**MUTYH-Associated Polyposis: MUTYH Gene Deletion/Duplication**

**Test Code:** QW  
**Turnaround time:** 2 weeks  
**CPT Codes:** 81228 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.mtsinai.on.ca/familialcancer/Diseases/MAP/default.htm](http://www.mtsinai.on.ca/familialcancer/Diseases/MAP/default.htm)

### Genes

**MUTYH**

### Indications

This test is indicated for:

- Individuals with a clinical diagnosis of polyposis who do not have a detectable *APC* mutation and in whom sequence analysis of the *MUTYH* gene was negative.
- Individuals at-risk for MAP due to family history in whom sequence analysis of the *MUTYH* gene was negative.
- Carrier testing in adults with a family history of MAP in whom sequence analysis of the *MUTYH* gene 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.

Please note that a “backbone” of probes across the entire genome are included on the array for analytical and quality control purposes. Rarely, off-target copy number variants causative of disease may be identified that may or may not be related to the patient's phenotype. Only known pathogenic off-target copy number variants will be reported. Off-target copy number variants of unknown clinical significance will not be reported.

### Detection

Detection is limited to duplications and deletions. The CGH array will not detect point or intronic mutations. The frequency of deletions/duplication in MAP is unknown.

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

* Preferred specimen type: Whole Blood
Type: Whole Blood

Specimen Requirements:

In EDTA (purple top) tube:
Infants (2 years): 3-5 ml
Older Children & Adults: 5-10 ml

Specimen Collection and Shipping: Refrigerate until time of shipment. Ship sample within 5 days of collection at room temperature with overnight delivery.

Type: Saliva

Specimen Requirements:

Oragene™ Saliva Collection kit (available through EGL) used according to manufacturer instructions.

Specimen Collection and Shipping: Store sample at room temperature. Ship sample within 5 days of collection 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

- **MUTYH-Associated Polyposis:** MUTYH Gene Sequencing (QV) is required before deletion/duplication.
- **MUTYH-Associated Polyposis:** Common Mutation Panel (TW).
- **Familial Adenomatous Polyposis:** APC Gene Sequencing (TV).
- **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.
- 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.