

An Introduction to Genetic Testing

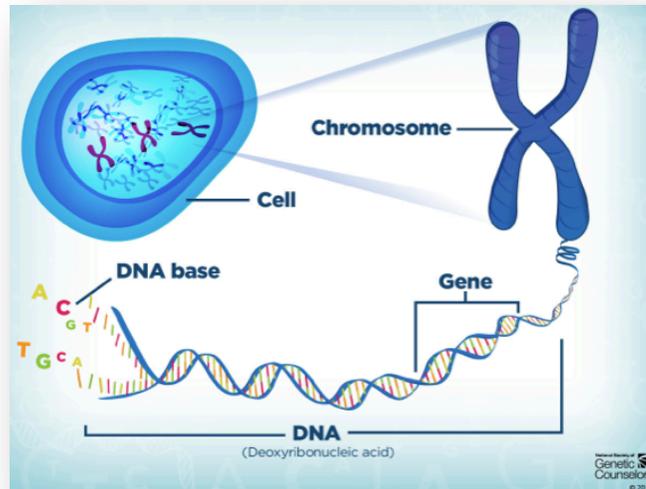
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Compiled by the Undiagnosed Diseases Network with thanks to

- National Society of Genetic Counselors
- Genetic Alliance

DNA Basics



We are all made up of *cells*.

Cells contain *DNA*, or instructions to tell our bodies how to work.

DNA is packaged into structures called *chromosomes*.

Each chromosome contains many *genes* and each gene contains *DNA bases* (A,T,C,G).

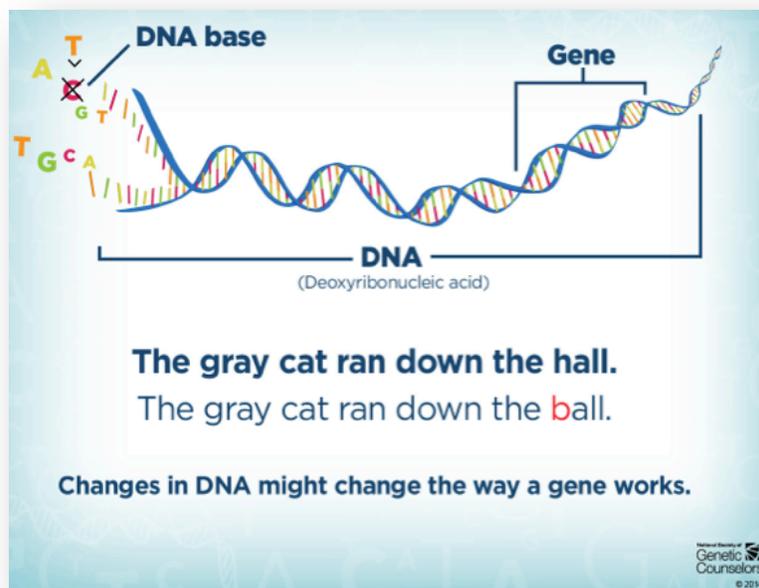
Exons are the parts of the gene that provide the instructions for proteins.

All the genetic material contained within chromosomes is called the *genome*.

What are genetic variants?

Genetic variants are changes in genes.

Variants are common! Most are harmless; however, some can change the function of a gene and cause the body to not work correctly.



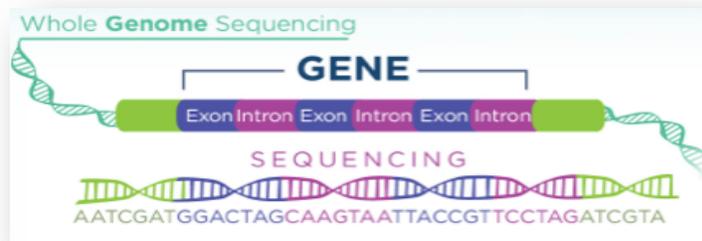
Examples of variants include:

- **Substitutions:** changes in a single DNA base
- **Insertions** or **deletions:** extra or missing pieces of DNA
- **Duplications:** copied pieces of DNA

What is sequencing?

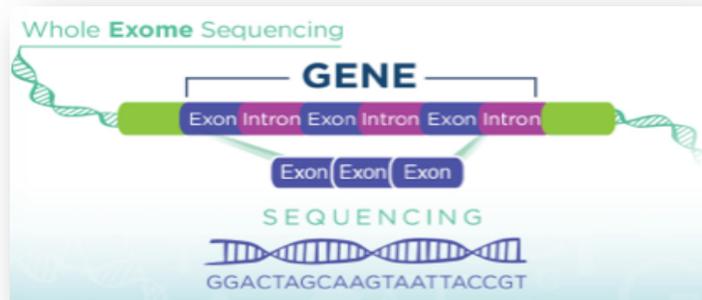
Sequencing is a type of genetic test used to look for variants. Sequencing “reads” each base, or letter, of the DNA to find changes that may cause or affect risk for a disease.

What is whole genome sequencing?



Whole genome sequencing (WGS) is a type of sequencing that reads the DNA looking for changes in the entire genome.

What is whole exome sequencing?



Whole exome sequencing (WES) is a type of sequencing that reads the DNA looking for changes in the exons of genes.

What will happen during the genetic testing process?

During the genetic testing process, patients (and sometimes family members) will:

- 1) Review the Informed Consent form
- 2) Sign the Informed Consent form
- 3) Have 1-2 teaspoons of blood taken from the arm
- 4) The blood sample or samples are then sent to the laboratory for testing.

Why might family members need to give blood?

It is helpful to get blood from family members to compare family member results with the patient's results. This helps researchers to figure out the meaning of the patient's results.

IMPORTANT: Review of the Informed Consent form is an important part of the genetic testing process. **Before** having genetic testing, patients should understand the test's purpose, possible impacts on medical care, alternatives to testing, and potential risks and benefits.

What types of results can a patient receive from genetic testing?

Primary findings: results RELATED to symptoms

<p>POSITIVE: a change is found that is known to cause or contribute to the patient's disease.</p> <p>NOTE: The test may be positive for a result that is or <i>is not</i> related to the patient's symptoms.</p>	<p>NEGATIVE: no changes were found that are known to cause or contribute to the patient's disease.</p>	<p>VARIANT OF UNCERTAIN SIGNIFICANCE (VUS): a change was found, but there is not enough information available to determine the meaning of the change.</p> <p>NOTE: Additional testing may be needed.</p>
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Secondary & incidental findings: results UNRELATED to symptoms

Results may also be identified that are unrelated to the patient's symptoms, but could have implications for his or her health. These can be broken down as:

- **Secondary findings:** laboratories look specifically for these findings (patients only)
- **Incidental findings:** laboratories discover these findings by chance

NOTE: As part of this study, patients and family members have the option to receive unexpected findings if they relate to:

Conditions with known treatment or management options (examples: hereditary cancer syndromes, cardiovascular syndromes, malignant hyperthermia susceptibility).

AND

For adult patients and family members only: The chances of having a child with certain conditions (referred to as **carrier status**; example: sickle cell anemia).

QUESTIONS TO THINK ABOUT BEFORE GENETIC TESTING



1. Am I prepared to receive results that are unexpected?
2. How would I feel about receiving results that are uncertain?
3. What would the results mean for my health?
4. Would I want to share the results with anyone?
5. What would the results mean for the health of my family members?
6. Would I want my employer or insurance company knowing about my genetic results?



What are the limitations?

- May not provide an explanation for the patient's symptoms.
- Will not find all genetic changes that cause disease.
- May not provide treatment options or information about what to expect in the future, even if a genetic explanation is found.

What are the benefits?

- Results may reveal the cause of the patient's symptoms.
- If a cause is found, it may help to:
 - Provide a better understanding of the condition and direct treatment.
 - Figure out if other family members have an increased chance of having or passing on the condition.

What are the risks?

- Learning about results can be emotionally challenging.
- Variants with uncertain implications may be found.
- Information discovered may affect the health of relatives.
- Issues of adoption and parentage (biological fatherhood or motherhood) may be discovered.
- Results may impact the ability to obtain life, long-term care, or disability insurance.