MAYO CLINIC LABORATORIES

NEW TEST

Notification Date: September 24, 2024
Effective Date: October 29, 2024

PKLR Full Gene Analysis, Varies

Test ID: PKLRZ

Genetics Information

This test utilizes next-generation sequencing to detect single nucleotide and copy number variants in PKLR. 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 pyruvate kinase deficiency.

Methodology:

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

Ordering Guidance:

Preliminary screening tests, such as complete blood cell count with peripheral smear, direct Coombs test, and pyruvate kinase enzyme activity assays (preferably as a part of EEEV1 / Red Blood Cell [RBC] Enzyme Evaluation, Blood) should be performed before ordering this test.

Targeted testing (also called site-specific or known variants testing) is available for variants identified in the PKLR gene. See FMTT / Familial Variant, Targeted Testing, Varies. To obtain more information about this testing option, call 800-533-1710.

Necessary Information

1. ***PKLR* Gene Sequencing Patient Information** is required. Testing may proceed without the patient information; however, it aids in providing a more thorough interpretation. Ordering healthcare professionals are strongly encouraged to complete the form and send it with the specimen.
2. Include healthcare professional's name and phone number with specimen.

Reference Values:

An interpretive report will be provided.

Specimen Requirements:

Patient Preparation: A previous bone marrow transplant from an allogenic donor will interfere with testing. For instructions for testing patients who have received a bone marrow transplant, call 800-533-1710.

Specimen Type: Whole blood
Preferred: Lavender top (EDTA)
Acceptable: Yellow top (ACD)
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

Specimen Stability Information:

Specimen Type	Temperature	Time
Varies	Varies	

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.
- If the patient has had an allogeneic hematopoietic stem cell transplant or a recent heterologous 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.
- For individuals who have received blood transfusions, the genotype usually reverts to that of the of the recipient within 6 weeks. For individuals who have received allogeneic blood or marrow transplantation, a pretransplant DNA specimen is recommended for testing. For patients who have been transfused within the preceding 6 weeks, the enzyme assay (PK1 / Pyruvate Kinase Enzyme Activity, Blood) will also be affected, so it is not an appropriate alternative test.
- Patients who have received an allogeneic blood or marrow transplant would be expected to convert to the PKLR status of the donor. However, if the patient's transplant was partially successful or if there is a relapse of an underlying hematologic malignancy, a mixture of donor and recipient genotypes may be seen on genetic analysis. The enzyme assay can be performed after transplantation; order PK1 / Pyruvate Kinase Enzyme Activity, Blood.

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 multiexon 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.

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 professionals 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.(3) 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 or intronic variants without known or suspected pathogenicity 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

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

Questions

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