Test Definition: PMPDD

PMP22 Gene, Large Deletion/Duplication Analysis, Varies

Overview

Useful For

Diagnosis of Charcot-Marie-Tooth type 1A or hereditary neuropathy with liability to pressure palsies

Genetics Test Information

This test assesses for large deletions and duplications only.

Testing Algorithm

For information see Hereditary Peripheral Neuropathy Diagnostic Algorithm

Special Instructions

- Informed Consent for Genetic Testing
- Hereditary Peripheral Neuropathy Diagnostic Algorithm
- Molecular Genetics: Neurology Patient Information
- Informed Consent for Genetic Testing (Spanish)

Method Name

Dosage Analysis by Polymerase Chain Reaction (PCR)/Multiplex Ligation-Dependent Probe Amplification (MLPA)

NY State Available

Yes

Specimen

Specimen Type

Varies

Specimen Required

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

Submit only 1 of the following specimens:

Specimen Type: Whole blood
Container/Tube:
Preferred: Lavender top (EDTA) or yellow top (ACD)
Acceptable: None
Specimen Volume: 3 mL
Collection Instructions:

1. Invert several times to mix blood.
2. Send whole blood specimen in original tube. **Do not aliquot**.
3. Whole blood collected postnatal from an umbilical cord is also acceptable. See Additional Information
Specimen Stability Information: Ambient (preferred) 4 days/Refrigerated 4 days/Frozen 4 days
Additional Information:
1. Specimens are preferred to be received within 4 days of collection. Extraction will be attempted for specimens received after 4 days, and DNA yield will be evaluated to determine if testing may proceed.
2. To ensure minimum volume and concentration of DNA is met, the requested volume must be submitted. Testing may be canceled if DNA requirements are inadequate.
3. For postnatal umbilical cord whole blood specimens, maternal cell contamination studies are recommended to ensure test results reflect that of the patient tested. A maternal blood specimen is required to complete maternal cell contamination studies. Order MATCC / Maternal Cell Contamination, Molecular Analysis, Varies on both the cord blood and maternal blood specimens under separate order numbers.

Specimen Type: Extracted DNA
Container/Tube:
Preferred: Screw Cap Micro Tube, 2mL with skirted conical base
Acceptable: Matrix tube, 1mL
Collection Instructions:
1. The preferred volume is at least 100 mcL at a concentration of 75 ng/mcL.
2. Include concentration and volume on tube.
Specimen Stability Information: Frozen (preferred) 1 year/Ambient/Refrigerated
Additional Information: DNA must be extracted in a CLIA-certified laboratory or equivalent and must be extracted from a specimen type listed as acceptable for this test (including applicable anticoagulants). Our laboratory has experience with Chemagic, Puregene, Autopure, MagnaPure, and EZ1 extraction platforms and cannot guarantee that all extraction methods are compatible with this test. If testing fails, one repeat will be attempted, and if unsuccessful, the test will be reported as failed and a charge will be applied. If applicable, specific gene regions that were unable to be interrogated due to DNA quality will be noted in the report.

Forms

1. **New York Clients-Informed consent is required.** Document on the request form or electronic order that a copy is on file. The following documents are available in Special Instructions:
-Informed Consent for Genetic Testing (T576)
-Informed Consent for Genetic Testing-Spanish (T576)
2. Molecular Genetics: Neurology Patient Information in Special Instructions
3. If not ordering electronically, complete, print, and send a Neurology Specialty Testing Client Test Request (T732) with the specimen.

Specimen Minimum Volume

See Specimen Required

Reject Due To

All specimens will be evaluated by Mayo Clinic Laboratories for test suitability.

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Varies		

Clinical & Interpretive

Clinical Information

This test is appropriate as a first-tier test for individuals with clinical features suggestive of Charcot-Marie-Tooth type 1A (CMT1A) and/or hereditary neuropathy with liability to pressure palsies (HNPP).

Charcot-Marie-Tooth type 1A is a dominantly inherited disease characterized by progressive distal muscle weakness and atrophy, sensory loss, and slow nerve conduction velocity starting early in life. Duplications of the *PMP22* gene are associated with CMT1A and are thought to account for 45%-50% of all CMT and up to 80% of demyelinating CMT.

Deletions of *PMP22* are associated with HNPP, a dominantly inherited disease resulting in peripheral neuronal demyelination. HNPP is characterized clinically by recurrent focal motor and sensory neuropathy in a single nerve that can manifest as numbness, muscular weakness, and atrophy. Deletions of *PMP22* are thought to account for up 80% of HNPP.

Reference Values

An interpretive report will be provided.

Interpretation

All detected alterations are evaluated according to American College of Medical Genetics and Genomics recommendations.(1) Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance.

Cautions

In addition to disease-related probes, the multiplex ligation-dependent probe amplification technique utilizes probes localized to other chromosomal regions as internal controls. In certain circumstances, these control probes may detect other diseases or conditions for which this test was not specifically intended. Results of the control probes are not normally reported. However, in cases where clinically relevant information is identified, the ordering physician will be informed of the result and provided with recommendations for any appropriate follow-up testing.

This test may not detect deletions/duplications present in very low levels of mosaicism.

Rare alterations (ie, polymorphisms) exist that could lead to false-negative or false-positive results. If results obtained do not match the clinical findings, additional testing should be considered.

Test results should be interpreted in the context of clinical findings, family history, and other laboratory data. Errors in our interpretation of results may occur if information given is inaccurate or incomplete.

Clinical Reference

1. Richards S, Aziz N, Bale S, et al. Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular

Pathology. Genet Med. 2015;17(5):405-424
2. van Paassen BW, van der Kooi AJ, van Spaendonck-Zwarts KY, Verhamme C, Baas F, de Visser M. PMP22 related neuropathies: Charcot-Marie-Tooth disease type 1A and Hereditary Neuropathy with liability to Pressure Palsies. Orphanet J Rare Dis. 2014;9:38
3. Li J, Parker B, Martyn C, Natarajan C, Guo J. The PMP22 gene and its related diseases. Mol Neurobiol. 2013;47(2):673-698
4. Bird TD. Charcot-Marie-Tooth Hereditary Neuropathy Overview. In: Adam MP, Feldman J, Mirzaa GM, et al, eds. GeneReviews [Internet]. University of Washington, Seattle; 1998. Updated August 1, 2024. Accessed January 16, 2025. Available at www.ncbi.nlm.nih.gov/books/NBK1358/
5. Chen L, Zhang H, Li C, Yang N, Wang J, Liang J. Literature review of clinical analysis of hereditary neuropathy with liability to pressure palsies. J Neurol. 2024;272(1):41. doi:10.1007/s00415-024-12839-7
6. Chrestian N. Hereditary Neuropathy with Liability to Pressure Palsies. In: Adam MP, Feldman J, Mirzaa GM, et al, eds. GeneReviews [Internet]. University of Washington, Seattle; 1998. Updated August 27, 2020. Accessed January 16, 2025. Available at www.ncbi.nlm.nih.gov/books/NBK1392/
7. Martinez Thompson JM, Klein CJ. Thirty Years Later, Case Closed: A Case of PMP22 Triplication From Anticipation. Mayo Clin Proc. 2016;91(5):687-688. doi:10.1016/j.mayocp.2015.12.019
8. Pisciotta C, Bertini A, Tramacere I, et al. Clinical spectrum and frequency of Charcot-Marie-Tooth disease in Italy: Data from the National CMT Registry. Eur J Neurol. 2023;30(8):2461-2470. doi:10.1111/ene.15860
9. Weterman MA, van Ruissen F, de Wissel M, et al. Copy number variation upstream of PMP22 in Charcot-Marie-Tooth disease. Eur J Hum Genet. 2010;18(4):421-428. doi:10.1038/ejhg.2009.186
10. Zhang F, Seeman P, Liu P, et al. Mechanisms for nonrecurrent genomic rearrangements associated with CMT1A or HNPP: rare CNVs as a cause for missing heritability. Am J Hum Genet. 2010;86(6):892-903. doi:10.1016/j.ajhg.2010.05.001

Performance

Method Description
Multiple ligation-dependent probe amplification (MLPA) is utilized to test for the presence of large deletions and duplications within the *PMP22* gene.(Unpublished Mayo method)

PDF Report
No

Day(s) Performed
Varies

Report Available
14 to 21 days

Specimen Retention Time
Whole blood: 28 days (if available); Extracted DNA: 3 months

Performing Laboratory Location

Mayo Clinic Laboratories - Rochester Main Campus

Fees & Codes

Fees

- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

Test Classification

This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. It has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

81324

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
PMPDD	PMP22 Gene, Deletion/Duplication	75384-8

Result ID	Test Result Name	Result LOINC® Value
113371	Result Summary	50397-9
113374	Result	75384-8
113375	Interpretation	69047-9
113376	Additional Information	48767-8
113377	Specimen	31208-2
113378	Source	31208-2
113379	Released By	18771-6