**Medullary Cystic Kidney Disease 2: UMOD Gene Deletion/Duplication**

**Test Code:** WI  
**Turnaround time:** 2 weeks  
**CPT Codes:** 81228 x1

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**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 in individuals who have tested negative for sequence analysis
- Individuals at-risk for UMOD-related kidney disease 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.

Please note that a “backbone” of probes across the entire genome are included on the array for analytical and quality control purposes. Rarely, off-target copy number variants causative of disease may be identified that may or may not be related to the patient’s phenotype. Only known pathogenic off-target copy number variants will be reported. Off-target copy number variants of unknown clinical significance will not be reported.

**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

* Preferred specimen type: Whole Blood

**Type: Whole Blood**

Specimen Requirements:

In EDTA (purple top) or ACD (yellow top) tube:
Infants (2 years): 3-5 ml

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Older Children & Adults: 5-10 ml

Specimen Collection and Shipping: Refrigerate until time of shipment. Ship sample within 5 days of collection at room temperature with overnight delivery.

**Type: Saliva**

Specimen Requirements:

Oragene™ Saliva Collection kit (available through EGL) used according to manufacturer instructions.

Specimen Collection and Shipping: Store sample at room temperature. Ship sample within 5 days of collection 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 Emory Genetics Laboratory, please submit a copy of the sequencing report with the test requisition.

**Related Tests**

- Sequencing analysis of the *UMOD* gene is available (WH) 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.