BACKGROUND:
Platelet-type von Willebrand disease (PT-VWD) and type 2B VWD are rare autosomal dominantly inherited bleeding disorder resulting from an abnormal high affinity interaction between platelet glycoprotein Ib/V/IX complex and von Willebrand factor (VWF). These disorders share many clinical and laboratory features including (1) mucosal bleeding and increased bleeding with surgery, (2) thrombocytopenia in a majority of cases, (3) reduced VWF levels with loss of the higher molecular weight multimers from plasma and (4) enhanced platelet aggregation response to low-dose ristocetin.

Distinction of PT-VWD from type 2B VWD is based on determining whether the enhanced interaction of platelets with VWF is platelet-based or plasma-based. In PT-VWD the defect is platelet-based, and is located in the platelet glycoprotein Ib/V/IX complex. In type 2B VWD the defect is plasma-based, and resides in VWF. Special low-dose ristocetin based platelet agglutination assays or VWF Exon 28 Sequence Analysis can be used to establish the diagnosis of type 2B VWD. Sequencing of GP1BA can be used to identify sequence variations in glycoprotein Ibα that cause PT-VWD.

In addition, DNA analysis can be used to differentiate PT-VWD and type 2B VWD. To date, all cases of PT-VWD have been traced to genetic variations of GP1BA, the gene for platelet glycoprotein Ibα. These include missense mutations altering the amino acid sequence from Glycine 249 to Methionine 255, and a 27 base pair deletion which encodes for deletion of Proline 436 through Serine 444.

METHOD:
PCR and bidirectional DNA sequence analysis of the coding region and intron-exon borders.

REASONS FOR REFERRAL:
Genetic analysis of the GP Ibα gene is useful to confirm a diagnosis of Platelet Type VWD, and may be helpful for genetic evaluation of family members.

ASSAY SENSITIVITY:
Analytical sensitivity and specificity is approximately 99%. The method detects nucleotide base alterations, small deletions and insertions within the regions analyzed. Large deletions and duplications have not been described in this disorder and are not detected by this assay. Rare sequence variations in primer binding sites may interfere with mutation detection.
Clinical sensitivity will be highest in patients with a phenotype consistent with the disorder. A positive test result confirms a diagnosis of PT-VWD. A negative test result argues strongly against a diagnosis of PT-VWD but does not exclude other variants forms of von Willebrand disease.
SPECIMEN REQUIREMENTS:
5 ml EDTA (lavender top) whole blood. Sample must be less than 1 month old when received by our laboratory.

SHIPPING REQUIREMENTS:
Ship on an ice pack or at room temperature. Place the specimen and the requisition into plastic bags and seal. Insert into a Styrofoam container; seal and place into a sturdy cardboard box, and tape securely. 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
Phone: 800-245-3117, ext. 6250

TURNAROUND TIME: 21 days

CPT CODES: 81479

ALSO AVAILABLE:
Von Willebrand Disease Type 2B Evaluation (includes VWF Multimer Analysis and Type 2B VWD Binding Assay)
VWF Exon 28 Sequence Analysis

REFERENCES:

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