

Overview

Useful For

Confirmation of suspected clinical diagnosis of familial or hereditary pancreatitis in patients with chronic pancreatitis

Identification of gene variants contributing to pancreatitis in an individual or family

Identification of gene variants to allow for predictive and diagnostic testing in family members

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
CULAF	Amniotic Fluid Culture/Genetic Test	Yes	No
_STR1	Comp Analysis using STR (Bill only)	No, (Bill only)	No
_STR2	Add'l comp analysis w/STR (Bill Only)	No, (Bill only)	No
CULFB	Fibroblast Culture for Genetic Test	Yes	No
MATCC	Maternal Cell Contamination, B	Yes	No

Genetics Test Information

This test utilizes next-generation sequencing to detect single nucleotide and copy number variants in 9 genes associated with an increased risk for pancreatitis: *CASR*, *CEL*, *CFTR*, *CLDN2*, *CPA1*, *CTRC*, *PRSS1*, *SPINK1*, *TRPV6*. See [Targeted Genes and Methodology Details for Expanded Pancreatitis Gene Panel](#) and Method Description for additional details.

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

Testing Algorithm

Skin biopsy:

For skin biopsy or cultured fibroblast specimens, fibroblast culture will be performed at an additional charge. If viable cells are not obtained, the client will be notified.

Cord blood:

For cord blood specimens that have an accompanying maternal blood specimen, maternal cell contamination studies will be performed at an additional charge.

Special Instructions

- [Informed Consent for Genetic Testing](#)
- [Blood Spot Collection Card-Spanish Instructions](#)

- [Blood Spot Collection Card-Chinese Instructions](#)
- [Informed Consent for Genetic Testing \(Spanish\)](#)
- [Blood Spot Collection Instructions](#)
- [Targeted Genes and Methodology Details for Expanded Pancreatitis Gene Panel](#)

Method Name

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

NY State Available

Yes

Specimen**Specimen Type**

Varies

Ordering Guidance

Patients who have had a previous bone marrow transplant from an allogenic donor should not have testing performed on blood, bone marrow, or saliva because any results generated will reflect the genome of the donor rather than the recipient. Testing on patients who have an active hematologic malignancy or hematologic disorder with clonal proliferation may identify both somatic mutations and germline variants, which may result in test failure or necessitate follow-up testing to determine whether the detected variant is germline or somatic. For these patients, testing a skin biopsy or cultured fibroblasts is recommended. For instructions for testing patients who have received a bone marrow transplant or have an active hematologic disorder, call 800-533-1710. For more information see Cautions.

This test does not analyze genes associated with hereditary pancreatic cancer risk. For genetic testing for pancreatic cancer risk, see PANCP / Hereditary Pancreatic Cancer Panel, Varies.

Customization of this panel and single gene analysis for any gene present on this panel are available. For more information see CGPH / Custom Gene Panel, Hereditary, Next-Generation Sequencing, Varies. To modify this panel via CGPH, use the Inborn Errors of Immunity/Bone Marrow Failure/Telomeropathy/Pulmonary Fibrosis/Very Early Onset IBD/Pancreatitis disease state for step 1 on the [Custom Gene Ordering Tool](#).

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

Specimen Required

Patient Preparation: A previous hematopoietic stem cell transplant from an allogenic donor will interfere with testing. For information about 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:** 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.**
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 are 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: Skin biopsy**Supplies:** Fibroblast Biopsy Transport Media (T115)**Container/Tube:** Sterile container with any standard cell culture media (eg, minimal essential media, RPMI 1640). The solution should be supplemented with 1% penicillin and streptomycin.**Specimen Volume:** 4-mm Punch**Specimen Stability Information:** Ambient (preferred) <24 hours/Refrigerated <24 hours**Additional Information:**

1. Specimens are preferred to be received within 24 hours of collection. Culture and extraction will be attempted for specimens received after 24 hours and will be evaluated to determine if testing may proceed.
2. A separate culture charge will be assessed under CULFB / Fibroblast Culture for Biochemical or Molecular Testing. An additional 3 to 4 weeks are required to culture fibroblasts before genetic testing can occur.

Specimen Type: Cultured fibroblasts**Source:** Skin or tissue**Container/Tube:** T-25 flask**Specimen Volume:** 2 Flasks**Collection Instructions:** Submit confluent cultured fibroblast cells from a skin or tissue biopsy. Cultured cells from a prenatal specimen will not be accepted.**Specimen Stability Information:** Ambient (preferred) <24 hours/Refrigerated <24 hours**Additional Information:**

1. Specimens are preferred to be received within 24 hours of collection. Culture and extraction will be attempted for specimens received after 24 hours and will be evaluated to determine if testing may proceed.
2. A separate culture charge will be assessed under CULFB / Fibroblast Culture for Biochemical or Molecular Testing. An additional 3 to 4 weeks are required to culture fibroblasts before genetic testing can occur.

Specimen Type: Extracted DNA

Container/Tube:

Preferred: Screw Cap Micro Tube, 2 mL with skirted conical base

Acceptable: Matrix tube, 1 mL

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.

Specimen Type: Blood spot

Supplies: Card-Blood Spot Collection (Filter Paper) (T493)

Container/Tube:

Preferred: Collection card (Whatman Protein Saver 903 Paper)

Acceptable: PerkinElmer 226 filter paper or blood spot collection card

Specimen Volume: 2 to 5 Blood spots

Collection Instructions:

1. An alternative blood collection option for a patient older than 1 year is a fingerstick. For detailed instructions, see [How to Collect a Dried Blood Spot Sample](#).
2. Let blood dry on the filter paper at ambient temperature in a horizontal position for a minimum of 3 hours.
3. Do not expose specimen to heat or direct sunlight.
4. Do not stack wet specimens.
5. Keep specimen dry

Specimen Stability Information: Ambient (preferred)/Refrigerated

Additional Information:

1. Blood spot specimens are acceptable but not recommended. Multiple extractions will be required to obtain sufficient yield for supplemental analysis, and there is significant risk for test failure due to insufficient DNA.
2. Due to lower concentration of DNA yielded from blood spot, some aspects of the test may not perform as well as DNA extracted from a whole blood sample. When applicable, specific gene regions that were unable to be interrogated will be noted in the report. Alternatively, additional specimen may be required to complete testing.
3. For collection instructions, see [Blood Spot Collection Instructions](#)
4. For collection instructions in Spanish, see [Blood Spot Collection Card-Spanish Instructions](#) (T777)
5. For collection instructions in Chinese, see [Blood Spot Collection Card-Chinese Instructions](#) (T800)

Specimen Type: Saliva

Patient Preparation: Patient should not eat, drink, smoke, or chew gum 30 minutes prior to collection.

Supplies:

DNA Saliva Kit High Yield (T1007)

Saliva Swab Collection Kit (T786)

Container/Tube:

Preferred: High-yield DNA saliva kit

Acceptable: Saliva swab

Specimen Volume: 1 Tube if using T1007 or 2 swabs if using T786

Collection Instructions: Collect and send specimen per kit instructions.

Specimen Stability Information: Ambient (preferred) 30 days/Refrigerated 30 days

Additional Information: Saliva specimens are acceptable but not recommended. Due to lower quantity/quality of DNA yielded from saliva, some aspects of the test may not perform as well as DNA extracted from a whole blood sample. When applicable, specific gene regions that were unable to be interrogated will be noted in the report. Alternatively, additional specimen may be required to complete testing.

Forms

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:

-[Informed Consent for Genetic Testing](#) (T576)

-[Informed Consent for Genetic Testing \(Spanish\)](#) (T826)

Specimen Minimum Volume

See Specimen Required

Reject Due To

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

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Varies		

Clinical & Interpretive**Clinical Information**

Hereditary pancreatitis (HP) is defined as 2 or more individuals in a family affected with pancreatitis involving at least 2 generations.(1) Variants in several genes, including *PRSS1*, *CFTR*, *CTRC*, and *SPINK1* have demonstrated genetic susceptibility to chronic pancreatitis. Disease susceptibility may be monogenic, as is the case with *PRSS1*, digenic or multigenic, and multifactorial in which multiple genes and environmental factors play a role in disease expression. Additional genes - *CASR*, *CEL*, *CPA1*, *CLDN2* and *TRPV6*, are also associated with an increased risk for pancreatitis, including early-onset chronic pancreatitis or progression from recurrent acute to chronic pancreatitis.

***PRSS1*:**

The most common monogenic cause of HP is the presence of a variant in the cationic trypsinogen (*PRSS1*) gene. Variants in the *PRSS1* gene are inherited in an autosomal dominant manner. It has been reported that as many as 80% of patients with symptomatic hereditary pancreatitis have a causative *PRSS1* variant.(1) HP cannot be clinically distinguished from other forms of pancreatitis. However, *PRSS1* variants are generally restricted to individuals with a family history of pancreatitis and are infrequently found in patients with alcohol-induced pancreatitis. Although several variants have been identified, the p.R122H, p.N29I, and p.A16V variants are the most common disease-causing variants in *PRSS1*.

associated with HP.(2) 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%.(3)

SPINK1:

Biallelic variants in the *SPINK1* gene have been associated with increased susceptibility to chronic pancreatitis especially in families without *PRSS1* variants; however, it is unknown if biallelic variants alone are sufficient to cause chronic pancreatitis. Additionally, heterozygous *SPINK1* variants appear to modify disease severity when observed in combination with variants in other genes.(1,2,4) Unlike *PRSS1* variants, *SPINK1* variants have been associated with alcohol-induced pancreatitis.(4)

CFTR:

Pancreatitis is a known manifestation of an atypical *CFTR*-related disorder, which results from biallelic disease-causing variants in the *CFTR* gene. However, *CFTR* variants can also co-occur with variants in *CTRC*, *SPINK1*, or *CASR* to confer pancreatitis disease susceptibility.(1-4) When observed in the context of a *SPINK1* variant, for example, heterozygous variants in *CFTR* are associated with a 2- to 5-fold increased risk for pancreatitis as compared to the general population.(4)

CTRC:

Variants in *CTRC* have been observed in individuals with chronic pancreatitis in association with other risk factors such as variants in *CFTR* or *SPINK1* or specific environmental risk factors. Thus, chronic pancreatitis may be attributable to the presence of *CTRC* variants in the context of other risk factors as opposed to *CTRC* variants alone.(1)

CASR:

Although disease-causing variants in *CASR* are typically associated with familial hypocalciuric hypercalcemia (FHH), some loss-of-function variants have been found to infer an increased risk for pancreatitis in individuals who also have variants in *PRSS1*, *SPINK1*, or *CFTR*. Gain-of-function variants in *CASR* have also been reported to be risk alleles for alcohol-induced pancreatitis.(3)

CEL:

Variants in *CEL* have been found to be associated with maturity-onset diabetes of the young (MODY8), which includes pancreatic atrophy secondary to exocrine pancreatic insufficiency. The exocrine pancreatic insufficiency may lead to chronic pancreatitis, suggesting that variants in *CEL* are associated with an increased risk for pancreatitis and are implicated in less than 1% of individuals with chronic pancreatitis.(1,5)

CPA1:

Monoallelic variants in the *CPA1* gene have been associated with an increased risk for early onset, nonalcoholic chronic pancreatitis. Specifically, risk allele variants have been more commonly observed in European populations and account for approximately 9.7% of cases of chronic pancreatitis in children younger than 10 years and approximately 1% of adult individuals. Some of these affected individuals have also been found to have a disease-causing variant in another hereditary pancreatitis gene such as *PRSS1*, *SPINK1*, *CFTR* and *CTRC*, although the majority of reported cases have not been found to have a second variant.(3,6,7)

CLDN2:

CLDN2 variants have been observed in individuals with chronic pancreatitis in association with other risk factors such as alcohol consumption. The gene is located on the X chromosome and therefore the risk for pancreatitis in association

with other risk factors is increased in hemizygous male patients and homozygous female patients. Variants have been reported to be associated with a mild-to-moderate risk of pancreatitis progression from recurrent acute pancreatitis to chronic pancreatitis.(3,7,8)

TRPV6:

Variants in the *TRPV6* gene have been found to increase the risk of early-onset chronic pancreatitis (individuals younger than 20 years). Previous studies have shown that loss-of-function variants are observed more frequently in a cohort of individuals with nonalcoholic chronic pancreatitis as compared to the unaffected control group. The majority of these individuals had either two disease-causing variants or were homozygous for a *TRPV6* variant. They also had other underlying factors that increased their risk for chronic pancreatitis, suggesting that *TRPV6* is a susceptibility gene.(3,9,10)

Reference Values

An interpretive report will be provided.

Interpretation

All detected variants are evaluated according to American College of Medical Genetics and Genomics recommendations.(11) Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance.

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 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.

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 mutations 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.

Genes may be added or removed based on updated clinical relevance. For the most up to date list of genes included in this test and 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 non-leukocyte reduced blood transfusion, results of tests performed on blood, bone marrow, or saliva specimens may be inaccurate due to the presence of donor DNA. Test orders for blood, bone marrow, or saliva will be canceled by the laboratory if there is a history of an allogeneic hematopoietic stem cell transplant. Similarly, blood, bone marrow, and saliva results will be impacted by presence of active hematologic malignancy or hematologic disorder with clonal proliferation. Call Mayo Clinic Laboratories for instructions for testing a skin biopsy or fibroblast culture for patients who have received a bone marrow transplant or have an active hematologic disorder.

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.(11) 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.

Clinical Reference

1. Raphael KL, Willingham FF. Hereditary pancreatitis: current perspectives. *Clin Exp Gastroenterol*. 2016;9:197-207

2. Suzuki M, Minowa K, Nakano S, Isayama H, Shimizu T. Genetic abnormalities in pancreatitis: An update on diagnosis, clinical features, and treatment. *Diagnostics (Basel)*. 2020;11(1):31
3. Shelton C, LaRusch J, Whitcomb DC. Pancreatitis overview. In: Adam MP, Feldman J, Mirzaa GM, et al. eds. *GeneReviews* [Internet]. University of Washington, Seattle; 2014. Updated July 2, 2020. Accessed March 31, 2025. Available at www.ncbi.nlm.nih.gov/books/NBK190101/
4. Hasan A, Moscoso DI, Kastrinos F. The role of genetics in pancreatitis. *Gastrointest Endosc Clin N Am*. 2018;28(4):587-603
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7. Khan E, Chakrabarty S, Shariff S, Bardhan M. Genetics and genomics of chronic pancreatitis with a focus on disease biology and molecular pathogenesis. *Glob Med Genet*. 2023;10(4):324-334. Published 2023 Nov 22. doi:10.1055/s-0043-1776981
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9. Dermine S, Masson E, Girodon-Boulandet E, et al. Diagnostic yield of repeat genetic testing in idiopathic chronic pancreatitis. *Clin Res Hepatol Gastroenterol*. 2024;48(6):102346. doi:10.1016/j.clinre.2024.102346
10. Masamune A, Kotani H, Sorgel FL, et al. Variants that affect function of calcium channel TRPV6 are associated with early-onset chronic pancreatitis. *Gastroenterology*. 2020;158(6):1626-1641.e8. doi:10.1053/j.gastro.2020.01.005
11. 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

Performance

Method Description

Next-generation sequencing (NGS) and/or Sanger sequencing is performed to test for the presence of variants in coding regions and intron/exon boundaries of the genes analyzed, as well as some other regions that have known disease-causing variants. The human genome reference GRCh37/hg19 build was used for sequence read alignment. At least 99% of the bases are covered at a read depth over 30X. Sensitivity is estimated at above 99% for single nucleotide variants, above 94% for deletions/insertions (delins) less than 40 base pairs (bp), above 95% for deletions up to 75 bp and insertions up to 47 bp. NGS and/or a polymerase chain reaction-based quantitative method is performed to test for the presence of deletions and duplications in the genes analyzed. Confirmation of select reportable variants may be performed by alternate methodologies based on internal laboratory criteria.

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. See [Targeted Genes and Methodology Details for Expanded Pancreatitis Gene Panel](#) for details regarding the targeted genes analyzed for each test and specific gene regions not routinely covered.(Unpublished Mayo method).

Genes analyzed: *CASR*, *CEL*, *CFTR*, *CLDN2*, *CPA1*, *CTRC*, *PRSS1*, *SPINK1*, *TRPV6*

PDF Report

Supplemental

Day(s) Performed

Varies

Report Available

28 to 42 days

Specimen Retention Time

Whole blood: 28 days (if available); Saliva: 30 days (if available); Extracted DNA: 3 months; Blood spots: 1 year (if available)

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

81223

81404 x2

81405 x2

81479

81479 (if appropriate for government payers)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
PANGP	Expanded Pancreatitis Gene Panel	106782-6

Result ID	Test Result Name	Result LOINC® Value
621966	Test Description	62364-5
621967	Specimen	31208-2
621968	Source	31208-2
621969	Result Summary	50397-9

621970	Result	82939-0
621971	Interpretation	69047-9
621972	Additional Results	82939-0
621973	Resources	99622-3
621974	Additional Information	48767-8
621975	Method	85069-3
621976	Genes Analyzed	82939-0
621977	Disclaimer	62364-5
621978	Released By	18771-6