

Privacy and Genetic Information

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Part I

- Science

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Laws of Inheritance: a reminder

Genes are UNITS of information (sequences of DNA) that are transmitted with high FIDELITY through time

Genes may have dominant, recessive or X-linked effects.

Note: Things are really much more complicated than this.

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Impact of the Human Genome Project

- A government program that finished three years ahead of schedule and under budget!
- It gave us the consensus DNA sequence of humanity ... the operating system for the hardware ... the blueprint.
- It did not tell us how many genes there are or what they do
- Bu, it provided the tools to permit access of vast amounts of information

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Beyond the Human Genome Project

- Much work now focused on understanding DNA variation
- Single DNA letter changes are known as SNPs
- Example: atagca.....atacca
- Two or more SNPs can be combined into haplotypes
- Soon: the Haplotype Map. This is a map of combinations of SNPS that permits a less complicated approach to establishing the role of gene variants in risk for disease.

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Gene-Environment Interactions

Genes determine little, but they influence a great deal.

Fact: impossible to untangle nature from nurture.

Goal: understand how genes and the environment interact.

Best approach: Nurture your nature.

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DNA is the Information Molecule

All the genetic information coding for a human is present in the first cell (union of sperm and egg)

The information is a long sequence written in a four letter alphabet (A, T, G, C)

The DNA sequence in germ cells is 3,100,000,000 letters

The human genome has about 30,000 genes

Our cells may use 150,000 proteins (We have learned that one gene may be the origin of several similar proteins).

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The DNA Paradox

Your DNA is 99.9 percent the same as that of the person next to you

The .1 percent difference is immensely important

It means we differ at 6 million letters

We are both very alike and very different

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The Power of Gene Variants

- People with mutations in the HGPRT gene engage in specific forms of self-mutilation.
- There is almost certainly a single gene that determines the capacity for perfect pitch (necessary, but not sufficient).
- A single base pair mutation (A155G) in the 12s rRNA mitochondrial gene greatly increases the risk of hearing loss from exposure to aminoglycoside antibiotics
- Mutations in Monomine oxidase A gene have been strongly associated with violent behavior
- Mutations in FOXP2 gene may be highly associated with a specific, severe impairment in the ability to use language

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Part II

- Impact of the Science

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Areas in Which Genetic Information Is Having a Major Impact

- Agriculture
- Medicine
- Criminal Law

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The biggest impact of genomics so far? In agriculture!

In the USA tens of millions of acres are planted with corn, soy beans, and cotton that are genetically engineered to resist a certain non-chemical pesticide.

The rice genome has been sequenced, and Chinese scientists have developed many strains of genetically modified rice.

Golden rice may prevent blindness from lack of vitamin A

In October 2002 plans were made to create an onion that will not make a person cry.

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Areas Which May Experience High Genomic Impact Over the Next Decade

- Public Health: expanded newborn screening
- Employment (discovery of genes influencing occupational diseases)
- Life Insurance (discovery of gene variants highly associated with differential life expectancy)
- Religion (genetic engineering, cloning, preimplantation diagnosis, selective abortion)
- Education (discovery of alleles that influence educability)

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Key Challenge in Medicine: Understand the role of gene variants in common disorders

Diabetes has reached epidemic proportions, largely due to overweight and lack of exercise. Yet the best predictor of risk is family history

Alzheimer's disease is epidemic – apparently merely as a result of increased life expectancy. Yet, the best predictor of risk (currently) is ApoE genotype.

Cancer is a set of genetic diseases. All cancers arise due to a set of mutations in a single cell

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Major Trends in Applied Genomics 2004

Cost of acquiring genetic data continues to fall

Correlation of gene variants with variation in human health continues to rise.

Major advances in study of proteins – proteomics.

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Impact of Trends in Applied Genomics 2004

Medicine - New diagnostic tools (microarrays)
Emergence of pharmacogenetics
Progress in behavioral genetics

Pharmaceutical Industry - Drug development

Agriculture - Genetically engineered crops to improve yields

Nutrition – Food industry becoming interested in nutritional genomics as a new approach to wellness

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Molecular Medicine

We will soon use microarrays to ask many questions about an individual's DNA or proteins to aid in diagnosis and choice of therapy.

In 2002 MIT scientists characterized the circuitry (on/off switches) for all the 6000 genes in the yeast genome. The feat will be replicated in humans within 5 years.

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Part III

- Privacy

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Some Ethical Issues in Genomic Medicine

- Moral status of fetus and embryo
 - Prenatal diagnosis and selective abortion
 - Therapeutic cloning
- Carrier screening
 - Impact on parenting
- GENETIC PRIVACY**
 - Impact of risk assessment testing
 - Long term storage of DNA and related data
 - Forensic DNA data banks
- Gene therapy
 - Safety issues
 - Informed consent

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Genetics and Privacy: Major Issues

- Impact on research and research oversight
- Impact on public health
- Impact on prenatal diagnosis
- Impact on confidentiality

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Impact on Research and its Oversight

- An IRB at a leading medical school required that explicit reference to risk of insurance discrimination be included in a consent document.
- Researchers have had great trouble in obtaining a sufficiently large CONTROL group. In a follow-up study, the vast majority of those who refused to participate cited the warning about insurance discrimination in the consent form as their reason for declining.
- Query: Is there sufficient basis to demand that such a warning be part of the consent process? Does it constitute a real risk?

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Impact on Public Health

- Context: Probable expansion of Newborn Screening to include DNA testing.
- An NIH funded study in Missouri is currently sequencing a gene in more than 20,000 newborns.
- This could (should?) lead to state based storage of DNA test results

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Prenatal Diagnosis: What is a Serious Genetic Disorder?

- From 1965 to 1995 the number of live born children with spina bifida in England and Wales declined by 95 percent.
- This was because of a screening test that could identify women with "high risk" pregnancies. Most women who learned of the diagnosis terminated the pregnancy.
- For most fetuses with spina bifida we cannot predict the severity of medical problems.

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Genetics and Confidentiality

- Genetic information is familial
- The physician may discover facts that are of great importance to other family members
- Discovery of inherited risk for serious disease raises issue of communication with other relatives

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Opportunity: Warn About Risk of Colon Cancer

- DNA test may indicate that a person carries a dominantly mutation that increases cancer risk
- Inference: his siblings and other relatives may have this mutation too
- Opportunity: early screening and curative surgery

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Problem

The patient tells the physician that he will not disclose his test results to relatives, and he forbids the physician to do so.

What is the proper ethical conduct for the physician?

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How Often has Violation of Confidentiality Actually Occurred?

No lawsuits (or published disciplinary actions) for violating patient's request.

Very few lawsuits for failure to warn.

I conclude this is not (yet) a problem, nor is it likely to become one.

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Opportunity: New Diagnostic Tests

Historically, it has been impossible in many cases to explain why a child has developmental delay

DNA tests (telomeric probes) may greatly improve our diagnostic and, perhaps, prognostic skills.

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Problem: Genetics and Self-Image

New tests to diagnose developmental delay could cause: parental guilt, diminished self-worth, and/or social stigmatization

How will genetic labels influence educational programs?

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Opportunity: Warning Healthy People about Risk of Future Disease

Cancer: about 5 -10 percent of people who develop cancer are born with a significantly increased risk

Tests available for breast and colon cancer now

How should we decide when to use a test for increased risk of future serious disease?

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Problem: Will Genetics Change our Ideas About Health?

Is a person who carries a mutation that increases his or her risk for a disease or disorder healthy or ill?

Consider: a 42 year old woman seeks oophorectomy because of her family history of ovarian cancer. Her insurer refuses to pay for the surgery because it was not performed to treat a "bodily disease." Should she be reimbursed? (Katskee v. Blue Cross of Nebraska)

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Problem: Risk of Genetic Discrimination

What evidence is there of such discrimination?

- How adequate are the current protections to prevent genetic discrimination?

What can we say about the risk that genetic discrimination will become more widespread in the future?

- Is it possible that miscalculations about the risks had harmful effects in medicine?

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Genetics and Health Insurance

- About 40 states have laws prohibiting group health plans from using genetic data to deny coverage for pre-existing conditions
- The federal HIPAA (Sect. 703) also forbids this
- Almost no evidence to suggest that genetic data has led to denial of access to health insurance

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Genetics and Life Insurance

- Some states address this issue; mso tdo not.
- Genetic tests not used in life insurance underwriting
- Insurers will demand to see results of tests that applicant has taken
- It will be impossible to prohibit life insurers from gaining access to genetic test results

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Genetics and Long Term Care Insurance

- Less than 10 percent of Americans purchase LTC, but the number is rising rapidly
- What if we develop a predictive test for Alzheimer's disease?

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Genetics and Employment: Conflicting Interests of EEOC and OSHA

- The ADA forbids using pre-employment medical testing
- The EEOC says that ADA rules protect persons denied employment on the basis of a genetic test
- OSHA exists to promote a safe workplace
- May employers use genetic tests for risk for occupational disease?

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Rise of Tissue/DNA Data Banks

- Pharmaceutical and biotech companies have a huge interest in correlating clinical history with DNA variation
- Tissue banks and medical records may have unanticipated commercial value
- DNA data banks are being aggressively compiled in the research setting

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Universal DNA Banking

Our society seems to be drifting in the direction of acquiring DNA data on everyone. We have been collecting blood on all newborns since the 1960s. Over the last few years some states have begun to save the samples.

The US military maintains a huge DNA data bank

Every state has a DNA forensic data bank

A few years ago, a consulting group estimated that there are 320 million human tissue samples banked in the USA, more than 1 per person.

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Human Behavioral Genetics

The search for genes that influence risk for autism, schizophrenia, bipolar disorder, and other common mental illnesses is underway.

Claims linking genes with intelligence will proliferate.

What will we do with such knowledge?

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How Will Genetic Data Be Used in the Future?

- Increasing use of genetic testing to avoid conception or birth of children with serious genetic disorders
- Genetic testing to plan wellness
- Nutritional products keyed to genetic profile
- Choice of therapy keyed to genetic profile
- Insurance products keyed to genetic profile
- Regulations to forbid use of genetics to deny insurance
- Universal DNA profiling?

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The End

Thank you.

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Biggest Recent Event in Genomics in 2002?

Complete sequence of the Malaria parasite (*P.falciparum*)

Complete sequence of *Anopheles gambiae*, its mosquito vector

In 2002 more than 100 million people developed malaria, and 3 million died of the disease.

A new therapeutic approach has already emerged from this work.

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Pharmacogenomics

Most drugs do not work in a significant fraction of patients
This is in part due to genes that influence drug metabolism

The era of one drug fits all will end in the next 10 years
Drug choice will be matched to patients' genetic background

Genomic knowledge will permit efficient development of
drugs that will have greater efficacy and fewer side effects

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Nutritional Genomics

Goal: Guide consumers to the most effective nutritional
supplement based on their genotypes

Example: Some people have a "pro-inflammatory" genotype.
The use of an anti-inflammatory nutritional supplement to
dampen the inflammatory response may help reduce the
risk of or delay the age of onset of chronic inflammatory
disorders such as coronary artery disease and osteoarthritis

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Ethical Issues in Gene Therapy

Gene therapy delivers a "normal" gene to a key cell line in an
effort to correct a very serious genetic disease.

The only successful use of gene therapy involves the transfer
of a gene to treat a rare, rapidly fatal immune disorder (in
children for whom no bone marrow donor is available). In
France this therapy has apparently cured 10 young
children. In one, however, the new gene has caused a fatal
form of T-cell leukemia (by interrupting a gene called
LMO2 which governs blood cell development).

Should the government permit this research? Should parents
be allowed to consent to have children undergo therapy?

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Xenotransplantation

- 79,000 Americans are waiting for organ donation; 16,000
will die while waiting.
- Pigs are being genetically altered so that their organs
express cell surface proteins that are human and can
therefore trick our immune systems. A line of pigs already
exists with kidneys that would not trigger a hyperacute
rejection.
- Assuming xenotransplantation is clinically safe, what
ethical limits (if any) are there on genetically engineering
mammals to serve us in fighting disease?

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