

Familial Adenomatous Polyposis: APC Gene Deletion/Duplication

Test Code: QP

Turnaround time: 2 weeks

CPT Codes: 81203 x1

Condition Description

APC-associated polyposis conditions result from a mutation in the APC gene and cause a predisposition for colon cancer. Disorders in this category include:

- Familial Adenomatous Polyposis (FAP)
- Attenuated FAP (AFAP)
- Gardner Syndrome
- Turcot Syndrome

FAP is an autosomal dominant disorder characterized by the development of hundreds to thousands of adenomatous colonic polyps, usually beginning during early adolescence. 95% of affected individuals develop polyps by age 35; without surgical intervention, these polyps will inevitably progress to colorectal cancer by the early forties. Extracolonic manifestations such as dental anomalies, polyps of the gastric fundus and duodenum, congenital hypertrophy of the retinal pigment epithelium (CHRPE), osteomas, desmoid tumors, soft tissue tumors, and other associated cancers may occur.

Attenuated FAP differs in that the overall polyp burden tends to be less (average of 30) and polyps are also more proximally located. Colorectal cancer generally occurs at a later age.

Gardner Syndrome is associated with colon polyps typical of FAP, in conjunction with osteomas, desmoid tumors, and other neoplasms.

Turcot Syndrome consists of colon polyps and central nervous system tumors.

The diagnosis of APC-associated polyposis conditions relies primarily on clinical findings. Molecular genetic testing of APC detects disease-causing mutations in up to 90% of individuals with typical FAP. Molecular genetic testing is most often used to confirm the diagnosis of FAP or attenuated FAP in individuals with equivocal findings (e.g., <100 adenomatous polyps) and to provide early diagnosis of at-risk family members. Phenotype variations may correlate with the specific location of the APC gene mutation. APC-associated polyposis conditions are inherited in an autosomal dominant manner. Approximately 75%-80% of individuals with APC-associated polyposis conditions have an affected parent. The APC gene (5q21-q22) has 15 exons. The specific function of the APC gene is the object much research and tumor suppressor activity is suspected.

Sequencing of the APC gene is recommended after a clinical diagnosis consistent with FAP or an APC-associated polyposis condition, and provides a complementary method to confirm the presence of mutations in a proband, identify at-risk individuals among the proband's relatives, [and provide prenatal diagnosis in families with known mutations](#). For patients in whom mutations are not identified by full gene sequencing, deletion/duplication analysis is appropriate.

Please [click here](#) for the GeneTests summary on this condition.

Genes

[APC](#)

Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of FAP or an APC-associated polyposis syndrome in an individual in whom sequence analysis was negative.
- Individuals at-risk for FAP or an APC-associated polyposis syndrome due to family history in whom sequence analysis was negative.

Methodology

DNA isolated from peripheral blood is hybridized to a CGH array to detect deletions and duplications. The targeted CGH array has overlapping probes which cover the entire genomic region.

Detection

Approximately 8%-12% of individuals with an APC-associated polyposis condition and 100 or more polyps have a partial or whole APC gene deletion. Detection is limited to duplications and deletions. The CGH array will not detect point or intronic mutations.

Results of molecular analysis should be interpreted in the context of the patient's clinical presentation and/or tumor pathology.

Specimen Requirements

Submit only 1 of the following specimen types

Type: Whole Blood (EDTA)

Specimen Requirements:

EDTA (Purple Top)

Infants and Young Children (2 years of age to 10 years old: 3-5 ml

Older Children & Adults: 5-10 ml

Autopsy: 2-3 ml unclotted cord or cardiac blood

Specimen Collection and Shipping:

Ship sample at room temperature for receipt at EGL within 72 hours of collection. Do not freeze.

Type: DNA, Isolated

Specimen Requirements:

Microtainer

3µg

Isolation using the Perkin Elmer™ Chemagen™ Chemagen™ Automated Extraction method or Qiagen™ Puregene kit for DNA extraction is recommended.

Specimen Collection and Shipping:

Refrigerate until time of shipment in 100 ng/µL in TE buffer. Ship sample at room temperature with overnight delivery.

Special Instructions

Please submit copies of pedigree or other family history information along with the sample. Contact the laboratory if further information is needed. Sequence analysis is required before deletion/duplication analysis by targeted CGH array. If sequencing is performed outside of EGL Genetics, please submit a copy of the sequencing report with the test requisition form.

Related Tests

- [Familial Adenomatous Polyposis: APC Gene Sequencing \(TV\)](#) is required before deletion/duplication.
- [MYH-Associated Polyposis: Common Mutation Panel \(TW\)](#), [MYH-Associated Polyposis: MYH Gene Sequencing \(QV\)](#), and [MYH-Associated Polyposis: MYH Gene Deletion/Duplication \(QW\)](#) are available for *MYH*-associated polyposis, and may be indicated for individuals with a clinical diagnosis of FAP or AFAP who do not have a detectable *APC* mutation.
- Prenatal testing is available to couples who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.