


Variants of Uncertain Significance (VUS)

Sometimes, mutations or “spelling errors” occur in your DNA. This can sometimes change the meaning of the DNA which can affect your body.



Let's use the spelling of  to help understand how these errors work.

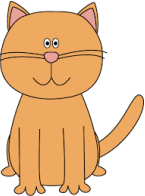
Normally, this animal's name is spelled C-A-T.

Sometimes, a person might misspell it K-A-T. Although spelling it with a K is technically wrong, you can still tell that they are referring to a .

In genetics, sometimes the strand of DNA is also “misspelled,” but like this example, the meaning doesn't change. This is “benign,” which means that the spelling error is not harmful and will not cause a genetic disorder.

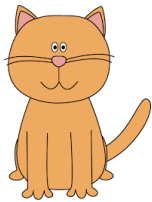
Other times, someone might misspell  as R-A-T.

This time, the meaning of the word has changed. Instead of referring to a  it refers to a .

This can cause a problem if the person wants to refer to a .

This can also happen with DNA, where the “spelling error” completely changes the meaning. This can be “pathogenic,” which means that this spelling error can cause a genetic disorder.

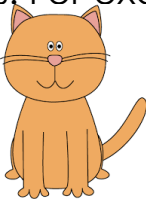
Other times, the spelling errors are not so understandable. If



is spelled C-R-T, C-E-T, or C-I-T, it is unclear what the person spelling the word is referring to.

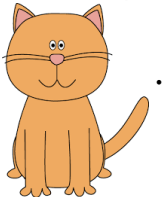
This can also happen in genetics. Sometimes geneticists don’t know yet how a “spelling error” can affect the meaning of your DNA and therefore if it causes genetic disorders or not. These spelling errors are called “Variants of Uncertain Significance.”

After some studies are done, scientists may know more about certain variants. For example, scientists may decide that C-E-T most likely means



In DNA, this means that the variant is “likely benign,” or likely to not cause disease.

Other variants might be reclassified as “likely pathogenic.” For example, scientists may decide that C-I-T is not likely to refer to a



This means that the variant is likely to cause a genetic disorder.

What Does that Mean for My Diagnosis?

If you get a test result back that says you have a Variant of Uncertain Significance, that means that doctors don't know yet if your "spelling error" causes a specific genetic diagnosis. This doesn't mean you have a disease, but it also doesn't mean that you are fine. Doctors simply don't know. Doctors will use family history and symptoms to address your current medical concerns. In the future, doctors may know more about your variant.

Sources

I have a VUS (Variant of Uncertain Significance): Now what? Rochester: Mayo Clinic, 2015

Ledbetter, Nancy. "Guest Blog: Genetic Variants of Uncertain Significance." Facing Our Risk of Cancer Empowered. Last Modified October 25, 2016.

<http://www.facingourrisk.org/get-involved/HBOC-community/BRCA-HBOC-blogs/FORCE/genetic-testing/guest-blog-genetic-variants-uncertain-significance/>

Mallory, Jen. "Variants of Uncertain Significance (VUS) in LFS." Living LFS. Last modified December 7, 2017. <https://www.livinglfs.org/variants-of-uncertain-significance-vus-in-lfs/>

"Uncertain Results Related to Patient Symptoms: Variants of Uncertain Significance." Clinical Sequencing Exploratory Research. Accessed July 31, 2018.

<https://www.ashg.org/education/csertoolkit/uncertainresults.html>

"Variant of Uncertain Significance (VUS): Your Child's genetic Test Result." Seattle Children's Hospital. Last modified September 2015.

<https://www.seattlechildrens.org/pdf/PE2118.pdf>

"Variant of Unknown Significance and Family Studies." Ambry Genetics. Last modified October 16, 2017.

https://www.ambrygen.com/file/material/view/579/FamilyStudy_VUSPatientGuide_1017_final.pdf

"Variants of Uncertain Significance (VUS)." Facing Our Risk of Cancer Empowered. Last modified on January 6, 2018. <http://www.facingourrisk.org/understanding-brca-and-hboc/information/hereditary-cancer/genetic-testing/basics/variants-of-uncertain-significance.php>

"Variants of Uncertain Significance: What You Need to Know." Myriad Pro. Accessed July 31, 2018. <https://www.myriadpro.com/blog/variants-of-uncertain-significance-what-you-need-to-know/>

"Variants of Unknown Significance." Breastcancer.org. Last modified on September 28, 2016. <https://www.breastcancer.org/symptoms/testing/genetic/variants>

Images:

"Cute Orange Cat." My Cute Graphics. Downloaded on August 6, 2018

<https://www.mycutegraphics.com/graphics/cats/cute-orange-cat.html>

"Brown Rat." Pixabay. Downloaded on August 6, 2018. <https://pixabay.com/en/rat-rodent-mouse-brown-animal-297866/>

Author

Grace S. Miller

Intern, Texas Health Institute

MSRGN would like to thank all the professionals, individuals and families who assisted in the review of the documents.

Acknowledgement

This project is supported by the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services (HHS) as part of an award totaling \$600,000 with 0 percentage financed with non-governmental sources. The contents are those of the author(s) and do not necessarily represent the official views of, nor an endorsement, by HRSA, HHS, or the U.S. Government.