Patient Name: <<patname>> **Accession #: <<accession>>**

Client: <<docnametitle>>	Patient Name: <<patname>>	Accession #: <<accession>>
Ordered By:	DOB: <<dob>>	Collected: <<collectdtm>>
Physician: <<refphys>>	Gender: <<sex>>	Accessioned:<<entrydtm>>
Test: Complete Cancer Panel	*Specimen Type: Oral Swab/Saliva*	Reported: <<reportdtm>>

Discover™ Hereditary Cancer Risk Assessment Report

Positive Result: Clinically Significant Alteration Detected

Test Result Summary

Gene	Classification	Zygosity	Variant Transcript
SDHA	Pathogenic	Heterozygous	NM_004168.4 (SDHA): c.1151C>G (p. Ser384Ter)

Additional Variant Details

Location: (GRCh37) Exon: 9/15, SDHA chr5: 235345
Consequence/Type: Stop gained, SNV
ClinVar/dbSNP: 230877/ rs151170408

Sample Level Metrics

Amplicon Mean Coverage: 741.4
Uniformity of Coverage: 94.03
Low Coverage Regions:

Test Methods

Patient genomic DNA (gDNA) was isolated from patient sample(s) (buccal swab or spittle sample) using bead-based extraction chemistry. gDNA is quantified and quality checked following extraction. Targeted coding exons and short segments of intronic regions are isolated through the library preparation process utilizing the panel created by illumina® for identification of variants within genomic regions with known hereditary cancer relationships. PCR amplification of regions of interest is followed by sequencing on the illumina® Next Generation Sequencing (NGS) platform. The bioinformatics pipeline utilized prioritizes variants based upon their consequence to protein function and ultimately their clinical significance. ACMG guidelines were utilized to compare sequencing results with evidence to support pathogenicity as reported here. As a result of updates to knowledge in the field of genomics, variant classification and/or interpretation may change over time as more information becomes available. Only variations of clinical significance (primary findings) are included in this report, secondary/incidental sequence variant(s) are not.

Interpretation

SDHA

Loss of function germline variants (pathogenic/likely pathogenic) in the SDHA gene are associated with autosomal dominant hereditary paraganglioma-pheochromocytoma syndromes (PGL-PCC) and increased risk of gastrointestinal stromal tumors (GIST). GIST tumors can develop anywhere along the GI tract including the esophagus, stomach, gallbladder, liver, small intestine, colon, rectum, anus, and the lining of the gut. PGL_PCC related tumors are neuroendocrine in nature and distributed throughout the body. There is preliminary evidence that suggests that individuals with loss of function SDHA variants are also at increased lifetime risk of renal cancer. These variants are also associated with autosomal recessive mitochondrial complex II deficiency. Although the risk of these types of cancer is increased above that of the general population risk, it is not necessary that an individual with one or two copies of loss of function variants will get cancer in their lifetime.

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Recommendations

- Always speak with a medical professional regarding your results
- Genetic counseling is recommended to discuss the implications of these test results
  - If you would like to discuss these results in further detail, please call our office directly at (201) 791-7293 to schedule an appointment with one of our genetic counselors.

Cancer Panels:

BreastDiscover, OvarianDiscover, UterineDiscover, ColorectalDiscover, MelanomaDiscover, PancreaticDiscover, GastricDiscover, ProstaticDiscover, LungDiscover, CNSDiscover, KidneyDiscover, BladderDiscover.

Targeted Regions for "Inherited Cancer Gene Panel", includes the whole regions of the genes indicated below:
Breast Discover: ATM, BARD1, BRCA1, BRCA2, BRIP1, CDH1, CHEK2, NBN, NF1, PALB2, PTEN, RAD50, STK11, TP53
Ovarian Discover: BARD1, BRCA1, BRCA2, BRIP1, DICER1, EPCAM, MLH1, MSH2, MSH6, PMS2, PTEN, RAD50, RAD51C, RAD51D, STK11, TP53
Uterine Discover: EPCAM, FH, MLH1, MSH2, MSH6, PMS2, PTEN, STK11, TP53
Colorectal Discover: APC, AXIN2, BMPR1A, CDH1, CHEK2, EPCAM, GPC3, MLH1, MSH2, MSH6, MUTYH, PMS2, POLD1, POLE, PTEN, SMAD4, STK11, TP53
Skin Discover: BAP1, BRCA2, CDK4, CDK2NA, MITF, PTCH1, PTEN, RB1, TP53
Pancreatic Discover: APC, ATM, BMPR1A, BRCA1, BRCA2, CDK2NA, EPCAM, MEN1, MLH1, MSH2, MSH6, PALB2, PMS2, SMAD4, STK11, TP53, VHL
Gastric Discover: APC, BMPR1A, CDH1, EPCAM, KIT, MLH1, MSH2, MSH6, NF1, PDGFRB, PMS2, SDHA, SDHB, SDHC, SDHD, SMAD4, STK11, TP53, TSC1, TSC2, VHL
Prostate Discover: ATM, BRCA1, BRCA2, CDK2NA, CHEK2, DICER1, EPCAM, FH, HOXB13, MLH1, MSH2, MSH6, NBN, NF1, PALB2, PMS2, RAD51D, SMAD4, TP53, WT1
Lung Discover: ALK, EGFR, EPCAM
CNS Discover: ALK, APC, CDKN1B, CDKN2A, DICER1, EPCAM, MEN1, MLH1, MSH2, MSH6, NBN, NF1, NF2, PHOX2B, PMS2, PRKAR1A, PTCH1, PTEN, SMARCB1, SMARCE1, SUFU, TP53, TSC1, TSC2, VHL
Renal Discover: BAP1, EPCAM, FH, FLCN, MET, MITF, MLH1, MSH2, MSH6, PMS2, PTEN, SDHA, SDHAF2, SDHB, SDHC, TP53, TSC1, TSC2, VHL, WT1
Bladder Discover: FH
Sarcoma Discover: BLM, EPCAM, FH, KIT, NF1, PDGFRB, PMS2, PRKAR1A, PTCH1, RB1, RECQL4, SDHA, SDHB, SDHC, SDHD, SUFU, TP53, WRN
Hematologic Discover: BLM, EPCAM, NF1, PMS2, RUNX1, TERT, TP53
Endocrine Discover: APC, CDC73, CDKN1B, MAX, MEN1, NF1, PRKAR1A, RET, SDHA, SDHAF2, SDHB, SDHC, SDHD, TMEM127, TP53, VHL

Test Indication:

Information provided indicates that this individual has a personal history of cancer.

All genes in panel are run for each patient, only clinically significant variants are reported. While not all genes will be found to be wildtype in their genetic code, any variations seen and not reported were benign/likely benign and therefore not known to cause disease according to current research.

Test Limitations

Variants may exist in genes other than the ones listed in this panel or in novel ways that have yet to be clinically characterized. As such, this test does not represent all of the possible variations in the entire exome or genome of the individual. Further testing should be discussed with a medical professional or genetic counselor based upon the coverage regions of this test and potential ability of other testing to elucidate information that may be clinically significant. Only the protein coding regions and splicing sites of these genes are included in the analysis and reported herein. Variations outside the sequenced regions of these genes are not included in the genetic risk analysis. Certain types of mutations other than single nucleotide changes or smaller deletions/duplications may not be identified based on the current Next Generation Sequencing analysis technology used for this test. Examples of mutations that are not covered under this test: mosaicism, chromosomal aberrations, insertions or deletions larger than 50bp, or copy number variants. False negatives can occur if DNA quality is suboptimal (but passes minimum thresholds for quality control), if patient has received a recent bone marrow transplant or blood transfusion, or if the variant is novel or in a region that is

not yet well studied. False positives can occur in some cases, particularly in patients with lymphoma or leukemia or with known chronic myeloid or lymphoid neoplasms. Based on study design and technology differences between laboratories, reported variants may not be the same from the same subject. The sensitivity and specificity of these tests varies between facilities due to differences in chemistry and bioinformatic analysis.

Disclaimer

This report was generated using the materials and methods described above, which required the use of various reagents, protocols, instruments, software, databases, and other items, some of which were provided or made accessible by third parties. A defect or malfunction in any such reagents, protocols, instruments, software, databases, and/or other items may compromise the quality or accuracy of the report. The report has been generated based on, and incorporates references to various scientific manuscripts, references, and other sources of information that were prepared by third parties that describe correlations between certain genetic mutations and particular diseases (and/or certain therapeutics that may be useful in ameliorating the effects of such diseases). Such information and correlations are subject to change over time in response to future scientific and medical findings. Biogenica makes no representation or warranty of any kind, expressed or implied, regarding the accuracy of the information provided by or contained in such manuscripts, references, and other sources of information. If any of the information provided by or contained in such manuscripts, references, and other sources is later determined to be inaccurate, the accuracy and quality of the report may be adversely impacted. Biogenica is not obligated to notify you of any impact that future scientific or medical research findings may have on the report. The report must always be interpreted and considered within the clinical context, and a physician should always consider the report along with all other pertinent information and data that a physician would prudently consider prior to providing a diagnosis to a patient or developing and implementing a plan of care for a patient. The report should never be considered or replied upon alone in making any diagnosis or prognosis. The manifestations of many diseases are caused by more than one gene variant, a single gene variant may be relevant to more than one disease, and certain relevant gene variants may not have been considered in the report. In addition, many diseases are caused or influenced by modifier genes, epigenetic factors, environment factors, and other variables that are not addressed by the report (or that are otherwise unknown). As such, the relevance of the report should be interpreted in the context of a patient's clinical manifestations. Medical knowledge annotation is constantly updated and reflects the current knowledge at the time. The test performance characteristics were determined by Biogenica. determined that such clearance or approval is not necessary. This laboratory is CLIA certified to perform high complexity testing.

The report was generated by Biogenica as required by the CLIA 1988 regulations. The report, and the tests used to generate the report, have not been cleared or approved by the U.S. Food and Drug Administration (FDA), since FDA has