

## Birt-Hogg-Dube Syndrome: *FLCN* Gene Deletion/Duplication

**Test Code:** VK

**Turnaround time:** 2 weeks

**CPT Codes:** 81228 x1

### Condition Description

Birt-Hogg-Dube syndrome (BHDS) is an autosomal dominant condition, the symptoms of which include hair follicle hamartomas, kidney tumors, and spontaneous pneumothorax. Individuals with BHDS usually present with multiple, small, skin-colored, dome-shaped papules distributed over the face, neck, and upper trunk. These cutaneous manifestations include fibrofolliculomas, trichodiscomas/angiofibromas, perifollicular fibromas, and acrochordons; only fibrofolliculomas, however, are specific for BHDS. Skin lesions typically first appear in early adulthood and increase in size and number with age. Renal tumors are typically bilateral, multifocal, and usually slow growing; median age of tumor diagnosis is 48 years. The most common renal tumors are renal hybrids of oncocytoma and chromophobe histologic cell types. Lung cysts are mostly bilateral and multifocal; most individuals are asymptomatic but have a high risk for spontaneous pneumothorax. Some families have renal tumor and/or autosomal dominant spontaneous pneumothorax without cutaneous manifestations. Disease severity can vary significantly even within the same family.

The *FLCN* gene (17p11.2) (also known as *BHD*) is the only gene known to be associated with BHDS. Sequence analysis detects mutations in *FLCN* in 88% of affected individuals; therefore, some affected individuals who fulfill clinical diagnostic criteria do not have an identifiable mutation. Molecular genetic testing is indicated in all individuals known to have or suspected of having BHDS, including individuals with one of the following:

- o Five or more facial or truncal papules with at least one histologically confirmed fibrofolliculoma, with or without a family history of BHDS
- o 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)
- o Multiple and bilateral chromophobe, oncocytic, and/or hybrid renal tumors
- o A single oncocytic, chromophobe, or oncocytic hybrid renal tumor and a family history of renal cancer with any of the above renal cell tumor types
- o A family history of autosomal dominant primary spontaneous pneumothorax without a history of smoking or COPD

The proportion of cases caused by *de novo* mutations is unknown because a sufficient number of parents have not been evaluated for subtle manifestation, nor are there sufficient data on clinically unaffected parents who have been evaluated by molecular genetic testing. Although some individuals diagnosed with BHDS have an affected parent, the family history may appear to be negative because of failure to recognize the disorder in family members, early death of the parent before the onset of symptoms, or late onset of the disease in the affected parent.

[Click here](#) for the GeneTests summary on this condition.

### Genes

#### [FLCN](#)

### Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of Birt-Hogg-Dube syndrome in individuals who have tested negative for sequence analysis
- Individuals at-risk for Birt-Hogg-Dube syndrome due to family history who have tested negative for sequence analysis

### Methodology

DNA isolated from peripheral blood is hybridized to a CGH array to detect deletions and duplications. The targeted CGH array has overlapping probes which cover the entire genomic region.

### Detection

Detection is limited to duplications and deletions. The CGH array will not detect point or intronic mutations. Results of molecular analysis must be interpreted in the context of the patient's clinical and/or biochemical phenotype.

### 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 24 hours of collection. Do not refrigerate or freeze.

**Type: DNA, Isolated****Specimen Requirements:**

Microtainer

3µg

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.

**Special Instructions**

Submit copies of diagnostic biochemical test results with the sample, if appropriate. Contact the laboratory if further information is needed.

Sequence analysis is required before deletion/duplication analysis by targeted CGH array. If sequencing is performed outside of EGL Genetics, please submit a copy of the sequencing report with the test requisition.

**Related Tests**

- Sequencing analysis of the *FLCN* gene is available (VJ) and is required before deletion/duplication analysis.
- Prenatal testing is available to individuals who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.