# Test Definition: PCGP

Porphyria Comprehensive Gene Panel, Varies

## Overview

### Useful For

Follow up for abnormal biochemical results suggestive of porphyria

Establishing a molecular diagnosis for patients with porphyria

Identifying variants within genes known to be associated with porphyria, allowing for predictive testing 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 porphyria: *ALAD*, *ALAS2*, *CLPX*, *CPOX*, *FECH*, *GATA1*, *HFE*, *HMBS*, *PPOX*, *UROD*, and *UROS*. See Targeted Genes and Methodology Details for Porphyria Comprehensive Gene Panel and Method Description for additional details.

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

The biochemical testing approach for diagnosis of patients with a suspected porphyria is most effective when done in a thoughtful manner. For recommendations for first-tier biochemical testing, the following algorithms are available:
-Porphyria (Acute) Testing Algorithm
-Porphyria (Cutaneous) Testing Algorithm

### Testing Algorithm

**Skin biopsy or cultured fibroblast specimens:**

For skin biopsy or cultured fibroblast specimens, a fibroblast culture will be performed at an additional charge. If viable cells are not obtained, the client will be notified.

**Prenatal specimens:**

If an amniotic fluid specimen or cultured amniocytes are received, an amniotic fluid culture will be performed at an additional charge.
If a chorionic villi specimen or cultured chorionic villi are 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.
For more information see:
-Porphyria (Acute) Testing Algorithm
-Porphyria (Cutaneous) Testing Algorithm

### Special Instructions

- Molecular Genetics: Biochemical Disorders Patient Information
- Informed Consent for Genetic Testing
- Porphyria (Acute) Testing Algorithm
- Porphyria (Cutaneous) Testing Algorithm
- Blood Spot Collection Card-Spanish Instructions
- Blood Spot Collection Card-Chinese Instructions
- Informed Consent for Genetic Testing (Spanish)
- Blood Spot Collection Instructions
- Targeted Genes and Methodology Details for Porphyria Comprehensive Gene 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

Upon request and after initial testing is complete, WESPR / Panel to Whole Exome Sequencing Reflex Test, Varies may be added to this test. To obtain more information about this option or add WESPR testing, call 800-533-1710.

Customization of this panel and single gene analysis for any gene present on this panel is available. For more information see CGPH / Custom Gene Panel, Hereditary, Next-Generation Sequencing, Varies. To modify this panel via CGPH, use the Inborn Errors of Metabolism 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. 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**.**

**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 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)
**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. Due to lower quantity/quality of DNA yielded from blood spots, 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.
2. Due to lower concentration of DNA yielded from blood spot, it is possible that 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:** 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:** Tissue biopsy
**Supplies:** Hank's Solution (T132)
**Container/Tube:** Sterile container with sterile Hank's balanced salt solution, Ringer's solution, or normal saline
**Specimen Volume:** 0.5 to 3 cm(3) or larger
**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**: Cultured fibroblasts
**Source**: Skin or tissue
**Container/Tube**: T-25 flask
**Specimen Volume**: 2 Flasks
**Collection Instructions**: Submit confluent cultured fibroblast cells from a 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**: Extracted DNA
**Container/Tube**:
**Preferred**: Screw Cap Micro Tube, 2mL with skirted conical base
**Acceptable**: Matrix tube, 1 mL
**Collection Instructions**:
1. The preferred volume is at least 100 mcL at a concentration of 75 ng/mcL.
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 Full 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: Biochemical Disorders Patient Information (T527)
3. If not ordering electronically, complete, print, and send a Biochemical Genetics Test Request (T798) 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

The porphyrias are a group of inherited disorders resulting from enzyme defects in the heme biosynthetic pathway. Depending on the specific enzyme involved, various porphyrins and their precursors accumulate in different specimen types. The patterns of porphyrin accumulation in erythrocytes and plasma and excretion of the heme precursors in urine and feces allow for the detection and differentiation of the porphyrias.(1)

The porphyrias are typically classified as erythropoietic or hepatic based upon the primary site of the enzyme defect. In addition, hepatic porphyrias can be further classified as acute hepatic or chronic cutaneous, based on their clinical presentation.(2)

The primary acute hepatic porphyrias: acute intermittent porphyria (AIP), hereditary coproporphyria (HCP), and variegate porphyria (VP), are associated with neurovisceral symptoms that typically onset during puberty or later. Common symptoms include severe abdominal pain, peripheral neuropathy, and psychiatric symptoms. A broad range of medications (including barbiturates and sulfa drugs), alcohol, infection, starvation, heavy metals, and hormonal changes may precipitate crises. Photosensitivity is not associated with AIP but may be present in HCP and VP. Aminolevulinic acid dehydratase deficiency porphyria (ADP) is a rare, autosomal recessive porphyria that has a variable age at presentation.(2,3)

Clinical manifestations of acute porphyria include attacks of neurologic dysfunction, commonly characterized as abdominal pain. However, these acute attacks are variable and can include vomiting, diarrhea, constipation, urinary retention, acute episodes of neuropathic symptoms, psychiatric symptoms, seizures, respiratory paralysis, tachycardia, and hypertension. Respiratory paralysis can progress to coma and death.

Hereditary coproporphyria and VP are also associated with cutaneous manifestations, including edema, sun-induced erythema, acute painful photodermatitis, and urticaria. In some cases, patients present with isolated photosensitivity.

Acute attacks may be prevented by avoiding both endogenous and exogenous triggers. These triggers include

porphyrogenic drugs, hormonal contraceptives, fasting, alcohol, tobacco, and cannabis.(1-3)

Acute hepatic porphyrias are caused by autosomal dominant variants in 1 of 3 genes: *HMBS*, associated with AIP; *CPOX*, associated with HCP; and *PPOX*, associated with VP. Variants in these genes show incomplete penetrance, and patients with a confirmed deleterious variant may be asymptomatic. ADP is inherited in an autosomal recessive manner, due to two disease-causing variants in *ALAD*.(2)

The recommended first-tier tests to screen for acute hepatic porphyria are quantitative urinary porphyrins analysis (PQNRU / Porphyrins, Quantitative, Random, Urine) and fecal porphyrins analysis (FQPPS / Porphyrins, Feces).

Cutaneous photosensitivity is associated with the chronic porphyrias: porphyria cutanea tarda (PCT) and the erythropoietic porphyrias; erythropoietic protoporphyria (EPP), X-linked protoporphyria (XLP), and congenital erythropoietic porphyria (CEP). Although genetic in nature, environmental factors may exacerbate symptoms, significantly impacting the severity and course of disease.

Congenital erythropoietic porphyria is an erythropoietic porphyria caused by uroporphyrinogen III synthase deficiency. Symptoms typically present in early infancy with red-brown staining of diapers, severe cutaneous photosensitivity with fluid-filled bullae and vesicles. Other common symptoms may include thickening of the skin, hypo- and hyperpigmentation, hypertrichosis, cutaneous scarring, and deformities of the fingers, eyelids, lips, nose, and ears. A few milder adult-onset cases have been documented as well as cases that are secondary to myeloid malignancies (sometimes referred to as erythropoietic uroporphyria).

Porphyria cutanea tarda is the most common form of porphyria and is most commonly sporadic (acquired), but approximately 25% of cases are inherited in an autosomal dominant manner. The most prominent clinical characteristics are cutaneous photosensitivity and scarring on sun-exposed surfaces. Patients experience chronic blistering lesions resulting from mild trauma to sun-exposed areas. These fluid-filled vesicles rupture easily, become crusted, and heal slowly. Secondary infections can cause areas of hypo- or hyperpigmentation or sclerodermatous changes and may result in the development of alopecia at sites of repeated skin damage. Liver disease is common in patients with PCT as evidenced by abnormal liver function tests and with 30% to 40% of patients developing cirrhosis. In addition, there is an increased risk of hepatocellular carcinoma.(5)

Hepatoerythropoietic porphyria (HEP) is observed when an individual inherits PCT from both parents. Patients exhibit a similar clinical presentation to what is seen in CEP.

The clinical presentation of EPP and XLP is identical with onset of symptoms typically occurring in childhood. Cutaneous photosensitivity in sun-exposed areas of the skin generally worsens in the spring and summer months. Common symptoms may include itching, edema, erythema, stinging or burning sensations, and occasionally scarring of the skin in sun-exposed areas.

Chronic porphyrias are caused by autosomal dominant disease-causing variants in *UROD* that are associated with inherited PCT or autosomal recessive variants in *UROD* that are associated with HEP. They are also due to autosomal recessive disease-causing variants in *UROS* or X-linked variants in *GATA1* that are associated with CEP, or autosomal recessive variants in *FECH* that are associated with EPP. In addition, autosomal dominant variants in *CLPX*, associated with EPP2, and X-linked variants in *ALAS2,* associated with XLP, are also causes of chronic porphyrias.(1,4)

A comprehensive gene panel is a helpful tool to establish a targeted diagnosis for patients with suggestive clinical and biochemical features of porphyria.

The recommended first-tier biochemical testing for patients with a suspected porphyria is most effective when following a stepwise approach.

The following algorithms are available:
-Porphyria (Acute) Testing Algorithm
-Porphyria (Cutaneous) Testing Algorithm

## Reference Values

An interpretive report will be provided.

## Interpretation

All detected alterations are evaluated according to American College of Medical Genetics and Genomics recommendations.(5) 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 at least one reportable variant in an affected family member would allow for more informative testing of at-risk individuals.

To discuss the availability of further 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.

Deletion/duplication events that extend past the genes included on the panel may occur. In these instances, genes included in the ordered test are provided on the report and interpreted, and genomic breakpoints are reported if they are confirmed. However, copy number variants for genes not listed in the Method Description are typically not reported or interpreted for haploinsufficiency/triplosensitivity. CMACB / Chromosomal Microarray, Congenital, Blood; WESPR / Panel to Whole Exome Sequencing Reflex Test, Varies; or WGSDX / Whole Genome Sequencing for Hereditary Disorders, Varies is recommended for a full interpretation of deletions/duplications predicted to extend past the genes included on the panel.

This test is not designed to detect low levels of mosaicism or to 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.

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. Due to broadening genetic knowledge, it is possible that the laboratory may discover new information of relevance to the patient. Should that occur, the laboratory may issue an amended report.

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.(1) 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.

Rarely, incidental or secondary findings may implicate another predisposition or presence of active disease. These findings will be carefully reviewed to determine whether they will be reported.

## Clinical Reference

1. Tortorelli S, White A, Raymond K. Disorders of porphyrin metabolism. In: Dietzen DJ, Wong ECC, Bennett MJ, Haymond S, eds. Biochemical and Molecular Basis of Pediatric Disease. 5th ed. AACC Press; 2020:chap 15
2. Siegesmund M, van Tuyll van Serooskerken AM, Poblete-Gutierrez P, Frank J. The acute hepatic porphyrias: current status and future challenges. Best Pract Res Clin Gastroenterol. 2010;24(5):593-605
3. Sardh E, Barbaro M. Acute intermittent porphyria. In: Adam MP, Feldman J, Mirzaa GM, et al, eds.. GeneReviews [Internet]. University of Washington, Seattle; 2005. Updated Feburary 8, 2024. Accessed November 18, 2025. Available at www.ncbi.nlm.nih.gov/books/NBK1193
4. Rudnick S, Phillips J, Bonkovsky H et. al. Familial porphyria cutanea tarda. In: Adam MP, Feldman J, Mirzaa GM, et al, eds.. GeneReviews [Internet]. University of Washington, Seattle; 2013. Updated June 9, 2024. Accessed November 18, 2025. Available at www.ncbi.nlm.nih.gov/books/NBK143129/
5. 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 to be over 99% for single nucleotide variants, over 94% for deletions-insertions (delins) less than 40 base pairs (bp), and over 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. See Targeted Genes and Methodology Details for Porphyria Comprehensive Gene Panel for details regarding the targeted genes analyzed and specific gene regions not routinely covered.(Unpublished Mayo method).

Genes analyzed: *ALAD, ALAS2, CLPX, CPOX, FECH, GATA1, HFE, HMBS, PPOX, UROD,* and *UROS.*

### PDF Report

No

### 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

81405
81406 x 2
81479
88233-Tissue culture, skin, solid tissue biopsy (if appropriate)
88240-Cryopreservation (if appropriate)
81479 (if appropriate for government payers)

### LOINC® Information

| Test ID | Test Order Name | Order LOINC® Value |
|---|---|---|
| PCGP | Porphyria Comprehensive Gene Panel | 105350-3 |

| Result ID | Test Result Name | Result LOINC® Value |
|---|---|---|
| 608680 | Test Description | 62364-5 |
| 608681 | Specimen | 31208-2 |
| 608682 | Source | 31208-2 |
| 608683 | Result Summary | 50397-9 |
| 608684 | Result | 82939-0 |
| 608685 | Interpretation | 69047-9 |
| 608686 | Resources | 99622-3 |
| 608687 | Additional Information | 48767-8 |
| 608688 | Method | 85069-3 |
| 608689 | Genes Analyzed | 48018-6 |
| 608690 | Disclaimer | 62364-5 |
| 608691 | Released By | 18771-6 |