

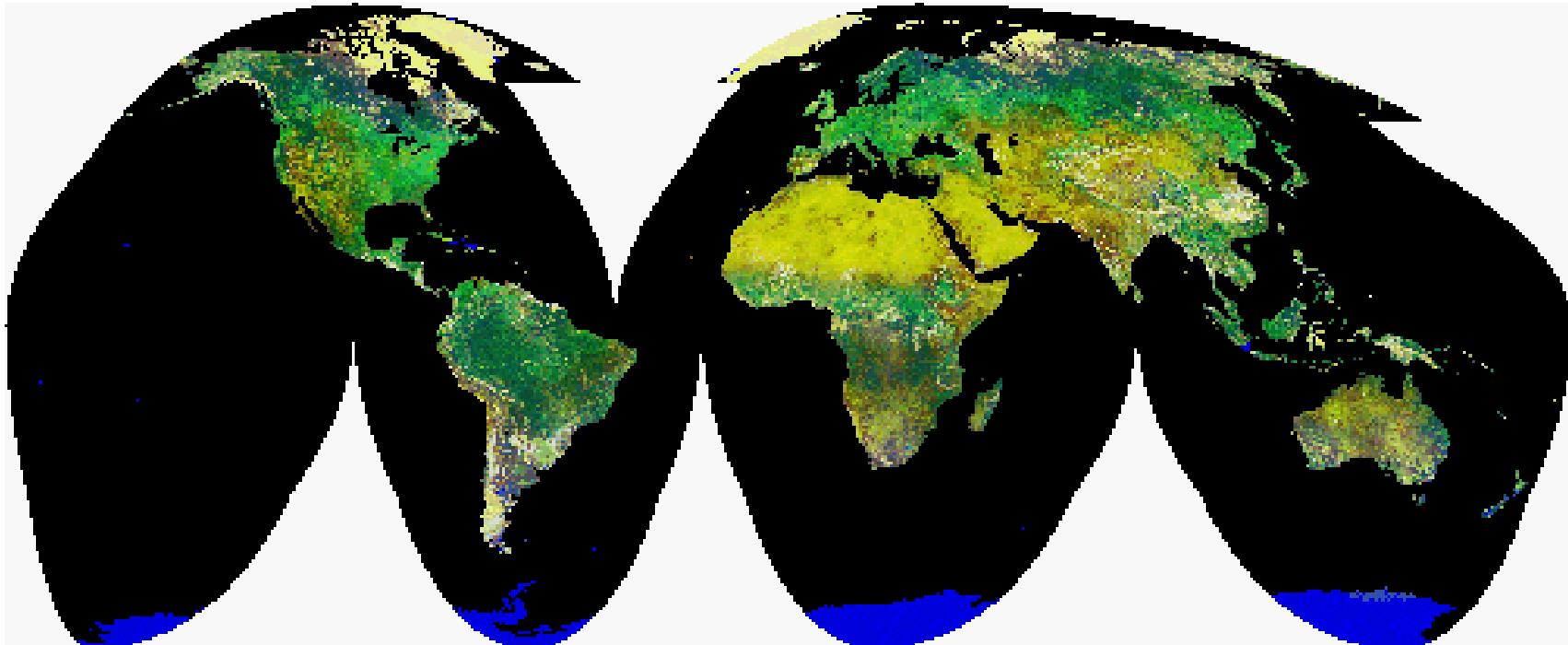
Engineering, Ethics and Society: Bioengineering Ethics

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

Lecture Contents

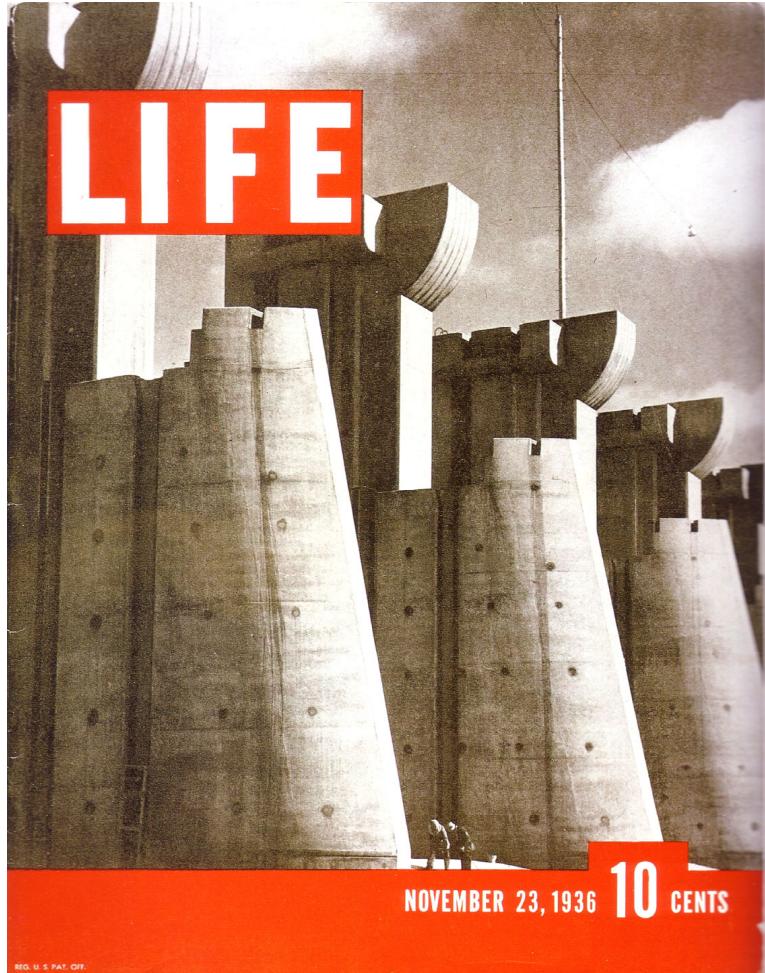
- DNA Bioengineering
 - History and objectives
 - Recombinant DNA technology
- Case I: GMO Applications
 - Objectives
 - Plants and Animals
 - Ethical Considerations
- Case 2: Hybrid Systems
 - Objectives
 - Materials and Mechanisms
 - Ethical Considerations
- Case 3: Embryonic Bioengineering
 - Objectives
 - Embryonic Cell Repair
 - CRISPR Gene Editing
 - 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.

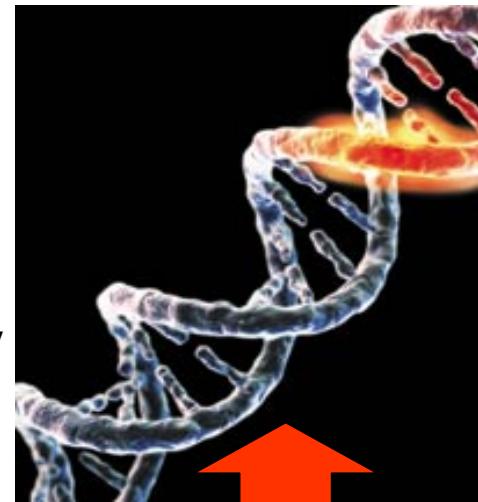
Our Focus: BioEngineering



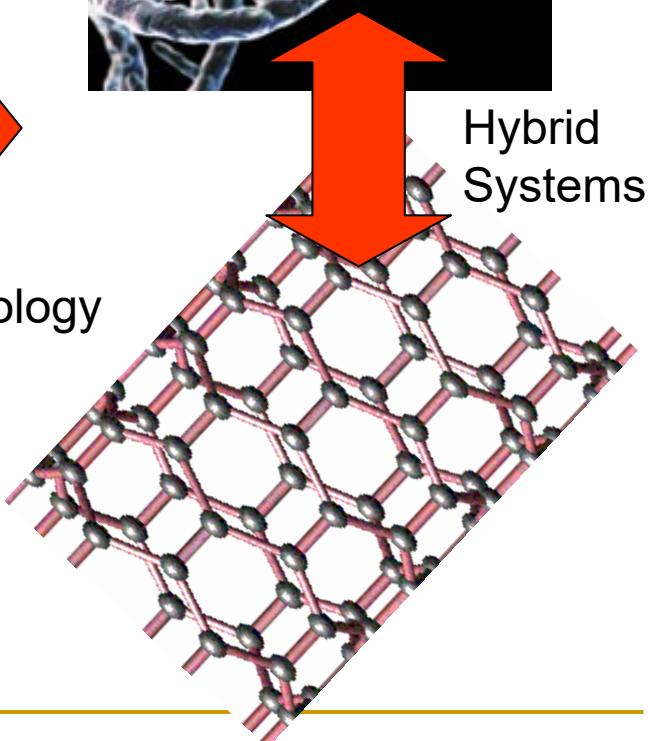
DNA-Based
Biotechnology

$\times 10^{-12}$

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

- Early Technology and Science
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 - 1870: Gregor Mendel's genetic experiments with flowers
 - 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

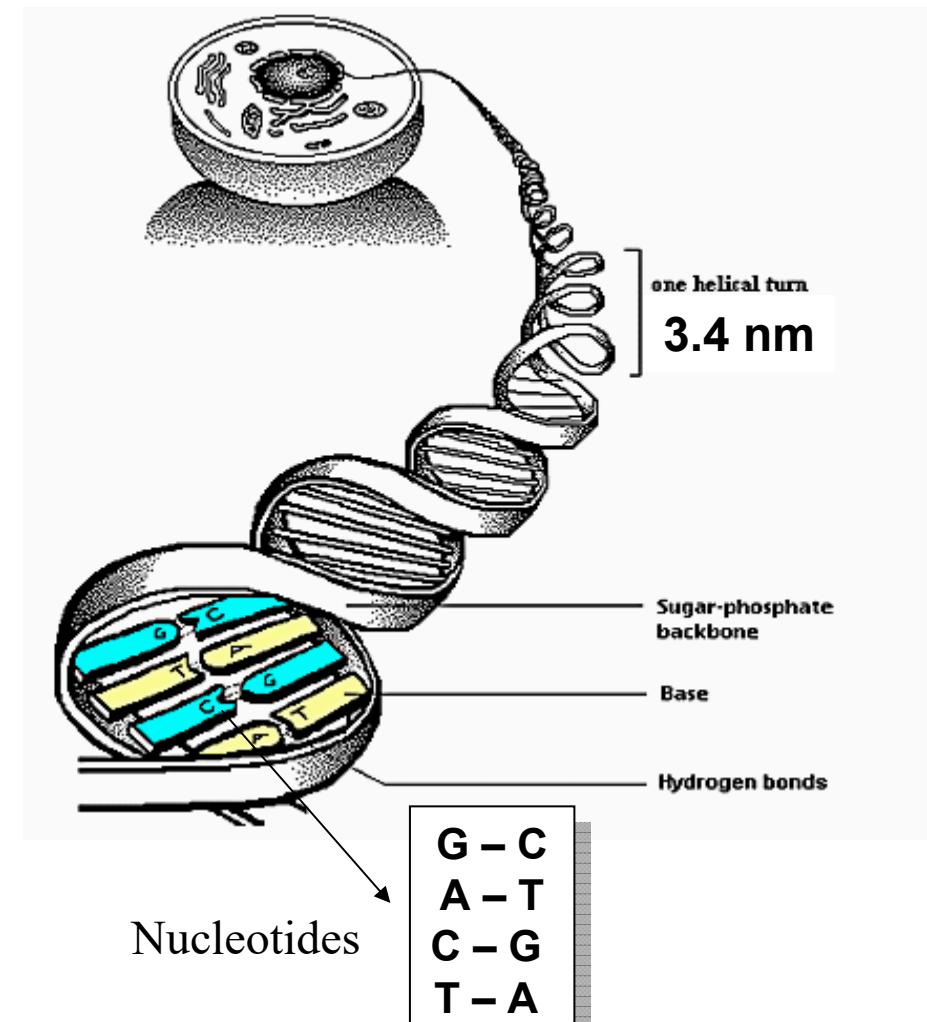
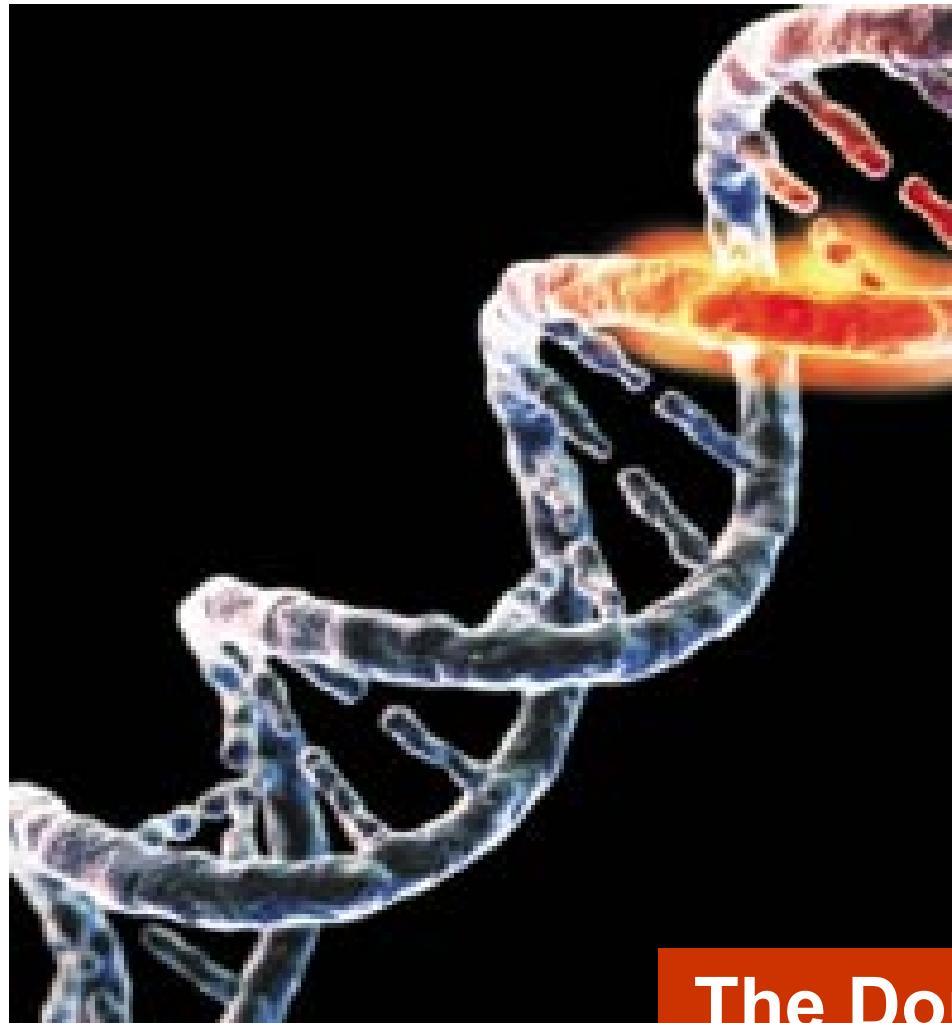
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"Back in 1953, all we wanted to do was find out how DNA provided the information and what the cellular machinery was for making proteins."

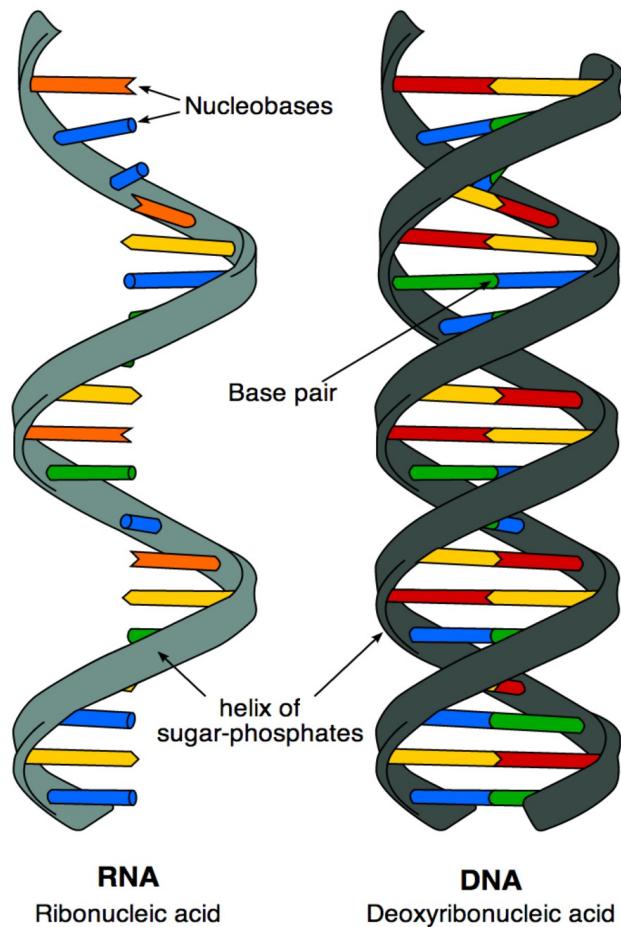
James Watson, 2003

Structure of DNA



The Double Helix

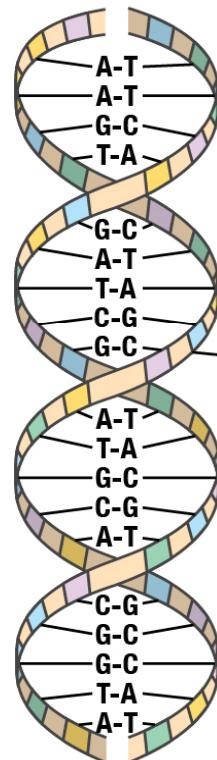
DNA and RNA



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

DNA, RNA and Protein Formation

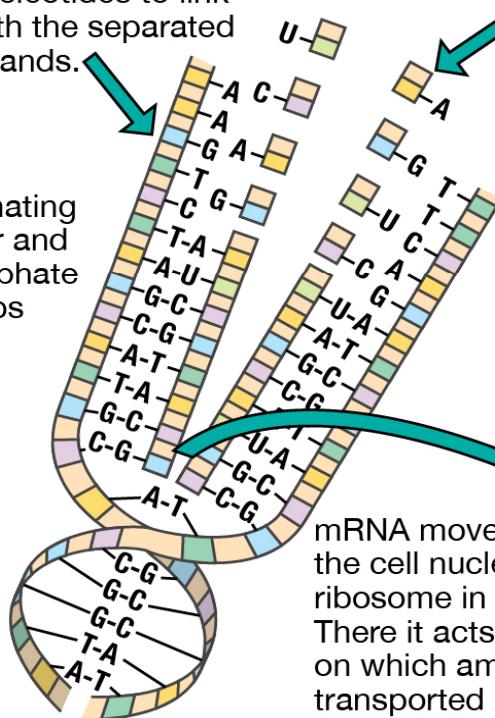
1. Double-stranded DNA in the cell nucleus



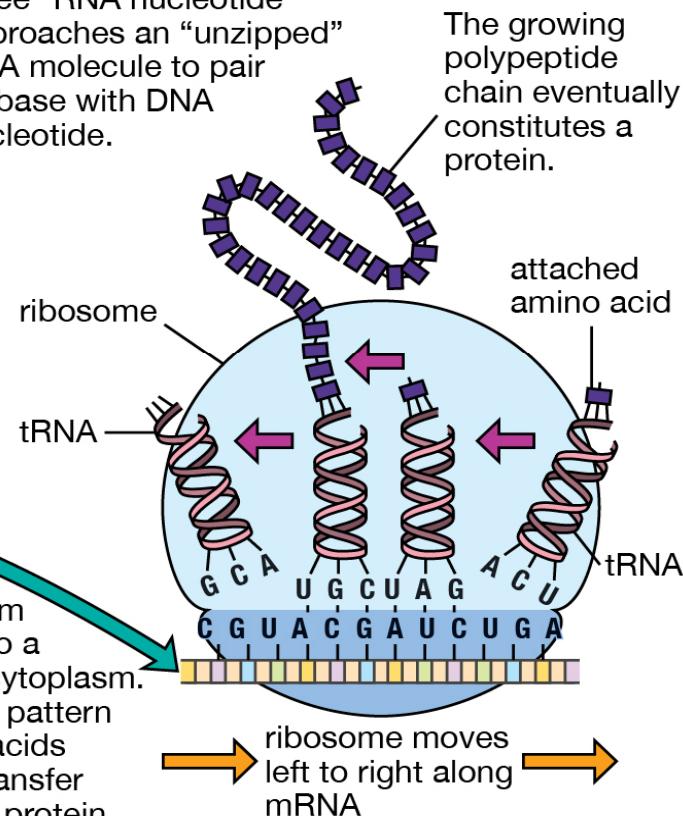
2. Messenger RNA (mRNA) forming on DNA strands

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.

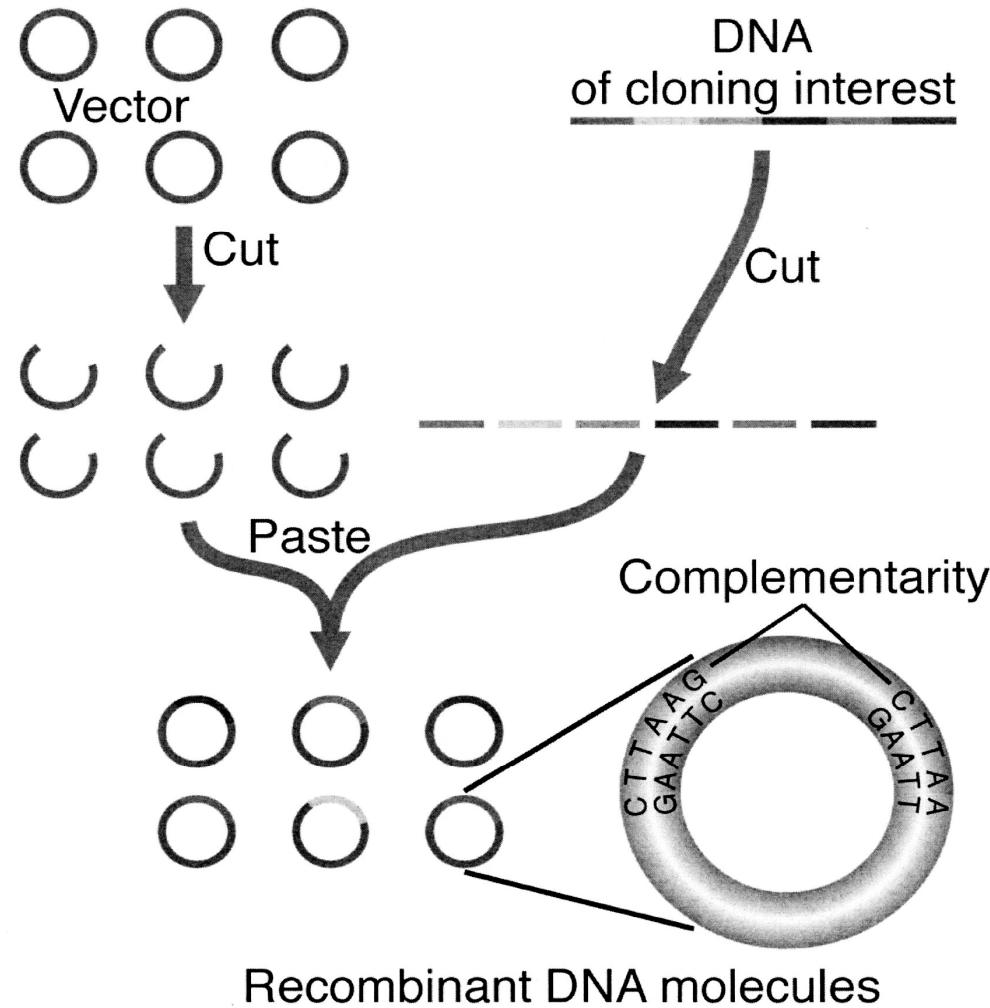
© Encyclopædia Britannica, Inc.

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

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.

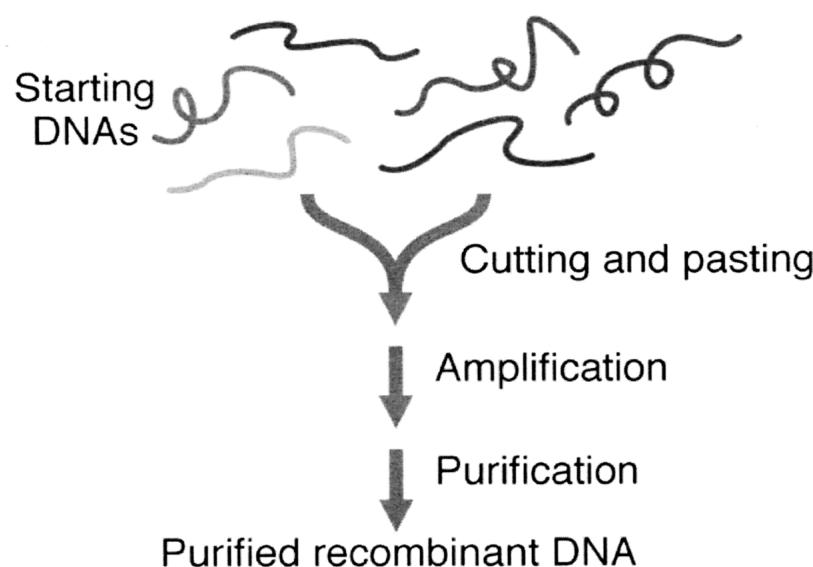
Basic Recombinant Approach



Key Objectives of Recombinant DNA



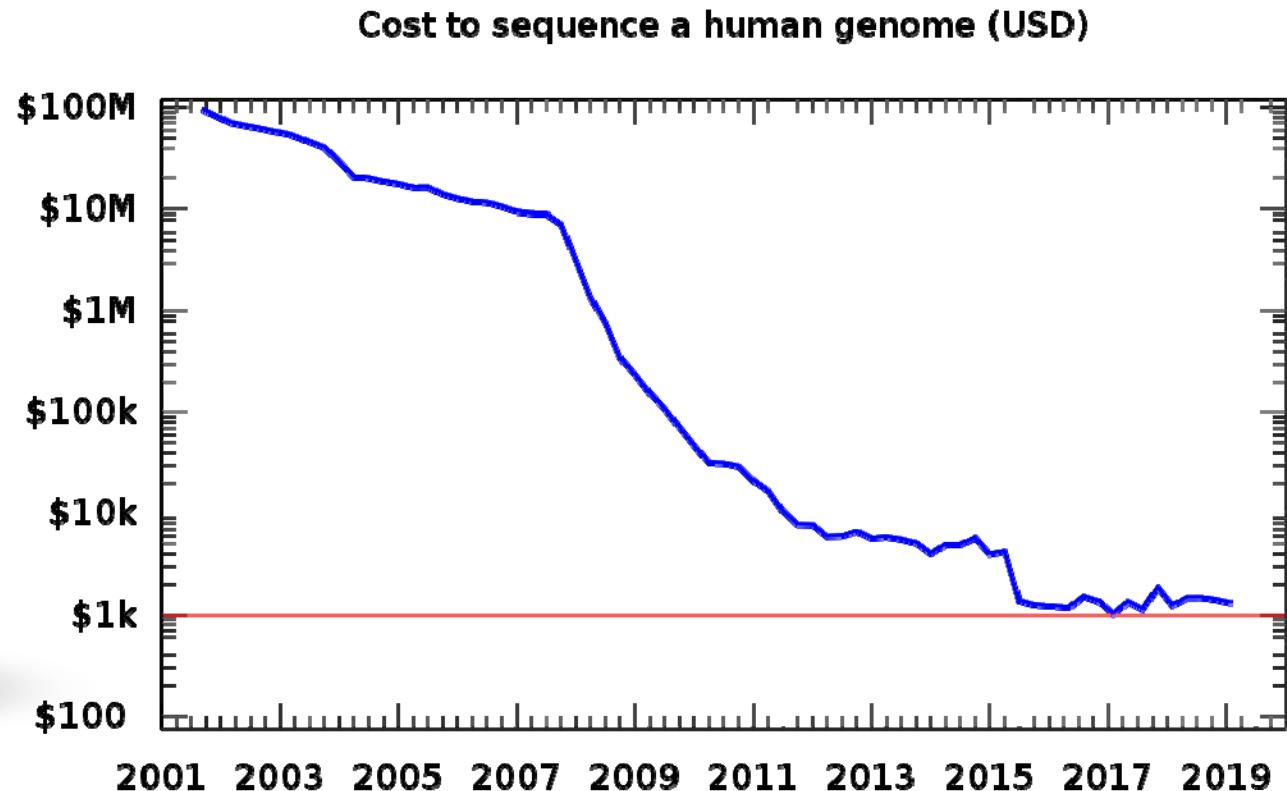
Scientists and engineers locate 30,000 genes within the 3 billion letters of the human genome.



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

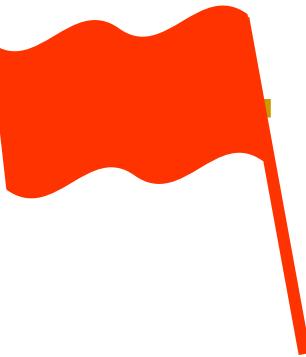
- Interactions among DNA, RNA, Ribosomes and Proteins
 - How do genes control protein formation?
 - What determines whether a given piece of DNA is functioning or is not functioning in the cell?
- Connection between DNA and Brain Function
 - How is information stored, retrieved and used?
 - How do genes 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
 - **Genetic Testing and Prediction**
 - **Genetically Targeted Drugs**
 - **Genetic Selection**
 - **Gene Repair**
 - **Replacement Cells and Organs**
 - **Exact Reproduction**
 - **Improved Characteristics**



Case 1: Genetically Modified Organisms (GMOs)



GMO Technologies :

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

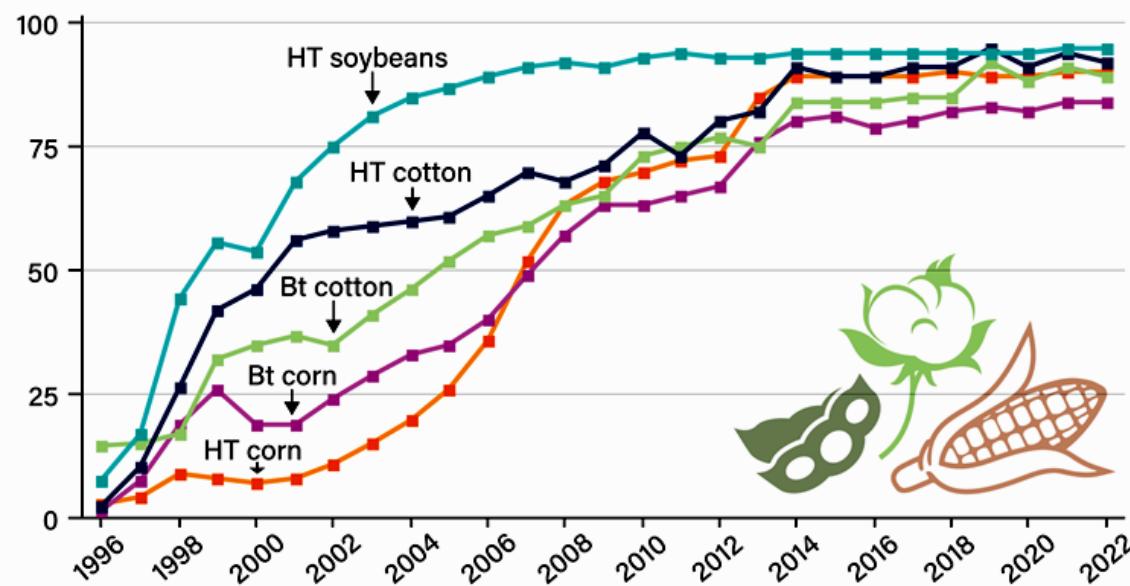
Genetically Modified Crops in the US

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



Economic Research Service
U.S. DEPARTMENT OF AGRICULTURE

Percent of planted acres



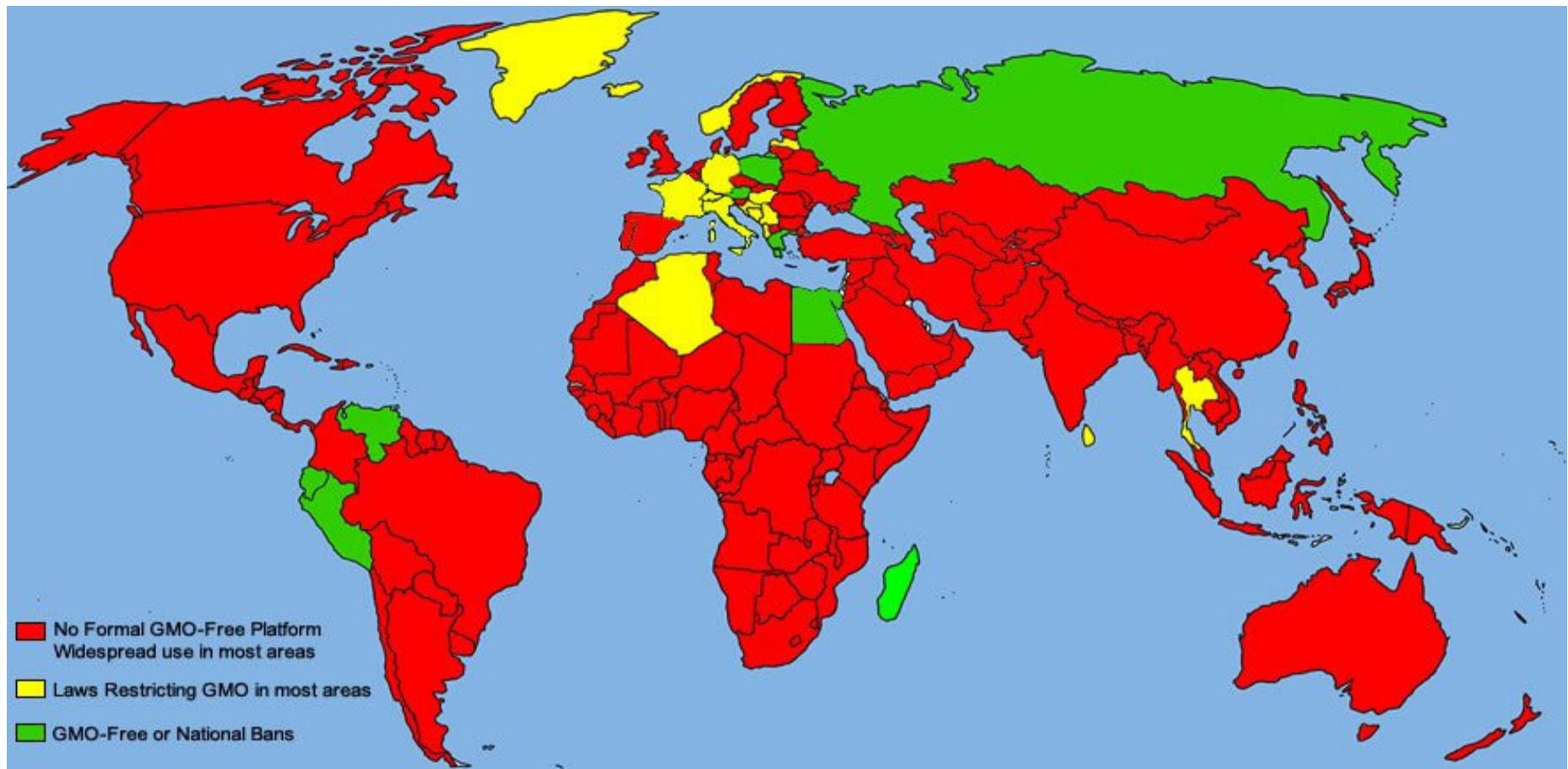
Notes: HT = herbicide-tolerant varieties. Bt = Insect-resistant varieties that contain genes from the soil bacterium *Bacillus thuringiensis*. HT and Bt corn and cotton categories include both the singular trait as well as varieties with overlapping HT and Bt traits, otherwise known as "stacked" traits.

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.



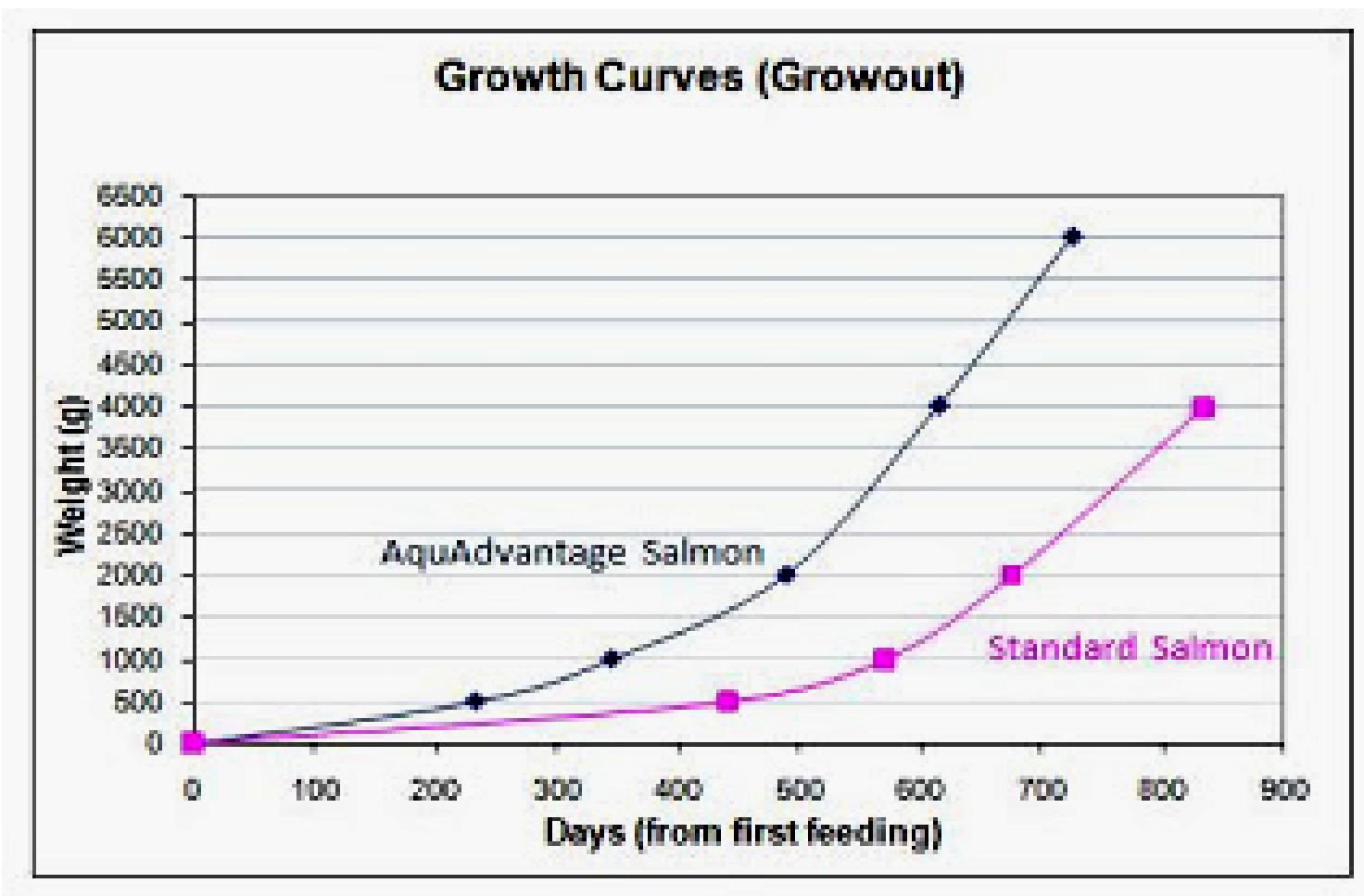
United States Department of Agriculture, Economic Research Service

Genetically Modified Crops Worldwide



https://gmo.geneticliteracyproject.org/wp-content/uploads/2016/02/gmo_world_map_large.jpg

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 viscosity.

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.

More than 90 percent of corn



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 GMOS

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.

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

After the pork recall, we use

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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

CA Political Battleground ~12 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.

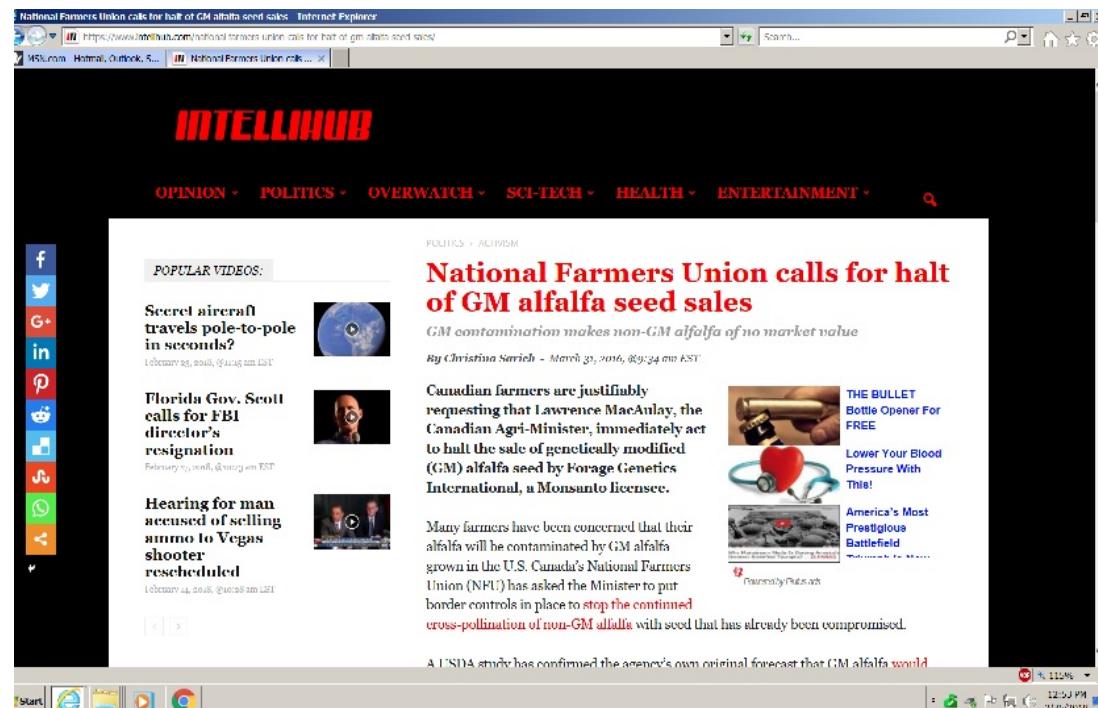
Laws and Regulations Adjust...

- 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.

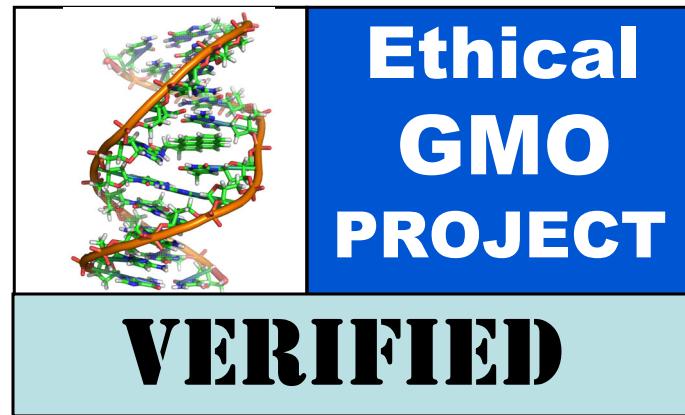


Laws and Markets Adjust

- Vermont recently 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 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.



A Modest Proposal



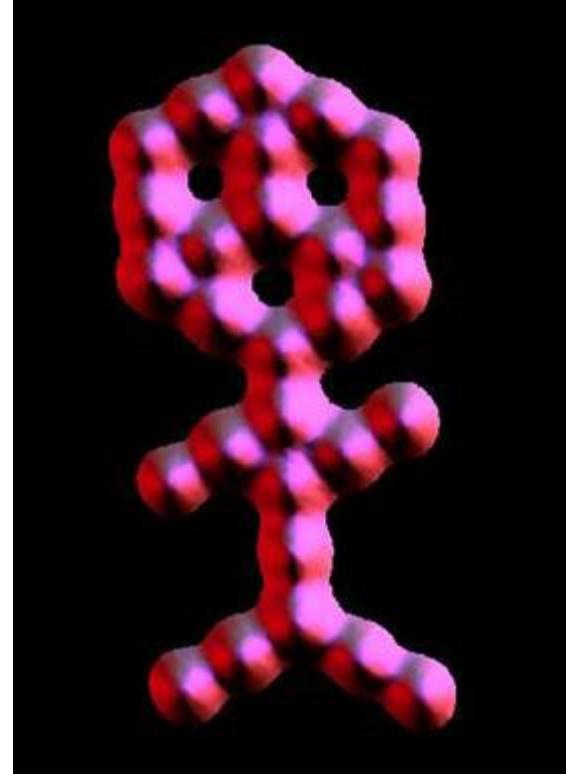
How about a label for the people who support genetic engineering?

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

Case 2: Hybrid Systems - Nano and Bio

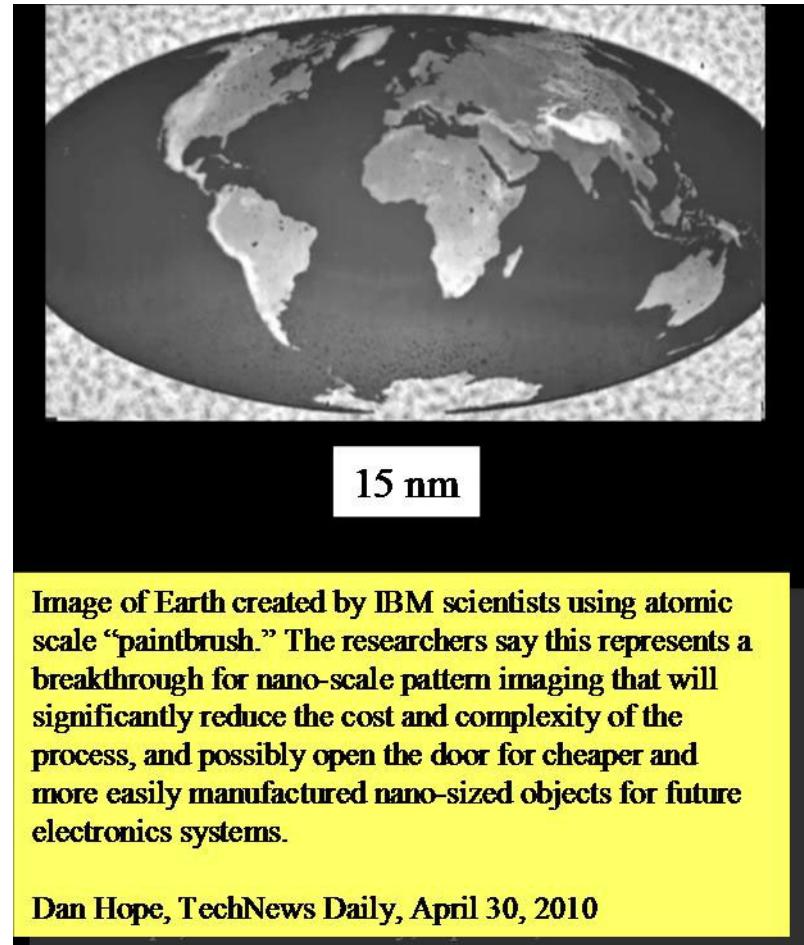
- Nanotechnology Objective
Manipulate the fundamental building blocks of nature to manufacture new classes of micro-products that are clean, strong, light and precise
- Requirements
 - Get atoms into the right place
 - Specify structures in molecular detail without violating physics
 - Have low manufacturing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



IBM Atom Man, c. 2005

Case 2: Hybrid Systems - Nano and Bio

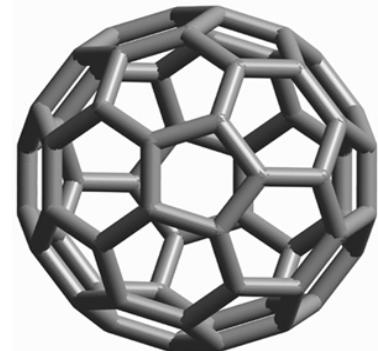
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Nano Materials

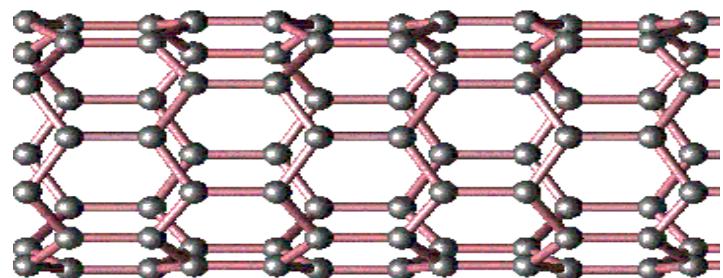
Buckyballs

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



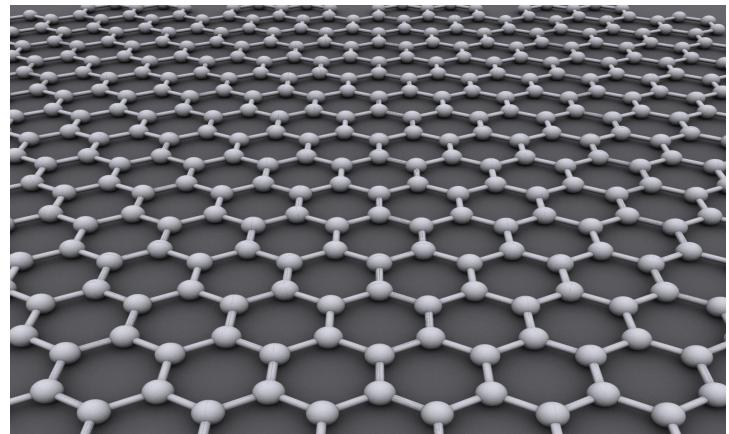
Nanotubes

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



Graphene

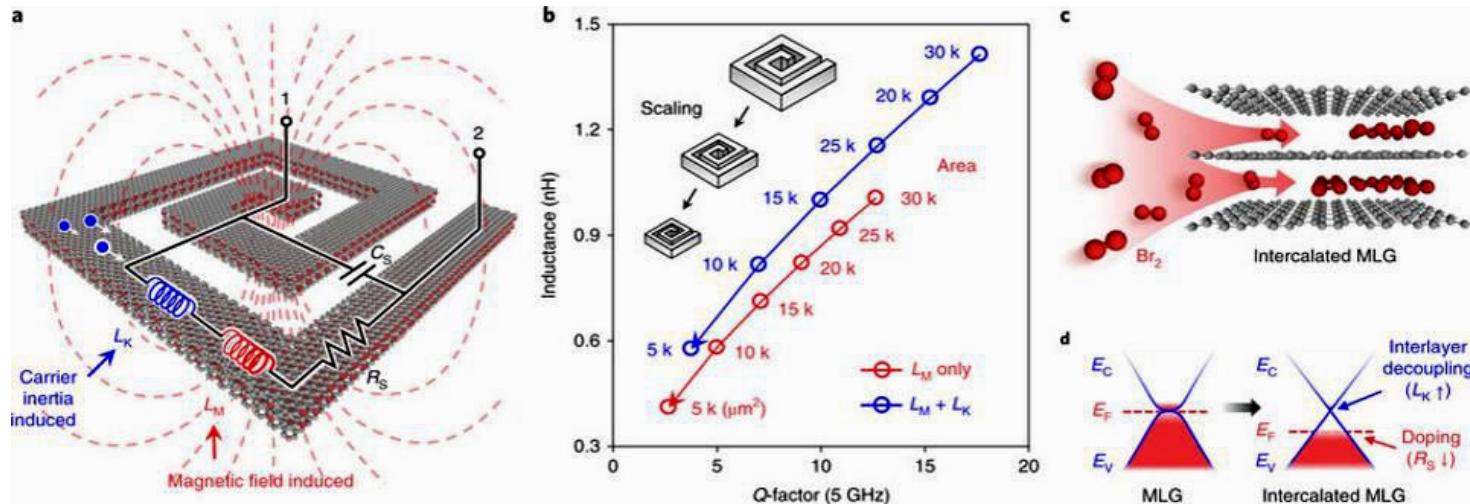
- Carbon atoms spread into 1-atom sheet
- Flexible and strong
- Exceptional electrical and thermal properties, and 100x strength of steel
- For display screens, batteries, lights, etc.



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

Nanomaterials: Example

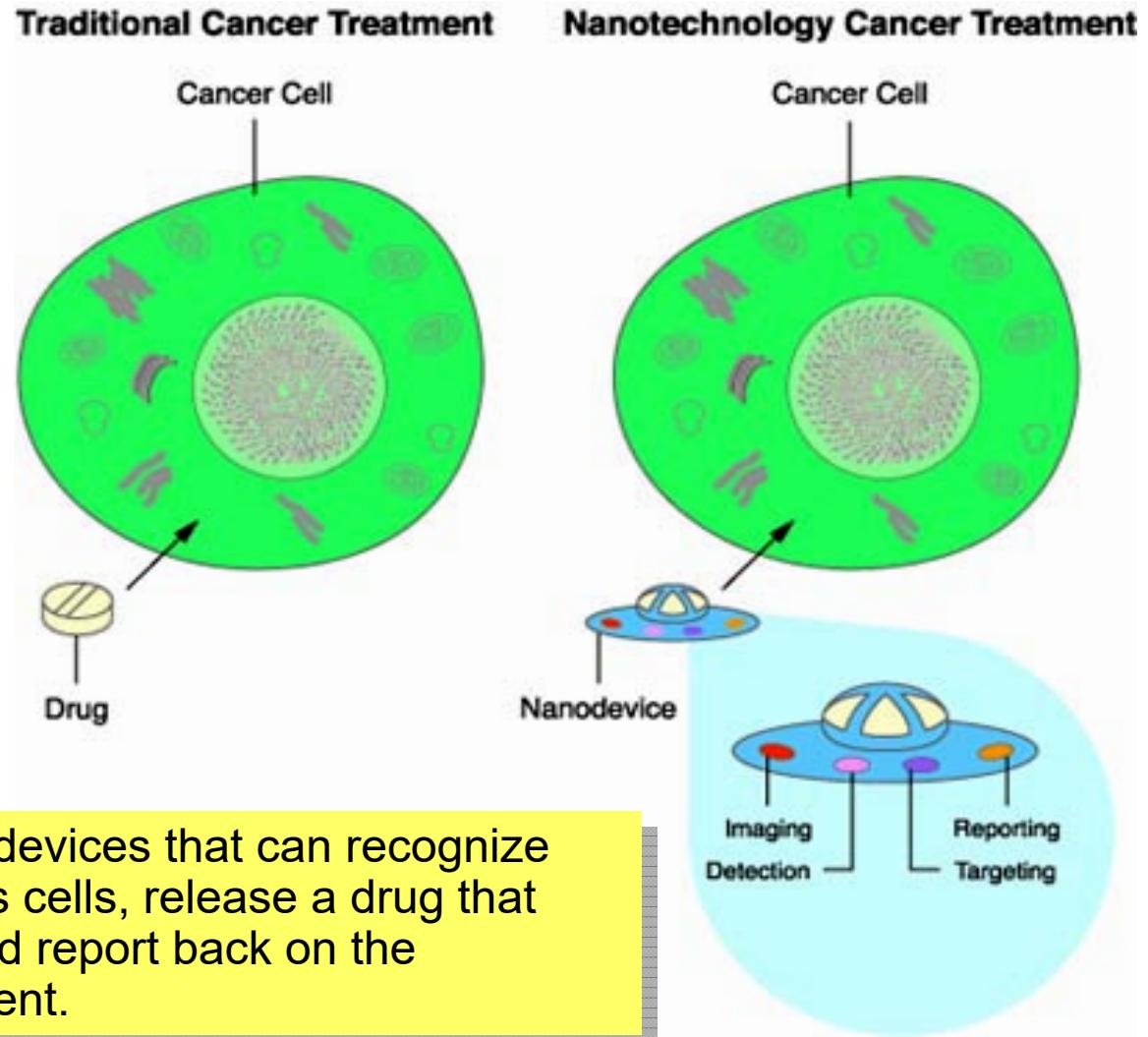
“The Last Barrier To Ultra-Miniaturized Electronics Is Broken, Thanks To A New Type Of Inductor”



“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

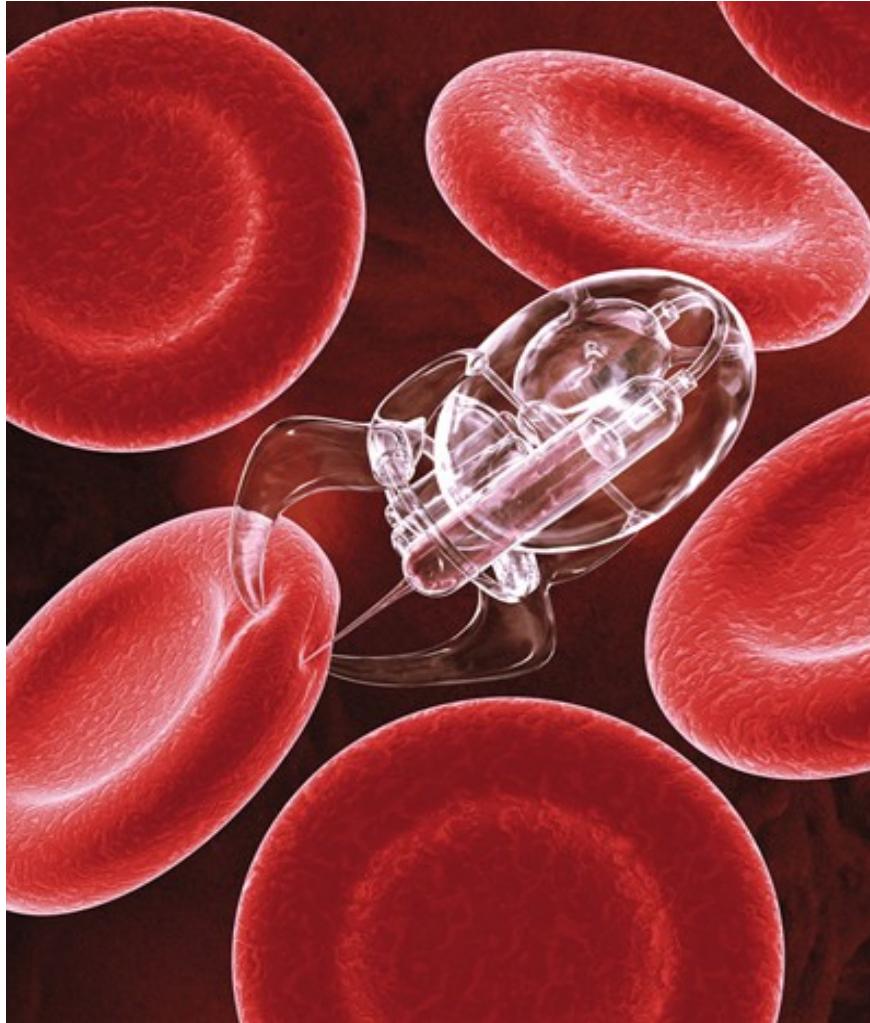


Illustration by Coneyly Jay for Ohio State University

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

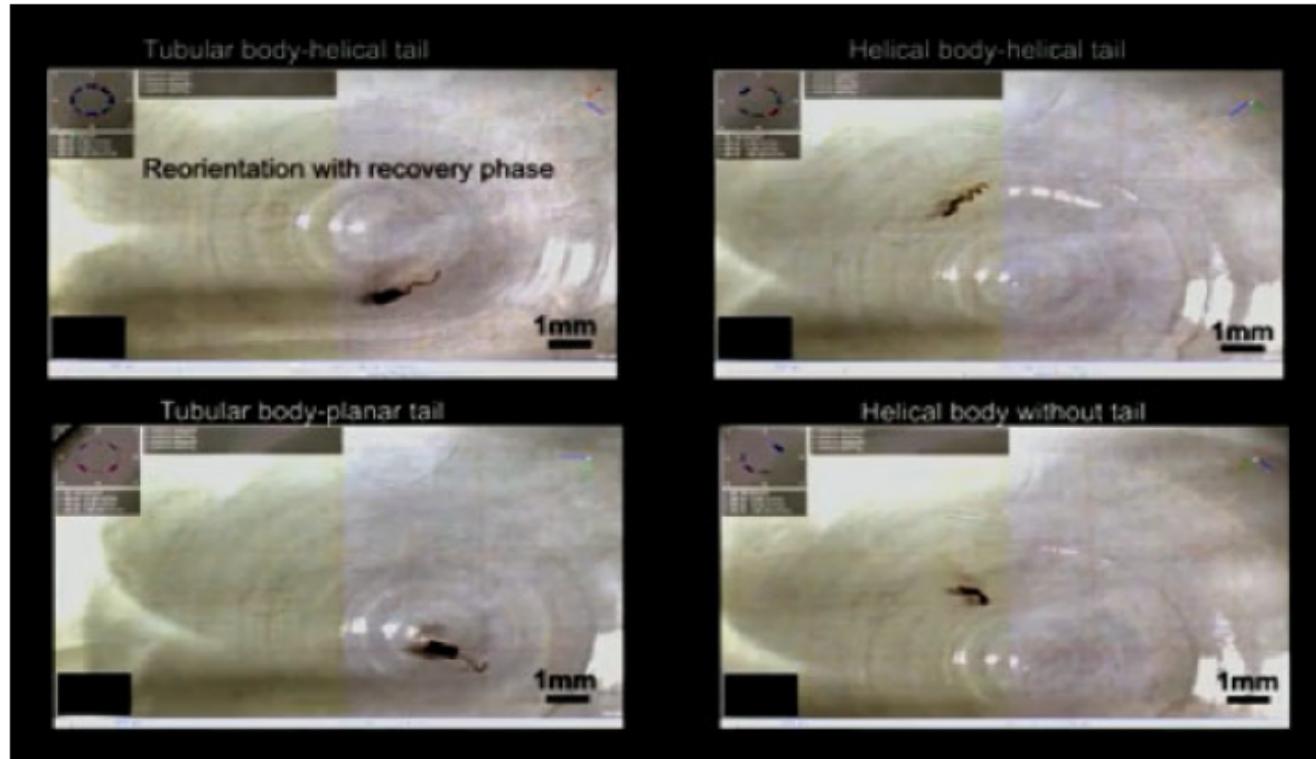
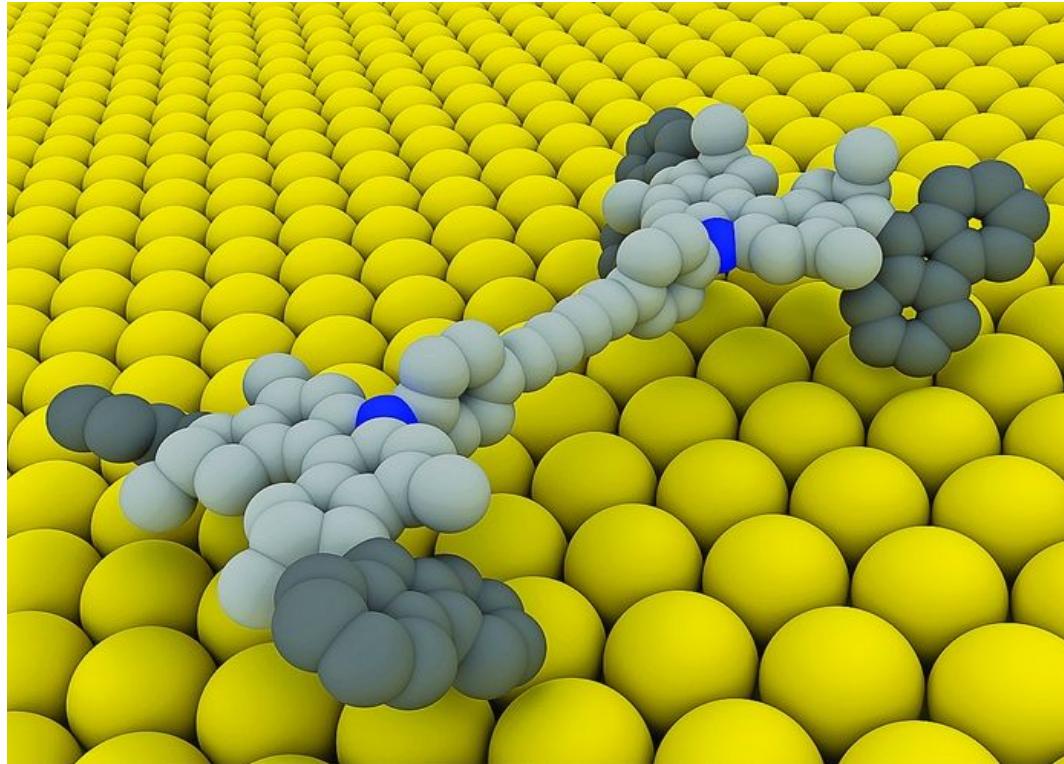


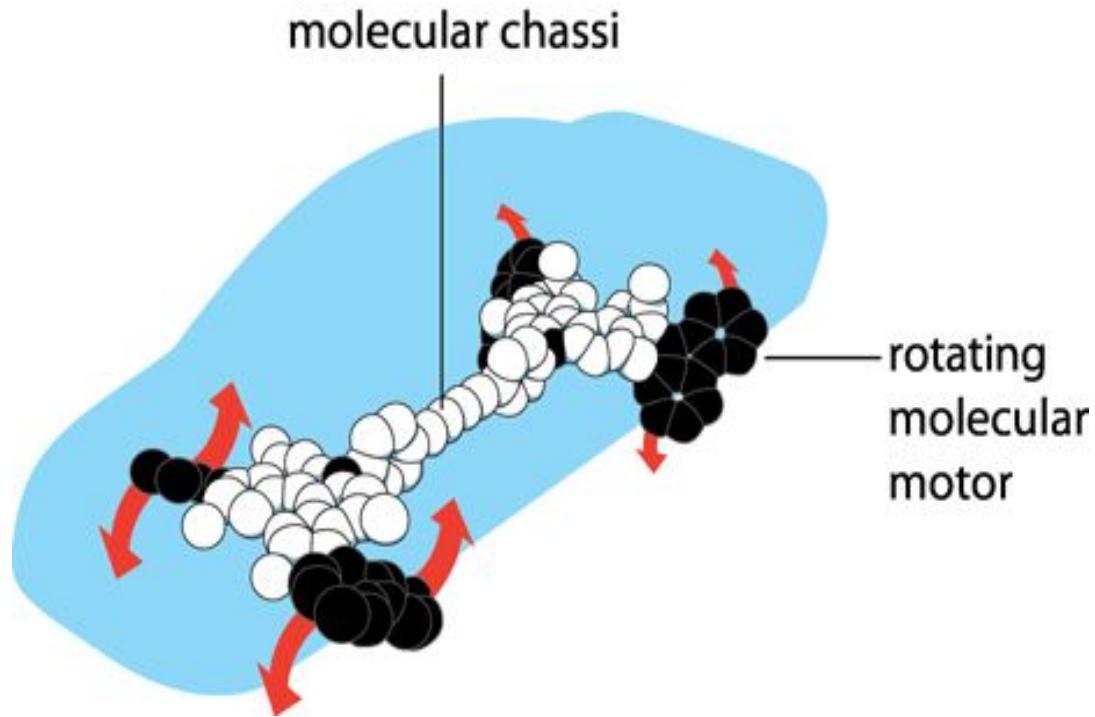
Image Credit: ETH Zurich

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.

Molecular Machines: Today

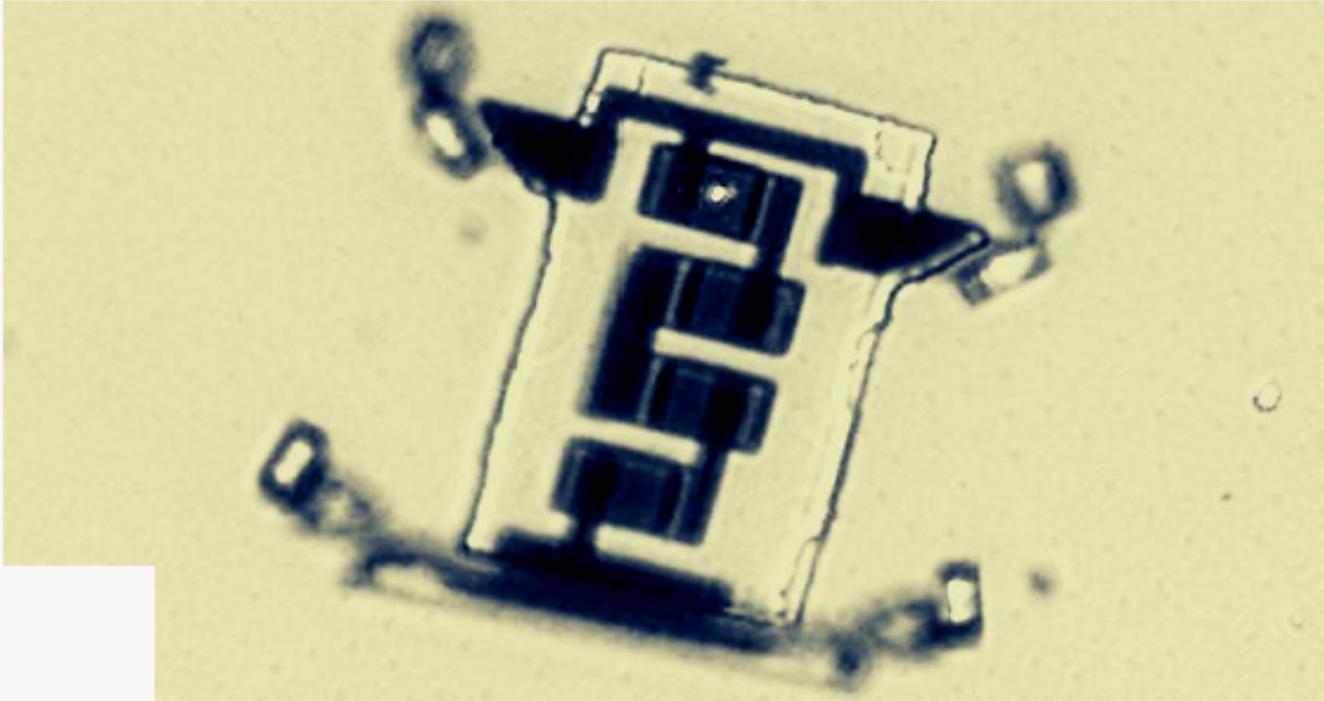


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Micro Robots: Today

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.

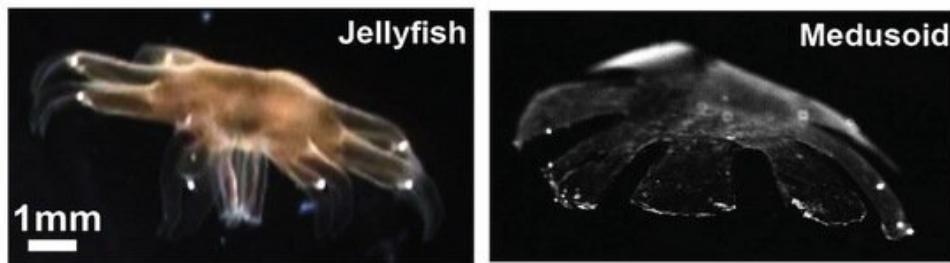
Hybrid Organisms...



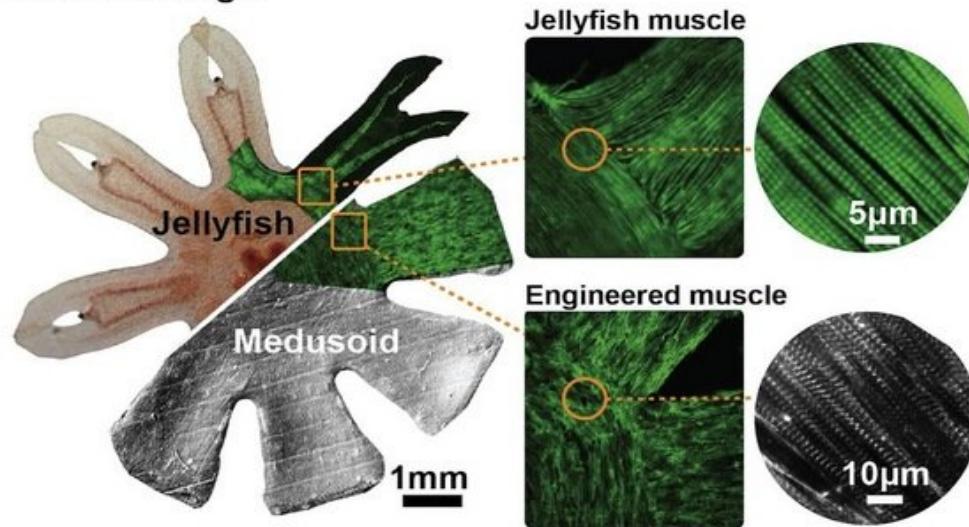
University of North Carolina Hybrid Bugs and Moths

...Hybrid Organic Structures...

Body design



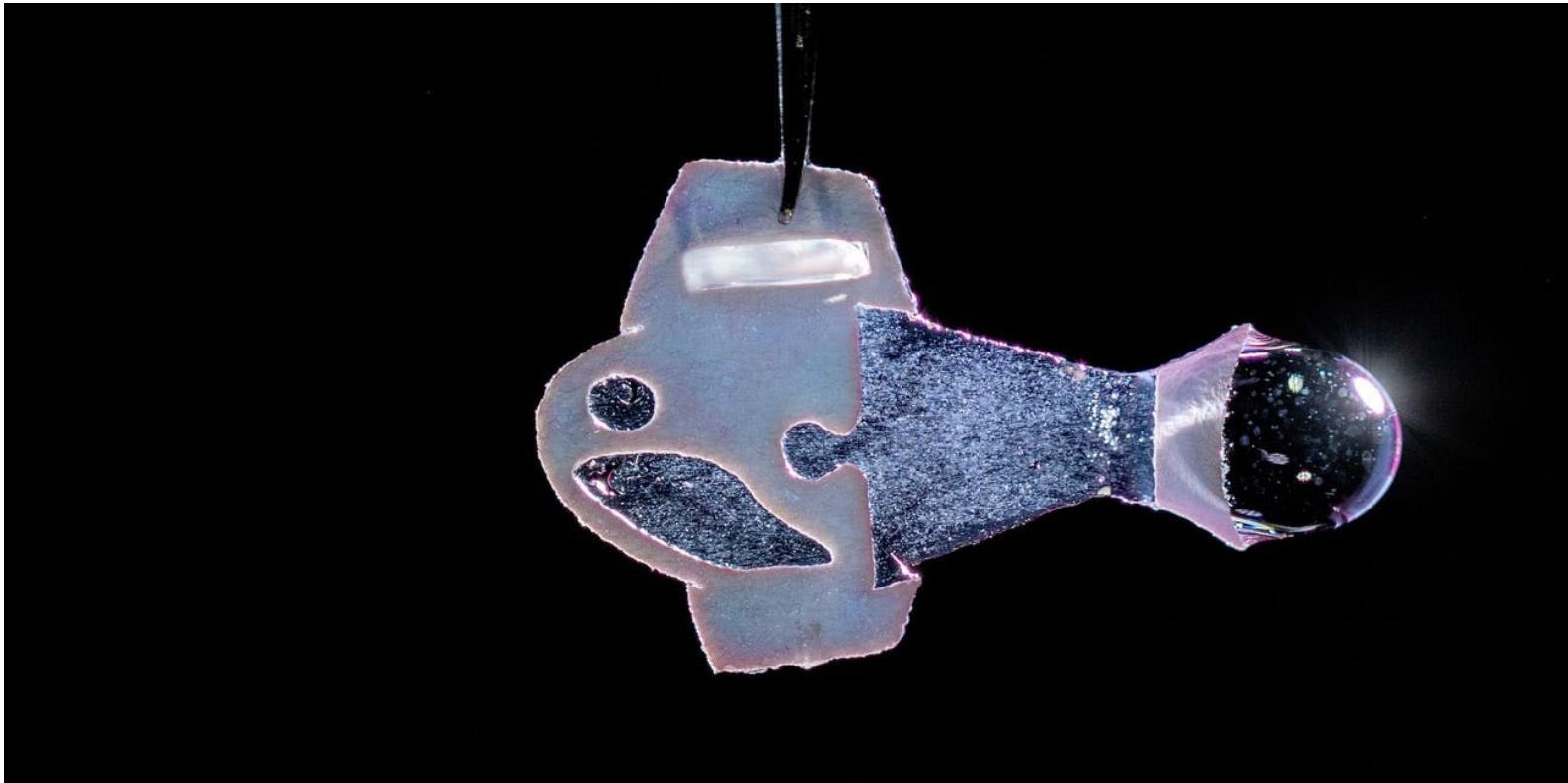
Muscle design



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>

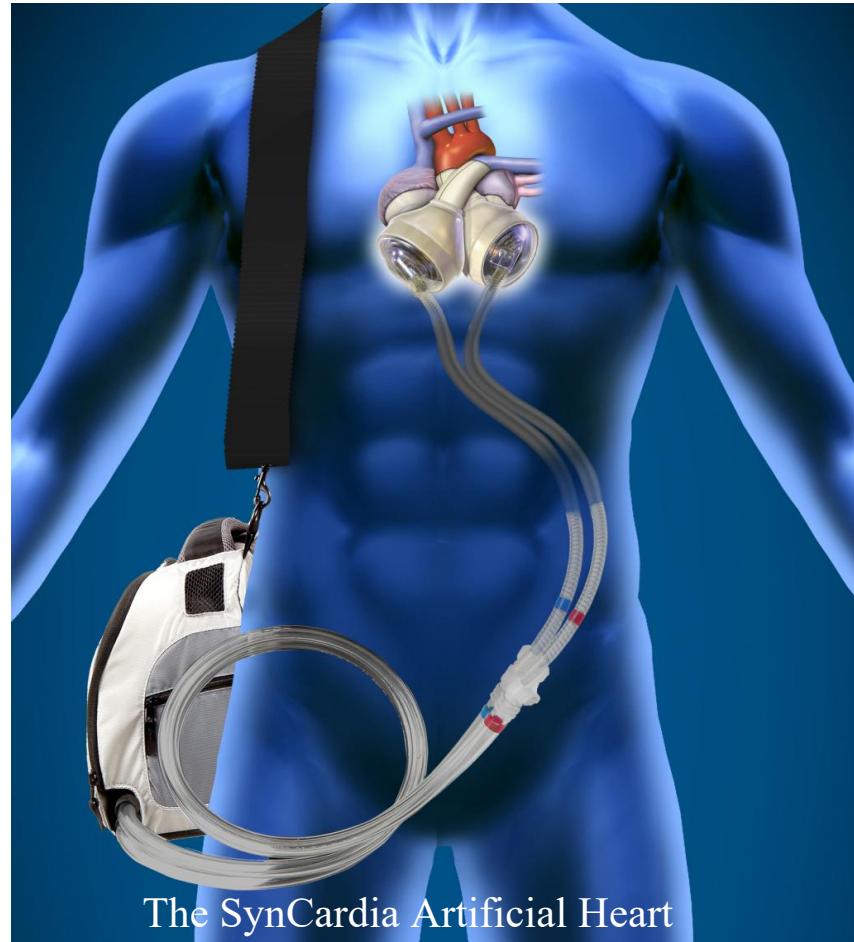
...Now Using Human Heart Tissue



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

The Goal: Improve On Interim Mechanisms...



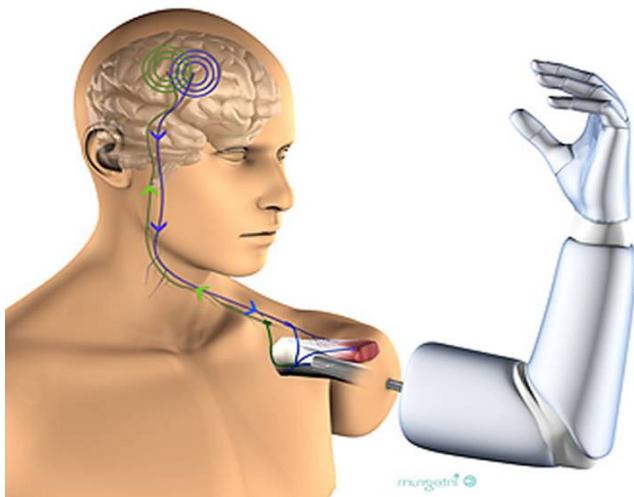
The SynCardia Artificial Heart

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...



For major improvements in:

- Limb Prostheses
- Vision Prostheses
- Hearing Prostheses
- Emotional Response

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/>

...Progress is Being Made...

• USA TODAY

From 'science fiction' to reality: Paralyzed man walks again thanks to brain and spine implants

Karen Weintraub, USA TODAY

Wed, May 24, 2023 at 10:30 AM PDT • 7 min read



Gert-Jan Oksam practices walking in a Swiss research laboratory.

A Dutch man whose spinal cord was injured in a bike accident a dozen years ago can now walk thanks to stimulators implanted on his brain and spinal cord, according to [a study published Wednesday](#).

...and Businesses Being Started

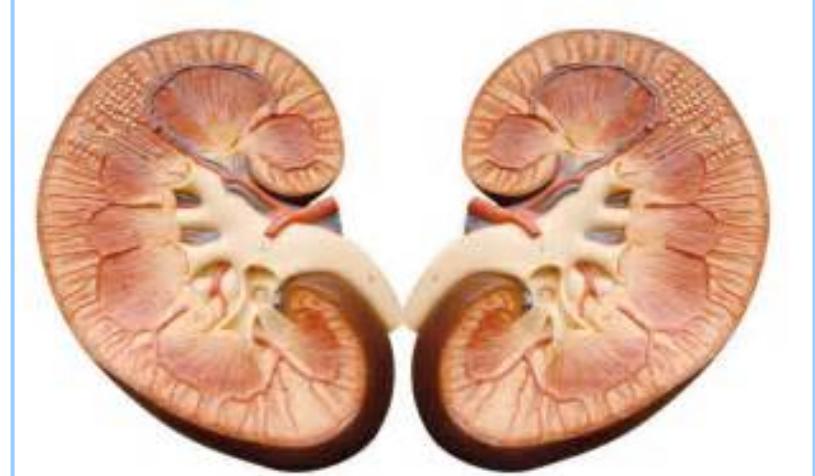
Elon Musk backed company is taking aggressive steps for FDA approval and to product sales.

Neuralink's First-in-Human Clinical Trial is Open for Recruitment

We are happy to announce that we've received approval from the reviewing independent institutional review board and our first hospital site to begin recruitment for our first-in-human clinical trial. The PRIME Study (short for **Precise Robotically Implanted Brain-Computer Interface**) – a groundbreaking investigational medical device trial for our fully-implantable, wireless brain-computer interface (BCI) – aims to evaluate the safety of our implant (N1) and surgical robot (R1) and assess the initial functionality of our BCI for enabling people with paralysis to control external devices with their thoughts.

Body Parts Can Be 3D Printed

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.

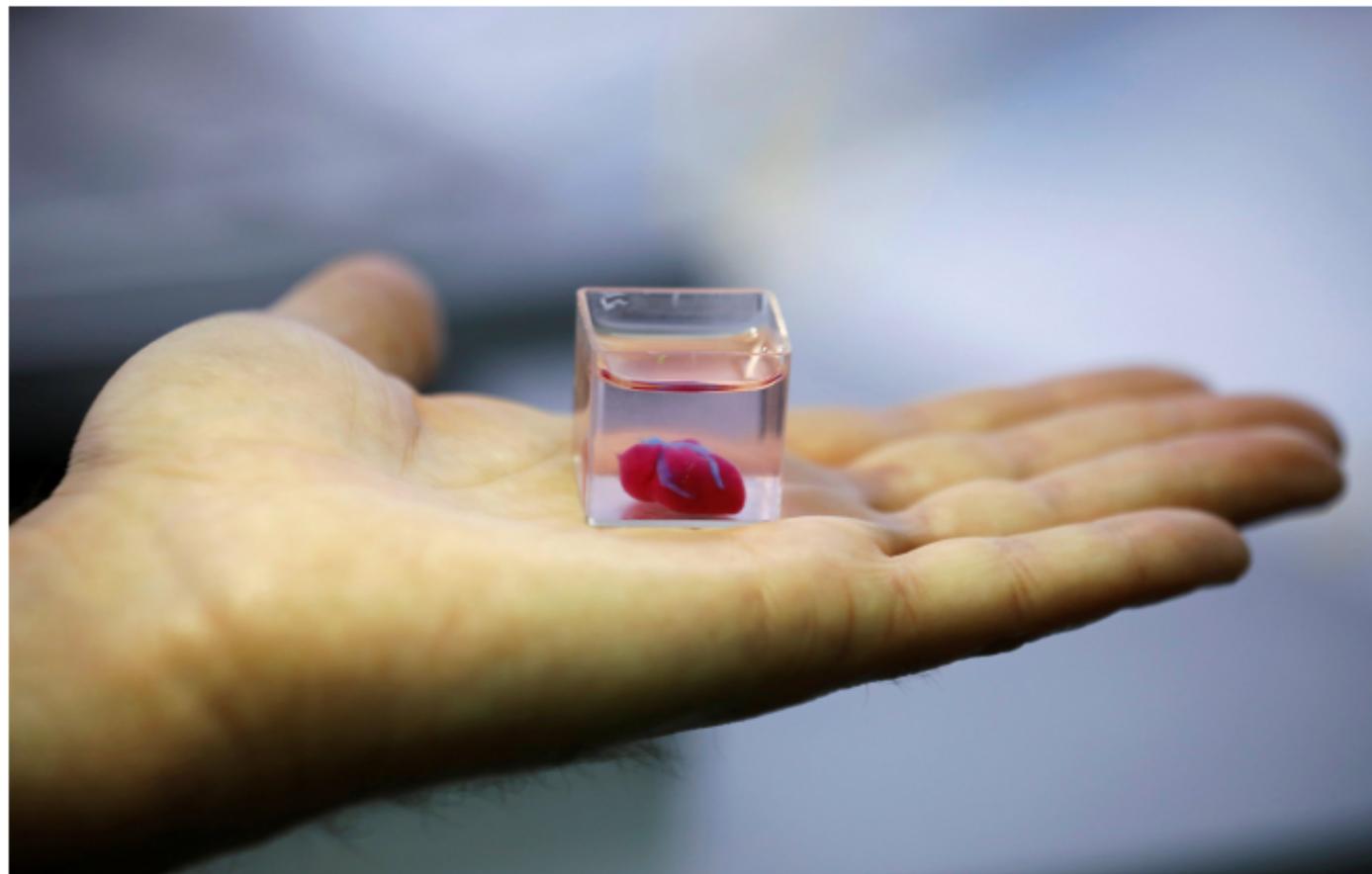


Lab picture from 3D The Voice of 3D Printing; kidney from <https://images.fastcompany.com>

3D Printed 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

Tissues Are Being Bioengineered

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

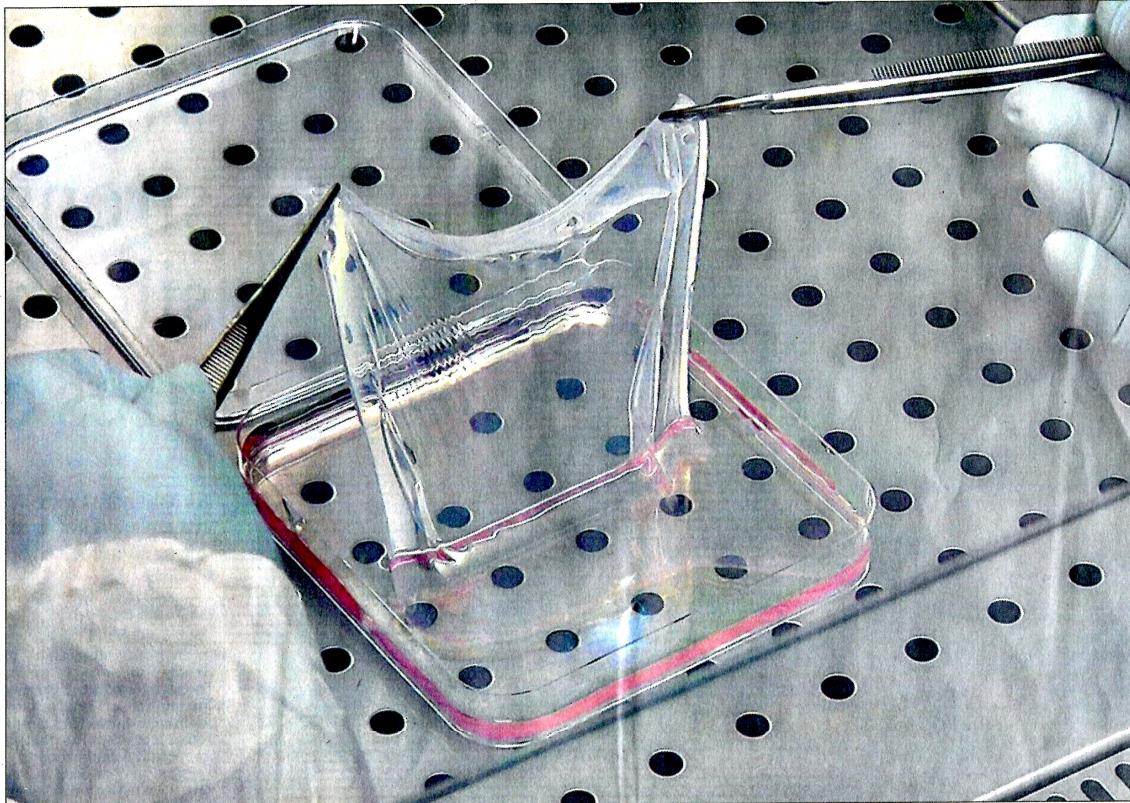
For a soccer-playing, holiday-loving boy on the brink of death from a rare inherited skin disease, doctors have accomplished a feat of genetic engineering, surgical stamina and raw nerve.

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.

CMR UNIMORE CMR Unimore

Los Angeles Times, November 11, 2017

Ethical Analysis: Prosthetic Bioengineering

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

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

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

Case 3: Embryonic Bioengineering

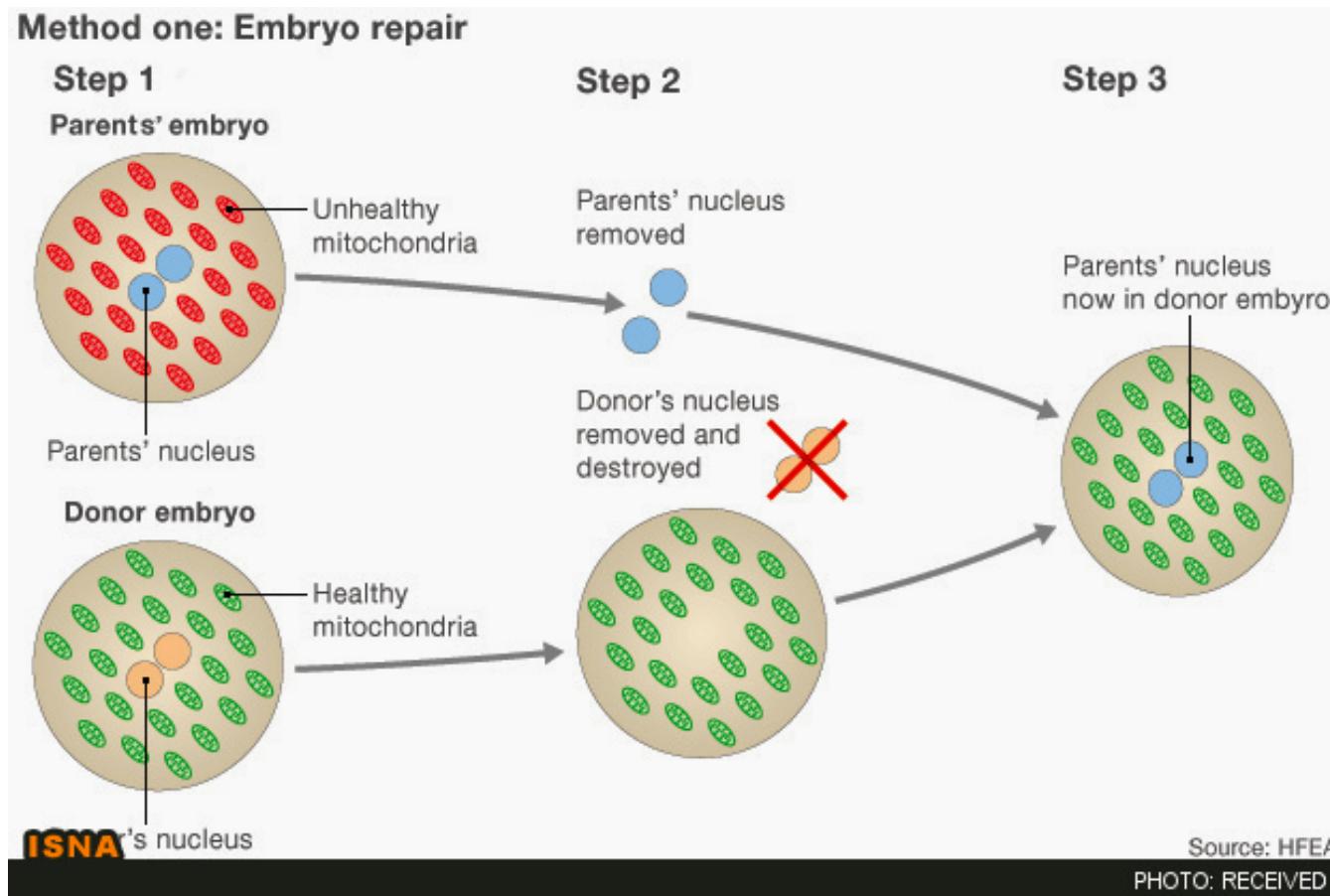
- *Mechanical Cloning:* Cells separated from embryos
 - Freed cells implanted in womb
 - Cells develop into twins, triplets, etc.
- *DNA Cloning:* DNA obtained from donor cell
 - Replaces original DNA in **ovum**, and egg develops into clone of donor
 - Replaces original DNA in embryonic **stem cells**,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



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

www.pbs.org

Human Cell Repair: “3-Parent Babies”



Bioengineering solution for defective mitochondria as performed in Britain.

Early Ethical Concerns



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

Early Ethical Concerns

Los Angeles Times
MONDAY, FEBRUARY 9, 2015 A15

OPINION

OP-ED

Modifying humans

By Marcy Darnovsky and Jessica Cussins

BRITAIN 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-

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

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

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.

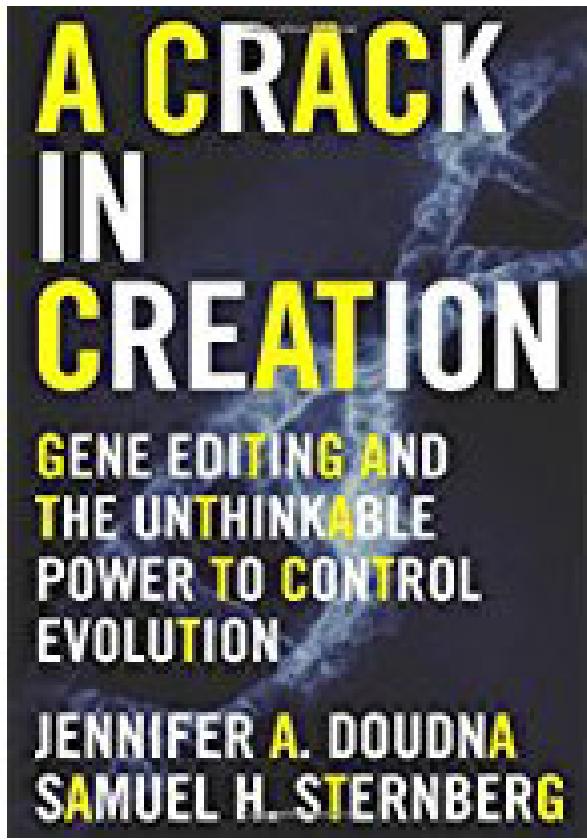
So when a Chinese team revealed last month that it

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

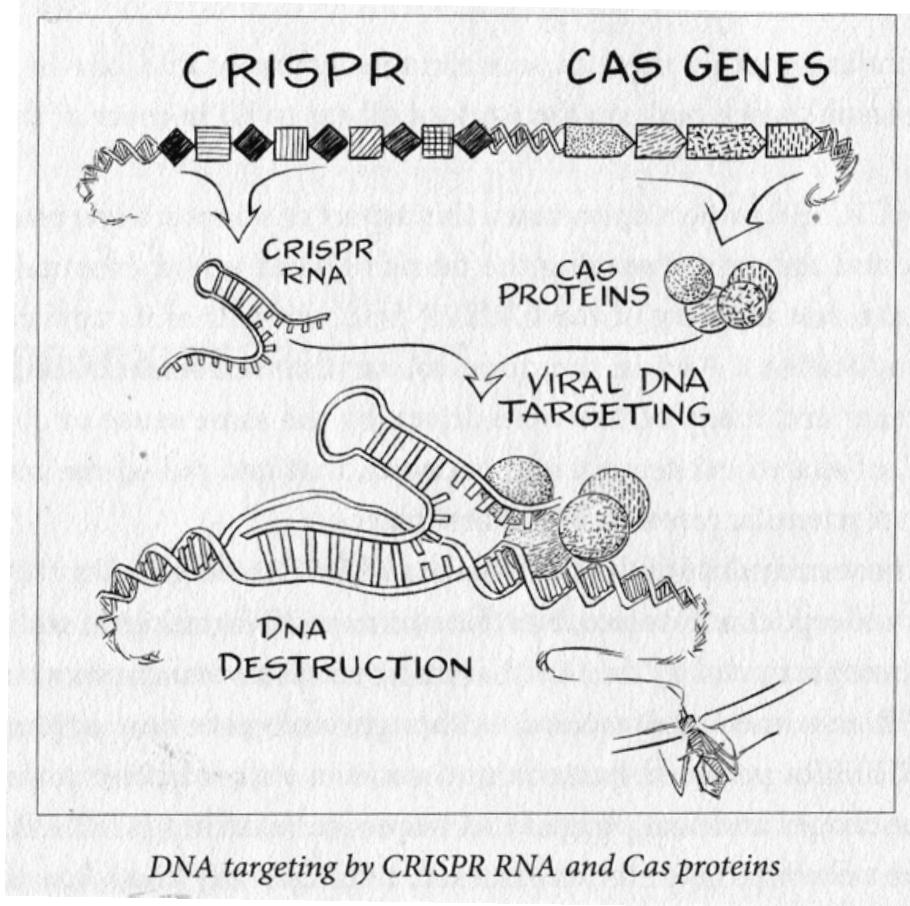
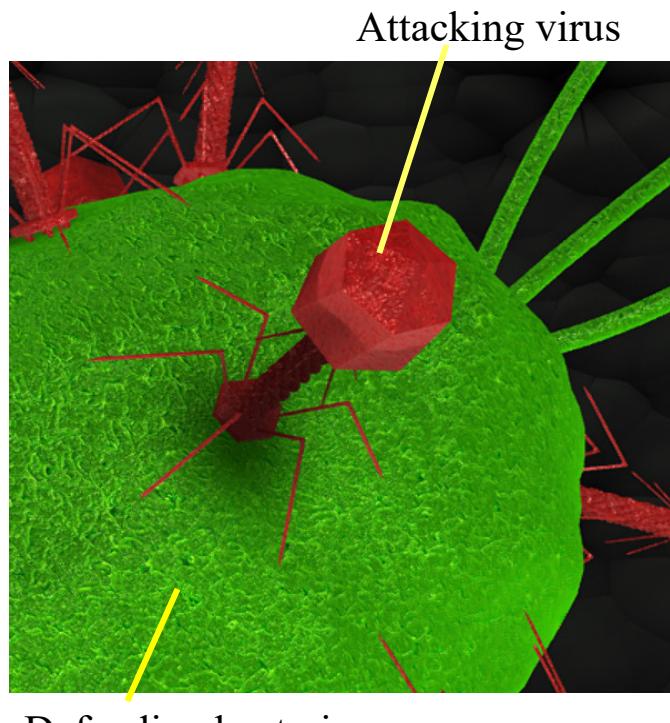


- CRISPR = Clustered Regularly Interspaced Short Palindromic Repeats
- CRISPR Uses DNA-cutting enzyme CAS9 that finds its target with the help of an RNA guide sequence that researchers can engineer to home in on any gene or DNA segment of interest.

"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."

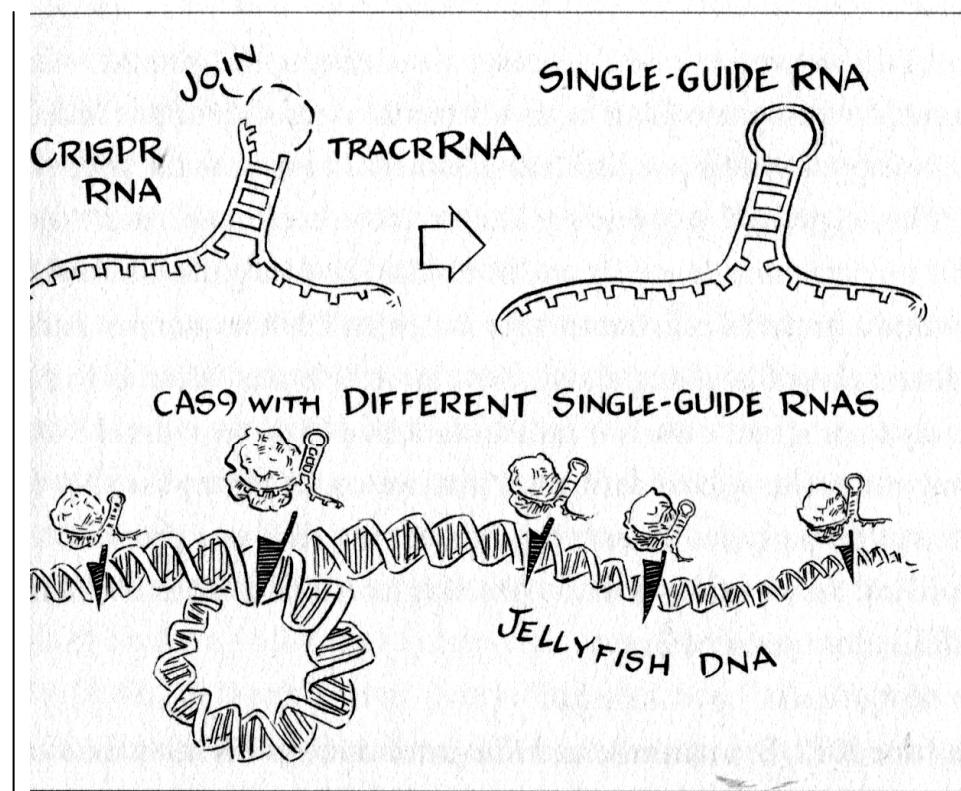
Prof. Jennifer Doudna, UC Berkeley, 2017

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.

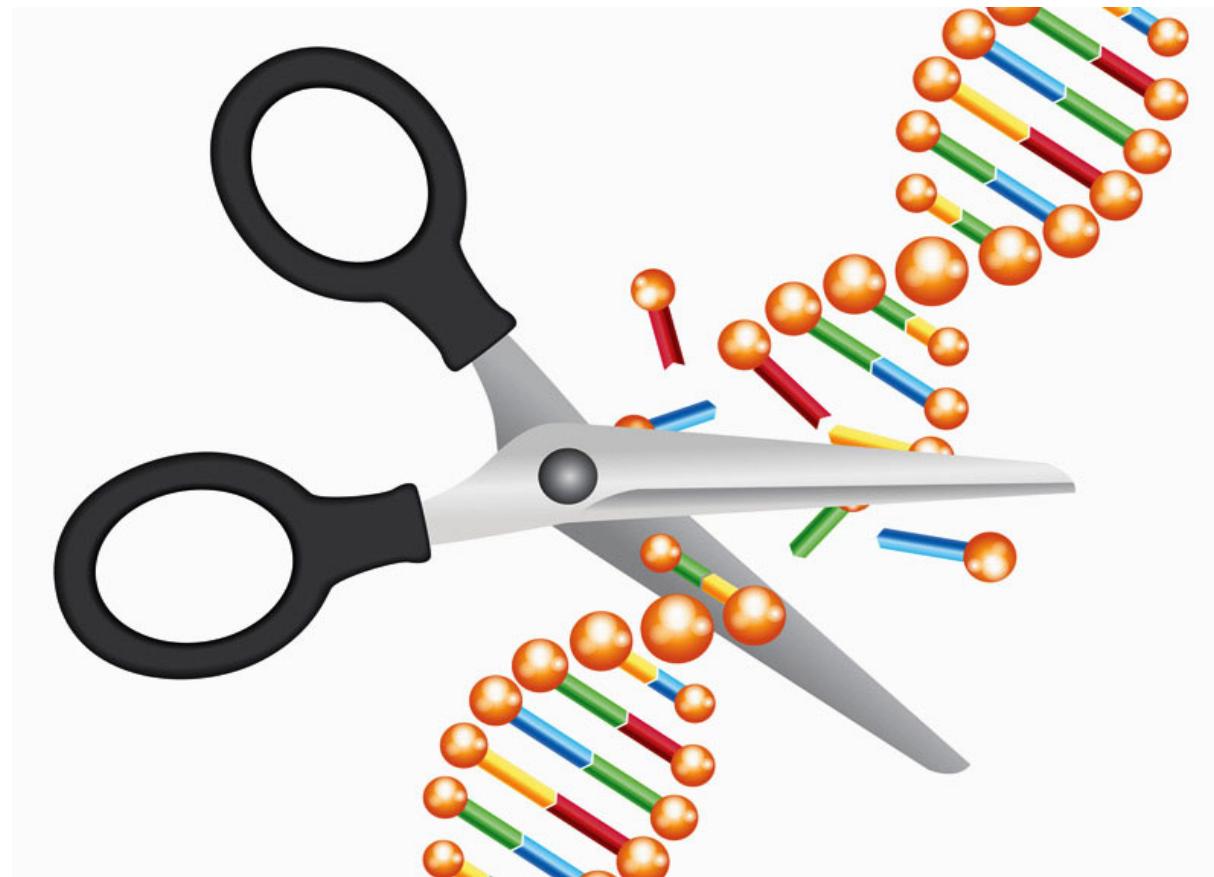
The Demonstration



Programmable DNA cutting by CRISPR-Cas9

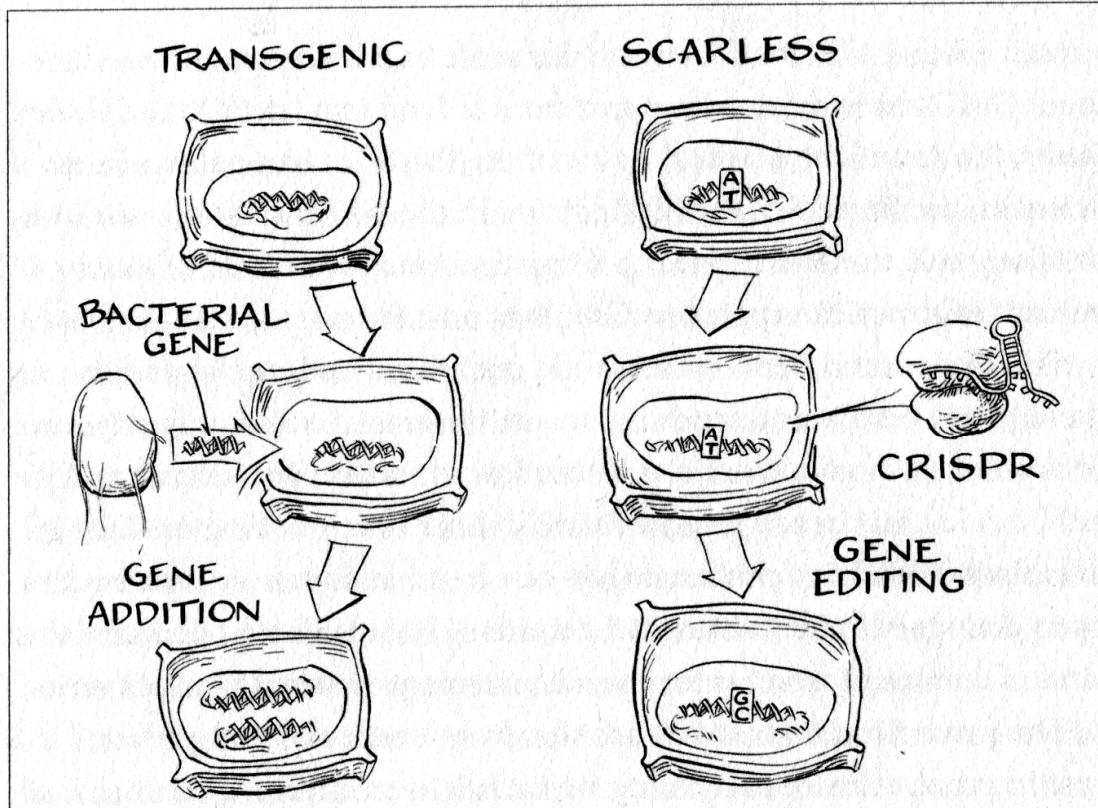
They then showed they could “engineer” RNA-CAS9 CRISPRs that would cut target DNA in precisely specified places – such as gene locations.

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.

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.

Ready Commercial Availability

The screenshot shows the homepage of the Synthego website. At the top, there is a navigation bar with links for 'First Look', 'Next-Generation GMP sgRNA Facility', 'Company', 'Support', 'Order', a search icon, 'Subscribe', a shopping cart icon, and user account options. Below the navigation bar, the Synthego logo is visible, along with 'Products', 'Workflows', and 'Learn' dropdown menus. A large, semi-transparent overlay features a photograph of three scientists in a lab setting. Overlaid on this image is the text 'GET A FREE CRISPR CONSULTATION' and a large, bold, green title: 'Access the Power of CRISPR in Your Research'. Below the title, a subtitle reads: 'Schedule a free discovery call and research project consultation with a genome engineering expert.' Two smaller text blocks provide additional information: 'You're the expert of your research project. We're the genome engineering experts. Let's work together!' and 'We'd love to help answer your complex CRISPR research questions so you can focus on making discoveries.' At the bottom of the page, there is a footer section with links to 'About', 'Careers', 'Contact', 'Privacy Policy', and 'Terms & Conditions'.

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 [Privacy 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.

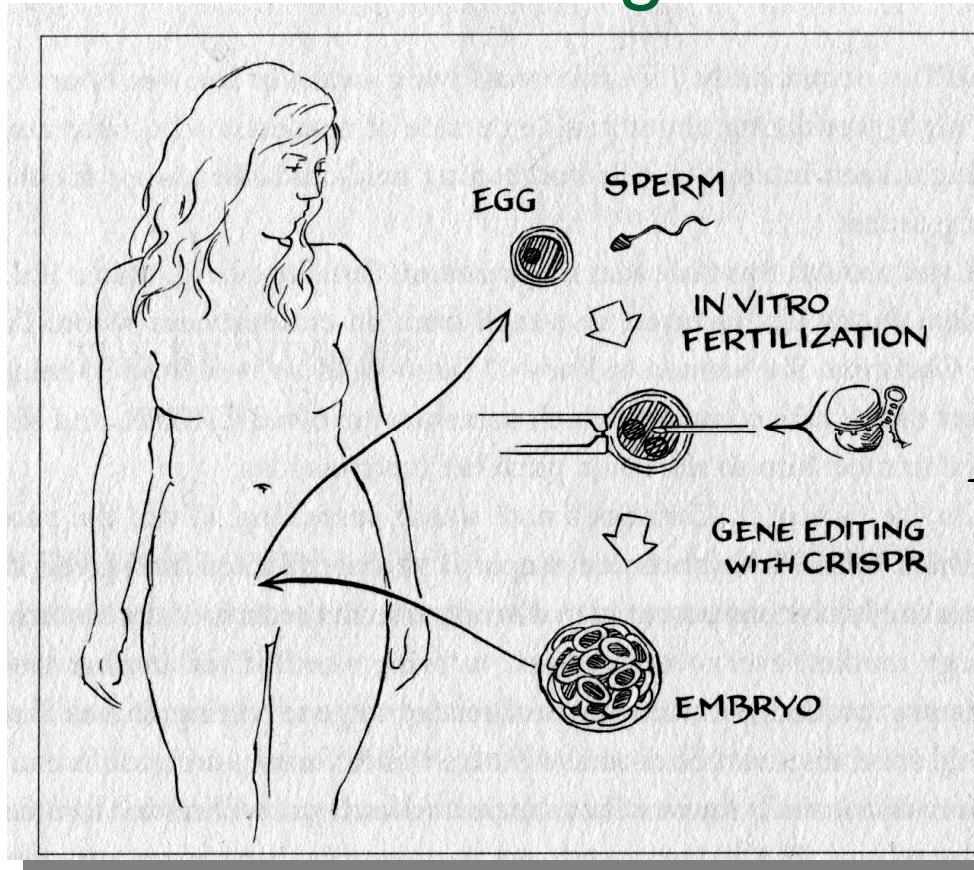
Pig-Human Transplant

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.

Human Gene Editing: “Promise and Peril”

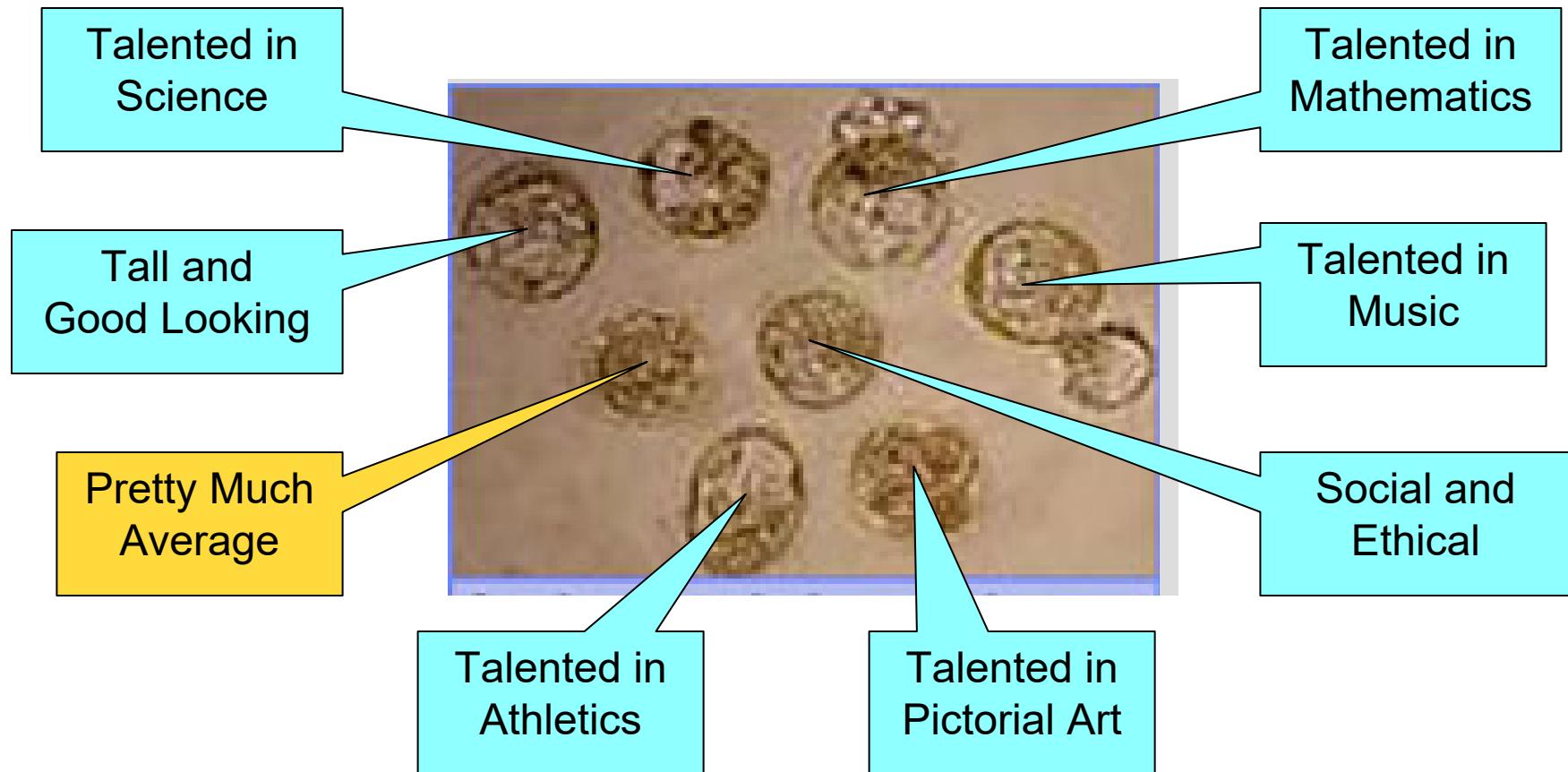


1. Selection
2. Health
3. Improvement

“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.¹

First Steps in Selection

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.

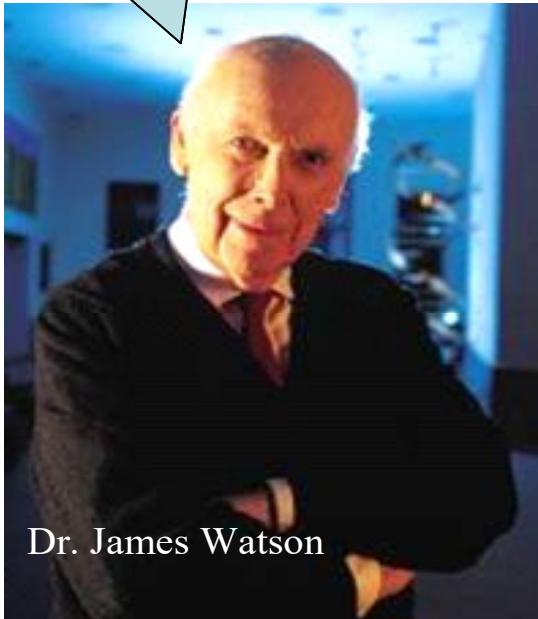
"Your results are based on currently available information in the medical literature and scientific databases ... that may be subject to change," the disclaimer reads. "This may result in a change in your risk assessment."

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-

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

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]

The Oregon Health and Science University reported that they had edited human embryos specially created for a study and not intended to survive it.

Real Embryo Editing: China, January 2018

He Jiankui: China condemns 'baby gene editing' scientist

© 21 January 2018

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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

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What might 'Mueller report' look like?

© 21 February 2019

ADVERTISEMENT

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.

Recent Cell Editing

F.D.A. Approves Sickle Cell Treatments, Including One That Uses CRISPR

People with the genetic disease have new opportunities to eliminate their symptoms, but the treatments come with obstacles that limit their reach.

 Share full article    3



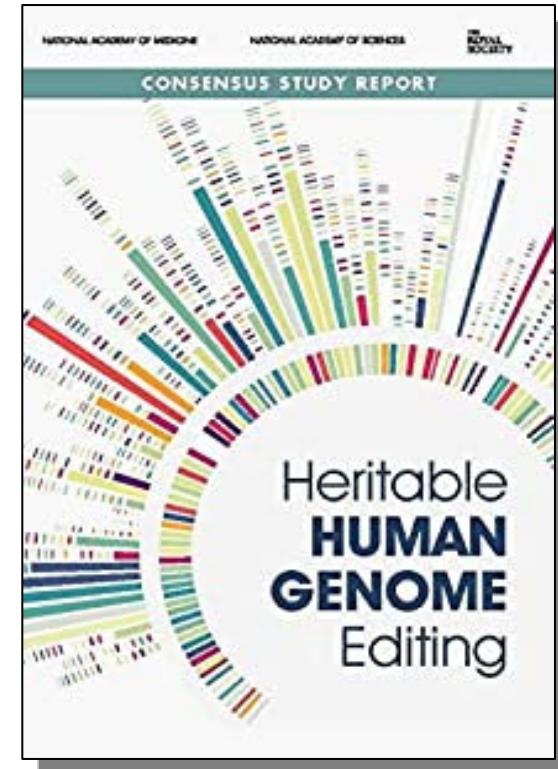
A vial of Vertex Pharmaceuticals's CRISPR Cas-9 gene therapy for sickle cell disease.
Vertex Pharmaceuticals

NY Times 12-8-23

Science Community 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.

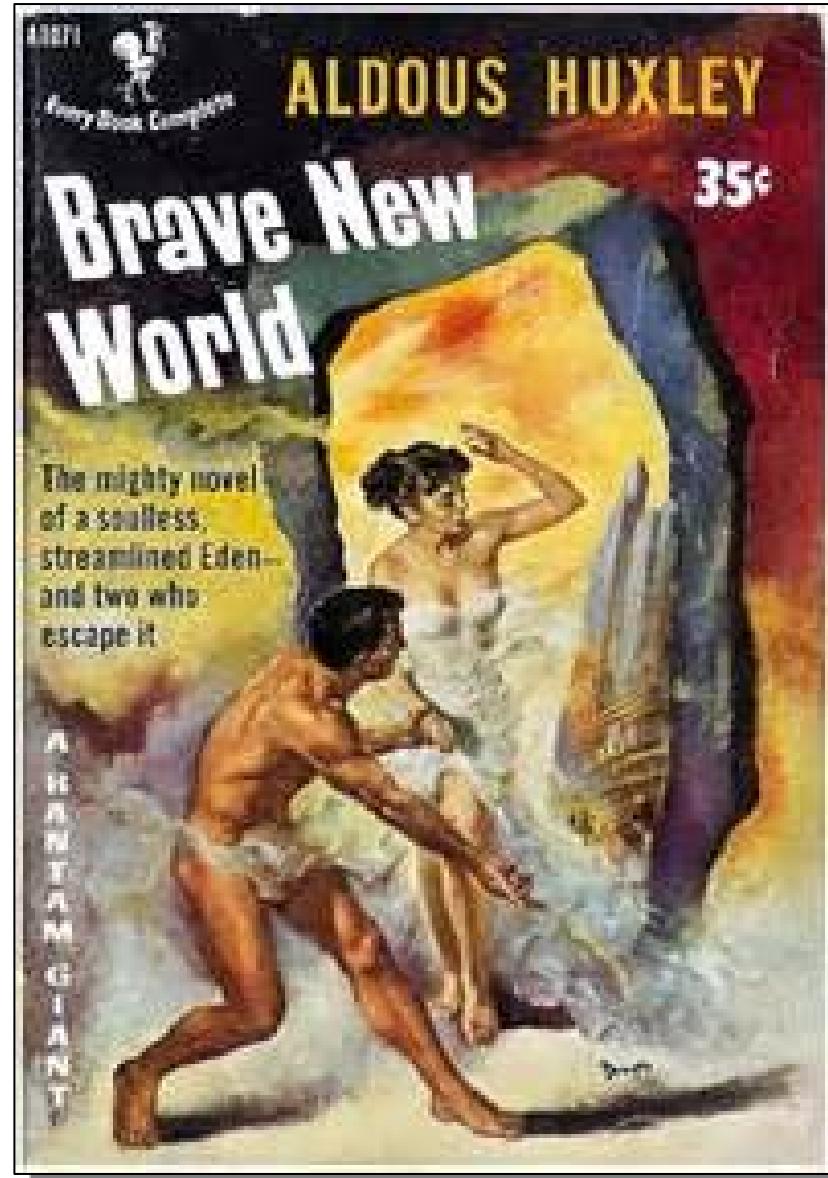


The implicit finding was that genome editing is inevitable, but requires great care.

...an Earlier 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. The novel was advertised as:

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

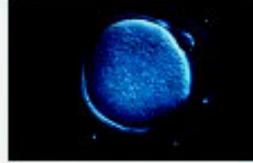


We're Getting Closer...

The screenshot shows a web page from the USC Fertility website. At the top left is the phone number 213.975.9990. The top center features the USC Fertility logo with the tagline "Hope for Today & Tomorrow". On the right side is a search icon and a "Select Language" dropdown menu. Below the header is a navigation bar with links: About USC Fertility, Getting Started, Testing, Treatments, IVF, Egg/Embryo/Sperm Freezing, LGBT Fertility, Donor/Surrogacy, and Pregnancy Loss. The main title of the article is "Making Human Eggs from Stem Cells". Below the title, it says "By Kristin Bendikson". To the left of the text is a small image of a blue egg cell. The text discusses research from Massachusetts General Hospital led by biologist Jonathan Tilly, which claims to have generated new eggs from human ovarian stem cells. It notes that this research, published in Nature Medicine, has the potential to open up a new field of reproductive biology. The text also mentions that women are born with a finite number of eggs and that the loss of eggs is a major barrier for fertility physicians. It describes how researchers have previously worked with mice and applied the same methods to human cells, marking reproductive cells (eggs) in the ovary, retrieving cells, sorting them, and growing them in the laboratory to produce immature egg cells. A circular arrow icon is in the bottom right corner.

Making Human Eggs from Stem Cells

By Kristin Bendikson



Researchers from Massachusetts General Hospital have claimed to generate new eggs cells from human ovarian stem cells. This groundbreaking research team, led by biologist Jonathan Tilly, was published online this past Sunday in the journal Nature Medicine. If validated, this research has the potential to open up a new field of reproductive biology that could have tremendous impacts on the field of infertility.

Women are born with a finite number of eggs in their ovaries. As a woman ages, the number and quality of eggs diminishes. The loss of eggs is a major barrier for fertility physicians as they assist older women conceive.

The researchers have previously worked with mice and have now applied the same methods to human cells. The research initially consisted of marking reproductive cells (eggs) in the ovary. They were then able to retrieve cells from the ovary and sort the cells to separate out the marked cells (eggs). The next step was to then grow the cells in the laboratory to produce immature egg cells. In the previous mice studies, they were able to generate viable egg cells that could be fertilized and produce embryos.

Even to Human Cloning...

Chinese scientists create cloned monkey

By [Katie Hunt](#), CNN

⌚ 4 minute read · Published 12:45 PM EST, Tue January 16, 2024

 Leave a comment



CNN

World

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Zhaodi Liao et al., Nature Communications

The cloned rhesus monkey was named Retro is doing well, according to the research team.

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**