Nephronophthisis: \textit{NPHP4} Gene Sequencing

\textbf{Test Code: SNPH4}

\textbf{Turnaround time:} 4 weeks

\textbf{CPT Codes:} 81479 x1

\begin{table}[h]
\centering
\begin{tabular}{|c|c|}
\hline
\textbf{Condition Description} & \\
\hline
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. & \\
\hline
\begin{tabular}{l}
\textbf{Nephronophthisis 4} \\
Mutations in the \textit{NPHP4} gene (1p36) cause nephronophthisis 4 (NPHP4), which has also been referred to as juvenile nephronophthisis. In these families, end-stage renal disease commenced within a wide age range, 11 to 34 years. The NPHP4 protein has been shown to interact with the NPHP1 protein. Mutations in \textit{NPHP4} have been associated with Senior-Loken syndrome-4, the association of nephronophthisis with autosomal recessive retinitis pigmentosa.
\end{tabular} & \\
\hline
\begin{tabular}{l}
For patients with suspected juvenile nephronophthisis/NPHP4, 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. \textcolor{blue}{Click here} for the OMIM summary on this condition. \\
\textbf{Genes} & \\
\textit{NPHP4} & \\
\textbf{Indications} & \\
This test is indicated for: \\
\begin{itemize}
\item Confirmation of a clinical/biochemical diagnosis of juvenile nephronophthisis/NPHP4
\item Carrier testing in adults with a family history of juvenile nephronophthisis/NPHP4
\end{itemize} & \\
\textbf{Methodology} & \\
\textbf{Detection} & \\
Clinical Sensitivity: Unknown. 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: \textcolor{blue}{\sim 99\%} & \\
\textbf{Specimen Requirements} & \\
\textit{Submit only 1 of the following specimen types} & \\
\textbf{Type: Saliva} & \\
\textbf{Specimen Requirements:} & \\
Orangene™ Saliva Collection Kit \\
Orangene™ Saliva Collection Kit used according to manufacturer instructions. Please contact EGL for a Saliva Collection Kit for patients that cannot provide a blood sample. & \\
\textbf{Specimen Collection and Shipping:} & \\
Please do not refrigerate or freeze saliva sample. Please store and ship at room temperature. & \\
\textbf{Type: Whole Blood (EDTA)} & \\
\textbf{Specimen Requirements:} & \\
EDTA (Purple Top) & \\
\textbf{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. & \\
\end{tabular}
\end{table}
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 unclothed 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™ 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 NPHP4 genes by CGH array is available for those individuals in whom sequence analysis is negative.
- 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.