Alabama Genomic
HEALTH INITIATIVE

FREQUENTLY ASKED QUESTIONS

PROGRAM OVERVIEW

- What are we testing for?
- What is the difference between research genomics screening and clinical genomics testing?
- What does the test involve?
- Where will the testing take place?
- What are the benefits?
- What does DNA stand for?
- What are genes?
- What is a genetic variant?
- What is the difference between genotyping and whole genome sequencing?
- Who is offered whole genome sequencing?
- What is required to participate?
- Should I enroll in the AGHI instead of undergoing clinical genetic testing my doctor has referred me to?

RECEIVING RESULTS

- How long do I have to wait to receive my results?
- If I receive a negative test result, does that mean that I am free of any genetic risk at least in the genes that are tested by the AGHI?
- I have a concerning family/personal health history but received a negative result. Why?
- What is the likelihood of getting a positive result?
- If I receive a positive result, what happens next?
- Is the cost for follow-up care covered by the study or by insurance?

PRIVACY, CONFIDENTIALITY, AND PARTICIPANT RE-CONTACT INFORMATION

- How does the AGHI protect my privacy? Can I control the way in which my results are communicated to me?
- Are there any laws protecting me from discrimination based on my genetic information?
- Should I say yes to biobank?
- What are possible reasons you would re-contact me if I participate in the AGHI?

PROGRAM OVERVIEW

What are we testing for?

We are testing participants for the presence of specific genetic variants (differences in a person's genetic code) that may predict the development of serious medical conditions, such as cancer or heart disease, that can be prevented or treated if the diagnosis is made early. Using a type of test called genotyping, about 1-3% of participants will be found to have such a genetic variant. These participants will be provided genetic counseling that will include recommendations to begin a monitoring or treatment plan.

For example, specific genetic differences in the BRCA1 or BRCA2 genes have been shown to significantly increase the likelihood of developing breast and ovarian cancer, as well as some other types of cancer. Other genetic differences in several genes are associated with greater risk for disorders such as cardiomyopathy (disease of the heart muscle), arrhythmia (irregular heart rate and risk of sudden death), and hypercholesterolemia (high levels of cholesterol in the blood). All of the genetic differences the AGHI tests for are "actionable", meaning there are existing prevention or medical action steps that can be taken that may prevent the disease from developing or reduce its impact.

What is the difference between research genomics screening and clinical genomics testing?

Research genomics screening, such as is done in AGHI, involves examination of DNA from a research participant for changes in a predetermined group of genes for changes that may be of medical significance. Although it can detect some medically important genetic changes, the technology used is known to miss some significant genetic changes. Clinical genetic testing, in contrast, examines a group of genes selected to specifically address a medical risk in a person based on his or her personal and family history. The technology used here is designed to detect virtually all of the medically significant genetic changes in these genes. Because of these differences, anyone who has a personal or family history of a genetic disorder should have clinical genetic testing and should not rely on research genetic screening, such as is offered by AGHI, as a substitute for clinical testing.

What does the test involve?

After being educated about the program and providing signed consent, participants will complete a brief health questionnaire and submit a small blood sample, which will be processed into DNA and tested in laboratories at UAB and the HudsonAlpha Institute for Biotechnology.

Where will the testing take place?

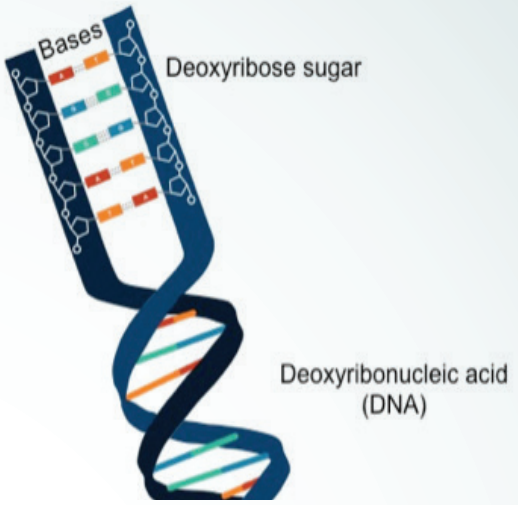
Recruitment locations include The Kirklin Clinic of UAB Hospital in Birmingham, North Alabama Children's Specialists in Huntsville, and UAB Medicine in Huntsville, Selma, and Montgomery. Additional enrollment events will be scheduled in other locations throughout the state of Alabama.

What are the benefits?

Participants found to have certain genetic variants can benefit from potentially lifesaving screening or treatment, which also can be offered to other members of their family who may face a similar risk for disease. The AGHI will also generate a wealth of knowledge that researchers can use to identify genetic factors that increase a person's chance of developing both rare and common disorders. It is hoped that this knowledge will lead to new approaches for preventing, diagnosing, and treating disease.

What does DNA stand for?

DNA stands for deoxyribonucleic acid. This term describes the different chemical building blocks that make up the structure of DNA. The structure of DNA is similar to a twisted ladder, known as a double helix. In this "ladder" the sides are made of a sugar called deoxyribose. Each "step" of the DNA "ladder" is made of a pair of bases. There are four bases, adenine (A), thymine (T), guanine (G) and cytosine (C). These four bases (A,T,C,G) are the "letters" of the genetic code that provide instructions for the human body to grow and work properly.

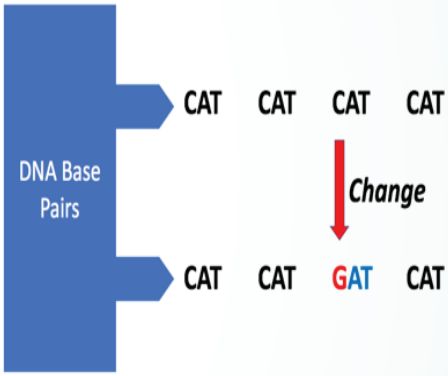


What are genes?

Genes are pieces of genetic information made of DNA that provide instructions to our body on how to grow and operate as it should. Genes are similar to sentences in an instruction manual. Each sentence provides a different instruction. Humans have over 22,000 genes. We know about many genes that provide important instructions for our body. Other genes we know little about.

What is a genetic variant?

A genetic variant is a difference in the genetic code of DNA. All people have differences in their DNA. This is part of what makes each person a unique individual. Genetic differences can range from very small, at the level of a single DNA letter, to very large that may affect hundreds of genes. Most of these differences are neutral, and are not related to a medical condition. Some differences are harmful and cause disease. This happens when a difference changes the way a gene reads, so that the body no longer gets the correct instruction.



What is the difference between genotyping and whole genome sequencing?

Genotyping can be thought of as a "spot check" of some of a person's DNA letters. The AGHI genotyping test we are using looks at only about 650,000 of these letters. This may sound like a large number, but compared to the 3 billion total letters in a person's genome, it is a small amount of information. These letters have been selected because we know they can be associated with a disease.

Whole genome sequencing looks at all of the letters in a person's genome. Although that means that all known disease-associated variants would be detected, it also means that a large number of variants may be found that are of unknown medical significance.

Who is offered whole genome sequencing?

A separate component of the AGHI uses a test called whole genome sequencing. The individuals that receive this type of test will be referred by their medical provider because it is believed there may be a genetic cause for their intellectual disability, autism, and/or an undiagnosed medical condition.

What is required to participate?
Participants in genotyping as part of the Alabama Genomic Health Initiative regardless of their health status or diagnosis must be at least 18 years. Those participants referred for whole genome sequencing as part of the Alabama Genomic Health Initiative may be of any age.

Should I enroll in the AGHI instead of undergoing clinical genetic testing my doctor has referred me to?
No. The genotyping test used by AGHI is designed as a broad population screen, not for genetic testing of a person with clinical indications for genetic testing. Clinical genetic testing is much more targeted and comprehensive, and detects a larger number of disease-associated genetic variants. A person who is referred for clinical genetic testing should not use AGHI as a substitute, and a person who has participated in AGHI who has received a negative test report should still consider clinical genetic testing if there are other indications, such as a family history of a possible genetic disorder.

RECEIVING RESULTS

How long do I have to wait to receive my results?
If you participate in genotyping as part of the Alabama Genomic Health Initiative, it takes several months to return results to you. If your result is negative, it will be mailed to the address you provided at the time of your enrollment. If your result is positive, a genetic counselor will first contact you by phone to review your results.

If I receive a negative test result, does that mean that I am free of any genetic risk at least in the genes that are tested by the AGHI?
No. The genotyping test only looks at a subset of the most well-understood genetic variants in these genes. There could be other variants that either are not detected by this type of test or are currently not known to be associated with disease. These unknown or undetectable variants still could cause disease risk. That is why this screening test does not replace a clinical test.

I have a concerning family/personal health history but received a negative result. Why?
A negative result means that no known harmful differences were found in the genes tested in this study. This result does not mean that you have no genetic risk factors, or that you will not develop a medical condition in the future. If you and/or members of your family have a history of a particular medical condition, a negative test result does not eliminate that history. It is possible that you or your family members have a difference in one or more of the genes tested that is not yet known to be harmful. Since there are over 20,000 genes, it is also possible that you or your family members have a medical condition due to a difference in a gene not included in the gene list selected for this study. Families often share many other things outside of genetics such as diet, habits, or environment. These non-genetic factors play a significant role in your health. You should continue to follow your physician's advice and receive recommended disease screenings such as mammograms or blood pressure and cholesterol checks just to name a few.

What is the likelihood of getting a positive result?
The likelihood of getting a positive result depends on your medical and family history. For those who have genotyping for the selected genes, we estimate that 1-3% will get a positive result. For those who have genome sequencing after being referred by their healthcare provider, previous experience shows that about 25-30% will get a positive result that explains the genetic reason for their health condition.

If I receive a positive result, what happens next?

A positive result means that a genetic difference was identified and confirmed in one or more of the genes tested that places you at increased risk for specific medical conditions. You will receive a call from one of the genetic counselors involved with the study to discuss the results and offer options for following up with a genetic counseling appointment. In some cases, telemedicine may be an option to complete this follow-up appointment. Genetic counseling can provide you information about the specific gene(s) in which a difference was found, how this may affect your health, and what this may mean for you and your family going forward. After you speak with the genetic counselor, a copy of your test result will be mailed to the address you provided at the time of enrollment. If you consented to share results with your provider, a copy of the genetic test report will also be sent to the doctor(s) you indicated at the time of enrollment. The genetic counselor that speaks to you will confirm your consent to do so before sending results to your provider.

Is the cost for follow-up care covered by the study or by insurance?

If you receive a positive result as a part of this study, your doctor may recommend a new or different medical management plan. The Alabama Genomic Health Initiative does not include any treatment or medical care that may be recommended based on the results of the genetic testing provided. The cost of follow-up medical care will be billed to you or your insurance company.

If you have health insurance coverage, the cost of follow-up care will be billed as usual through your insurance. Whether or not your follow-up care will be covered by your insurance depends on a number of factors including what treatment or testing is being provided, who your health insurance provider is (Medicare, Medicaid, Viva, Blue Cross Blue Shield of Alabama, etc.), and the specific details of your plan.

PRIVACY, CONFIDENTIALITY, AND PARTICIPANT RE-CONTACT INFORMATION

How does the AGHI protect my privacy? Can I control the way in which my results are communicated to me?

You can choose one of the following three ways to receive your results, and you can indicate your decision on the informed consent form:

1. You allow the AGHI team to directly send the results to both you AND your medical provider. If you choose this option, you can discuss the results with your doctor immediately after you receive the results, and your doctor will be able to follow-up with recommendations for genetic counseling and/or medical care based on the result. Even if you receive a negative result, your doctor will be able to explain what it means to you and your current and future health.

2. You allow the AGHI team to directly send the results only to you, but NOT to your medical provider. If you choose this option, you can decide whether or not to share your results with your doctor after receiving the results yourself first.

3. You can choose NOT to know the result yourself, and NOT to share the results with your medical provider. If you choose this option, neither you nor your doctor will be informed of your genetic test results, positive or negative. You may choose this option if you simply want to donate your blood sample to the biobank for the purpose of advancing future medical research.

There are some factors that you may consider in making this decision such as the timeliness of discussing your genetic test results with your doctor, concerns about the privacy of your genetic information, and the opportunity to contribute to medical/genetic research. Whichever option you choose, your decision will be respected by the AGHI team.

Are there any laws protecting me from discrimination based on my genetic information?

There are some protections available to prevent genetic discrimination, but they have important limitations and may not prevent discrimination in all settings. The Genetic Information Nondiscrimination Act (GINA) is a federal law that was passed in 2008 to provide protection from discrimination in health insurance coverage or employment based on genetic information. First, GINA makes it against the law for a health insurance company to use a genetic test result or family health history as a reason to deny you health insurance coverage or to decide how much you are going to pay. Second, GINA makes it against the law for an employer to use a genetic test result or family health history to make choices regarding your employment.

There are limitations to the protections GINA provides, however. GINA's protections for insurance only apply to health insurance. They do not apply to life, long-term care, or disability insurance. Employment protections of GINA do not apply to small businesses/employers with less than 15 employees, or to those in the US Military or employees of the federal government. Signed in to law in 2000, Executive order 13145 protects federal employees from genetic discrimination in employment.

If you have concerns about genetic discrimination, you should discuss these with a genetic counselor or other healthcare provider before undergoing genetic testing, including the genetic testing offered by the AGHI.

Should I say yes to biobank?

If you say yes to biobank, your blood sample will be coded (that is, your name will be removed from your blood sample and the sample will be given a unique seven-digit number) and then stored in the biobank. Stored blood samples in the biobank will enable researchers to conduct future scientific research on various health conditions that may benefit you as well as many others who have genetic features similar to you. As such, the AGHI research team regards the biobank as a key research tool for future medical breakthroughs. Respecting your decisions about participation in research is one of the most important ethical principles the AGHI team cherishes. The decision about whether or not to have your blood sample stored in the AGHI Biobank is a personal one, and will not affect your ability to participate in other aspects of this study. There are some potential factors that you may consider in making this decision such as concerns about the privacy of your genetic information and the opportunity to contribute to medical / genetic research.

What are possible reasons you would re-contact me if I participate in the AGHI?

One of the ways you may be re-contacted is to provide feedback to us about your experience in the AGHI to inform our community engagement research efforts. Participants for this research will be invited to participate in AGHI-related surveys or events by phone or mail, at the number and address they provided when they enrolled. The invitation to participate in these community engagement efforts will not contain any language that discloses that a participant has enrolled in the AGHI.

Community engagement research helps us know how we can improve our recruitment, education, and enrollment efforts for the AGHI and other future research projects. Other reasons we may contact you in the future are to inform you of additional research studies that may be of interest to you.