

Pancreatitis Panel

Pancreatitis is a relatively common disorder with multiple etiologies that causes inflammation in the pancreas. Acute pancreatitis (AP) is a result of sudden inflammation, and patients may present with increased pancreatic enzyme concentrations. Chronic pancreatitis (CP) is a syndrome of progressive inflammation that may lead to permanent damage to pancreatic structure and function. Genetic testing can be utilized to determine a genetic cause of idiopathic or hereditary AP or CP and/or to assess risk of disease in family members.

Disease Overview

Incidence/Prevalence

- Chronic pancreatitis
 - Incidence: ~4-12/100,000 per year¹
 - Prevalence: ~37-42/100,000¹

Symptoms and Etiology

	Symptoms/Presentation	Etiologies
AP	<p>Sudden onset of pain in the upper abdomen, nausea and vomiting, orthostatic hypotension, confusion, and shortness of breath</p> <p>Duration is <6 months</p> <p>Increased concentrations of pancreatic enzymes (ie, lipase, amylase)</p> <p>Characteristic findings of pancreatic inflammation on abdominal imaging</p>	<p>Most acute pancreatitis is caused by gallstones, alcohol use, hypertriglyceridemia, or is idiopathic</p>
RAP	<p>>1 episode of acute pancreatitis, separated by ≥3 months</p>	<p>Nonhereditary RAP and CP are typically associated with ≥1 risk factor, divided into the following TIGAR-O categories:</p>
CP	<p>Abdominal pain, nausea, vomiting, weight loss, diarrhea, oily stools</p> <p>Duration is >6 months</p> <p>At advanced stages, pain often decreases, and malabsorption and diabetes may occur</p> <p>Patients with CP have an increased risk of pancreatic cancer after age 50</p>	<ul style="list-style-type: none"> • Toxic-metabolic • Idiopathic • Autoimmune • Recurrent or severe acute pancreatitis • Obstructive <p>44-65% of CP cases are alcohol-related¹; alcohol use and smoking are independent risk factors but together have a multiplicative effect on risk¹</p>

RAP, recurrent acute pancreatitis

Source: Conwell, 2014¹; Shelton, 2020²; Shelton, 2019³

Tests to Consider

[Pancreatitis Panel \(CFTR, CTRC, PRSS1, SPINK1\), Sequencing 3004788](#)

Method: Massively Parallel Sequencing/Sequencing

- Use for individuals with a personal history of idiopathic pancreatitis
- Use to detect sequence variants in the *CFTR*, *CTRC*, *PRSS1*, and *SPINK1* genes

Related Tests

[Familial Mutation, Targeted Sequencing 2001961](#)

Method: Polymerase Chain Reaction/Sequencing

- Recommended test for a known familial sequence variant previously identified in a family member
- A copy of the family member's test result documenting the familial variant is required.

Genetics

Genes

- *CFTR* (NM_000492), *CTRC* (NM_007272), *PRSS1* (NM_002769), *SPINK1* (NM_003122)
 - 90% of individuals affected with *PRSS1*-related hereditary pancreatitis have the *PRSS1* sequence variant R122H (p.Arg122His)⁴
 - Other genes (*CLDN2*, *CPA1*, *CASR*, *CEL*, *TRPV6*) have been reported to be associated with CP but are not currently assessed at ARUP Laboratories.²

Inheritance

- *PRSS1*: autosomal dominant with gain-of-function variants
- *CFTR*, *CTRC*, *SPINK1*: autosomal recessive/digenic

Test Interpretation

Methodology

This test is performed using the following sequence of steps:

- Selected genomic regions, primarily coding exons and exon-intron boundaries, from the targeted genes are isolated from extracted genomic DNA using a probe-based hybrid capture enrichment workflow.
- Enriched DNA is sequenced by massively parallel sequencing (MPS; also known as next generation sequencing [NGS]) followed by paired-end read alignment and variant calling using a custom bioinformatics pipeline.
- Sanger sequencing is performed as necessary to fill in regions of low coverage or known low quality, and in certain other situations to confirm variant calls.

Sensitivity/Specificity

Clinical Sensitivity

CFTR, *CTRC*, *PRSS1*, and *SPINK1* pathogenic variants which contribute to or explain idiopathic pancreatitis: ~48%⁵

Analytical Sensitivity

Variant Class	Analytical Sensitivity (PPA) Estimate ^a (%) and 95% Credibility Region (%)	Analytical Specificity (NPA) (%)
SNVs	>99 (96.9-99.4)	>99.9
Deletions 1-10 bp ^b	93.8 (84.3-98.2)	>99.9
Insertions 1-10 bp ^b	94.8 (86.8-98.5)	>99.9

^aGenes included on this test are a subset of a larger methods-based validation from which the PPA values are derived.

^bVariants greater than 10 bp may be detected, but the analytical sensitivity may be reduced.

bp, base pairs; NPA, negative percent agreement; PPA, positive percent agreement; SNVs, single nucleotide variants

Results

Result	Interpretation
--------	----------------

Result	Interpretation
Positive	One of the following: <ul style="list-style-type: none"> • One <i>PRSS1</i> pathogenic variant or copy number variant detected • Two pathogenic <i>CFTR</i>, <i>SPINK1</i>, or <i>CTRC</i> gene variants detected • Two pathogenic variants detected, one in each of two different genes (digenic inheritance) • One pathogenic variant detected in <i>CFTR</i>, <i>CTRC</i>, or <i>SPINK1</i> genes (may increase the risk for pancreatitis but is not causative)
Negative	No pathogenic variants detected in any of the genes; reduces the risk for hereditary pancreatitis but genetic etiology is not excluded
Uncertain	Variant(s) of uncertain clinical significance detected; may be disease-causing or benign

Limitations

- A negative result does not exclude a genetic etiology for pancreatitis.
- Diagnostic errors can occur due to rare sequence variations.
- Interpretation of this test result may be impacted if this patient has had an allogeneic stem cell transplantation.
- The following will not be evaluated:
 - Variants outside the coding regions and intron-exon boundaries of targeted genes
 - Regulatory region and deep intronic variants other than 5T (IVS8), c.1680-886A>G (c.1679+1.6kbA>G), and c.3718-2477C>T in the *CFTR* gene
 - Large deletions/duplications in any of the tested genes
 - Variants in currently unknown genes that may be associated with pancreatitis
- The following may not be detected:
 - Deletions/duplications/insertions of any size by massively parallel sequencing
 - Noncoding transcripts
 - Low-level somatic variants
 - Certain other variants due to technical limitations in the presence of pseudogenes or repetitive/homologous regions

References

1. Conwell DL, Lee LS, Yadav D, et al. [American Pancreatic Association practice guidelines in chronic pancreatitis: evidence-based report on diagnostic guidelines](#). *Pancreas*. 2014;43(8):1143-1162.
2. Shelton C, LaRusch J, Whitcomb DC. [Pancreatitis overview](#). In: Adam MP, Ardinger HH, Pagon RA, et al, eds. GeneReviews. University of Washington, Seattle; 1993-2022. [Updated: Jul 2020; Accessed: Feb 2022]
3. Shelton C, Solomon S, LaRusch J, et al. [PRSS1-related hereditary pancreatitis](#). In: Adam MP, Ardinger HH, Pagon RA, et al, eds. GeneReviews, University of Washington, Seattle; 1993-2020. [Last Update: Apr 2019; Accessed: Feb 2022]
4. Rebours V, Boutron-Ruault MC, Schnee M, et al. [The natural history of hereditary pancreatitis: a national series](#). *Gut*. 2009;58(1):97-103.
5. Masson E, Chen JM, Audrézet MP, et al. [A conservative assessment of the major genetic causes of idiopathic chronic pancreatitis: data from a comprehensive analysis of PRSS1, SPINK1, CTRC and CFTR genes in 253 young French patients](#). *PLoS One*. 2013;8(8):e73522.

Additional Resources

- Gupte A, Goede D, Tuite R, et al. [Chronic pancreatitis](#). *BMJ*. 2018;361:k2126.
- LaRusch J, Whitcomb DC. [Genetics of pancreatitis](#). *Curr Opin Gastroenterol*. 2011;27(5):467-474.
- Yadav D, Lowenfels AB. [The epidemiology of pancreatitis and pancreatic cancer](#). *Gastroenterology*. 2013;144(6):1252-1261.

Related Information

[Acute Pancreatitis](#)

Chronic Pancreatitis

ARUP Laboratories is a nonprofit enterprise of the University of Utah and its Department of Pathology, 500 Chipeta Way, Salt Lake City, UT 84108
(800) 522-2787 | (801) 583-2787 | aruplab.com | arupconsult.com
Content Review February 2022 | Last Update August 2022

© 2022 ARUP Laboratories. All Rights Reserved.

Client Services - (800) 522-2787