Ciliopathies: Sequencing Panel

**Condition Description**

The ciliopathies are a group of disorders caused by mutations in genes that encode proteins involved in the formation and function of cilia. Cilia are microtubule-based, hair-like cytoplasmic extensions that extend from the cell surface. The cilium is a highly conserved organelle that is structurally complex with approximately 1000 different recognized polypeptides.

Cilia can be classified as either motile cilia or primary cilia (often called sensory cilia). Motile cilia, sometimes referred to as flagella, are typically found on epithelia cells that line the brain ventricles, oviducts, and respiratory tract. They can appear in bundles of 200-300 and can create movement of the extracellular fluid. Primary cilia are found on the surface of almost all cell types. They sense a wide variety of extracellular signals and transmit them to the interior of the cell. They are critical for developmental and physiological functions. Recent research suggests that motile cilia can be chemosensory as well.

Cilia are a component of almost all cells, so defects in the cilium can lead to conditions that have features involving multiple organ systems, such as renal disease, cerebral anomalies, and retinal degeneration. Additional features include diabetes, skeletal dysplasia, obesity, and congenital fibroptic dyscytotic diseases of the pancreas and liver; however, the specific phenotype depends on the specific cilia involved.

Diseases tested by the panel include primary ciliary dyskinesia, nephronphthisis, Senior-Loken syndrome, Leber congenital amaurosis, Meckel-Gruber syndrome, Joubert and related syndromes, Bardet-Biedl syndrome, and many others. Please refer to the below list for all genes on the ciliopathies panel.

**Genes**

\[ \text{ACVR2B, ADGRV1, AHI1, APL1, ARL13B, ARL5, ATXN10, B9D1, B9D2, BBS1, BBS10, BBS12, BBS2, BBS4, BBS5, BBS7, BBS9, CC2D2A, } \\
\text{CCDC28B, CCDC39, CCDC40, CDH23, CEP164, CEP290, CEP41, CFTR, CLRN1, CPLANE1, CRB1, CRELD1, CRX, DNAF1, DNAF2, DNAF3, } \\
\text{DNAH11, DNAH5, DNAI1, DNAI2, DNAI1, DYNC2H1, EVC, EVC2, FOXH1, GDF1, GLIS2, GUCY2D, HYS1, IFT43, IFT30, IMDH1, INVS, IQCB1, } \\
\text{KCNJ13, KIF7, LCAS, LEFTY2, LRAT, MKKS, MKS1, MYO7A, NEK1, NEK8, NKO2, SNE, NODAL, NPHP1, NPHP3, NPHP4, ODF1, PCARE, } \\
\text{PCDH15, PKD2, PKHD1, RCSD1, RPE65, RPR5, RPRGRIP1, RPRGRIP1L, RSPH4A, RSPH9, SCNN1A, SCNN1A, SCNN1B, } \\
\text{SCNN1G, SDCCAG8, SPATA7, TCTN1, TCTN2, TMEM138, TMEM216, TMEM230, TMEM237, TMEM237, TMEM67, TOPOPS, TRIM32, TSC1, } \\
\text{TSC2, TTC21B, TTC8, TULP1, UMOD, USH1C, USH1G, USH2A, VHL, WDPCP, WDR19, WDR35, WHRN, XPNP0P3, ZIC3, ZNF423} \]

**Indications**

This test is indicated for:

- Individuals with a suspected ciliopathy.

**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 more 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.

**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**

Submit only 1 of the following specimen types

**Type:** Whole Blood

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.
Specimen Requirements:

In EDTA (purple top) tube:
Infants (2 years): 3-5 ml
Older Children & Adults: 5-10 ml.

Specimen Collection and Shipping: Ship sample at room temperature with overnight delivery.

**Type: Isolated DNA**

Specimen Requirements:

In microtainer: 60 ug

Isolation using the Qiagen™ Puregene kit for DNA extraction is recommended.

Specimen Collection and Shipping: Refrigerate until time of shipment in 100 ng/μl of TE buffer. Ship sample at room temperature with overnight delivery.

**Related Tests**

- Individual gene sequencing and deletion/duplication analysis is available for some genes on this panel.
- A comprehensive Eye Disorders Panel is also available.
- Custom diagnostic mutation analysis (KM) is available to family members if mutations are identified by targeted mutation testing or sequencing analysis.
- Ciliopathies: Deletion/Duplication Panel.