Familial Adenomatous Polyposis: APC Gene Sequencing

**Test Code:** TV  
**Turnaround time:** 4 weeks  
**CPT Codes:** 81201 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, and 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 may occur, including:

- dental anomalies
- polyps of the gastric fundus and duodenum
- congenital hypertrophy of the retinal pigment epithelium (CHRPE)
- osteomas
- desmoid tumors
- soft tissue tumors
- other associated cancers

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., more than 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 of much research and tumor suppressor activity is suspected.

### Methodology

**Next Generation Sequencing:** In-solution hybridization of all coding exons is performed on the patient's genomic DNA. Although some deep intronic regions may also be analyzed, this assay is not meant to interrogate most promoter regions, deep intronic regions, or other regulatory elements, and does not detect single or multi-exon deletions or duplications. Direct sequencing of the captured regions is performed using next generation sequencing. The patient's gene sequences are then compared to a standard reference sequence. Potentially causative variants and areas of low coverage are Sanger-sequenced. Sequence variations are classified as pathogenic, likely pathogenic, benign, likely benign, or variants of unknown significance. Variants of unknown significance may require further studies of the patient and/or family members.

### Detection

**Clinical Sensitivity:** Sequence analysis of the APC gene detects disease-causing mutations in approximately 90% of individuals with typical FAP. Mutations in the promoter region, some mutations in the introns and other regulatory element mutations, and large deletions cannot be detected by this analysis.

**Analytical Sensitivity:** ~99%.

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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: Saliva

Specimen Requirements:
Oragene™ Saliva Collection Kit
Oragene™ Saliva Collection Kit used according to manufacturer instructions. Please contact EGL for a Saliva Collection Kit for patients that cannot provide a blood sample.

Specimen Collection and Shipping:
Please do not refrigerate or freeze saliva sample. Please store and ship at room temperature.

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
8µg
Isolation using the Perkin Elmer™ 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.

Related Tests

- Familial Adenomatous Polyposis: APC Gene Deletion/Duplication (QP) is available for those individuals in whom sequence analysis is negative.
- MYH-Associated Polyposis: MYH Common Mutation Panel (TW), MYH-Associated Polyposis: MYH Gene Sequencing (QV), and MYH-Associated Polyposis: MYH Gene Deletion/Duplication (QW) may be indicated for individuals with a clinical diagnosis of FAP or AFAP who do not have a detectable APC mutation.
- Known Mutation Testing (KM) is available to family members if mutations are identified by sequencing.
- 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.