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.

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

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

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

<table>
<thead>
<tr>
<th>Specimen Type</th>
<th>Temperature</th>
<th>Time</th>
<th>Special Container</th>
</tr>
</thead>
<tbody>
<tr>
<td>Varies</td>
<td>Ambient (preferred)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Frozen</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Refrigerated</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Clinical and 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


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) and Time(s) Test Performed

Performed weekly; Varies

Analytic Time

14 days

Maximum Laboratory Time

20 days

Specimen Retention Time

Whole Blood: 2 weeks (if available) Extracted DNA: 3 months

Performing Laboratory Location

Rochester

Fees and 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 Regional Manager. 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. This test has not been cleared or approved by the U.S. Food and Drug Administration.

CPT Code Information

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

LOINC® Information

<table>
<thead>
<tr>
<th>Test ID</th>
<th>Test Order Name</th>
<th>Order LOINC Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRSSZ</td>
<td>PRSS1 Gene, Full Gene Analysis</td>
<td>94215-1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Result ID</th>
<th>Test Result Name</th>
<th>Result LOINC Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>52464</td>
<td>Result Summary</td>
<td>50397-9</td>
</tr>
<tr>
<td>52465</td>
<td>Result</td>
<td>82939-0</td>
</tr>
<tr>
<td>52466</td>
<td>Interpretation</td>
<td>69047-9</td>
</tr>
<tr>
<td>52467</td>
<td>Additional Information</td>
<td>48767-8</td>
</tr>
<tr>
<td>Result ID</td>
<td>Test Result Name</td>
<td>Result LOINC Value</td>
</tr>
<tr>
<td>-----------</td>
<td>------------------</td>
<td>-------------------</td>
</tr>
<tr>
<td>52468</td>
<td>Specimen</td>
<td>31208-2</td>
</tr>
<tr>
<td>52469</td>
<td>Source</td>
<td>31208-2</td>
</tr>
<tr>
<td>52470</td>
<td>Released By</td>
<td>18771-6</td>
</tr>
</tbody>
</table>