Understanding Genetic Variants

Oncology Nursing Society

Your genes are made up of many base pairs, and these base pairs line up in an expected order. Genetic testing looks for the expected order and reports any changes. These changes are called variants. Variants may be inherited or acquired.

VARIANTS MAY BE

INHERITED (GERMLINE)

Change is passed down from parents.
Change is in every cell of the body.

OR

ACQUIRED (SOMATIC)

Change is developed over a lifetime.
Change is only in the tumor.

There may be a combination of variants found in your genetic test results.

Genetic changes may be benign (harmless), pathogenic (harmful), or of uncertain significance (there is not enough information to determine whether it is harmful or harmless). Sometimes using an analogy is helpful for explaining concepts. One way to explain the differences between variants is to think about how changing an ingredient in a recipe can affect the taste of the food.

Harmless change that does not lead to cancer: "Benign"

A blueberry cake recipe calls for a stick of butter. Unfortunately, we only have margarine, which we substitute for the butter. We bake the cake and it tastes delicious, getting rave reviews from the entire family. This can be compared to a benign variant: The change in the recipe did not affect the taste and consistency of the cake: It is a harmless change in the recipe.

These findings will usually not be noted on the genetic test report.

Not enough data to determine whether a change is harmful: "Variant of uncertain significance"

A chocolate cake recipe calls for a stick of butter. Unfortunately, we only have margarine, which we substitute for the butter. We serve the cake and some family members like it, yet others say they do not think it tastes very good. This can be compared to a variant of unknown clinical significance: The meaning of the change is not clear. In this example, there is not agreement about the impact of the ingredient substitution in the recipe.

Reclassification will occur when enough data are available to determine whether the variant is benign or pathogenic. Treatment decisions are not based on this finding but based on the patient and family medical history.

Harmful change that may lead to cancer growth: "Pathogenic"

A lemon pound cake recipe calls for a stick of butter. The recipe emphasizes avoiding substitution of margarine for butter. As we don't have butter, we use margarine. The pound cake does not rise as much as usual, and every family member complains that the cake's unappealing flavor is nothing like they are used to. This can be compared to a pathogenic variant: It is a harmful change in the recipe.

This is an actionable finding. Cancer screening and treatment decisions will be made based on these findings as well as the patient and family medical history.

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