Steroid-Resistant Nephrotic Syndrome: Sequencing Panel

Test Code: MM620
Turnaround time: 6 weeks
CPT Codes: 81406 x1, 81404 x1, 81405 x1, 81407 x1

**Condition Description**

Nephrotic syndrome is a collection of signs and symptoms that occur when glomeruli (the filtering units of the kidneys) leak protein into the urine. Clinical findings include increased proteinuria, edema (swelling), hyperlipidemia, and hypoalbuminemia. Nephrotic syndrome is one of the most commonly diagnosed kidney diseases in childhood and can occur in adulthood. Every year, 2-4 out of every 100,000 children and 3 out of every 100,000 adults are diagnosed with primary nephrotic syndrome in North America.

Nephrotic syndrome can present as an isolated finding or in association with nephritis syndrome or another syndrome. Several diseases may cause nephrotic syndrome and prognosis varies depending on causation. Primary causes include minimal-change nephropathy, focal glomerulosclerosis, membranous nephropathy, and hereditary nephropathies. Secondary causes include diabetes mellitus, lupus erythematosus, viral infections, and preeclampsia. Progressive forms of nephrotic syndrome can lead to chronic kidney disease and/or end-stage renal disease.

Genetic disorders account for the majority of cases of nephrotic syndrome that begin within the first year of life and in childhood. Treatment may be available depending on causation of the syndrome, and/or underlying genetic defect. Identification of mutations may modify genetic counseling and recurrence risks after renal transplantation. Phenotypic variation has been demonstrated in patients with the same mutations and/or mutations within the same gene. When a hereditary disorder is suspected, age of onset, presence of extrarenal abnormalities, and type of renal histologic lesions should be considered to determine the appropriate gene(s) to test.

**References:**

2. Medscape (Pediatric Nephrotic Syndrome and Nephrotic Syndrome)

**Genes**

ACTN4, ARHGDIA, CD2AP, CFH, COL4A3, COL4A4, COL4A5, COQ2, COQ6, COQ8B, CRB2, CUBN, DGKE, EMP2, INF2, ITGA3, ITGB4, KANK1, KANK2, LAMB2, LMX1B, MEFV, MYO1E, NEIL1, NPHS1, NPHS2, NUP107, NXF5, OCRL, PA2X, PDSS2, PLCG1, PPM1D, PTPRO, SCARB2, SMARCD1, TRPC6, TTC21B, WDR73, WT1

**Indications**

The test is indicated for:

- Individuals with a clinical diagnosis of nephrotic syndrome.

**Methodology**

**Next Generation Sequencing:** In-solution hybridization of all coding exons is performed on the patient's genomic DNA. Although some deep intronic regions may also be analyzed, this assay is not meant to interrogate most promoter regions, deep intronic regions, or other regulatory elements, and does not detect single or multi-exon deletions or duplications. Direct sequencing of the captured regions is performed using next generation sequencing. The patient's gene sequences are then compared to a standard reference sequence. Potentially causative variants and areas of low coverage are Sanger-sequenced. Sequence variations are classified as pathogenic, likely pathogenic, benign, likely benign, or variants of unknown significance. Variants of unknown significance may require further studies of the patient and/or family members.

Due to pseudogenes, exons 8-10 and exons 20-22 of the \( CFH \) gene and exons 41-50 and exons 63-67 of the \( CUBN \) gene cannot be analyzed at this time.

**Detection**

**Next Generation Sequencing:** 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/duplications will not be detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient’s clinical/biochemical phenotype.

Analytical Sensitivity: ~99%.

**Specimen Requirements**
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 24 hours of collection. Do not refrigerate or freeze.

Type: DNA, Isolated

Specimen Requirements:
Microtainer
15µg
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.