Primary Ciliary Dyskinesia Panel

Primary ciliary dyskinesia (PCD), also known as Kartagener syndrome, is a rare inherited condition that results from an underlying defect in the structure or function of motile cilia, impacting multiple body systems. Patients with PCD typically first present with neonatal respiratory distress, chronic oto-sinopulmonary disease, and year-round wet coughing. Chronic airway infection in patients with PCD often leads to bronchiectasis and obstructive lung disease, and hearing loss (either transient or permanent) can result from recurrent ear infection. Approximately half of patients with PCD will have a laterality defect such as situs inversus totalis or heterotaxy (see Heterotaxy and Situs Inversus Panel Test Fact Sheet). PCD is also associated with infertility and ectopic pregnancy due to ciliary dysfunction.

Tests to Consider

Primary Ciliary Dyskinesia Panel, Sequencing 3001621

Method: Massively Parallel Sequencing

- Use to detect variants in genes related to primary ciliary dyskinesia, which can present with laterality defects such as situs inversus or heterotaxy as well as pulmonary disease.
- Regions of low coverage and reported variants are confirmed by Sanger sequencing as necessary.

See Related Tests.

Disease Overview

Prevalence

Approximately 1 in 16,000

Genetics

Etiology

Pathogenic variants in genes related to structure and function of the motile cilia

Penetrance

100%

Inheritance

Autosomal recessive; rare X-linked recessive forms have been reported

Test Interpretation

Clinical Sensitivity

Variable; dependent on phenotype/condition

Analytical Sensitivity

For massively parallel sequencing:

Variant Class	Analytical Sensitivity (PPA) Estimate[a] (%)	Analytical Sensitivity (PPA) 95% Credibility Region[a] (%)
SNVs	99.2	96.9-99.4

[a]Genes included on this test are a subset of a larger methods-based validation from which the PPA values are derived.

bp, base pairs; PPA, positive percent agreement; SNVs, single nucleotide variants

Variant Class	Analytical Sensitivity (PPA) Estimate[a] (%)	Analytical Sensitivity (PPA) 95% Credibility Region[a] (%)
Deletions 1-10 bp	93.8	84.3-98.2
Deletions 11-44 bp	99.9	87.8-100
Insertions 1-10 bp	94.8	86.8-98.5
Insertions 11-23 bp	99.9	62.1-100

[a]Genes included on this test are a subset of a larger methods-based validation from which the PPA values are derived.

bp, base pairs; PPA, positive percent agreement; SNVs, single nucleotide variants

Limitations

- A negative result does not exclude a diagnosis of primary ciliary dyskinesia.
- Diagnostic errors can occur due to rare sequence variations.
- Interpretation of this test result may be impacted if this patient has had an allogeneic stem cell transplantation.
- The following will not be evaluated:
  - Variants outside the coding regions and intron-exon boundaries of targeted genes
  - Regulatory region and deep intronic variants
  - Noncoding transcripts
  - The following exons are not sequenced due to technical limitations of the assay:
    - ARMC4(NM_001290020) exon 9
    - ARMC4(NM_001290021) exon 13
    - ARMC4(NM_001312689) exon 4
    - ARMC4(NM_018076) exon 9
    - CCDC103(NM_001258397) exon 4
    - CCDC114(NM_001364171) exon 3
    - CCDC114(NM_001364171) partial exon 4(Chr19:48822049-48822069)
    - CCDC40(NM_001243342) exon 18
    - CFAP298(NM_001350335) partial exon 5(Chr21:33975399-33975450)
    - CFAP298(NM_001350337) partial exon 6(Chr21:33974534-33974561)
    - DNAAF5(NM_017802) exon 1
    - DNAI2(NM_001353167) exon 13
    - SPAG1(NM_001374321) partial exon 11(Chr8:101225456-101225529)
    - SPAG1(NM_003114) partial exon 11(Chr8:101225456-101225529)
    - SPAG1(NM_172218) partial exon 11(Chr8:101225456-101225529)
- The following may not be detected:
  - Deletions/duplications/insertions of any size by massively parallel sequencing
  - Some variants due to technical limitations in the presence of pseudogenes, repetitive, or homologous regions
  - Low-level somatic variants

Genes Tested

Gene Name	MIM #	Associated Disorder	Inheritance Pattern
ARMC4	615408	PCD	AR
CCDC103	614677	PCD	AR
CCDC114	615038	PCD	AR
CCDC151	615956	PCD	AR

AR, autosomal recessive; XLR, X-linked recessive

Gene Name	MIM #	Associated Disorder	Inheritance Pattern
CCDC39	613798	PCD	AR
CCDC40	613799	PCD	AR
CCDC65	611088	PCD	AR
CCNO	607752	PCD	AR
CFAP298	615494	PCD	AR
DNAAF1	613190	PCD	AR
DNAAF2	612517	PCD	AR
DNAAF3	614566	PCD	AR
DNAAF4	608706	PCD	AR
DNAAF5	614864	PCD	AR
DNAH1	603332	PCD	AR
DNAH11	603339	PCD	AR
DNAH5	603335	PCD	AR
DNAI1	604366	PCD	AR
DNAI2	605483	PCD	AR
DNAL1	610062	PCD	AR
DRC1	615288	PCD	AR
GAS8	605178	PCD	AR
LRRC6	614930	PCD	AR
MCIDAS	614086	PCD	AR
NME8	607421	PCD	AR
PIH1D3	300933	PCD	XLR
RSPH1	609314	PCD	AR
RSPH3	615876	PCD	AR
RSPH4A	612647	PCD	AR
RSPH9	612648	PCD	AR

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Gene Name	MIM #	Associated Disorder	Inheritance Pattern
SPAG1	603395	PCD	AR
ZMYND10	607070	PCD	AR

AR, autosomal recessive; XLR, X-linked recessive

Additional Resources

Knowles MR, Daniels LA, Davis SD, et al. Primary ciliary dyskinesia. Recent advances in diagnostics, genetics, and characterization of clinical disease. Am J Respir Crit Care Med. 2013;188(8):913-922.

Shapiro AJ, Davis SD, Polineni D, et al. Diagnosis of primary ciliary dyskinesia. an official American Thoracic Society Clinical Practice guideline. Am J Respir Crit Care Med. 2018;197(12):e24-e39.

Related Information

Heterotaxy and Situs Inversus Panel

Related Tests

Heterotaxy & Situs Inversus Panel, Sequencing 3002682

Method: Massively Parallel Sequencing

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