

Patient Name		Affix barcode label of Patient's sample here
Date of Birth		

Test Information

The benefits and risks of the OncoAlly Hereditary Cancer Analyses are described below. It is recommended that you receive genetic counseling from a licensed healthcare provider who can answer your questions about genetic testing and provide information about alternatives. Information about genetic counselors in your area is available at <https://www.nsgc.org/>.

Background

The purpose of OncoAlly™ Hereditary Cancer testing is to identify changes in the DNA sequence that may predispose individuals to specific types of cancers. This test uses a PCR-free protocol that produces comprehensive and consistent coverage of all exons and non-coding regions of an individual's genome. The resulting data is subjected to in-silico analyses, for subsets of genes, optimized for the detection of sequence analysis (single nucleotide variants, deletions/insertions and characterized intronic variants), copy number variants, duplications/deletions, mobile element insertions, and inversions. Detailed information and gene list of each of the offered tests can be found at www.variantyx.com.

Technical Limitations

Genetic testing is accurate, but may not always identify a genetic variant even though one exists. This test attempts to evaluate the entire DNA sequence (within the scope described for the test), but may not be able to detect all DNA changes due to limitations in current technology. Certain regions of the DNA may not be well covered. Certain variant types may not be detectable such as methylation abnormalities, variants in genes with highly homologous pseudogenes and variants in regions that are difficult to assay based on current technology. Unusual circumstances including bone marrow transplantation, blood transfusion, and variants that exist in only a small fraction of cells (mosaicism) may interfere with variant identification. Deletions, duplications and copy number variants between 50 and 300 nucleotides are detected with a lower sensitivity. Additionally, interpretation of the results is limited by the current medical understanding of disease and available scientific information. This test requires high-quality DNA. In some cases, an additional sample may be needed if the volume, quality and/or condition of the initial sample is not sufficient. Samples submitted as genomic DNA will only be processed if the extraction was performed in a CLIA/CAP accredited laboratory. This test does not consider somatic variants.

The following genes are not fully covered: *SOS1*, *PTCH1*, *STK11*, *CEBPA*. Therefore there may be variants in certain regions of these genes that are not identified with this test. The following genes have regions that are not unique: *SDHA*, *PMS2*. Therefore there may be variants in these genes that cannot be assigned to the correct location and limit the interpretation. Performance characteristics were not determined for the Boland inversion detection and therefore may not be identified with this assay.

Possible Test Results

Positive - A positive result indicates that one or more genetic variants were identified that indicate an increased risk of developing the disorder in the future. Individuals with positive results may wish to consider further independent testing and/or consultation with their physician or genetic counselor.

Carrier Status - A Carrier status result will be reported only for a single pathogenic/likely pathogenic variant in a gene associated with autosomal recessive hereditary cancer predisposition. Carriers may have a lower risk of developing cancer than individuals with biallelic variants in this gene, but a greater risk than the general population. Individuals with Carrier status result may wish to consider further independent testing and/or consultation with their physician or genetic counselor.

Uncertain - A variant of uncertain significance was identified by this test. This means that a genetic variant was identified, but based on available information in the medical literature and research and scientific databases it is not certain whether the variant may cause the disorder. The variant could be a normal genetic change that does not cause the disorder. Without further information, the effects of the variant cannot be known and an "uncertain/clinically inconclusive" result may be reported. The uncertainty may be resolved over time if additional information becomes available. Periodic reanalysis of the sequence data or further analysis, including testing of additional family members, may be recommended.

Negative - A negative result indicates that no genetic variant explaining the disorder was identified by this test. This reduces the likelihood of, but does not exclude the possibility of, the disorder being genetic in nature.

Indeterminate - An indeterminate result indicates that there may be relevant genetic variant(s) identified in the analysis, but that it is uncertain whether they are true variants or artifacts. Furthermore, it is considered that a repeat test will not resolve the technical uncertainty and orthogonal confirmation is necessary to resolve the result.

Inconclusive - A technically inconclusive result indicates that there was an issue with the patient sample that resulted in data that the lab cannot interpret. It is considered that a repeat test will likely resolve the technical uncertainty and therefore a repeat sample is recommended to complete the analysis.

Reporting Standards

All reportable variants in the clinical report will be categorized as pathogenic, likely pathogenic or a variant of uncertain significance (VUS) utilizing the American College of Medical Genetics and Genomics (ACMG)/Association for Molecular Pathology (AMP) guidelines as published by Richards et al. 2015 (for more information see: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4544753/>). Variants may have a strong phenotypic correlation with the reported patient phenotype(s) and be considered a strong causal candidate for the disorder or may have some phenotypic overlap with the reason for testing but not be considered the sole genetic cause for the phenotype(s) in the patient. Both types of variants may be reported. Even if this test finds DNA changes that are responsible for the reported symptoms, the testing may not completely predict the severity of the disorder, possible future problems, or response to treatment. Variants of uncertain clinical significance will only be reported if found to be associated with patient phenotype. Variants of uncertain clinical significance will not be reported in targeted analysis (phenotypic based analyses) unless sufficient clinical information was provided.

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Variantyx reviews clinical notes provided with the test submission and may report results from other labs for detection of the variant on our platform. This is possible if there is detailed information in the notes provided with the test requisition. Information required includes (but is not limited to): reference genome, chromosome location/gene name, variant change (c./p. or breakpoints), and transcript. It is recommended to include previous test results containing the required information.

Patient Confidentiality

To maintain confidentiality, test results will only be released to the ordering healthcare provider or ordering laboratory, and upon your request, to additional healthcare provider(s) indicated on this test requisition form. Test results will only be disclosed to others by your written consent and/or if demanded by a court of competent jurisdiction. It is your responsibility to consider the possible impact of test results on insurance rates, the ability to obtain disability, life or long-term care insurance and employment. The Genetic Information Non-discrimination Act (GINA), enacted by the US Federal Government, provides some protection against discrimination by health insurance companies and employers based on genetic test results, but does not cover life, disability or long-term care insurance. Information about GINA is available at <https://www.genome.gov/10002328>.

Anonymized information obtained from the test may be included in variant and allele frequency databases used to help healthcare providers and scientists understand human disease, as well as in scientific publications. Names and personal identifying information will not be revealed. Separate from the above, if there are opportunities to participate in research relevant to your condition, and you have consented for recontact, Variantyx may contact you or your healthcare provider for research purposes.

Turnaround time

The turnaround time (TAT) of this test can be found on the [Variantyx website](#), which begins at the time of sample receipt. Please note that the following scenarios will likely result in extension of the turnaround time (1) when the DNA sample fails QC and is determined to be insufficient for testing, requiring collection of a new sample; (2) when the test is sent for orthogonal confirmation at an external laboratory. In the second scenario, the turnaround time can be expected to be extended by the turn around time of the external laboratory plus 1 week.

Sample Retention

DNA extracted from submitted samples may be stored for at least 3 months following completion of testing and may be discarded thereafter. Extracted DNA is not returned unless requested prior to testing (additional fees apply). After completion of testing, anonymized DNA may be used for test development and improvement, internal validation, quality assurance and training purposes before being discarded.

NY state residents: No other test shall be performed on this sample except the test ordered by the clinician, unless waived by the patient or authorized individual. In addition, the patient's biological sample will be destroyed within 60 days or upon the completion of testing, unless waived by the patient or authorized individual. Orthogonal confirmation of results at a reference lab cannot be performed unless the patient or authorized individual provides permission to do so.

