Nephronophthisis: INVS Gene Deletion/Duplication

**Test Code:** DINVS  
**Turnaround time:** 2 weeks  
**CPT Codes:** 81228 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 2**

In one study, individuals with infantile nephronophthisis (NPHP2) presented within the first months of life with severe renal failure and acidosis, which could be associated with hypertension and/or polyuria and/or severe cholestatic liver disease. A renal biopsy, performed in all patients, showed similar features characterized by a diffuse chronic tubulointerstitial nephritis and particularly by the presence of microcystic dilatation of proximal tubules and Bowman space. Progression of the renal disease was extremely rapid and patients can reach end-stage renal failure before the age of 2 years (11 to 22 months).

In another study, phenotypic presentation ranged from a Potter-like syndrome to hyperechogenic kidneys, renal insufficiency, hypertension, and hyperkalemia. Affected individuals showed rapid deterioration of kidney function, leading to end-stage renal failure within 3 years. The manifestations range from prenatal fetal oliguria and oligohydramnios resulting in postnatal respiratory failure and death to postnatal onset of disease later than 30 months of age. None of the postnatally diagnosed patients had a history of either oligohydramnios or neonatal respiratory symptoms. All affected individuals developed anemia, hyperkalemic metabolic acidosis, and increased serum creatine. None of the affected subjects had polyuria, polydypsia, or associated ocular or hepatic complications.

The specific clinical features of this disease are its early onset and rapid progression to end-stage renal failure. Pathologically, it differs from later-onset nephronophthisis by the absence of medullary cysts and thickened tubular basement membranes and by the presence of cortical microcysts. NPHP2 is caused by mutations in the *INVS* gene (also known as *NPHP2* (9q31)). The protein product of the *INVS* gene, inversion, has been shown to interact with that of the *NPHP1* gene, nephrocystin.

Click here for the OMIM summary on this condition.

### Genes

**INVS**

### Indications

This test is indicated for:

- Confirmation of a clinical/biochemical diagnosis of infantile nephronophthisis in individuals who have tested negative for sequence analysis
- Carrier testing in adults with a family history of infantile nephronophthisis 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
- 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 INVS gene is available and is required before deletion/duplication analysis.
- 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.