Genome Editing and CRISPR

August 17th, 2022
Maine State House

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KEN BURNS PRESENTS
THE GENE
AN INTIMATE HISTORY

2022

New advances in genetics are becoming personal

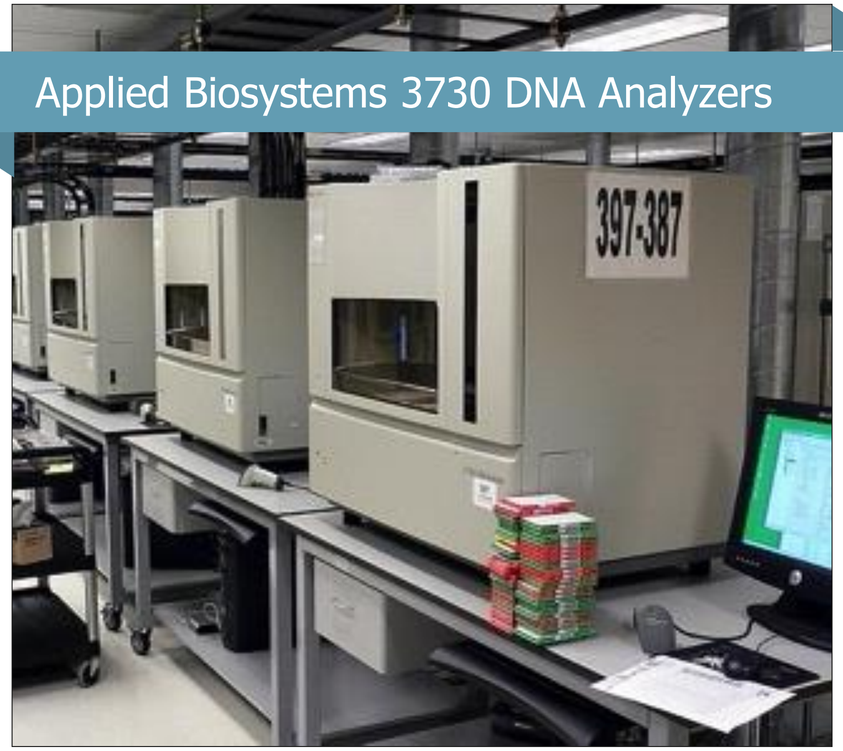
Learning about our DNA can offer:

- Insights about our health, behavior, family history and other traits.
- Information with personal, social and familial impact.
- Improved health care.
- Complicated questions about how to use genetics personally and as a society.
- Challenges about how to ensure fairness and equity in genetic advances.

Technology out of the lab and into the world: Rapid, portable DNA analysis is on the horizon

2002

Applied Biosystems 3730 DNA Analyzers



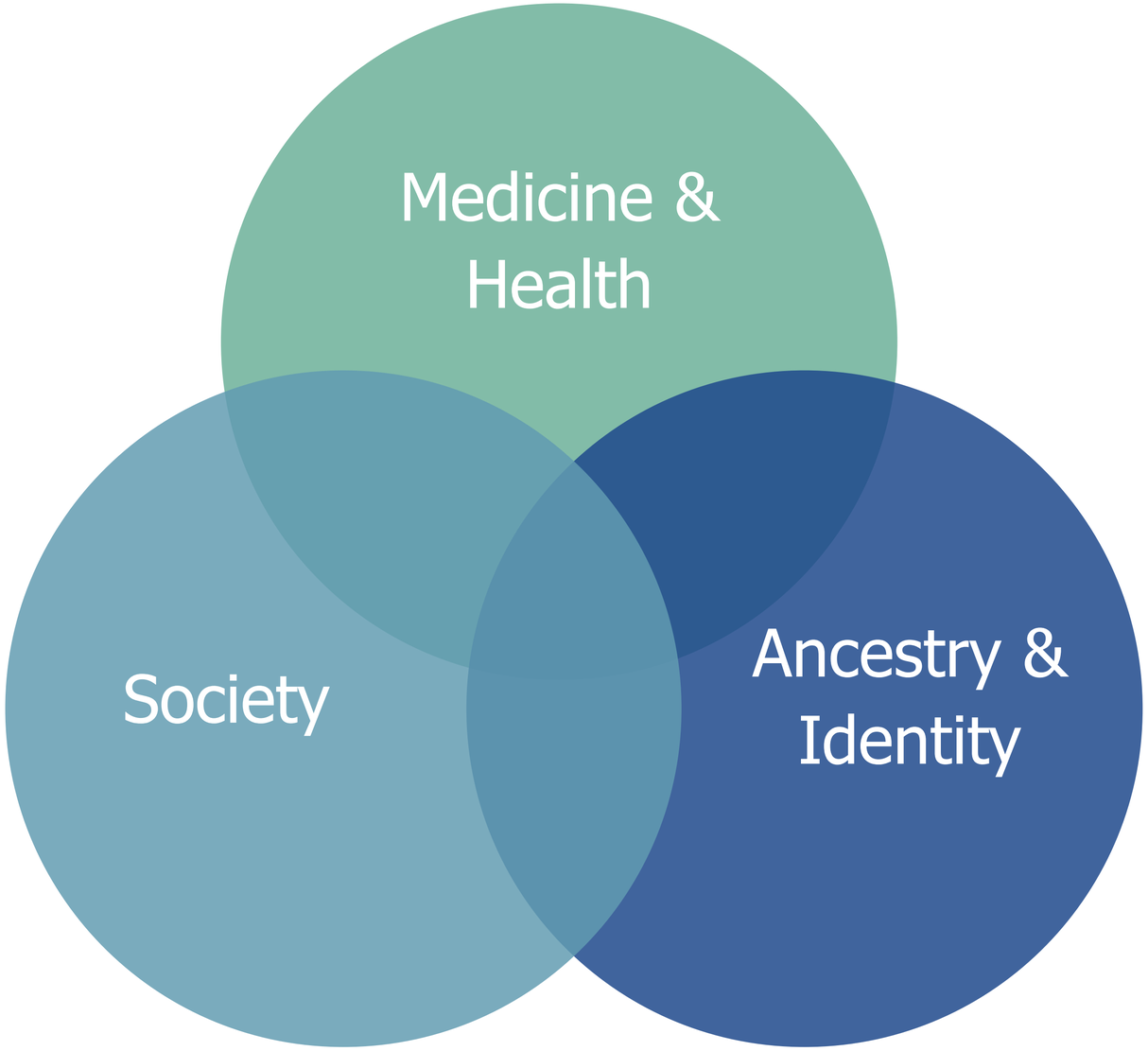
Jurvetson, CC BY 2.0

2019

MinION DNA Sequencer

NASA

How is personal genetics affecting real people?



Genetic testing:

Solving medical mysteries
& connecting families

2022 Update: there are now over 130 patients and the condition has a name – Hao-Fountain Syndrome.

Personal choices based on genetic information

Actor Angelina Jolie reveals she chose to undergo a double mastectomy.

Jolie had a genetic test and found she carried a mutation in the BRCA1 gene. Doctors estimated there was a very high chance she would get breast cancer.

Genetics can determine safety and effectiveness of certain medications

CYP2D6 gene, involved in converting codeine to morphine - 100 known variants and counting!

Typical metabolizer - medication works as expected

Slow metabolizer - gets very little effect from the medicine

Rapid metabolizer - standard dose of medication can be lethal

Adapted from http://www.ensrmedical.com/pharmacogenetics/

Genetic testing during pregnancy: More information and at an earlier date

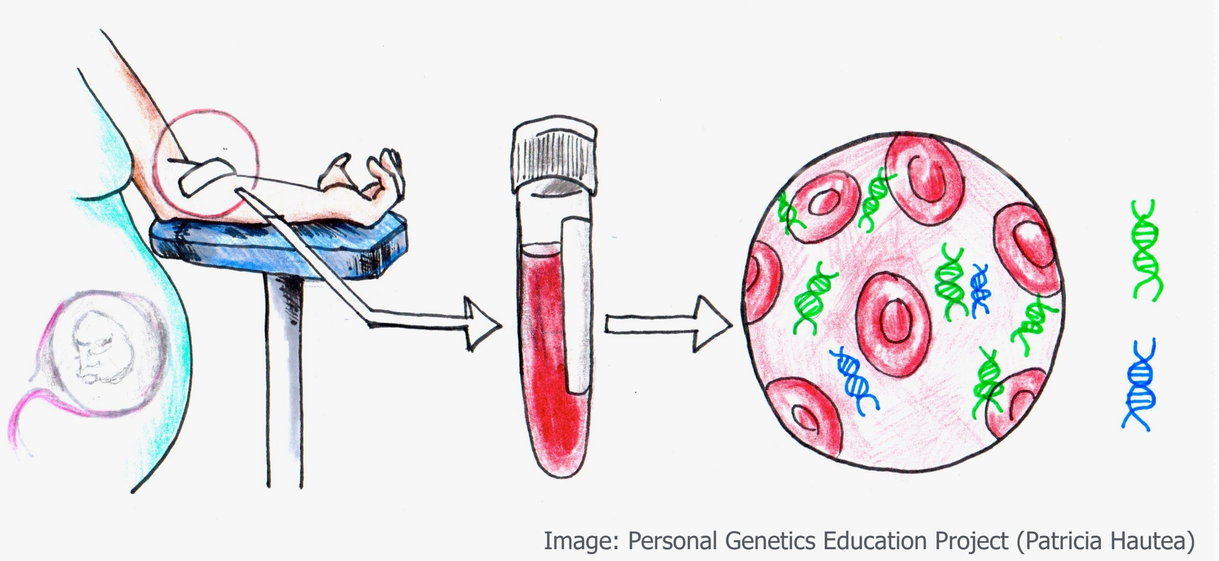


Image: Personal Genetics Education Project (Patricia Hautea)

- **Non-invasive prenatal testing (NIPT)** involves analyzing a blood sample taken from a pregnant person to learn about traits of the fetus.
- This test looks at small pieces of DNA that circulate in the pregnant person’s bloodstream.
- Some of these pieces of DNA come from cells of the placenta that broke open and can reveal information about the developing fetus.

Reproductive technology opens the door to analyze embryos for certain genetic traits

- Eggs, harvested from ovaries, can be combined with sperm in a petri dish in a process called in-vitro fertilization (IVF).
- After 3-5 days of development, one or more cells can be removed from the embryo and assessed for certain traits in a process called pre-implantation genetic diagnosis (PGD).

“Golden State Killer” suspect arrested in April 2018

The search was aided by a DNA match from a database created to find relatives for family history/genealogy hobbyists.

[GED match] Tools for DNA and Genealogy Research

Photo via Sacramento county policy department

Forensic genetic genealogy in use in Maine

Maine man to stand trial for 1993 Alaska murder after genetic genealogy tied him to crime scene DNA

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Updated: 6:48 PM EDT Apr 29, 2021

Infinite Scroll Enabled

Phil Hirschkorn
Political Reporter

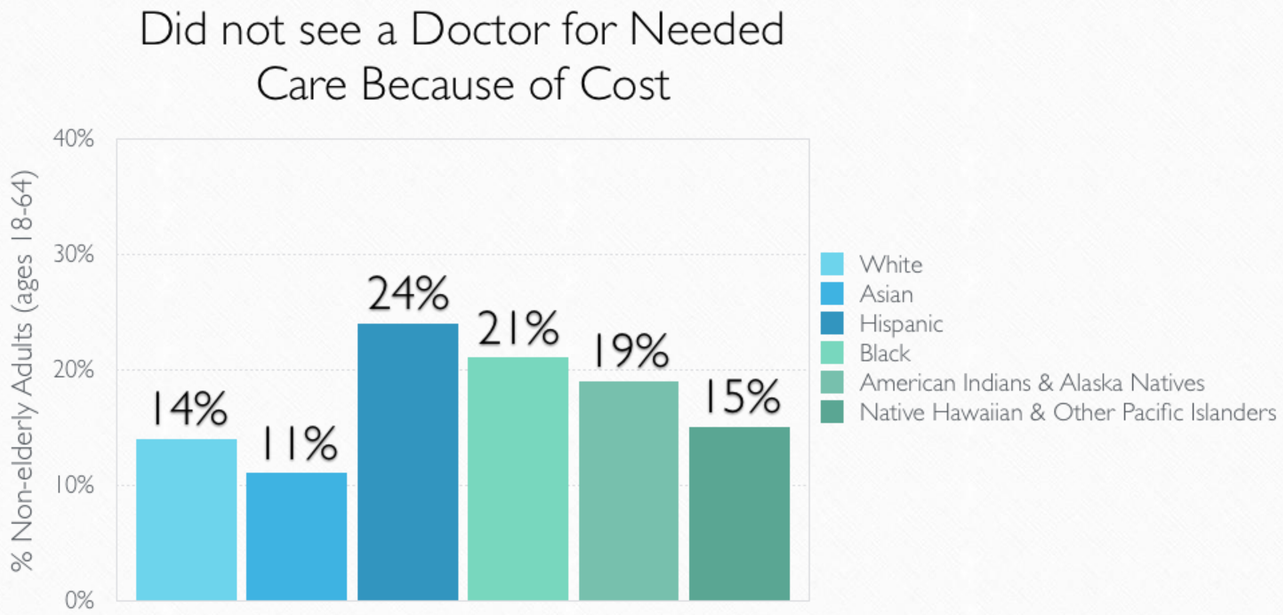
A key step is comparing crime scene DNA with DNA profiles accessible from two popular consumer DNA testing sites, GEDmatch and FamilyTreeDNA, which currently store a combined 1.6 million profiles.

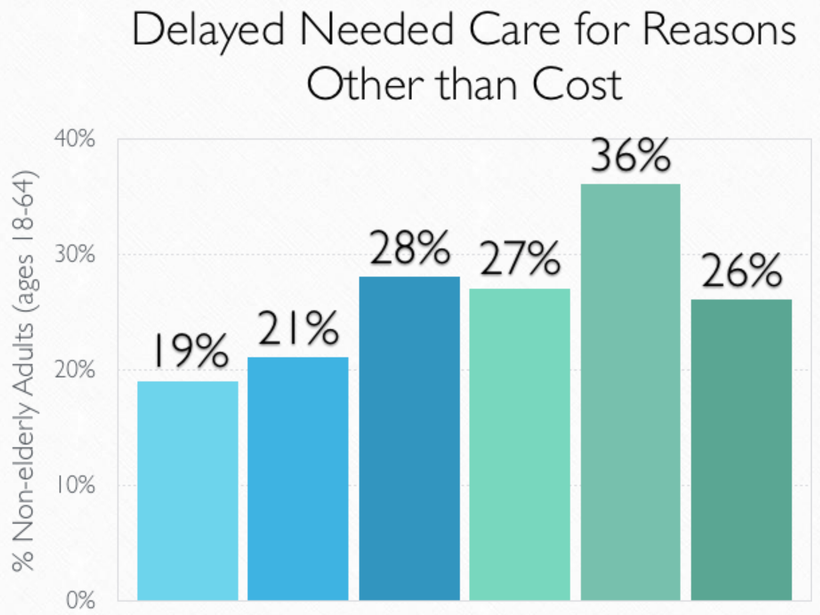
"We reverse engineering people's family tree," Moore said. "But we're not actually accessing anyone's DNA file or DNA code. All we're getting is a list of matches, which is generated through comparing the unknown crime-scene DNA to all those DNA files of the people that are participating in those two databases."

https://www.wmtw.com/article/maine-man-to-stand-trial-for-1993-alaska-murder-after-genetic-genealogy-tied-him-to-crime-scene-dna/36292803

Healthcare access is key to personal genetics being shared fairly

Percent of Non-elderly Adults in US who did not Receive or Delayed Care in past 12 months by Race/Ethnicity (2014)





Data from Kaiser Family Foundation analysis of CDC Behavior Risk Factor Surveillance System (2014)

Diné (Navajo Nation) setting their own terms: Making decisions regarding their participation in genetic research

dbking, CC-BY 2.0

"To us, any part of ourselves is sacred. Scientists say it's just DNA. For an Indian, it is not just DNA, it's a part of a person, with a deep religious significance. It is part of the essence of a person."
– Frank Dukepoo, Hopi geneticist

Erin Blakemore, *History* (Nov 3, 2017)

Navajo Nation reconsiders ban on genetic research

Tribal leaders are developing a policy for genetic research and data sharing, potentially ending a 15-year moratorium

Sara Reardon, *Nature* (Oct 6th, 2017)

Proposed policy included power for Nation to:

- Approve or reject research proposals
- Maintain control over the samples

Where does CRISPR fit in to this conversation?

What is **CRISPR**?

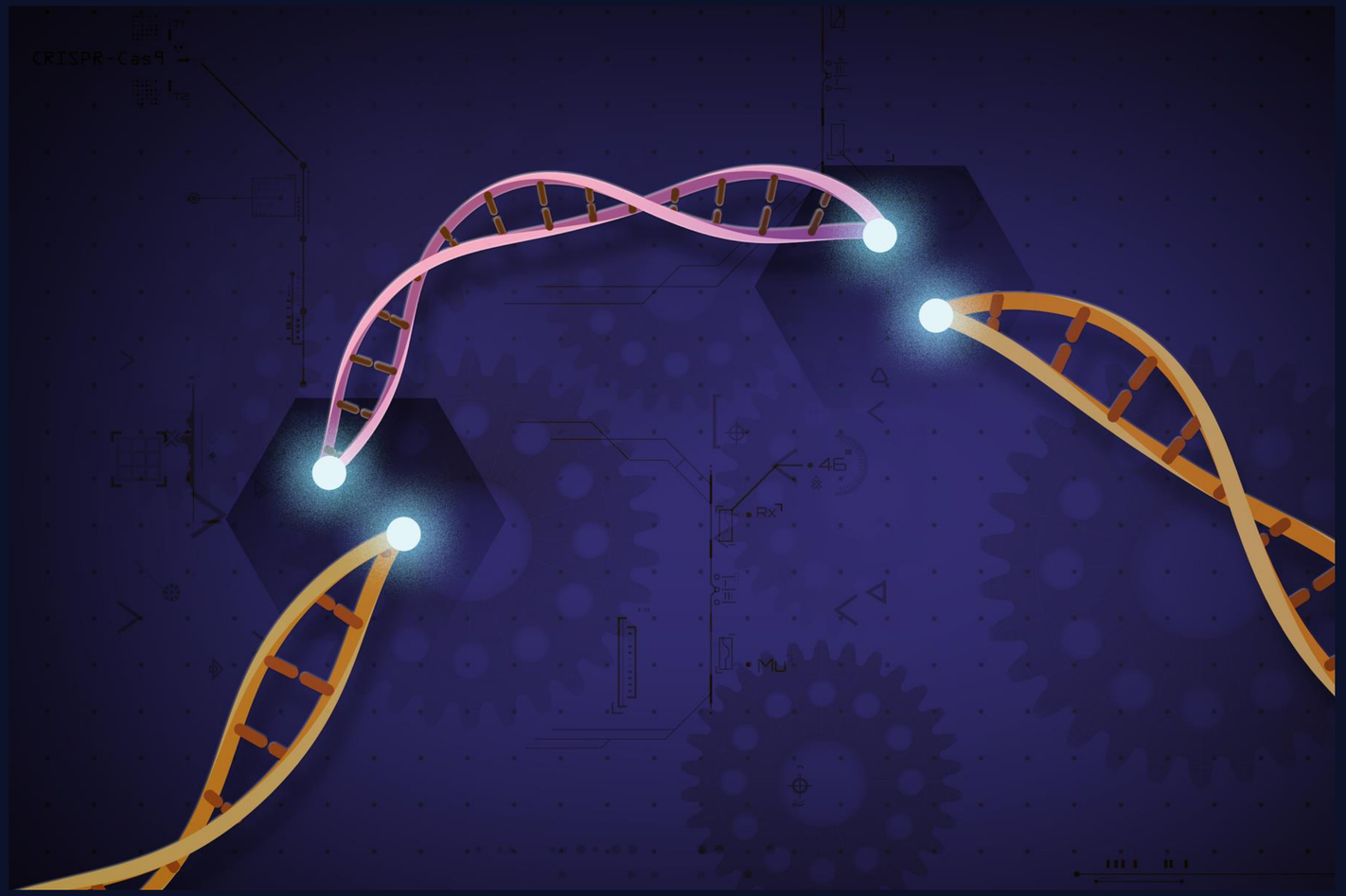
(Clustered regularly interspaced short palindromic repeats)

A genome editing technique that:

- Targets a specific section of DNA
- Makes a precision cut/break at the target site
- Can do one of two things:
  - Makes a gene non-functional
  - Replace one version of a gene with another

What are the potential applications of CRISPR to human health?

What is genome editing?

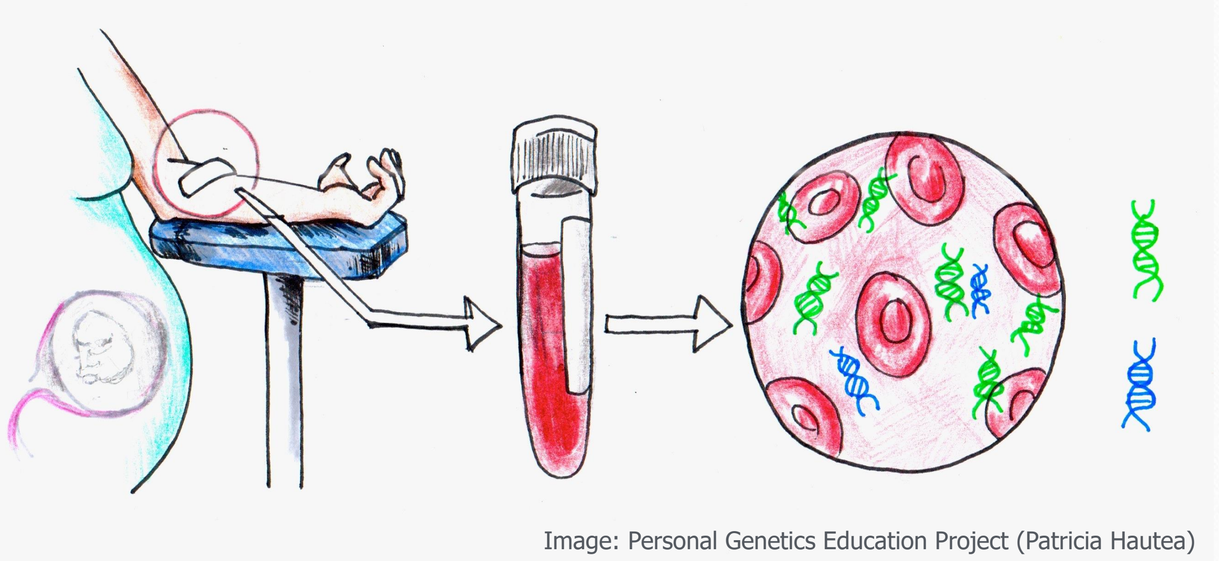


Ernesto del Aguila III

Genome editing is making a change to an organism's DNA at a specific site.

CRISPR is a genome editing tool that can be used to make these specific DNA changes.

Genetic testing during pregnancy: More information and at an earlier date



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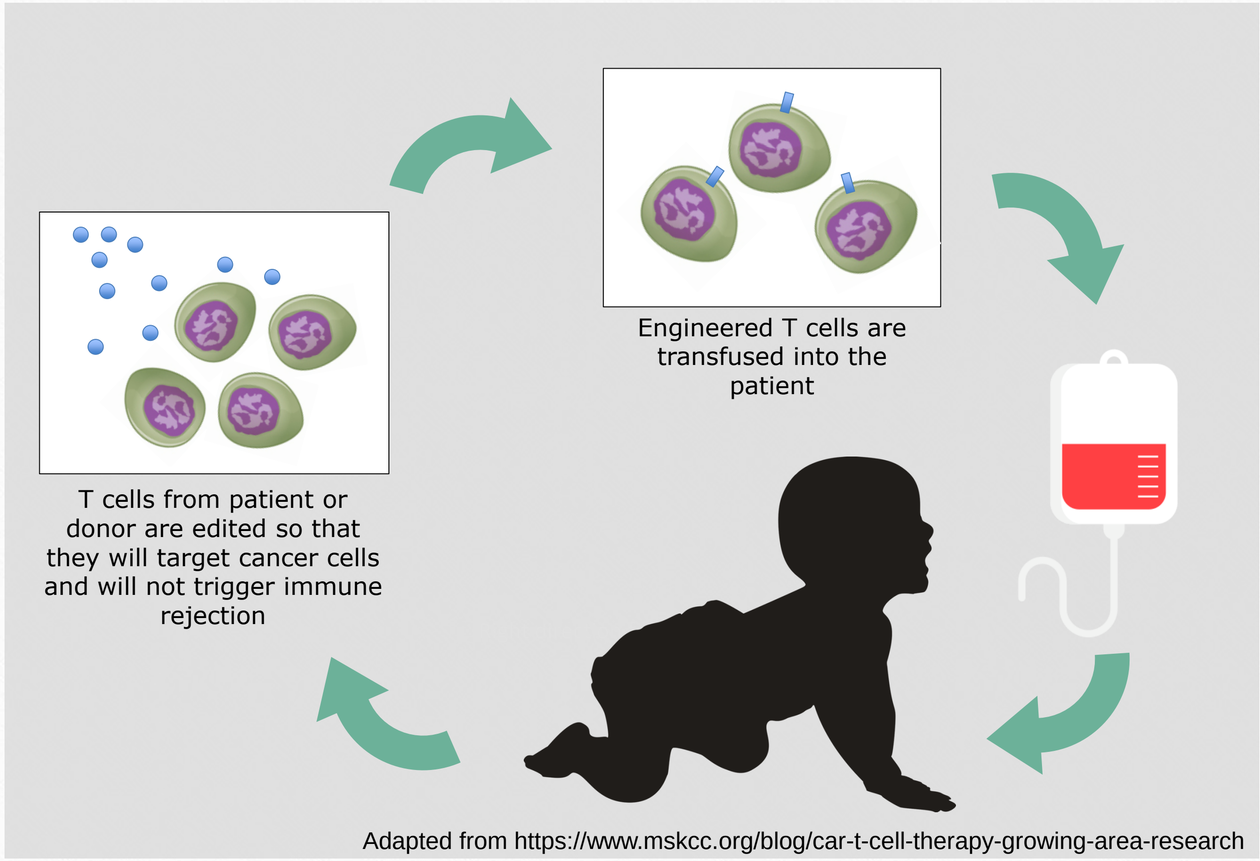


The possibility of changing your DNA

Layla Richards: the first success of genome editing-based gene therapy

Do Now: Discuss the following with the person (or people) next to you:

Imagine you've been offered a deal from a genomics company. You can get a free genome sequence – an analysis of all your DNA that includes a report of your ancestry, traits and a medical profile. The medical profile tells you about diseases for which you have a low risk of getting, and also those you have a high risk of getting.

Are you interested? Why or why not?

Do Now: Discuss the following with the person (or people) next to you:

For the first 100 volunteers, the company is offering to ”correct” several of the disease-related genes found by the analysis. Imagine this were a very new procedure approved by the government for safety, but without a great deal of long-term study.

Would you volunteer for this added service?

(This service is not currently available and will not be in the near future, so use your imagination.)

Watch this clip from *The Gene: An Intimate History*

https://ny.pbslearningmedia.org/resource/9795d5d3-2b03-4d50-b193-ae6eb918392f/genome-editing-and-crispr/

What is Gene Therapy?

Research is on-going to develop gene therapies for conditions such as cystic fibrosis and sickle cell disease

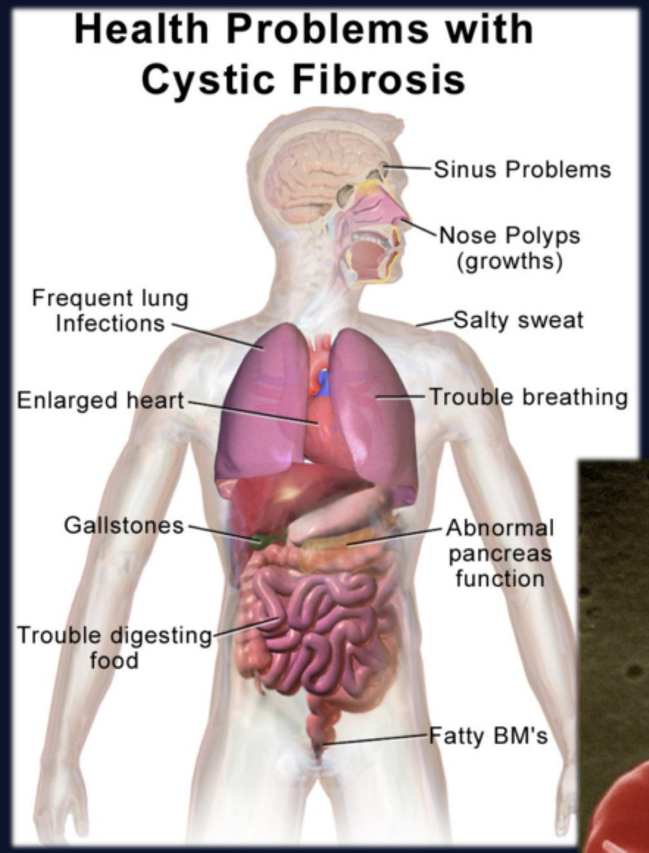


Image: Blausen.com staff, CC BY 3.0

Image: Wellcome Images, CC BY-NC-ND 2.0

Researchers have used genome editing to cure a type of liver disease in adult mice

Image: Lex McKee, CC BY-NC 2.0

This type of research is an important step towards developing new gene therapies in humans

Image: Maidiel1, CC BY-SA 4.0

Might genome editing one day lead to a solution to the global shortage of organs?

Should genome editing be used in the hopes of reducing malaria?

Image: YoHandy, CC BY-NC-ND 2.0

› Philos Trans R Soc Lond B Biol Sci. 2019 May 13;374(1772):20180105.
doi: 10.1098/rstb.2018.0105.

Mice Against Ticks: an experimental community-guided effort to prevent tick-borne disease by altering the shared environment

Joanna Buchthal [1], Sam Weiss Evans [2 3 4], Jeantine Lunshof [1 5 6], Sam R Telford 3rd [7], Kevin M Esvelt [1]

Affiliations + expand

PMID: 30905296 PMCID: PMC6452264 DOI: 10.1098/rstb.2018.0105

Free PMC article

Abstract

Mice Against Ticks is a community-guided ecological engineering project that aims to prevent tick-borne disease by using CRISPR-based genome editing to heritably immunize the white-footed mice (Peromyscus leucopus) responsible for infecting many ticks in eastern North America. Introducing

https://pubmed.ncbi.nlm.nih.gov/30905296/#:~:text=Mice%20Against%20Ticks%20is%20a,ticks%20in%20eastern%20North%20America.

Image: The National Academies, CC BY-NC-SA 2.0

2018: Claims of CRISPR being used to edit genomes of twin girls

“New eugenics” and “designer babies”: What are the underlying concerns?

Eugenics lurk in the shadow of CRISPR

Robert Pollack, *Science* (May 22, 2015)

What’s the difference between genetic engineering and eugenics?

Robert Gebelhoff, *Washington Post* (February 22, 2016)

Designer babies aren’t futuristic. They’re already here.

Are we designing inequity into our genes?

Laura Hercher, *MIT Technology Review* (October 22, 2018)

Scientists confront the ghost of eugenics

Amy Marcus, *Wall Street Journal* (August 17, 2018)

American eugenics movement

- Began in US in early 1900s
- Social movement that worked to "improve" society by encouraging or discouraging people to have babies
- Promoted reproduction by people or groups with "positive" qualities
- Discouraged or sometimes stopped reproduction by groups with "negative" qualities
- State and Federal laws addressing issues ranging from immigration to mandatory sterilization

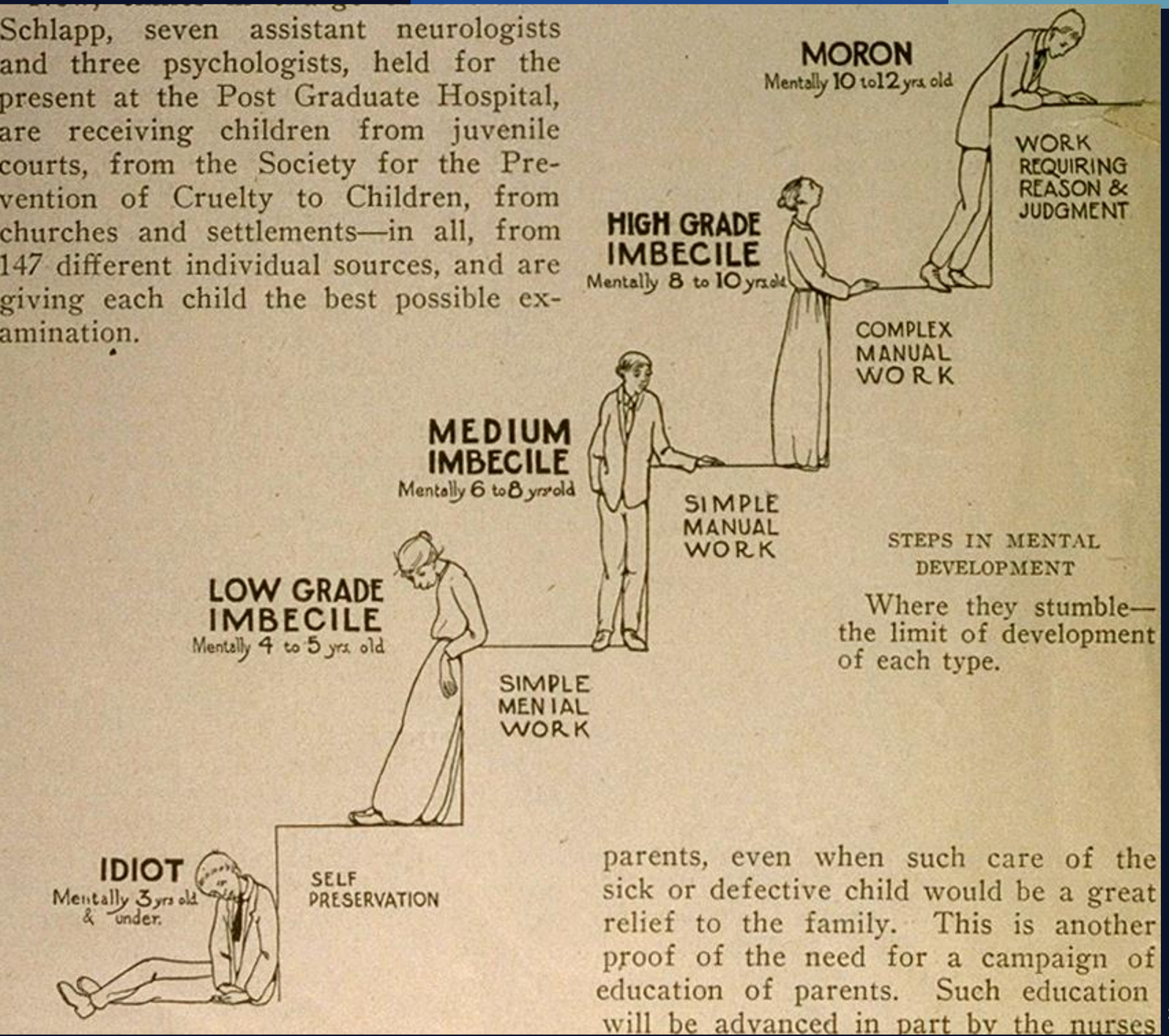
OCTOBER 29, 1926.

HEREDITY IS BIG PROBLEM

Home for Feeble-Minded Is Filled With Those Whose Parents Were Not as Carefully Selected as Dairymen Breed Cattle

The Women's Auxiliary to the dairymen, who met in the roof garden of the Hotel Vermont yesterday afternoon, listened to talks by Miss Sara M. Holbrook, department of education, U. V. M., and Prof. H. F. Perkins of the University, head of the zoology department.

Schlapp, seven assistant neurologists and three psychologists, held for the present at the Post Graduate Hospital, are receiving children from juvenile courts, from the Society for the Prevention of Cruelty to Children, from churches and settlements—in all, from 147 different individual sources, and are giving each child the best possible examination.



STEPS IN MENTAL DEVELOPMENT

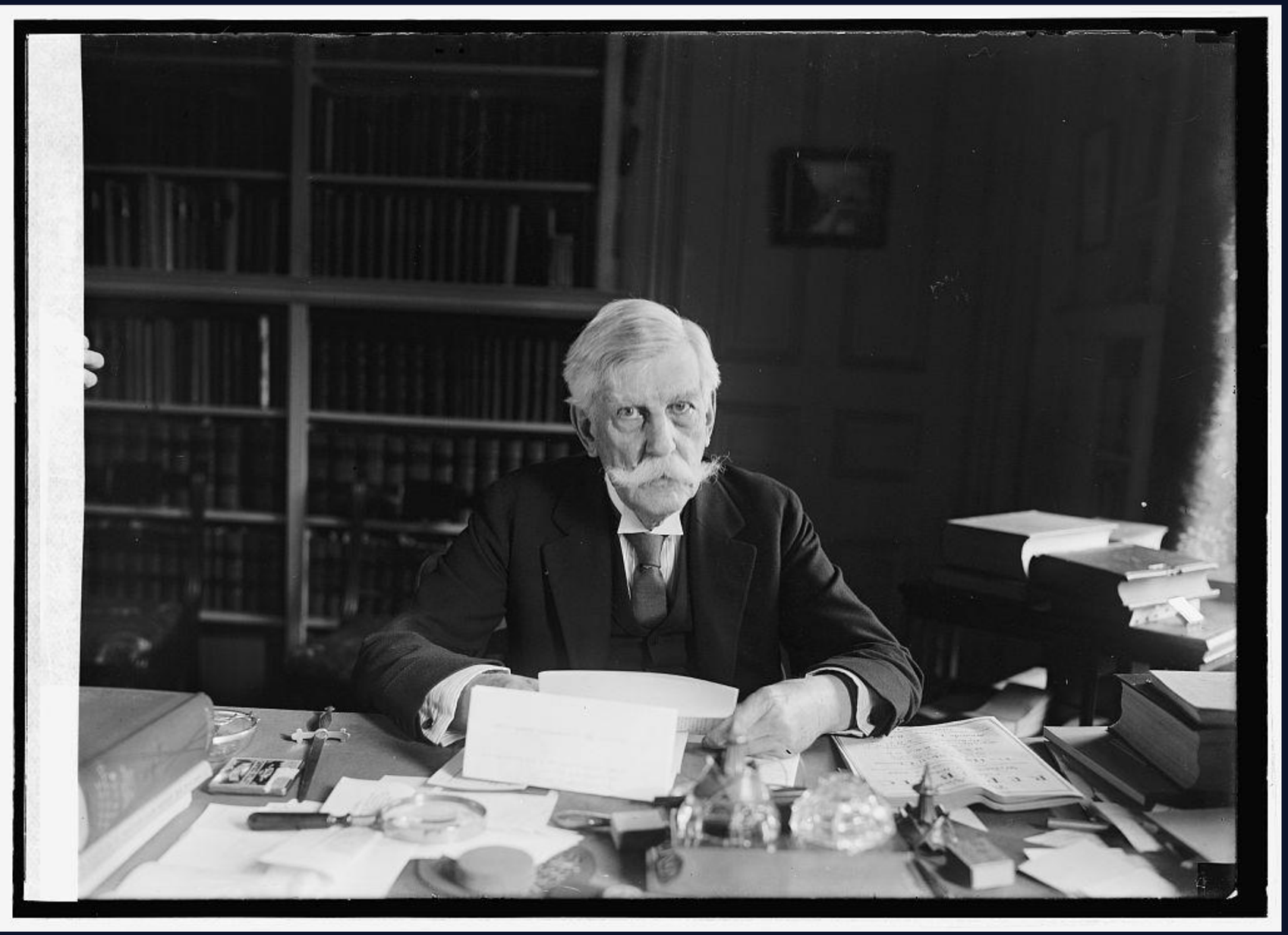
Where they stumble—the limit of development of each type.

parents, even when such care of the sick or defective child would be a great relief to the family. This is another proof of the need for a campaign of education of parents. Such education will be advanced in part by the nurses

Making the case for eugenics:

Arguing certain people are destined to become a "burden"

Photo: 1906. Source: American Philosophical Society, ERO, MSC77,Ser1,Box35: Trait Files



US Library of Congress

Supreme Court ruling: Buck v. Bell allows forced sterilization

"...society can prevent those who are manifestly unfit from continuing their kind... Three generations of imbeciles are enough."
-Justice Oliver Wendell Holmes, Jr.

Quote source: Buck v. Bell, 274 US 200 – Supreme Court 1927

Pedigrees used to justify sterilization

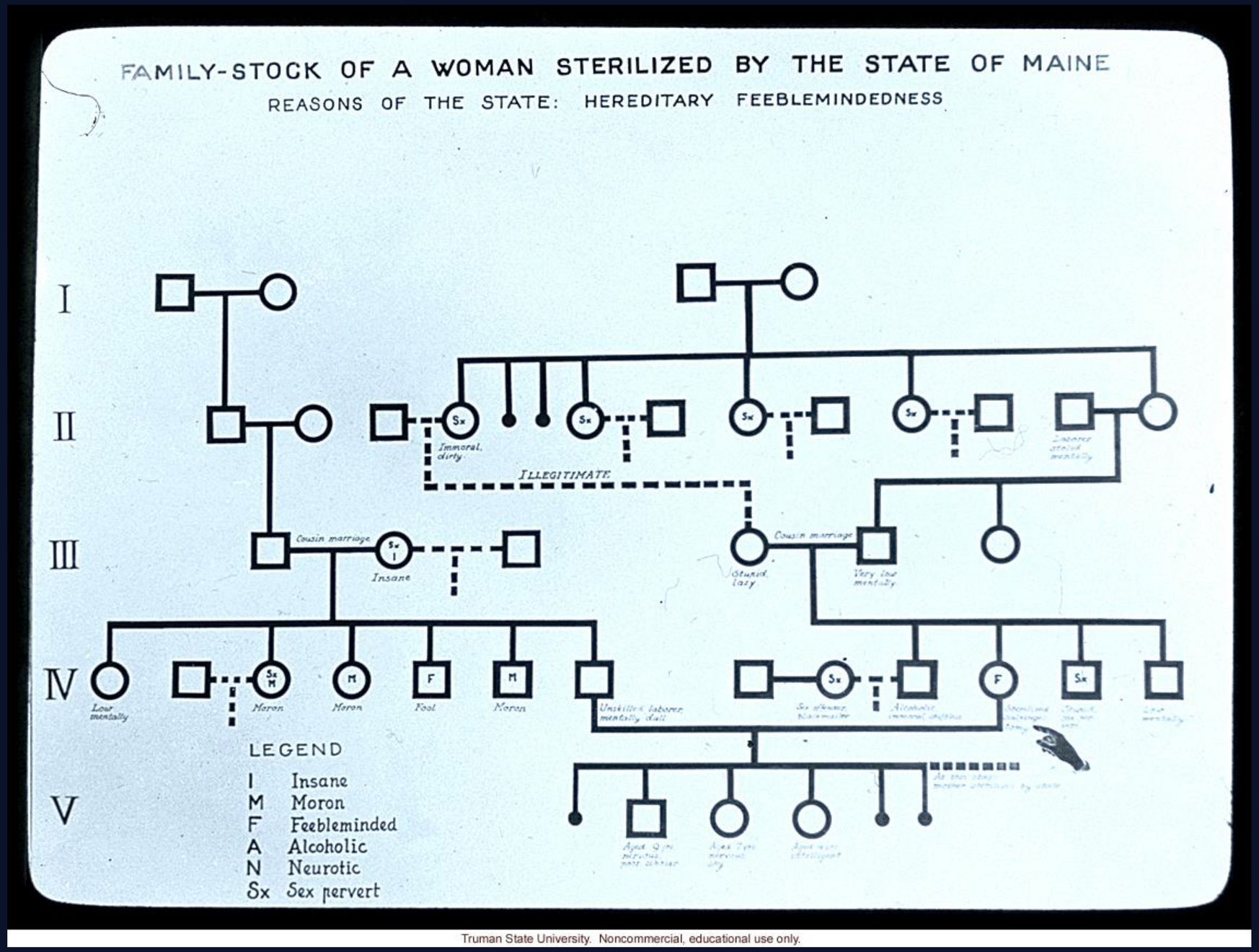


Photo: circa 1935. Source: The Harry H. Laughlin Papers, Truman State University, Lantern Slides, IBM Box,Box 10

Echoes of the past: Sterilization in the 2000s

Judge to inmates: Get sterilized and I'll shave off jail time

Derek Hawkins, *Washington Post* (July 21, 2017)

Following reports of forced sterilization of female prison inmates, California passes ban

Hunter Schwarz, *Washington Post* (September 26, 2014)

Many perspectives are needed to forge a path forward

Upcoming webinars in this series

Difference, not deficit: Reframing the conversation around genetics, deafness, and disability

CRIPSR has extensive medical and health implications – but what about other sectors of society?

How could genome editing impact our environment?

Cassava

pxfuel.com
Neil Palmer, CC BY-SA 2.0

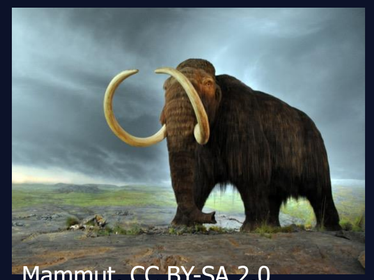
Agriculture case study: Using genome editing to lower the toxicity of an important food crop – cassava.

Honeycreeper

USFWS – Pacific Region,
CC BY-NC 2.0

Insect-borne disease case study: Using genome editing to engineer mosquitoes to prevent them from infecting Hawaiian honeycreepers with avian malaria.

Mammoth



Mammut, CC BY-SA 2.0

De-extinction and permafrost preservation case study: Using genome editing to bring back the woolly mammoth to help prevent thawing of permafrost.

Cassava

Do Now: Discuss the following with the person (or people) next to you:

You live in a rural village and your relatives are suffering from Konzo, a disease that causes paralysis. You rely on a plant called cassava as your main source of food. Cassava naturally produces a toxin. At high concentration, this toxin can make people sick with Konzo. However, soaking the cassava in water for a couple of days before eating it prevents this problem.

Scientists have proposed to genetically alter the cassava plant to make it less dangerous. You wonder whether providing a clean source of water, such as a well, to your village could be a better solution. What are the questions you have for the scientists about their plan?

Cassava

Cassava is an important food crop for over 800 million people worldwide

Colombia, South America

Ghana, Africa

Vietnam, Asia

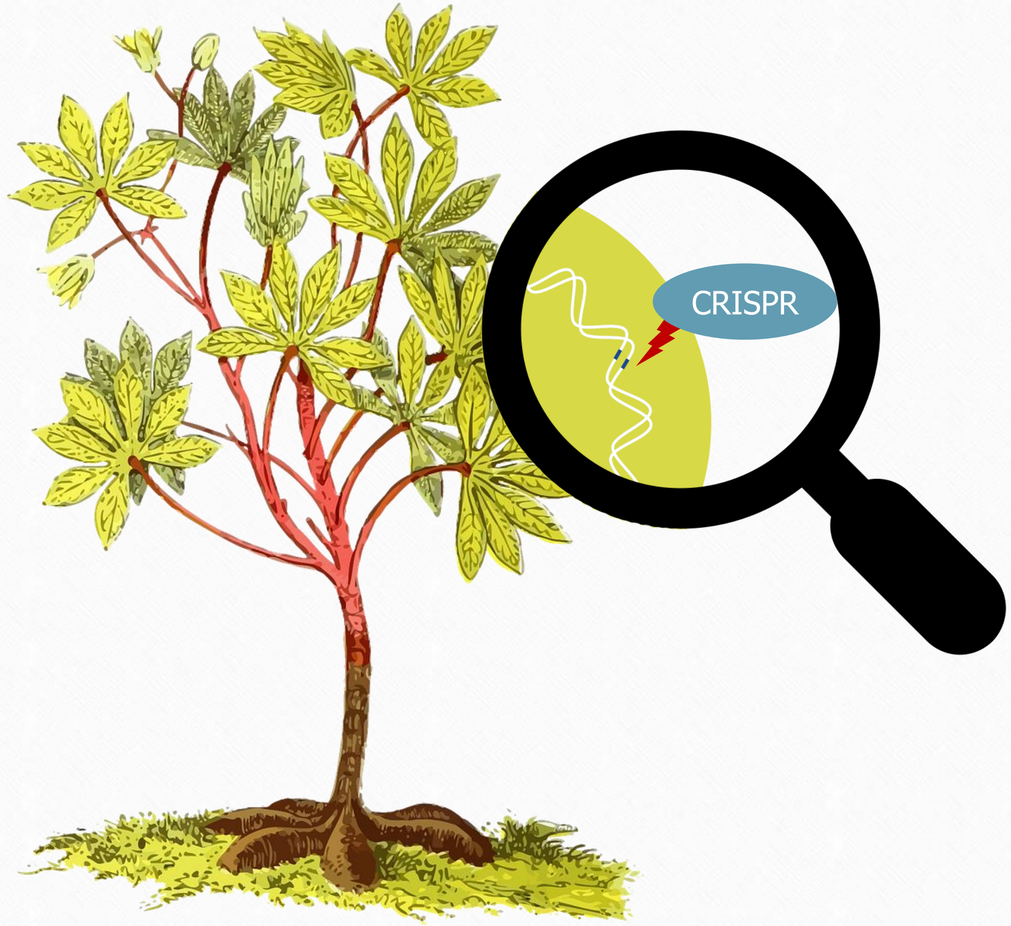
Cassava

Cassava can cause a disease called Konzo

- Cassava naturally produces a toxin, which is present at higher levels when the plant is grown in drought conditions.
- At high levels, this toxin can cause Konzo, a disease that leads to paralysis and can potentially be deadly.
- Soaking the cassava in water and eating a protein-rich diet can prevent Konzo and make cassava a safe source of food.
- Konzo is a disease of poverty, because poverty often limits access to water and a protein-rich diet.

Cassava

Genome editing of the cassava's DNA could be used to lower the plant's toxicity.



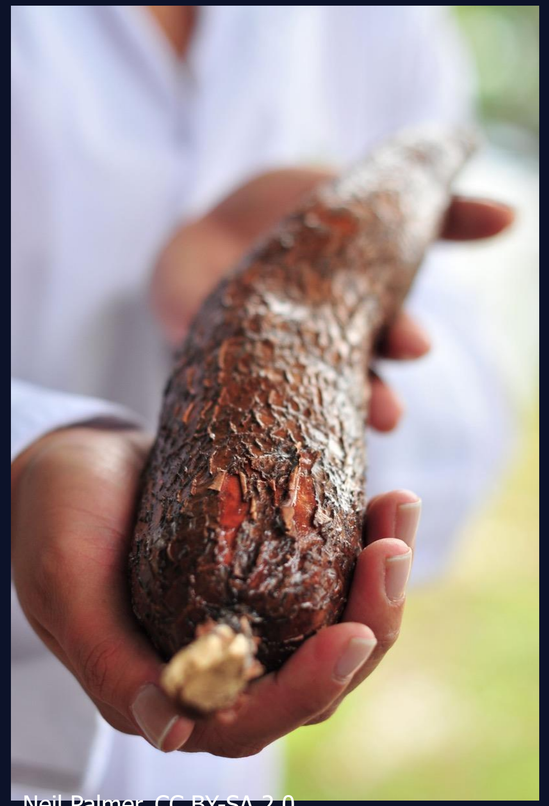
- Cassava has 2 genes that are responsible for the plant's toxic effects.
- CRISPR could be used to edit these genes to reduce the toxicity of cassava.

Schematic created by pgEd (Nadine Vincenten)

Cassava

Major questions and considerations

- Could genome editing negatively affect the plant's drought-tolerance, a very beneficial trait for many regions across the globe?
- Could genome editing of cassava make the plant more vulnerable to insects? If so, would farmers need to use pesticides to grow their crop?
- Will someone own the edited plants? What about the seeds?
- Should efforts in preventing Konzo lie with this genome editing approach? Or should the focus be on breaking the cycle of poverty? Might a combination of approaches be the best way forward?



This CRISPR pioneer wants to capture more carbon with crops

New research at Jennifer Doudna's institute aims to create faster-growing, carbon-hungry plants using the gene-editing tool.

By Casey Crownhart June 14, 2022

INNOVATIVE GENOMICS INSTITUTE

https://www.technologyreview.com/2022/06/14/1053843/carbon-capture-crispr-cro

Agricultural issues closer to home?

nature › horticulture research › review articles › article

Review Article | Open Access | Published: 01 January 2021

Can gene editing reduce postharvest waste and loss of fruit, vegetables, and ornamentals?

Emma N. Shipman, Jingwei Yu, Jiaqi Zhou, Karin Albornoz & Diane M. Beckles

Horticulture Research **8**, Article number: 1 (2021) | Cite this article

11k Accesses | **22** Citations | **54** Altmetric | Metrics

Abstract

Approximately 33% of the produce that is harvested is never consumed since these products naturally have a short shelf-life…This loss, however, could be reduced by breeding new crops that retain desirable traits and accrue less damage over the course of long supply chains.

New gene-editing tools promise the rapid and inexpensive production of new varieties of crops with enhanced traits more easily than was previously possible.

https://www.nature.com/articles/s41438-020-00428-4

Agricultural issues closer to home?

AP

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Maine's blueberry crop faces climate change peril

By PATRICK WHITTLE June 5, 2021

SYSTEMATIC REVIEW article

Front. Sustain. Food Syst., 07
September 2021
Sec. Crop Biology and Sustainability
https://doi.org/10.3389/fsufs.2021.685801

Application of Gene Editing for Climate Change in Agriculture

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[4] Horticultural Sciences Department, University of Florida, Gainesville, FL, United States
[5] Department of Global Development, Cornell University, Ithaca, NY, United States

Mechanism of CRISPR gene editing system