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Understanding your Genetic Test Result

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BHD syndrome is a genetic condition. When it is suspected patients have it, it is recommended they take a genetic test. This guide will help you understand your own genetic test result and interpret the “code” you are given when you get your DNA sequencing results.This code allows you to understand where in your DNA we found variants that may be related to BHD.

Please note that your result may look different depending on the test provider. If there is something in your result you don’t understand, please ask your clinician or genetic counsellor, or contact us for further help.

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What do the numbers mean?

- Your DNA sequencing result may look something like c.1285del, c.1429C>T, c.927_954dup, c.610_611delinsTA, or perhaps something like c.872-?_1062+?del.

- This "code" relates to the particular variant in the folliculin (FLCN) gene, which is the gene associated with BHD Syndrome. It enables the classification of the variant and helps understand if it is likely to be causing your condition.

- The numbers in the sequencing result relate to how far along in the FLCN gene the variant occurs e.g. c.1285del indicates the variant is at nucleotide 1285.

- Nucleotides are the building blocks of our DNA, and are represented by the letters 'A' (adenine) 'C' (cytosine) 'G' (guanine) and 'T' (thymine).

What do the letters mean?

- There are a few different types of letter(s) found in the sequencing result, which have different meanings.

- Firstly, the small 'c.' at the beginning of the result means a coding DNA reference sequence was used. Nucleotides are building blocks of DNA. Not all the nucleotides in a gene are used to make (code) the protein. Some bits are cut out. A coding DNA reference therefore refers to only the nucleotides used to make the protein.

- If there is an 'A', 'C', 'G' and/or 'T' in your result this refers to which nucleotide(s) are altered (e.g. deleted or inserted).

- Finally, if there is an abbreviation such as 'del' or 'dup' then this indicates what has happened to cause the variant. These are explained in the section below.

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What do the words mean?

- del: one or more letters of the DNA code are missing (deleted).
- dup: one or more letters of the DNA code are present twice (duplicated).
- ins: one or more letters of the DNA code have been added (inserted).
- delins: one or more letters of the DNA code are missing (deleted) and have been replaced by one or more new letters (inserted).

What do the symbols mean?

- There are several different symbols you might see in your sequencing result and they have various meanings. The most common ones are as follows:
- _ (underscore) indicates a range.
- > (greater than) indicates a substitution from one nucleotide to another one.
- + (plus) or – (minus) indicate the variant occurs within an intron. An intron is part of a nucleotide sequence that is not used to build the final DNA code.
- ? (question mark) indicates unknown positions.

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How do I put it all together?

- Now you have all the pieces of the puzzle to understand your sequencing result!
- Here are some examples of FLCN variants found in the LOVD database:
- c.1285del: The nucleotide at position 1285 has been deleted.
- c.1429C>T: The nucleotide at position 1429 has been swapped from a C to a T.
- c.927_954dup: The nucleotides between position 927 and 954 (inclusive) have been duplicated.
- c.610_611delinsTA: The nucleotides at position 610 and 611 have been deleted and a T and an A have been inserted.
- c.872-?_1062+?del: There has been a deletion of several nucleotides, although the exact location has not been identified. The start point is located in the intron following the nucleotide at position 872, and the end point is in the intron before nucleotide at position 1062.

What does this all mean?

- Now you can understand your sequencing result, what does it actually mean?

You may see the one of the following terms on your test result:

- Pathogenic: There is sufficient evidence that this variant is capable of causing the manifestations seen in BHD.
- Likely Pathogenic: There is strong evidence that this variant is capable of causing manifestations seen in BHD.
- Variant of Unknown Significance: There is currently not sufficient evidence to suggest this variant is capable of causing the manifestations seen in BHD.

- These terms do not determine whether or not you will develop any of the manifestations associated with BHD, and reflect the degree of evidence for the development of BHD symptoms in individuals with specific variants.

- It is therefore recommended that if you are diagnosed with BHD, you have your kidneys checked regularly. We also suggest you share with your family members that you have BHD and encourage them to consider testing for BHD.

- The BHD Foundation website has a letter you can use to inform your family members, and can answer any questions you have surrounding BHD and testing.

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If you would like to get in touch with the BHD Foundation, please email our team: contact@bhdsyndrome.org

For more information about our work and BHD, you can visit our website: www.thebhdfoundation.org