

Patient Name	DOB	Sex	MRN	Invitae #
Norma Bates	07.30.1980	Female	12344321	RQ654845
Clinical Team	Report Date	Sample Type	Sample Collection Date	Sample Accession Date
Festus Ezeli	03.20.2019	Saliva	03.06.2019	03.08.2019

Test Performed
Sequence analysis and deletion/duplication testing of the gene listed in the results section below.

Reason for Testing
Family history

Targeted Variants

Gene	Variant	Zygosity	Classification	Result
PRRT2	c.115G>A (p.Ala39Thr)	heterozygous	Likely Benign	Detected

The table above reflects the information for the requested variant(s) based on the date this report was issued.

- Based on the results of family testing, the c.115G>A (p.Ala39Thr) variant in PRRT2 has been reclassified as Likely Benign. Benign and Likely Benign variants are not included in this report but a full list is available upon request.

Summary

Negative result. No Pathogenic sequence variants or deletions/duplications identified.

Clinical Summary

- No reportable genetic variants were identified by this analysis. This individual may still be at risk for certain medical conditions based on other factors, such as family history, genetic causes not evaluated with this test, or other environmental influences. Follow up of this individual and surveillance of their family members may still be warranted.
- Please note, familial variant analysis includes full gene sequencing and deletion/duplication testing unless otherwise indicated. The presence or absence of the familial variant(s) is always reported. Pathogenic or Likely Pathogenic variants elsewhere in the gene(s), if present, would also be reported. Variants of Uncertain Significance elsewhere in the gene(s), if present, would not be reported.
- These results should be interpreted within the context of additional laboratory results, family history, and clinical findings. Genetic counseling is recommended to discuss the implications of this result. For access to a network of genetic providers, please contact Invitae at clientservices@invitae.com, or visit www.nsgc.org or tagc.med.sc.edu/professional_organizations.asp.

Complete Results

The following genes were evaluated for sequence changes and exonic deletions/duplications:
PRRT2

Results are negative unless otherwise indicated

Benign and Likely Benign variants are not included in this report but are available upon request. An asterisk (*) indicates that this gene has a limitation. Please see the Limitations section for details.

Methods

- Genomic DNA obtained from the submitted sample is enriched for targeted regions using a hybridization-based protocol, and

sequenced using Illumina technology. Unless otherwise indicated, all targeted regions are sequenced with $\geq 50\times$ depth or are supplemented with additional analysis. Reads are aligned to a reference sequence (GRCh37), and sequence changes are identified and interpreted in the context of a single clinically relevant transcript, indicated below. Enrichment and analysis focus on the coding sequence of the indicated transcripts, 10bp of flanking intronic sequence (20bp for BRCA1/2), and other specific genomic regions demonstrated to be causative of disease at the time of assay design. Promoters, untranslated regions, and other non-coding regions are not otherwise interrogated. For some genes only targeted loci are analyzed (indicated in the table above). Exonic deletions and duplications are called using an in-house algorithm that determines copy number at each target by comparing the read depth for each target in the proband sequence with both mean read-depth and read-depth distribution, obtained from a set of clinical samples. All clinically significant observations are confirmed by orthogonal technologies, except individually validated variants and variants previously confirmed in a first-degree relative. Confirmation technologies include any of the following: Sanger sequencing, Pacific Biosciences SMRT sequencing, MLPA, MLPA-seq, Array CGH. Array CGH confirmation of NGS CNV calling performed by Invitae Corporation (1400 16th Street, San Francisco, CA 94103, #05D2040778). The following analyses are performed if relevant to the requisition. For PMS2 exons 12-15, the reference genome has been modified to force all sequence reads derived from PMS2 and the PMS2CL pseudogene to align to PMS2, and variant calling algorithms are modified to support an expectation of 4 alleles. If a rare SNP or indel variant is identified by this method, both PMS2 and the PMS2CL pseudogene are amplified by long-range PCR and the location of the variant is determined by Pacific Biosciences (PacBio) SMRT sequencing of the relevant exon in both long-range amplicons. If a CNV is identified, MLPA or MLPA-seq is run to confirm the variant. If confirmed, both PMS2 and PMS2CL are amplified by long-range PCR, and the identity of the fixed differences between PMS2 and PMS2CL are sequenced by PacBio from the long-range amplicon to disambiguate the location of the CNV. Technical component of confirmatory sequencing is performed by Invitae Corporation (1400 16th Street, San Francisco, CA 94103, #05D2040778).

- The following transcripts were used in this analysis: PRRT2 (NM_145239.2).
- A PMID is a unique identifier referring to a published, scientific paper. Search by PMID at <http://www.ncbi.nlm.nih.gov/pubmed>.
- An rsID is a unique identifier referring to a single genomic position, and is used to associate population frequency information with sequence changes at that position. Reported population frequencies are derived from a number of public sites that aggregate data from large-scale population sequencing projects, including ExAC (<http://exac.broadinstitute.org>), gnomAD (<http://gnomad.broadinstitute.org>), and dbSNP (<http://ncbi.nlm.nih.gov/SNP>).
- A MedGen ID is a unique identifier referring to an article in MedGen, NCBI's centralized database of information about genetic disorders and phenotypes. Search by MedGen ID at <http://www.ncbi.nlm.nih.gov/medgen>. An OMIM number is a unique identifier referring to a comprehensive entry in Online Mendelian Inheritance of Man (OMIM). Search by OMIM number at <http://omim.org/>.
- Invitae uses information from individuals undergoing testing to inform variant interpretation. If "Invitae" is cited as a reference in the variant details this may refer to the individual in this requisition and/or historical internal observations.

Limitations

- Based on validation study results, this assay achieves >99% analytical sensitivity and specificity for single nucleotide variants, insertions and deletions <15bp in length, and exon-level deletions and duplications. Invitae's methods also detect insertions and deletions larger than 15bp but smaller than a full exon but sensitivity for these may be marginally reduced. Invitae's deletion/duplication analysis determines copy number at a single exon resolution at virtually all targeted exons. However, in rare situations, single-exon copy number events may not be analyzed due to inherent sequence properties or isolated reduction in data quality. Certain types of variants, such as structural rearrangements (e.g. inversions, gene conversion events, translocations, etc.) or variants embedded in sequence with complex architecture (e.g. short tandem repeats or segmental duplications), may not be detected. Additionally, it may not be possible to fully resolve certain details about variants, such as mosaicism, phasing, or mapping ambiguity. Unless explicitly guaranteed, sequence changes in the promoter, non-coding exons, and other non-coding regions are not covered by this assay. Please consult the test definition on our website for details regarding regions or types of variants that are covered or excluded for this test. This report reflects the analysis of an extracted genomic DNA sample. In very rare cases, (circulating hematology neoplasm, bone marrow transplant, recent blood transfusion) the analyzed DNA may not represent the patient's constitutional genome.

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This report has been reviewed and approved by:

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NOT FOR RELEASE

UNSIGNED
Nobody

Disclaimer

DNA studies do not constitute a definitive test for the selected condition(s) in all individuals. It should be realized that there are possible sources of error. Errors can result from trace contamination, rare technical errors, rare genetic variants that interfere with analysis, recent scientific developments, and alternative classification systems. This test should be one of many aspects used by the healthcare provider to help with a diagnosis and treatment plan, but it is not a diagnosis itself. This test was developed and its performance characteristics determined by Invitae. It has not been cleared or approved by the FDA. The laboratory is regulated under the Clinical Laboratory Improvement Act (CLIA) as qualified to perform high-complexity clinical tests (CLIA ID: 05D2040778). This test is used for clinical purposes. It should not be regarded as investigational or for research.