MAYO CLINIC LABORATORIES

Test Definition: PRSSZ

PRSS1 Gene, Full Gene Analysis, Varies

Overview

Useful For

Confirmation of suspected clinical diagnosis of hereditary pancreatitis (HP) in patients with chronic pancreatitis

Identification of familial *PRSSI* mutation to allow for predictive and diagnostic testing in family members

Genetics Test Information

Testing consists of full gene sequencing of the *PRSS1* gene. Includes the following commonly observed mutations: R122H, N29I, and A16V.

Special Instructions

- Molecular Genetics: Congenital Inherited Diseases Patient Information
- Informed Consent for Genetic Testing
- Informed Consent for Genetic Testing (Spanish)

Highlights

-Full sequencing of the *PRSS1* gene includes R122H, N29I, and A16V mutations
-Mutations in the *PRSS1* gene are the most common cause of hereditary pancreatitis
-Useful for diagnostic confirmation of hereditary pancreatitis

Method Name

Polymerase Chain Reaction (PCR) Amplification followed by DNA sequencing

NY State Available

Yes

Specimen

Specimen Type

Varies

Shipping Instructions

Specimen preferred to arrive within 96 hours of draw.

Specimen Required

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.
Specimen Type: Whole blood
Container/Tube:
Preferred: Lavender top (EDTA) or yellow top (ACD)

Acceptable: Any anticoagulant
Specimen Volume: 3 mL
Collection Instructions:
1. Invert several times to mix blood.
2. Send specimen in original tube.
Specimen Stability Information: Ambient (preferred)/Refrigerated

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 (T826)
2. Molecular Genetics: Congenital Inherited Diseases Patient Information (T521) in Special Instructions

Specimen Minimum Volume

1 mL

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	Ambient (preferred)		
	Refrigerated		
	Frozen		

Clinical & Interpretive

Clinical Information

Hereditary pancreatitis (HP) is a rare autosomal dominant disorder associated with approximately 80% penetrance. HP is characterized by early onset acute pancreatitis during childhood or early adolescence. The acute pancreatitis in these patients generally progresses to chronic pancreatitis by adulthood and can eventually lead to both exocrine and endocrine pancreatic insufficiency. Patients with HP are also at an increased risk for developing pancreatic cancer. Studies have estimated the lifetime risk of developing pancreatic cancer to be as high as 40%.

Mutations in the protease serine 1 or cationic trypsinogen (*PRSS1*) gene are a common cause of HP. It has been reported that as many as 80% of patients with symptomatic hereditary pancreatitis have a causative *PRSS1* mutation. HP cannot be clinically distinguished from other forms of pancreatitis. However, *PRSS1* mutations are generally restricted to individuals with a family history of pancreatitis. *PRSS1* mutations are infrequently found in patients with alcohol-induced and tropical pancreatitis.

Although several mutations have been identified, the R122H, N29I and A16V mutations are the most common disease-causing mutations associated with HP. Data suggest that the R122H mutation results in more severe disease and earlier onset of symptoms than the A16V mutation. Although these 3 alterations account for >90% of mutations

detected in the cationic trypsinogen gene, the inability to identify mutations in approximately 20% of families with HP suggests the involvement of other loci or unidentified mutations in the cationic trypsinogen gene.

Mutations in other genes, such as *SPINK1, CFTR* and *CTRC* have been associated with hereditary and familial pancreatitis. Abnormalities in these genes are not detected by this assay. However, genetic testing for these genes simultaneously, including *PRSS1*, is available by ordering HPPAN / Hereditary Pancreatitis Panel.

Reference Values

An interpretive report will be provided.

Interpretation

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

Cautions

Some individuals who have a diagnosis of hereditary pancreatitis and/or involvement of *PRSS1* may have a mutation that is not identified by this method (eg, large genomic deletions or duplications, promoter mutations, deep intronic mutations). The absence of a mutation, therefore, does not eliminate the possibility of a diagnosis of hereditary pancreatitis. For predictive testing of asymptomatic individuals, it is important to first document the presence of an *PRSS1* gene mutation in an affected family member.

In some cases, DNA alterations of undetermined significance may be identified.

Rare 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 May;17(5):405-424
2. Teich N, Mossner J: Hereditary chronic pancreatitis. Best Pract Res Clin Gastroenterol 2008;22(1):115-130
3. Rebours V, Levy P, Ruszniewski P: An overview of hereditary pancreatitis. Dig Liver Dis 2012;44(1):8-15
4. Ellis I: Genetic counseling for hereditary pancreatitis-the role of molecular genetics testing for the cationic trypsinogen gene, cystic fibrosis and serine protease inhibitor Kazal type 1. Gastroenterol Clin North Am 2004;33:839-854
5. Solomon S, Whitcomb DC, LaRusch J. *PRSS1*-Related Hereditary Pancreatitis. In: GeneReviews. Edited by RA Pagon, MP Adam, HH Ardinger HH, et al: University of Washington, Seattle. 1993-2014. 2012 Mar 1. Available at www.ncbi.nlm.nih.gov/books/NBK84399

Performance

Method Description

Bidirectional sequence analysis is used to test for the presence of a mutation in all coding regions and intron/exon boundaries of the *PRSS1* gene.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed

Varies

Report Available

14 to 20 days

Specimen Retention Time

Whole Blood: 2 weeks (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

81404-PRSS1 (protease, serine, 1 [trypsin 1]) (eg, hereditary pancreatitis), full gene sequence

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
PRSSZ	PRSS1 Gene, Full Gene Analysis	94215-1

Result ID	Test Result Name	Result LOINC® Value
52464	Result Summary	50397-9
52465	Result	82939-0
52466	Interpretation	69047-9
52467	Additional Information	48767-8
52468	Specimen	31208-2

52469	Source	31208-2
52470	Released By	18771-6