Overview

Useful For

Confirmation of suspected clinical diagnosis of *MUTYH*-associated polyposis (MAP) in patients with adenomatous polyps or early-onset colorectal cancer

Identification of familial *MUTYH* mutations to allow for predictive or diagnostic testing in family members

Genetics Test Information

This test includes next-generation sequencing to evaluate for mutations in the coding region of the *MUTYH* gene. Sanger sequencing may also be performed to confirm any detected variants.

Testing Algorithm

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/Targeted Next-Generation Sequencing followed by Polymerase Chain Reaction (PCR) and Sanger Sequencing

NY State Available

Yes

Specimen

Specimen Type

Varies

Shipping Instructions

Specimen preferred to arrive within 96 hours of draw.

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.

Additional Information: To ensure minimum volume and concentration of DNA is met, the preferred volume of blood must be submitted. Testing may be canceled if DNA requirements are inadequate.

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 by 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

Biallelic germline mutations in the *MUTYH* gene (also known as *MYH*) cause *MUTYH*-associated polyposis (MAP) syndrome, an autosomal recessive form of hereditary colorectal cancer. MAP is a polyposis syndrome typically associated with 10 to 100 adenomatous colon polyps, which in turn confer a significantly increased risk for colorectal cancer. Therefore, phenotypic overlap exists between MAP and attenuated familial adenomatous polyposis (FAP). However, the number of cumulative polyps is variable and can mimic both classic FAP, associated with hundreds to thousands of polyps, and Lynch syndrome, which is generally associated with very few (1-5) adenomatous polyps. Therefore, evaluation for *MUTYH* should be considered in patients with early onset colorectal cancer in whom a DNA

mismatch repair (MMR) defect has not been identified.

Patients with biallelic *MUTYH* mutations are at risk for extracolonic manifestations including upper gastrointestinal polyps or cancer as well as other tumors. Congenital hyperpigmentation of the retinal epithelium (CHRPE), dental anomalies, dermal cysts, desmoid tumors, and osteomas may also occur, but to a lesser extent than what is observed in patients with FAP.

Literature suggests that monoallelic carriers may also be at increased risk for colon, gastric, breast, and endometrial cancer. Approximately 1% to 2% of mixed European Caucasian individuals are predicted to carry a *MUTYH* mutation. Therefore, the reproductive partners of monoallelic and biallelic carriers should be offered carrier screening to adequately assess the risk of their offspring to have MAP.

Two mutations, G396D and Y179C (originally known as G382D and Y165C), account for approximately 85% of the disease-causing *MUTYH* mutations in affected mixed European Caucasian individuals.

Reference Values

An interpretive report will be provided.

Interpretation

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

Cautions

Clinical Correlations:

Some individuals who have a diagnosis of *MUTYH*-associated polyposis (MAP) or involvement of *MUTYH* may have a mutation that is not identified by this method (eg, promoter mutations, deep intronic mutations). The absence of a mutation, therefore, does not eliminate the possibility of a diagnosis of *MUTYH*-associated polyposis. For predictive testing of asymptomatic individuals, it is important to first document the presence of *MUTYH* gene mutations in an affected family member.

In some cases, DNA alterations of undetermined significance may be identified. 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. We strongly recommend that patients undergoing predictive testing receive genetic counseling both prior to testing and after results are available.

Technical Limitations:

Due to the limitations of next-generation sequencing, we can detect more than 93% of insertions and deletions up to 20 bases and 43 bases, respectively. If a diagnosis is still suspected, consider full gene sequencing using traditional Sanger methods. If results obtained do not match the clinical findings, additional testing should be considered.

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 reported or predicted to cause disease, alterations found deep in the intron or alterations that do not result in an amino acid substitution are not reported. These and common polymorphisms identified for this patient are available upon request.

Reclassification of Variants-Policy:

All detected alterations are evaluated according to American College of Medical Genetics and Genomics recommendations.(1) Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance. At this time, it is not standard practice for the laboratory to systematically re-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 CS, Bale S, Bellissimo DB, et al: ACMG recommendations for standards for interpretation and reporting of sequence variations: Revisions 2007. Genet Med 2008;10(4):294-300

2. Goodenberger M, Lindor NM: Lynch syndrome and MYH-associated polyposis: review and testing strategy. J Clin Gastroenterol 2011;45(6):488-500

3. Lindor NM, McMaster ML, Lindor CJ, et al: Concise handbook of familial cancer susceptibility syndromes. Second edition. J Natl Cancer Inst Monogr 2008;(38):1-93

4. Win AK, Cleary SP, Dowty JG, et al: Cancer risks for monoallelic *MUTYH* mutation carriers with a family history of colorectal cancer. Int J Cancer 2011;129(9):2256-2262

5. *MUTYH*-Associated Polyposis-GeneReviews-NCBI Bookshelf. Available atÂ www.ncbi.nlm.nih.gov/books/NBK107219/

Performance

Method Description

Next-generation sequencing (NGS) is performed to test for the presence of a mutation in the *MUTYH* gene.(Pritchard CC, Smith C, Salipante SJ, et al: ColoSeq provides comprehensive Lynch and polyposis syndrome mutational analysis using massively parallel sequencing. J Mol Diagn 2012;14[4]:357-366)

Reported variants detected by NGS will be confirmed by Sanger sequencing.

PDF Report

No

Day(s) and Time(s) Test Performed

Performed weekly; Varies

Analytic Time

14 days

Maximum Laboratory Time

20 days

Specimen Retention Time

Whole Blood: 2 weeks (if available) Extracted DNA: Indefinitely

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

81406

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
MYHZ	MUTYH Full Gene Analysis	94228-4

Result ID	Test Result Name	Result LOINC Value
BA1637	Result Summary	50397-9
BA1638	Result	82939-0
BA1639	Interpretation	69047-9
BA1640	Additional Information	48767-8
BA1641	Specimen	31208-2
BA1642	Source	31208-2
BA1643	Released By	18771-6