Nephronophthisis: *NPHP1* Gene Deletion/Duplication

**Test Code:** WZ  
**Turnaround time:** 2 weeks  
**CPT Codes:** 81405 x1

### Condition Description

Nephronophthisis, an autosomal recessive cystic kidney disease, is the most frequent monogenic cause of renal failure in childhood. There are four forms of nephronophthisis caused by mutations in four different genes. Clinically, there is a statistically different age at onset at end-stage renal disease: terminal renal failure develops at median ages of 13 years, 1 year, 19 years, and 11-34 years in *NPHP1*, *NPHP2*, *NPHP3*, and *NPHP4* respectively. Hallmarks of familial nephronophthisis are tubular basement membrane disruption, interstitial lymphohistiocytic cell infiltration, and development of cysts at the corticomedullary border of the kidneys. The histology in later stages of NPH always merges into a chronic sclerosing tubulointerstitial nephropathy, which is found in chronic renal failure of all origins.

#### Nephronophthisis 1

Clinical features of familial juvenile nephronophthisis (NPHP1) include anemia, polyuria, polydipsia, isosthenuria, and death in uremia. Hypertension and proteinuria are conspicuous in their absence. Excessive urinary loss of sodium accounts for the rarity of hypertension. Symmetrical destruction of the kidneys involving both tubules and glomeruli (which were hyalinized) is observed. The age at death ranges from about 4 to 15 years. This is the second most common cause of childhood chronic renal failure. 65 to 75% of NPHP1 patients exhibit large homozygous deletions in the 2q13 region that includes the *NPHP1* gene.

Joubert syndrome is an autosomal recessive multisystem disease characterized by cerebellar vermis hypoplasia with prominent superior cerebellar peduncles (resulting in the ‘molar tooth sign,’ or MTS, on axial MRI), mental retardation, hypotonia, irregular breathing pattern, and eye movement abnormalities. Some individuals with JS have retinal dystrophy and/or progressive renal failure characterized as nephronophthisis. The disorder in such patients is referred to as cerebellooculorenal syndrome, or CORS. Individuals with a mild form of JS have been shown to have a homozygous deletion of the *NPHP1* gene identical, by mapping, to that in subjects with nephronophthisis alone. Senior-Loken syndrome, the association of nephronophthisis with autosomal recessive retinitis pigmentosa, has been observed in patients with homozygous deletion of the *NPHP1* gene.

Click here for the OMIM summary on this condition.

### Indications

This test is indicated for:
- Confirmation of a clinical/biochemical diagnosis of familial juvenile nephronophthisis
- Carrier testing in adults with a family history of familial juvenile nephronophthisis

### 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

Disclaimer: This information is confidential and subject to change without notice. It may not be reproduced in whole or part unless authorized in writing by an authorized EGL representative.
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
- 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**

Deletion/duplication analysis is recommended before sequence analysis.

**Related Tests**

- Custom diagnostic mutation analysis is available to family members if mutations are identified by targeted mutation testing or sequencing analysis.
- Prenatal testing is available to couples who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.