BLOODCENTER of WISCONSIN™

VWF D1472H RISTOCETIN-BINDING POLYMORPHISM

BloodCenter of Wisconsin's Hemostasis Reference Laboratory offers testing for detection of the D1472H polymorphism within von Willebrand factor.

BACKGROUND:

Type 2M von Willebrand disease (VWD) is characterized by a qualitative defect in von Willebrand factor (VWF). Type 2M VWD is diagnosed by a disproportionate decrease in VWF ristocetin cofactor activity (VWF:RCo) as compared with VWF antigen (VWF:Ag). The VWF:RCo assay is a functional measure of VWF binding to platelets, exploiting the capacity of ristocetin to induce a conformational change in VWF that leads to VWF binding to platelet glycoprotein Ib (GPIb). The decreased VWF:RCo in type 2M VWD is attributable to mutations in the VWF A1 domain that disrupt the VWF platelet binding site. However, an A1 domain polymorphism, D1472H, decreases ristocetin-mediated VWF-platelet interaction, presumably through alteration of the ristocetin-binding site on VWF, leading to decreased VWF:RCo results in individuals with normal VWF function. The D1472H VWF polymorphism is found in 63% of African American and 17% of Caucasian healthy individuals. In D1472H-positive individuals the VWF:RCo/VWF:Ag ratio may lead to the classification of the patient as VWD type 2M, when in reality, the discrepancy between VWF:RCo and VWF:Ag may be an artifact of the current functional assay.

REASONS FOR REFERRAL:

- Evaluation of patients with abnormal VWF:RCo/VWF:Ag ratio
- Diagnosis of patients with type 2M VWD

METHOD:

PCR amplification and bi-directional DNA sequence analysis are performed from cDNA nucleotides 4354-4747 The sequence analyzed is compared to NC_000012.10 reference sequence. Sequence variations are reported using the standard nomenclature recommendations of the Human Genome Variation Society.

LIMITATIONS:

Analytical sensitivity is >99%. Rare polymorphisms within primer or probe regions may interfere with detection of gene variants. The presence of the VWF D1472H polymorphism cannot rule out a diagnosis of type 2M VWD, as bona fide type 2M mutations could be present. It is important to consider each patient's bleeding history, taking into account historical challenges and family history.

REPORTABLE RANGE/NORMAL VALUES:

Results are reported as negative, heterozygous or homozygous for D1472H.

PO Box 2178
Milwaukee, WI 53201-2178
Location/Sample Deliveries:
638 N. 18th St. Milwaukee, WI 53233-2121
p800-245-3117 | f414-937-6202 | www.bcw.edu

SPECIMEN REQUIREMENTS:
5 mL EDTA (lavender top) whole blood, collected and shipped at room temperature.
Sample should be less than 7 days old when received at our laboratory.

SHIPPING REQUIREMENTS:
Place the specimen and the test requisition into plastic bags and seal. Insert into a Styrofoam container; place into a sturdy cardboard box, tape securely, and ship by an overnight carrier. Ship the package in compliance with your overnight carrier guidelines. Label with the following address:

Client Services/Hemostasis Reference Laboratory
BloodCenter of Wisconsin
638 N. 18th St.
Milwaukee, WI 53233
800-245-3117, ext. 6250

TURNAROUND TIME: 7 - 10 days

CPT CODES: 81479

REFERENCES:
1. Sadler JE, Budde U, Eikenboom JC et al. Update on the pathophysiology and classification of von Willebrand disease: a report of the Subcommittee on von Willebrand Factor. J.Thromb.Haemost. 2006;4:2103-2114.
2. Flood VH, Gill JC, Morateck PA et al. Common VWF exon 28 polymorphisms in African Americans affecting the VWF activity assay by ristocetin cofactor. Blood 2010;116:280-286.
3. Flood VH, Friedman KD, Gill JC et al. Limitations of the ristocetin cofactor assay in measurement of von Willebrand factor function. J.Thromb.Haemost. 2009;7:1832-1839.

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