KEY POINTS:

- A VUS is a genetic difference that is not well understood at this time.
- Finding a VUS is very common.
- A VUS result usually does not change your medical care.

What are genetic variants?

Genetic variants are parts of the DNA that don’t match the usual DNA sequence. Having variants is normal. They’re what makes each of us different. Every person has variants that are unique to their family. There are even some variants that are unique to you. Most are harmless and do not change how a gene works.

Genetic tests are done to look for variants that change how a gene works and might cause genetic conditions (pathogenic and likely pathogenic variants). These are uncommon. However, as part of genetic testing, other types of variants are often found, including those called variants of uncertain significances (VUS).

Types of variants

- “Benign” or “Likely Benign”
  These are harmless variants. They are not expected to impact a person’s health. These are not included in the lab report.

- “Pathogenic” or “Likely pathogenic”
  These are variants that are expected to change how a gene works. They may cause a genetic disease or health risk.

- “Variants of uncertain significance” or “VUS”
  There is not enough information about these variants to know if they are harmless or could cause a genetic condition.

Why are some variants called “uncertain”?

The laboratory uses computer programs and genetic databases to help figure out if a variant will change how a gene works. But sometimes, there just isn’t enough information to know for sure. Many variants have never been seen before. These type of variants get called VUS. Sometimes, labs disagree on what to call a variant. One lab may call it benign, but another lab calls the same variant a VUS. This shows how hard it can be to understand some results.
Could a VUS result get changed?

A VUS result could get changed to either benign or pathogenic with new information. For some variants, a different test can measure if the gene is working or not. Or a future study may describe how the variant affects the gene. We may learn that the variant is found in healthy people, or in people with a genetic condition. Sometimes it takes months or years to learn more about a variant. Some VUS results may never get changed. Most of the time when we learn more, we find that the VUS is actually benign (harmless). Fewer than 1 in 10 (10%) VUS results are changed to pathogenic or likely pathogenic.

Should others in the family be tested for the VUS?

It is not usually helpful to test family members for a VUS. Your provider will let you know if there is a reason to do family testing. Sometimes finding the same VUS in a healthy relative (like a parent) suggests the variant is benign. If there are many people in the family with the same condition, testing others may find out if the VUS is connected. Family testing only works for genes and conditions that are expected to affect everyone with the variant, such as serious childhood diseases. Family testing is not usually useful for a VUS result in a cancer risk gene. Unless a VUS is found to be harmful, this result does not change any recommended screening or medical care for you or your relatives.

Do I need to do anything more?

We recommend that you check back with your healthcare provider every few years. New information about the VUS may be available in the future. There could also be other genetic testing available at some point.

You may be interested in participating in a research study on the gene involved or the condition in your family. You can find out more on the NIH website: [How to Get Involved in Research](https://www.nih.gov)