MAYO CLINIC LABORATORIES

NEW TEST

Notification Date: March 27, 2023
Effective Date: March 30, 2023

Red Blood Cell Membrane Disorders Gene Panel, Next-Generation Sequencing, Varies

Test ID: NMEM

Genetics Information:

This test utilizes next-generation sequencing to detect single nucleotide and copy number variants in 12 genes associated with red blood cell (RBC) membrane disorders including hereditary spherocytosis, hereditary elliptocytosis, hereditary pyropoikilocytosis, Southeast Asian ovalocytosis, hereditary stomatocytosis (both overhydrated and dehydrated/hereditary xerocytosis subtypes), and cryohydrocytosis(1-3): ABCB6, ANK1, EPB41, EPB42, GYPC, KCNN4, PIEZO1, RHAG, SLC2A1, SLC4A1, SPTA1, and SPTB. See Method Description for additional details.

Identification of a disease-causing variant may assist with diagnosis, prognosis, clinical management, recurrence risk assessment, familial screening, and genetic counseling for RBC membrane disorders.

Useful for:

Providing a comprehensive genetic evaluation for patients with a personal or family history suggestive of a red blood cell (RBC) membrane disorder

Second-tier testing for patients in whom previous targeted gene variant analyses were negative for a specific RBC membrane disorder

Establishing a diagnosis of a hereditary RBC membrane disorder, allowing for appropriate management and surveillance of disease features based on the gene involved, especially if splenectomy is a consideration(5)

Identifying variants within genes associated with phenotypic severity, allowing for predictive testing and further genetic counseling

Methodology:

Sequence Capture and Targeted Next-Generation Sequencing (NGS) followed by Polymerase Chain Reaction (PCR) and Sanger Sequencing

Reference Values:

An interpretive report will be provided.

Specimen Requirements:

Specimen Type: Whole blood
Patient Preparation: A previous bone marrow transplant from an allogenic donor will interfere with testing. Call 800-533-1710 for instructions for testing patients who have received a bone marrow transplant.
Container/Tube:

Preferred: Lavender top (EDTA)
Acceptable: Yellow top (ACD), green top (sodium heparin)
Specimen Volume: 3 mL
Collection Instructions:
1. Invert several times to mix blood.
2. Send whole blood specimen in original tube. **Do not aliquot.**
Specimen Stability Information: Ambient (preferred) 4 days/Refrigerated
Minimum Volume: 1ml

Cautions:

Clinical Correlations:

- Test results should be interpreted in the context of clinical findings, family history, and other laboratory data. Misinterpretation of results may occur if the information provided is inaccurate or incomplete.
- If testing was performed because of a clinically significant family history, it is often useful to first test an affected family member. Detection of a reportable variant in an affected family member would allow for more informative testing of at-risk individuals.
- To discuss the availability of additional testing options, or for assistance in the interpretation of these results, contact the Mayo Clinic Laboratories genetic counselors at 800-533-1710.

Technical Limitations:

- Next-generation sequencing may not detect all types of genomic variants. In rare cases, false-negative or false-positive results may occur. The depth of coverage may be variable for some target regions; assay performance below the minimum acceptable criteria or for failed regions will be noted. Given these limitations, negative results do not rule out the diagnosis of a genetic disorder. If a specific clinical disorder is suspected, evaluation by alternative methods can be considered.
- There may be regions of genes that cannot be effectively evaluated by sequencing or deletion and duplication analysis as a result of technical limitations of the assay, including regions of homology, high guanine-cytosine (GC) content, and repetitive sequences. Confirmation of select reportable variants will be performed by alternate methodologies based on internal laboratory criteria.
- This test is validated to detect 95% of deletions up to 75 base pairs (bp) and insertions up to 47 bp. Deletions-insertions (delins) of 40 or more bp, including mobile element insertions, may be less reliably detected than smaller delins.

Deletion/Duplication Analysis:

- This analysis targets single and multi-exon deletions/duplications; however, in some instances, single exon resolution cannot be achieved due to isolated reduction in sequence coverage or inherent genomic complexity. Balanced structural rearrangements (such as translocations and inversions) may not be detected.
- This test is not designed to detect low levels of mosaicism or to differentiate between somatic and germline variants. If there is a possibility that any detected variant is somatic, additional testing may be necessary to clarify the significance of results.
- For detailed information regarding gene-specific performance and technical limitations, see Method Description or contact a laboratory genetic counselor.
- If the patient has had an allogeneic hematopoietic stem cell transplant or a recent blood transfusion, results may be inaccurate due to the presence of donor DNA. Call Mayo Clinic Laboratories for instructions for testing patients who have received a bone marrow transplant.

Reclassification of Variants:

- Currently, it is not standard practice for the laboratory to systematically review previously classified variants on a regular basis. The laboratory encourages healthcare providers to contact the laboratory at any time to learn how the classification of a particular variant may have changed over time. Due to broadening genetic knowledge, it is possible that the laboratory may discover new information of relevance to the patient. Should that occur, the laboratory may issue an amended report.

Variant Evaluation:

- Evaluation and categorization of variants are performed using published American College of Medical Genetics and Genomics and the Association for Molecular Pathology recommendations as a guideline.(6) Other gene-specific guidelines may also be considered. Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance. Variants classified as benign or likely benign are not reported.
- Multiple in silico evaluation tools may be used to assist in the interpretation of these results. The accuracy of predictions made by in silico evaluation tools is highly dependent upon the data available for a given gene, and periodic updates to these tools may cause predictions to change over time. Results from in silico evaluation tools should be interpreted with caution and professional clinical judgment.
- Rarely, incidental or secondary findings may implicate another predisposition or presence of active disease. These findings will be carefully reviewed to determine whether they will be reported.

CPT Code:

81405
81479
81479 (if appropriate for government payers)

Day(s) Performed: Varies **Report Available:** 28 to 42 days

Questions

Contact Connie Penz, Laboratory Resource Coordinator at 800-533-1710.