Congenital Thrombotic Thrombocytopenia Purpura

ADAMTS13 Sequence Analysis

Description: Congenital TTP, also known as Schulman-Upshaw syndrome, is classically characterized by neonatal onset of recurrent episodes of thrombocytopenia and hemolytic anemia, fever, and neurologic symptoms that are responsive to plasma infusion or plasmapheresis. However, the phenotype is highly variable, even among family members. Delayed onset of symptoms has been described, especially in regards to women who initially develop TTP during pregnancy. Congenital TTP is caused by biallelic mutations in the *ADAMTS13* gene that impair the protein's ability to cleave von Willebrand Factor (vWF), resulting in thrombotic microangiopathy and tissue injury.

Indications:

- Individuals with congenital thrombotic thrombocytopenia purpura
- Women who develop TTP during pregnancy
- Females with a history of TTP who are contemplating pregnancy
- Targeted mutation analysis of at-risk relatives of patient with *ADAMTS13* mutation
- Prenatal diagnosis of an at-risk fetus (after confirmation of parental carrier status).

Specimen: At least 3 mls whole blood in purple top (EDTA) tube. Label tube with patient's name, birth date, and date of collection. Phlebotomist must initial tube to verify patient's identity.

Testing Methodology:

PCR-based sequencing of the coding regions and their exon/intron boundaries of the *ADAMTS13* gene.

Sensitivity:

Clinical Sensitivity: PCR-based sequencing of the coding regions and their exon/intron boundaries of the *ADAMTS13* gene detects the vast majority of mutations in patients with congenital TTP. Several deletions of ~30 basepairs in *ADAMTS13* have been described, which may not be detected with this test methodology.

The sensitivity of PCR-based DNA sequencing is over 99% for the detection of nucleotide base changes, small deletions and insertions in the regions analyzed. Mutations in regulatory regions or other untranslated regions are not detected by this test. Multiple exon deletions, large insertions, genetic recombinational events and rare, primer site mutations may not be identified using this methodology. Rare primer site mutations may lead to erroneous results.

Cincinnati Children's
Human Genetics

Cytogenetics and Molecular Genetics Laboratories
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www.cchmc.org/genetics

Turn-Around Time: 4 weeks.

CPT Codes:

ADAMTS13 sequence analysis	81479
ADAMTS13 family specific mutation analysis	81403

Please call 1-866-450-4198 for current pricing or with any billing questions.

Results: Each test report includes a detailed interpretation of the genetic findings, the clinical significance of the result, and specific recommendations for clinical management and additional testing, if warranted. Biochemical and functional test results will be incorporated, when available. Results will be reported to the referring physician or health care provider as specified on the test requisition form.

Ancillary Testing: Results from ADAMTS13 activity, inhibition and antibody tests confirm a diagnosis of congenital or idiopathic TTP. Ancillary tests are available by calling 513-636-4530 or by visiting www.cincinnatichildrens.org/tma.

Shipping Instructions

Please enclose **test requisition** with sample. **All information must be completed before sample can be processed**. Place samples in Styrofoam mailer and ship at room temperature by overnight Federal Express to arrive Monday through Friday.

Ship to:

Cytogenetics and Molecular Genetics Laboratories
3333 Burnet Avenue NRB 1042
Cincinnati, OH 45229

References:

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Camilleri, R. S., et al. (2012). J Thromb Haemost, 10(9), 1792-1801.

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Kremer Hovinga, J. A., et al. (2012). Hematology Am Soc Hematol Educ Program, 2012, 610-616.

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