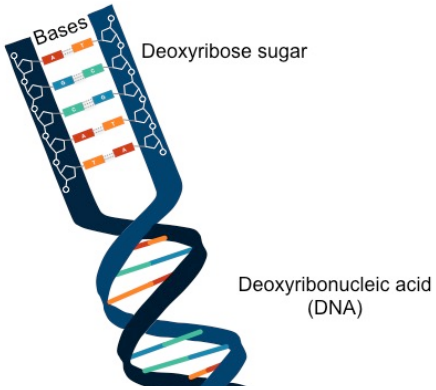
Alabama Genomic HEALTH INITIATIVE

Frequently Asked Questions

Genetics Defined

What does DNA stand for?

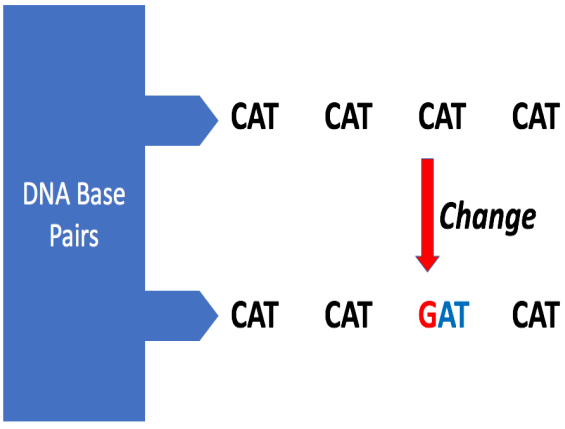
DNA stands for *deoxyribonucleic acid*. This term describes the different chemical building blocks that make up the structure of DNA. The structure of DNA is similar to a twisted ladder, known as a double helix. In this "ladder" the sides are made of a sugar called deoxyribose. Each "step" of the DNA "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 difference 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.

AGHI Genetic Testing Information

Where did the gene list come from?

The list of 59 genes selected for this study was created by a group of genetics doctors and experts from the American College of Medical Genetics and Genomics (ACMG). These genes were selected for two main reasons. First, genetic differences in these genes are known to increase the risk for certain medical conditions such as cancers or cardiovascular diseases. Second, if you are found to have a difference in one of these genes, there are specific actions you and your doctors may take to help prevent disease or to detect it at an earlier, more treatable stage. This list does not include all genes that have been linked to medical conditions. As our knowledge of genetics increases, it is possible that new genes will be added to this list in the future that are not currently part of the 59 gene list.

What is the difference between genotyping and whole genome sequencing?

Genotyping involves detection of thousands of genetic variants in your DNA; each variant is a difference in the genetic code in one of the 3 billion genetic "letters" that make up your genetic information. Any individual will have millions of such differences, but only a small number of these are associated with increased risk of medical problems. The genotyping test we are using detects only about 650,000 of these variants. Although these have been selected to enrich a list of variants associated with disease, not all disease-associated variants are known yet. Whole genome sequencing identifies all of the variants in a person's genome. Although that means that all possible 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 small percentage of participants will be invited to participate in whole genome sequencing as part of the Alabama Genomic Health Initiative. These people will be invited because they have a medical condition that is believed to have a genetic cause that has not yet been found. The study coordinators will identify these individuals for which whole genome sequencing may find a genetic cause for their medical condition.

Why doesn't everyone who participates in AGHI get whole genome sequencing?

As noted above, genome sequencing detects all possible variants, but a large number of these are of unknown medical significance. For the screening of individuals in the general population, genotyping is much less expensive and identifies variants that are clearly known to be associated with risk of disease. The limitation is that many disease-associated variants are not detected by this method, but the low cost and clear relationship of detected variants and medical problems make it the preferred approach at this time for population screening.

How old do you have to be in order to participate?

Those invited to participate in genotyping as part of the Alabama Genomic Health Initiative regardless of their health status or diagnosis must be 18 years old in order to participate. Those invited to participate in whole genome sequencing as part of the Alabama Genomic Health Initiative may be of any age.

I have been referred for clinical genetic testing or have been considering asking for such a referral. Should I enroll in AGHI instead?

No. The genotyping test used by AGHI is designed for 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.

AGHI Information on Possible 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.

Why did I not receive results at the same time as other participants that enrolled the same day as me?

If you enrolled on the same day as a friend or family member, you may not receive results at the same time and this is not necessarily cause for concern. By the time results are ready to be returned to participants, the original order in which samples are received for testing is not maintained. In some cases, testing of samples is repeated to ensure accuracy of results before returning information to participants. If you have any questions about this process or would like to check on the status of your information, you may call (205) 934-9525 or email aghi@uab.edu at any time.

I understand that the population screen genotyping tests only looks at 59 genes, and that a negative test does not mean that I don't have a variant in some other gene. However, if I receive a negative test report does that mean that I am free of any genetic risk at least in these 59 genes?

No. The genotyping test only looks at a subset of the best understood genetic variants in these 59 genes. There could be other variants that either are not detected by this method or are currently not known to be associated with disease that still could indicate disease risk. That is why this screening test does not replace a clinical test if one is indicated based on personal history or family history.

I received a negative result, what about my family/personal history?

A negative result means that no known harmful differences were found in the 59 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 59 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 59-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 screening 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 59 selected genes, we estimate that 1-3% will get a positive result. For those who have genome sequencing based on their medical history, 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? Who will contact me?

A positive result means that a genetic difference was identified and confirmed in one or more of the 59 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 set up an appointment to discuss the result in more detail. This appointment may be in-person or done via telemedicine based on your preference. The genetic counselor 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. If you consented to share results with your provider, a copy of the genetic test report will 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 included in the study? Is it covered 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.

AGHI Privacy, Confidentiality, and Participant Recontact Information

If I get a positive genetic test result, are there any laws protecting me from discrimination?

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.

Who has access to my data?

Members of the trained personnel on the AGHI team have access to your identifiable data and data that is connected to your identity by a confidential code made up of a unique set of numbers. Potential future researchers would have access only to this data, from which personal identifying information has been removed and which is labeled with your unique set of numbers that only trained study personnel can relate to your identity.

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. Such 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.

Should I give my doctor access to these results?

There are three ways you might take action on your genetic test results, and you can indicate your decision on the informed consent form:

1) You allow the AGHI team to directly send the results to 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 the genetic counseling and/or medical care you receive following the genetic test 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.

What are possible reasons you would re-contact me if I consented to participate in the Alabama Genomic Health Initiative?

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.

I have heard about the story of Henrietta Lacks; how can I be sure that will not happen to me?

Henrietta Lacks was a young African-American woman whose life was cut short by cervical cancer in 1951. Before her death, a sample of her cancer cells was taken without her knowledge or permission to be used in research. These cells were then used in medical research without her family's knowledge or permission for several decades after her passing. It is because of stories like that of Ms. Lacks that regulation of medical research was created to protect the rights of participants in research, and to ensure that research is done in an ethical way. Ethical use of genetic information and samples collected as a part of the Alabama Genomic Health Initiative is of great importance. For this reason, we provide you with specific information about what the study involves and how your samples may be used in research *before* you decide to participate. As a part of this study, you can choose whether or not you would like for your sample to be kept for use in future research.