

Overview

Useful For

Evaluating patients with a personal or family history suggestive of a hereditary paraganglioma and pheochromocytoma (PGL/PCC) syndrome

Establishing a diagnosis of a hereditary PGL/PCC, allowing for targeted surveillance based on associated risks

Identifying genetic variants associated with increased risk for PGL/PCC, allowing for predictive testing and appropriate screening of at-risk family members

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
_STR1	Comp Analysis using STR (Bill only)	No, (Bill only)	No
_STR2	Add'l comp analysis w/STR (Bill Only)	No, (Bill only)	No
CULFB	Fibroblast Culture for Genetic Test	Yes	No
CULAF	Amniotic Fluid Culture/Genetic Test	Yes	No
MATCC	Maternal Cell Contamination, B	Yes	No

Genetics Test Information

This test utilizes next-generation sequencing to detect single nucleotide and copy number variants in 11 genes associated with hereditary paraganglioma and/or pheochromocytoma (PGL/PCC): *FH*, *MAX*, *NF1*, *RET*, *SDHA*, *SDHAF2*, *SDHB*, *SDHC*, *SDHD*, *TMEM127*, and *VHL*. For more information see Method Description and [Targeted Genes and Methodology Details for Hereditary Paraganglioma/Pheochromocytoma Panel](#).

Identification of a disease-causing variant may assist with diagnosis, prognosis, clinical management, familial screening, and genetic counseling for hereditary PGL/PCC.

Testing Algorithm

Skin biopsy:

If skin biopsy is received, fibroblast culture will be added at an additional charge. If viable cells are not obtained, the client will be notified.

Prenatal specimens:

If an amniotic fluid specimen is received, an amniotic fluid culture will be performed at an additional charge.  
If chorionic villi, cultured chorionic villi, or cultured amniocyte specimen is received, a fibroblast culture will be performed at an additional charge.

For any prenatal specimen that is received, maternal cell contamination testing will be performed at an additional charge.

**Cord blood:**

For cord blood specimens that have an accompanying maternal blood specimen, maternal cell contamination studies will 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 \(Spanish\)](#)
- [Targeted Genes and Methodology Details for Hereditary Paranganglioma/Pheochromocytoma Panel](#)

**Method Name**

Sequence Capture and Targeted Next-Generation Sequencing (NGS) followed by Polymerase Chain Reaction (PCR) and Sanger Sequencing

**NY State Available**

Yes

**Specimen**

**Specimen Type**

Varies

**Ordering Guidance**

Customization of this panel and single gene analysis for any gene present on this panel are available. For more information see CGPH / Custom Gene Panel, Hereditary, Next-Generation Sequencing, Varies. To modify this panel via CGPH, use the Hereditary Cancer disease state for step 1 on the [custom gene ordering tool](#).

Targeted testing for familial variants (also called site-specific or known mutations testing) is available for the genes on this panel. For more information see FMTT / Familial Variant, Targeted Testing, Varies. To obtain more information about this testing option, call 800-533-1710.

**Specimen Required**

**Patient Preparation:** A previous hematopoietic stem cell transplant from an allogenic donor will interfere with testing. For information about testing patients who have received a hematopoietic stem cell transplant, call 800-533-1710.

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**Submit only 1 of the following specimens:**

**Specimen Type:** Whole blood

**Container/Tube:**

**Preferred:** Lavender top (EDTA) or yellow top (ACD)

**Acceptable:** Green top (Sodium heparin)

**Specimen Volume:** 3 mL

**Collection Instructions:**

1. Invert several times to mix blood.
2. Send whole blood specimen in original tube. **Do not aliquot.**
3. Whole blood collected postnatal from an umbilical cord is also acceptable. See Additional Information

**Specimen Stability Information:** Ambient (preferred) 4 days/Refrigerated 4 days/Frozen 4 days

**Additional Information:**

1. Specimens are preferred to be received within 4 days of collection. Extraction will be attempted for specimens received after 4 days, and DNA yield will be evaluated to determine if testing may proceed.
2. To ensure minimum volume and concentration of DNA are met, the requested volume must be submitted. Testing may be canceled if DNA requirements are inadequate.
3. For postnatal umbilical cord whole blood specimens, maternal cell contamination studies are recommended to ensure test results reflect that of the patient tested. A maternal blood specimen is required to complete maternal cell contamination studies. Order MATCC / Maternal Cell Contamination, Molecular Analysis, Varies on both the cord blood and maternal blood specimens under separate order numbers.

**Specimen Type:** Saliva

**Patient Preparation:** Patient should not eat, drink, smoke, or chew gum 30 minutes prior to collection.

**Supplies:**

DNA Saliva Kit High Yield (T1007)

Saliva Swab Collection Kit (T786)

**Container/Tube:**

**Preferred:** High-yield DNA saliva kit

**Acceptable:** Saliva swab

**Specimen Volume:** 1 Tube if using T1007 or 2 swabs if using T786

**Collection Instructions:** Collect and send specimen per kit instructions.

**Specimen Stability Information:** Ambient (preferred) 30 days/Refrigerated 30 days

**Additional Information:** Saliva specimens are acceptable but not recommended. Due to lower quantity/quality of DNA yielded from saliva, some aspects of the test may not perform as well as DNA extracted from a whole blood sample. When applicable, specific gene regions that were unable to be interrogated will be noted in the report. Alternatively, additional specimen may be required to complete testing.

**Specimen Type:** Blood spot

**Supplies:** Card-Blood Spot Collection (Filter Paper) (T493)

**Container/Tube:**

**Preferred:** Collection card (Whatman Protein Saver 903 Paper)

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**Acceptable:** PerkinElmer 226 filter paper or blood spot collection card

**Specimen Volume:** 2 to 5 Blood spots

**Collection Instructions:**

1. An alternative blood collection option for a patient older than 1 year is a fingerstick. For detailed instructions, see [How to Collect a Dried Blood Spot Sample](#).
2. Let blood dry on the filter paper at ambient temperature in a horizontal position for a minimum of 3 hours.
3. Do not expose specimen to heat or direct sunlight.
4. Do not stack wet specimens.
5. Keep specimen dry.

**Send:** Ambient (preferred)/Refrigerated

**Additional Information:**

1. Blood spot specimens are acceptable but not recommended. Multiple extractions will be required to obtain sufficient yield for supplemental analysis, and there is significant risk for test failure due to insufficient DNA.
2. Due to lower concentration of DNA yielded from blood spot, some aspects of the test may not perform as well as DNA extracted from a whole blood sample. When applicable, specific gene regions that were unable to be interrogated will be noted in the report. Alternatively, additional specimen may be required to complete testing.
3. For collection instructions, see [Blood Spot Collection Instructions](#)
4. For collection instructions in Spanish, see [Blood Spot Collection Card-Spanish Instructions](#) (T777)
5. For collection instructions in Chinese, see [Blood Spot Collection Card-Chinese Instructions](#) (T800)

**Specimen Type:** Cultured fibroblasts

**Source:** Skin

**Container/Tube:** T-25 flask

**Specimen Volume:** 2 Flasks

**Collection Instructions:** Submit confluent cultured fibroblast cells from a tissue biopsy.

**Specimen Stability Information:** Ambient (preferred) <24 hours/Refrigerated <24 hours

**Additional Information:**

1. Specimens are preferred to be received within 24 hours of collection. Culture and extraction will be attempted for specimens received after 24 hours and will be evaluated to determine if testing may proceed.
2. A separate culture charge will be assessed under CULFB / Fibroblast Culture for Biochemical or Molecular Testing. An additional 3 to 4 weeks are required to culture fibroblasts before genetic testing can occur.

**Specimen Type:** Skin biopsy

**Supplies:** Fibroblast Biopsy Transport Media (T115)

**Container/Tube:** Sterile container with any standard cell culture media (eg, minimal essential media, RPMI 1640). The solution should be supplemented with 1% penicillin and streptomycin.

**Specimen Volume:** 4-mm Punch

**Specimen Stability Information:** Ambient (preferred) <24 hours/Refrigerated <24 hours

**Additional Information:**

1. Specimens are preferred to be received within 24 hours of collection. Culture and extraction will be attempted for specimens received after 24 hours and will be evaluated to determine if testing may proceed.
2. A separate culture charge will be assessed under CULFB / Fibroblast Culture for Biochemical or Molecular Testing. An additional 3 to 4 weeks are required to culture fibroblasts before genetic testing can occur.

**Specimen Type:** Extracted DNA

**Container/Tube:**

**Preferred:** Screw Cap Micro Tube, 2 mL with skirted conical base

**Acceptable:** Matrix tube, 1 mL

**Collection Instructions:**

1. The preferred volume is at least 100 mL at a concentration of 75 ng/mL.
2. Include concentration and volume on tube.

**Specimen Stability Information:** Frozen (preferred) 1 year/Ambient/Refrigerated

**Additional Information:** DNA must be extracted in a CLIA-certified laboratory or equivalent and must be extracted from a specimen type listed as acceptable for this test (including applicable anticoagulants). Our laboratory has experience with Chemagic, Puregene, Autopure, MagnaPure, and EZ1 extraction platforms and cannot guarantee that all extraction methods are compatible with this test. If testing fails, one repeat will be attempted, and if unsuccessful, the test will be reported as failed and a charge will be applied. If applicable, specific gene regions that were unable to be interrogated due to DNA quality will be noted in the report.

#### PRENATAL SPECIMENS

**Due to its complexity, consultation with the laboratory is required** for all prenatal testing; call 800-533-1710 to speak to a genetic counselor.

**Specimen Type:** Amniotic fluid

**Container/Tube:** Amniotic fluid container

**Specimen Volume:** 20 mL

**Specimen Stability Information:** Ambient (preferred) <24 hours/Refrigerated <24 hours

**Additional Information:** Specimen will only be tested after culture.

1. Specimens are preferred to be received within 24 hours of collection. Culture and extraction will be attempted for specimens received after 24 hours and will be evaluated to determine if testing may proceed.
2. A separate culture charge will be assessed under CULAF / Culture for Genetic Testing, Amniotic Fluid. An additional 2 to 3 weeks are required to culture amniotic fluid before genetic testing can occur.
3. **All prenatal specimens must be accompanied by a maternal blood specimen;** order MATCC / Maternal Cell Contamination, Molecular Analysis, Varies on the maternal specimen.

**Specimen Type:** Confluent cultured amniocytes

**Container/Tube:** T-25 flask

**Specimen Volume:** 2 Flasks

**Collection Instructions:** Submit confluent cultured amniocytes from another laboratory

**Specimen Stability Information:** Ambient (preferred) <24 hours/Refrigerated <24 hours

**Additional Information:**

1. Specimens are preferred to be received within 24 hours of collection. Culture and extraction will be attempted for specimens received after 24 hours and will be evaluated to determine if testing may proceed.
2. A separate culture charge will be assessed under CULFB / Fibroblast Culture for Biochemical or Molecular Testing.
3. **All prenatal specimens must be accompanied by a maternal blood specimen;** order MATCC / Maternal Cell Contamination, Molecular Analysis, Varies on the maternal specimen.

**Specimen Type:** Chorionic villi  
**Container/Tube:** 15-mL tube containing 15 mL of transport media  
**Specimen Volume:** 20 mg  
**Specimen Stability Information:** Ambient (preferred) <24 hours/Refrigerated <24 hours  
**Additional Information:** Specimen will only be tested after culture.  
1. Specimens are preferred to be received within 24 hours of collection. Culture and extraction will be attempted for specimens received after 24 hours and will be evaluated to determine if testing may proceed.  
2. A separate culture charge will be assessed under CULFB / Fibroblast Culture for Biochemical or Molecular Testing. An additional 3 to 4 weeks are required to culture fibroblasts before genetic testing can occur.  
3. **All prenatal specimens must be accompanied by a maternal blood specimen;** order MATCC / Maternal Cell Contamination, Molecular Analysis, Varies on the maternal specimen.

**Specimen Type:** Cultured chorionic villi  
**Container/Tube:** T-25 flasks  
**Specimen Volume:** 2 full flasks  
**Collection Instructions:** Submit confluent cultured cells from another laboratory  
**Specimen Stability Information:** Ambient (preferred) <24 hours/Refrigerated <24 hours  
**Additional Information:**  
1. Specimens are preferred to be received within 24 hours of collection. Culture and extraction will be attempted for specimens received after 24 hours and will be evaluated to determine if testing may proceed.  
2. A separate culture charge will be assessed under CULFB / Fibroblast Culture for Biochemical or Molecular Testing.  
3. **All prenatal specimens must be accompanied by a maternal blood specimen;** order MATCC / Maternal Cell Contamination, Molecular Analysis, Varies on the maternal specimen.

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:  
[-Informed Consent for Genetic Testing \(T576\)](#)  
[-Informed Consent for Genetic Testing-Spanish \(T826\)](#)  
2. [Molecular Genetics: Inherited Cancer Syndromes Patient Information Sheet \(T519\)](#)  
3. If not ordering electronically, complete, print, and send a [Oncology Test Request \(T729\)](#) with the specimen.

**Specimen Minimum Volume**  
See Specimen Required

**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	Varies		

## Clinical & Interpretive

### Clinical Information

Parangangliomas (PGL) and pheochromocytomas (PCC) are rare neuroendocrine tumors that arise from autonomous ganglia. Tumors located within the adrenal medulla (the largest sympathetic ganglion) are called pheochromocytomas, while those that stem from either parasympathetic or sympathetic ganglia are designated parangangliomas.

Parangangliomas and pheochromocytomas have a germline genetic basis in up to 30% of cases.(1) The genes implicated in hereditary PGL/PCC syndrome include *MAX*, *TMEM127*, *FH*, and the *SDHx* genes.

The genes most frequently associated with hereditary PGL/PCC syndromes are the succinate dehydrogenase-associated genes *SDHA*, *SDHAF2*, *SDHB*, *SDHC*, and *SDHD*.

Germline alterations in the *MAX* gene are typically associated with increased risk for PCC, although some individuals have been identified with PGL. *MAX* variants occur in approximately 1% of patients with hereditary PGL/PCC syndromes.(2)

*TMEM127* variants are associated most frequently with PCC and rarely PGL.(1) Alterations of *TMEM127* account for approximately 2% of individuals with hereditary PGL/PCC.(2)

Recent evidence suggests that disease-causing variants in *FH* also increase risk for PGL/PCC.(3,4) Individuals with disease-causing *FH* variants carry a significantly increased risk for cutaneous or uterine leiomyomata and renal tumors.(5)

Alterations in *VHL*, *NF1*, and *RET* also increase risk for PGL/PCC, in addition to other types of tumors.(6)

Disease-causing variants in the *VHL* gene are associated with a syndrome called von Hippel Lindau (VHL) syndrome. In addition to PGL/PCC, individuals with VHL syndrome are at increased risk for hemangioblastomas, renal cell carcinoma, pancreatic cysts, neuroendocrine tumors, endolymphatic sac and epididymal tumors.(7)

*NF1* gene variants are associated with neurofibromatosis type I (NF1). Individuals with NF1 are at increased risk for pheochromocytomas in addition to neurofibromas and central nervous system gliomas, such as optic nerve gliomas. NF1 is also characterized by other features such as cafe-au lait macules, axillary/inguinal freckling, and Lisch nodules.(8)

Disease-causing *RET* variants result in a syndrome called multiple endocrine neoplasia type 2 (MEN2) or familial medullary thyroid cancer (FMTC). In addition to an increased risk for PGL/PCC, individuals with MEN2/FMTC have a very high risk of developing medullary thyroid cancer. Individuals with MEN2 may also have other features, such as primary hyperparathyroidism, mucosal neuromas, ganglioneuromatosis, and distinctive facial features.(9)

The National Comprehensive Cancer Network and the American Cancer Society provide recommendations regarding the medical management of individuals with hereditary PGL/PCC syndromes.(10)

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**Reference Values**

An interpretive report will be provided.

**Interpretation**

All detected variants are evaluated according to American College of Medical Genetics and Genomics recommendations.<sup>(11)</sup> Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance.

**Cautions**

Clinical Correlations:

Test results should be interpreted in the context of clinical findings, family history, and other laboratory data.

Misinterpretation of results may occur if the information provided is inaccurate or incomplete.

If testing was performed because of a clinically significant family history, it is often useful to first test an affected family member. Detection of a reportable variant in an affected family member would allow for more informative testing of at-risk individuals.

To discuss the availability of additional testing options or for assistance in the interpretation of these results, contact the Mayo Clinic Laboratories genetic counselors at 800-533-1710.

Technical Limitations:

Next-generation sequencing may not detect all types of genomic variants. In rare cases, false-negative or false-positive results may occur. The depth of coverage may be variable for some target regions; assay performance below the minimum acceptable criteria or for failed regions will be noted. Given these limitations, negative results do not rule out the diagnosis of a genetic disorder. If a specific clinical disorder is suspected, evaluation by alternative methods can be considered.

There may be regions of genes that cannot be effectively evaluated by sequencing or deletion and duplication analysis as a result of technical limitations of the assay, including regions of homology, high guanine-cytosine (GC) content, and repetitive sequences. Confirmation of select reportable variants will be performed by alternate methodologies based on internal laboratory criteria.

This test is validated to detect 95% of deletions up to 75 base pairs (bp) and insertions up to 47 bp. Deletions-insertions (delins) of 40 or more bp, including mobile element insertions, may be less reliably detected than smaller delins.

This analysis targets single and multi-exon deletions/duplications; however, in some instances single exon resolution cannot be achieved due to isolated reduction in sequence coverage or inherent genomic complexity. Balanced structural rearrangements (such as translocations and inversions) may not be detected.

This test is not designed to detect low levels of mosaicism or differentiate between somatic and germline variants. If there is a possibility that any detected variant is somatic, additional testing may be necessary to clarify the significance of results.



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Genes may be added or removed based on updated clinical relevance. For detailed information regarding gene specific performance and technical limitations, see Method Description or contact a laboratory genetic counselor.

If the patient has had an allogeneic hematopoietic stem cell transplant or a recent non-leukocyte reduced blood transfusion, results may be inaccurate due to the presence of donor DNA. Call Mayo Clinic Laboratories for instructions for testing patients who have received a bone marrow transplant.

#### Reclassification of Variants:

Currently, it is not standard practice for the laboratory to systematically review previously classified variants on a regular basis. The laboratory encourages healthcare professionals to contact the laboratory at any time to learn how the classification of a particular variant may have changed over time.

#### Variant Evaluation:

Evaluation and categorization of variants are performed using published American College of Medical Genetics and Genomics and the Association for Molecular Pathology recommendations as a guideline.(11) Other gene-specific guidelines may also be considered. Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance. Variants classified as benign or likely benign are not reported.

Multiple in silico evaluation tools may be used to assist in the interpretation of these results. The accuracy of predictions made by in silico evaluation tools is highly dependent upon the data available for a given gene, and periodic updates to these tools may cause predictions to change over time. Results from in silico evaluation tools should be interpreted with caution and professional clinical judgment.

#### Clinical Reference

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4. Castro-Vega LJ, Buffet A, De Cubas AA, et al. Germline mutations in *FH* confer predisposition to malignant pheochromocytomas and paragangliomas. *Hum Mol Genet*. 2014;23(9):2440-2446. doi:10.1093/hmg/ddt639
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8. Friedman JM. Neurofibromatosis 1. In: Adam MP, Feldman J, Mirzaa GM, et al, eds. GeneReviews [Internet]. University of Washington, Seattle; 1998. Updated April 3, 2025. Accessed June 16, 2025. Available at [www.ncbi.nlm.nih.gov/books/NBK1109/](http://www.ncbi.nlm.nih.gov/books/NBK1109/)

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10. Benn DE, Gimenez-Roqueplo AP, Reilly JR, et al. Clinical presentation and penetrance of pheochromocytoma/paranganglioma syndromes. J Clin Endocrinol Metab. 2006;91(3):827-836

11. 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;17(5):405-424

**Performance**

**Method Description**

Next-generation sequencing (NGS) and/or Sanger sequencing are performed to test for the presence of variants in coding regions and intron/exon boundaries of the genes analyzed, as well as some other regions that have known disease-causing variants. The human genome reference GRCh37/hg19 build was used for sequence read alignment. At least 99% of the bases are covered at a read depth over 30X. Sensitivity is estimated at above 99% for single nucleotide variants, above 94% for deletion-insertions (delins) less than 40 base pairs (bp), above 95% for deletions up to 75 bp and insertions up to 47 bp. NGS and/or a polymerase chain reaction-based quantitative method is performed to test for the presence of deletions and duplications in the genes analyzed.

There may be regions of genes that cannot be effectively evaluated by sequencing or deletion and duplication analysis as a result of technical limitations of the assay, including regions of homology, high guanine-cytosine (GC) content, and repetitive sequences. For details regarding the targeted genes analyzed or specific gene regions not routinely covered see [Targeted Genes and Methodology Details for Hereditary Paranganglioma/Pheochromocytoma](#). (Unpublished Mayo method)

Confirmation of select reportable variants may be performed by alternate methodologies based on internal laboratory criteria.

Genes analyzed: *FH*, *MAX*, *NF1*, *RET*, *SDHA*, *SDHAF2*, *SDHB*, *SDHC*, *SDHD*, *TMEM127*, and *VHL*

**PDF Report**  
Supplemental

**Day(s) Performed**  
Varies

**Report Available**

14 to 21 days

Specimen Retention Time

Whole blood: 28 days (if available); Saliva: 30 days (if available); Extracted DNA: 3 months; Blood spots: 1 year (if available)

Performing Laboratory Location

Mayo Clinic Laboratories - Rochester Main Campus

Fees & 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 account representative. 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. It has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

81437

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
HPGLP	Hereditary PGL/PCC Panel	In Process

Result ID	Test Result Name	Result LOINC® Value
614731	Test Description	62364-5
614732	Specimen	31208-2
614733	Source	31208-2
614734	Result Summary	50397-9
614735	Result	82939-0
614736	Interpretation	69047-9
614737	Resources	99622-3
614738	Additional Information	48767-8
614739	Method	85069-3
614740	Genes Analyzed	48018-6
614741	Disclaimer	62364-5
614742	Released By	18771-6