

# Ethics and Genomics

*Cinnamon S. Bloss, Ph.D.*

*March 6, 2018*

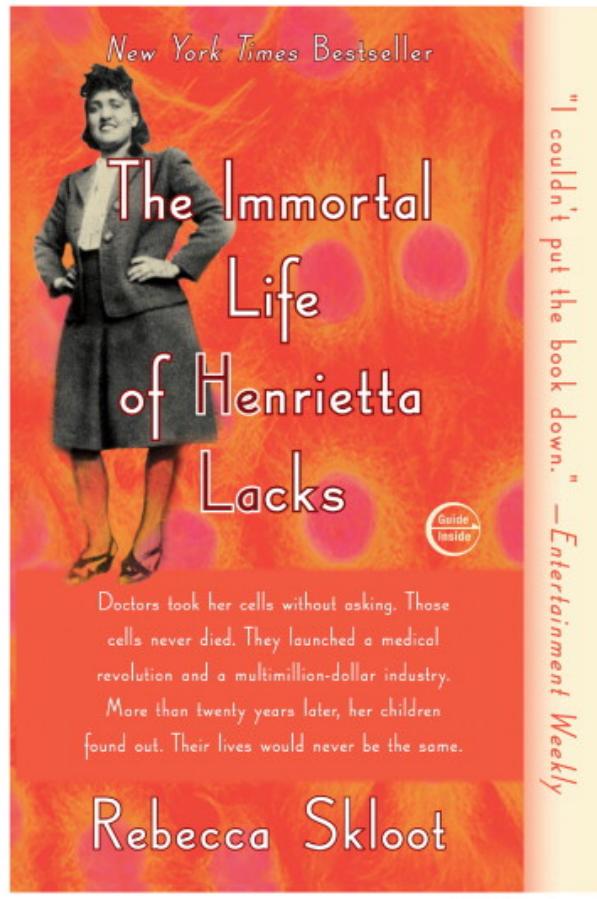


*"We are here to celebrate the completion of the first survey of the entire human genome. Without a doubt, this is the most important, most wondrous map ever produced by humankind."*

**President Bill Clinton, June 26, 2000**

Why consider ethics in  
regards to genomic data?

# Henrietta Lacks



# Direct-to-Consumer Genomics

The screenshot shows the 23andMe website. At the top left is the 23andMe logo with a stylized DNA helix icon. To its right is a user profile placeholder with a blue and pink shape. Further right are links for "Cinnamon Bloss | Sign out |" and a shopping cart icon showing "0". Below the header is a navigation bar with links: "welcome", "ancestry", "health", "how it works" (which is highlighted in purple), "store", "search", and "help".

## Personal Genome Service®

Get to know your DNA. All it takes is a little bit of spit.

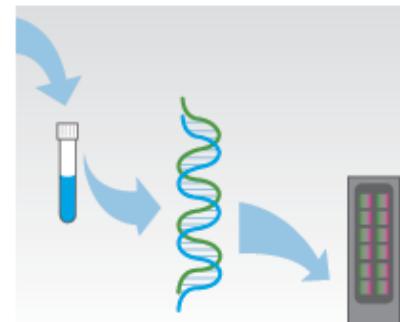
Here's what you do:



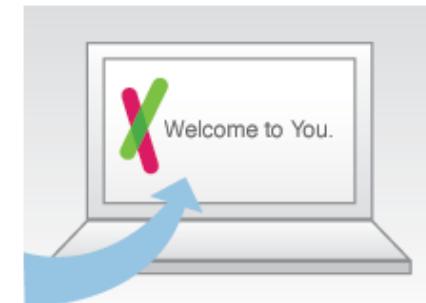
1. Order a kit from our [online store](#).



2. [Register your kit](#), spit into the tube, and send it to the lab.



3. Our CLIA-certified lab analyzes your DNA in 6-8 weeks.



4. [Log in](#) and start exploring your genome.

# ASU vs. Havasupai Indian Tribe



*TRENDS in Genetics*



About the  
HGP

Research

# Human Genome Project Information

Education

News

Medicine

Ethical, Legal,  
Social Issues

# What is ELSI?

- U.S. DOE and NIH devote 3-5% of their annual Human Genome Project budgets toward “ethical, legal and social issues (ELSI)” surrounding the availability of genetic information
- This represents the worlds largest bioethics program
- Genomics has presented new and complex ethical and policy issues for individuals and society
- Programs that identify and address these implications an integral part of the U.S. HGP since its inception
- These have resulted in a body of work that promotes education and helps guide the conduct of genetic research and the development of related medical and public policies



Home > Research Funding > Research Funding Divisions > Division of Genomics and Society > The ELSI Research Program

Division of Genomics and Society

Division Outreach and Activities

Division Planning and Evaluation

Division Staff

The ELSI Research Program

Centers of Excellence in ELSI Research

ELSI Planning and Evaluation History

ELSI Publications and Products Database

ELSI Research Priorities

ELSI Research Program Abstracts and Activities Database

ELSI Sample Applications and Summary Statements

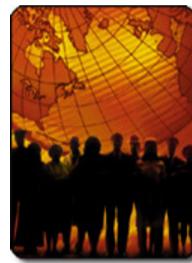
## ELSI Research Program

### *The Ethical, Legal and Social Implications (ELSI) Research Program*

[ELSI Research Program](#) | [DG&S Planning and Evaluation](#) | [Abstracts and Activities Database](#)

[Publications and Products Database](#) | [Program Reports](#) |

[Genomics and Society Working Group](#) | [Sample Applications and Summary Statements](#)



- [Overview](#)
- [Research Priorities](#)
- [Research Funding Opportunities](#)
- [Workshops](#)
- [Centers of Excellence in ELSI Research](#)
- [Research Program Staff](#)

No other area of biomedical research has sustained such a high level of commitment, backed by \$\$, to ethical issues – genomics unique.

# Uniqueness of Genetic Information

- **Identifying:** Genetic information is identifying not only on an individual level but a familial (and parentage) level as well.
- **Ubiquitous:** Identity and genetic status can be gathered from a small amount of material and is permanent rather than transitory information.
- **Longevity:** Genetic samples and data can be kept for indeterminate periods of time.
- **Predictive:** Can be diagnostic, predictive, or provide risk information.
- **Individual and familial nature:** Most genetic information flows between generations. These implications may extend beyond the family to larger groups of closely linked people with common ancestry, for example, indigenous, ethnic or ethno-religious communities.
- **Shared Information:** Genetic information as shared information affects who may be regarded as the 'patient' since it may be the individual as well as the family. This raises unique challenges for individual autonomy and consent as well as the duty to warn and the right not to know.
- **Informational risks:** Genetic information may put individuals, families and communities at risk of discrimination and stigmatization.
- **Symbolic meaning:** Genetic information tends to be regarded as particularly symbolic in part due to its social perception as a human blueprint representing the essence of life.

# ELSI Issues

- Fairness in the use of genetic information
- Privacy and confidentiality\*
- Psychological/behavioral impact
- Stigmatization, and discrimination\*
- Reproductive issues & Forensics
- Clinical issues (regulation, education of providers)
- Uncertainties (as related to susceptibilities to complex conditions)
- Conceptual and philosophical implications (human responsibility, free will vs. genetic determinism)
- Health and environmental issues concerning genetically modified foods
- Commercialization of products including property rights (patents, copyrights, and trade secrets)

Focus:

- 1) Ethical Management of Genomic Data
- 2) Genetic Privacy
- 3) Genomic Medicine Education

# Ethical Management of Genomic Data

Why is the ethical management of genomic data so challenging?

# 1. Genomic data can reveal health risks

- Growing informational richness of genomic data facilitate answers to questions, but also magnifies potential for misuse
- Different from targeted genetic data
- Or even SNP data

## 2. “Comprehensiveness” of Genomic Data

- Potential for re-identification
  - Previously required a reference sample
  - Now can consult genetic genealogy databases
- Actual extent of risk is unknown, but
- Amplifies concerns about who should be able to have, and control, access

### 3. Complexity and uncertain meaning of genomic data

- Enhances possibility that, if shared, data will be misunderstood
- Challenges for researchers and clinicians who have to decide which individual findings to return
- Incidental findings inevitable, not simply possible

# Pre-genomic Approaches to Management of Data

# From ‘Genetics’ to ‘Genomics’

- 15-20 years ago, studies were generally highly targeted
- Straightforward informational risks
- Consents focused on:
  - Breach of privacy
  - Insurance and employment main areas of concern
- Low tech data security
- (pre-dated the development of massive genomic databases)

# Earlier Consent Forms

- Rarely addressed return of results, default was that results not returned
- Targeted nature meant IF risk low
  - Apart from undisclosed adoption or misattributed paternity
- Narrow consent language
  - Only described immediate study
  - Broad consent for an unspecified range of future studies was the exception
  - “Silence” on future sharing

# Influential Paper 1995

## Consensus Statement

# Informed Consent for Genetic Research on Stored Tissue Samples

Ellen Wright Clayton, MD, JD; Karen K. Steinberg, PhD; Muin J. Khoury, MD, PhD; Elizabeth Thomson, MS, RN;  
Lori Andrews, JD; Mary Jo Ellis Kahn, MSN, RN; Loretta M. Kopelman, PhD; Joan O. Weiss, LCSW

**Objective.**—To develop recommendations for obtaining adequate informed consent in the future when gathering tissue samples that may be used for genetic studies and defining the circumstances under which it is necessary to obtain further consent if tissue samples already in hand are to be used for such research.

**Participants.**—Scientists, ethicists, lawyers, and consumers selected by the National Center for Human Genome Research and the Centers for Disease Control and Prevention to represent a wide array of opinions

**Evidence.**—Statutes, regulations, and cases

**Consensus Process.**—Initial workshop, followed by a period of public comment on this document with opportunities for comment by individuals, organizations, and other participants as well as smaller meetings involving participants

**Conclusions.**—Genetic research using stored tissue samples can provide important benefits and risks to individuals, researchers, and society. Workshop participants conclude that (1) informed consent is required for most genetic research using linkable samples unless conditions for waiver are met; (2) informed consent is not required for genetic research using de-identified samples; (3) identifiers may be considered if identifiers are to be removed before samples are used for genetic research; and (4) informed consent is warranted for research that poses a significant risk to subjects.

rent concerns that some individuals have about this research must be considered. As evidence of this sort of balancing, it is widely accepted that informed consent must be obtained for the many projects that involve the direct prospective involvement of individual subjects. The role of

**Consents began to be written with greater specificity about whether, with whom, and for what purposes, samples and data would be shared.**

**But...recommendation was often interpreted as applying only to prospectively collected samples...**

Movement Toward  
Broader Sharing &  
Expanding  
Applications

# Commitment to Broad Data Release

- First enshrined in 1996 Bermuda Principles, subsequently reaffirmed
  - Maximize pace of research to benefit society
- NIH GWAS Data Access Policy adopted in 2008
  - Need for large samples to power GWAS
  - Informatics technology made it cheaper and easier to share
  - Requires deposition of data into NIH Database of Genotypes and Phenotypes
- Enactment of GINA in 2008



## ***dbGaP Overview***

The **database of Genotypes and Phenotypes** (dbGaP) was developed to archive and distribute the results of studies that have investigated the interaction of genotype and phenotype. Such studies include genome-wide association studies, medical sequencing, molecular diagnostic assays, as well as association between genotype and non-clinical traits. The advent of high-throughput, cost-effective methods for genotyping and sequencing has provided powerful tools that allow for the generation of the massive amount of genotypic data required to make these analyses possible.

dbGaP provides two levels of access - [open](#) and [controlled](#) - in order to allow broad release of non-sensitive data, while providing oversight and investigator accountability for sensitive data sets involving personal health information. Summaries of studies and the contents of measured variables as well as original study document text are generally available to the public, while access to individual-level data including phenotypic data tables and genotypes require varying levels of authorization. More complete descriptions of the dbGaP system are available in [Pub Med Central](#) and the [NCBI Bookshelf](#).

### [View Certificate of Confidentiality](#)

The data in dbGaP will be pre-competitive, and will not be protected by intellectual property patents. Investigators who agree to the terms of dbGaP data use may not restrict other investigators' use of primary dbGaP data by filing intellectual property patents on it. However, the use of primary data from dbGaP to develop commercial products and tests to meet public health needs is encouraged.

## ***Submission Policy***

Submitters who are not Federally-funded and affiliated with an NIH IC will need to work with an NIH [DAC](#) so that proposed submission can be reviewed for consistency with appropriate policies to protect the privacy of research participants and confidentiality of their data. Submissions to dbGaP will not be accepted without assurance that the submitting institution approves the submission and has verified that the data submission is consistent with all applicable laws and regulations, as well as institutional policies. Submitters must also identify any Data Use limitations that are specifically set for each individual research participants, (e.g., through their informed consent). Please see [NIH data sharing policy](#) website for more details.

# Trend Toward Broader Sharing of Samples

- Usually via large biorepositories
- Capability of new sequencing technologies to work with smaller quantities of material
- Investigators more willing to share

# Sense of Discomfort Remains

- Proliferation of genomic information across society and potential for misuse
- Emergence of data in settings far removed from research labs and clinics
  - Criminal justice system
  - Private sector activities (e.g., DTC genomics, genetic genealogy)

# Renewed Concerns about Identifiability

# Re-identification

- Potential for re-identification
  - Previously required a reference sample
  - Now can consult genetic genealogy databases
- Actual extent of risk is unknown, but
- Amplifies concerns about who should be able to have, and control, access
- But, growing sense that participants in genomics research should be informed explicitly
- Ushered in trend toward more frequent use of broad consent

# Broad Consent

- Consent forms describe explicitly the possible downstream deposition of genomic (and other) info in public databases
- Sharing with multiple researchers for use in many types of studies
- Seek authorization for the distribution of samples to secondary researchers (expansion of biobanks)

# Receptivity to Broad Consent

- Some prefer, others have been less amenable
  - Populations that have historically suffered research abuses
- Reported unease among some about inability to control future uses of data/sample
  - Two recent lawsuits challenging the research use of stored bloodspots from state NBS programs w/o parental consent

# Level of Risk

- Shouldn't overstate risk of re-identification and subsequent suffering of harm
- Most data shared through controlled-access databases, limited to “qualified” investigators

# “Open Consent” and the Citizen Science Movement

# Genomes inherently identifiable

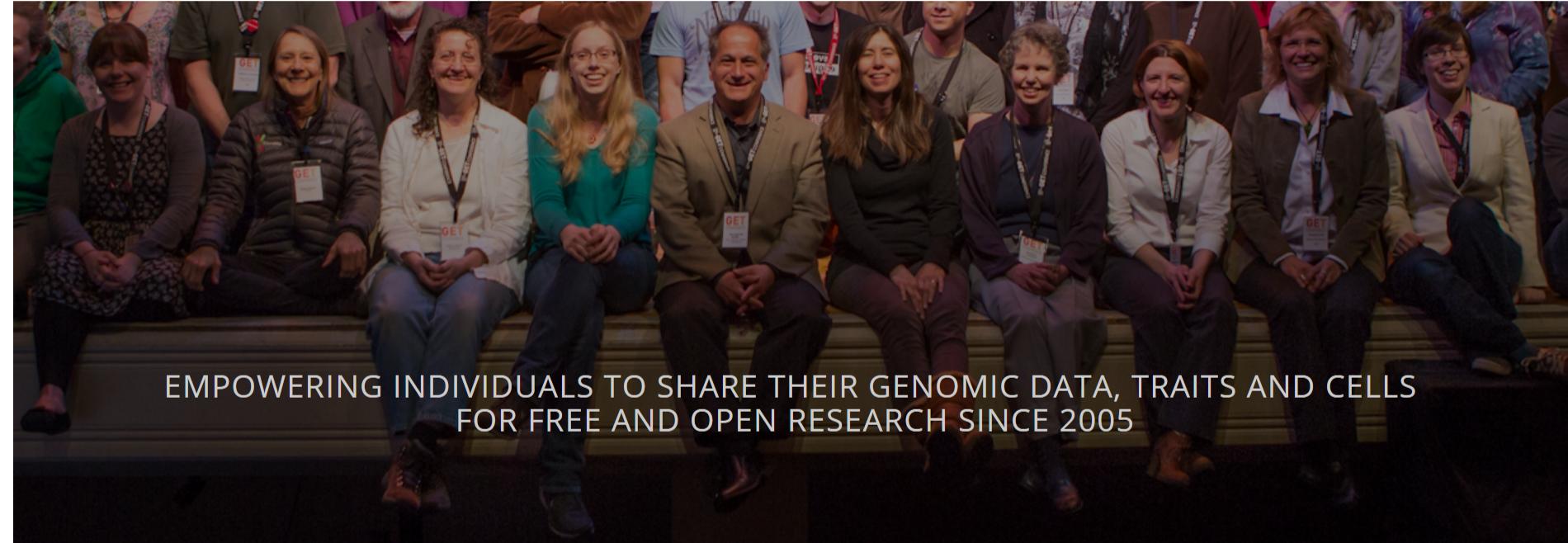
- Some suggest that continuing to try to take measures to reduce identifiability are misguided
- Example: Personal Genome Project
  - Forgo any expectation of privacy
  - Data shared openly over the internet
  - Volunteers must pass an enrollment exam
  - Participants highly self-selected
  - Solution for general public will involve multiple strategies
- Key: Improved Transparency
  - Consistent with people's expectations, which are realistic



# The Harvard Personal Genome Project

we are open for science

[About](#) | [Participate](#) | [Use Data](#) | [Donate](#) | [Participant login](#)



EMPOWERING INDIVIDUALS TO SHARE THEIR GENOMIC DATA, TRAITS AND CELLS  
FOR FREE AND OPEN RESEARCH SINCE 2005



ADNA test kit from Ancestry.com includes a tube for customers to spit in.

COURTESY OF ANCESTRYDNA

## Rewriting Life

# 2017 was the year consumer DNA testing blew up

More people took genetic ancestry tests last year than in all previous years combined.

by Antonio Regalado   February 12, 2018

The number of people who have had their DNA analyzed with direct-to-consumer genetic genealogy tests more than doubled during 2017 and now exceeds 12 million, according to industry estimates.



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# The future of health begins with AllofUs

The *All of Us* Research Program is a historic effort to gather data from one million or more people living in the United States to accelerate research and improve health. By taking into account individual differences in lifestyle, environment, and biology, researchers will uncover paths toward delivering precision medicine.

[WATCH VIDEO](#) 

# Rethinking consent paradigms

- Improved transparency
- Tiered consent
- Opt-out mechanisms
- Citizen science
- Issues with generalizability

# Discussion

## “Food for Thought” Questions

- Who owns and controls genetic information and how will it be used?
- How do we prepare the public to make informed choices?
- How do we as a society balance current scientific limitations and social risk with long-term benefits?
- How does personal genetic information affect an individual and society's perceptions of that individual?
- How does genomic information affect members of minority communities?

# Genetic Privacy

Genetic Information Nondiscrimination Act  
(GINA)

# History of GINA

*First federal legislation to prevent the misuse of genetic information*

- Forward-looking vs. premature
- Human seq starting ~300 genetic tests available

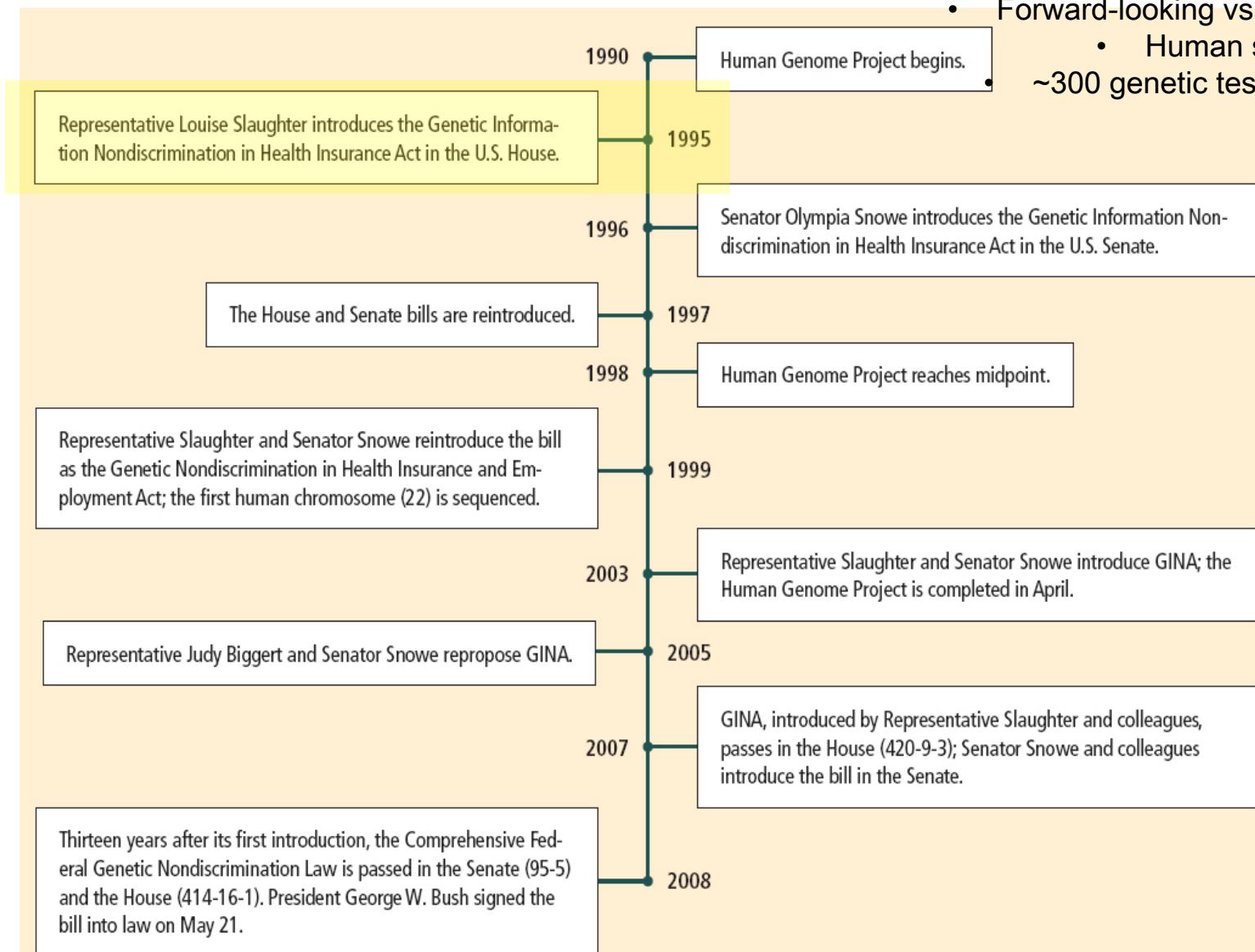


Figure 1. Genetic Information Nondiscrimination Act (GINA) Legislative History

# May 21, 2008



Passed by overwhelming majorities in the House of Representatives and the Senate.

President George W. Bush signs H.R. 493, the Genetic Information Nondiscrimination Act of 2008 among legislators in the Oval Office of the White House.

# First Major New Civil Rights Bill of the New Century

**“GINA is the first major new civil rights bill of the new century”**

*- Senator Edward Kennedy (GINA Co-sponsor)*

- First U.S. federal antidiscrimination statute crafted to address an area where there was no well-documented history of widespread discrimination and no stigmatized group to protect.
- Statute proposes:
  - 1) “to fully protect the public from discrimination” and also to
  - 2) “allay their concerns about the potential for discrimination, thereby allowing individuals to take advantage of genetic testing, technologies, research and new therapies”



*Bush praised Sen. Edward Kennedy, who was instrumental in pushing the legislation through Congress. The Massachusetts Democrat was diagnosed with a malignant brain tumor the week the bill was signed.*

# What does GINA do?

*Protects from genetic discrimination in health insurance and employment.*

## Health Insurance Protections

It is against the law for health insurers to request, require, or use genetic information

- Eligibility for health insurance
- Health insurance premiums, contribution amounts, or terms of coverage

Health insurers can legally ask for genetic information for the purposes of making decisions about paying for certain tests or treatments, but once they have it they cannot use it to discriminate in the ways described above.

It is also against the law for health insurers to:

- Consider family history or a genetic test result a pre-existing condition
- Ask or require that you have a genetic test
- Use any genetic information they do have to discriminate against you, even if they did not mean to collect it

# Definition of Genetic Information

## *Genetic Information in GINA*

- An individual's genetic tests or the genetic tests of the individual's family members, and the manifestation of a disease or disorder in the individual's family members
- The request or receipt of genetic services or participation in clinical research that includes genetic services, for both the individual and the individual's family members

## *Family Member*

- First-, second-, third- or fourth-degree relative

## *Genetic Services*

- Receipt of genetic testing, genetic counseling, genetic education, or participation in a research study

## *Genetic Test*

- Analysis of human DNA, RNA, chromosomes, proteins, or metabolites that detects genotypes, mutations, or chromosomal changes

# What does GINA do?

*Protects from genetic discrimination in health insurance and employment.*

## **Employment Protections**

It is against the law for employers to use genetic information to:

- Make decisions about hiring, firing, promotion, or pay
- Limit, segregate, classify, or otherwise mistreat an employee

also illegal for an employer to request, require, or purchase genetic information.

There are some exceptions to when an employer can legally have an employee's genetic information, and when this occurs, the employer must keep it confidential and in a separate medical file.

GINA applies to all employers with 15 or more employees with the exception of U.S. military and federal employees (however both have other relevant policies in place).

# What does GINA NOT do?

## Current Health Status

- GINA does not prevent health insurers from making decisions about eligibility, coverage, or premiums based on a person's current symptoms or diagnosis of a disease or health condition
- This is true even if the condition is a genetic disease or was diagnosed in part by a genetic test (other policies are relevant here)

Adapted from: Rothstein, M.A. (2008), J Law Med Ethics. 36(4): 837–840.	Asymptomatic	Mild, Temporary, Presymptomatic	Impairment/ Disease
Genetic Information Nondiscrimination Act	Yes	No	No
Americans with Disabilities Act	No	No	Yes

*ADA – Prohibits discrimination, including employment discrimination, on the basis of disability (an impairment that constitutes a substantial limitation of a major life activity).*

ACA  
(health insurance)  
Employment?

## Other Types of Insurance

- GINA does not apply to life, disability, and long-term care insurance.

## Some Federal Health Services and Systems

# GINA Case Study: DTC Example



## GINA and Direct-to-Consumer Genetic Testing

A 25-year-old male undergoes genetic screening through a direct-to-consumer (DTC) commercial company. The results demonstrate an apolipoprotein E4 (apoE4) genotype, increasing his risk for cardiovascular disease and Alzheimer disease. The patient makes an appointment with his medical provider for a physical examination and lipid profile.

### **Issues:**

1. The patient's genetic profile obtained through his DTC test is protected by GINA.
2. The patient-related discussions and medical history obtained by his medical provider also are protected.
3. Because he is 25 years of age and is too young for current lipid profile screening recommendations, his insurer likely will not cover laboratory testing without review of the DTC results that demonstrate his increased cardiovascular risk by genotype.
4. The insurer can request the DTC results to determine medical necessity for lipid profile screening and surveillance, and Alzheimer surveillance later in life.
5. Under GINA, he cannot be denied health insurance because of his apoE4 genotype.

# Impact of GINA & Public Awareness

## ***Tests of GINA's Authority***

- EEOC estimated that in fiscal year 2013 there were 333 GINA-related charges of employment discrimination (vs. 90,000 in other areas), and most also included ADA-related claims (Green, Lautenbach & McGuire, NEJM 2015)

## ***Public Awareness Tests of GINA's Authority***

J Genet Counsel (2015) 24:512–521  
DOI 10.1007/s10897-014-9771-y

PROFESSIONAL ISSUES

### **Public Awareness of Genetic Nondiscrimination Laws in Four States and Perceived Importance of Life Insurance Protections**

Alicia A. Parkman • Joan Foland • Beth Anderson • Debra Duquette •  
Holly Sobotka • Mary Lynn • Shelley Nottingham • William David Dotson •  
Katherine Kolor • Summer L. Cox

- In 2010 multistate survey, less than 20% of adult respondents were aware of GINA
- More recent evidence suggests that after reading a description of GINA, some fraction of individuals may become MORE concerned about discrimination

# Genomic Medicine Education

How do we prepare healthcare providers?

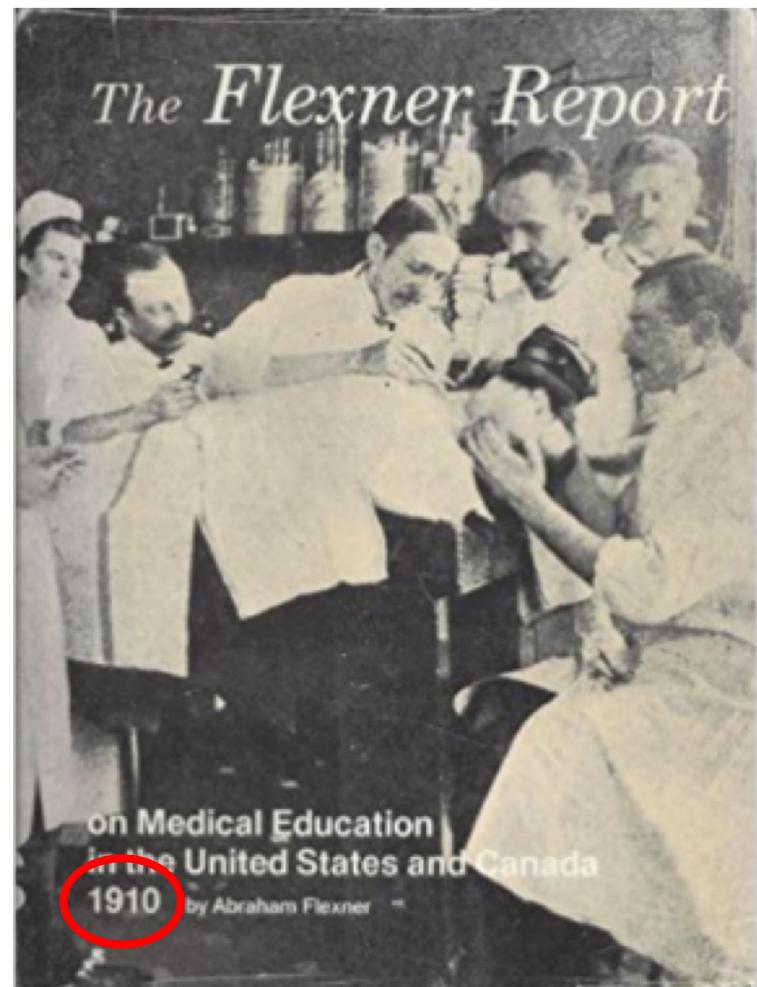
# Unreadiness Among Healthcare Providers

- **Physicians in short supply (~850k in the US), overloaded with patient care responsibilities, and ill prepared to integrate new body of knowledge**
- **Nearly half are over 50 years of age with training that occurred before completion of the Human Genome Project and advances in genomic medicine**
- **In 2011 only 135 medical geneticists and 331 genetic counselors were certified, and there are cumulatively <3500 of these professionals for a country of over 300 million people – trained in Mendelian genetics**
- **Paradox that 90% of consumers regard physicians as best resource for guidance about their genomic information, but over 90% of physicians reported lacking confidence and being underprepared in using genetic information to guide their practice**

# Move Medical Education into the 21<sup>st</sup> Century



850k US Physicians  
+  
1 Million All of Us  
Volunteers



# Current Genomics Education Landscape

- Currently non-genetics specialties have no knowledge or core competency requirements in genomics
- In 2013 less than 15% of AAMC accredited schools had any offerings related to genomics
- Models Proposed to Fill the Gap
  - Traditional course(s)
  - Independent study projects
  - Track or degree emphasis area
  - Online education resources
  - Hands on genomic analysis opportunities (e.g., cadaver, donor or personal genomes)

Genetics inMedicine | SPECIAL ARTICLE

© American College of Medical Genetics and Genomics

**Framework for development of physician competencies in genomic medicine: report of the Competencies Working Group of the Inter-Society Coordinating Committee for Physician Education in Genomics**

Bruce R. Korf, MD, PhD<sup>1</sup>, Anna B. Berry, MD<sup>2,3</sup>, Melvin Limson, PhD<sup>4</sup>, Ali J. Marian, MD<sup>5</sup>, Michael F. Murray, MD<sup>6</sup>, P. Pearl O'Rourke, MD<sup>7</sup>, Eugene R. Passamani, MD<sup>8</sup>, Mary V. Reiling, PharmD<sup>9</sup>, John Tooker, MD, MBA<sup>10</sup>, Gregory J. Tsongalis, PhD<sup>11,12</sup> and Laura L. Rodriguez, PhD<sup>8</sup>

JAMA February 9, 2016 Volume 315, Number 6

VIEWPOINT

Integrating Cadaver Exome Sequencing Into a First-Year Medical Student Curriculum

Glenn S. Gerhard, MD  
Lewis Katz School of Medicine, Temple University, Philadelphia, Pennsylvania.

The rapid growth in the use of genetics in medical care, driven largely by the Human Genome Project and the emergence of next-generation DNA sequencing technology, has outpaced the education and training capabilities of clinicians and providers at all levels. This has led to the formation of the Inter-Society Coordinating We therefore decided to integrate modern genetics and genetics teaching into the first-year medical student curriculum through the use of exome sequencing of DNA obtained from cadavers used to teach anatomy. This exposes every member of the first-year class to next-generation DNA sequencing and avoids any of the nega-

Genetics inMedicine | ORIGINAL RESEARCH ARTICLE

© American College of Medical Genetics and Genomics

**How do students react to analyzing their own genomes in a whole-genome sequencing course?: outcomes of a longitudinal cohort study**

Saskia C. Sanderson, PhD<sup>1</sup>, Michael D. Linderman, PhD<sup>1,2</sup>, Randi Zinberg, MS<sup>1</sup>, Ali Bashir, PhD<sup>1,2</sup>, Andrew Kasarskis, PhD<sup>1,2</sup>, Micol Zweig, MPH<sup>1</sup>, Sabrina Suckiel, MS<sup>1</sup>, Hardik Shah, BS<sup>1,2</sup>, Milind Mahajan, PhD<sup>1,2</sup>, George A. Diaz, MD, PhD<sup>1</sup> and Eric E. Schadt, PhD<sup>1,2</sup>

OPEN ACCESS Freely available online

PLOS ONE

Evidence That Personal Genome Testing Enhances Student Learning in a Course on Genomics and Personalized Medicine

Keyan Salari<sup>1\*</sup>, Konrad J. Karczewski<sup>1</sup>, Louanne Hudgins<sup>2</sup>, Kelly E. Ormond<sup>1,3</sup>

<sup>1</sup> Department of Genetics, Stanford University, Stanford, California, United States of America, <sup>2</sup> Department of Pediatrics, Division of Medical Genetics, Stanford University, Stanford, California, United States of America, <sup>3</sup> Stanford Center for Biomedical Ethics, Stanford University, Stanford, California, United States of America

# Thanks!

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