Overview

Useful For
Genetic diagnosis of Birt-Hogg-Dube syndrome for clinical management, risk assessment for related clinical symptoms, and genetic counseling for family members

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/DNA Sequencing and Deletion Detection by Multiplex Ligation-Dependent Probe Amplification (MLPA)

NY State Available
Yes

Specimen

Specimen Type
Varies

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: Specimen preferred to arrive within 96 hours of collection.

Specimen Stability Information: Ambient (preferred)/Refrigerated

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 by Mayo Clinic Laboratories for test suitability.

**Specimen Stability Information**

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<th>Specimen Type</th>
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<th>Time</th>
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**Clinical and Interpretive**

**Clinical Information**

The clinical characteristics of Birt-Hogg-Dube syndrome (BHDS) include cutaneous manifestations (fibrofolliculomas, trichodiscomas/angiofibromas, perifollicular fibromas, and acrochordons), pulmonary cysts/history of pneumothorax, and various types of renal tumors. Skin lesions typically appear during the third and fourth decades of life and typically increase in size and number with age. Lung cysts are mostly bilateral and multifocal; most individuals are asymptomatic but have a high risk for spontaneous pneumothorax. Individuals with BHDS have an increased risk of renal tumors that are typically bilateral and multifocal and usually slow growing; median age of tumor diagnosis is 48 years with a range from 31 to 71 years. Some families have renal tumor and/or autosomal dominant spontaneous pneumothorax without cutaneous manifestations.

BHDS is inherited in an autosomal dominant manner and penetrance is considered to be very high. *FLCN* (also known as folliculin or *BHD*) is the only gene known to be associated with BHDS. Sequence analysis detects mutations in *FLCN* in 88% of affected individuals. Recent studies have reported that multi-exonic deletions can account for up to 5% to 10% of additional mutations.(2, 3)

Molecular genetic testing is indicated in all individuals known to have or suspected of having BHDS, including individuals with one of the following:

- Five or more facial or truncal papules with at least 1 histologically confirmed fibrofolliculoma, with or without a family history of BHDS
- Facial papules histologically confirmed to be angiofibroma in an individual who does not fit the clinical criteria of tuberous sclerosis complex (TSC) or multiple endocrine neoplasia type 1 (MEN1)
- Multiple and bilateral chromophobe, oncocytic, and/or hybrid renal tumors
- A single oncocytic, chromophobe, or oncocytic hybrid renal tumor and a family history of renal cancer with any of these renal cell tumor family history of renal cancer with any of the above renal cell tumor types

- A family history of autosomal dominant primary spontaneous pneumothorax without a history of smoking or chronic obstructive pulmonary disease (COPD)

In the absence of an increased risk of developing childhood malignancy, the American Society of Clinical Oncology (ASCO) recommends delaying genetic testing in at-risk individuals until they reach age 18 years and are able to make informed decisions regarding genetic testing.

Reference Values
An interpretive report will be provided.

Interpretation
All detected alterations will be evaluated according to American College of Medical Genetics and Genomics (ACMG) recommendations. Variants will be 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 Birt-Hogg-Dube syndrome may have a mutation that is not identified by this method (eg, deep intronic mutations, promoter mutations). The absence of a mutation, therefore, does not eliminate the possibility of a diagnosis of Birt-Hogg-Dube syndrome. For predictive testing of asymptomatic individuals, it is important to first document the presence of a FLCN gene mutation in an affected family member.

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

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

Rare polymorphisms 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.

Clinical Reference


Performance

Method Description
DNA sequencing is utilized to test for the presence of a mutation in all coding regions and intron/exon boundaries of the folliculin (FLCN) gene. Additionally, gene dosage analysis (MLPA) is used to test for the presence of large
deletions and duplications in this gene. (Unpublished Mayo method)

**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**

81479-Unlisted molecular pathology procedure code

**LOINC® Information**

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Test Definition: FLCNZ
FLCN Gene, Full Gene Analysis