

MUTYH-Associated Polyposis: MUTYH Gene Sequencing

Test Code: QV

Turnaround time: 4 weeks

CPT Codes: 81406 x1

Condition Description

MUTYH-associated polyposis (MAP) results from mutations in the *MUTYH* gene. MAP is an autosomal recessive disorder characterized by the development of multiple adenomatous polyps in the colon, stomach, or duodenum and an increased risk for cancer. This accounts for a proportion of patients with a clinical diagnosis of familial adenomatous polyposis (FAP) or attenuated FAP (AFAP) who do not have a detectable *APC* gene mutation. Studies from multiple FAP registries suggest that approximately 7% to 17% of patients with the FAP or AFAP phenotype carry biallelic mutations in the *MUTYH* gene. In these individuals, the polyp burden ranges from only a few to the hundreds typical of classic FAP.

The *MUTYH* gene (1p34.3-1p32.1), also referred to as the *MYH* gene, has 16 exons and is involved in DNA mismatch repair. Although this condition is newly described, some studies have found that 1% of Caucasians will carry one of two common mutations, p.Y179C (previously reported as p.Y165C or p.Y176C) and p.G396D (previously reported as p.G382D or p.G393D), in *MUTYH*. Prevalence of *MUTYH* mutations in other ethnic groups is currently unknown.

Testing of the *MUTYH* gene is recommended in individuals with a suspected clinical diagnosis of FAP or AFAP in whom no *APC* gene mutation was identified. Testing can confirm the presence of mutations in a proband, identify at-risk or carrier individuals among the proband's relatives, and provide prenatal diagnosis in families with known mutations.

For Caucasian patients with suspected MAP, a common mutation panel is available to test for the two common mutations found in that population. For non-Caucasian patients with suspected MAP, or Caucasian patients with suspected MAP in whom common mutation analysis did not identify two mutations, sequence analysis is recommended as the first or next step in mutation identification. For patients in whom mutations are not identified by full gene sequencing, deletion/duplication analysis is appropriate.

Please [click here](#) for the National Cancer Institute summary on this condition.

References:

<http://www.cancer.net/patient/Cancer+Types/MYH-Associated+Polyposis>

<http://www.mtsinai.on.ca/familialcancer/Diseases/MAP/default.htm>

Sieber, O.M.; Lipton, L.; Crabtree, M.; Heinemann, K.; Fidalgo, P.; Phillips, R.K.S.; Bisgaard, M.L.; Orntoft, T.F.; Aaltonen, L.A.; Hodgson, S.V.; Thomas, H.J.W.; Tomlinson, I.P.M.: Multiple colorectal adenomas, classic adenomatous polyposis, and germ-line mutations in MYH. *New Eng. J. Med.* 348: 791-799, 2003.

Aretz S, Uhlhaas S, Goergens H, Siberg K, Vogel M, Pagenstecher C, Mangold E, Caspari R, Propping P, Friedl W. *MUTYH*-associated polyposis: 70 of 71 patients with biallelic mutations present with an attenuated or atypical phenotype. *Int J Cancer*. 2006; 119: 807-814.

Genes

[MUTYH](#)

Indications

This test is indicated for:

- Non-Caucasian individuals with a clinical diagnosis of polyposis who do not have a detectable *APC* mutation.
- Caucasian individuals with a clinical diagnosis of polyposis who do not have a detectable *APC* mutation and who test negative for the two mutations common in Caucasians.
- Individuals at-risk for MAP due to family history.
- Carrier testing in adults with a family history of MAP.

Methodology

PCR amplification of 16 exons contained in the *MUTYH* gene is performed on the patient's genomic DNA. Direct sequencing of amplification products is performed in both forward and reverse directions using automated fluorescence dideoxy sequencing methods. The patient's gene sequences are then compared to a normal reference sequence. Sequence variations are classified as mutations, benign variants unrelated to disease, or variations of unknown clinical significance. Variants of unknown clinical significance may require further studies of the patient and/or family members. This assay does not interrogate the promoter region, deep intronic regions, or other regulatory elements, and does not detect large deletions.

Detection

Clinical Sensitivity:

The number of individuals with unexplained polyposis who will have biallelic mutations in *MUTYH* identified on sequence analysis is unknown. Data from Aretz et al. shows that the detection rate may vary by the extent and age of onset of polyposis, with 27% detection in individuals with 100+ polyps diagnosed between the ages of 35 and 45.

Mutations in the promoter region, some mutations in the introns, other regulatory element mutations, and large deletions cannot be detected by this analysis.

Analytical Sensitivity: ~99%.

Results of molecular analysis should be interpreted in the context of the patient's clinical presentation and family history.

Specimen Requirements

Submit only 1 of the following specimen types

Type: DNA, Isolated

Specimen Requirements:

Microtainer

8µg

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.

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: 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.

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

- [MUTYH-Associated Polyposis: Common Mutation Panel \(TW\)](#).
- [MUTYH-Associated Polyposis: MUTYH Gene Deletion/Duplication \(QW\)](#) is available for those individuals in whom sequence analysis is negative.
- [Familial Adenomatous Polyposis: APC Gene Sequencing \(TV\)](#) and [Familial Adenomatous Polyposis: APC Gene Deletion/Duplication \(QP\)](#) are available for APC-associated polyposis conditions, and may be indicated for individuals with a clinical diagnosis of polyposis who do not have a detectable MYH mutation.
- [Known Mutation Analysis \(KM\)](#) 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.