



Understanding Genetics:

How-To Guide on Reading and Understanding a Genetic Testing Report

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This guide is for general education only and is not medical advice. Please talk with your child's doctor or a genetic counselor about your child's specific results





Genetic testing reports can feel overwhelming. They often include technical words, numbers, and unfamiliar concepts. This guide walks through what each section means and defines common terms in plain language.

Step 1: Look for the Gene Name

Your report will list the genes where each change was found.

Genes are written in **capital letters** and are usually ***italicized***.

Example:



KCNQ2

SCN2A

BRCA1



Your report may include results for more than one gene. Be sure to read each gene name and its result separately.

Step 2: Understand the Variant

Next on the report, you will see something like:

c.842C>T (p.Ala281Val)

This describes the exact genetic change (or **variant**) that occurred in the gene.

The “c.” and “p.” notations describe the same variant, just from two different angles: one at the DNA level, and one at the protein level.

You don’t need to decode this completely, but here’s what it means:

c.

= the change at the DNA level

p.

= the resulting change at the protein level

Numbers

= the location where the change occurred

Letters

= what changed



Breaking it Down

So if your *KCNQ2* variant is the one in the example:

c.842C>T

When you look at your **DNA**, at **position 842** on the *KCNQ2* gene, there was **supposed to be a C but instead there's a T**.

p.Ala281Val

When you look at the resulting **protein**, at **position 281**, there was **supposed to be an Ala but now there is a Val**.

Note: Sometimes the “p.” notation is written in **shorthand** and looks a little different.

For example, **p.Ala281Val** might instead appear as **p.A281V**.

These single-letter codes are used in the place of three-letter codes at times, but they describe the exact same thing.

This example shows how **missense** variants are typically written. Missense variants are the **most common** variant type found in people with *KCNQ2*-related disorders, but your own genetic report may look a little different.



If you'd like to understand more about your specific variant, it's best to talk with a genetic counselor who can walk you through exactly what your report means for you.

Step 3: Look for Zygosity

Everyone has two copies of a gene, **zygosity** tells you how many copies of the gene are affected by a variant.



Heterozygous: One copy of the gene has the change (most common in *KCNQ2*-related disorders)



Homozygous: Both copies have the change



Breaking it Down cont'd

Step 4: Look for Inheritance

Reports often say whether the variant is:



De novo: New change not inherited from either parent



Inherited: Passed from a parent



Unknown: Parents usually not tested yet

Step 5: Find the Classification

Most genetic reports include a summary or results section near the beginning that tells you how a genetic variant is classified. Look for words like:

Pathogenic

Likely Pathogenic

Variant of Uncertain Significance (VUS)

Likely Benign

Benign

Negative

These terms describe how confident the laboratory is that a genetic change is related to disease or symptoms.

To make this determination, genetic testing laboratories evaluate many different sources of information, including:



Large population databases that show how common a variant is in the general population



Previously reported patients with the same genetic change



Clinical classification databases, such as ClinVar



Published scientific and medical research



Computer prediction tools



Laboratory and functional studies (when available)

The laboratory combines all of this evidence using standardized guidelines to determine the most appropriate classification for a variant.



What These Words Mean

Pathogenic:

A genetic change that is known to cause disease.

This classification requires a large amount of well-established evidence from research studies, clinical reports, and other scientific data. Pathogenic variants are considered disease-causing and can often help explain a person's symptoms or diagnosis.

Likely Pathogenic:

A genetic change that is very likely to cause disease, but there is slightly less evidence available than for a pathogenic variant.

In most clinical situations, healthcare providers use likely pathogenic variants similarly to pathogenic variants when making medical decisions.

Important: "Pathogenic" and "likely pathogenic" describe how much scientific evidence exists linking a variant to disease, **not** how severe symptoms will or should be.

"Likely pathogenic" simply means researchers haven't yet published enough studies on that specific variant to call it definitive. Someone can have a pathogenic variant and mild symptoms, or a likely pathogenic variant and severe symptoms.



What These Words Mean

Variant of Uncertain Significance (VUS):

A genetic change that has been identified, but there is currently not enough evidence to determine whether it causes disease or is a harmless genetic difference.

A VUS should not usually be used by itself to make major medical decisions.

As more research is published and more individuals undergo genetic testing, a VUS may eventually be:



Reclassified as **pathogenic** or **likely pathogenic**



Reclassified as **benign** or **likely benign**

Because of this, genetic results may be reviewed again as scientific knowledge grows.

Likely Benign:

A genetic change that is very unlikely to cause disease.

There is strong evidence suggesting that this variant is a normal part of human genetic variation, but not quite enough information to classify it as definitively benign.

Likely benign variants are generally **not considered medically significant** and are not expected to explain a person's symptoms.

Benign:

A genetic change that is not associated with disease.

These variants are considered normal differences in our DNA and are commonly found throughout the general population.

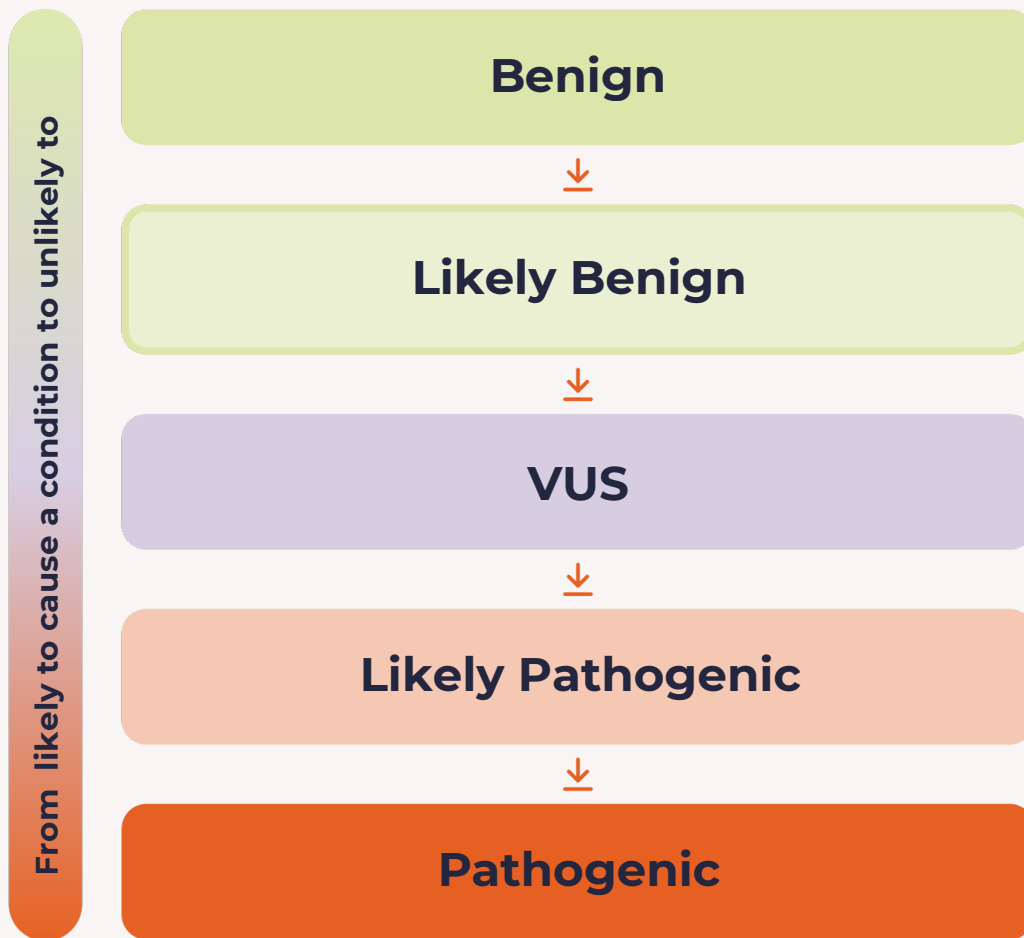
Everyone has many benign genetic variants.

Benign variants are **not expected to cause symptoms or affect health.**



Variant Classification Spectrum

As scientists learn more about genetics and more individuals undergo testing, variants may move along this spectrum as new evidence becomes available.



Most genetic changes found in our DNA are actually benign and do not cause disease. The goal of genetic testing is to identify which changes are medically meaningful and which are simply part of normal human variation.



Variant Types

Most reports will describe the variant type, which tells you what exact kind of change occurred in the DNA.

To see how these variant types differ, it helps to think of a gene as a sentence spelled out in DNA letters. For example:

THE CAT SAT

Missense

One letter changed in the DNA of the gene

THE MAT SAT

A protein is made but may not work correctly

Nonsense

A stop signal appears too early in the gene

THE CAT []

A protein is shortened or not made at all

Frameshift

DNA letters added or removed in a number that isn't a multiple of 3

TEC ATS AT_

Little or no working protein is made

Deletion

A piece of DNA in the gene is missing

THE [] SAT

A protein may be made with missing pieces, or little or no working protein is made.

Duplication

A piece of DNA is copied twice in the gene

THE CAT CAT SAT

A protein may be made with extra pieces, or little or no working protein is made.

Insertion

Extra DNA added to the gene

THE FAT CAT SAT

A protein may be made with extra pieces, or little or no working protein is made.



Other Important Report Terms

A few more words your report may use to talk about a variant:



Phenotype

Symptoms or features seen in a person



Genotype

Your genetic result



Penetrance

How likely it is that someone with the variant will show symptoms



Expressivity

How severe the symptoms may be



Mosaicism

Only some cells carry the genetic change



Recurrence

The chance a condition will occur again in another child from the same family



Segregation

Whether the variant tracks with disease in a family



Still puzzled?

Ask your care team or genetic counselor. No question is too small.



Lab Interpretation

This is often very technical; it's okay to focus on the summary.

What to Look for in the Recommendations Section

Some reports include:

- ☒ suggested follow-up testing
- ☒ specialist referrals
- ☒ family testing
- ☒ medical management considerations

These are guidelines, not strict instructions.

Questions to Ask Your Provider

- ☐
 - Is this variant known to cause disease?
- ☐
 - Is there evidence this causes a loss- or gain-of-function effect?
- ☐
 - Was this inherited or de novo?
- ☐
 - Does this explain the symptoms?
- ☐
 - Should family members be tested?
- ☐
 - Will this change treatment?

Important Things to Remember

-  Genetic testing does not predict everything
-  Results may change as science advances
-  Two people with the same variant may differ
-  VUS results may be reclassified over time