Exome Sequencing for Healthcare Interpreters

Funded by the National Institutes of Health National Human Genome Research Institute U01 HG007292

Principal Investigators
Katrina Goddard and Benjamin Wilfond

Content Development Team
Galen Joseph, Cynthia Roat, Gary Ashwal, Claudia Guerra, Leslie Riddle, Alan Rope, Jamilyn Zepp, Amy Wade

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Booster Shot Media

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What to expect

1. Online class (today)
2. Vocabulary exercises (on your own)
3. Bilingual glossary of terms
4. List of additional resources
Basic concepts

Exome sequencing

Genetic specialists
What is genetics?
What is genetics?

The field of science and medicine that studies the biologic basis of heredity…
What is genetics?

The field of science and medicine that studies the biologic basis of heredity…

…and how the instructions for life are used by all living organisms.
What is genetics?

What is DNA?
Adenine
Thymine
Guanine
Cytosine
GTCAGCAGAGCAACCGAGCTTTTC ACGGGTACGCCGACCTCCCGA
Quiz!

● What is the function of DNA in our bodies?

● What is a chromosome?

● What is a gene?
What is genetics?

What is DNA?

How do we pass on DNA?
DOMINANT

recessive
Blonde  Blonde
Quiz!

- How many chromosomes does a person typically have?
- How many chromosomes does an egg or sperm have?
- What does “replicate” mean?
- What does it mean if a gene is “dominant” or “recessive?”
What is genetics?
What is DNA?
How do we pass on DNA?
How can DNA change unexpectedly?
Extra chromosome
Extra chromosome

Missing chromosome
Extra chromosome

Missing chromosome

Pair from one parent
Extra chromosome
Missing chromosome
Pair from one parent
Fragment duplicated
In genetics, a change at the gene-level is called a variant.
Change letters
Change letters
Change letters

Mix Up letters
Change letters

Mix Up letters
Change letters

Mix Up letters

Delete letters
Change letters

Mix Up letters

Delete letters
Change letters

Mix Up letters

Delete letters

Add letters
1: Inherited
1: Inherited
1: Inherited
1: Inherited
2: De Novo
2: De Novo
2: De Novo
“Benign”
Variant but no harm
“Benign”
Variant but no harm

“Deleterious” or “Pathogenic”
Variant may cause harm or increase risk
“Benign”
Variant but no harm

“Deleterious” or “Pathogenic”
Variant may cause harm or increase risk
Additional Chromosome
Thousands of genes!
Quiz!

- What is a genetic change at the chromosomal level called?
- What is a genetic change at the gene level called?
- What does it mean if a change is “benign”?
- What does it mean if a change is “deleterious?”
Got all that?
My job as a genetic counselor is to help people understand their risk for conditions that may run in families, like cancer sometimes does.
My job as a genetic counselor is to help people understand their risk for conditions that may run in families, like cancer sometimes does. I’ll take a health history for you, and for your family. Then I’ll tell you about genetic testing, if it seems like that might be helpful.
My job as a genetic counselor is to help people understand their risk for conditions that may run in families, like cancer sometimes does.

I’ll take a health history for you, and for your family. Then I’ll tell you about genetic testing, if it seems like that might be helpful.

And if you DO decide to get tested, I’ll be here afterward to explain the results and to help you decide what to do next.
Pedigree
(Family Tree)
I don’t know what my dad’s parents died of. I know my grandmother on my mom’s side had some kind of cancer, but I don’t know what kind.
I don’t know what my dad’s parents died of. I know my grandmother on my mom’s side had some kind of cancer, but I don’t know what kind.

I guess I could ask. But half the family is back in Mexico, and we don’t like to talk about things like this.
It's just bad luck, right?

But what does this have to do with genetics?
Environmental causes or random mutations
Environmental causes or random mutations

Gene mutation or variant
Single site analysis
Individual gene testing

ACCGAGCTTTTCTC
Gene panel

cccctgtgtcgg
acccgagcttttctc
tctgaaaaacgaatc
ccatgtgtcgg
Exome sequencing
So, this test would tell us if I have cancer? Or if I’m going to get cancer?
Genetic testing can tell us if a person has certain genetic conditions, but it doesn’t tell you if you have cancer.
Genetic testing can tell us if a person has certain genetic conditions, but it doesn’t tell you if you have cancer.

It tells you if you have a gene that makes it more likely for you to get certain cancers in the future.
Genetic testing can tell us if a person has certain genetic conditions, but it doesn’t tell you if you have cancer. It tells you if you have a gene that makes it more likely for you to get certain cancers in the future. But even then, we can’t know if you would develop the disease or condition for sure.
Exome sequencing also provides a lot of other genetic information. From this test, we can learn about whether you have other genetic conditions that are unrelated to cancer.
Exome sequencing also provides a lot of other genetic information. From this test, we can learn about whether you have other genetic conditions that are unrelated to cancer.

We can also learn if you are a carrier of any gene variants that are related to particular illnesses. In this case, you wouldn’t get the illness yourself because the gene is recessive.
But you could pass the affected gene on to your children. If your partner also passes on an affected gene, your children could get the illness.
But you could pass the affected gene on to your children. If your partner also passes on an affected gene, your children could get the illness.

You can decide if you want this other information or only the information about cancer genes.
What can exome sequencing tell Manuel?

Information he may want to know:

- Cancer risk

Information he may **NOT** want to know:

- Risk of other non-cancer illness
- Carrier status of other genes
Only looks at 1% – 2% of a person’s entire genome.
May find an unknown variant in a known gene.
May find a change in a gene whose function is unknown.
Some types of changes are not visible.
Quiz!

- What is genetic testing?
- Why would a genetic counselor recommend genetic testing?
- What is looked at in single site analysis?
- What is looked at in individual gene testing?
- What is looked at in gene panel testing?
- What is looked at in exome testing?
- What is looked at in genome testing?
- What are some limitations to gene sequencing?
It sounds like this test can tell me if I have certain genetic conditions, but I don’t have any symptoms of those.
It sounds like this test can tell me if I have certain genetic conditions, but I don’t have any symptoms of those.

And I guess it could tell me if I carry some gene variant that I might pass to my children. I’m most worried about cancer.
This test just tells me if I have a higher risk than everyone else of getting cancer, right?
This test just tells me if I have a higher risk than everyone else of getting cancer, right?

But so what? If I’m going to get cancer, there’s nothing I can do about it, right?
This test just tells me if I have a higher risk than everyone else of getting cancer, right?

But so what? If I’m going to get cancer, there’s nothing I can do about it, right?

So why bother getting tested? What does it matter?
“It actually does matter...”
"It actually does matter..."
"It actually does matter..."
“It actually does matter...”
“It actually does matter...”
“It actually does matter...”
"It actually does matter..."
I wonder how much this will cost? What do you want to bet my insurance won’t pay for it?
And what if it turns out that I DO have this genetic mutation? It will just make me worry.

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And what if it turns out that I DO have this genetic mutation? It will just make me worry.

And if my family finds out I have a genetic mutation, what will they think of me?

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I wonder how much this will cost? What do you want to bet my insurance won’t pay for it?

And if my family finds out I have a genetic mutation, what will they think of me?

It would be like God is punishing me for something.
And what if it turns out that I DO have this genetic mutation? It will just make me worry.

It would be like God is punishing me for something.

I wonder how much this will cost? What do you want to bet my insurance won’t pay for it?

And if my family finds out I have a genetic mutation, what will they think of me?

Or what if they terminate my health insurance because they know I’m going to get cancer?

It would be like God is punishing me for something.
And what if it turns out that I DO have this genetic mutation? It will just make me worry.

I wonder how much this will cost? What do you want to bet my insurance won’t pay for it?

Or what if they terminate my health insurance because they know I’m going to get cancer?

If they find out at work, could I get fired?

And if my family finds out I have a genetic mutation, what will they think of me?

It would be like God is punishing me for something.
Manuel, you look worried. What’s going through your mind?
An Act
To prohibit discrimination on the basis of genetic information with respect to health insurance and employment.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

SECTION 1. SHORT TITLE; TABLE OF CONTENTS.
(a) Short Title.—This Act may be cited as the “Genetic Information Nondiscrimination Act of 2008.”
(b) Table of Contents.—The table of contents of this Act is as follows:

Sec. 1. Short title; table of contents.
Sec. 2. Findings.

TITLE I—GENETIC NONDISCRIMINATION IN HEALTH INSURANCE
Sec. 101. Definitions.
Sec. 102. Employer practices.
Sec. 103. Labor organization practices.
Sec. 104. Health plans.
Sec. 105. Certification.
Sec. 106. Enforcement.
Sec. 107. Remedies.
Sec. 110. Civil rights.
Sec. 111. Rulemaking.

TITLE II—PROHIBITING EMPLOYMENT DISCRIMINATION ON THE BASIS OF GENETIC INFORMATION
Sec. 201. Definitions.
Sec. 203. Labor organization practices.
Sec. 204. Employment programs.
Sec. 205. Employment practices.
Sec. 206. Certification.
Sec. 207. Enforcement.
Sec. 208. Remedies.
Sec. 209. Civil rights.

TITLE III—MISCELLANEOUS PROVISIONS
Sec. 301. Repeal.
Sec. 302. Child labor protections.

SEC. 2. FINDINGS.
Congress makes the following findings:

(1) Deciphering the sequence of the human genome and other advances in genetics open major new opportunities for medical progress. New knowledge about the genetic basis of illness will allow for earlier detection of illnesses, often before symptoms have begun. Genetic testing can allow individuals to take steps to reduce the likelihood that they will contract
Section 1. Short Title; Table of Contents.
(a) Short Title.—This Act may be cited as the “Genetic Information Nondiscrimination Act of 2008.”

“A. In General.—For purposes of this section, a group health plan, and a health insurance issuer offering group health insurance coverage in connection with a group health plan, may not adjust premium or contribution amounts for the group covered under such plan on the basis of genetic information.
TITLE I—GENETIC NONDISCRIMINATION IN HEALTH INSURANCE

“(3) No group-based discrimination on basis of genetic information.—

“(A) In general.—For purposes of this section, a group health plan, and a health insurance issuer offering group health insurance coverage in connection with a group health plan, may not adjust premium or contribution amounts for the group covered under such plan on the basis of genetic information.

TITLE II—PROHIBITING EMPLOYMENT DISCRIMINATION ON THE BASIS OF GENETIC INFORMATION

(a) Discrimination Based on Genetic Information.—It shall be an unlawful employment practice for an employer—

(1) to fail or refuse to hire, or to discharge, any employee, or otherwise to discriminate against any employee with respect to the compensation, terms, conditions, or privileges of employment of the employee, because of genetic information with respect to the employee; or

(2) to limit, segregate, or classify the employees of the
Manuel can choose which test results to get:

**Primary findings:**
- Cancer risk

**Secondary findings:**
- Risk of other non-cancer illness
- Carrier status of other genes
Quiz!

- What’s the purpose of genetic testing?
- What could be some of the benefits to genetic testing?
- Why might some people be wary of testing?
- What is GINA?
- Does a patient have to hear all the results from exome testing?
- Why might a patient NOT want to hear all the results?
"Negative"
(Normal)
"Negative"
(Normal)

"Positive"
(Deleterious mutation)
"Negative" (Normal)

"VUS" (Variant of uncertain significance)

"Positive" (Deleterious mutation)
Manuel, our test found that you do have an altered MLH1 gene.
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That means that you are at higher risk than the general public to get a number of cancers such as colorectal cancer, liver cancer, pancreatic cancer and others.
Manuel, our test found that you do have an altered MLH1 gene.

That means that you are at higher risk than the general public to get a number of cancers such as colorectal cancer, liver cancer, pancreatic cancer and others.

This condition is called “Lynch Syndrome.”
So, let's set up an appointment for a colonoscopy for you. It would probably be a good idea to do them more frequently than usual, now that we know you have a high risk of colon cancer.
So, let's set up an appointment for a colonoscopy for you. It would probably be a good idea to do them more frequently than usual, now that we know you have a high risk of colon cancer.

We know that removing polyps can help prevent cancer, AND catch it early if it starts.
That makes sense. Let's make that appointment.
Wow, this is good to know. My wife and I have been talking about having children.
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So, if she’s NOT a carrier, we’re OK, right?
Wow, this is good to know. My wife and I have been talking about having children.

So, if she’s NOT a carrier, we’re OK, right?

But if she IS a carrier, like me, then we have a one-in-four chance of having a baby with cystic fibrosis.
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But if she IS a carrier, like me, then we have a one-in-four chance of having a baby with cystic fibrosis.

I need to talk to her about this. Can she get tested to find out if she is a carrier?
Absolutely. Have her call in for an appointment and she can get “carrier testing” too.
Quiz!

- What sort of sample is taken to do genetic testing?
- What does it mean to have a positive result?
- What does it mean to have a negative result?
- What does it mean to variant of uncertain significance?
- What does it mean to be a carrier of a genetic condition?
QUESTIONS?