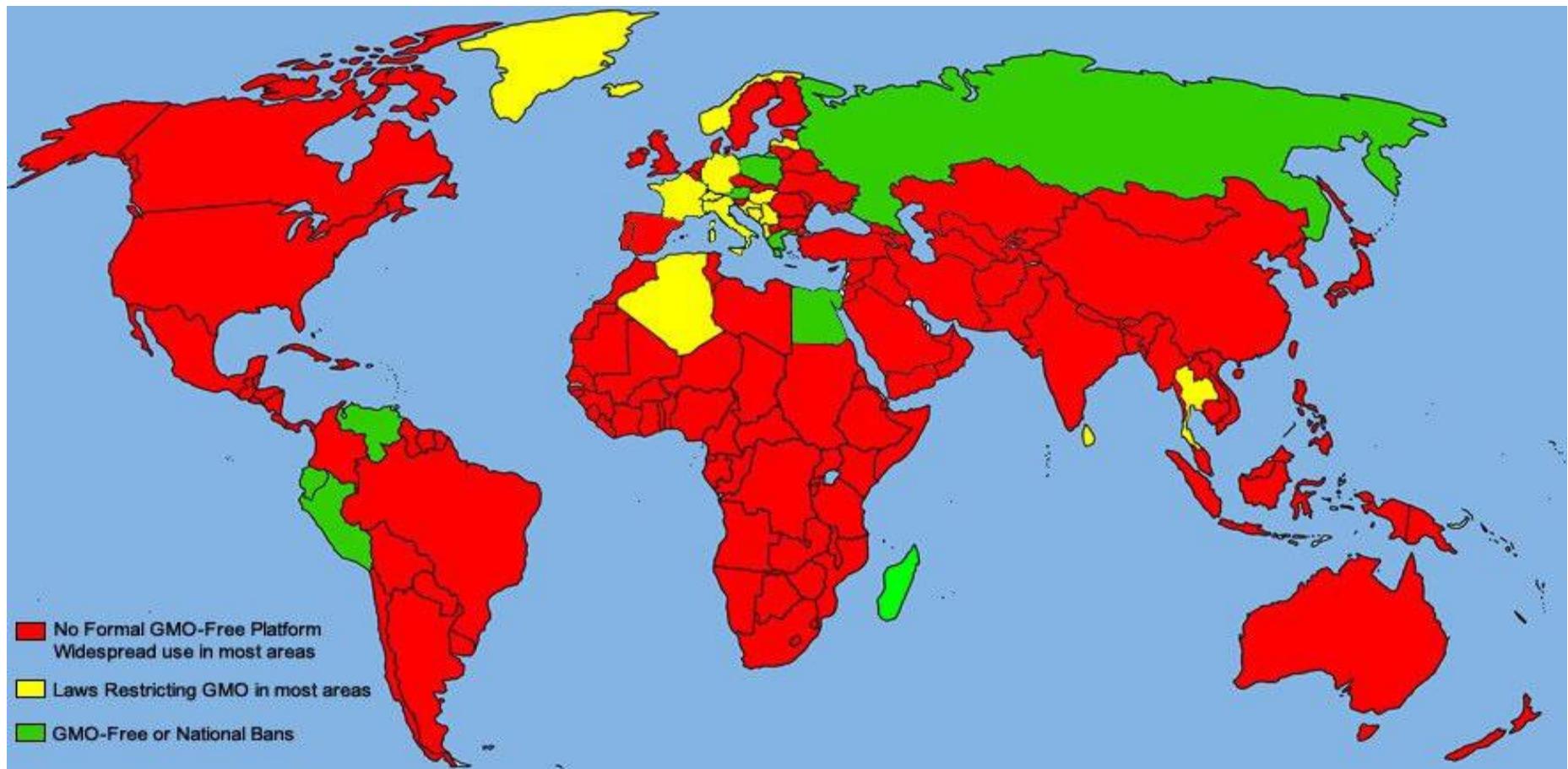
Notes: HT = herbicide-tolerant varieties. Bt = Insect-resistant varieties that contain genes from the soil bacterium *Bacillus thuringiensis*. HT and Bt corn and cotton categories include both the singular trait as well as varieties with overlapping HT and Bt traits, otherwise known as "stacked" traits.

Source: USDA, Economic Research Service (ERS) using data from the 2002 ERS report Adoption of Bioengineered Crops for 1996-99 and National Agricultural Statistics Service, (annual) June Agricultural Survey for 2000-22.



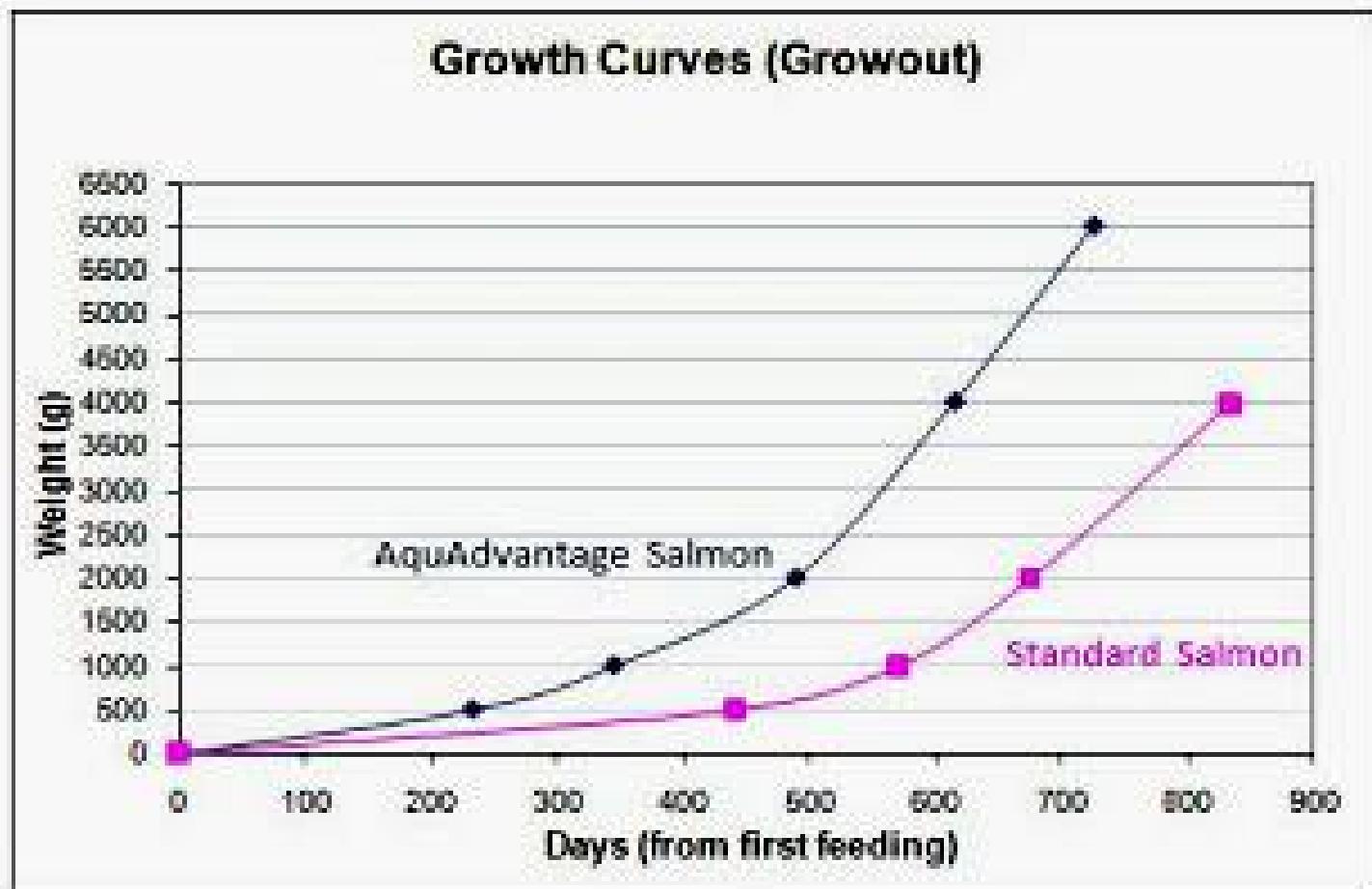
United States Department of Agriculture, Economic Research Service

# Genetically Modified Crops Worldwide



[https://gmo.geneticliteracyproject.org/wp-content/uploads/2016/02/gmo\\_world\\_map\\_large.jpg](https://gmo.geneticliteracyproject.org/wp-content/uploads/2016/02/gmo_world_map_large.jpg)

# GMO Food Animals: Salmon



# GMO Salmon are Impressive...



Genetically modified salmon at one year compared to natural salmon

# ...but GMO Chickens are Scary



# Societal Reactions to GMO Technology



## Avenues of Response

- Public Concern
- Embargoes/Restrictions
- Labeling Regulations

# Responses Have Varied: Against GMO

B2 □ Y

THE NEW YORK TIMES, MONDAY, APRIL 27, 2015

## *Chipotle to Stop Serving Genetically Altered Food*

By STEPHANIE STROM

In a first for a major restaurant chain, Chipotle Mexican Grill on Monday will begin serving only food that is free of genetically engineered ingredients.

"This is another step toward the visions we have of changing the way people think about and eat fast food," said Steve Ells, founder and co-chief executive of Chipotle. "Just because food is served fast doesn't mean it has to be made with cheap raw ingredients, highly processed with preservatives and fillers and stabilizers and artificial colors and flavors."

In 2013, Chipotle was the first restaurant chain to indicate which items contained genetically modified organisms, and a small but growing number of restaurants, largely in fine dining, also now label their menus.

Grocers, too, are moving to offer consumers more products free of genetically altered ingredients. The shelves and cases in Whole Foods stores are to be free of products containing such ingredients by 2018, and Walmart is vastly expanding its selection of organic foods, which are free of genetic alteration by law.

Even big food companies are moving to take genetically modified ingredients, or G.M.O.s, out of their products or to label products so that consumers know which are free of them.

Whether other major restaurant chains will follow Chipotle's lead is uncertain. The increased demand for such products has made them more expensive and difficult to obtain in the amounts that big businesses need.

"Say that to live up to the promise of being non-G.M.O., you need a non-G.M.O. ingredient

and soy grown in the United States is genetically modified, and Chipotle used soy oil to fry its chips and tortillas. Canola oil comes from rapeseed, another large G.M.O. crop.

Getting rid of genetically engineered corn was easiest. Chipotle's primary tortilla supplier was already producing non-G.M.O. corn flour in small amounts, and it agreed to increase its production.

But one oil can't simply replace another. Different oils have different smoking temperatures. They impart different flavors and having varying viscosities.

Chipotle's chefs preferred sunflower oil but finding enough was tricky. Chipotle found a farmer willing to increase his production of sunflower, but the company needed more oil than he could produce.

So instead of using one oil for the majority of its needs, Chipotle now uses sunflower to fry its chips and tortillas, while a non-G.M.O. rice bran oil will be mixed into rice and used to fry fajita vegetables.

The flour tortillas posed a bigger problem. "The shortening had an oil in it that was derived from soybeans," said Chris Arnold, Chipotle's spokesman. "We won't use lard for tortillas because of our vegan and vegetarian customers, and we can't use palm oil because of the environmental impact."

So Chipotle's flour tortillas are now made with a non-G.M.O. canola oil, which costs more, and the company said last week that it might have to raise prices slightly this year.

But Mr. Ells said the cost of going G.M.O.-free was "de minimis." "It's really mostly about beef," he said.

KIRSTEN LUCE FOR THE NEW YORK TIMES

Starting Monday, nothing at Chipotle's more than 1,800 restaurants will contain genetically modified organisms, or G.M.O.s.



# Responses Have Varied Against GMO

B2 □ Y

**Chipotle to Stop Serving GM Foods**

By STEPHANIE STROM

In a first for a major restaurant chain, Chipotle Mexican Grill on Monday will begin serving only food that is free of genetically engineered ingredients.

**Chipotle's junk science**

TIMES, MONDAY, APRIL 27, 2015

**Altered Food**

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**In 2003, the International Council for Science, a nongovernmental body representing more than 100 national science academies and dozens of international scientific unions, reviewed 50 independent and authoritative studies. It concluded that the GMOs Chipotle banned this week "are safe to eat." Period.**

make them more expensive and difficult to obtain in the amounts that big businesses need.

"Say that to live up to the promise of being non-G.M.O., you need a non-G.M.O. ingredient

After an audit found suppliers had failed to meet standards for raising cattle, Chipotle said it would stop using beef from cattle fed GM corn.

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# Responses Have Varied: For GMO

**ENVIRONMENT**

## Engineered food holds our future

BY HOPE JAHREN



ON THE OCCASIONAL clear-frost autumn night, my dog takes the opportunity to remind me that she is not a dog. Bewitched by sounds that I cannot hear and by smells that I cannot imagine, she plants her four feet stolidly apart and raises her head up toward the treetops. Through her slack jaw she emanates a long, low, warbling bellow that echoes across the empty wood. After the last note fades, she is herself again and comes tripping back to my side. I rub her head and continue hiking through the dark forest with my GMO wolf.

Yes, my best friend is a genetically modified organism; deliberate selection has produced the blunt-toothed, small-pawed wonder that walks by my side. Millennia passed as the most trusting puppy was selected from the litter born of a mother who herself had been the most trusting puppy, forever changing the original pattern of genes within the DNA. Now I live with a *Canis* species that sees food as a gift and can't hunt to save her life but has somehow retained the ability to howl.

Our world is changing rapidly. In my 47 years of life, global population has fully doubled, with 3.7 billion hungry mouths added to our planet. During this same time span, the amount of land suitable for agriculture has increased by only 5%. Miraculously, this did not result in the great global famine one

Genetically modified plants in agricultural products are a safe and productive way to feed the world

ABOVE: HENRIK SPOHLER; ILLUSTRATIONS BY ALEX FINE FOR TIME

78 TIME October 24, 2016

# CA Political Battleground 10 Years Ago

November 11, 2012

HUFF  
POST

LOS ANGELES

## Prop 37 Defeated: California Voters Reject Mandatory GMO-Labeling

The Huffington Post | By Anna Almendrala  
Posted: 11/07/2012 11:39 am EST Updated: 11/08/2012 3:54 pm EST

California voters rejected [Prop 37](#), which would have required retailers and food companies to label products made with genetically modified ingredients.

Millions of dollars, mostly from outside of California, were poured into campaigns both for and against Prop 37. But the donations that came in weighed heavily in favor of Prop 37's opponents.

Companies like Monsanto and The Hershey Co. contributed to what was eventually a \$44 million windfall for "No on Prop 37," while proponents were only able to raise \$7.3 million, [reports California Watch](#).

Still, despite the lopsided campaign funding power, voting on Prop 37 was relatively close. As of this story's publish time (98.5 percent of precincts reporting), Prop 37 was able to gain 47 percent of California's vote.

Opponents of Prop 37 [blitzed California with campaign ads](#) on a variety of different reasons GMO labeling would be costly for consumers and punitive to businesses like small farms and mom-and-pop stores. The anti-Prop 37 movement also gained endorsements from prominent publications like the [Los Angeles Times](#) and the [San Francisco Chronicle](#) -- not necessarily because the newspapers were against GMO labeling, but because of the way the ballot initiative was written.

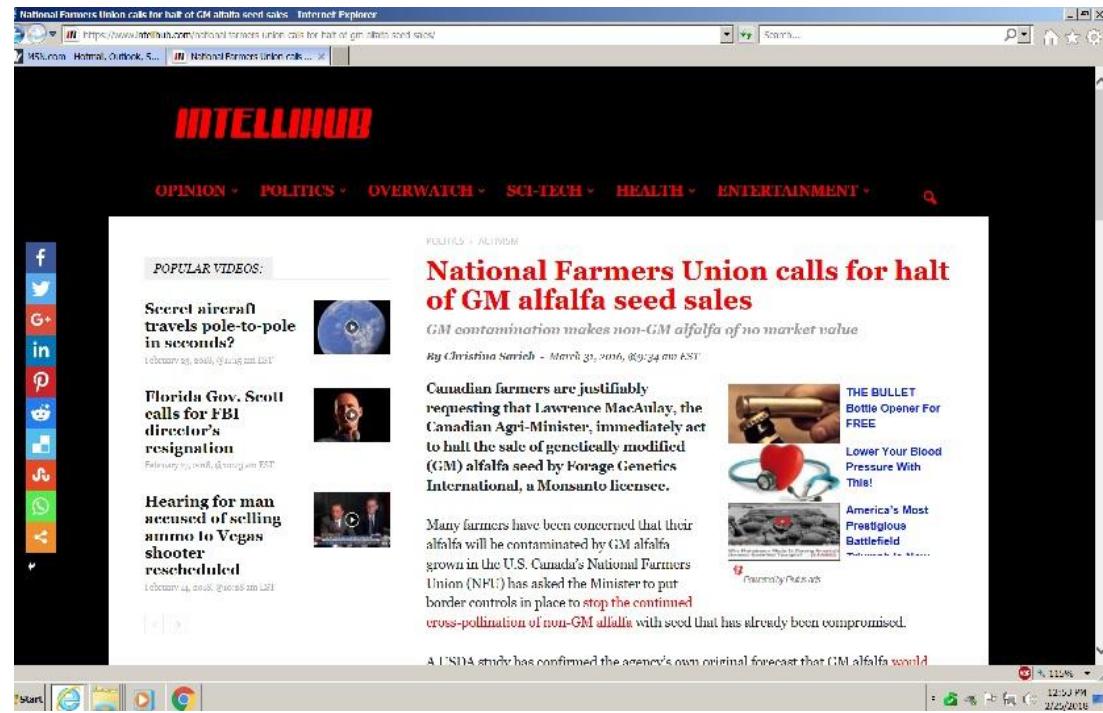
# Laws and Regulations Adjust...

- Vermont passed a law requiring the labeling of food with GMO contents starting on July 1, 2016
- The US congress then passed a law blocking states from imposing their own GMO labeling rules and exempting animal products, but
- The National Bioengineered Food Disclosure Standard regulates labeling of bioengineered food. As of January 1, 2022, foods meeting requirements identified in the Standard *must* bear a disclosure.



# ...and Markets Adjust

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- Some food producers are independently opting out.



# Laws and Markets Adjust

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- The US congress then passed a law blocking states from imposing their own GMO labeling rules and exempting animal products, but
- The National Bioengineered Food Disclosure Law of July 29, 2016 charges Dept. of Agriculture with developing a national mandatory system for disclosing the presence of “bioengineered material”
- But some food producers are independently opting out
- And many food product companies are now adding NON GMO in their package labeling.



# GMO Ethical Analysis

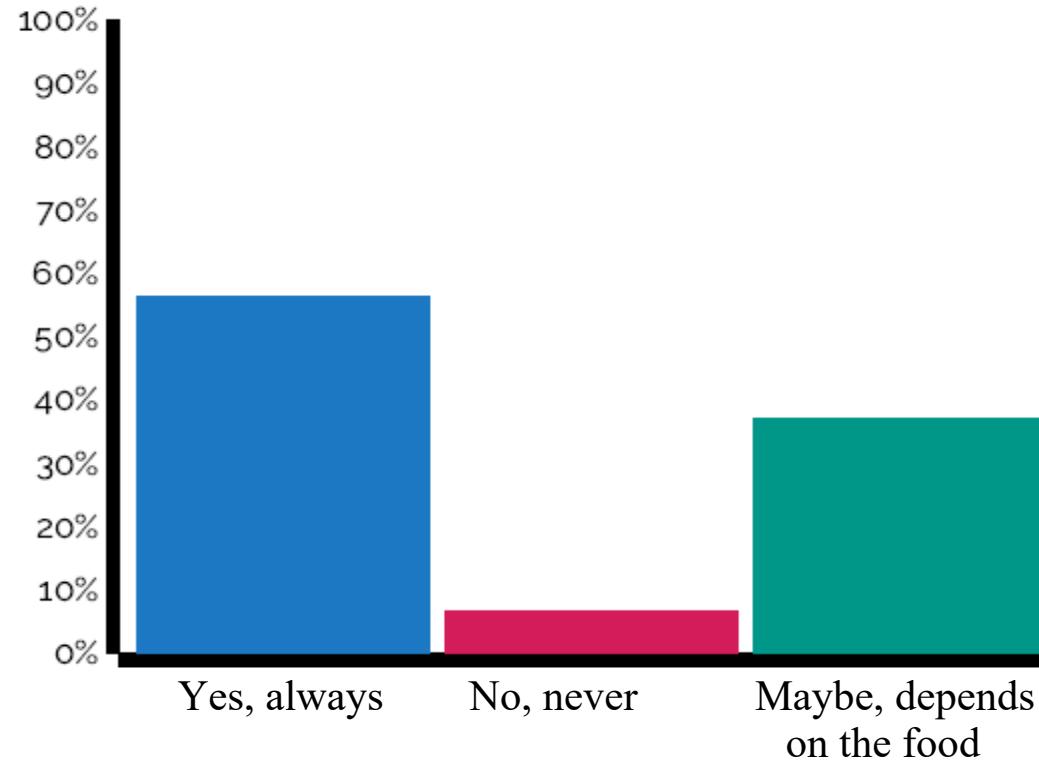
- Beneficial Factors
  - ❑ Increased productivity, to feed 2050 human population
  - ❑ Greater resistance, against weeds, pests and disease
  - ❑ Environmental agriculture, e.g., less plowing and irrigation needs
  - ❑ Designed products, e.g., food with health protective value
- Risk Factors
  - ❑ Uncontrolled spread of transgenic crops
  - ❑ Cross-pollination: Superweeds or worse
  - ❑ Harmful direct effects: Wildlife and food animals
  - ❑ Ecological disasters: Biodiversity, wildlife, sustainability
  - ❑ Human health and heredity: Top of the food chain
- Moral & Ethical Issues
  - ❑ Health and ecological risks vs. benefits
  - ❑ Agendas set by giant corporations
  - ❑ Poorer populations most likely to suffer bad effects

# Online Poll: GMOs and Labeling

- Log on to UCLA\_WIFI
- Go to <https://onlinepoll.ucla.edu>
- Search for GMO Labeling
- Password: 1234
- Answer the 1 multiple choice question
- Hit “SUBMIT”

# Online Poll: GMO Labeling

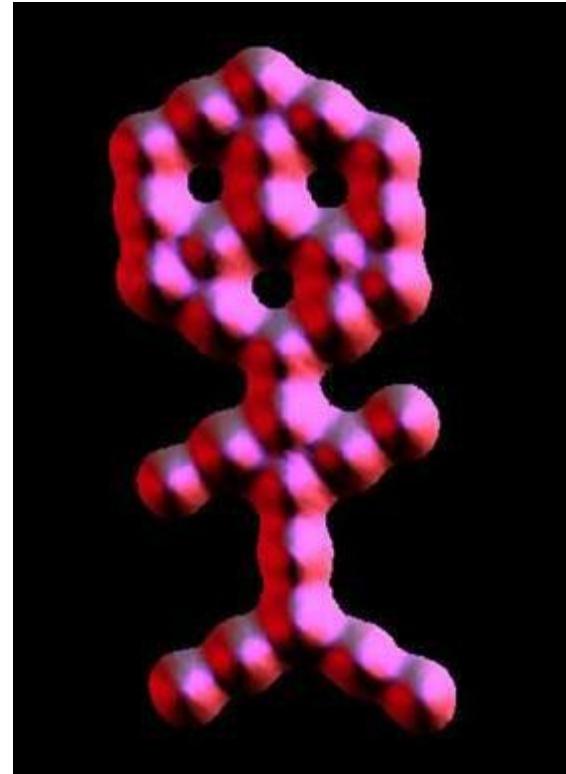
Should the presence of GMO contents be included in food labels?



Engr 183EW classes are definitely for labeling; the total of ~95% for combined 'Yes' and 'depends on the food' is about the same quarter to quarter.

# Case 2: Hybrid Systems - Nano and Bio

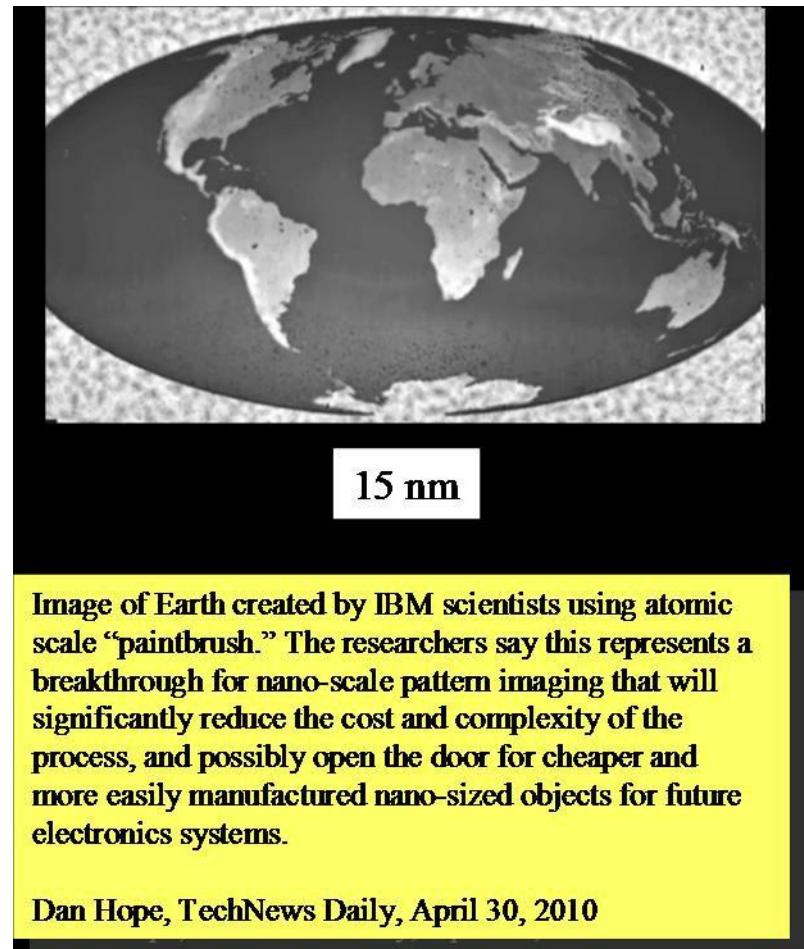
- Nanotechnology Objective  
Manipulate the fundamental building blocks of nature to manufacture new classes of micro-products that are clean, strong, light and precise
- Requirements
  - Get atoms into the right place
  - Specify structures in molecular detail without violating physics
  - Have low manufacturing costs
- Related Concepts
  - Nano Mechanisms
  - Hybrid NanoBio Systems
  - Self Replication?



IBM Atom Man, c. 2005

# Case 2: Hybrid Systems - Nano and Bio

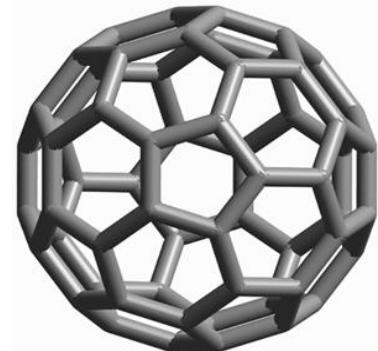
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# Nano Materials

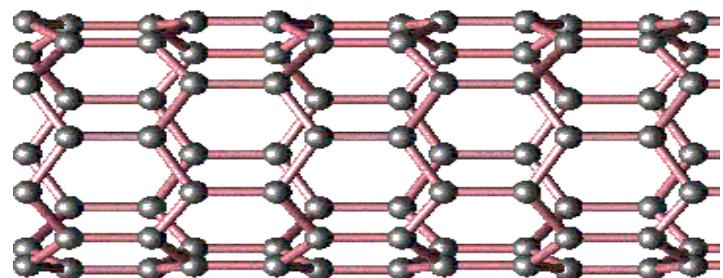
## Buckyballs

- Carbon atoms arranged as spheres
- For superhard substances such as synthetic diamonds



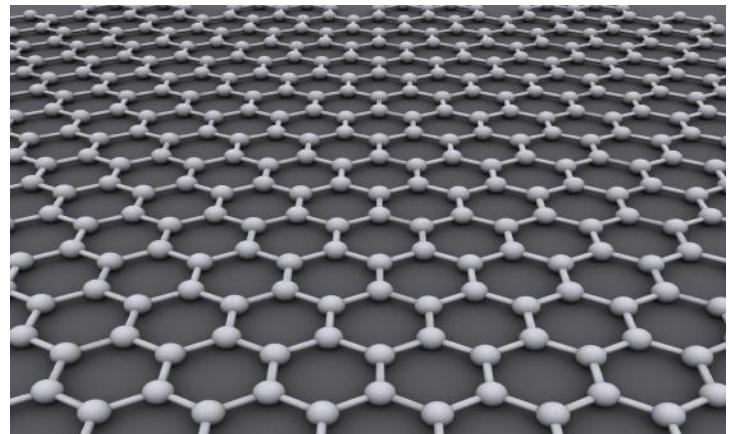
## Nanotubes

- Carbon atoms rolled into cylinders
- Exceptional electrical, thermal and structural properties
- 100x as strong as steel
- For batteries, implants, prostheses, etc.



## Graphene

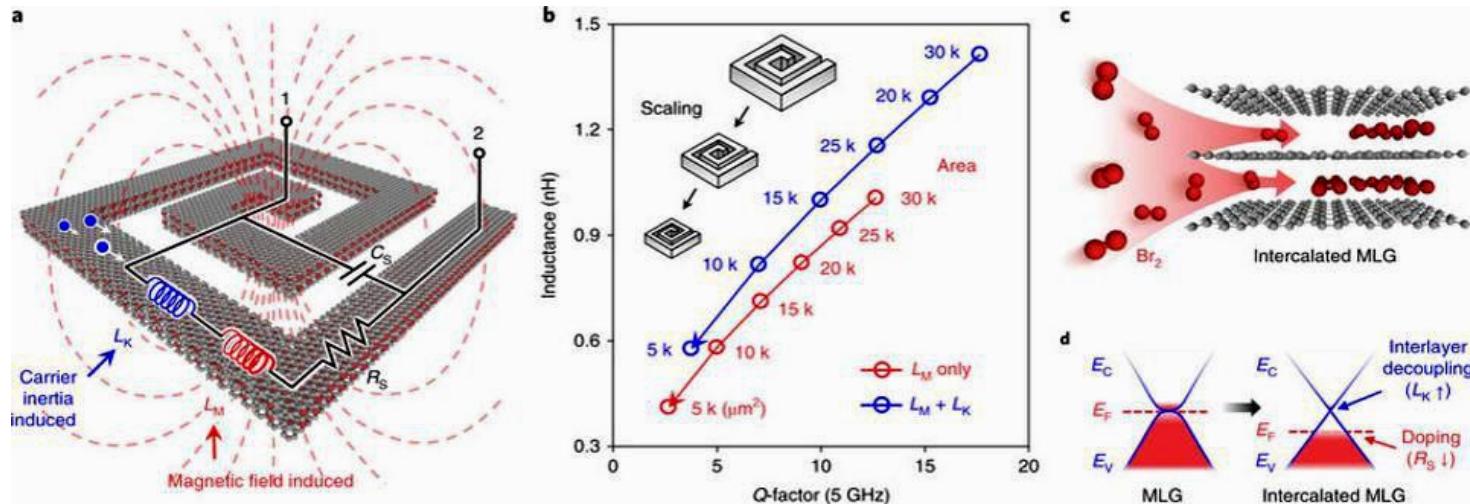
- Carbon atoms spread into 1-atom sheet
- Flexible and strong
- Exceptional electrical and thermal properties, and 100x strength of steel
- For display screens, batteries, lights, etc.



NMR Studies of Fullerenes and their Complexes, University of Cambridge, UK, 2005

# Nanomaterials: Example

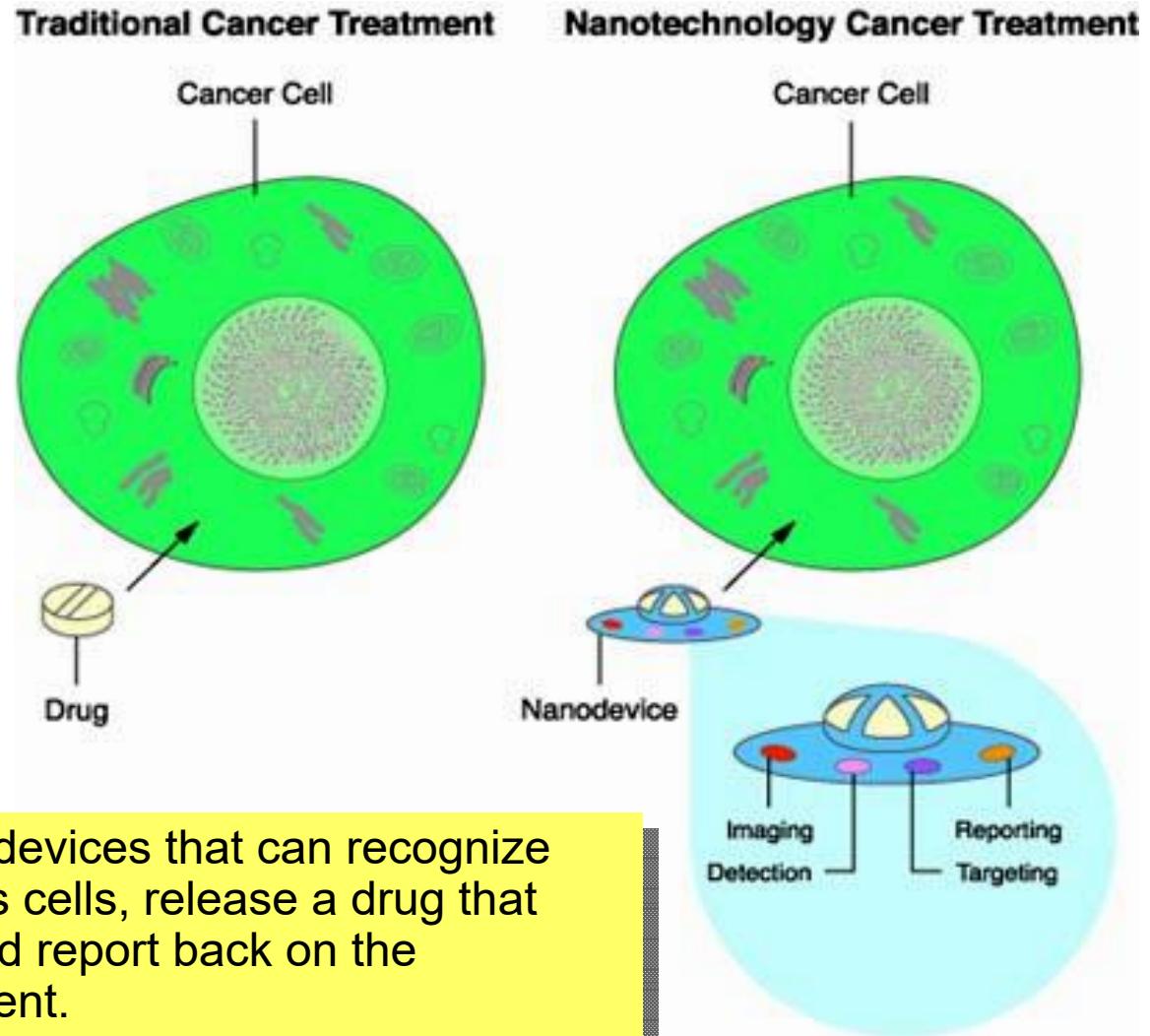
“The Last Barrier To Ultra-Miniaturized Electronics Is Broken, Thanks To A New Type Of Inductor”



*“We essentially engineered a new nanomaterial to bring forward the previously ‘hidden physics’ of kinetic inductance at room temperature and in a range of operating frequencies targeted for next-generation wireless communications.”*

Kaustav Banejee  
Nanoelectronics Research Lab  
UC Santa Barbara, July 2020

# Nanodevices: Example Benefit



One goal is to create nanodevices that can recognize precancerous or cancerous cells, release a drug that targets only those cells, and report back on the effectiveness of the treatment.

# Nanodevices: Tomorrow

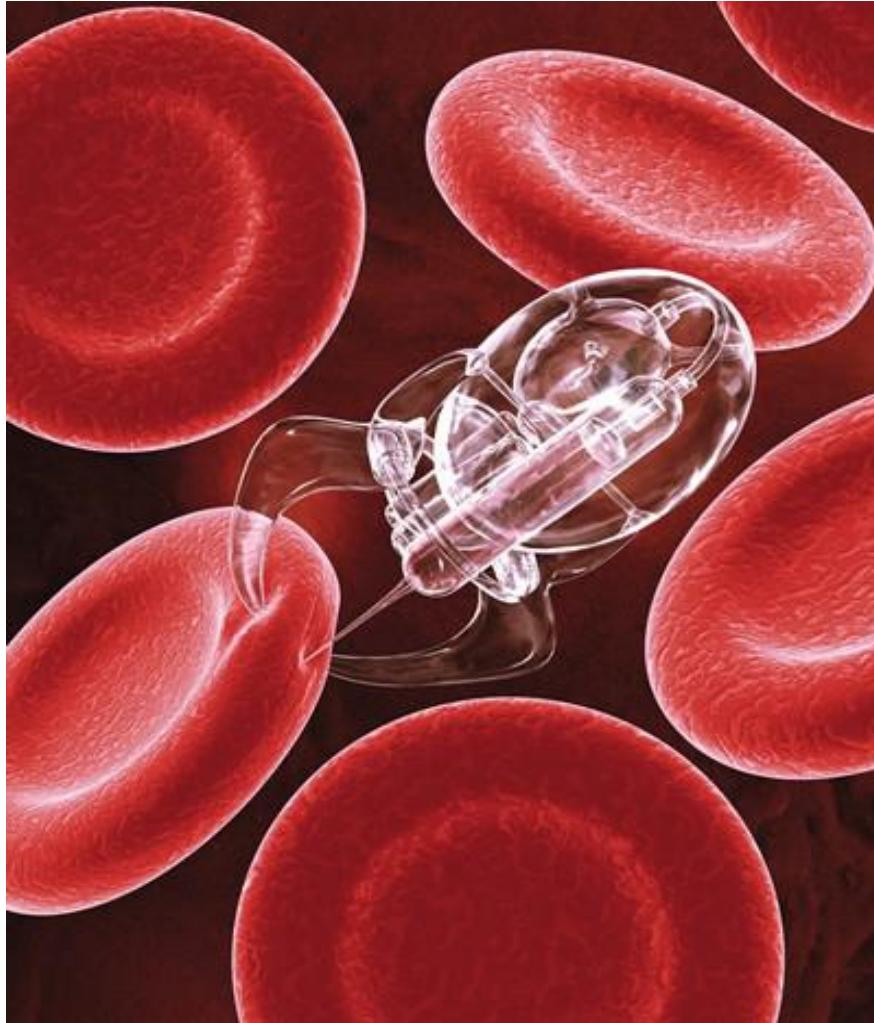


Illustration by Coneyly Jay for Ohio State University

In this speculative image a mobile nano mechanism moves among red blood cells sensing problems and injecting medication

# Nanodevices: Today

BUSINESS

Researchers develop flexible nanobots to deliver drugs inside your body

KYLE WIGGERS @KYLE\_L\_WIGGERS JANUARY 18, 2019 1:58 PM

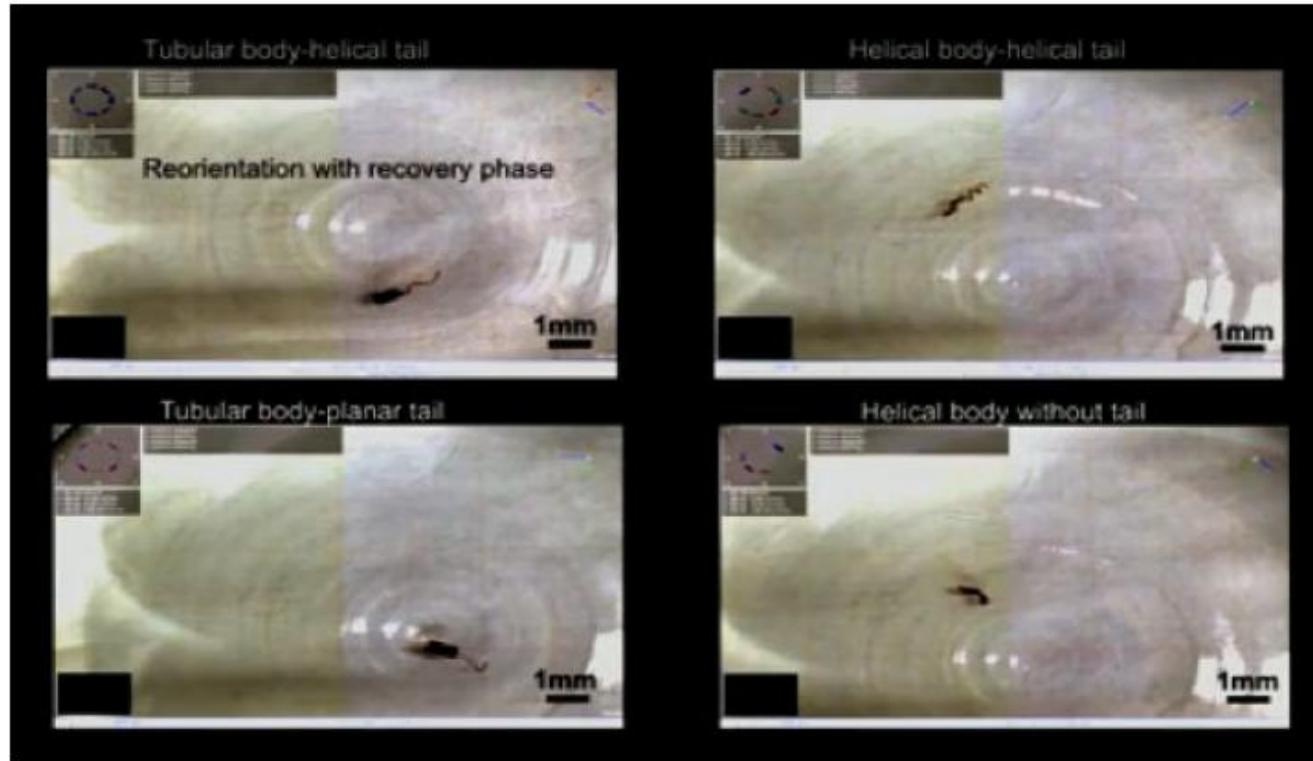
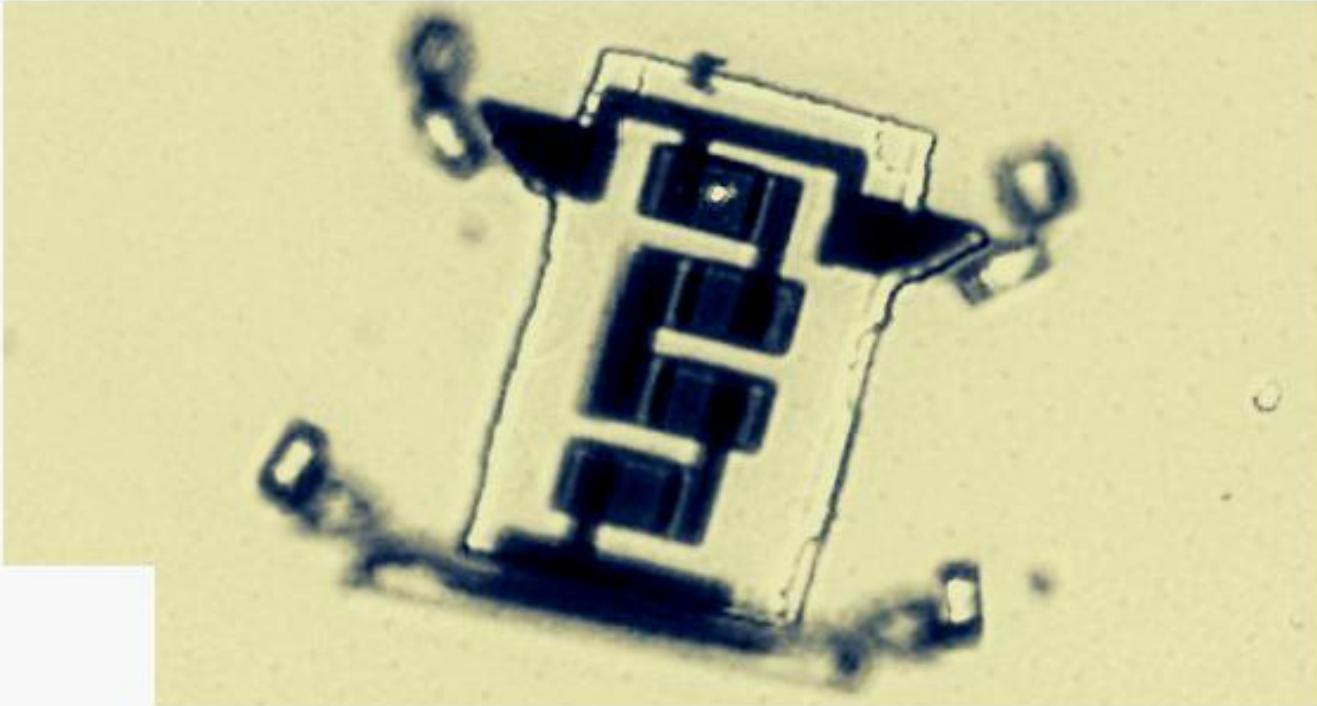


Image Credit: ETH Zurich

# Micro Robots: Today

**BBC** |  | Home | News | Sport | More ▾ | 

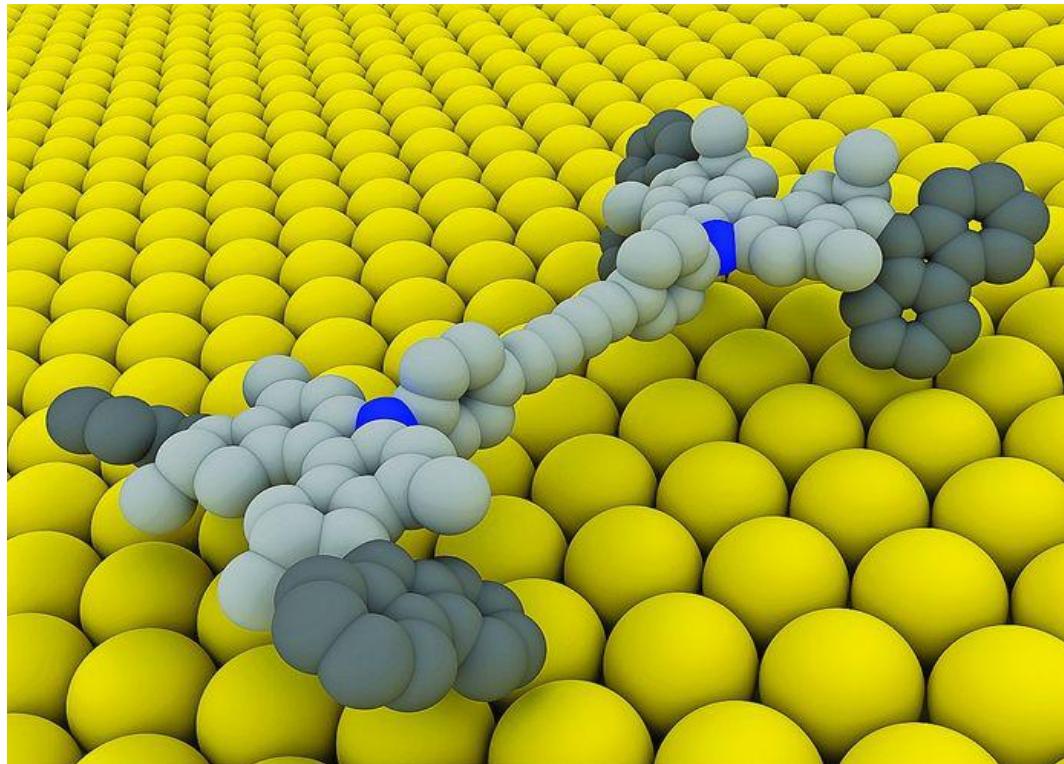
<https://www.bbc.com/news/av/technology-54327412> | Menu



**Scientists create a microscopic robot that 'walks'**

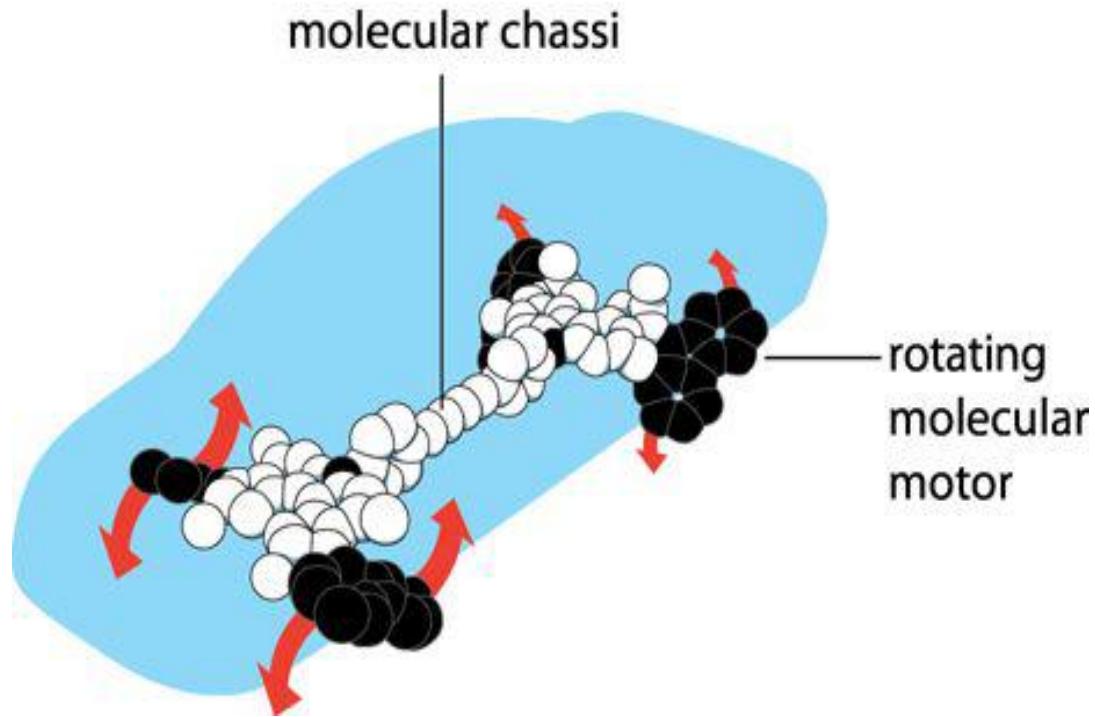
Scientists at Cornell University have created a tiny micro-robot that "walks" using four legs. Invisible to the naked eye, 10 of the computer chip bots could fit within the full stop at the end of this sentence.

# Molecular Machines: Today



The 2016 Nobel Prize in Chemistry was jointly awarded to Jean-Pierre Sauvage, Sir J. Fraser Stoddart and Bernard Feringa "for the design and synthesis of molecular machines" that can do work when energy is added.

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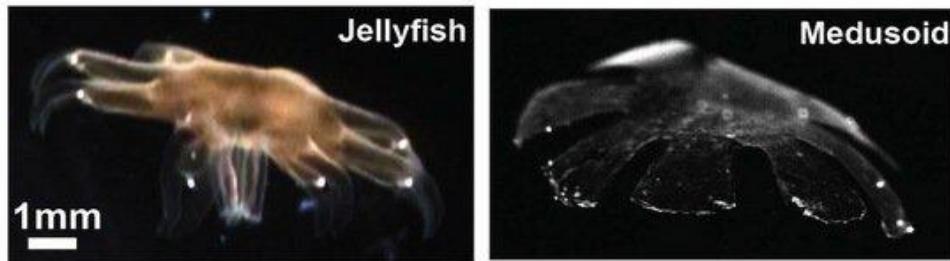
# Hybrid Organisms...



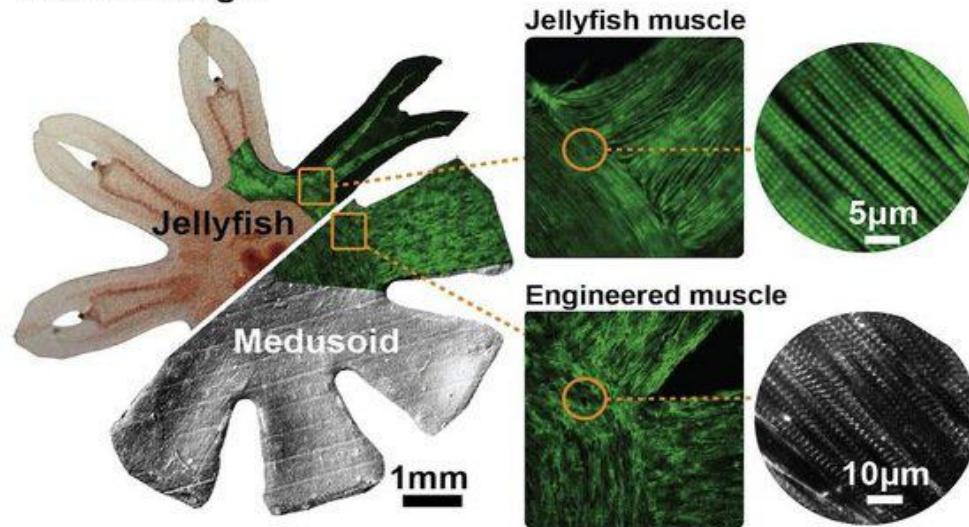
University of North Carolina Hybrid Bugs and Moths

# ...Hybrid Organic Structures...

## Body design



## Muscle design



Using **rat heart cells** and **silicone polymer**, researchers bioengineered a "jellyfish" that knows how to swim. A bioengineered jellyfish mimic swims in ocean-like saltwater. Researchers reported the creation of this mimic July 22, 2012 in the journal Nature Biotechnology. The odd jellyfish mimic, dubbed a "Medusoid" by its creators, is more than a curiosity. It's a natural biological pump, just like the human heart. That makes it a good model to use to study cardiac physiology, said study researcher Kevin Kit Parker, a bioengineer at Harvard University.

<http://news.yahoo.com/swimming-jellyfish-built-rat-cells-silicone-172816992.html>

## ...Now Using Human Heart Tissue

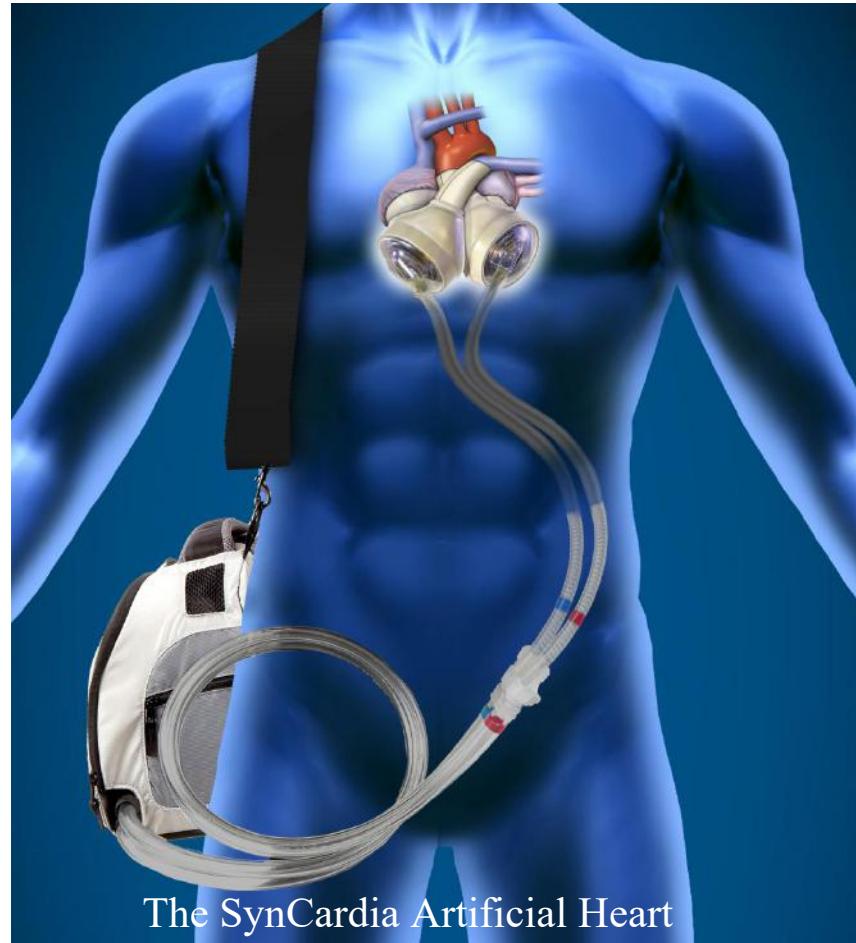


Scientists at Harvard have built a school of robotic fish powered by human heart cells. The fish, which swim on their own, show how lab-grown heart tissue can be designed to maintain a rhythmic beat indefinitely, a team reports in the journal *Science*.

Jon Hamilton, NPR All Things Considered, February 10, 2022

Copyright Gershon Weltman, 2022

# The Goal: Improve On Interim Mechanisms...

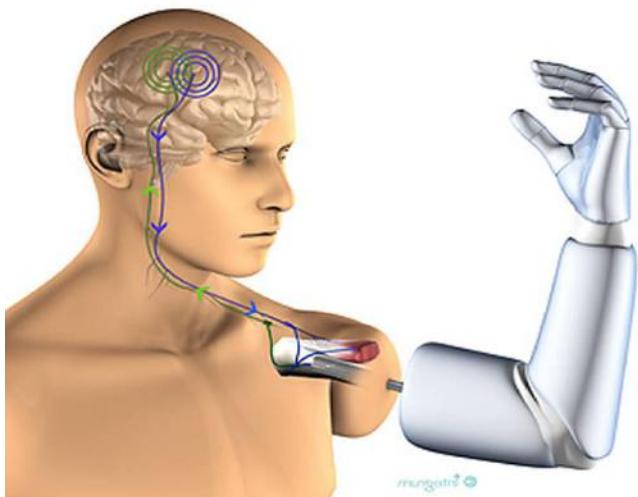


The SynCardia heart is designed to sustain patients awaiting transplants.

# ... Build New Physical Prostheses...

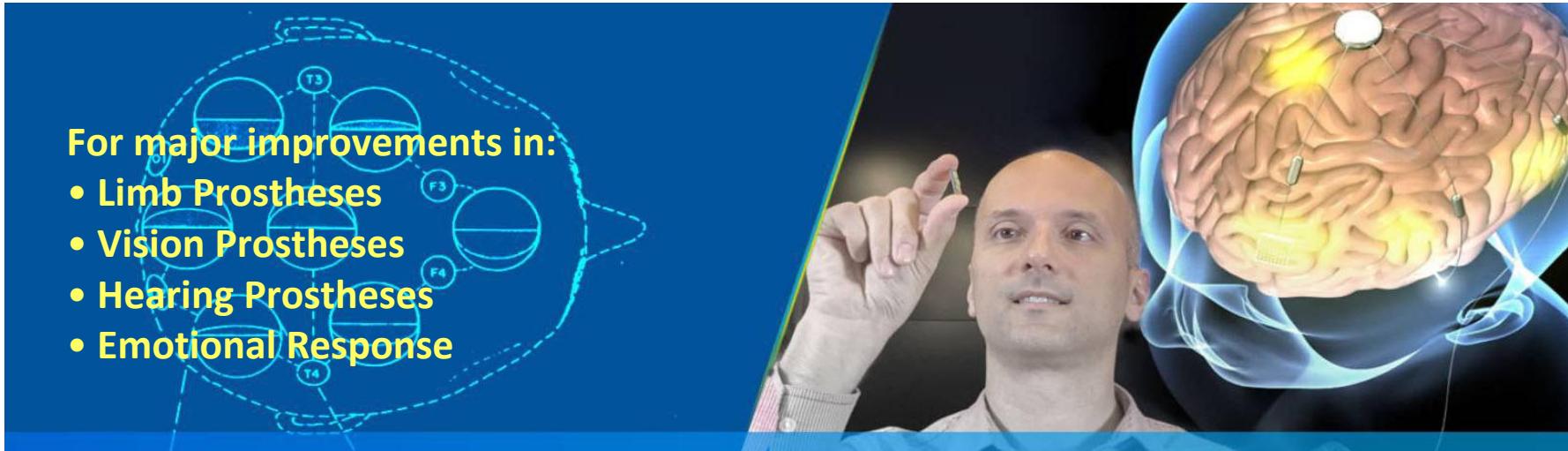


The state of the art is electromyographic (EMG) control via signals from remaining muscles



The goal is control by thought commands via existing brain and nerve pathways

# ...New Brain-Computer Interfaces...



In 1973, UCLA computer science professor Jacques Vidal published a landmark paper, *"Toward direct brain-computer communication"* that both coined the term “brain-computer interface” and set the foundation for an emerging field.

Today, Dejan Markovic, UCLA SEAS professor of electrical and computer engineering and leader of the Parallel Data Architecture Laboratory says, *“The real question is: Can we build technologies that enable those types of things that are clinically sustainable, efficacious, and attractive to patients?”*

<https://samueli.ucla.edu/brain-computer-interface/>

# ...Grow Body Parts...



Researchers at Massachusetts General Hospital (MGH) have taken the first step toward developing artificial, lab-grown limbs, building a rat forelimb with functioning vascular and muscular tissue, built on a natural, cleaned matrix.

# ...3D Print Body Parts...

Research laboratories around the world are racing to print tissues and organs including patients' own stem cells as bio ink. Russian scientists have set their sights on the thyroid gland. Hangzhou Dianzi University in China created the biomaterial 3D printer Regenovo, and printed a small working kidney that lasted four months. Other labs and companies are working on printing tissues such as skin for grafts and prosthesis covers and replacement blood vessels. Bioprinting can be combined with nano materials such as graphene and with artificial biomaterials such as alginate to create complex structures. It is clear that this technology will accelerate rapidly due to the demand for better prostheses and transplants.

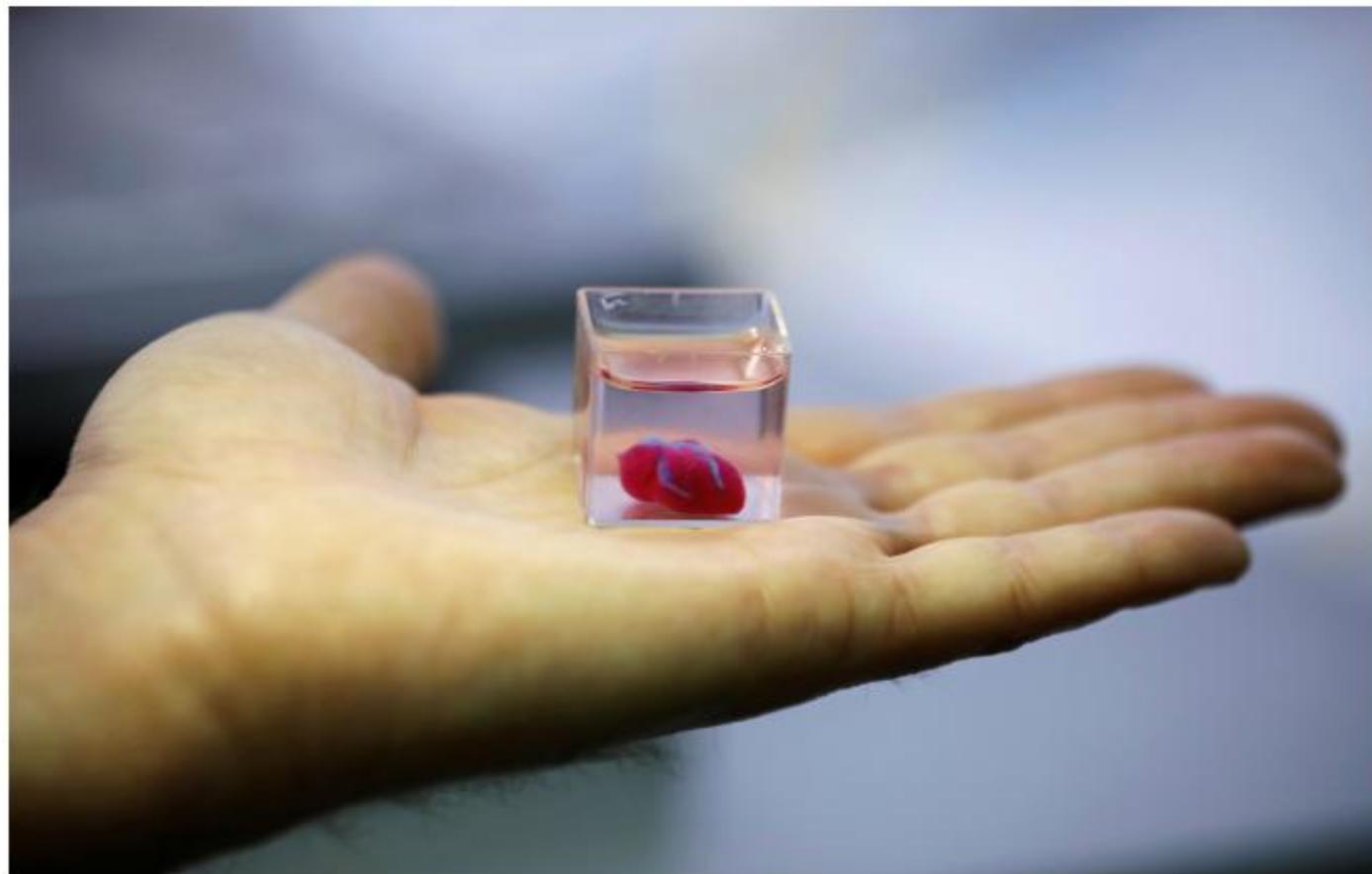


Lab picture from 3D The Voice of 3D Printing; kidney from <https://images.fastcompany.com>

# 3D Printed Body Parts: Miniature Heart

**Israeli scientists create world's first 3D-printed heart using human cells**

The team created a cell-containing "bioink" and used it to 3D print the organ layer by layer.



A scientist holds the world's first 3D-printed, vascularized engineered heart in Tel Aviv on April 15. AMIR COHEN / Reuters

<https://www.nbcnews.com/mach/science/israeli-scientists-create-world-s-first-3d-printed-h...> 4/19/2019

# ...and Bioengineer Tissues

SCIENCE FILE

## For dying boy, a new set of skin

Bold gene therapy that saved a child with rare disease offers hope to heal others.

MELISSA HEALY

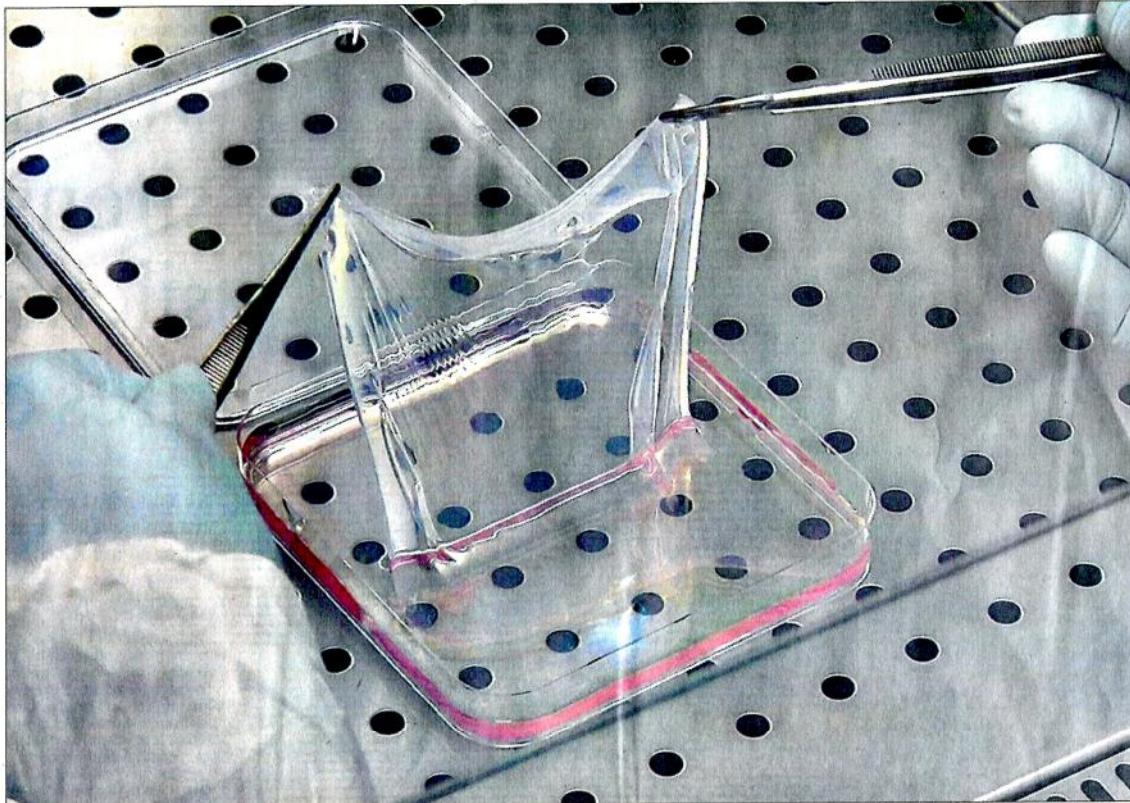
For a soccer-playing, holiday-loving boy on the brink of death from a rare inherited skin disease, doctors have accomplished a feat of genetic engineering, surgical stamina and raw nerve.

Infections arising from blisters and sores had destroyed 60% of his skin. Just 7 years old when he arrived at a burn unit in Bochum, Germany, the child was in excruciating pain despite round-the-clock morphine. He suffers from junctional epidermolysis bullosa, or JEB, a disorder that is generally fatal in the first few years of life. Though the boy had outlived most with the disease, he clearly appeared that he was about to die.

A team of German and Italian physicians had a bold idea to spare him that grim fate.

Over a five-month period in the fall and winter of 2015, they harvested some of the boy's few remaining healthy skin cells.

Using a virus to invade the cells, they introduced a corrected version of the mutated gene that had caused the catastrophic failure of his epidermis, the body's largest organ.



A MEDICAL team used a pioneering technique to build a healthy new epidermis for a boy in Germany with junctional epidermolysis bullosa, or JEB, a disorder that destroyed much of his skin. Above, a sample of engineered skin.

Los Angeles Times, November 11, 2017

# Ethical Analysis: Prosthetic Bioengineering

Features	Technical/Ethical Issues
<b>Non-Living Prostheses</b> <ul style="list-style-type: none"><li>■ Limb Replacement</li><li>■ Sensor Replacement</li><li>■ Memory &amp; Learning</li></ul>	<ul style="list-style-type: none"><li>■ Safety (e.g., Batteries, Runaways, BMI)</li><li>■ Pain and Discomfort</li><li>■ AI versus Voluntary Control</li><li>■ <b>Prosthetic Advantage/Difference</b></li><li>■ <b>Cost Barriers</b></li><li>■ <b>Socio-Economic Inequality</b></li></ul>
<b>Living Tissue Prostheses</b> <ul style="list-style-type: none"><li>■ Tissue Building</li><li>■ Organ Building</li><li>■ Hybrid Mechanisms</li></ul>	<ul style="list-style-type: none"><li>■ Health and Well Being</li><li>■ Standards and Regulation</li><li>■ Tissue Sources</li><li>■ Long Term Viability</li><li>■ <b>Cost Barriers</b></li><li>■ <b>Socio-Economic Inequality</b></li></ul>

*Socio-economic inequality is a recurring issue in biotechnical ethics.*

# Case 3: Embryonic Bioengineering

- *Mechanical Cloning:* Cells separated from embryos
  - Separated cells implanted in womb
  - Cells develop into twins, triplets, etc.
- *DNA Cloning:* DNA obtained from donor cell
  - Replaces original DNA in **ovum**, and egg develops into clone of donor
  - Replaces original DNA in embryonic **stem cells**, and cells develop into tissue or organ in the body or for transplanting back into donor or into closely matched recipient



Microscopic image shows several human embryos in the 8-cell stage

[www.pbs.org](http://www.pbs.org)

*Much ethical controversy centers on the embryonic origin of most stem cells*

# Case 3: Embryonic Bioengineering

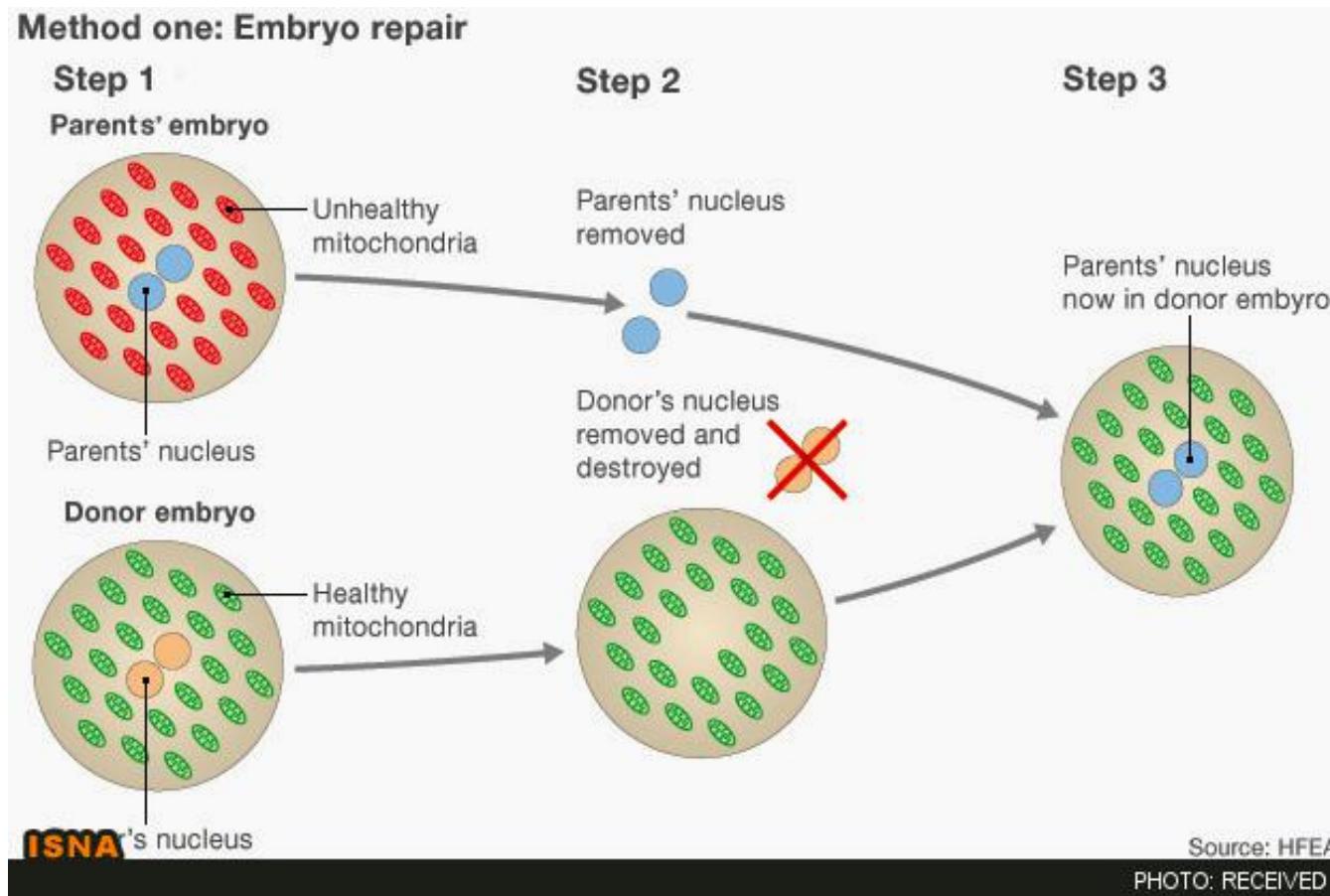
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- *Cell Repair:* Components integrated from different cells



Microscopic image shows several human embryos in the 8-cell stage

[www.pbs.org](http://www.pbs.org)

# Human Cell Repair: “3-Parent Babies”



Bioengineering solution for defective mitochondria as performed in Britain.

# Early Ethical Concerns

Los Angeles Times MONDAY, FEBRUARY 9, 2015 A15

## OPINION

OP-ED

# Modifying humans

By Marcy Darnovsky and Jessica Cussins

**B**RITAIN IS ABOUT to become the only country in the world to explicitly allow the inheritable genetic modification of humans. With a vote Feb. 3 in the House of Commons, the country has paved the way for "three-person in vitro fertilization," which combines genetic material from two women and a man.

Creating high-tech procedures like this to help women have healthy babies seems worthy of unquestioning support. But it's not so simple — and promises to soon get more complicated.

The techniques at immediate issue are relatively crude. They work by removing the nucleus from the egg (or embryo) of an intended mother, and inserting it into one provided by a second woman. Any resulting child would inherit its nuclear DNA from the intended mother and father and its mitochondrial DNA from the second woman.

mitochondrial diseases, and most also involve genetic mutations in the nucleus. About 15% of cases stem from solely defective mitochondria, and only these women — estimated to be fewer than 15 per year in Britain — would be candidates for three-person in vitro fertilization.

Later this month, the House of Lords will get the final say on the regulations. If the bill is approved, it will carve out an exception to British law against the inheritable genetic modification of humans and put the country at odds with laws in 45 countries and provisions in several international treaties.

Crossing this threshold raises a profound societal question that until now has been hypothetical: As biotechnologies improve and enable us to make more specific genetic changes in our offspring, how far will we go? Will "mission creep" expand the genetic manipulations performed on future generations?

Genetic-engineering techniques now being developed, including "precision gene edit-

Britain is moving too quickly on 'three-person in vitro fertilization.'

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Genetic-engineering techniques now being developed, including "precision gene edit-

Britain is moving too quickly on 'three-person in vitro fertilization.'

tal preference or fertility industry marketing, exacerbate existing social inequalities?

Women affected by devastating mitochondrial diseases understandably would want to give cutting-edge methods a try — if they were safe, and if there were no better alternatives. But neither of these caveats holds in this case. In February 2014, an expert committee convened by the U.S. Food and Drug Administration reviewed the same evidence available in Britain and concluded that three-person in vitro fertilization wasn't even ready for clinical trial. Yet Britain is barreling ahead to offer it in approved fertility clinics, outside a research context. Even more concerning, there is no required follow-up to study the

## Editing human DNA? That door may open soon

A new technique is used in embryos, igniting a furious ethical debate.

BY ERYN BROWN

It's a scenario that has haunted biologists since the dawn of the DNA age: the evil scientist custom-crafting a human being with test tubes and petri dishes.

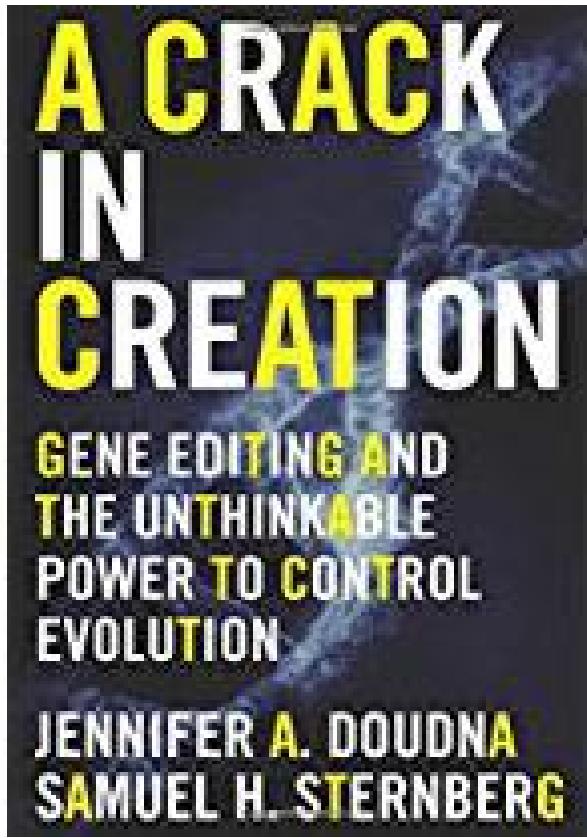
So when a Chinese team revealed last month that it

change the DNA in any organism. The negative side is, it allows regular biologists to change the DNA in any organism," said Harvard Medical School geneticist George Church. "You can twist any technology into something bad."

In the last few months, many researchers have come to realize that the new gene editing tool, known as CRISPR/Cas9, might pro-

[See Genetics, A18]

# The Door Opens: CRISPR-CAS9

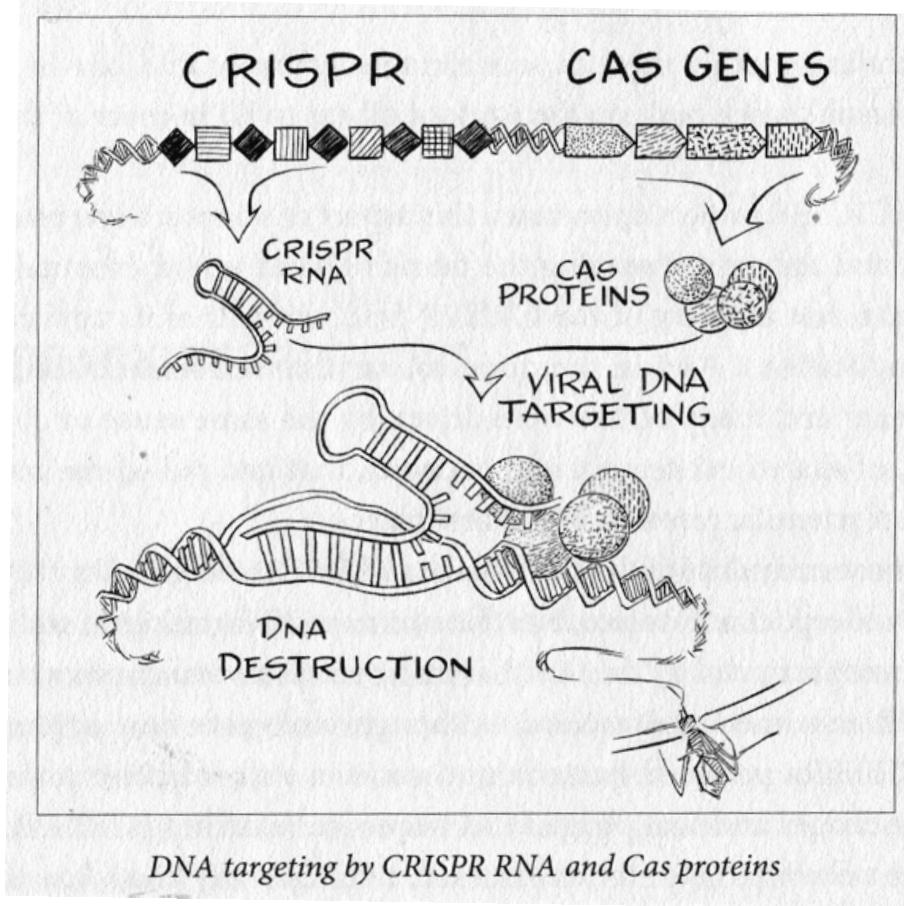
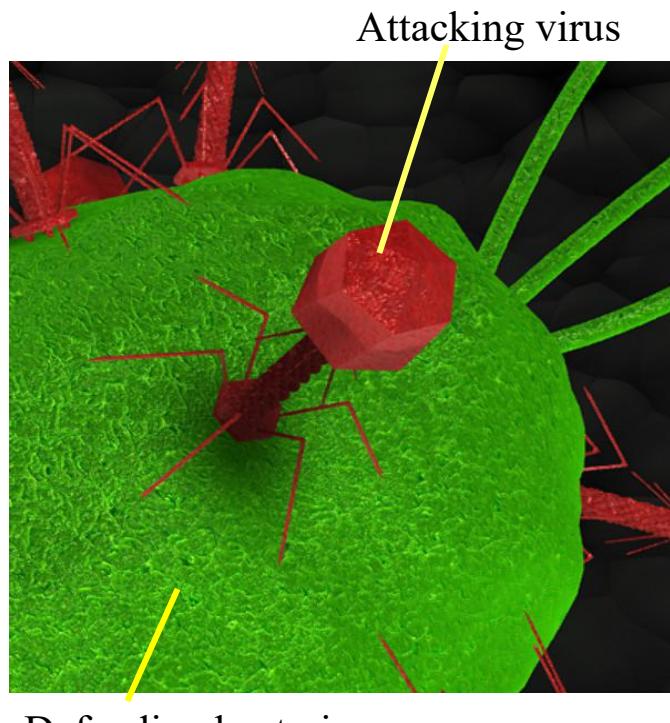


- CRISPR = Clustered Regularly Interspaced Short Palindromic Repeats
- CRISPR Uses DNA-cutting enzyme CAS9 that finds its target with the help of an RNA guide sequence that researchers can engineer to home in on any gene or DNA segment of interest.

*"with...CRISPR-CAS9 (CRISPR for short) an organism's genome –including all its genes – has become almost as editable as a simple piece of text."*

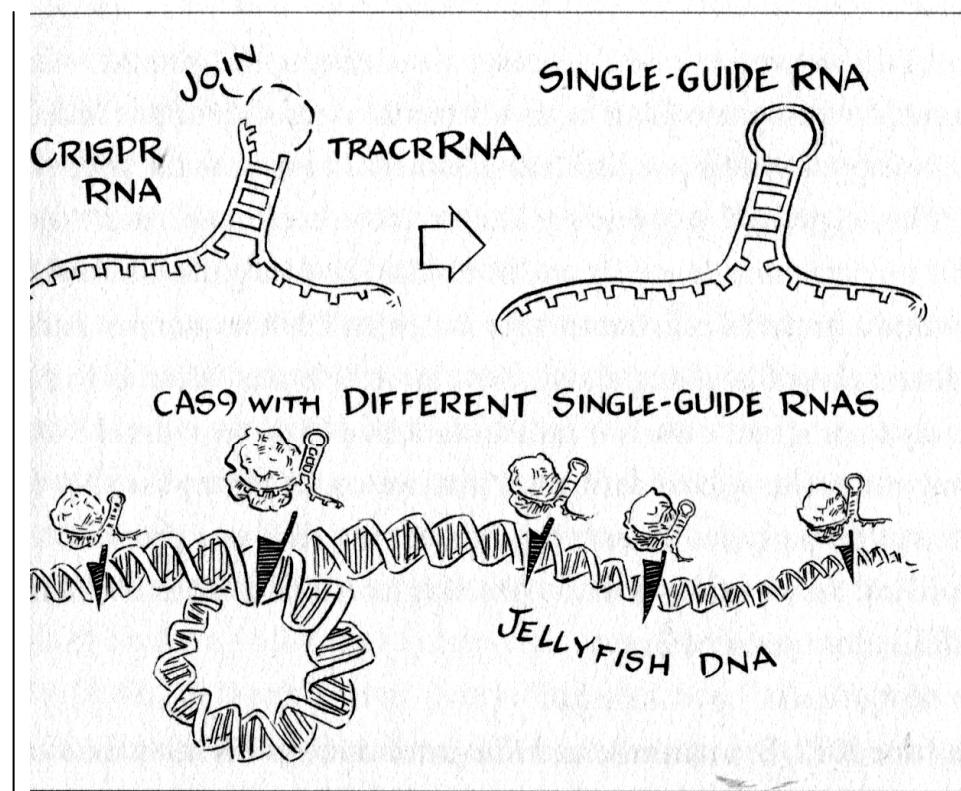
*Prof. Jennifer Doudna, UC Berkeley, 2017*

# The Discovery



Dr. Doudna and colleagues found that bacteria protect themselves against viruses by using a RNA copy of the virus' critical DNA to seek and destroy.

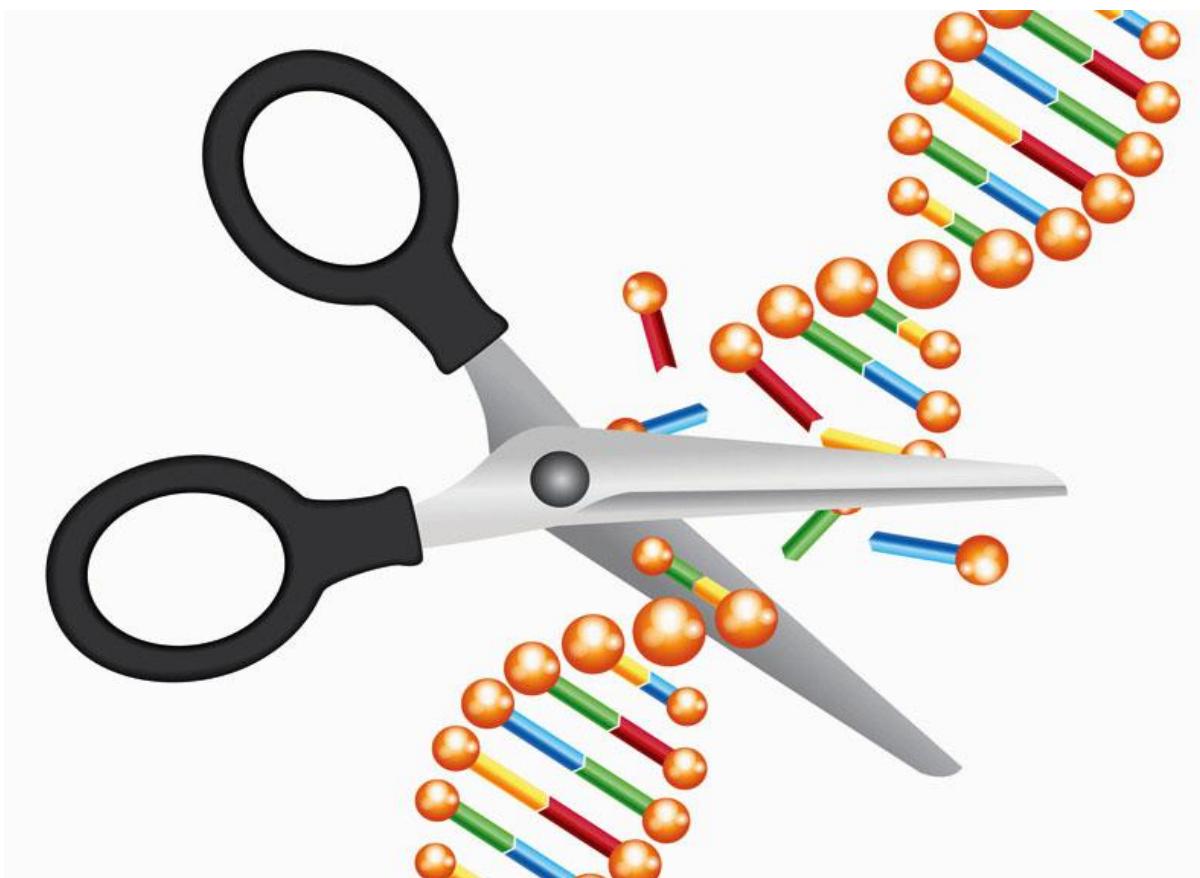
# The Demonstration



*Programmable DNA cutting by CRISPR-Cas9*

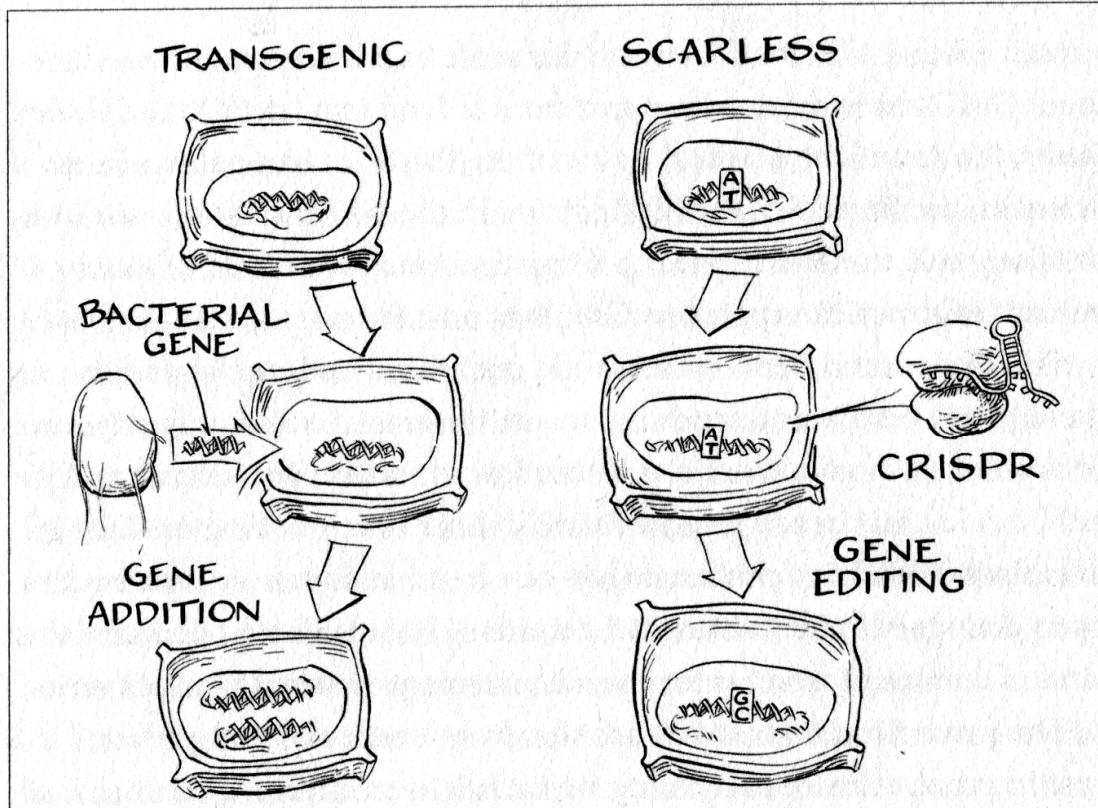
They then showed they could “engineer” RNA-CAS9 CRISPRs that would cut target DNA in precisely specified places – such as gene locations.

# Ubiquitous Symbolism: CRISPR Scissors



But CAS proteins can be selected to perform other editing functions as well.

# The Difference



*Transgenic GMOs versus scarless gene-edited organisms*

The CRISPR technique enables precise editing to modify protein formation using an organism's own genes rather than genes from an outside source.

# Ready Commercial Availability

The screenshot shows the Sigma-Aldrich website with a red header bar. The main title is "CRISPR/Cas Nuclease RNA-guided Genome Editing". Below it, a paragraph discusses the company's new genome editing tools, Sigma CRISPRs. A sidebar on the right lists various support options like SDS, Certificates, and Customer Support. A "Related Article" section includes links to "Tips for Cell Engineering using CRISPR" and "A CRISPR/Cas-GFP Vector for Rapid Expression Verification". A "Categories" section lists Cell culture, Gene expression, FMSL, and Transfection.

File Edit View Favorites Tools Help

Forward https://www.sigmataldrich.com/ Suggested Sites Web Slice Gallery

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SDS Certificates Customer Support Technical Service Quality Management Web Help Web Toolbar Worldwide Offices

**CRISPR Use License Agreement**

**Related Article**

[Tips for Cell Engineering using CRISPR](#)

[A CRISPR/Cas-GFP Vector for Rapid Expression Verification](#)

[View CRISPR Webinar](#)

**Categories**

- Cell culture
- Gene expression
- FMSL
- Transfection

http://www.sigmaltdrich.com/safety\_center.html

# Early CRISPR Targets

- “Double muscled” dogs
- Micro pigs
- Superior goats
- Humanized pig DNA
- Disease-resistant rice
- Slower ripening tomatoes
- Healthier potatoes
- Proto woolly mammoths
- De-diseased mosquitoes
- Etc., etc.



# Engineered Mosquitoes



TheScientist  
EXPLORING LIFE, INSPIRING INNOVATION

NEWS & OPINION MAGAZINE SUBJECTS MULTIMEDIA CAREERS SUBSCRIBE

Study: Gene Drive Wipes Out Lab Mosquitoes

No females were produced after eight generations, causing the population to collapse.

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Please read our [Online Policy](#) to learn how we use cookies to provide you with a better experience.

I UNDERSTAND

Researchers at Imperial College London used CRISPR to edit genes so that females did not lay eggs; after 8 generations no eggs were laid at all. There are questions if the lab results will translate to the wild – or if they should.

# Pig-Human Transplant

Newsweek, Nov 8/Nov 15, 2021

## Pig kidney transplant successful

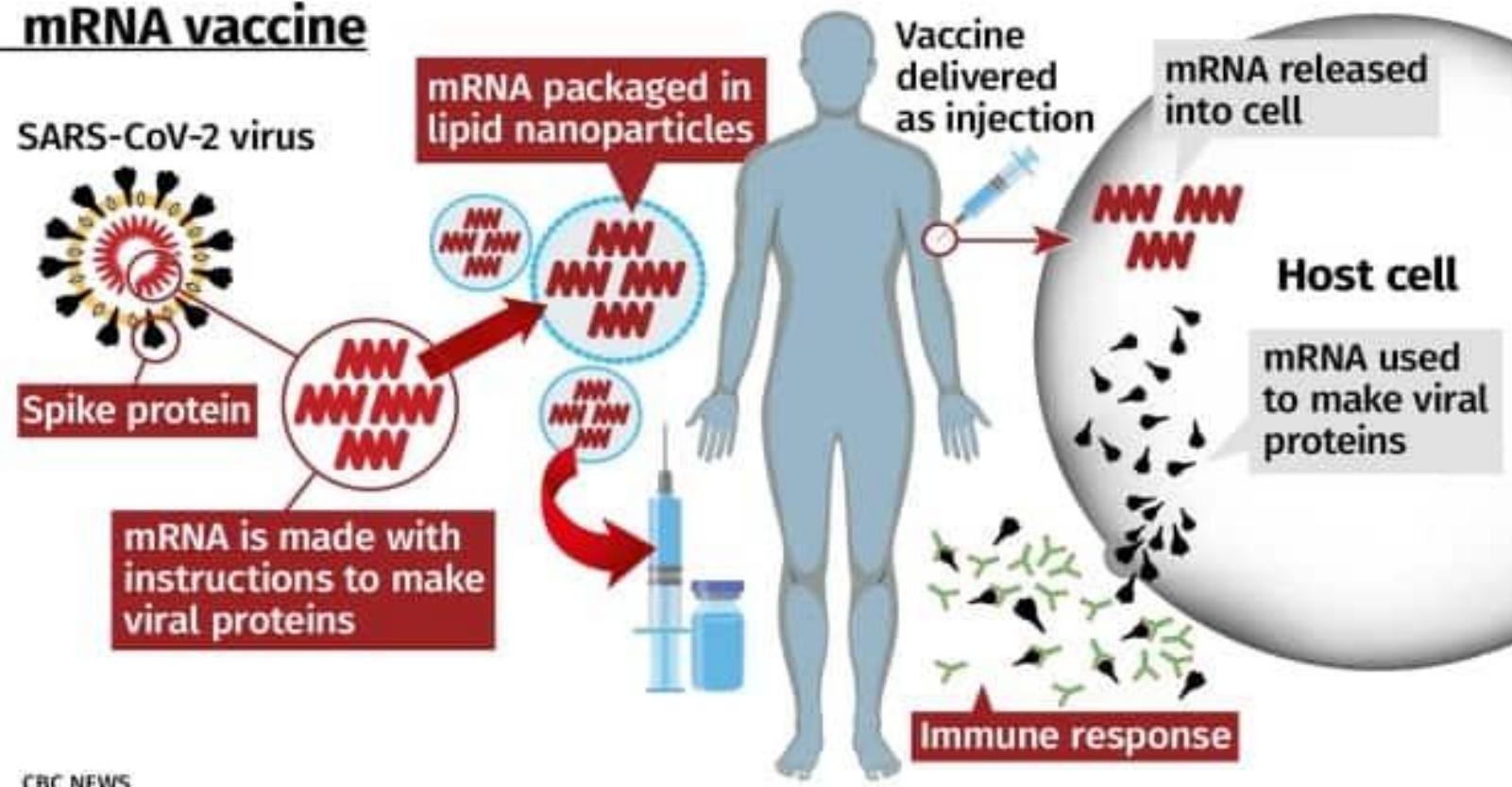
Surgeons in New York City announced Oct. 21 that they had **attached a kidney grown in a genetically altered pig to a brain-dead human patient**—where it worked normally for 54 hours. As the first successful operation of its kind, it could suggest a path forward for accessing organs for transplant patients.

# Related Technology: Covid-19 Vaccine



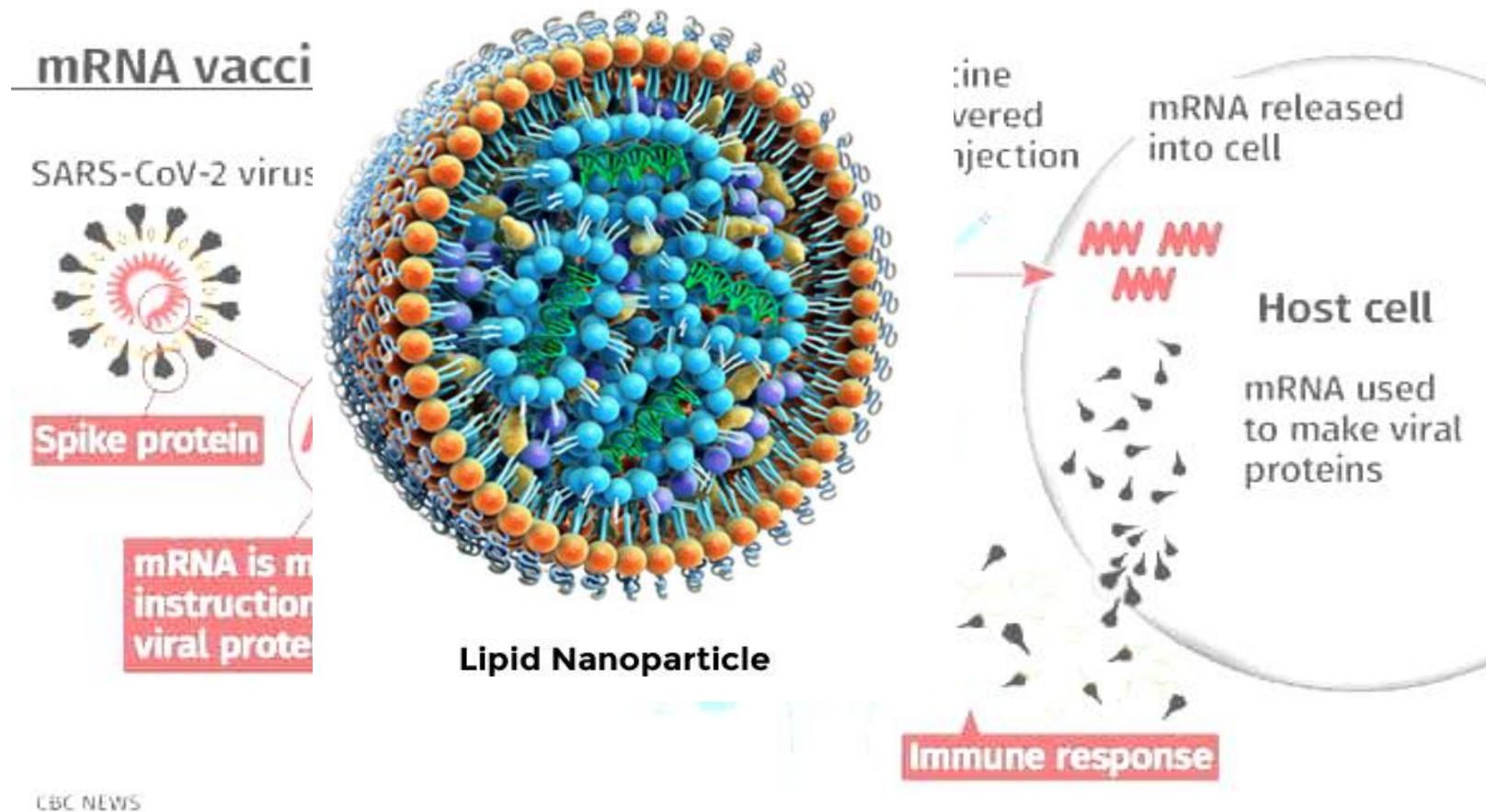
# Related Technology: Covid-19 Vaccine

## mRNA vaccine

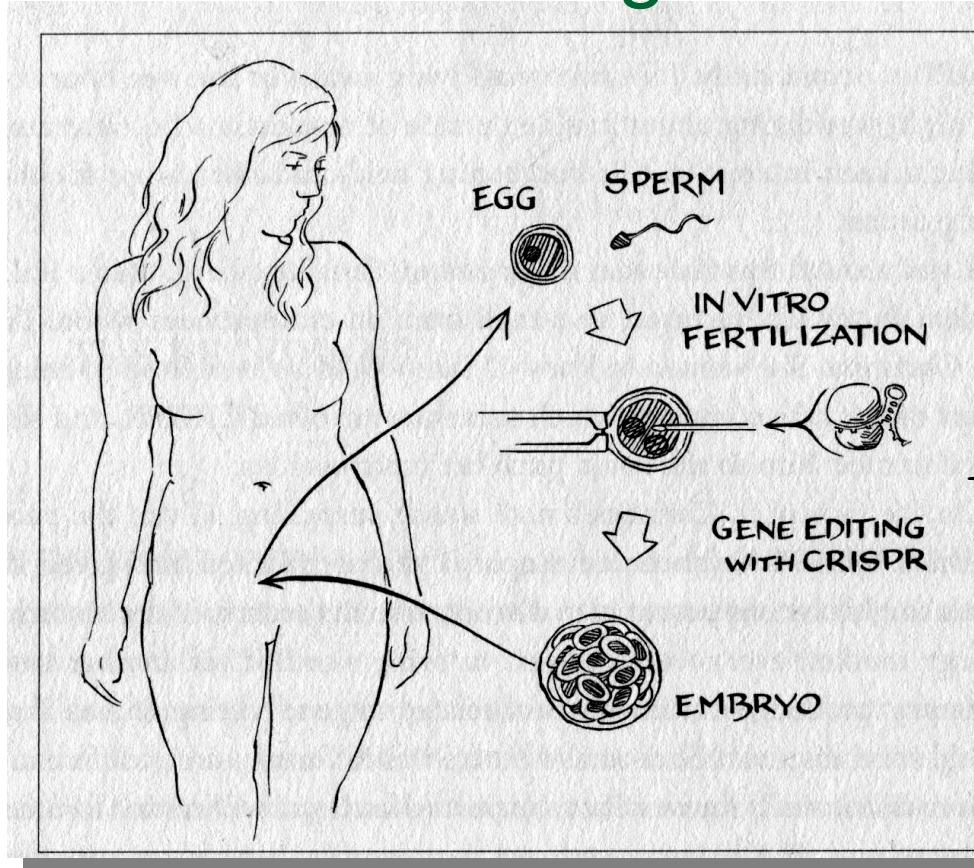


CBC NEWS

# Related Technology: Covid-19 Vaccine



# Human Gene Editing: “Promise and Peril”

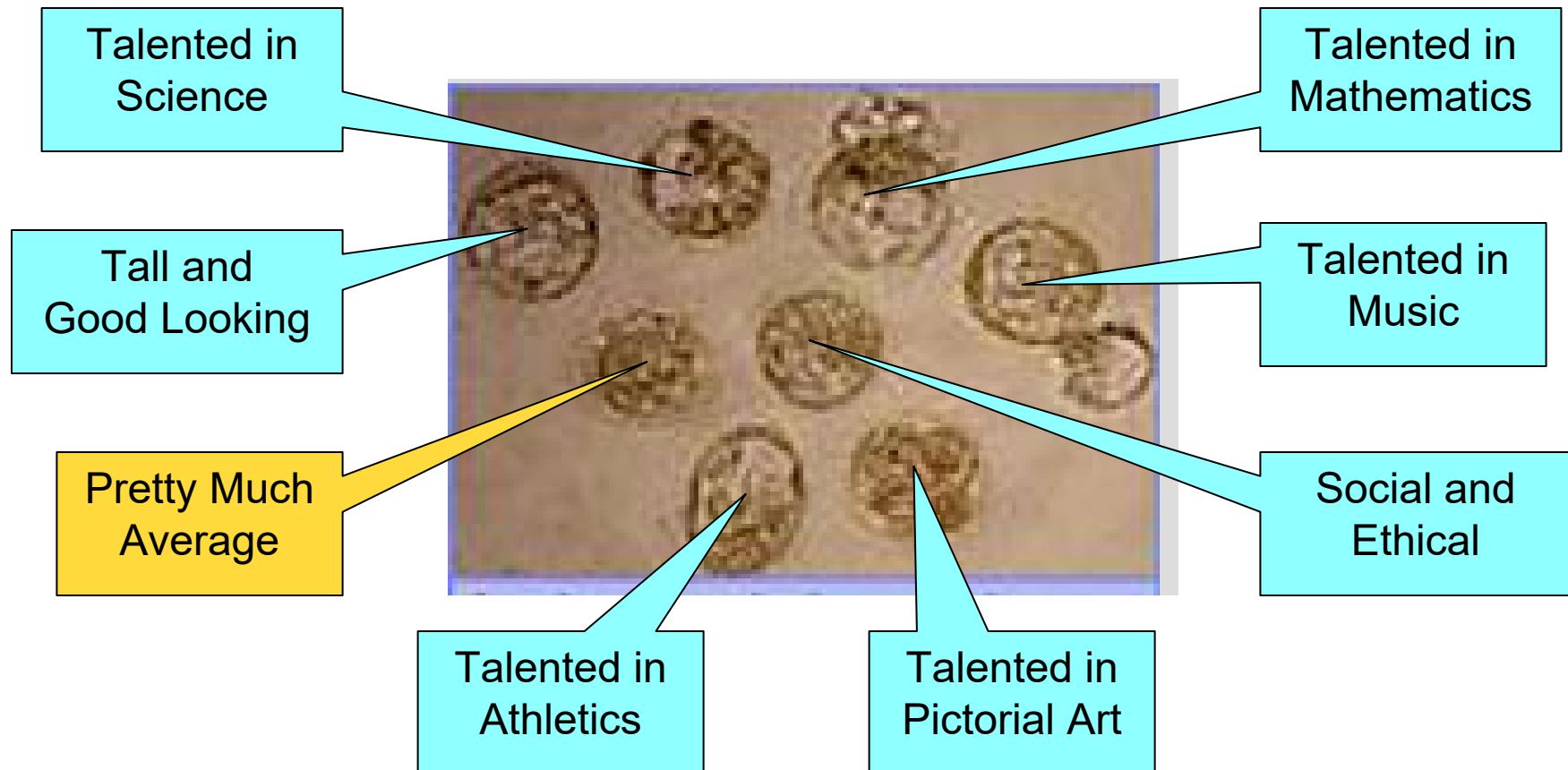


1. Selection
2. Health
3. Improvement

“While applications in the planet’s flora and fauna are exciting, it’s the impact of gene editing on our own species that offers both the greatest promise and the greatest peril for the future of humanity.”

Jennifer Doudna, 2017

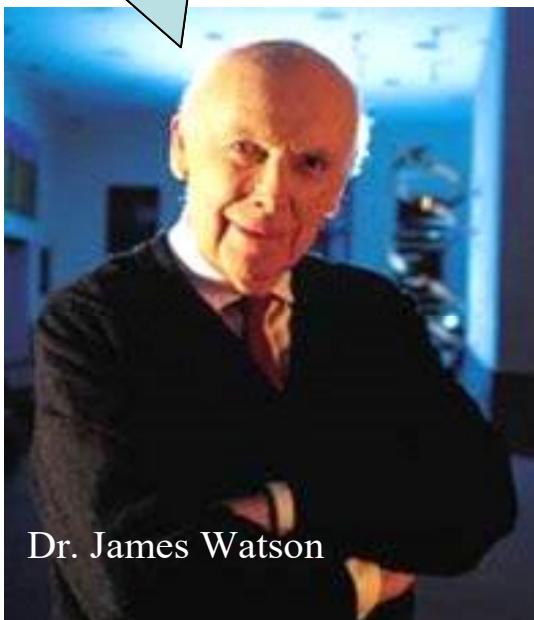
# Potential Selection for Attributes



The Chinese company B.G.I. has said that while people may initially resist the ability to “custom design” their children, if it’s available everybody will want to use it.<sup>1</sup>

# The Pioneers Opine

“People say, ‘Well, these would be designer babies, and I say what’s wrong with designer clothes?’”



Dr. James Watson

ScientificAmerican.com, April 2003

“if we can walk the narrow line between prohibiting CRISPR to the detriment of certain individuals’ health and *overusing* it and subverting our society’s values – we will be able to use this technology in a way that is unequivocally good.”



Dr. Jennifer Doudna

J. Doudna and S. Sternberg, A Crack in Creation, 2017

Jennifer Doudna and Emmanuelle Charpentier are 2020 Nobel Prize awardees.

# Noble Prize Recognition

“In any prize in the world of science, there are many people who contribute along the way and that certainly is true in the case of CRISPR,”



ALEXANDER HENK/PICTURE ALLIANCE/GETTY IMAGES

Jennifer Doudna and Emmanuelle Charpentier are 2020 Nobel Prize awardees.

# Lab Human Editing: Oregon, August 2017

## Alteration of human embryos marks a first

Scientists remove a malevolent mutation from DNA through a gene-editing process.

By MELISSA HEALY

Using a powerful gene-editing technique, scientists have rid human embryos of a mutation responsible for an inherited form of heart disease that's often deadly to healthy young athletes and adults in their prime.

The experiment marks the first time that scientists have altered the human genome to erase a disease-causing mutation not only from the DNA of the primary subject but from the genes of

his or her progeny as well.

The controversial procedure, known as "germ-line editing," was conducted at Oregon Health and Science University in Portland using human embryos expressly created for the purpose. It was reported Wednesday in the journal *Nature*.

Scientists' ultimate goal is to fix gene mutations that lead to debilitating or fatal diseases, and to prevent the propagation of those mutations to future generations.

Study leader Shoukhrat Mitalipov, a biologist at OHSU, said the new findings might correct genetic variants that can cause breast and ovarian cancer, cystic fibrosis and muscular dystrophy in those who inherit

[See **Embryos**, A5]

In 2017 the Oregon Health and Science University edited human embryos specially created for a study and not intended to survive it.

# Real Human Editing: China, January 2018

## He Jiankui: China condemns 'baby gene editing' scientist

© 21 January 2019

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### Top Stories

#### Clashes as Venezuela aid row intensifies

At least one person dies and others are injured as civilians confront troops at the border with Brazil.

© 39 minutes ago

#### Smollett suspended from Empire TV show

© 34 minutes ago

#### What might 'Mueller report' look like?

© 211 February 2019

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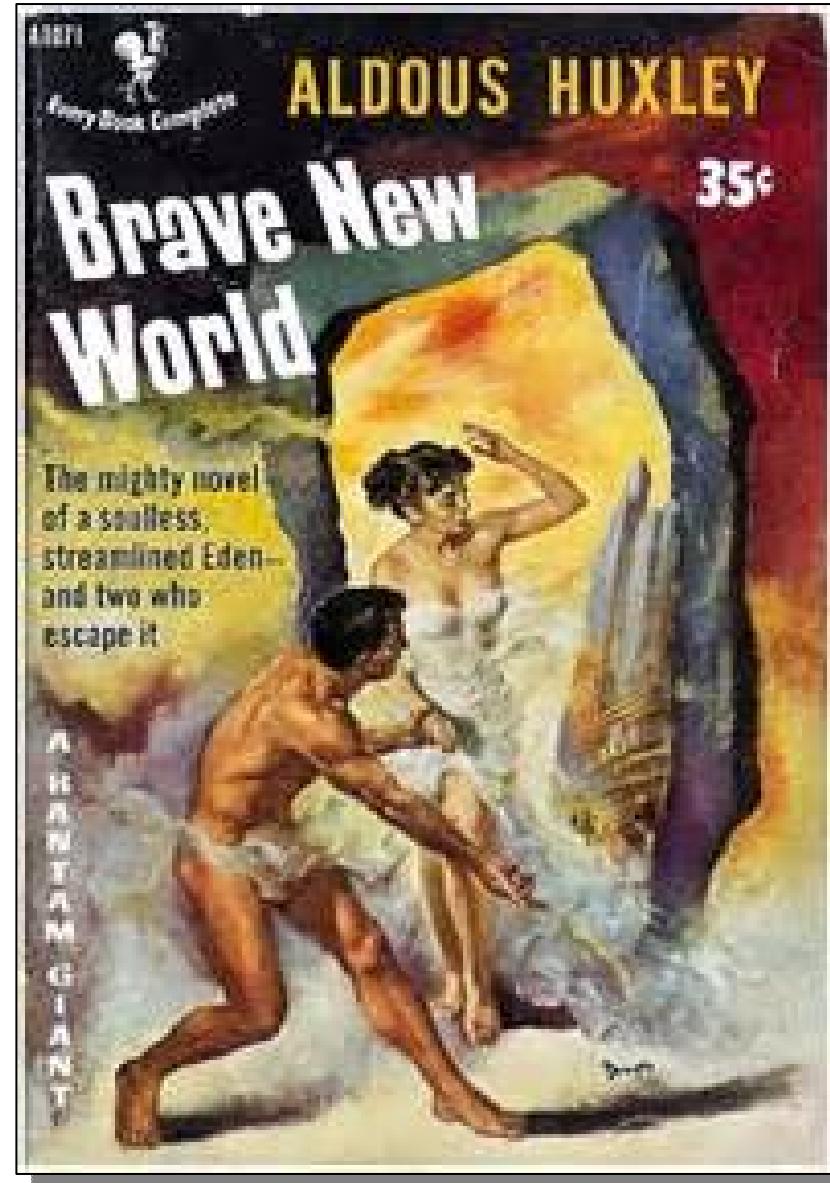
This Chinese scientist reported that he had used CRISPR to edit the genes of two twins to increase HIV resistance; his action caused an ethical storm.

# Prescient Warning

Published in 1932, Aldous Huxley's novel *Brave New World* describes a society where people are born in test tubes, segmented into levels of ability and achievement, and controlled by propaganda and the drug SOMA.

Advertised as:

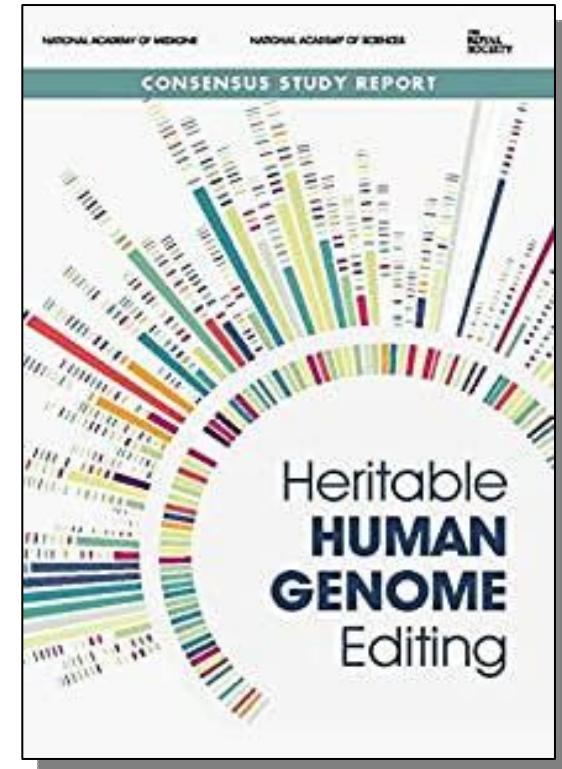
*"The mighty novel of a soulless, streamlined Eden, and two who escape it."*



# Expert Scientific Caution...

The U.S. National Academy of Medicine and National Academy of Sciences, together with the U.K. Royal Society jointly concluded in their 2020 report that:

- CRISPR is currently *not technically safe enough* for heritable genome editing;
- *A path to heritable genome editing is feasible*, but should first be used only in rare cases when no other paths to a healthy child are available;
- *Individual nations* should decide whether or not to use heritable genome editing;
- The decisions should be based on the *views of their citizens*; and
- There should be *national and international governance* of human genome editing activities.



The implicit finding was that genome editing is inevitable, but requires great care.

# ...and Societal Concern

## Disquiet over startup's genetic testing

BY MELODY PETERSEN

The decision of whether to have a child can be hard even under the best of circumstances. For those with a family history of debilitating disease, it's often gut-wrenching. If only there were some way to answer the all-important question: Will my child be healthy?

To those potential parents, a San Francisco startup is offering a solution: a genetic test of their embryos so they can select the one with the lowest risk of disease.

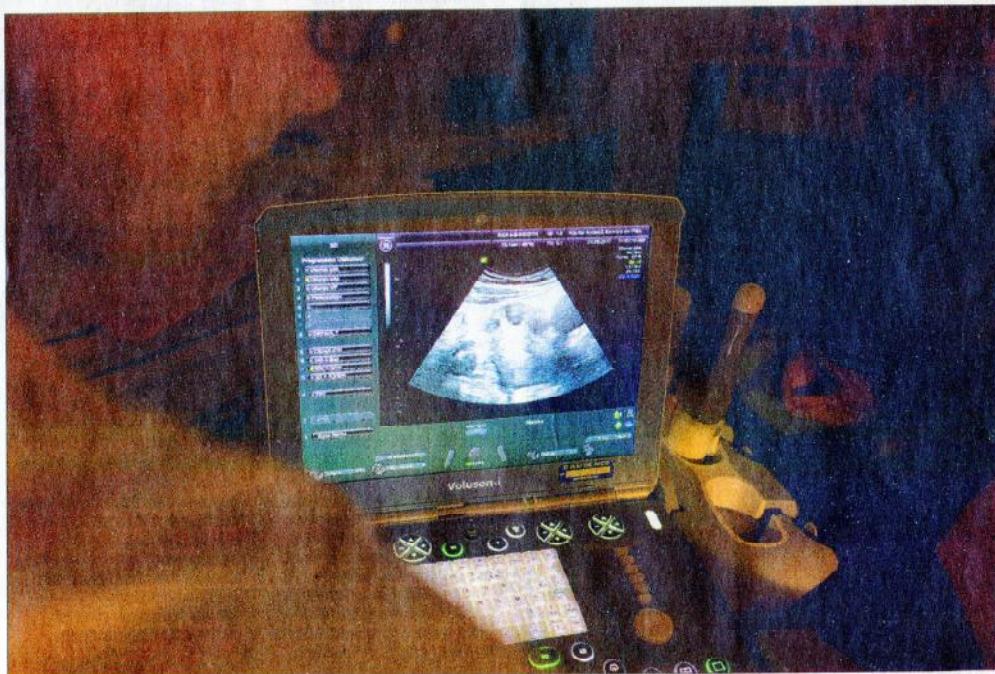
"We help couples have healthy babies," Orchid Inc. says of its tests for schizophrenia, Alzheimer's, cancer and seven other diseases. As much as health information, the 2-year-old company sells peace of mind. "I was apprehensive about having kids due to my family history, but after going through our report I feel in control," reads one testimonial on Orchid's website.

Scientists say it isn't that simple.

Peter Kraft, a Harvard professor of epidemiology, helped to develop the so-called polygenic risk scores that Orchid says are the backbone of its tests. He said the way Orchid uses them concerns him, raising the possibility that, for instance, parents could select an embryo said to be at a re-

Orchid Inc. says it can help parents select embryos with the lowest likelihood of developing cancer and other diseases.

But there are scientific and ethical concerns.



BSIP / Universal Images Group

**IF YOU PICK** an embryo that's at low risk for breast cancer, you may actually be increasing your risk for other traits," said Harvard professor Peter Kraft. Above, an ultrasound of an embryo transfer.

op breast cancer, diabetes or other conditions between 70% and 90% of the time.

Tellier pointed out that Orchid has not yet published any studies.

On its website, Orchid calls its test "the most advanced genetic risk assessment available." Yet it also has a disclaimer in its terms of service requiring users to "waive any and all claims against Orchid for any amendment or modification" to its test report.

"Your results are based on currently available information in the medical literature and scientific databases ... that may be subject to change," the disclaimer reads. "This may result in a change in your risk assessment."

To use the companies' embryo tests, couples must choose to undergo IVF, an expensive and painful process aimed at helping those who have trouble conceiving. In the Mendelsohn interview, Siddiqui suggested that even fertile couples might want to consider using IVF in order to "mitigate disease risk with our embryo report."

An IVF procedure that might result in the creation of five embryos involves weeks of hormone shots and then medical procedures to collect eggs and later to implant the embryos. That cycle can cost \$15,000 before adding the costs of the ge-

# Ethical Issues of Human DNA Engineering

- General
  - Not natural, playing God
  - Inadequate control & regulation
- Germ Line (inheritable individual changes)
  - Abandoning evolution
  - Unforeseen consequences
- Gene Drive (inheritable population changes)
  - Unforeseen ecological effects
  - Potential use as bio-weaponry
- Selection, Health and Improvement
  - Culturing and killing of embryos (violating anti-abortion laws)
  - Inaccurate editing (unforeseen individual consequences)
  - Eugenics renewal (discredited selective human breeding)
  - **Economic and social polarization**
  - **Marginalization and discrimination**

# Ethical Issues of Human DNA Engineering

- General
  - Not natural

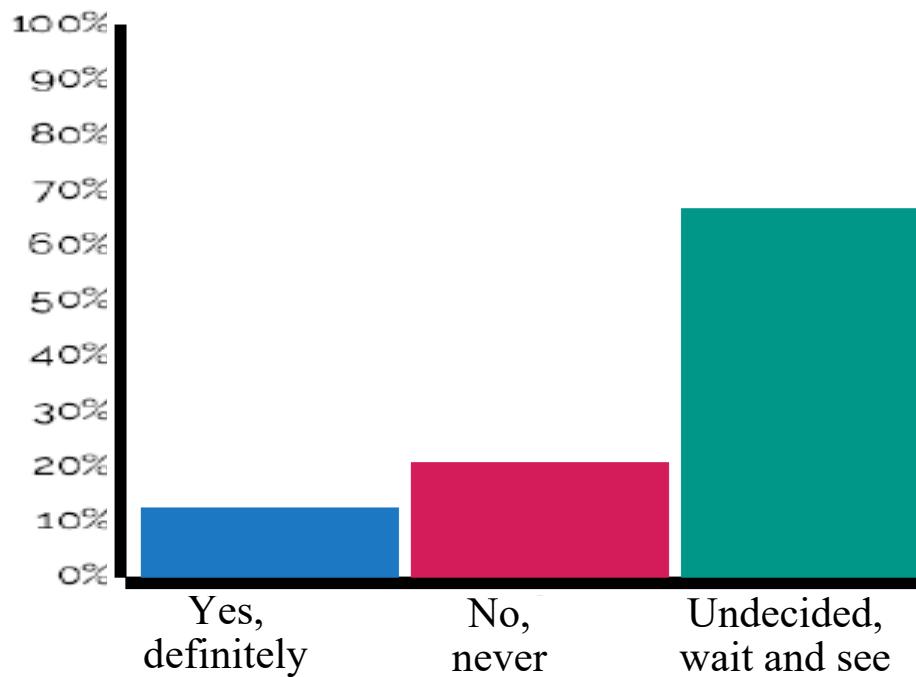
“Our discomfort around designer babies has always had to do with the fact that it makes the playing field less level – taking existing inequities and turning them into something inborn. If ... we don’t address these disparities, we risk creating a society where some groups, because of culture or geography or poverty, bear a greater burden of genetic disease.”

Laura Hercher  
MIT Technology Review  
October 22, 2018

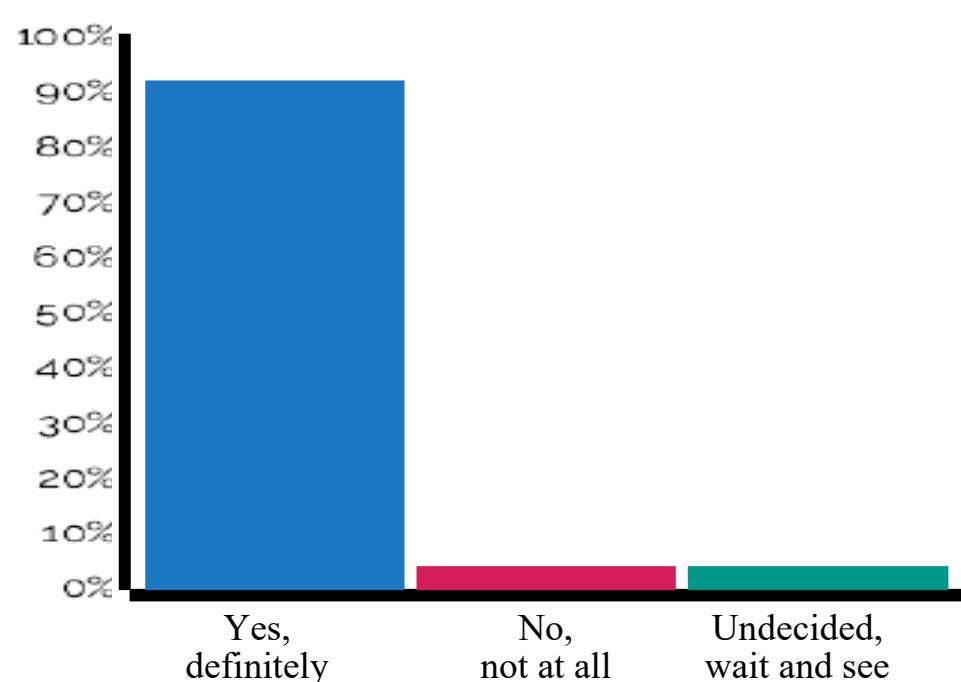
- Renewal of “eugenics” (discredited selective human breeding)
- **Economic and social polarization**
- **Marginalization and discrimination**

# Engr 183EW: Online Poll on Gene Editing

Would you choose your children's characteristics if you could?



Do you see value in human gene editing and replacement?



Fall 2020 only 10% of students said they would definitely chose their children's features, and 90% said they definitely see value in human gene editing. Both of these results are encouraging, but could be changeable.

# Online Poll: Where do You Stand?

- Log on to UCLA\_WIFI
- Go to <https://onlinepoll.ucla.edu>
- Search for [Engr 183EW – Gene Editing](#)
- Password: 1234
- Answer the 2 multiple choice questions
- Hit “SUBMIT”