Warde Medical Laboratory

# LABORATORY REPORT

Example Client, XYZ123
1234 Warde Road
Ann Arbor MI 48108

**EXAMPLE, REPORT W**
WX0000003826 F 12/05/1988 34 Y

## Referral Testing

Collected: 09/01/2023 10:01 Received: 09/01/2023 10:01

| Test Name | Result | Flag | Ref-Ranges | Units | Site |
|---|---|---|---|---|---|

### von Willebrand Disease Gene Sequencing

| | | | | | |
|---|---|---|---|---|---|
| vWF Disease Gene Seq | SEE NOTE | | | | QCRL |

RESULT: HETEROZYGOUS FOR THE c.6859C>T (p.Arg2287Trp) VARIANT OF UNCERTAIN SIGNIFICANCE IN THE VON WILLEBRAND FACTOR GENE

INTERPRETATION: This test has identified one copy of the c.6859C>T (p.Arg2287Trp) variant in the VWF gene. In the published literature, the variant has been reported in affected individuals with Type 1 or Type 2A von Willebrand disease (vWD) (PMID: 16985174 (2007), 23340442 (2013)), but it has also been reported in healthy individuals (PMID: 22197721 (2012), 23216583 (2013)). In in-vivo functional studies, this variant caused mild intracellular retention and impaired secretion of VWF protein (PMID: 16985174 (2007), 19566550 (2009), 23340442 (2013), 31035301 (2019)). The frequency of this variant in the general population, 0.008 (199/24962 chromosomes, http://gnomad.broadinstitute.org), is uninformative in assessment of its pathogenicity. ClinVar contains an entry for this variant (URL: www.ncbi.nlm.nih.gov/clinvar, Variation ID: 100450). Analysis of this variant using bioinformatics tools (e.g. MutationTaster and PolyPhen-2) for the prediction of the effect of amino acid changes on protein structure and function yielded conflicting predictions that this variant is benign or damaging. Please note that these prediction tools are not fully validated and should be viewed with caution. Based on the available information, we are unable to determine the clinical significance of this variant. Testing affected family members could help clarify the clinical significance of this variant. Genetic counseling is recommended. Laboratory results and submitted clinical information reviewed by Timothy Trieu D. Vo, PhD, FACMG, CGMB.

von Willebrand disease (VWD) is the most common inherited bleeding disorder, affecting approximately 1% of the general population. It results from quantitative or qualitative defects of the von Willebrand factor (VWF) protein. Pathogenic variants in the VWF gene (located on chromosome 12p13.3) can cause reduced synthesis of VWF protein, or structural and functional abnormalities in the VWF protein, leading to various types of VWD.

In this assay, sheared genomic DNA fragments representing the entire coding region and the splice junction sites of the VWF gene (NM 000552.3) are selectively enriched through exon capture, and then subjected to nucleotide sequence analysis on a massively parallel sequencing platform. To avoid pseudogene interference, long range PCR (LR-PCR) is performed for exons 23-28. The LR-PCR product is processed and included in the sequencing reaction. Exon level, copy number variants are detected by bioinformatic analysis of the sequencing and

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confirmed by a custom targeted microarray. However, due to the pseudogene, exons 23-28 are excluded from copy number analysis. This analysis will identify variants associated with Type II (subtypes, A, B, M, and N) and some forms of Type I and Type III VWD (see http://www.shef.ac.uk/vwf/vwd.html). Since genetic variation and other factors can affect the accuracy of this test, results should always be interpreted in light of clinical and familial data. Benign and likely benign variants with no known clinical significance are reported only by request.

The classification and interpretation of the variants identified in this DNA assessment reflect the current state of Quest Diagnostics' understanding at the time this report was issued. Variant classification and interpretation are subject to professional judgment, and may change for a variety of reasons, including but not limited to, improvements in classification techniques, availability of additional information, and observation of a variant in more patients. Health care providers should verify a variant's classification prior to taking any clinical action. This test result should be used in conjunction with the health care provider's clinical evaluation and other medically established means to help with a diagnosis and treatment plan. For questions regarding variant classification updates, please call Quest Diagnostics at 866-GENEINFO (436-3463) to speak to a genetic counselor or laboratory director.

This test was developed and its analytical performance characteristics have been determined by Quest Diagnostics Nichols Institute San Juan Capistrano. It has not been cleared or approved by FDA. This assay has been validated pursuant to the CLIA regulations and is used for clinical purposes.
Test Performed at:
Quest Diagnostics Nichols Institute
33608 Ortega Highway
San Juan Capistrano, CA 92675-2042 I Maramica MD, PhD, MBA

Clinical Indication: NA

QCRL

Performing Site:
QCRL: QUEST DIAGNOSTICS REFERENCE LAB CAPISTRANO 33608 Ortega Highway San Juan Capistrano CA 92675

**Reported Date:** 2023.09.01 10:01 VONWI