Test Definition: CDH1Z

CDH1 Gene, Full Gene Analysis

Overview

Useful For

Confirmation of suspected clinical diagnosis of hereditary diffuse gastric cancer

Identification of familial *CDH1* variant to allow for predictive testing in family members

Predictive testing of an asymptomatic child **is not recommended**.

Additional Tests

Test ID	Reporting Name	Available Separately	Always Performed
COLAB	Hereditary Colon Cancer CGH Array	Yes, (order FMTT)	Yes

Testing Algorithm

When this test is ordered, array comparative genomic hybridization will always be performed at an additional charge.

Special Instructions

- Molecular Genetics: Inherited Cancer Syndromes Patient Information
- Informed Consent for Genetic Testing
- Informed Consent for Genetic Testing (Spanish)

Method Name

Polymerase Chain Reaction (PCR) Amplification followed by DNA Sequencing

COLAB: Gene Dosage Analysis by Array Comparative Genomic Hybridization (aCGH)

NY State Available

Yes

Specimen

Specimen Type

Varies

Shipping Instructions

Specimen preferred to arrive within 96 hours of collection.

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.

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

Specimen Minimum Volume

1 mL

Reject Due To

All specimens will be evaluated at 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

Hereditary diffuse gastric cancer (HDGC) is a rare autosomal dominant hereditary cancer syndrome associated with germline variants in the *CDH1*gene,which encodes the protein E-cadherin. HDGC is predominantly characterized by increased susceptibility to diffuse gastric cancer and lobular breast cancer. HDGC is highly penetrant since the risk for developing gastric cancer is 80% by age 80. Women also have an approximately 40% to 60% risk of breast cancer by age 80. Colorectal cancer has been reported in individuals with germline *CDH1* variants, however, the specific lifetime risk for colorectal cancer is unknown.

The International Gastric Cancer Linkage Consortium proposes clinical criteria for the selection of individuals who are at increased risk of having a germline *CDH1* variant as follows: 1) two or more cases of diffuse gastric cancer (histopathological confirmation in at least 1 case) in first- or second-degree relatives in which at least 1 individual is

diagnosed prior to age 50; 2) three or more documented cases of diffuse gastric cancer in first- or second-degree relatives regardless of age of onset; 3) individuals diagnosed with diffuse gastric cancer before the age of 40 regardless of family history; 4) personal or family history of diffuse gastric cancer and lobular breast cancer in first and second relatives with at least 1 diagnosis occurring before age 50.

Reference Values

An interpretive report will be provided.

Interpretation

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

Cautions

Some individuals who have a diagnosis of hereditary diffuse gastric cancer may have a variant that is not identified by this method (eg, deep intronic alterations, promoter alterations). The absence of a variant, therefore, does not eliminate the possibility of a diagnosis of hereditary diffuse gastric cancer. For predictive testing of asymptomatic individuals, it is important to first document the presence of a *CDH1* gene variant in an affected family member.

In some cases, DNA alterations of undetermined significance may be identified.

It is strongly recommended that asymptomatic patients undergoing predictive testing receive genetic counseling both prior to testing and after results are available.

Rare alterations exist that could lead to false-negative or false-positive results. If results obtained do not match the clinical findings, additional testing should be considered.

Test results should be interpreted in the context of clinical findings, family history, and other laboratory data. Errors in the interpretation of results may occur if information given is inaccurate or incomplete.

Clinical Reference

1. Richards S, Aziz N, Bale S, et al: Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. Genet Med. 2015 May;17(5):405-424

2. Lindor NM, McMaster ML, Lindor CJ, Greene MH; National Cancer Institute, Division of Cancer Prevention, Community Oncology and Prevention Trials Research Group. Concise handbook of familial cancer susceptibility syndromes - second edition. J Natl Cancer Inst Monogr. 2008;(38):1-93

3. Fitzgerald RC, Hardwick R, Huntsman D, et al: Hereditary diffuse gastric cancer: updated consensus guidelines for clinical management and directions for future research. J Med Genet. 2010;47:436-444

4. Kaurah P, Huntsman DG: Hereditary diffuse gastric cancer. In: Adams MP, Ardinger HH, Pagon RA, et al, eds. GeneReviews (Internet). University of Washington, Seattle; 2002. Updated March 22, 2018. Accessed August 12, 2020 Available at www.ncbi.nlm.nih.gov/books/NBK1139/

Performance

Method Description

Bidirectional sequence analysis is performed to test for the presence of a mutation in all coding regions and intron/exon boundaries of the *CDH1* gene.(Unpublished Mayo method)

Additionally, array comparative genomic hybridization (aCGH) is used to test for the presence of large deletions and duplications.(Aradhya S, Lewis R, Bonaga T, et al: Exon-level array CGH in a large clinical cohort demonstrates increased sensitivity of diagnostic testing for Mendelian disorders. Genet Med. 2012;14[6]:594-603)

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: 3 months

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

Hereditary Colon Cancer CGH Array, additional test

81228

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
CDH1Z	CDH1 Gene, Full Gene Analysis	94240-9

Result ID	Test Result Name	Result LOINC Value
52487	Result Summary	50397-9
52488	Result	82939-0

Result ID	Test Result Name	Result LOINC Value
52489	Interpretation	69047-9
52490	Additional Information	48767-8
52491	Specimen	31208-2
52492	Source	31208-2
52494	Array Billed?	No LOINC Needed
52495	Released By	18771-6