**Potential FAQs for Return of Results to Individuals**

1. **What is the APOL1 gene and why is it important to kidney disease?**

Genes are like tiny instruction manuals that tell our bodies how to look, grow, and work. Genes are in every cell in our bodies. Genes are made of DNA (deoxyribonucleic acid). The APOL1 gene helps the immune system fight infections, particularly from a parasite that causes African sleeping sickness. There are some variants (or versions) of this gene, called G1 and G2, that are good at fighting infections, but, unfortunately, they are also associated with people developing kidney disease and kidney failure. The usual version of the gene is called G0. G0 is not associated with a higher risk of getting kidney disease.

The G1 and G2 variants are much more common in people whose ancestors and relatives come from sub-Saharan Africa, such as people who are African American, Afro-Caribbean, Hispanic Black and African.

Everybody has two copies of the APOL1 gene – one copy is inherited from our biological mothers, and the other copy is inherited from our biological fathers. The word ‘genotype” refers to whatever combination of a specific gene a person has. Your APOL1 genotype is the combination of versions of the APOL1 gene you have. People who have two copies of the G1 and/or G2 variants have what is called APOL1 “high-risk genotypes.” This means that they are at increased risk for getting kidney disease. The good news is that most people who have a “high-risk genotype” will not develop kidney disease. It is important to remember that people who do not have the high-risk genotype still can get kidney disease.

Although no treatments are currently approved for kidney disease in people with the high-risk APOL1 genotype, doctors are doing research to try to find treatments. You may wish to speak with your doctor to learn if you can participate in that kind of clinical trial.

1. **Should I get my APOLLO APOL1 genotype results?**

Some people wish to know their APOL1 test results, and others do not. Both choices are completely valid. Neither choice is wrong. The decision about whether to get your results is entirely up to you, and no one else.

Here are reasons why some people choose to get their APOL1 test results:

* + Knowing about your APOL1 status can give you some information about your risk for kidney disease.
  + Your results may help you make more informed and/or proactive decisions about your health behaviors and choices.
  + You might want to know your results so they can share them with your family members. Having this information could help to understand kidney health patterns in a family.
  + Learning about your results may offer relief from worrying and anxiety.

Here are reasons why some people choose not to get their APOL1 test results:

* + Learning about genetic information might be stressful for some people.
  + You might worry about others finding out about your results. Or, you might worry that people will ask you about your results.
  + You might worry about someone else using your test results to discriminate against you.
  + Some people do not believe the information will be useful to them.

There are many things to consider when choosing whether or not to receive your APOL1 results. These are just a few reasons that someone might or might not want their APOL1 test results. You might have other reasons you want or do not want to get your results. Remember, there is no “right” or “wrong” choice. The decision is entirely up to you.

1. **What do the different results mean? Does it matter if I have different combinations of the gene?** (The diagram attached here might help to make this information more clear.)

There are three categories of results: high-risk, low-risk carrier, and low-risk non-carrier. These three categories of results are explained below. Remember that genotype means whatever combination of two versions of the APOL1 gene that a person has:

**APOL1 high-risk genotypes: G1+G1, G1+G2, or G2+G2.** People who have any two of the high-risk variants of the APOL1 gene in the cells of the body have what is called a high-risk genotype. This means that they are at more risk than other people of getting kidney disease. Research is being done to find out whether the G1 and G2 variants have different effects on risk. Because only about 15% of people with high-risk genotypes ultimately get kidney disease, there must be some other factor besides their genes that leads those people to get kidney disease. Otherwise, everyone with the high-risk genotype would get kidney disease. But, most do not. We do not know all of the things that might lead people with the high-risk genotype to get kidney disease. But we do know of three things that can lead people with high-risk genotypes to get kidney disease. These three things are: HIV infection, COVID infection, and being treated with a medicine called “interferon”. Scientists are working to identify other important factors that might lead to kidney disease in people with a high-risk genotype.

**APOL1 low-risk genotype carriers: G1+G0 or G2+G0.** People who have one copy of the low risk version of the APOL1 gene (G0) and one copy of either G1 or G2 are called low-risk carriers. This means that they are not at increased risk for getting kidney disease, but they can pass a kidney-disease risk variant of the APOL1 gene on to some of their children.

**APOL1 low-risk genotype (non-carriers): G0G0.** People with low-risk genotypes are not at higher risk for developing kidney disease that is associated with APOL1. They cannot pass a risk variant on to their children. However, they can still develop kidney disease for other reasons.

It is important to remember that while the APOL1 gene plays a role in kidney disease risk, it is just one piece of the puzzle. Many other things contribute to a person’s chances of getting kidney disease. Regardless of APOL1 genotype, adopting healthy habits is important to minimizing the risk for all kidney diseases. This includes eating a healthy diet, exercising regularly, avoiding smoking, limiting how much alcohol you drink, and seeing your doctor or other healthcare provider for routine check-ups.

About 7% of African American people will develop end-stage kidney disease (ESKD) in their lifetime. About 2% of European Americans will develop ESKD in their lifetime. Taking proactive steps to care for your overall health is important for everyone. It does not matter what races or ethnicities people identify with.

A. If I have an APOL1 high-risk genotype, what’s the chance that I will get kidney disease? What is likely to trigger it?

Having a high-risk genotype does not guarantee that you will develop kidney disease. Instead, it means that you have a higher chance than other people of getting kidney disease. About 15% of people with an APOL1 high-risk genotype will develop kidney disease. This means that about 15 out of 100 people with the higher risk genotype will get kidney disease. Or, more than four out of five people with the high-risk genotype do not get kidney disease. Things that likely lead to people with a high-risk genotype to get kidney disease are HIV and COVID infections.

B. If I have a low-risk genotype, what’s the chance that I will get kidney disease? What’s likely to trigger it?

People with APOL1 low-risk genotypes are less likely to get kidney disease, but they still can get it. People with APOL1 low-risk genotypes still need to protect their kidney health by getting regular medical check-ups, eating a healthy diet, exercising, avoiding smoking, and limiting how much alcohol they drink. One common trigger for developing kidney disease in people without APOL1 high-risk genotypes is diabetes mellitus, but there are many other causes.

1. **What can I do about it? Is there anything that I can do now to preserve my kidneys? Is there anything I can do to prevent myself from getting kidney disease?**

Remember, while the APOL1 gene variants play a role in kidney disease, it is just one piece of the puzzle. Many other things affect how likely you are to get kidney disease. Some things that everyone can do to lower their risk of getting kidney disease include: eating a healthy diet, exercising, avoiding smoking, limiting how much alcohol they drink, and seeing their doctor or other healthcare provider for routine check-ups. Routine medical check-ups should include measuring blood pressure, blood sugar, serum blood urea nitrogen (BUN) and creatinine concentrations, and urine testing.

1. **What does this mean for my family?**

Some African American or Black families have several people with kidney disease, treated with dialysis or a kidney transplant. It is likely that APOL1 gene kidney-risk variants may be the cause of kidney disease in some of these families. We suggest that relatives inform their doctors of their family history of kidney disease and get regular check-ups, as in Question 4, above.

1. **Who should I tell? Should I share my results?**

This is a personal decision. It is completely up to you. To protect your privacy, the APOLLO Study will not provide this information to anyone other than you. The decision regarding whether you want your family, friends, or medical providers to know is very important.

Reasons that some people may not want to tell others their APOL1 result include - they worry about discrimination, they don’t want others to ask them about the results, or they don’t think the information will be useful. Reasons that some people may want to tell others their result include – they want to share information with their family, or they think the information may be helpful. You should balance these pros and cons when deciding whether (and with whom) to share your results.

APOLLO will not put your test results in your medical record or tell your doctor about your test results. If you want your doctor to know your APOL1 test results, then you need to tell your doctor. Importantly, if you tell your doctor or other healthcare provider about your APOL1 results, this information could become part of your medical record. The Genetic Information Nondiscrimination Act (GINA) is a federal law that protects you from discrimination on the basis of your genetic information by health insurance companies and most employers. However, this law does not protect you from discrimination by all employers or by other types of insurance, including life insurance, disability insurance, cancer insurance, and long-term care coverage. For more information about the benefits and limitations of GINA, you may visit: <https://www.ashg.org/advocacy/gina/>

1. **Where are we in the research process?**

The breakthrough that APOL1 G1 and G2 variants are associated with kidney disease was made in 2010. Since then, testing for these gene variants has become widely available, and clinical trials are underway to find treatments that will help patients with kidney disease that is associated with having an APOL1 high-risk genotype. In addition, the National Institutes of Health started the APOLLO Study to determine whether APOL1 gene testing can improve outcomes in kidney transplantation and make it safer for African American and Black people to be living kidney donors. Breakthroughs from ongoing treatment trials and APOLLO may improve the lives of people with, and at risk for, kidney disease.

1. **Where can I learn more?**

Additional information is available on the APOLLO Website:

[www.TheApolloNetwork.org](http://www.TheApolloNetwork.org) and the APOLLO Patient and Community Website: <https://www.apollocommunity.net>