Test Definition: APCZ

APC Gene, Full Gene Analysis

Overview

Useful For

Confirmation of familial adenomatous polyposis (FAP) diagnosis for patients with clinical features

Highlights

APC gene sequence analysis for 5' UTR and exons 1 through 15.

Array comparative genomic hybridization (aCGH) is used to test for the presence of large deletions and duplications encompassing the coding regions as well as promoter 1A and 1B of the *APC* gene.

Additional Tests

Test ID	Reporting Name	Available Separately	Always Performed
COLAB	Hereditary Colon Cancer CGH Array	Yes, (order FMTT)	Yes

Testing Algorithm

When this test is ordered, comparative genomic hybridization will always be performed at an additional charge.

See Colonic Polyposis Syndromes Testing Algorithm in Special Instructions.

Special Instructions

- Molecular Genetics: Inherited Cancer Syndromes Patient Information
- Informed Consent for Genetic Testing
- Colonic Polyposis Syndromes Testing Algorithm
- Informed Consent for Genetic Testing (Spanish)

Method Name

Custom Sequence Capture and Targeted Next-Generation Sequencing

COLAB: Array Comparative Genomic Hybridization (aCGH)

NY State Available

Yes

Specimen

Specimen Type

Varies

Advisory Information

This test should be ordered only for individuals with symptoms suggestive of familial adenomatous polyposis (FAP). Asymptomatic patients with a family history of FAP should not be tested until a variant has been identified in an affected family member.

Shipping Instructions

Specimen preferred to arrive within 96 hours of collection.

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.

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: Inherited Cancer Syndromes Patient Information (T519) in Special Instructions

3. If not ordering electronically, complete, print, and send 1 of the following forms with the specimen:

-Oncology Test Request (T729)

-Gastroenterology and Hepatology Client Test Request (T728)

Specimen Minimum Volume

1 mL

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	Ambient (preferred)		
	Frozen		
	Refrigerated		

Clinical and Interpretive

Clinical Information

Familial adenomatous polyposis (FAP) is an autosomal dominant condition caused by alterations in the *APC* gene located on the long arm of chromosome 5 (5q21). Classic FAP is characterized by progressive development of hundreds to thousands of adenomatous colon polyps. Polyps may develop during the first decade of life, and the majority of untreated FAP patients will develop colon cancer by age 40. Typically, there is a predominance of polyps on the left side of the colon; however, other areas of the colon may also be affected. The presence of extracolonic manifestations is variable and includes gastric and duodenal polyps, ampullary polyps, osteomas, dental abnormalities (unerupted teeth), congenital hypertrophy of the retinal pigment epithelium (CHRPE), benign cutaneous lesions, desmoids tumors, hepatoblastoma, and extracolonic cancers. Common constellations of colonic and extracolonic manifestations have resulted in the designation of 3 clinical variants: Gardner syndrome, Turcot syndrome, and hereditary desmoid disease.

Gardner syndrome is characterized by colonic polyps of classic FAP with epidermoid skin cysts and benign osteoid tumors of the mandible and long bones.

Turcot syndrome is characterized by multiple colonic polyps and central nervous system (CNS) tumors. Turcot syndrome is an unusual clinical variant of FAP, as it is also considered a clinical variant of hereditary nonpolyposis colorectal cancer (HNPCC). Individuals with Turcot syndrome have CNS tumors in addition to adenomatous polyps. The types of CNS tumor observed helps to distinguish Turcot-FAP variant patients from Turcot-HNPCC variant patients. The predominant CNS tumor associated with the Turcot-FAP variant is medulloblastoma, while glioblastoma is the predominant CNS tumor associated with Turcot-HNPCC.

Hereditary desmoid disease (HDD) is a variant of FAP with multiple desmoids tumors as the predominant feature. Many patients with HDD may not even show colonic manifestations of FAP. *APC* germline testing may assist clinicians in distinguishing a sporadic desmoid tumor from that associated with FAP.

Attenuated FAP (AFAP) is characterized by later onset of disease and a milder phenotype (typically <100 adenomatous polyps and fewer extracolonic manifestations) than classic FAP. Typically individuals with AFAP develop symptoms of the disease at least 10 to 20 years later than classically affected individuals. Individuals with AFAP often lack a family history of colon cancer and/or multiple adenomatous polyps. Of note, clinical overlap is observed between AFAP and *MYH*-associated polyposis (MAP), an autosomal recessive polyposis syndrome typically associated with fewer than 100 polyps. Although the clinical phenotype of MAP remains somewhat undefined, extracolonic manifestations, including CHRPE have been described in affected patients. Given the phenotypic overlap of AFAP and MAP, these tests are commonly ordered together or in a reflex fashion.

See Colonic Polyposis Syndromes Testing Algorithm in Special Instructions for additional information.

Reference Values

An interpretive report will be provided.

Interpretation

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

Cautions

A small percentage of individuals who are carriers or have a diagnosis of familial adenomatous polyposis (FAP) may have an alteration that is not identified by this method (eg, promoter alterations, deep intronic alterations, biallelic alterations in *MYH* gene). The absence of a alteration, therefore, does not eliminate the possibility of positive carrier status or the diagnosis of FAP. For carrier testing, it is important to first document the presence of an *APC* gene alteration in an affected family member.

Rare alterations 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.

It is strongly recommended that patients undergoing predictive testing receive genetic counseling both prior to testing and after results are available.

Technical Limitations:

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

Due to the limitations of next-generation sequencing, 90% of insertions and deletions up to 28 bases and 38 bases, respectively, can be detected. If a diagnosis of one of the syndromes on this panel is still suspected, consider full gene sequencing using traditional Sanger methods. Single or multiexon deletions as well as whole gene deletions will be detected by array comparative genomic hybridization (aCGH).

Evaluation Tools:

Multiple in-silico evaluation tools were used to assist in the interpretation of these results. These tools are updated regularly; therefore, changes to these algorithms may result in different predictions for a given alteration. Additionally, the predictability of these tools for the determination of pathogenicity is currently not validated.

Unless predicted to cause disease, alterations found deep in the intron or alterations that do not result in an amino acid substitution are not reported.

Reclassification of Variants-Policy:

At this time, it is not standard practice for the laboratory to systematically review likely deleterious alterations or variants of uncertain significance that are detected and reported. The laboratory encourages health care providers to contact the laboratory at any time to learn how the status of a particular variant may have changed over time.

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. American Society of Clinical Oncology. American Society of Clinical Oncology policy statement update: genetic testing for cancer susceptibility Clin Oncol. 2003;21:2397-2406

3. Half E, Bercovich D, Rozen P: Familial adenomatous polyposis. Orphanet J Rare Dis. 2009 Oct 12;4:22

4. Croner RS, Brueckl WM, Reingruber B, et al: Age and manifestation related symptoms in familial adenomatous polyposis. BMC Cancer. 2005 Mar 2;5:24

Performance

Method Description

Next-generation sequencing is performed to test for the presence of an alteration in all coding regions and intron/exon boundaries of the *APC* gene.(Unpublished Mayo method)

Additionally, array comparative genomic hybridization (aCGH) is used to test for the presence of large deletions and duplications encompassing the coding regions as well as promoter 1A and 1B of the *APC* 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

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

81201

Hereditary Colon Cancer CGH Array, additional test

81228

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
APCZ	APC Gene, Full Gene Analysis	94188-0

Result ID	Test Result Name	Result LOINC Value
53568	Result Summary	50397-9
53569	Result	82939-0
53570	Interpretation	69047-9
53571	Additional Information	48767-8
53572	Specimen	31208-2
53573	Source	31208-2
53574	Array Billed?	No LOINC Needed
53575	Released By	18771-6