

Bioethics of Personalized Genomics and Genetic testing



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Bioethics:



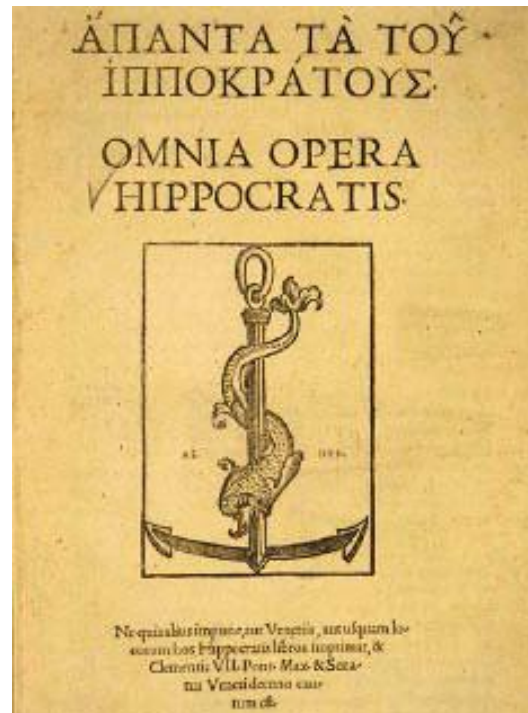
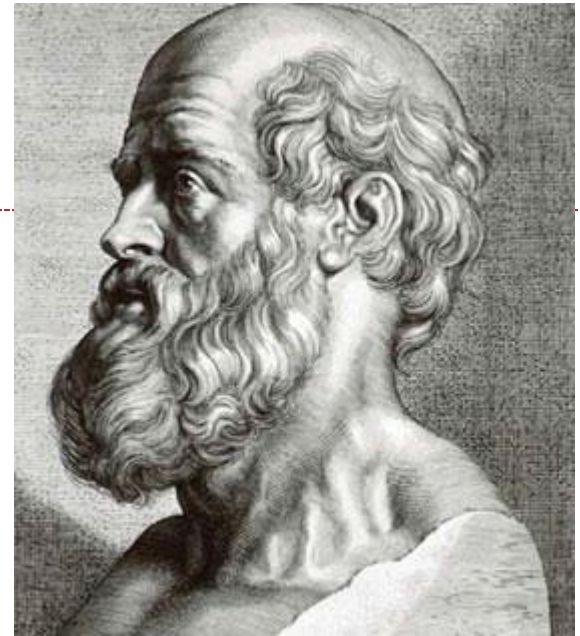
***NOUN, “THE ETHICS
OF BIOLOGICAL AND
MEDICAL RESEARCH”***

“Bioethics”



- Examines ethical issues in health care, health science, and health policy.
- Questions our attitude to basic human values and society’s responsibilities for the life and health of its members
- Evaluates how medical technology can change meaning of health and the effect on the way we live and die.
- Considers the right and wrong of decisions

The Hippocratic Oath



Hippocratic Oath (Modern version)

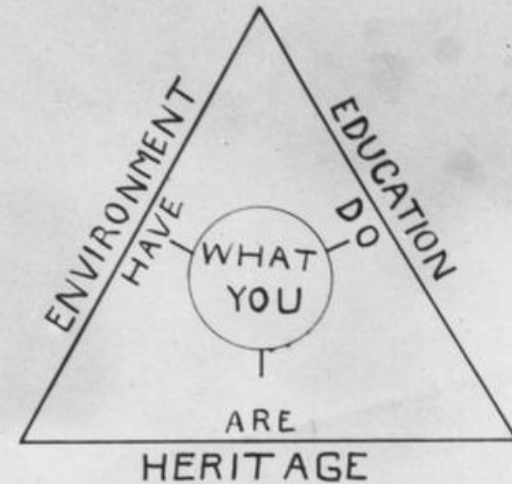
I swear to fulfill, to the best of my ability and judgment, this covenant:

I will respect the hard-won scientific gains of those physicians in whose steps I walk, and gladly share such knowledge as is mine with those who are to follow. I will apply, for the benefit of the sick, all measures which are required, avoiding those twin traps of overtreatment and therapeutic nihilism. I will remember that there is art to medicine as well as science, and that warmth, sympathy, and understanding may outweigh the surgeon's knife or the chemist's drug. I will not be ashamed to say "I know not," nor will I fail to call in my colleagues when the skills of another are needed for a patient's recovery. **I will respect the privacy of my patients, for their problems are not disclosed to me that the world may know.** Most especially must I tread with care in matters of life and death. If it is given me to save a life, all thanks. But it may also be within my power to take a life; this awesome responsibility must be faced with great humbleness and awareness of my own frailty. Above all, I must not play at God. I will remember that I do not treat a fever chart, a cancerous growth, but a sick human being, whose illness may affect the person's family and economic stability. My responsibility includes these related problems, if I am to care adequately for the sick. **I will prevent disease whenever I can, for prevention is preferable to cure. I will remember that I remain a member of society, with special obligations to all my fellow human beings, those sound of mind and body as well as the infirm.** If I do not violate this oath, may I enjoy life and art, respected while I live and remembered with affection thereafter. May I always act so as to preserve the finest traditions of my calling and may I long experience the joy of healing those who seek my help.

UNFIT HUMAN TRAITS

SUCH AS FEEBLEMINDEDNESS
EPILEPSY, CRIMINALITY,
INSANITY, ALCOHOLISM,
PAUPERISM AND MANY OTHERS,
RUN IN FAMILIES AND ARE
INHERITED IN EXACTLY THE
SAME WAY AS COLOR IN
GUINEA-PIGS. IF **ALL**
MARRIAGES WERE **EUGENIC**
WE COULD **BREED OUT**
MOST OF THIS UNFITNESS
IN **THREE GENERATIONS.**

THE TRIANGLE OF LIFE



YOU CAN IMPROVE YOUR **EDUCATION**,
AND EVEN CHANGE YOUR **ENVIRONMENT**;
BUT WHAT YOU REALLY **ARE** WAS ALL
SETTLED WHEN YOUR PARENTS WERE
BORN.
SELECTED PARENTS WILL HAVE
BETTER CHILDREN **THIS**
IS THE GREAT AIM OF **EUGENICS**

History of Unethical Research



- Nazi research by Mengele
 - Twins to study genetics, hypothermia, head injuries
- Guatemala syphilis study (1946-1948): prisoners and mental asylum patients purposefully infected with syphilis
- Tuskegee Experiment (1932-1972)-American researchers purposely withheld treatment for 399 African-American people with syphilis for the sole purpose of studying the long term effects of the disease.

History of Unethical Research

- Willowbrook Study (1963-1966)-Children with developmental disabilities were deliberately infected with Hepatitis (some were even fed fecal matter). Purpose of the study was to examine the course of the disease and to test a potential immunization
- Human radiation experiments by the US Department of Defense & Atomic Energy Commission.
- Zimbardo's Stanford Prison Experiment (1971). Study had to be ended prematurely because of abusive behaviors generated participants who where assigned as guards over those subjects that were assigned as prisoners.
 - <http://www.prisonexp.org/>

Issues in the era of modern bioethics



- Distinguishing “benefit” from “harm”
- The rights of the individual versus society
- Economics & law
- How to distribute benefits and burdens of research and health care amongst individuals and society

Birth of modern bioethics: Declaration of Helsinki (1964)



- <http://www.wma.net/en/30publications/10policies/b3/index.html>
- The World Medical Association (WMA) is a statement of ethical principles for medical research involving human subjects, including research on identifiable human material and data.
- Primarily addresses physicians but encourage those whose research involves human subjects to adopt these principles.

Birth of modern bioethics in U.S.



- 1968 Congressional Hearing
 - Led by Mondale
 - Mandated a national debate on directions of medical science in America
- 1975 The National Research Act
 - Established 11-member National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research.
 - "to identify the basic ethical principles that should underlie the conduct of biomedical and behavioral research involving human subjects and to develop guidelines that should be followed in such research"
 - Established IRB system

Belmont report 1978



**THE MAJOR ETHICAL
STATEMENT GUIDING
HUMAN RESEARCH IN
THE UNITED STATES**

Belmont Report defined boundaries between research and practice



Term	Definition	Outcome
Practice	Interventions designed solely to enhance well being of the individual	Reasonable expectation of success
Research	Activity to test a hypothesis: contributes to general knowledge	Permits a conclusion to be drawn

Three principles of the Belmont Report



1. Respect for persons
2. Beneficence
3. Justice



Belmont Report: Respect for persons



- Treat people as *autonomous* (the right to self-govern)
- Protect those who have diminished autonomy
 - *Vulnerable* populations, ie. Children, prisoners, elderly
- ❖ *Voluntary participation*
- ❖ *Informed consent*
- ❖ *Protection of privacy & confidentiality*
- ❖ *Right to withdraw without penalty*

Belmont Report: Beneficence



- Do no harm
 - Maximize benefits
 - Minimize risks
 - Obligation
-
- ❖ *Justice risks by benefits*
 - ❖ *Minimize risks*
 - ❖ *Avoid conflict of interest to avoid bias*

Belmont Report: Justice



- Distribute benefit and burden
- 5 formulations:
 1. Everyone receives equal share
 2. Distribution based on need
 3. Distribution based on individual effort
 4. Distribution based on societal contribution
 5. Distribution according to merit

Belmont Report Applied

Respect

- Informed consent
 - Obtain consent
 - No coercion
 - Protect privacy

Beneficence

- Risks/benefits
 - Minimize risks
 - Risks reasonable in relation to benefits
 - Maintain confidentiality

Justice

- Enrollment
 - Equal selection
 - Avoid exploitation of vulnerable population

Issues in bioethics



- Contraception & abortion
- Conception & reproductive technology
- Cloning
- Neonatal ethics
- Organ donation

- Stem cells
- Consent
- Disability
- End of life
- Euthanasia

Bioethics of genetic research



- **Genomic Research:** issues arising from coupling individual genome information to private health information
- **Genomic Health Care.**
- **Broader Societal Issues.** Implications of research on health & disease and the responsibility of the individual to society
- **Legal, Regulatory and Public Policy Issues.**

Issues in Genetics Research



- Genetic testing
 - Coverage and reimbursement
 - Personalized medicine
- Intellectual property and genomics
 - Gene patenting
- Genetic Discrimination
 - Privacy

Genetic testing: Personalized medicine



Genetic testing: direct to consumer (DTC) genetic testing companies



- Navigenics: purchased by Life Technologies
- Pathway Genomics: “physician order only”
 - “Order online and Pathway will provide a physician who will authorize your testing services.”
- deCODEme: purchased by Amgen
- 23andme
- Lumingenix: Australia based
- DNA DTC (Gene-by-Gene): started in 2012

DTC available in all states except New York
DTC banned in most of Europe
Allowed in Britain and Belgium

DTC should be available to consumer



- Greater autonomy
- Empowerment: “knowledge is power”
 - Informed choices on lifestyle choices, diet, reproduction
 - Couples can learn about their carrier status, disabilities of the fetus to guide decision about abortion or fetal treatment
- Maintain privacy (genetic information separate from health insurance companies and medical records)

Benefits of knowing genetic status



The New York Times

Google Co-Founder Has Genetic Code Linked to Parkinson's

By Miguel Heft

Published: September 18, 2008

MOUNTAIN VIEW, Calif. —Sergey Brin, a Google co-founder, said Thursday that he has a gene mutation that increases his likelihood of contracting Parkinson's disease, a degenerative disorder of the central nervous system that can impair speech, movement and other functions.

Mr. Brin, who made the announcement on a blog, says he does not have the disease and that the exact implications of the discovery are not clear. Studies show that his likelihood of contracting Parkinson's disease in his lifetime may be 20 percent to 80 percent, Mr. Brin said.

“...I carry the G2019S mutation and when my mother checked her account, she saw she carries it too.

The exact implications of this are not entirely clear. ...Nonetheless it is clear that I have a markedly higher chance of developing Parkinson's in my lifetime than the average person. In fact, it is somewhere between 20% to 80% depending on the study and how you measure....

This leaves me in a rather unique position. **I know early in my life something I am substantially predisposed to. I now have the opportunity to adjust my life to reduce those odds ...**

I feel fortunate to be in this position. Until the fountain of youth is discovered, all of us will have some conditions in our old age only we don't know what they will be. **I have a better guess than almost anyone else for what ills may be mine -- and I have decades to prepare for it.”** Sergey Brin

DTC should NOT be available to consumer



- Lack of regulation
 - Inaccuracy of testing
- Lack of counseling or education
- Lack of safeguards for consumers
- Unclear goal of DTC companies
- Unsupported claims made by DTC testing
 - False expectations regarding benefits of testing
 - Consumers can make irrevocable decisions based on results, ie. Terminate pregnancy, choice in spouse, forgo treatment

DTCs can be misleading



- United States Government Accountability Office (2006):
 - “misleading test results further complicated by deceptive marketing and other questionable practices”
 - “test results are misleading and of little or no practical use.”
 - GAO donors received disease risk predictions that varied across the four companies, indicating that identical DNA samples yield contradictory results. One donor was told that he was at below average, average, and above average risk for prostate cancer and hypertension.”



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Study shows knowing
your genetic make-up
may increase **Success**
of losing weight.

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Benefits of the Inborn Talent Genetic Test:

- Understand your child's natural talents and personality and shape his/her future development on this knowledge.
- Better utilise and invest your efforts, resources and time to develop the gifted areas to maximise the returns on your investments.
- Tailor-make the development process around your child's personality
- Plan for your child's future more effectively and efficiently
- Choose the right course to major during college years
- Provide a guideline for career choices

The Inborn Talent Genetic Test helps parents identify their children's hidden talents that may not be obvious at young age. Furthermore, it also reveals some personality traits that the child may possess, judging from his/her genetic make-up.

Since knowledge is power, early identification will help you take control and maximize the development of your children. Not only you will be able to find out which areas of your child's development you should concentrate on in order to maximise his/her potential, you will also be able to plan the way to develop these talents, according to the child's personality. By building a strong foundation at an early age, your child has a much better probability of success later in life!



Love is no coincidence!
Matching people by analyzing their
DNA
Order a GenePartner Test
Dating Sites & Matchmakers

<http://www.genepartner.com/index.php/>


DTC should NOT be available to consumer



- Most genetic information have little impact on behavior or outcome
- Most early customers of DTCs driven by curiosity rather than concern for health
- Negates personal responsibility and behavior
 - Smoking, diet, exercise
- Risk of non-consensual testing
 - Testing potential spouses
 - Testing children to confirm paternity
- Economics of genetic testing

Limitations of genetic testing



- Having positive genetic testing  developing disease.
- Risk for developing disease may not be accurate based on current research
 - Most risks from GWAS data have low odds ratios for developing disease
- Does not predict *when* a person *may* show symptoms of a disease
- Does not predict severity of symptoms

Risks



- Personal implications
 - Risk for a disease
 - ✦ Neurological disease without known treatment or cure: Alzheimer's disease or Parkinson's disease
 - ✦ Psychiatric diseases: schizophrenia
 - ✦ Cancer genes- BrCA1 and 2
- Confidentiality issues
 - ✦ Others may find out test results

Personalized Genomics: BrCA gene



- <http://well.blogs.nytimes.com/2012/12/31/carrying-a-cancer-gene-unsure-i-want-to-know/>
- *“But then I clicked away. The Bible doesn’t tell us if Eve ate any more apples, but I have had my fill of revelations. I am 21 years old, and I want to be free to live a normal life: fate unbound by double helix, future exploding with possibility. I don’t want to know.” Stanford graduate student, Emma Pierson*

Psychological outcome from genetic information



- Anxiety/Stress
- Confusion
- Impact on family:
 - In some cases, genetic testing creates tension within a family because the results can reveal information about other family members in addition to the person who is tested.

Using Alzheimer's as a model for revealing genetic test results



- AD is incurable
- REVEAL study assessed patients who were told their APOE4 genetic status
 - No difference between those who received positive APOE4 results from those who had negative results.
 - Suggest that those who receive their genetic information under controlled circumstances are not at greater risk for harm.
 - Test specific stress is significant but transient if patients receive proper post-test genetic counseling

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Connect to your past.



Health
Learn for the present.



Research
Participate for the future.

Learn valuable health & ancestry information.



\$99

Order Now

Ancestry



- Find information about your immediate family background that may not have been disclosed
 - Jewish?
 - African-American?
- Adoption history not disclosed
- Raises question of paternity

Do others want to know?



Do family members or society have the “right” to know genetic results?



Case: Right of the individual *vs* right of family/society



- J.D. develops symptoms and seeks medical attention.
- He receives diagnosis of an incurable neurodegenerative disease
 - He decides not to disclose the result to his wife and 4 kids
- His daughter wants to have children, but first asks her father, J.D., the result of his genetic test result
 - He *lies* to her and says he is negative
- She becomes pregnant.
 - Out of remorse, J.D. discloses to her his positive genetic test result
 - His daughter is distraught and decides to have herself tested as well.
 - Her predictive genetic testing is also positive

Rights of the individual vs rights of society



- What would you do if you were the genetic counselor to J.D.?
 - Would you disclose his test result to his family?
- Should J.D's daughter have gotten predictive testing?

Other “risks” for genetic testing



- False positives
 - Anxiety/Stress
 - Harm from undergoing unnecessary tests or procedures
- False negatives:
 - Ignoring a disease when genetic testing is negative
 - ✦ Diseases can occur sporadically

“I *will* have PD”



Case 1: 57 year old woman with a family history of Parkinson’s disease who is asymptomatic

- ✦ She has a SNP associated with mildly increased risk for developing PD
- ✦ She travels from another state every year for neurological examination by a movement disorders specialist to evaluate for signs of PD
- ✦ She has planned her life to account for developing PD:
 - Early retirement
 - Bought long term care insurance
 - Moved into a single story home

How would you counsel her?

“But I can’t have PD because I don’t have the gene!”



- Case 2: 69 year old retired lawyer with a 8 year history of parkinsonism on exam
 - He does not carry any SNPs associated with PD
 - Sequencing for LRKR2 mutation is negative
 - He refutes the diagnosis of PD because he does not have the gene and refuses to take medications to treat the symptoms
 - ✦ He is now in a wheelchair
 - ✦ Moved into a nursing home



Take a more active role in managing your health

Knowing how your genes may impact your health can help you plan for the future and personalize your healthcare with your doctor.

Add to Cart »

23andMe estimates your genetic chances of getting
Type 2 Diabetes



AS LOW AS

8 %



AS HIGH AS

52 %



23andMe will tell you:
**Your genetic risk
What you can do**

*This result based on our calculations for males with European ancestry



Plan for the future

Find out if your child will be at risk for 48 inherited conditions and learn about steps you can take.

[about carrier status](#)



Be on the lookout now

Knowing your health risks will help you and your doctor figure out health areas to keep an eye on.

[about disease risks](#)



Plan with your doctor

Personalize your healthcare by knowing in advance how you will respond to certain medications like Warfarin.

[about drug response](#)

Genetic testing currently does not alter behavior: AAT and smoking cessation



- **Does genetic testing result in behavioral health change? Changes in smoking behavior following testing for alpha-1 antitrypsin deficiency. Carpenter et al. 2007**

- **PURPOSE:**

- This study examines the impact of genetic testing for alpha-1 antitrypsin (AAT) deficiency, a condition that usually results in emphysema in individuals exposed to cigarette smoke. We evaluated whether AAT testing, performed in the home and with minimal contact (reading materials including advice on cessation), results in quit attempts and abstinence.

- **METHODS:**

Identified smokers (N = 199) from a larger study of genetic testing were surveyed 3 months following receipt of their AAT genotype. The primary endpoint was the incidence of quit attempts.

- **RESULTS:**

Smokers who tested severely AAT deficient were significantly more likely to report a 24-hr quit attempt (59%) than were those who tested normal (26%). Carriers had a 34% quit attempt rate. Severely AAT deficient smokers were more likely than both carriers and normals to seek information on treatment, use pharmacotherapy for smoking cessation, and report greater reductions in their smoking. There were no group differences in 3-month abstinence rates.

- **CONCLUSIONS:**

Knowledge of severe AAT deficiency, but not carrier status, may motivate smokers toward cessation. The AAT testing experience may have consequences for outcomes of other genetic conditions with modifiable health behaviors.

REVEAL study in Alzheimer's: behavioral changes



- No change in smoking cessation or modification of dietary or exercise habits.
- Favor biological intervention over behavior (ie. Lifestyle) changes
 - Most common change is addition of vitamins or nutritional supplements
- Patients also bought long term care insurance
 - REVEAL study patients are four times more likely to buy LTC at one year follow up.
 - GINA does not cover LTC insurance
 - ✦ Will LTC companies require genetic testing prior to issuing coverage?

ORIGINAL ARTICLE

Effect of Direct-to-Consumer Genomewide Profiling to Assess Disease Risk

Cinnamon S. Bloss, Ph.D., Nicholas J. Schork, Ph.D., and Eric J. Topol, M.D.

Table 3. Primary Outcome Measures before and after Receipt of Results of Genetic Testing for 2037 Subjects Who Completed Follow-up.*

Outcome Measure	Baseline Score	Follow-up Score	P Value [†]
Anxiety	35.2±9.6	34.6±10.0	0.80
Dietary fat intake	16.0±7.9	15.2±7.5	0.89
Exercise [‡]	28.6±23.0	28.6±22.9	0.61

* Plus-minus values are means ±SD. The assessment tools and ranges of scores for each category are listed in Table 2.

[†] All P values were calculated with the use of the Wilcoxon signed-rank test after adjustment for covariates.

[‡] A total of 1943 subjects were included in this analysis.

RESULTS

From a cohort of 3639 enrolled subjects, 2037 completed follow-up. Primary analyses showed no significant differences between baseline and follow-up in anxiety symptoms ($P=0.80$), dietary fat intake ($P=0.89$), or exercise behavior ($P=0.61$). Secondary analyses revealed that test-related distress was positively correlated with the average estimated lifetime risk among all the assessed conditions ($\beta=0.117$, $P<0.001$). However, 90.3% of subjects who completed follow-up had scores indicating no test-related distress. There was no significant increase in the rate of use of screening tests associated with genomewide profiling, most of which are not considered appropriate for screening asymptomatic persons in any case.



**WHAT ARE THE ECONOMIC
COST AS RESULT OF
PERSONALIZED MEDICINE?**



Should genetic testing be by prescription only?



Yes

- Physician involved in explaining results
- This is the case in France, Germany, the Netherlands, Portugal and Switzerland
- Genetic test result determined to affect outcome or benefit

No

- Lack of autonomy for patients
- Paternalistic medicine
- Physicians don't currently understand value genetic test results

Blumer v. Acu-Gen Biolabs



- 2005 lawsuit against Acu-Gen Biolab
 - DTC to determine gender of fetus
 - Claim of 99.9% accurate
 - Also advised results of genetic defects
 - ✦ Many woman had additional testing and procedures to test for chromosomal abnormality
 - ✦ Caused unnecessary anxiety
 - ✦ Created additional expense for patient and health care system
 - ✦ Caused potential harm to expectant mothers and their fetus due to additional procedures
 - Company declared bankruptcy before going to trial

Laws & Bioethics



Legal ramifications of genetic test result



Can patients sue the physician for missing a “treatable” condition based on genetic test results?

Can defense attorneys use genetic predisposition of their client as part of their defense?

Legal case: lawsuit



- On the heels of a nearly \$3 million verdict for a Portland-area couple whose baby was born with Down syndrome, another couple has filed a \$6.25 million lawsuit claiming doctors conducting prenatal tests failed to detect a serious genetic disorder in their child.

The suit claims that medical staff at Oregon Health & Science University and Kaiser Permanente misinterpreted a January 2010 amniocentesis and other tests, leading them to tell North Portland residents Anna and Cory Miller that their future child likely wouldn't have major disabilities.

Based on that information, the Millers chose to continue the pregnancy, according to the suit filed Tuesday in Multnomah County Circuit Court. Their daughter was born on May 28, 2010, and days later they learned she had Charge syndrome, a condition that often includes heart defects, breathing problems, swallowing problems and hearing and vision impairments. It occurs in 1 in about 10,000 births, and can require months of hospitalization, repeated surgeries and years of developmental therapy and extra care.

Legal case: lawsuit



- Like in many so-called "wrongful birth" lawsuits, the Millers had to declare that they would have terminated the pregnancy had they known their daughter, now 2, would be born with major disabilities.

The suit seeks \$2 million to pay for medical care, therapy, medication, educational expenses and the extra costs of raising a child with a disability; \$3 million for their daughter's living, medical and therapy expenses once she becomes an adult; \$250,000 for wages Anna Miller has lost and will lose in caring for their daughter; and \$1 million for "the emotional distress, anxiety and depression experienced" by the Millers

Hypothetical example of legal ramifications of DTC testing



- “X non-consensually obtains a saliva sample from Y’s beer glass, analyses her DNA through a home-test kit, and sells to a newspaper(which publishes it) the information that Y has a particular genetic condition.
- The same process could be performed through a mail-order laboratory service, by shipping the wrongfully obtained genetic sample to a DTC company’s laboratory, for a wider genetic scan. This could produce Y’s genetic-profile, providing plentiful personal information. Should Y be a public figure, publicizing information pertaining to her future health risks—her status as a carrier of the gene mutation linked to the early onset of Alzheimer’s, for instance—entails an additional professional and monetary harm.”

Hypothetical example of unintended consequences



- G, a 15-year-old minor, sends his genetic sample to an Internet-based DTC company, in order to have it analyzed for Huntington's disease. He has a family history (his father has Huntington's disease) and he is, therefore, well acquainted with this horrendous condition. His parents have refused to allow him to take the test, or to consult a genetic counselor to have his risk assessed.
- The company's on-line consent form, accepted by G, contains a disclaimer, according to which the consumer declares that he is an adult. Following the receipt of the test results by e-mail, confirming that G carries the gene for Huntington's disease, G commits suicide.

Ethical considerations in testing minors



- Psychological harm to the minor
- Adverse effect on minor's self-esteem
- Loss of autonomy as an adult
- May limit future

- For some minors, a genetic test result could be “liberating”
 - Guide personal and career choices
 - Provide additional time to prepare for future
 - ✦ However, consequences of genetic information are not fixed in stone. A seemingly “terminal” result may change with advances in medicine

Guidelines in testing minors



- Test should promote minor's best interest & well being
 - Who determines the minor's best interest?
- Medical benefits available
 - Pre-emptive or therapeutic treatment available
- Pre-testing for adult onset disorders is inappropriate
- Pre-testing for carrier status should also be deferred until the minor/patient reaches reproductive age.

Case Discussion: testing of minor & disclosure of information



- **BACKGROUND**

- Dr. Hallmayer is the principal investigator of a twin study of autism, in collaboration with a number of other institutions, including the Autism Genetic Research Exchange in Los Angeles (which is conducting assessments for the project), the California Health Department, Kaiser Permanente, and UCSF (Neil Risch, statistics). Stanford is the primary site, and the study has received IRB approval from all participating institutions.
-
- For this study, subjects were drawn via the California Health Department, which has records of all people diagnosed with autism in California (where the diagnosis is generally made by regional centers). Approximately 700 twin pairs have been identified in which at least one twin had a diagnosis of autism since 1988. The CATS study seeks to enroll 300 twin pairs (including both monozygotic and dizygotic twins) and their parents, and 30 families have already been enrolled.
-
- The study involves a number of psychological and behavioral assessments performed for research purposes, by research staff. None of the assessments are performed by licensed clinical psychologists or MDs, but are performed by people trained to administer the specific tests. The study also involves a blood draw or buccal swab of the children for Fragile X testing (by PCR analysis, performed by Dr. Hallmayer's group) and determination of zygosity, and measurement of head circumference. The assessments include the following tests of the children (taking up to 4 or 5 hours):

Case from Stanford's Center for Integration of Research on Genetics and Ethics

Case Discussion: testing of minor & disclosure of information



- What needs to be reported to families?
- In which form should families be notified of results?
- Do cognitive tests need to be reported to parents?
- Should we only report on the affected children?
- Should learning disabilities or behavior issues observed during assessment (but not specifically obtained for the purposes of the study) be reported to parents?
- What should be done in cases where research/test results differ from parents knowledge? (i.e. if a “typical” child has a low IQ score or scores indicate a diagnosis of autism?)
- What information do we give regarding Fragile X or zygosity results?

Genetic discrimination: What does GINA do?

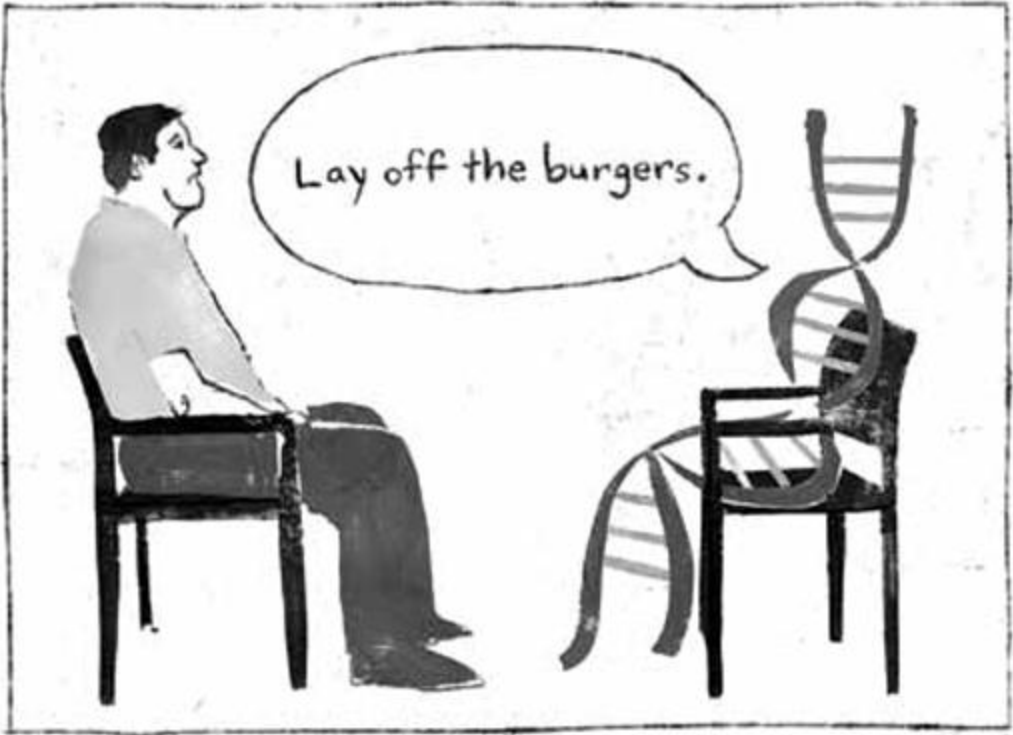


- Prevents health insurance plan from collecting genetic information including family medical history prior to, or in connection, with enrollment for purposes of underwriting.
- What is “underwriting?”
 - Rules for or determination of eligibility (including enrollment and continued eligibility) for benefits under the plan or coverage (including changes in deductibles or other cost-sharing mechanisms in return for activities such as completing a health risk assessment (HRA) or participating in a wellness program);
 - Computation of premium or contribution amounts under the plan (including discounts, rebates, payments in kind, or other premium differential mechanisms in return for activities such as completing an HRA or participating in a wellness program);
 - The application of any preexisting condition exclusion under the plan; and
 - Other activities related to the creation, renewal, or replacement of a contract of health insurance or health benefits.
- Prevents employers from requesting genetic information prior to employment

Genetic Privacy



- Online information
- Accidental disclosure of your genetic information to potential employers
- Who owns your data?
 - Navigenics sold to Life Technologies
 - deCODEme sold to Amgen



Obligation of researchers: Cultural implications in genetic research



- The warrior gene in modern Polynesians:
 - 2007 report (Lea et al.) identified MAO-A as the “warrior” gene in Polynesians (Maori)
 - Implied adventure & fearlessness that inspired great migration across Pacific
 - But also implied that this gene is responsible for violence in contemporary Polynesian communities

Swift rebuttal by scientific community, but wide spread interest by media already caused damage as the Maoris were associated with a gene that makes them *inherently* aggressive, unpredictable, and violent.

Obligations of researchers: **Indian Tribe Wins Fight to Limit Research of Its DNA**



Members of the tiny, isolated tribe had given DNA samples to university researchers starting in 1990, in the hope that they might provide genetic clues to the tribe's devastating rate of diabetes. But they learned that their blood samples had been used to study many other things, including mental illness and theories of the tribe's geographical origins that contradict their traditional stories

Obligations of researchers: Indian Tribe Wins Fight to Limit Research of Its DNA



But months later, tribe members learned more about the research when a university investigation discovered two dozen published articles based on the blood samples that Dr. Markow had collected. One reported a high degree of inbreeding, a measure that can correspond with a higher susceptibility to disease.

Ms. Tilousi found that offensive. “We say if you do that, a close relative of yours will die,” she said.

Another article, suggesting that the tribe’s ancestors had crossed the frozen Bering Sea to arrive in North America, flew in the face of the tribe’s traditional stories that it had originated in the canyon and was assigned to be its guardian.

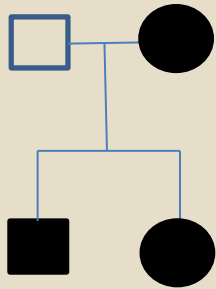
http://www.nytimes.com/2010/04/22/us/22dna.html?emc=eta1&_r=0

Case: Obligation of researcher

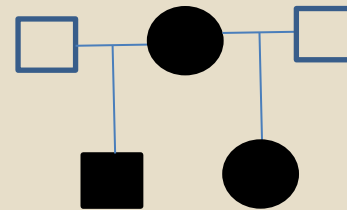


- Two siblings, of Asian descent, present with a neurological condition
- Their mother was reportedly affected, but now deceased
- Their father is still alive and agrees to genetic testing as well

Case: Obligation of researcher family pedigree



What do you disclose to the family?



Actual Pedigree

For more readings



- Stanford Center of Biomedical Ethics
<http://bioethics.stanford.edu/>
- Stanford Center for Integration of Research on Genetics and Ethics <http://cirge.stanford.edu/>
- National Human Genome Research Institute
<http://www.genome.gov/Issues/>