

## Diffuse Gastric Cancer Syndrome: *CDH1* Gene Sequencing

**Test Code:** SCDH1

**Turnaround time:** 4 weeks

**CPT Codes:** 81406 x1

### Condition Description

Diffuse gastric cancer (DGC) is a genetic cancer susceptibility syndrome characterized by a high risk for stomach and lobular breast cancer and is inherited in an autosomal dominant pattern. Gastric cancers that occur in this syndrome are of the diffuse-type, as opposed to intestinal, and often have signet ring cells through the stomach wall causing thickening, without forming a discrete mass.

Women with a *CDH1* pathogenic variant have a 39-52% lifetime risk for lobular breast cancer and a 63-93% risk of developing diffuse gastric cancer. Men have an estimated 40-67% lifetime risk of developing diffuse gastric cancer. Diffuse gastric cancer generally occurs before age 50 in *CDH1* pathogenic variant carriers, though cases under the age of 18 have been reported with a family history of hereditary diffuse gastric cancer.

References:

- GeneReviews.
- Kaurah P, MacMillan A, et.al. Founder and recurrent *CDH1* mutations in families with hereditary diffuse gastric cancer. *JAMA*. 2007;297:2360–72.
- Pharoah PD, Guilford P, Caldas C. Incidence of gastric cancer and breast cancer in *CDH1* (E-cadherin) mutation carriers from hereditary diffuse gastric cancer families. *Gastroenterology*. 2001;121:1348–53.
- Guilford P, Hopkins J, Harraway J, McLeod M, McLeod N, Harawira P, Taite H, Scoular R, Miller A, Reeve AE. E-cadherin germline mutations in familial gastric cancer. *Nature*. 1998;392:402–5.

### Genes

[CDH1](#)

### Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of diffuse gastric cancer syndrome.

### Methodology

PCR amplification of 16 exons contained in the *CDH1* 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 pathogenic variants, 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:** Unknown. Pathogenic variants in the promoter region, some pathogenic variants in the introns and other regulatory element pathogenic variants cannot be detected by this analysis. Large deletions will not be detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient's biochemical phenotype.

Analytical Sensitivity: ~99%.

### Specimen Requirements

**Submit only 1 of the following specimen types**

#### 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™ 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: 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.

**Related Tests**

- Gastrointestinal and Colorectal Cancer: Sequencing Panel
- Hereditary Cancer Syndrome: Sequencing Panel