

GenomeDx® (Microarray) Variant Testing Program (VTP)

Laboratories classify genetic changes as variants of uncertain significance (VUS) if there is incomplete or conflicting information about the health consequences of the variant. In some cases, testing family members for the presence or absence of the VUS may contribute to a better understanding of the variant and may be one piece of evidence leading to eventual reclassification of a VUS as a pathogenic, likely pathogenic, benign, or likely benign variant. For such cases, GeneDx has established a Variant Testing Program (VTP).

How do I determine if a variant is eligible for the GenomeDx® VTP?

GeneDx considers requests for the GenomeDx® Variant Testing Program for any individual found to have a VUS identified through whole genome microarray at our laboratory. In some circumstances we also offer the Variant Testing Program to parents of an individual with a likely pathogenic (LPATH) variant. There is no charge for variant testing for approved family members. GeneDx will make the final determinations for VTP in its sole discretion.

Application process for the GenomeDx® VTP:

- In some cases, the 'Recommendations' section of the proband's report may specify that testing for a VUS is available at no additional charge through the VTP for the biological mother and biological father of the proband. **Clinical information on the parents (and proband) must be provided at the time of testing in order for targeted testing to be performed at no charge, but no additional prior approval is required for these cases.**
- If parents are not available, there may be other informative family members eligible for our VTP. Requests to consider testing for relatives other than the biological parents, or requests for other variants not specified in the 'Recommendations' section of the report, should be submitted for advance review.
- Please fax a detailed pedigree and any relevant clinical information/evaluations to the GeneDx array genetic counselors at [301-519-2892](tel:301-519-2892), email genedx@genedx.com, or call [301-519-2100](tel:301-519-2100) and ask to speak with an array genetic counselor. Please be sure to indicate that you are submitting the information for VTP consideration **and include the name and/or GeneDx accession number of the proband.**
- Our team will review the case and will determine if there are informative family members appropriate for evaluation through the VTP. Cases are typically reviewed within a few days, but please allow up to 3 weeks after receipt of the application for a reply.
- A member of our team will contact the ordering clinician after the case has been reviewed to let him/her know if the family has been accepted in the VTP. If we are extending an offer for family member variant testing, we will discuss logistics of sample submission at that time.

Reasons why a family might not be accepted into the GenomeDx® Variant Testing Program:

- The VUS is in a genomic region that varies in copy number in the general population or for which there is no currently described phenotype.
- There are no informative family members available for testing.
- In certain circumstances, it may be more informative to perform more comprehensive diagnostic genetic testing in affected family member(s) instead of targeted testing of one or more unaffected relatives for a VUS.
- Segregation studies involving genes with incomplete penetrance or variable age-of-onset are challenging, especially in unaffected individuals; therefore, VTP studies are less likely to be approved for such genes.

Revising the classification of variants of uncertain significance takes a great deal of data and information from multiple sources. Therefore, there is no guarantee that participation in the VTP will lead to an updated classification of a VUS based on information from a single family, although cumulative data collected from multiple families over time may lead to a more definitive classification for a variant.

For more information please contact:

The GeneDx Array Genetic Counselors at [301-519-2100](tel:301-519-2100).