How Will You Learn What Was Found by WES?

The UNC Hospitals' Molecular Genetics Laboratory (MGL) will confirm all **diagnostic** and **medically actionable incidental** results found by WES before we discuss them with you during your second study visit.

People who are randomized to decide about learning non-medically actionable incidental information will be given more information about which ones will be confirmed and how various types can be learned.

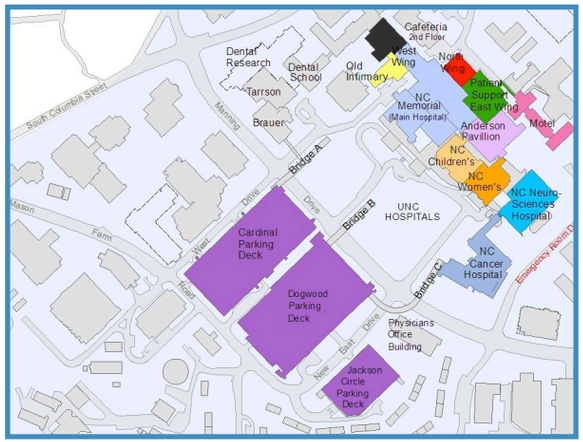
Will the Information Learned from WES Be Put Into Your Medical Record?

You will be asked if you want the confirmed results placed in your UNC Hospitals Electronic Medical Record (EMR). If you agree, you will sign a consent form and an official report will be entered. If you do not agree, these results will not be placed in your record.

Will You Be Re-contacted by NCGENES?

Genetic variants do <u>not</u> change over time, but we might gain new knowledge that changes how we interpret these variants in the future. We will review your WES information once a year (for up to 4 years) and will contact you if new information becomes available that would affect your medical care.

Genetic Medicine Building



UNC Hospitals

NCGenes

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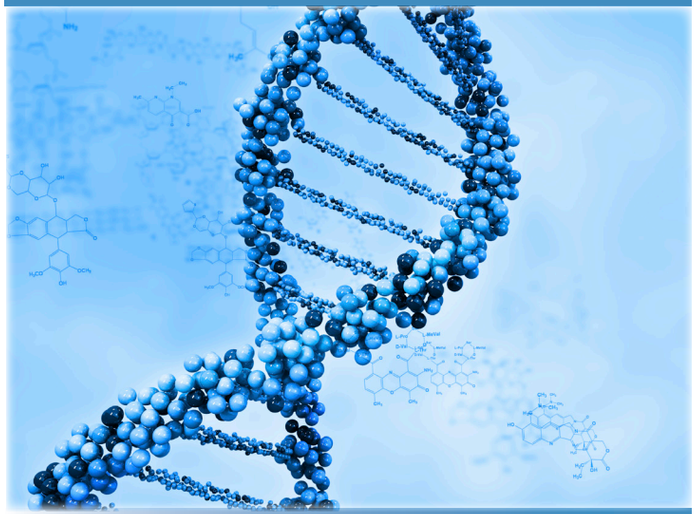
WHAT CAN I LEARN FROM WHOLE EXOME SEQUENCING?



NCGenes

North Carolina Clinical Genomic Evaluation by Next-generation Exome Sequencing

NCGENES

North Carolina Clinical Genomic Evaluation by Next-generation Exome Sequencing

What is Whole Exome Sequencing (WES)?

WES is a new genetic test that can find genetic causes of some kinds of health problems. The test studies the **exome**, which contains the genetic information used by our cells to make the different proteins in our body. Proteins, along with our environment, affect how our bodies work.

All genes have the same four DNA bases: "A", "C", "T", and "G". The order of these DNA bases in a gene is called the "**sequence.**" The DNA sequences tell the cell which protein to make and how to make it.

The DNA sequence of a gene is not exactly the same in everyone. WES reads the sequences of **many genes at the same time** and finds many thousands of differences, called "**variants**".

Some variants that WES finds may give you information about your health, but most will not. Most often we don't know whether or not a variant will have an effect on health. And, WES will not find all the variants that could possibly affect your health.

WES Finds Different Kinds of Information

I. Diagnostic Information

The main reason that you had WES was to see if it could find genetic variants that explain the health problem or the **diagnosis** that led you to join NCGENES. A group of genes that are related to your diagnosis will be studied in-depth.

There are three types of diagnostic results:

Positive result: a gene variant was found that explains your diagnosis and/or family history. This may help your doctor treat your symptoms.

Possible result: a gene variant was found that **might** explain your diagnosis and/or family history but we don't know for sure. We may recommend that you or your relatives have further testing to help us understand this result.

Negative result: no gene variant was found that explains your diagnosis and/or family history. Your WES will be re-studied in a year.

Everyone in NCGENES will learn his or her diagnostic result.

II. Incidental Information

WES can find many **other** variants that are **not** related to your diagnosis but that **may** affect your health in other ways. That's because WES finds the DNA sequences of **many** genes at the same time. Most of these genes are **not** related to your diagnosis. The information that you can learn from these kinds of **unrelated** genetic variants is called "**incidental information.**"

In NCGENES, There Are Three Types of Incidental Information

1. Information That Is Medically Actionable:

In rare cases, incidental information Is "medically actionable".

WES may find genetic variants that cause a serious disease that is **unrelated** to your diagnosis. **In very rare cases,** knowing this information can lead you and your doctor to take clear steps to prevent or successfully treat the disease. We call the information learned from these genetic variants "**medically actionable**" because there are definite ways to use it to help protect your health.

In NCGENES, we will look for variants in a group of genes that give medically actionable information. If your WES finds variants in this group, and after they are confirmed in the UNC Hospitals' Molecular Genetics Laboratory, you will be told this medically actionable incidental

2. Incidental Information That Is Not Medically Actionable:

In some cases, WES may find genetic variants that could give you information about an unrelated health concern, but this information **does not** lead you and your doctor to take specific steps to prevent it. We call the information learned from these variants "**non-medically actionable**" because there are no definite ways to use it to help protect your health.

3. Information That Has No Known Medical Value:

The great majority of variants have no known medical value so these will **not** be interpreted or reported to people in NCGENES

Making Decisions about Learning Non-Medically Actionable Incidental Information

Some adults NCGENES will be asked to decide whether or not they would like to learn any types of non-medically actionable incidental information that may be available from WES.

Some people might decide to learn this kind of information because they think it is important or they are interested in learning it. Other people may decide not to learn any of this kind of information or to learn only some types of it.

The value of this information to people and their doctors is uncertain. There are no definite steps for you and your doctor to take to protect your health after learning this type of information.

We are studying how people decide whether or not to learn this information, which types they decide to learn, and how these decisions affect them. This will be important to understand because many more people will be faced with these decisions as more clinics offer WES.

To study these decisions, adults in NCGENES will be divided into two groups by "randomization," which is like flipping a coin.

Group 1: will learn 1) diagnostic and 2) medically actionable, incidental results **only.**

Group 2: will learn 1) diagnostic and 2) medically actionable, incidental results **AND** 3) will be asked to decide if they want to learn other types of incidental information that is **not medically actionable.** These people will be given additional information about making this decision.