VWF FULL GENE SEQUENCE ANALYSIS

BloodCenter of Wisconsin’s Hemostasis Reference Laboratory offers direct DNA sequencing for the entire von Willebrand Factor gene.

BACKGROUND:
von Willebrand disease (VWD) is the most common inherited bleeding disorder with a prevalence as high as 1 percent in the general population. The symptoms of VWD are due to a quantitative or qualitative dysfunction of vWF protein. A variety of point mutations, insertions, and deletions in the VWF gene have been described (Keeney S. (2001). Clin. Lab. Haem. 23: 209-230). VWD is classified into three different subtypes (Nichols et al, NHLBI VWD report, Dec 2007). Type 1 accounts for approximately 70 percent of cases with deficiency of VWF, and is usually inherited as an autosomal dominant trait. Type 3 affects approximately 1 percent of cases and is characterized by very low or undetectable levels of plasma VWF. Type 3 is inherited as an autosomal recessive disease with either homozygous or compound heterozygous mutations. Affected individuals have severe bleeding that can be life-threatening if not recognized and treated.

CLINICAL UTILITY:
Persons with Type 1 or Type 3 VWD may possess mutation scattered anywhere in the VWF gene.

Two studies recently showed that in persons with Type 1 VWD, approximately 1/3 possess identifiable mutations in their VWF gene (Goodeve, Blood 2007, James, Blood 2007). The studies also showed the likelihood of finding a potential mutation increases as the patients’ VWF level decreases. The quantitative VWF deficiency that occurs in type 1 VWD is caused by dominant VWF mutations that affect VWF secretion or clearance without substantially altering multimer assembly or platelet binding (Sadler, Blood 2007).

Mutations associated with type 3 VWD are found throughout the entire coding region of the VWF gene. Sequence analysis of the entire coding region identifies mutations in 80%-90% of type 3 VWD patients. The detection of the presence of a causative mutation of Type 3 VWD in utero can be helpful in planning delivery and treatment for an affected child and for genetic counseling of the affected family.

REASONS FOR REFERRAL:
• Confirm diagnosis of type 1 or 3 von Willebrand Disease
• Facilitate appropriate factor replacement therapy
• Facilitate genetic counseling and prenatal diagnosis.
• Evaluation of a patient with type 2 VWD where targeted sequence evaluation failed to detect a mutation.

METHOD:
PCR-direct DNA sequencing.
REFERENCE INTERVAL:
Normal - Normal DNA sequence.
Abnormal - Presence of mutation or sequence variation.

SPECIMEN REQUIREMENTS:
5 ml EDTA (lavender top) whole blood.
Sample must be less than one 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; 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: 81408