

## Medullary Cystic Kidney Disease 2: *UMOD* Gene Sequencing

**Test Code:** WH

**Turnaround time:** 4 weeks

**CPT Codes:** 81479 x1

### Condition Description

The spectrum of *UMOD*-related kidney disease (uromodulin-associated kidney disease) includes familial juvenile hyperuricemic nephropathy (FJHN) and medullary cystic kidney disease type 2 (MCKD2). Clinical findings typically include reduced fractional excretion of uric acid resulting in hyperuricemia and gout (or precocious gout); interstitial kidney disease usually appearing between ages 15 and 40 years and leading to end-stage renal disease (ESRD) ten to 20 years later; and normal or small-sized kidneys. Medullary cysts (i.e., in the medulla or at the corticomedullary junction) are a late finding and may not be seen on imaging because of their small size. The age at ESRD varies both between and within families.

*UMOD*-related kidney disease is defined by: the presence of a mutation in *UMOD*, the gene encoding uromodulin; increased Tamm-Horsfall protein (THP) immunostaining on renal biopsy; and decreased uromodulin urinary excretion. *UMOD* (16p12.3), which encodes uromodulin (Tamm-Horsfall glycoprotein, or THP), the most abundant urinary protein, is the only gene associated with *UMOD*-related kidney disease. Over 90% of families with *UMOD*-related kidney disease have been found to have mutations. Most individuals diagnosed with *UMOD*-related kidney disease have an affected parent.

Testing of the *UMOD* gene is appropriate for individuals who have hereditary kidney disease of unknown cause in which the urinary sediment shows no hematuria or proteinuria (especially those with a strong family history of gout) and for those who have interstitial kidney disease of unknown cause (especially young individuals with a history of precocious gout). *UMOD*-related kidney disease is rare, being responsible for fewer than 1% of cases of end-stage kidney disease. However, *UMOD*-related kidney disease has been chronically under-diagnosed and prevalence rates may be somewhat higher.

For patients with *UMOD*-related kidney disease, sequence analysis is recommended as the first step in mutation identification. For patients in whom mutations are not identified by full gene sequencing, deletion/duplication analysis is appropriate.

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

### Genes

[UMOD](#)

### Indications

This test is indicated for:

- Confirmation of a clinical/biochemical diagnosis of *UMOD*-related kidney disease
- Individuals at-risk for *UMOD*-related kidney disease due to family history.

### Methodology

PCR amplification of 11 exons contained in the *UMOD* 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 mutations, 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:** Over 90% of families with *UMOD*-related kidney disease have been found to have mutations. *UMOD*-related kidney disease is responsible for fewer than 1% of cases of end-stage kidney disease. Mutations in the promoter region, some mutations in the introns and other regulatory element mutations 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: 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.

**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.

**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**

- Deletion/duplication analysis of the *UMOD* gene by CGH array is available for those individuals in whom sequence analysis is negative (WI).
- [Custom diagnostic mutation analysis \(KM\)](#) is available to family members if mutations are identified by targeted mutation testing or sequencing 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.