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Breast Cancer Patient Test Report

SUBJECT INFORMATION

Pre-Screening Subject No.: _____

Subject Initials (first/middle/last): _____

Date of Birth (dd/mmm/yyyy): _____

Gender: ☐ Male ☐ Female

SPECIMEN INFORMATION

Accession No.:_____ Date Specimen Received: _____ Date Reported: _____

Summary

Positive result. Pathogenic variant identified in BRCA1.

Clinical Summary

- A Pathogenic variant, c.4327C>T (p.Arg1443*), was identified in BRCA1.
  - The BRCA1 gene is associated with autosomal dominant hereditary breast and ovarian cancer (HBOC) syndrome (MedGen UID: 151793)
  - This Pathogenic variant is consistent with a with a diagnosis of HBOC. These results should be interpreted within the context of addtional laboratory results, family history and clinical findings.
  - HBOC syndrome is characterized by an increased lifetime risk for breast cancer, contaralateral brest cancer, male breast cancer, ovarian cancer, prostate cancer, pancreatic cancer, and other cancers (PMID:12237281). The lifetime risk for female breast cancer in individuals with a pathogenic BRCA1 sequence change is 40-87% (PMID: 10498392, 7907678). The risk for contralateral breast cancer in these individuals is up to 43% within ten years of the initial breast cancer diagnosis (PMID: 15197194). The lifetime risk for mail breast cancer in individuals with a pathogeic BRCA1 sequence change is 1.2% (PMID: 18042939). The lifetime risk for ovarian, fallopian tube, or peritoneal cancer in females is 16-44% (PMID: 7907678, 9145676). Clinical management guidelines for HBOC syndrome can be found at www.nccn.org.
  - Close relatives (children, siblings, and each parent) have up to a 50% chance of being a carrier of this Pathogenic variant. More distant relatives may also be carriers. Site-specific testing for this variant is available.
- Genetic counseling is recommended to discuss the implications of this result, For a listing of genetic counselors, please visit www.nsgc.org.

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Complete Results

Table 2: Complete Test Results (Style I)

Gene	Exon	Nucleotide Change	Amno acid Change	Zygosity	Mutation Type	Mutation Effect
BRCA1	11	2345delG	Ser782fs	Hetero	FS	NR
BRCA2	10	865A>C	Asn289His	Hetero	MS	P
BRCA2	11	2229T>C	His743His	Hetero	Syn	P
FS=Frameshift Mutation, NS=Nonsense Mutation, MS=Missense Mutation P=Polymorphism, S=Splice, IFI=In Frame Insertion, IFD=In Frame Deletion IVS=Intervenning Sequence, UV=Unclassified variant, Syn=Synonymous and NR=Not Reported						

Table 3: Complete Test Results (Style II)

Gene	Condition Group	Variant	Zygosity	Variant Classification
BRCA1	Hereditary Cancers (Breast)	c.4327C>T (p.Arg1443*)	heterozygous	PATHOGENIC
BRCA1	Hereditary Cancers (Breast)	c.4327C>T (p.Arg1443*)	heterozygous	PATHOGENIC
BRCA1	Hereditary Cancers (Breast)	c.4327C>T (p.Arg1443*)	heterozygous	PATHOGENIC
BRCA1	Hereditary Cancers (Breast)	c.4327C>T (p.Arg1443*)	heterozygous	PATHOGENIC
The folowing genes were evaluated for sequence changes and exonic deletions/duplications: BRCA1, BRCA2 Results are negative unless otherwise indicated				

Variant classification

After the sequence change has been thoroughly researched and the relevant information has been gathered, a formal variant classification is assigned to the sequence change.

A formal classification is meant to help answer two questions about the clinical significance of the sequence change.

- From a diagnostic perspective: Does this sequence change, in the correct genetic background, provide an explanation for disease in an affected individual?
- From a predictive perspective, narrowly applied to highly penetrant conditions: Is an individual who inherits this sequence change likely to develop disease?

The ACMG has recommended a five-tier classification system According to this system, a sequence change can be classified as:

- **Pathogenic**: This sequence change directly contributes to the development of disease. Some pathogenic sequence changes may not be fully penetrant. In the case of recessive or X-linked conditions, a single pathogenic sequence change may not be sufficient to cause disease on its own. Additional evidence is not expected to alter the classification of this sequence change.
- **Likely pathogenic**: This sequence change is very likely to contribute to the development of disease; however, the scientific evidence is currently insufficient to prove this conclusively. Additional evidence is expected to confirm

this assertion of pathogenicity, but we cannot fully rule out the possibility that new evidence may demonstrate that this sequence change has little or no clinical significance

- **Uncertain significance**: There is not enough information at this time to support a more definitive classification of this sequence change.
- **Likely benign**: This sequence change is not expected to have a major effect on disease; however, the scientific evidence is currently insufficient to prove this conclusively. Additional evidence is expected to confirm this assertion, but we cannot fully rule out the possibility that new evidence may demonstrate that this sequence change can contribute to disease.
- **Benign**: This sequence change does not cause disease.

Databases reviewed

- **Population databases:**
  - 1000 Genomes (http://browser.1000genomes.org)
  - NHLBI GO Exome Sequencing Project (ESP) (http://evs.gs.washington.edu/EVS)
  - dbSNP (http://www.ncbi.nlm.nih.gov/snp)
  - dbVar (http://www.ncbi.nlm.nih.gov/dbvar)
- **Disease databases:**
  - ClinVar (http://www.ncbi.nlm.nih.gov/clinvar)
  - ClinVitae (http://clinvitae.invitae.com)
  - Online Mendelian Inheritance in Man (OMIM) (http://www.omim.org)
  - Human Gene Mutation Database (HGMD) (http://www.hgmd.org)
  - Human Genome Variation Society (HGVS) (http://www.hgvs.org)
  - Leiden Open Variation Database (LOVD) (http://www.lovd.nl)
  - DECIPHER (http://decipher.sanger.ac.uk)
- **Sequence databases:**
  - NCBI genome (http://www.ncbi.nlm.nih.gov/genome)
  - RefSeq Gene (http://www.ncbi.nlm.nih.gov/refseq/rsg
  - Locus Reference Genomic (LRG) (http://www.lrg-sequence.org)
  - MitoMap (http://www.mitomap.org/MITOMAP/HumanMitoSeq)

Reporting

Our clinical report documents the evidence and logic supporting each variant interpretation to enable the ordering clinician to evaluate and, if appropriate, discuss the evidence with their patients. All language used to describe genetic variants and variant interpretation is systematic and consistent with ACMG and Human Genome Variation Society (HGVS) recommendations.

This report includes:

- **Summary**: A clear statement summarizing the high-level result of the genetic test — positive, negative, or clinically inconclusive

- **Clinical summary**: a description of the relevance of the genetic results to the patient based on their clinical and family history
- **Complete results table**: A table of the genes in which genetic variants were identified, and a complete list of all genes analyzed in the test
- **Variant details**: a summary of the evidence and logic used to justify the interpretation of the sequence change

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