



# Scientific Overview: Introduction to Genetics and Genomics

Genetics and the Law, PHG 523/LAW H 520

Sarah Nelson, MPH, PhD

January 6<sup>th</sup>, 2021

# Learning objectives



Understand different types of genetic variation



Describe the relationship between genotype and phenotype



Recognize major milestones in the history of genetic research



Identify applications of genomics relevant to legal issues

*Overall goal: Gain basic scientific understanding of genetics in order to apply the law and legal concepts in cases that involve genetics*

# Outline

I. Basic Biology

II. Genetic Research

III. Applications



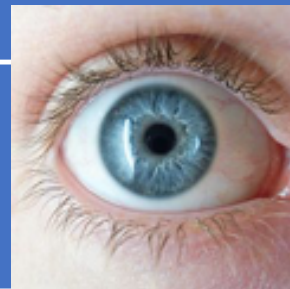
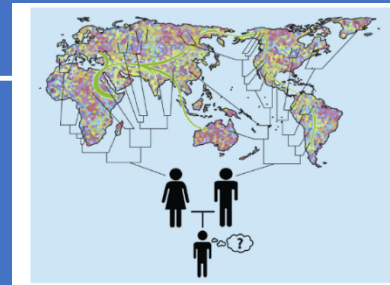
# “Many orientedness” of DNA

Family relationships

Ancestry/population  
history

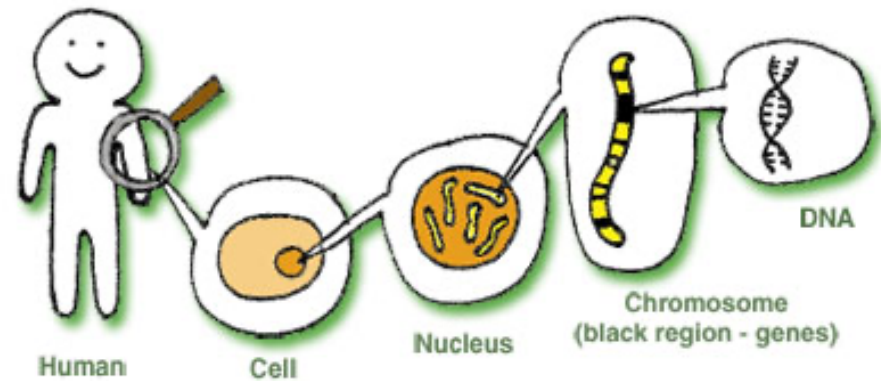
Disease risk/susceptibility

Non-medical traits

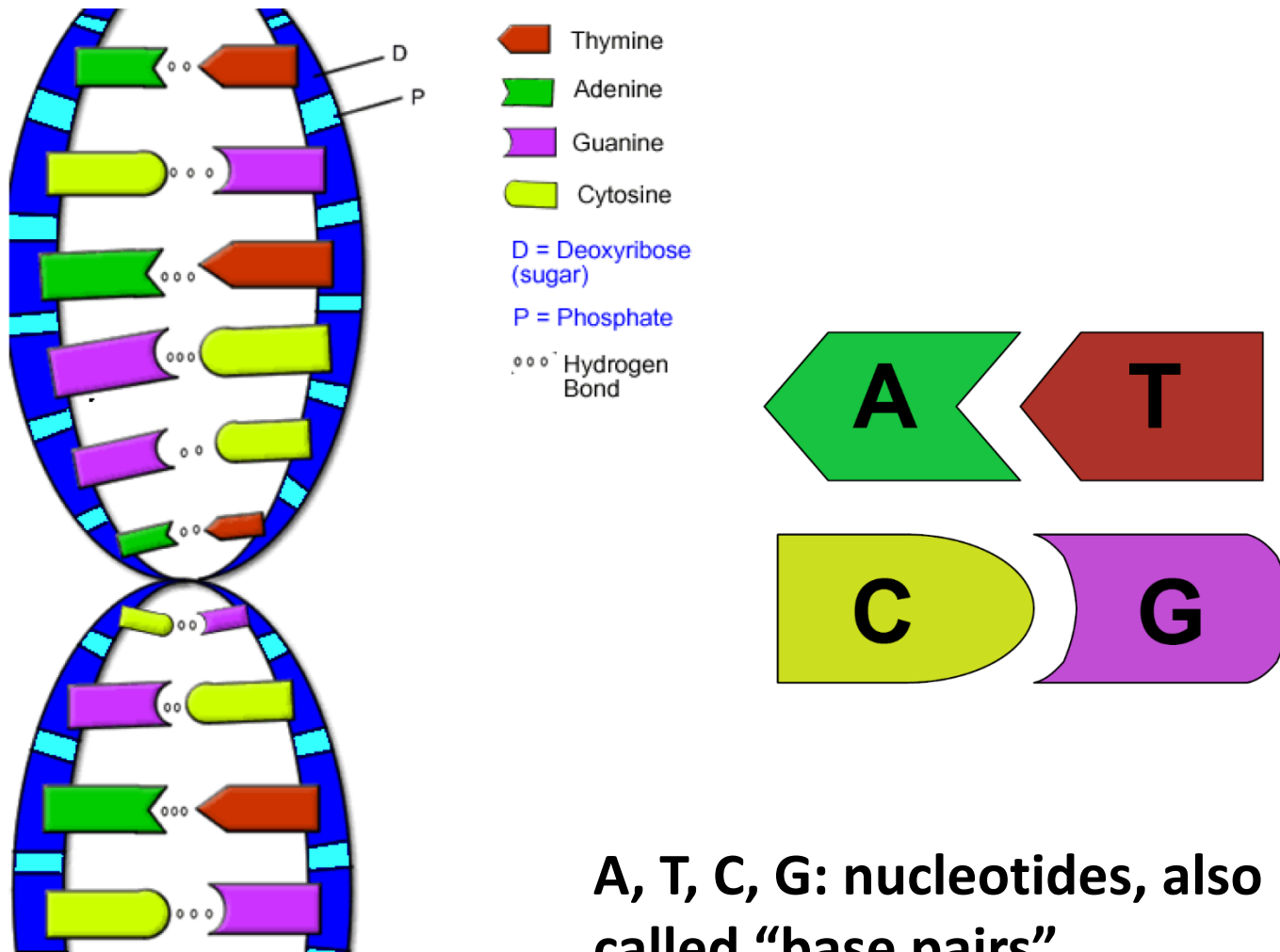


# Basic Biology: overview

- DNA
  - Molecule that carries genetic information
- Genes
  - Protein-coding units of DNA
  - ~20K genes in human genome
- Chromosomes
  - Organized packages of DNA
  - Located in nucleus of the cell
- Human genome
  - Entire set of genetic instructions found in a cell



# What Does DNA Look Like?



**A, T, C, G: nucleotides, also called “base pairs”**

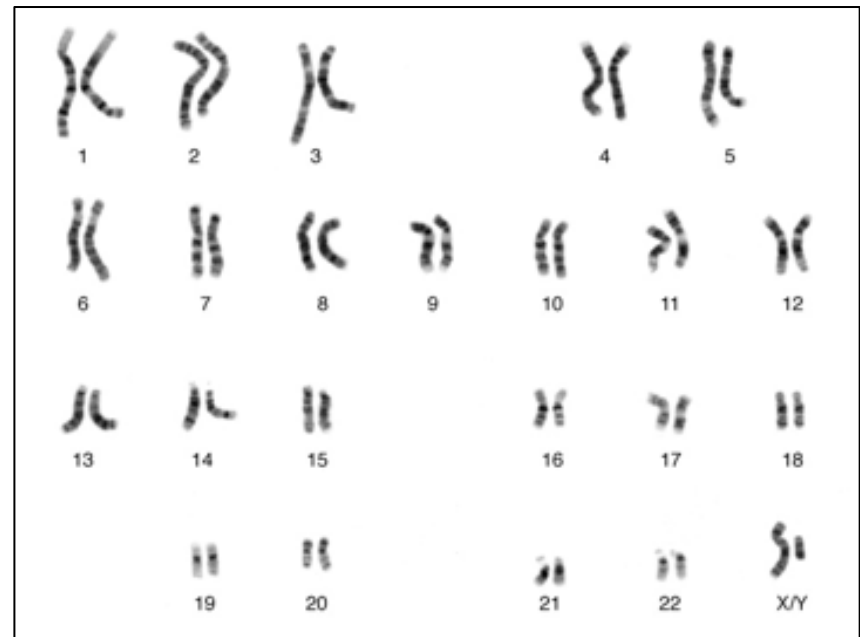
# DNA is organized into chromosomes

## Chromosomes

- Humans: chromosomes 1-22 (autosomes) and sex chromosomes (X, Y)
- One set of chromosomes from each parent

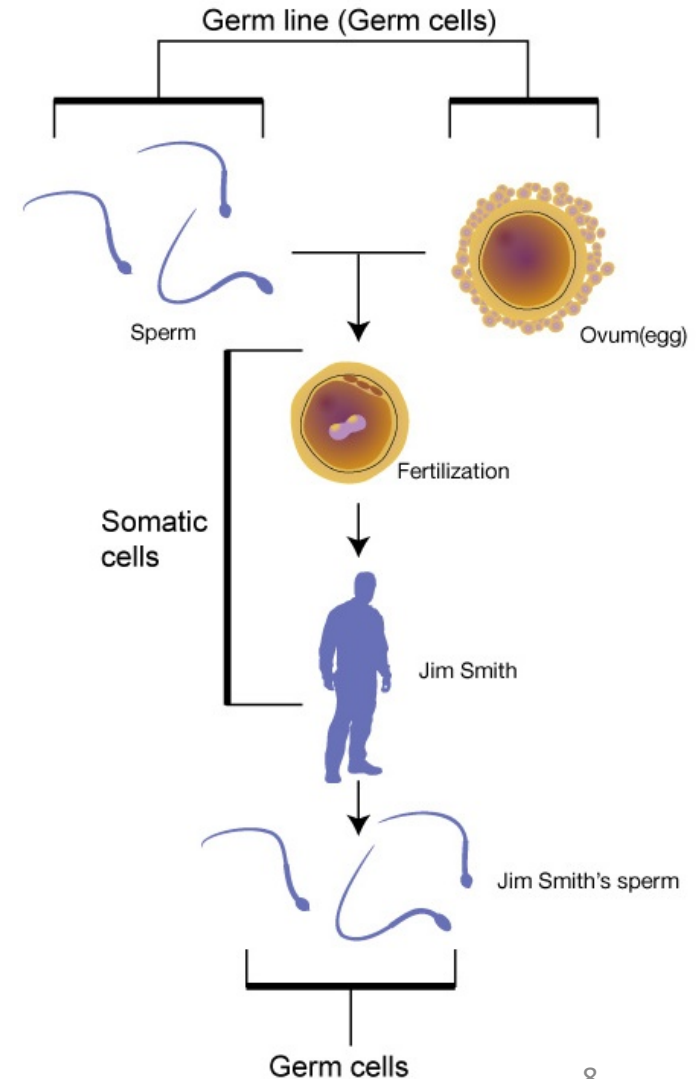
## Karyotype

- An individual's collection of chromosomes
- Laboratory visualization technique



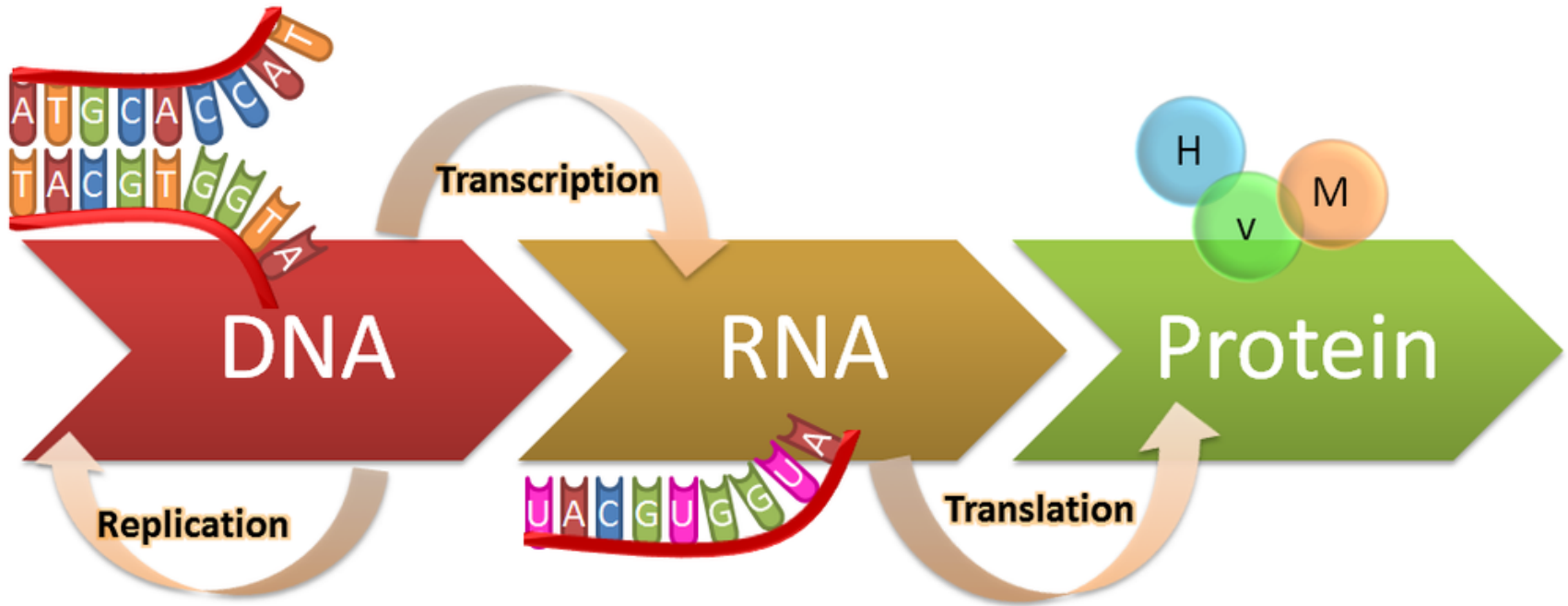
# Somatic vs. Germline genome

- Germ cells
  - Reproductive cells (i.e., sperm and egg)
  - Genetic content passed onto offspring
- Somatic cells
  - Non-germline
    - Your other body tissues and parts (heart, blood, liver, etc.)
    - “soma” = body in Greek
  - Genetic content NOT passed onto offspring
    - Can be “passed on” to daughter cells during cell division, in the same person)





# “Central Dogma” of Biology

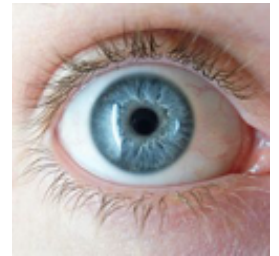


# Genotype and Phenotype

- Genotype: genetic information



- Phenotype: outward expression of a trait



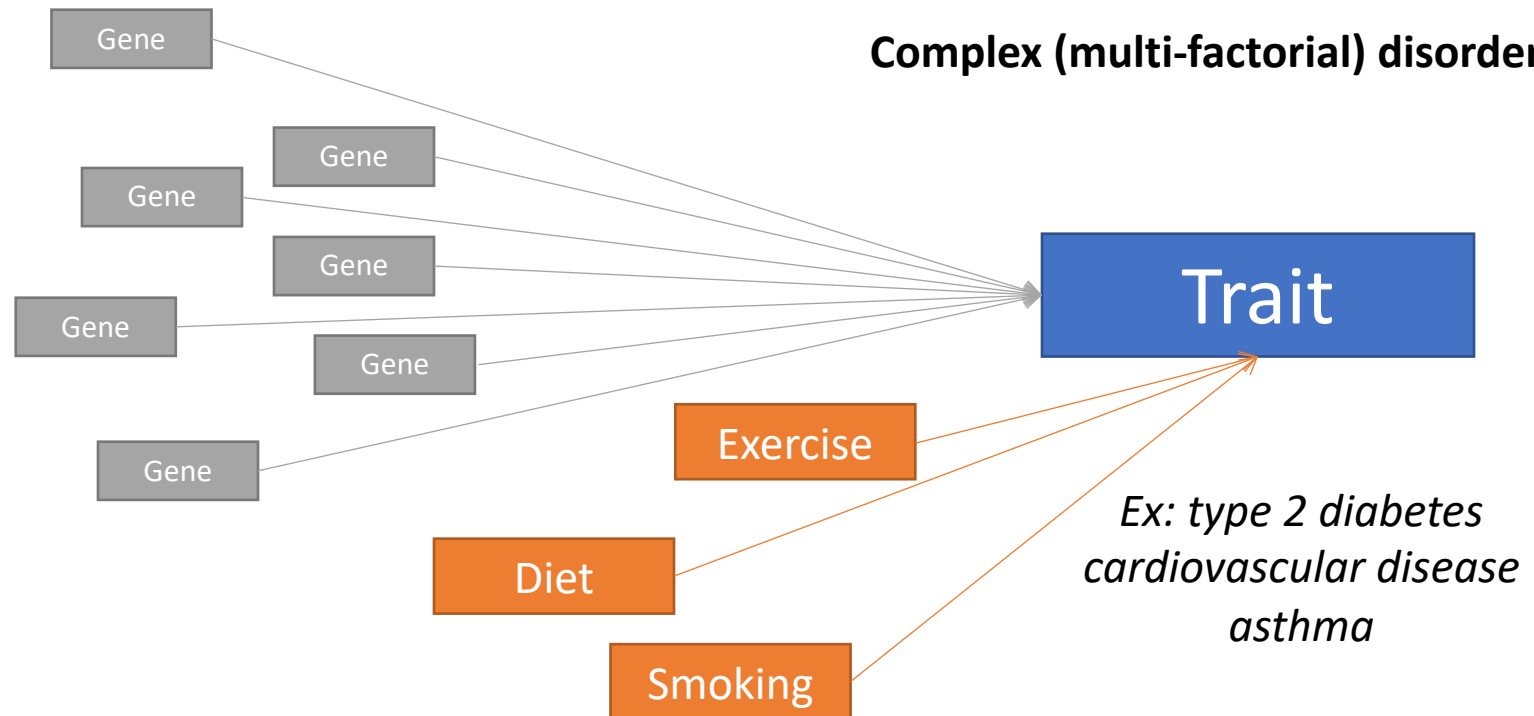
- Genotype matters more for some phenotypes than others...

# Genotype and Phenotype

## Mendelian (single gene) disorder

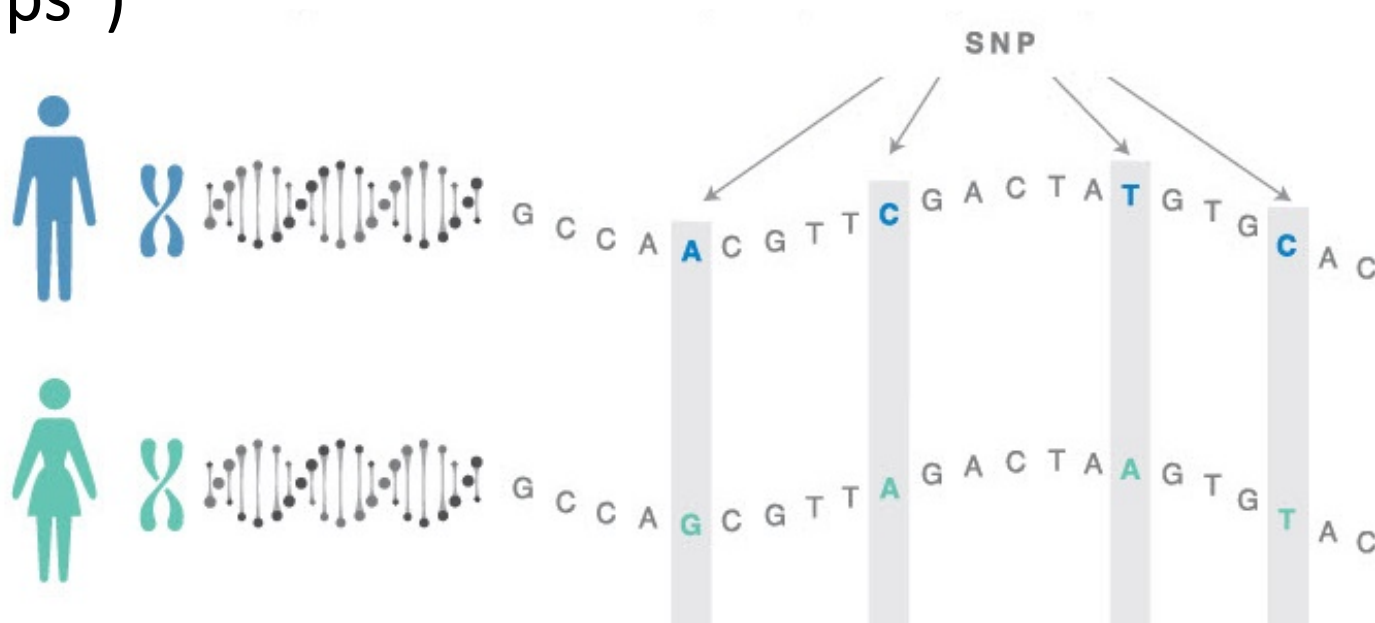


## Complex (multi-factorial) disorder



# Types of genetic variation

## 1) Single Nucleotide Polymorphisms (SNPs, or “snips”)

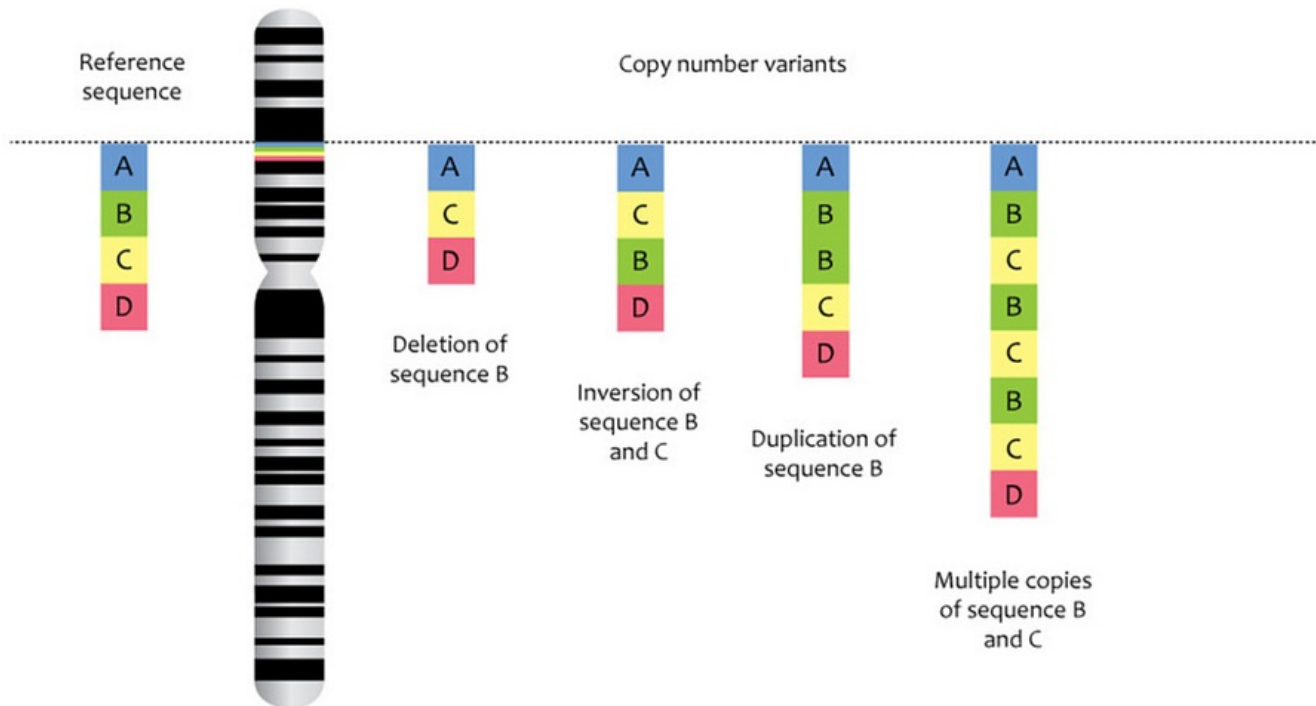


**Legal application: investigative genetic genealogy**

# Types of variation

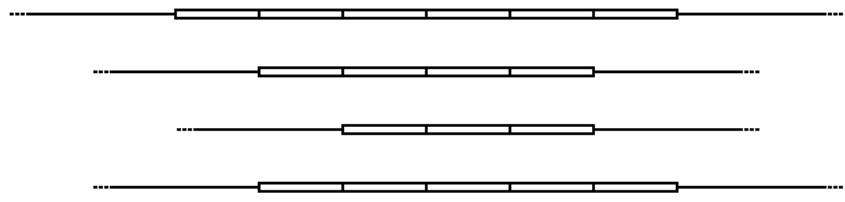
## 2) Copy number variation (CNV)

- also referred to as structural variation

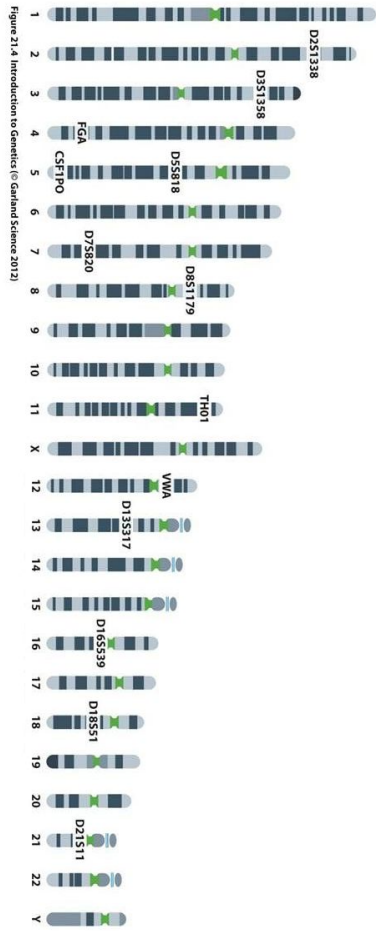
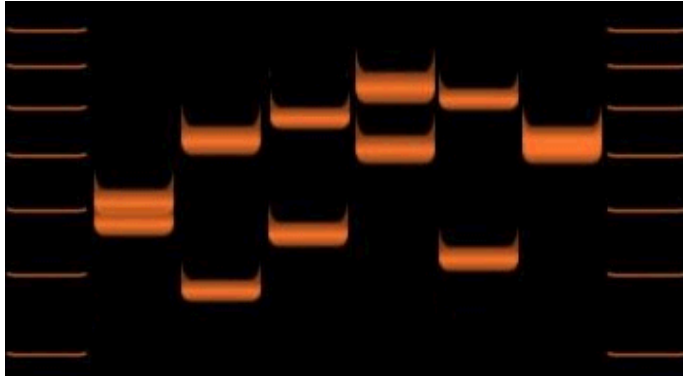


# Short Tandem Repeats (STRs)

- Repeating sequences of 2-6 base pairs of DNA
- Multi-allelic



- Specimen DNA amplified, and samples are separated by size

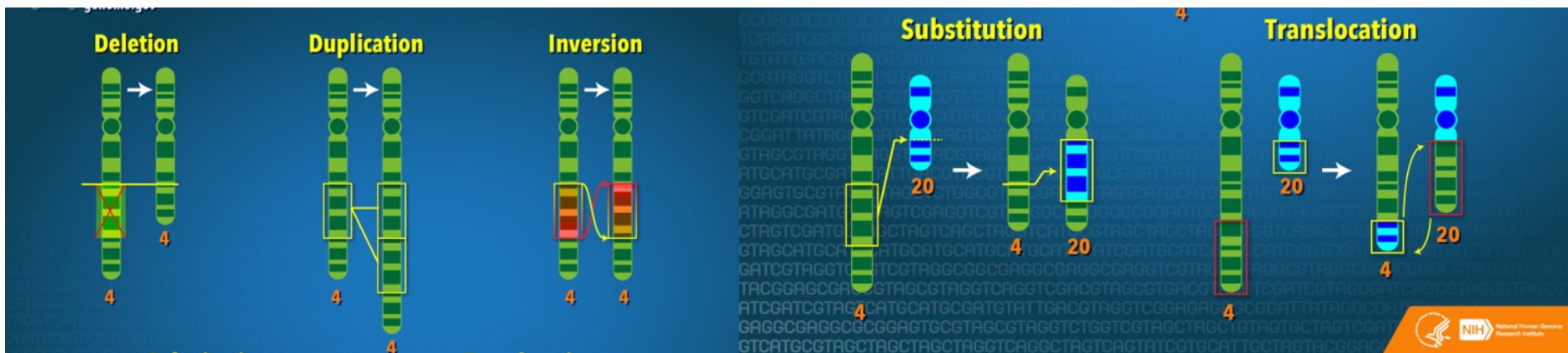


**Legal application: Combined DNA Index System (CODIS)**

# Type of variation

## 3) Chromosomal anomalies

- Large pieces of chromosomes deleted, duplicated, or rearranged



- Also whole chromosome deletions or duplications
  - e.g., Trisomy 21 – 3 copies of chrom21 – Down syndrome
  - Sex chromosome aneuploidies: XXX, XXY, XYY, XO

# Types of Genetic Variation

## GERMLINE

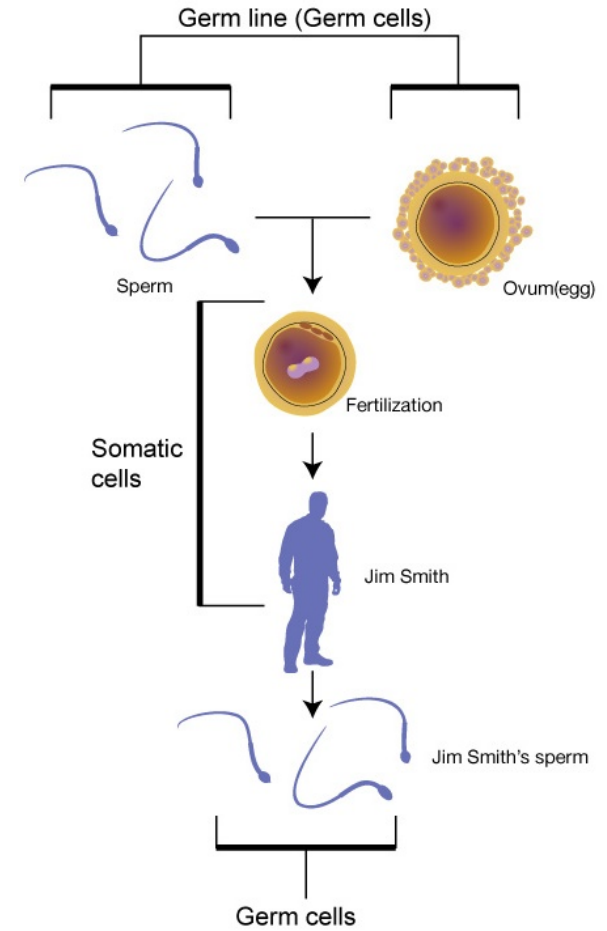
- Inherited from parents
- New (de novo) mutations in sperm or egg cells (germline)

CAN be passed on to offspring

## SOMATIC

- Acquired variation in non-germ cells, e.g. from....
- Errors in DNA replication
- DNA damage from environment
- Intentional modification (gene therapy)

CANNOT be passed on to offspring







# Variation: additional terms

- **Locus:** specific physical location of a gene or other DNA sequence on a chromosome (plural=“loci”)
  - Could be a single SNP or an entire gene
- **Allele:** one of two or more versions of a locus
  - E.g.: a SNP with two alleles, A and G
  - Alleles can also refer to longer stretches of a DNA
    - E.g., a neighboring set of SNPs, called a “haplotype” or a whole gene
- **Homozygous:** both alleles are the same (e.g., AA)
- **Heterozygous:** two alleles are different (e.g., AG)



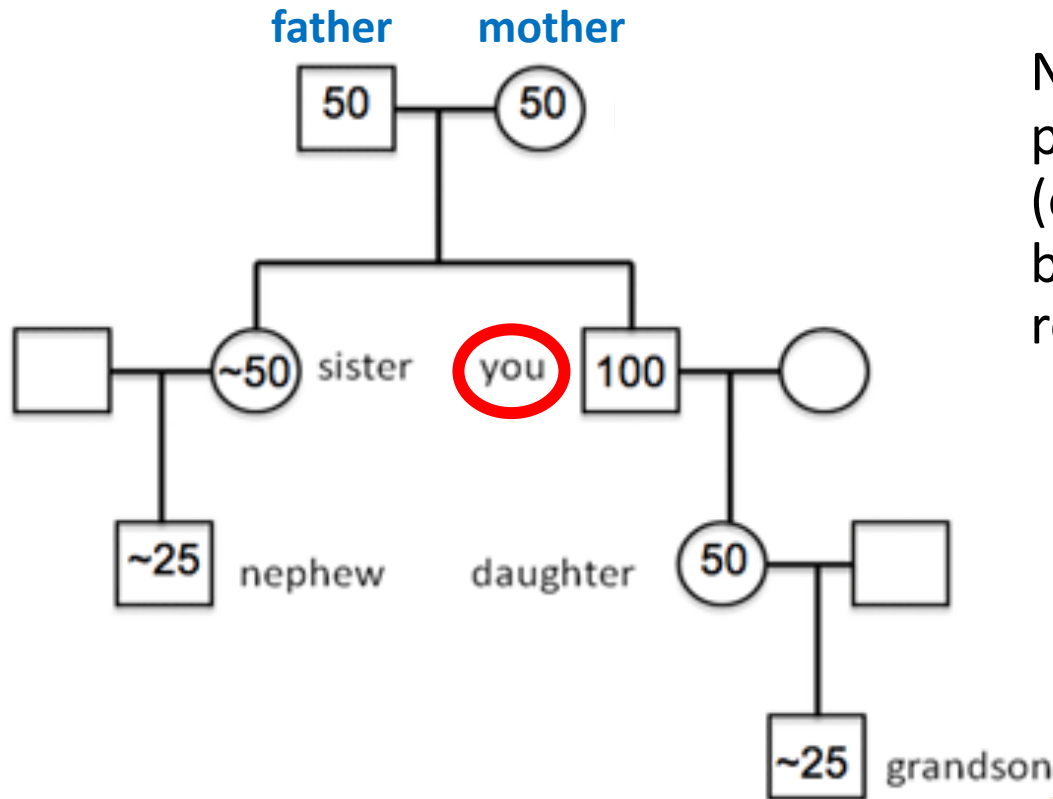
# Variation on what?

---

- Being a DNA “variant” typically means the DNA sequence varies/differs from the **human genome reference sequence**
  - Generated during Human Genome Project (more later)
  - A consensus sequence based on ~20 anonymous donors
  - Not comprehensive representative of human genetic variation worldwide
  - But practically useful for measuring and describing DNA variation
    - E.g., at a given position, does a chromosome contain the “reference” vs an “alternative” allele

# Relatedness

Pedigree: common way of depicting family relationship



Numbers given are the percent of genetic material (on average) shared between these different relative pair types



**Legal applications: Family law; familial searching**

## II. GENETIC RESEARCH

# Learning objectives



Understand different types of genetic variation



Describe the relationship between genotype and phenotype



Recognize major milestones in the history of genetic research



Identify applications of genomics relevant to legal issues

*Overall goal: Gain basic scientific understanding of genetics in order to apply the law and legal concepts in cases that involve genetics*

# II. Genetic Research

- Overall goal

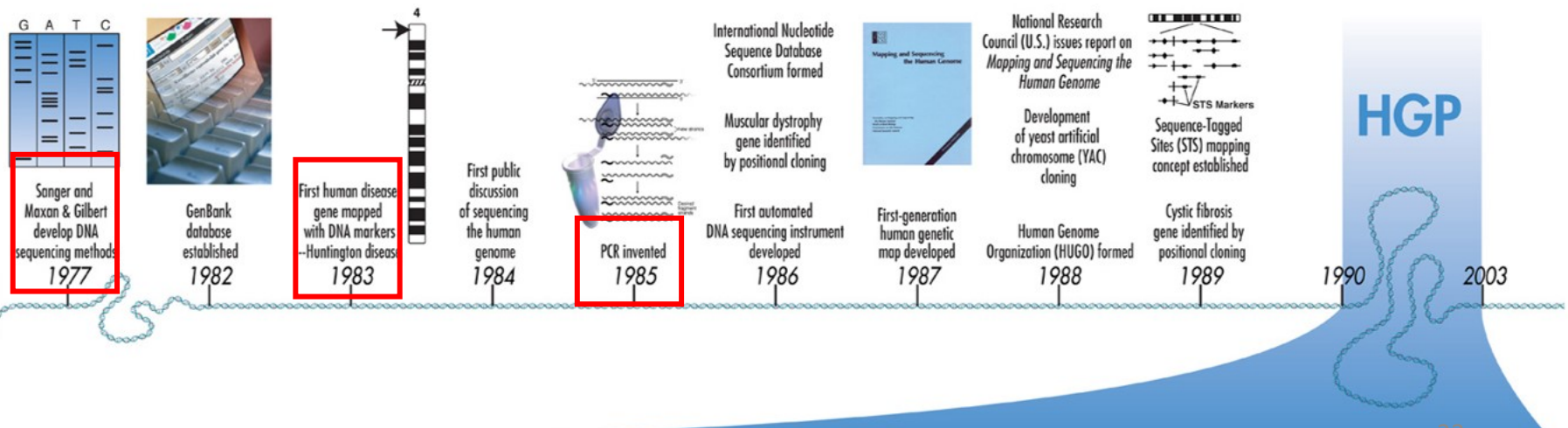
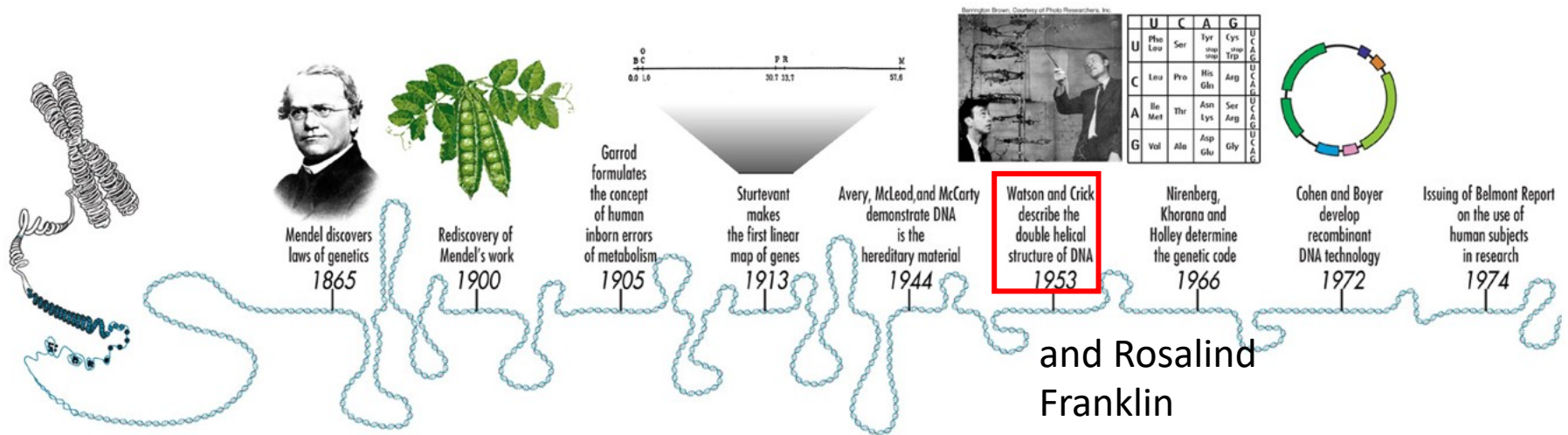
To **understand** human biology and disease in order to **improve** individual and population health

- Basic → clinical → translational (“bench to bedside”)

- Theme

Advances in laboratory technologies, bioinformatics, and statistical techniques have allowed new research directions

# Genetic research pre 21<sup>st</sup> century



# Research highlights

## Project

## Technical side note

Human Genome Project

Sanger sequencing

HapMap Project

Genome-wide association studies (GWAS) & genotyping microarrays (“SNP chips”)

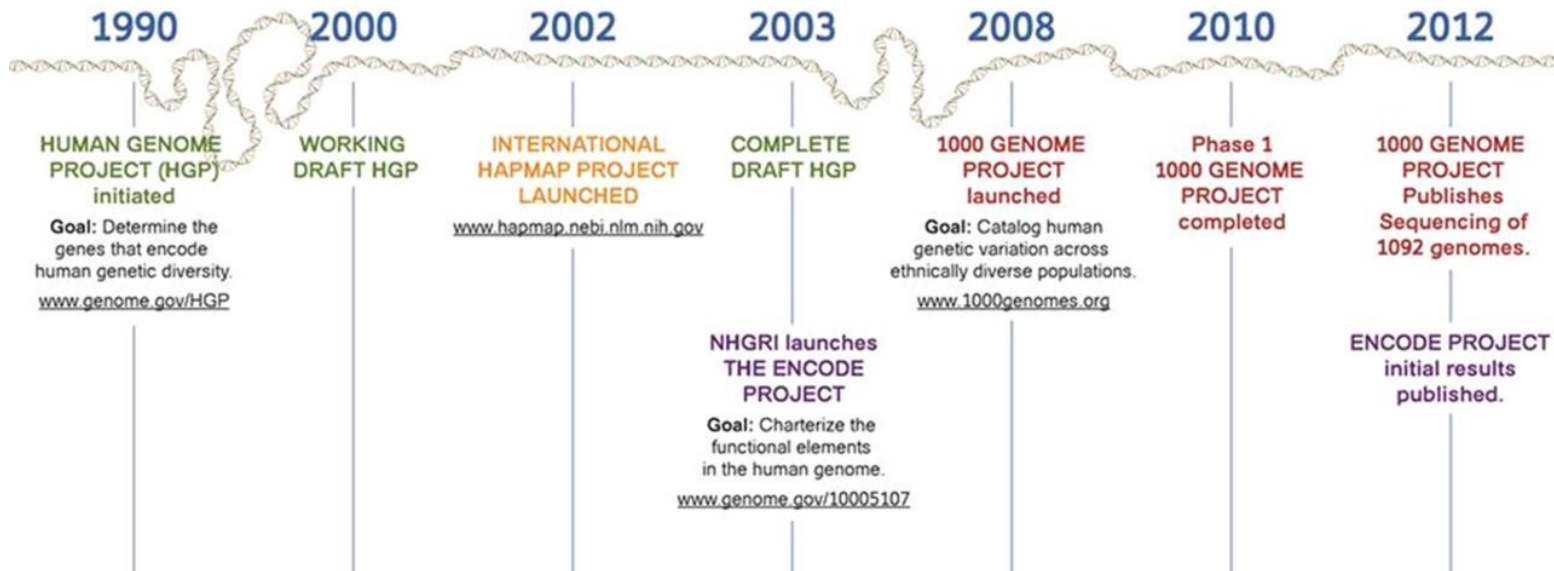
1000 Genomes Project

Next-generation sequencing

Precision Medicine Initiative

Combine genomics with other “omics”

## HUMAN GENOMICS TOOLS TIMELINE





# Human Genome Project

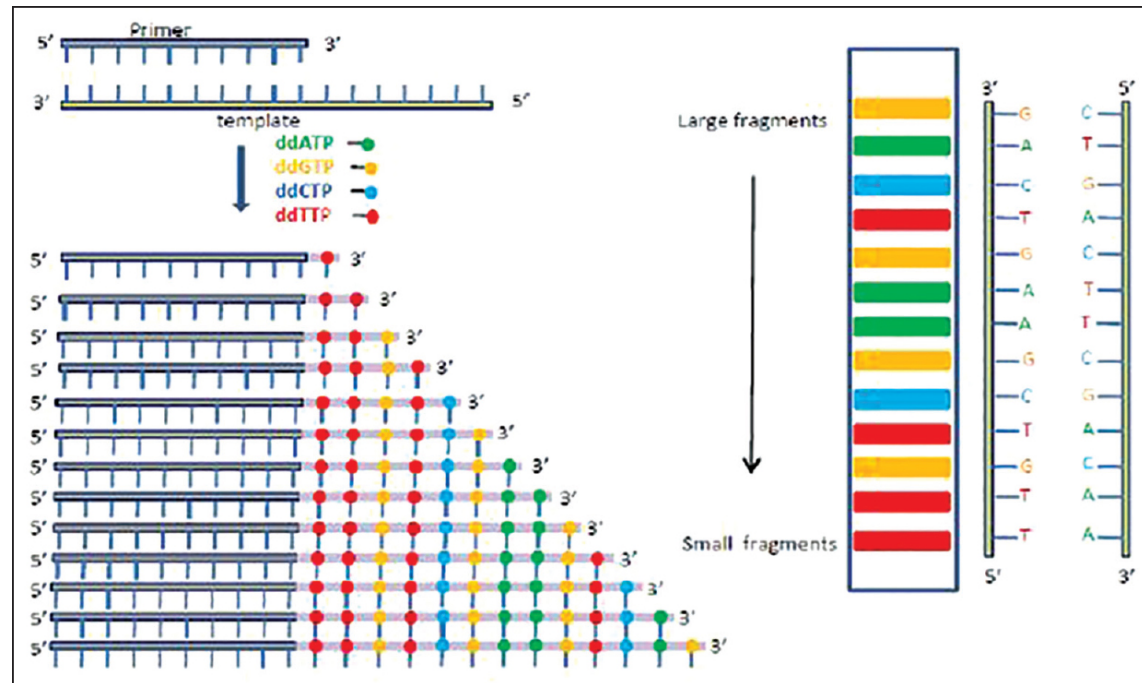


- International, collaborative research program to “map” (determine the sequence of) the human genome
  - In US, led by National Institutes of Health (NIH) and Department of Energy (DOE)
- Launched in 1990, completed in April 2003
  - National Human Genome Research Institute (NHGRI) created in 1997
- Total cost: \$2.7 billion in FY 1991 dollars
  - Cost to US taxpayers
- 5% of NHGRI budget dedicated to examining ethical, legal, and social implications (ELSI) of genetics

# HGP, cont.

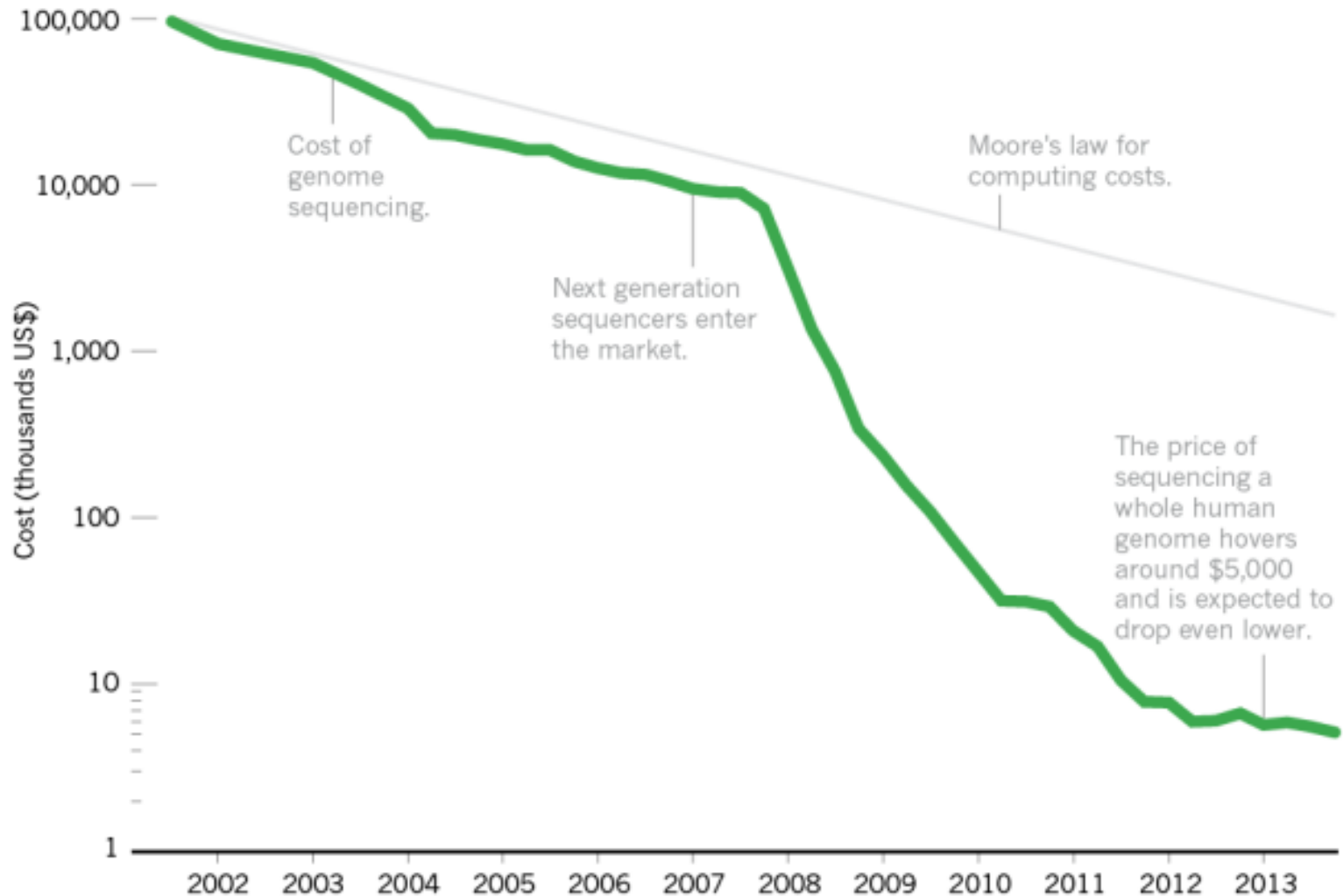
- “human genome reference sequence”
  - Composite sequence of a few (~20) anonymous individuals
- Sanger sequencing technology

- Slow
- Expensive



# Falling fast

In the first few years after the end of the Human Genome Project, the cost of genome sequencing roughly followed Moore's law, which predicts exponential declines in computing costs. After 2007, sequencing costs dropped precipitously.



# Post-HGP Research Initiatives



- Multi-national project 2002-2009
- Goal of identifying “tag” SNPs that are informative about genotype for other polymorphic loci
  - i.e. catalog **common variants**
- Initially 4 populations but expanded to 11 in final phase

[www.hapmap.ncbi.nlm.nih.gov](http://www.hapmap.ncbi.nlm.nih.gov)

## Technical development:

- SNP microarray or “chip”
  - High throughput
  - Genotype hundreds of thousands to millions of SNPs in one experiment
  - Initially content focused on HapMap “tag” SNPs



# GWAS - Genome-wide Association Studies

NHGRI FACT SHEETS

genome.gov

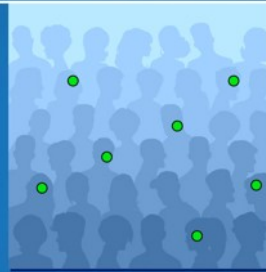
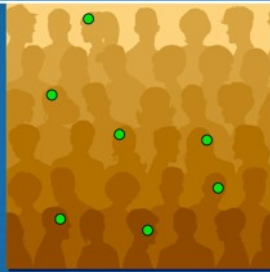
Individuals with disease

Individuals without disease



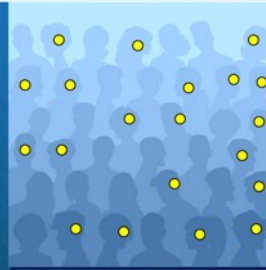
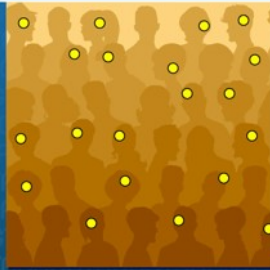
Using a CHIP can genotype  
500,000 - 5 Million SNPs

SNP 1



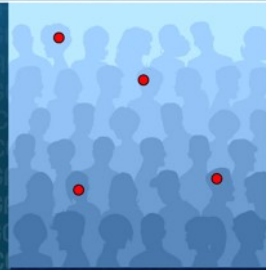
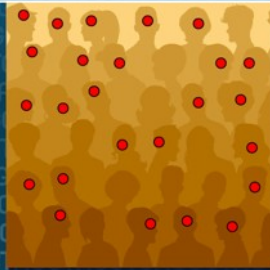
SNP 1  
No association  
to disease

SNP 2



SNP 2  
No association  
to disease

SNP 3



SNP 3  
Associated  
to disease



HapMap Project helps bring us SNP chips which in turn usher in the age of GWAS (2007 – present, though waning)

# NHGRI-EBI GWAS Catalog



This diagram shows all SNP-trait associations with  $p\text{-value} \leq 5.0 \times 10^{-8}$ , published in the GWAS Catalog.

<http://www.ebi.ac.uk/gwas/diagram>

- Digestive system disease
- Cardiovascular disease
- Metabolic disease
- Immune system disease
- Nervous system disease
- Liver enzyme measurement
- Lipid or lipoprotein measurement
- Inflammatory marker measurement
- Hematological measurement
- Body measurement
- Cardiovascular measurement
- Other measurement
- Response to drug
- Biological process
- Cancer
- Other disease
- Other trait

# Post-HGP Research Initiatives, cont.

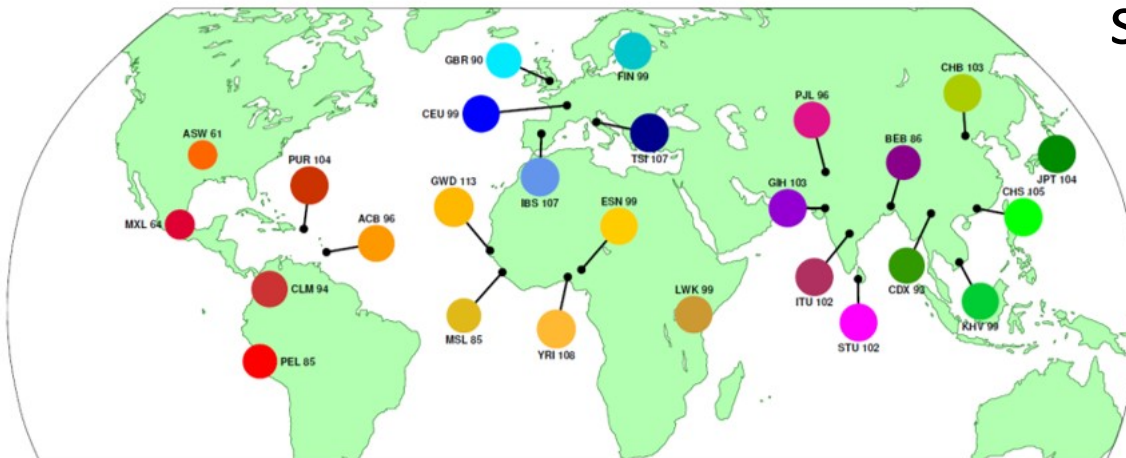
## 1000 Genomes

### A Deep Catalog of Human Genetic Variation

- Multi-national project, 2008-2012
- Sequence the genomes of 2,504 individuals
- Goal of identifying >95% of genetic variation
  - Structural variation
  - Rare variation in genes
  - Population allele frequencies
  - Haplotypes and linkage disequilibrium patterns
- Samples from 26 populations worldwide

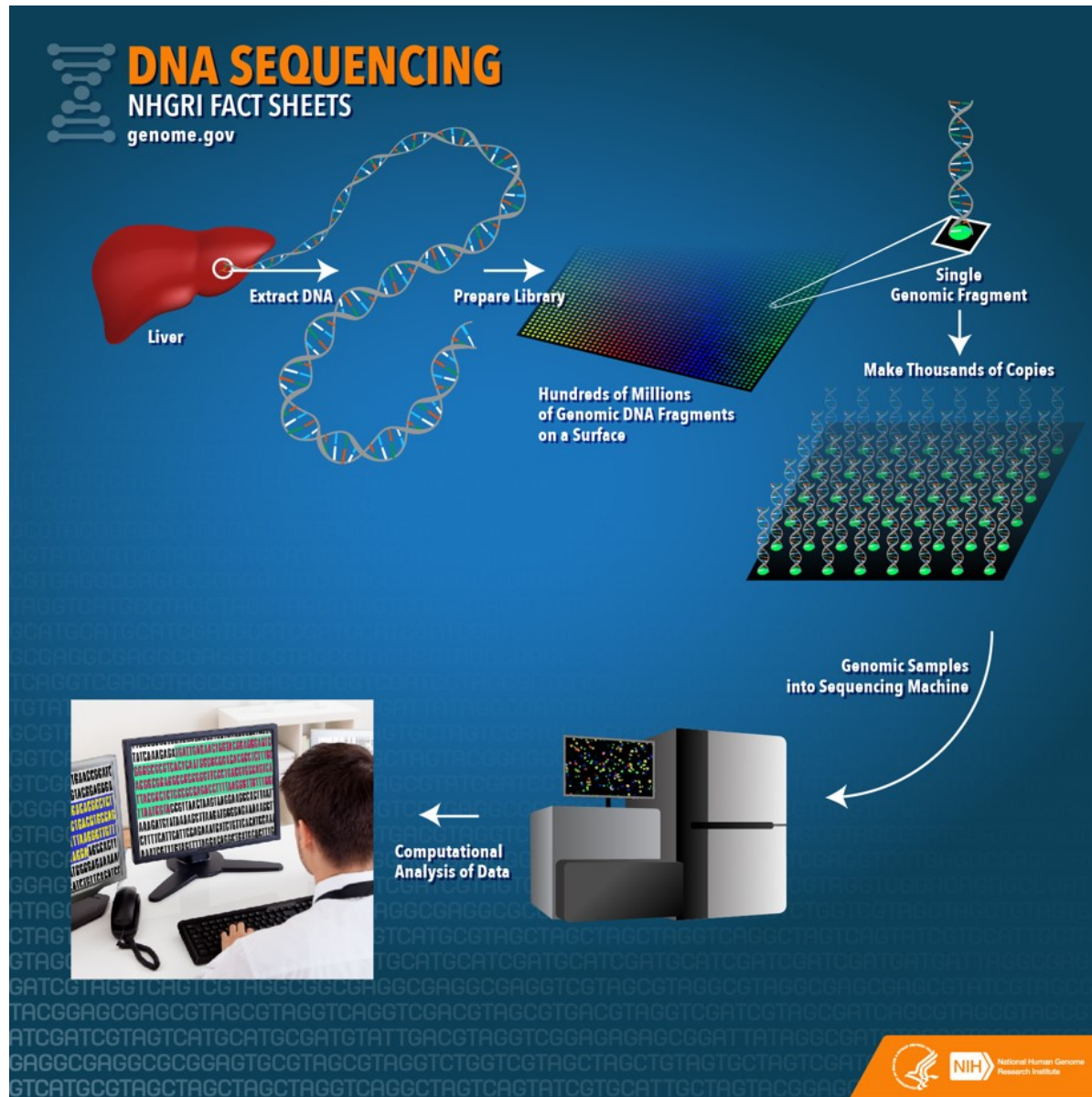
### Technical development:

- Next-generation sequencing (NGS)
- Much quicker and cheaper than Sanger and other earlier sequencing methods



*Image: G. Abecasis slides, ASHG 2014.  
bubble size indicates sample size*

# Next generation DNA sequencing





# Precision Medicine Initiative

- Launched by President Obama during 2015 State of the Union
- Long-term focus: “bringing precision medicine to all areas of health and healthcare on a large scale”
- Now recruiting 1M person **research cohort**, “All of Us”



**All of Us<sup>SM</sup> Research Program**

**WHAT IS IT?**

**Precision medicine** is a groundbreaking approach to disease prevention and treatment based on people's individual differences in environment, genes and lifestyle.

The *All of Us* Research Program will lay the foundation for using this approach in **clinical practice**.

**WHAT ARE THE GOALS?**

Engage a group of **1 million or more U.S. research participants** who will share biological samples, genetic data and diet/lifestyle information, all linked to their electronic health records. This data will allow researchers to develop more precise treatments for **many diseases and conditions**.

Pioneer a new model of research that emphasizes **engaged research participants, responsible data sharing and privacy protection**.

Research based on the cohort data will:

- Lay **scientific foundation** for precision medicine
- Help identify new ways to **treat and prevent disease**
- Test whether **mobile devices**, such as phones and tablets, can encourage healthy behaviors
- Help develop the **right drug** for the **right person** at the **right dose**

**WHY NOW?**

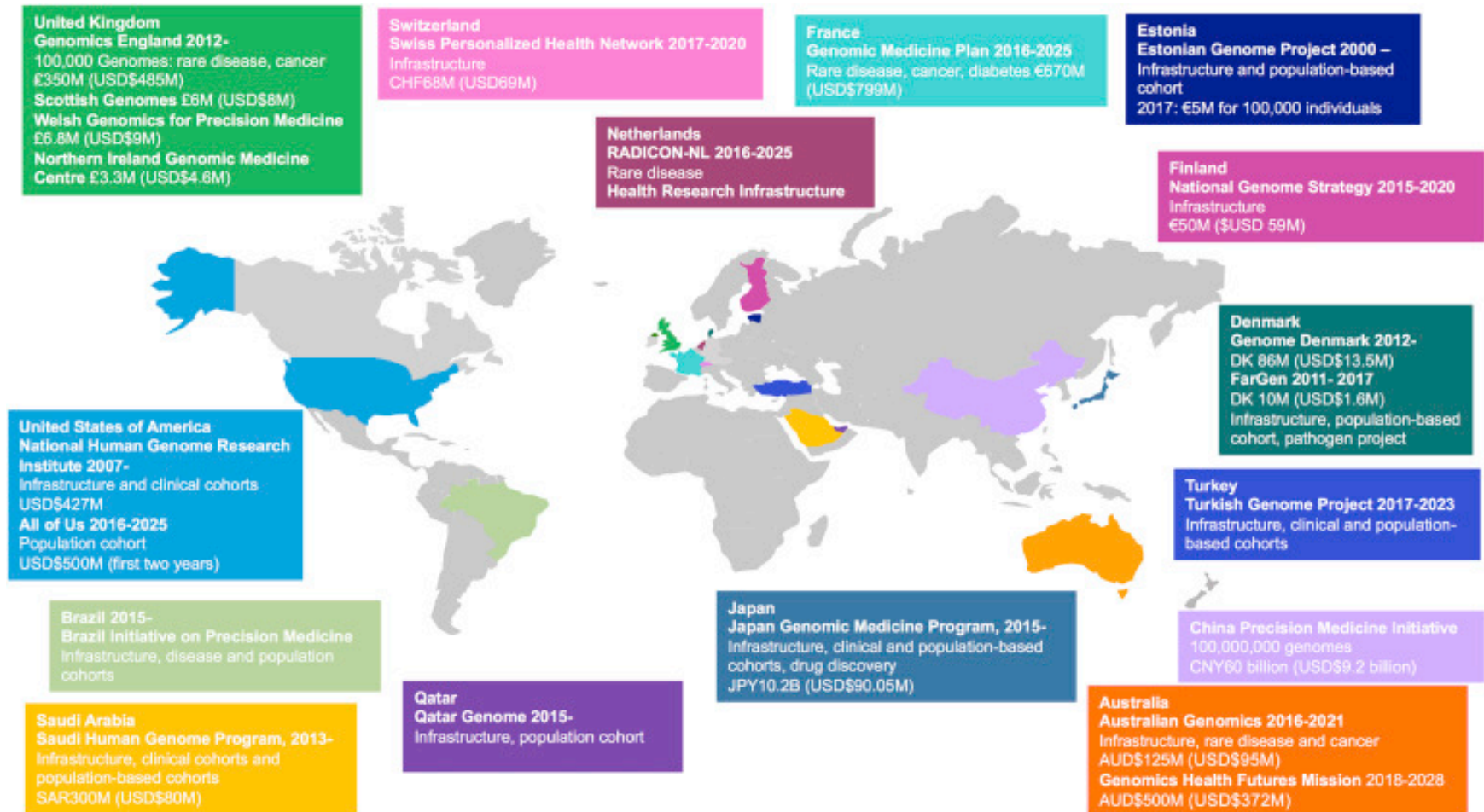
The **time is right** because:

- We have a greater understanding of human genes
- People are more engaged in healthcare and research
- We have the tools to track health information and use large databases
- Research technologies have improved

Follow the Program's progress and be one of the first to join this landmark effort.

[www.nih.gov/AllofUs-Research-Program](http://www.nih.gov/AllofUs-Research-Program)

# Research initiatives for translational genomics: global context



# Large-scale human genetic research: Ethical and legal questions



- Can participants give **broad consent** or should they have input on **specific proposed uses** of their biobanked samples and associated clinical info?
- Do researchers have ethical or legal responsibility to **return results** (clinically relevant or otherwise) to participants?
  - What about when participant is deceased? Or notifying family members who may also be implicated?
- Can participants request that their sample and/or data be destroyed?

# Beyond the genome: “-Omics”

- Other areas of research interest

- Transcriptomics (RNA)

- Proteomics (protein)

- Metabolomics

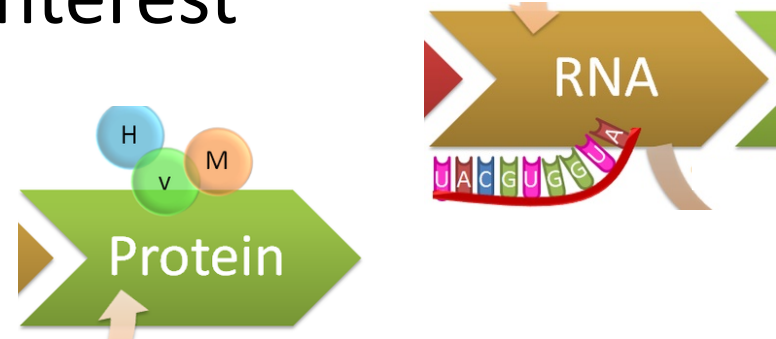
- Study of small molecules (“metabolites”)

- Epigenomics

- Study of chemical marks that regulate gene expression

- Microbiome

- Study of genomes of the many microorganisms that live in/on our bodies (e.g., gut, skin)



# III. APPLICATIONS

Medicine and Public Health

Consumer Genomics

Forensics

Biotechnology (CRISPR)

# Learning objectives



Understand different types of genetic variation



Describe the relationship between genotype and phenotype



Recognize major milestones in the history of genetic research

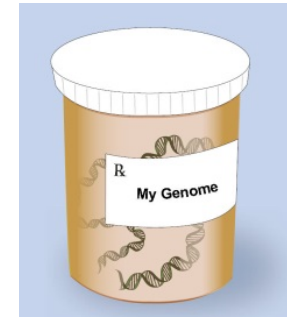


Identify applications of genomics relevant to legal issues

*Overall goal: Gain basic scientific understanding of genetics in order to apply the law and legal concepts in cases that involve genetics*

# III-A. Medicine and Public Health

- Genetic information can be used to guide the **prevention, diagnosis, and treatment** of disease



- **Personalized/precision medicine**

- Alternative to “one size fits all” health care that takes into account individual differences in people’s genes, environments, and lifestyles
  - Goal of the Precision Medicine Initiative and “All of Us” Research cohort: to lay the groundwork for clinical implementation of genetics and precision medicine



# GENETIC TESTING

NHGRI FACT SHEETS

genome.gov

## Genetic Tests Can Help to:



**Diagnose Your Disease**



**Pinpoint Genetic Factors That Caused Your Disease**



**Predict How Severe Your Disease Might Be**



**Choose the Best Medicine and Correct Dose**



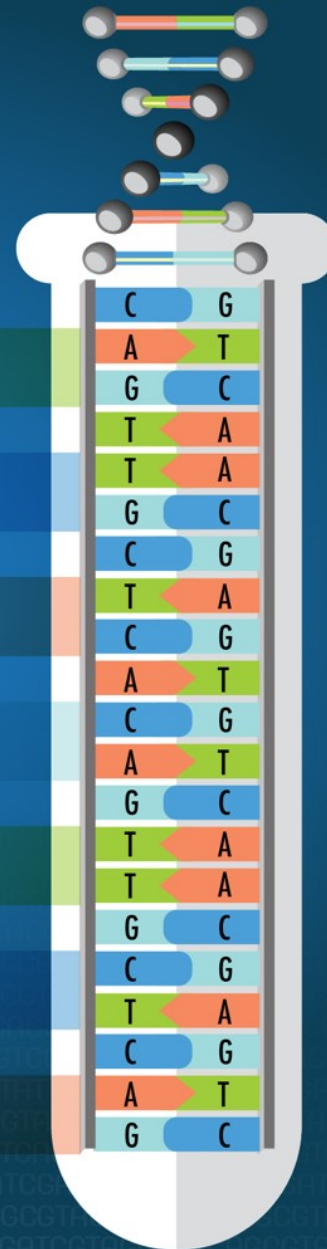
**Discover Genetic Factors That Increase Your Disease Risk**



**Find Genetic Factors That Could Be Passed to Your Children**



**Screen Newborns for Certain Treatable Conditions**



National Human Genome Research Institute



# Variant of Uncertain Significance

- Clinical interpretation of a genetic variant:

- Pathogenic
- Likely pathogenic
- VUS
- Likely benign
- Benign



- VUS: Common problem in clinical sequencing

- e.g. 5% of results for BRCA1/2 breast cancer; can go up to 20% for other diseases
- Sequencing DNA is now easy compared to interpreting



*Legal application: liability for labs that don't update a VUS in a clinical report once more info is available?*

# Public Health

- Newborn screening
  - Best example of large scale public health genetic screening in US
  - State run
  - Blood test w/in 1-2 days of birth
  - Began in 1960's
  - Recommended Uniform Screening Panel: 32 conditions
  
- Other applications
  - Infectious disease surveillance
  - Characterizing and tracking outbreaks



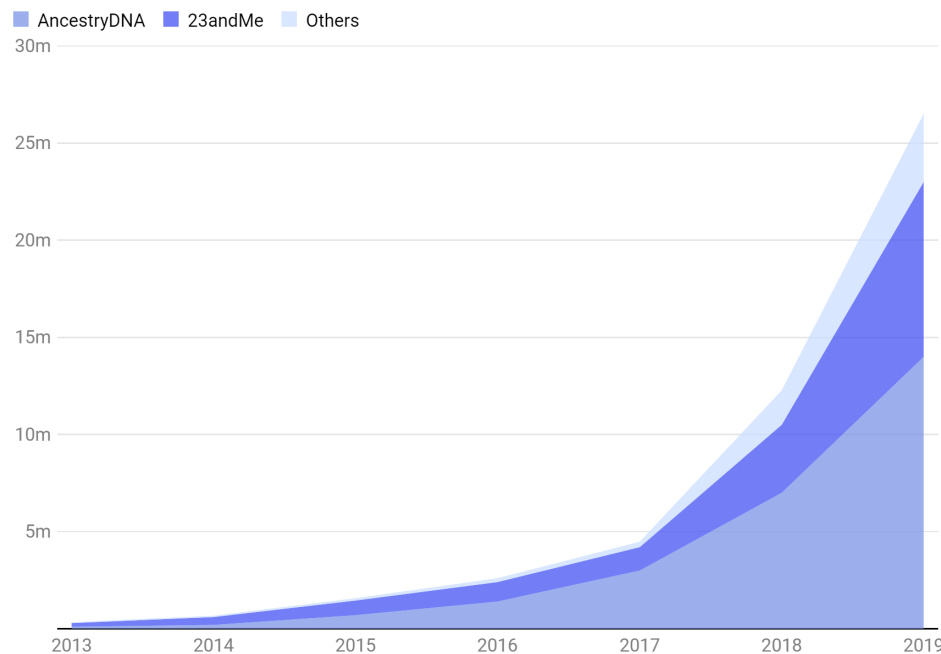
<http://www.biopoliticaltimes.org/article.php?id=5477>

# III-B. Consumer Genomics

- Genetic testing available direct-to-consumer (DTC) since ~2007
- Industry estimates: > 26M people tested

## Everybody's doing DNA tests

Total number of people tested by consumer genetics companies through January 2019, in millions



# DTC genetic testing process

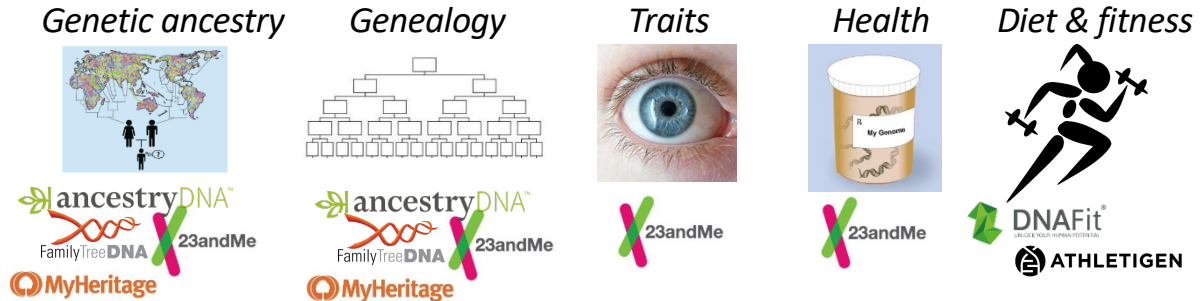
## Customer

(1) Mail saliva sample using company-provided spit kit



## DTC company

(2) Extracts customer's DNA  
(3) Measures (genotypes) DNA at ~1M variants  
Using SNP microarray technology  
(4) Analyzes **subset** of genotyped variants to provide **interpreted reports**:



(5) Provides to customer:



- **interpreted reports**
- **raw data file** of all ~1M measured variants

## Hey, soldiers and spies — think twice about that home genetic ancestry test

Lawmakers appear to be concerned that China could access genetic and health data of U.S. soldiers and secret agents through home ancestry tests



In this photo illustration, an Ancestry.com logo is displayed on a smartphone. (SOPA Images/LightRocket via Getty Images)

- Omnibus spending package passed by Congress end of Dec 2020
- Asks GAO to examine risks to intelligence community and military from use of DTC tests

# III-C. Forensic Uses

- **Relatedness**

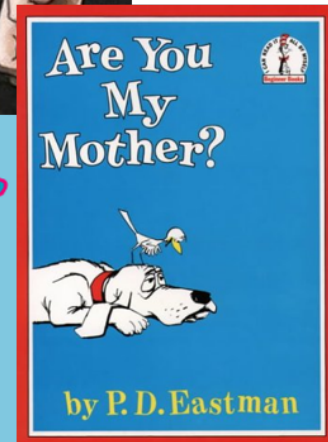
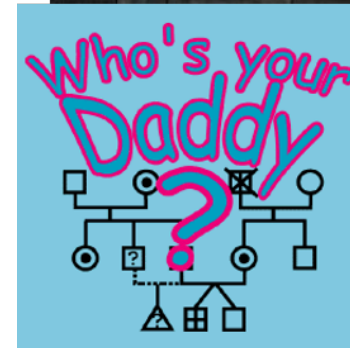
- Determine kinship, including paternity

- **Comparative DNA Profiling**

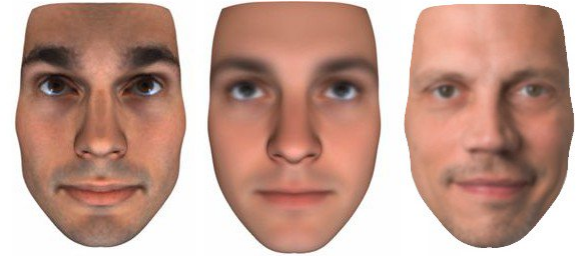
- Evaluation of the extent of genetic similarity between a known individual and an unidentified sample (eg. Blood stain from crime scene)
- Match probability based on population allele frequencies

- **ELSI Concerns**

- Familial searches?
- Use of consumer-facing databases (GEDmatch)?
- DNA samples taken at arrest?
- Overrepresentation of racial and ethnic minorities in criminal databases?



# Phenotypic profiling



- Predicting facial features based on DNA
- Controversial “face prediction” paper in 2017
  - J. Craig Venter’s company, Longevity
  - Heavily critiqued by scientific community
- Implications for DNA forensics in courts:
  - Admissibility as evidence?
  - Standards for evaluating evidence?

# Consumer genomics meets forensics

SCIENCE

## How a Genealogy Website Led to the Alleged Golden State Killer

Powerful tools are now available to anyone who wants to look for a DNA match, which has troubling privacy implications.

SARAH ZHANG APR 27, 2018

---

- April 2018: law enforcement announce use of consumer-facing, publicly available genealogy database (GEDMatch) to lead to arrest in Golden State Killer case
  - Via “spoofing” the data format used by DTC companies
- Opened floodgates on use of this technique (vs. government DNA databases such as CODIS)
- Over 50 “cold cases” solved





# III-D. Biotechnology

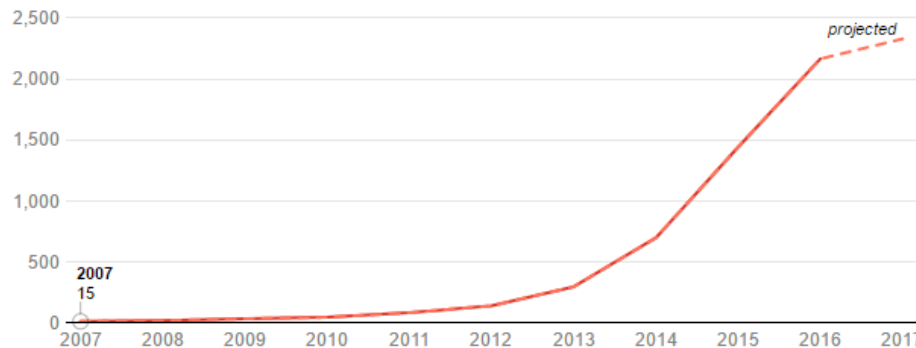
Focusing on a BIG game changer...

- **CRISPR**

- =“clustered regularly interspaced short palindromic repeats”
- Based on natural bacterial defense system
- Gene-editing technique harnessed in past decade

## CRISPR research publications

According to a Scopus database search of journal article titles and abstracts, the number of scientific publications that mention the word "CRISPR" is expected to reach an all-time high by the end of the year. As of May, 885 have already been published just in 2017.

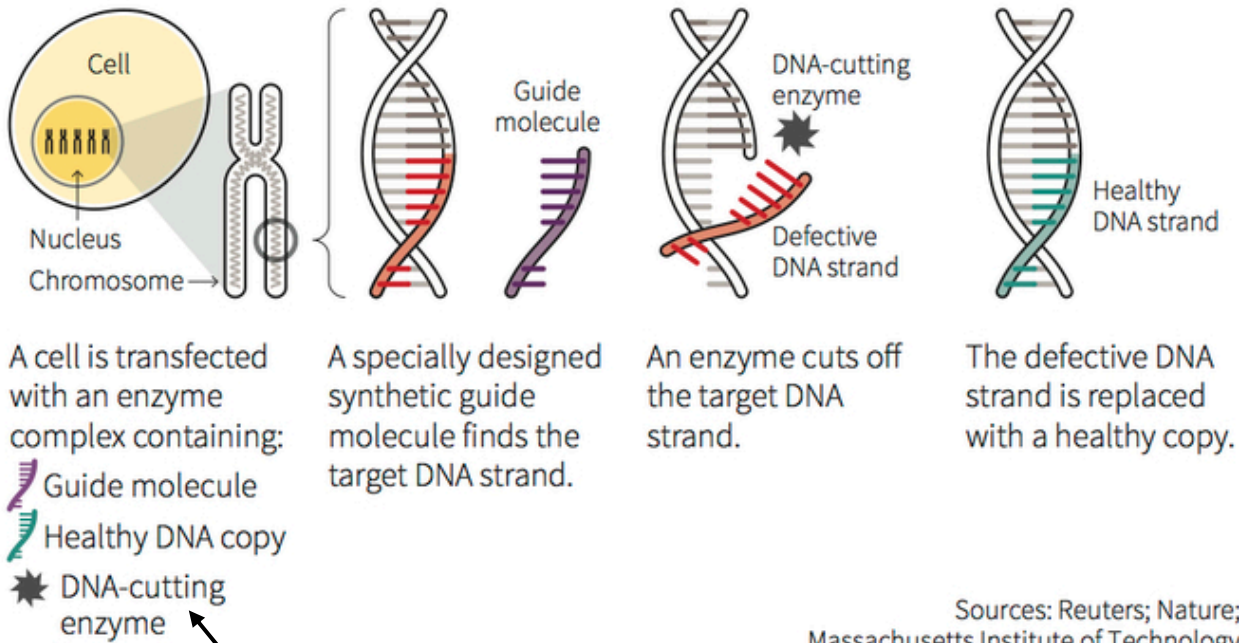


# CRISPR: how does it work?

## DNA editing

A DNA editing technique, called CRISPR/Cas9, works like a biological version of a word-processing programme's "find and replace" function.

### HOW THE TECHNIQUE WORKS



W. Foo, 24/04/2015

Cas9 protein

Sources: Reuters; Nature;  
Massachusetts Institute of Technology

REUTERS

Compared to the original DNA, the inserted DNA sequence can be a deletion, insertion, OR single base pair change

Incredibly precise compared to previous gene editing techniques  
"Molecular scissors"

Relatively "easy" (cost, time, materials required)

"transfection" = getting cell to express the Cas9 protein and guide RNA molecule. May involve viral vectors

# CRISPR: how can it be used?

- Many possible applications in research and medicine, in both humans and non-humans e.g.:
  - Generate “gene knockout” animal models for research
  - Treat infectious diseases
  - GMO/GM crops



# CRISPR: how can it be used? (cont)

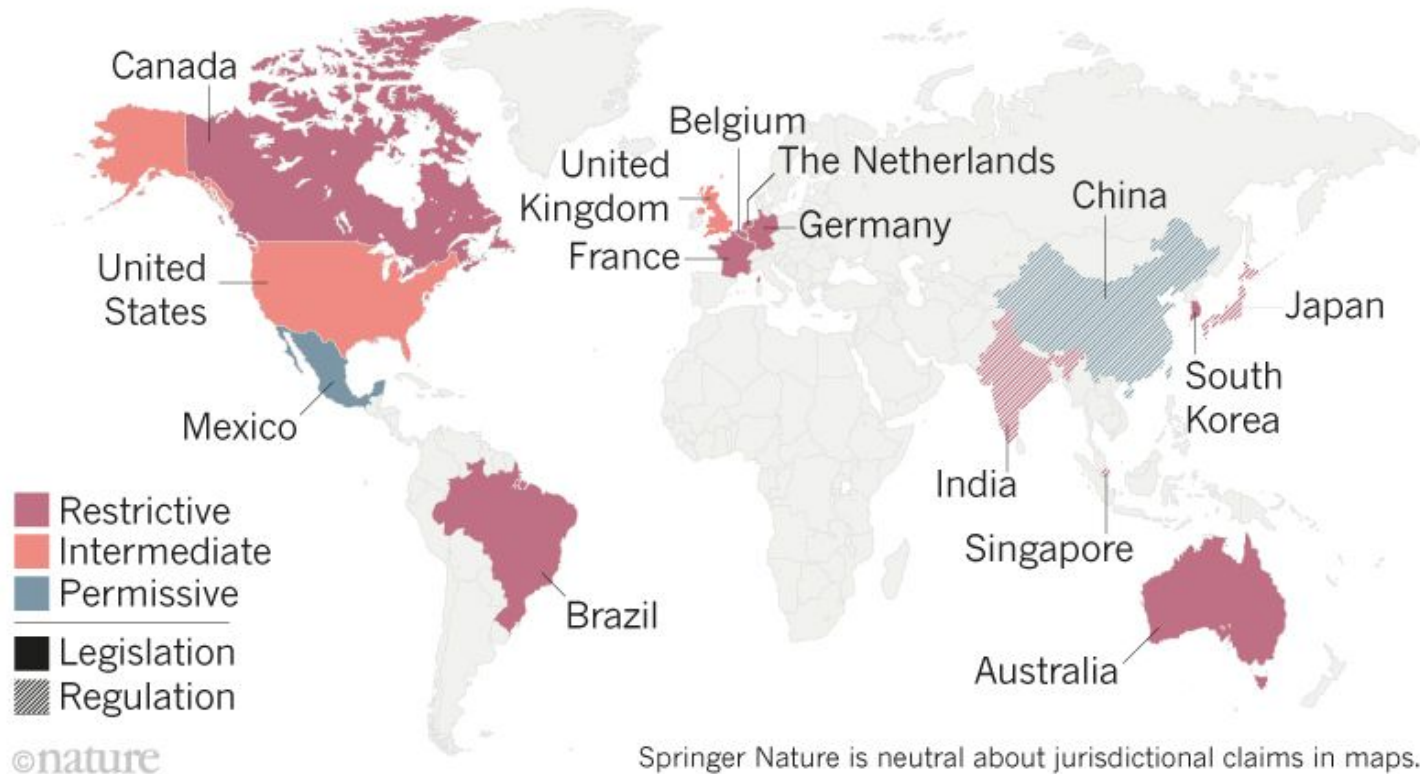
- Gene therapy/gene transfer
  - Concept not new: first clinical trials > 20 yrs ago (not much success)
- “Correcting” genetic diseases
  - Somatic gene therapy \*changes NOT passed down
  - Germline gene therapy \*changes passed down
    - Nov 2018: claim of first “CRISPR” babies in China
- First FDA approvals for CRISPR drugs started in 2017
  - E.g., Dec 2017: Luxturna, the first gene therapy for an inherited disease, a form of blindness
    - Expected to cost \$850k/tx





# THE LEGAL LANDSCAPE

A 2016 survey in *Science* examined existing laws (legislation) and documented policies (regulation) that explicitly govern gene editing or might be applied to such activities. The survey labelled countries as restrictive, permissive or something in between. But specialists disagree over whether rules in some nations might be interpreted to permit gene editing.



# General references

National Human Genome Research Institute (NHGRI) resources:

- Talking Glossary of Genetic Terms, <https://www.genome.gov/glossary/>
- Genetics, DNA, and Heredity: The Basics, [https://www.genome.gov/pages/education/modules/basicspresentation\\_vs2.pdf](https://www.genome.gov/pages/education/modules/basicspresentation_vs2.pdf)
- Issues in Genetics, <https://www.genome.gov/10000006/issues-in-genetics/>
- Fact Sheets: <https://www.genome.gov/10000202/fact-sheets/>

Genetics Home Reference, <https://ghr.nlm.nih.gov/>

University of Utah, Learn Genetics, <http://learn.genetics.utah.edu>

# Supplementary Slides

# Codons

Base pair triplets (“codons”) specify different amino acids, the building blocks of all proteins

		Second nucleotide					
		U	C	A	G		
First nucleotide	U	UUU Phe UUC UUA Leu UUG	UCU UCC Ser UCA UCG	UAU Tyr UAC UAA STOP UAG STOP	UGU Cys UGC UGA STOP UGG Trp	U C A G	
	C	CUU Leu CUC CUA CUG	CCU Pro CCC CCA CCG	CAU His CAC CAA Gln CAG	CGU Arg CGC CGA CGG	U C A G	
	A	AUU Ile AUC AUA AUG Met	ACU Thr ACC ACA ACG	AAU Asn AAC AAA Lys AAG	AGU Ser AGC AGA Arg AGG	U C A G	
	G	GUU Val GUC GUA GUG	GCU Ala GCC GCA GCG	GAU Asp GAC GAA Glu GAG	GGU Gly GGC GGA GGG	U C A G	
						Third nucleotide	



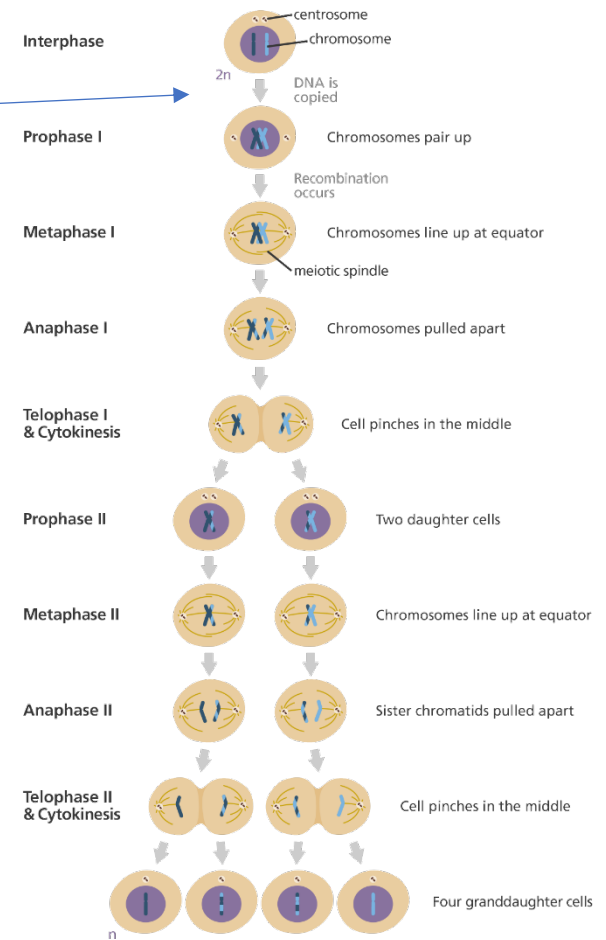
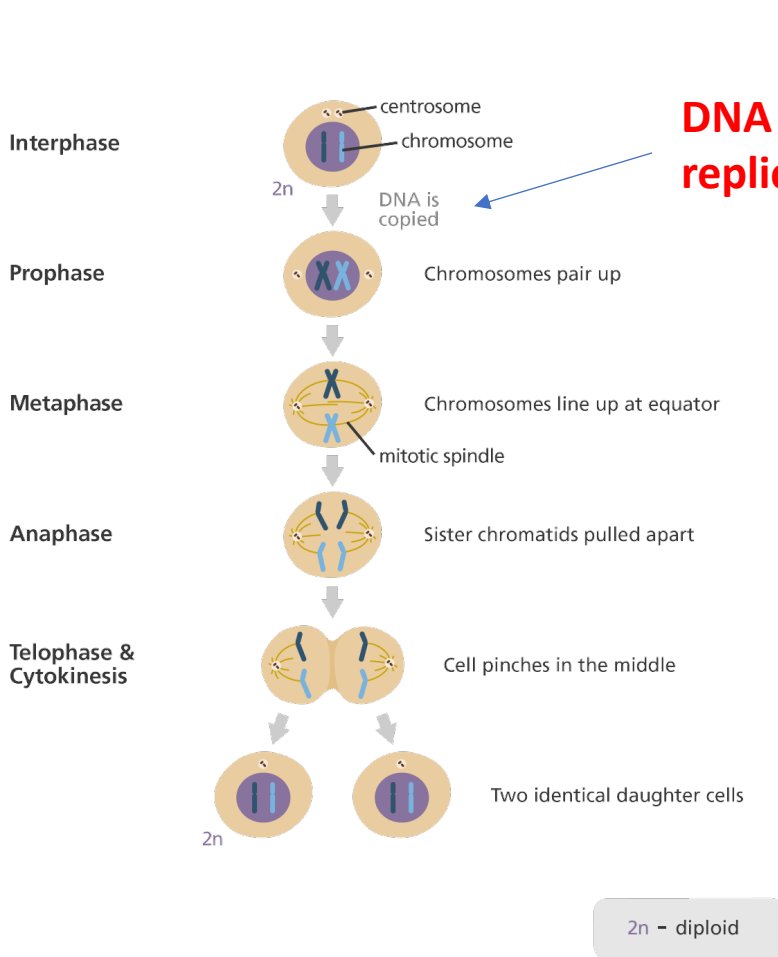
# Cell Division

## Mitosis

one cell divides once to form **two** identical, **diploid** daughter cells

## Meiosis

one cell divides twice to form **four** non-identical **haploid** cells



# Clinical Genetic Testing



**Prenatal testing**

**Case study 2:** Sofia is pregnant with her first child. Wanting to do everything to ensure a healthy newborn, she opts for whole-exome sequencing. The sequencing results identify pathogenic variants in PKU, which have been associated with phenylketonuria. Armed with this information, Sofia immediately begins a low-phenylalanine diet during pregnancy and arranges for the availability of a special dietary infant formula to avoid neonatal exposure to phenylalanine. With this treatment plan, the baby is expected to develop normally and lead a healthy adult life.



**Preconception testing**

**Case study 1:** Bob and Julie are considering having a child and seek preconception genetic testing. Julie is found to carry seven pathogenic variants for recessive diseases and Bob is found to carry five. There is one gene, SMN1, for which both are carriers. This result puts the couple at a 25% risk of having a child with spinal muscular atrophy, a progressive muscle-wasting disease. Julie and Bob decide to pursue preimplantation genetic diagnosis to avoid a pregnancy with an affected fetus by selecting embryos that do not inherit both pathogenic variants.



**Newborn screening and paediatric care**

**Case study 3:** Mei has just given birth to a healthy baby girl. She decides to have her daughter's genome assessed using exome sequencing. This test reveals two pathogenic variants in *GJB2*, putting the newborn at risk of hearing loss that can be progressive. Although the child passed a newborn baby hearing screening test, a diagnostic audiological test reveals mild hearing loss, often missed in newborn screening. The baby is fitted with hearing aids to facilitate normal auditory development. The baby's hearing is monitored yearly, and if it progresses to profound deafness, the option for cochlear implantation surgery can be offered to the family.



**Elderly health**

**Case study 6:** John had watched his father suffer a long end-of-life battle with Alzheimer disease. Curious about his own risks, he elected to obtain genetic testing through a direct-to-consumer testing company and learned that he harbours two copies of the *APOE ε4* variant, putting him at heightened risk of Alzheimer disease. He also learned that his ancestral origins were more diverse than he had previously realized and was able to connect with several distant relatives through an online ancestry portal.



**Adult medicine**

**Case study 4:** Joseph was interested in pursuing genomic sequencing to learn about his own health risks. He ordered a whole-genome sequencing test through a medical geneticist offering concierge services and discovered that he harbours a pathogenic variant for hypertrophic cardiomyopathy. This finding prompted a cardiac evaluation, which revealed normal cardiac morphology and conduction systems; however, a detailed family history assessment identified suspicion for hereditary sudden cardiac death on his mother's side based on unexplained drowning of a sibling and two maternal uncles who died of heart attacks at 55 and 60 years of age. Given the incomplete penetrance of hypertrophic cardiomyopathy, Joseph's actual risk of disease is unclear, but with a positive at-risk genotype, he will pursue regular cardiac evaluations and inform family members of their possible risk.



**Adult medicine**

**Case study 5:** Jessica is seeing a genetic counsellor (GC) to discuss her risk of breast cancer after her grandmother and aunt died of breast cancer and her mother was recently diagnosed. She brings a copy of her aunt's laboratory report from 2008 that notes a pathogenic variant identified and cites a publication to support the variant interpretation. Jessica's GC quickly looks up the variant in ClinVar and discovers that five clinical laboratories now interpret the variant as benign, citing more recent evidence accumulated from clinical testing. The GC suggests that her aunt's testing probably did not identify the correct cause of disease in her family and suggests that Jessica's mother undergo testing to identify another potential cause of hereditary breast cancer that may not have been examined in 2008. If a cause of breast cancer is found in her mother, Jessica would be able to pursue testing to inform her own risk.

# Race, ethnicity, and identity

physical characteristics

categorization

biology

racism

sociology

psychology

oppression



discrimination

skin color

social construction

difference

language

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

anthropology

culture

divisive

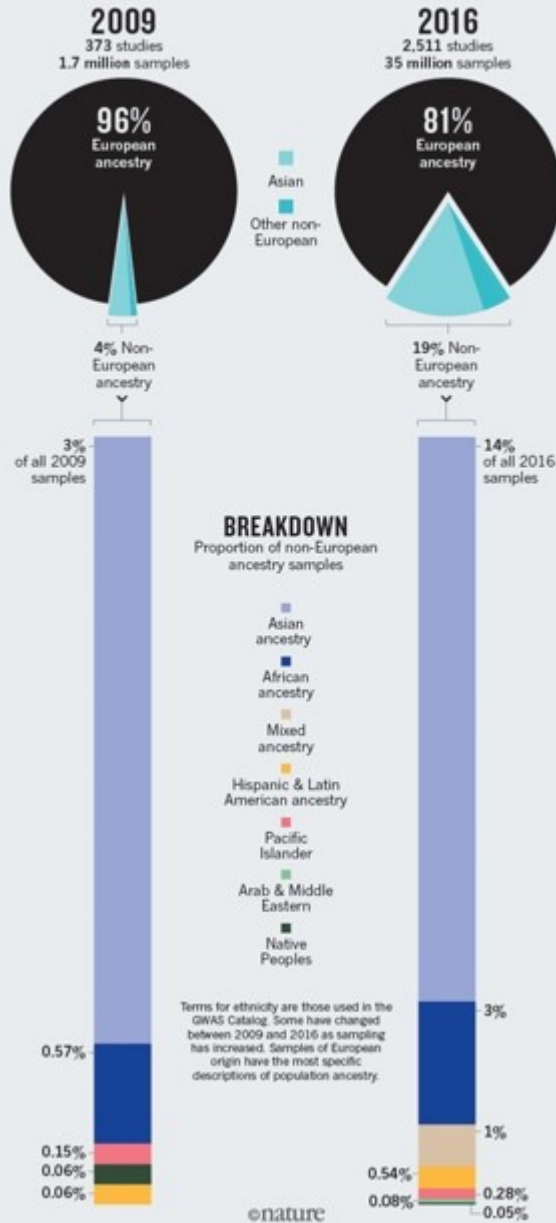
history

colonialism

inferiority/superiority

## PERSISTENT BIAS

Over the past seven years, the proportion of participants in genome-wide association studies (GWAS) that are of Asian ancestry has increased. Groups of other ancestries continue to be very poorly represented.



# Genetic research and diversity

nature

International weekly journal of science

Home | News & Comment | Research | Careers & Jobs | Current Issue | Archive | Audio & Video

Archive > Volume 538 > Issue 7624 > Comment > Article

NATURE | COMMENT

## Genomics is failing on diversity

Alice B. Popejoy & Stephanie M. Fullerton

12 October 2016

An analysis by Alice B. Popejoy and Stephanie M. Fullerton indicates that some populations are still being left behind on the road to precision medicine.

# Genetic research and health disparities



New Online

Views **6,785** | Citations **0** |  **0**



Viewpoint

ONLINE FIRST FREE



March 27, 2017

More ▾

## Genomics, Health Disparities, and Missed Opportunities for the Nation's Research Agenda

Kathleen McGlone West, MS, MPH<sup>1</sup>; Erika Blacksher, PhD<sup>2</sup>; Wylie Burke, MD, PhD<sup>2</sup>

[» Author Affiliations](#) | [Article Information](#)

*JAMA*. Published online March 27, 2017. doi:10.1001/jama.2017.3096

The completion of the Human Genome Project occurred at a time of increasing public attention to health disparities. In 2004, Sankar and colleagues<sup>1</sup> suggested that this coincidental timing resulted in an inappropriate emphasis on the contribution of genomics to health disparities, conflating racial patterns of disease with genetic ancestry, and distracting attention from the large and compelling body of scientific evidence pointing to social determinants of health disparities.<sup>2</sup> For example, genomic research has emphasized discovery of genetic contributors to diabetes risk, but the recent increase in the prevalence of obesity and type 2 diabetes, which disproportionately affects minority populations, cannot be attributed to genetic changes and rather

# Ownership of DNA

- Who owns your genetic information?
  - Court precedent that donors do not have property rights in their biological samples
    - E.g., Moore v. Regents of the University of California (1990)
  - Many direct-to-consumer companies sell customer data to third parties
    - Genetic data often more useful/valuable in the aggregate, e.g., as an R&D tool, than it is for the individual
- Ongoing case, Peerenboom v. Perlmutter, that may go against Moore precedent
  - See Genome Magazine Winter 2018 article, “Do You Belong to you?”

# Genetic Discrimination



- The Genetic Information Nondiscrimination Act (GINA) of 2008
  - Protects Americans from discrimination based on their genetic information in both health insurance (Title I) and employment (Title II)
- Does not apply to other insurance (e.g., life, long term disability)
- Legal issue: largely untested in court

# Ploidy

- Diploid

- Two **sets** of chromosomes ( $2n$ )

- One from father (paternal)
- One from mother (maternal)

- Human (non-germ) cells are diploid

- Most Eukaryotes (species whose cells have nuclei) are diploid

- Haploid

- One set of chromosomes ( $1n$ )

- **Germ cells** (sperm and egg) are haploid

- Polyploidy

- Multiple sets of chromosomes ( $>2n$ )

- Common in plants

- Fun fact: strawberries are octaploid ( $8n$ )





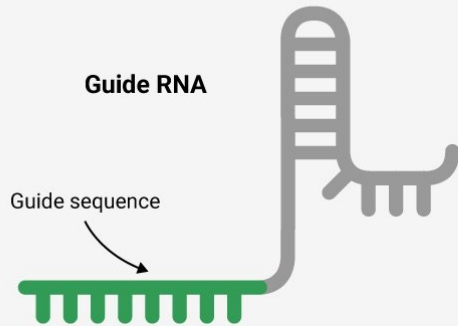
# “CRISPR baby” controversy

- First gene-edited babies reported Nov 2018, from an academic group in Shenzhen, China
  - Twin girls born
- Edited *CCR5* gene in embryos prior to transplant to woman's uterus
  - Attempt to create resistance to HIV, smallpox, and cholera
- Generated much controversy in scientific and medical communities
- Dec 2019: the lead scientist (He Jiankui) sentenced to 3 yrs in prison and ~\$430K fine for “illegal medical practice by knowingly violating the country's regulations and ethical principles with their experiments”

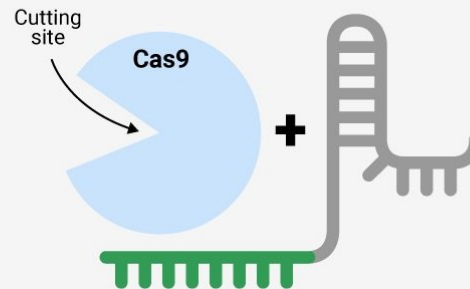
# CRISPR: how does it work?

## EDITING A GENE USING THE CRISPR/CAS9 TECHNIQUE

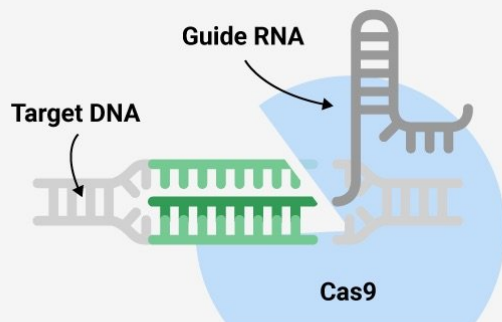
- 1** Scientists create a genetic sequence, called a "guide RNA," that matches the piece of DNA they want to modify.



- 2** This sequence is added to a cell along with a protein called Cas9, which acts like a pair of scissors that cut DNA.



- 3** The guide RNA homes in on the target DNA sequence, and Cas9 cuts it out. Once their job is complete, the guide RNA and Cas9 leave the scene.



- 4** Now, another piece of DNA is swapped into the place of the old DNA, and enzymes repair the cuts. Voilà, you've edited the DNA!

