Pancreatitis Panel

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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: Approximately 4-12/100,000 per year[1]
  - Prevalence: Approximately 37-42/100,000[1]

Symptoms and Etiology

	Symptoms/Presentation	Etiologies
AP	Sudden onset of pain in the upper abdomen, nausea and vomiting, orthostatic hypotension, confusion, and shortness of breath Duration is <6 months Increased concentrations of pancreatic enzymes (ie, lipase, amylase) Characteristic findings of pancreatic inflammation on abdominal imaging	Most acute pancreatitis is caused by gallstones, alcohol use, hypertriglyceridemia, or is idiopathic
RAP	>1 episode of acute pancreatitis, separated by ≥3 months	Nonhereditary RAP and CP are typically associated with ≥1 risk factor, divided into the following TIGAR-O categories: • Toxic-metabolic • Idiopathic • Autoimmune • Recurrent or severe acute pancreatitis • Obstructive 44-65% of CP cases are alcohol-related[1]; alcohol use and smoking are independent risk factors but together have a multiplicative effect on risk[1]
CP	Abdominal pain, nausea, vomiting, weight loss, diarrhea, oily stools Duration is >6 months At advanced stages, pain often decreases, and malabsorption and diabetes may occur Patients with CP have an increased risk of pancreatic cancer after age 50	

RAP, recurrent acute pancreatitis

Source: Conwell, 2014[1]; Shelton, 2020[2]; Shelton, 2019[3]

Featured ARUP Testing

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

If a familial sequence variant has been previously identified, targeted sequencing for that variant may be appropriate; refer to the Laboratory Test Directory for additional information.

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]

Analytic Sensitivity

Variant Class	Analytic Sensitivity (PPA) Estimate[a] (%) and 95% Credibility Region (%)	Analytic 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

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

[b]Variants 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
Positive	One of the following: • One *PRSS1* pathogenic variant or copy number variant detected • Two pathogenic *CFTR*, *SPINK1*, or *CTRC* gene variants detected • Two pathogenic variants detected, one in each of two different genes (digenic inheritance)

Result	Interpretation
	• One pathogenic variant detected in *CFTR*, *CTRC*, or *SPINK1* 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.

Related Information

Acute Pancreatitis
Chronic Pancreatitis

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