

Kartagener’s Syndrome or Heterotaxy with Chronic Respiratory Infections Gene Sequencing Panel – Test #745

Brief Description of Clinical Features: Primary Ciliary Dyskinesia (PCD; OMIM 244400) is a genetically heterogeneous disorder affecting the function of motile cilia (reviewed by Leigh et al. *Genetics in Medicine* 11:473-487, 2009). The hallmark features of PCD are neonatal respiratory distress, chronic coughing, and recurrent sinus and/or ear infections; 80-100% of all PCD patients have one or more of these symptoms. In 20-50% of individuals with PCD, the major visceral organs are reversed from their normal positions (also called *situs inversus*) (reviewed in Sutherland and Ware, *Am J Med Genet Part C Semin Med Genet* 151C:307-317, 2009). Kartagener’s syndrome is a condition defined by the symptomatic triad of situs inversus, sinusitis and bronchiectasis. Patients with PCD can also have abnormal orientation of some organs but not others (a condition called situs ambiguus or heterotaxy) (Kennedy et al. *Circulation* 115:2814-2821, 2007). Prompt diagnosis of PCD in patients with laterality defects is critical for the prevention of secondary respiratory complications, such as bronchiectasis, pneumonia and/or progressive loss of lung function.

Genetics: To date, recessive mutations in one of 9 genes (see table below) have been found to cause laterality defects (i.e. situs inversus or heterotaxy) in patients with PCD (Frischer et al. *Eur Respir J* 34:1264-1276, 2009; Merveille et al. *Nat Genet* 43:72-78, 2011; Becker-Heck et al. *Nat Genet* 43:79-84, 2011). This panel tests all known genes responsible for either Kartagener’s Syndrome or Heterotaxy with chronic airway infections in the most cost effective manner possible. Each test can also be ordered separately as well (see individual test descriptions on our website).

Description of This Particular Test: This test involves bidirectional DNA sequencing of the genes listed below, plus ~50 bp of flanking non-coding DNA on either side of each exon. Sequencing of each gene is performed in the order listed in the table, unless otherwise specified by the client. We will test each gene sequentially until a likely causative mutation is found.

Gene	Disease/Symptoms	NC_Ref_Seq	NM_Ref_Seq	NP_Ref_Seq	CCDS
<i>DNAH5</i>	PCD, KS	000005.9	001369.2	001360.1	3882.1
<i>DNAI1</i>	PCD, KS	000009.11	012144.2	036276.1	6557.1
<i>CCDC39</i>	PCD, KS, HT	000003.11	181426.1	852091.1	46964.1
<i>CCDC40</i>	PCD, KS, HT	000017.10	017950.2	060420.2	42395.1
<i>DNAI2</i>	PCD, KS	000017.10	023036.4	075462.3	11697.1
<i>DNAH11</i>	PCD, KS	000007.13	003777.3	003768.2	NA
<i>KTU/C14orf104</i>	PCD, KS	000014.8	018139.2	060609.2	9691.2
<i>LRRC50</i>	PCD, KS	000016.9	178452.4	848547.4	10943.2
<i>TXNDC3</i>	PCD, KS	000007.13	016616.3	057700.3	5452.1

Indications for Test: Candidates for this panel test are patients with Kartagener’s Syndrome (situs inversus, sinusitis, bronchiectasis) or Heterotaxy (situs ambiguus) and chronic upper and lower airway infections.

Sensitivity of Test: The overall sensitivity of this panel test is predicted to be ~80-90% for patients with Kartagener’s Syndrome. The sensitivity for patients with Heterotaxy is currently unknown.

Turnaround Time: Maximum of 100 calendar days.

Specimen Requirements: See page 4 of Requisition Form.

Prices (\$): Total Panel (if all 9 genes are tested) = \$11,050

CPT Codes	<i>DNAH5</i> Tier 1	+ <i>DNAH5</i> Tier 2	+ <i>DNAI1</i>	+ <i>CCDC39</i>	+ <i>CCDC40</i>	+ <i>DNAI2</i>	+ <i>DNAH11</i>	+ <i>KTU</i>	+ <i>LRRC50</i>	+ <i>TXNDC3</i>
83890	30	30	30	30	30	30	30	30	30	30
83891	40	40	40	40	40	40	40	40	40	40
83898	120	1150	1500	1840	2210	2250	3250	3460	3700	3960
83904	180	1720	2260	2740	3270	3430	4820	5140	5510	5890
83894	30	220	280	340	400	440	610	640	680	720
83912	90	190	230	260	290	320	350	370	390	410
Totals	\$490	\$3350	\$4340	\$5250	\$6240	\$6510*	\$9100*	\$9680*	\$10,350*	\$11,050*

* These prices reflect a 15% discount when 5 or more of the genes are tested.

Accreditation: CLIA ID:52D1027685 (expires 1/18/13) CAP ID:7185561, AU ID:1407125 (expires 12/20/12)

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