

## Epidemiology of rare paediatric respiratory diseases

### Paediatric respiratory epidemiology

#### **PA-67581 - Evaluating gene-disease relationships in motile ciliopathies: an international ClinGen and BEAT-PCD ERS CRC collaboration.**

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Genetic diagnosis of motile ciliopathies is conducted by healthcare, commercial and private laboratories. 88 genes have been implicated in

motile ciliopathies (PCD, male infertility and associated disorders). Gene-disease relationships are uncertain where evidence is limited, risking inaccurate reporting and diagnosis.

The ClinGen Motile Ciliopathy Gene Curation Expert Panel (GCEP) was set up collaboratively with BEAT-PCD ERS CRC in 2021. The GCEP comprises geneticists, pulmonologists and biocurators (Canada, France, Germany, Norway, Poland, Spain, Tunisia, UK, USA) tasked with classifying clinical validity of gene-disease relationships in motile ciliopathies to aid interpretation of genetic results. As an early step, the GCEP drew up guidelines to capture the critical details of motile ciliopathy cases and to score genetic and experimental evidence conservatively and consistently. The GCEP meets monthly and so far has curated 33 gene-disease relationships (<https://clinicalgenome.org/affiliation/40102/>). 22 curations have reached a definitive classification as the role of the gene in disease has been repeatedly demonstrated and upheld over time, 4 were disputed.

Classification	PCD	Infertility
Definitive	CCDC39 CCDC40 CCDC103 CCNO CFAP300 DNAAF3 DNAH11 DNAH5 DNAI1 DNAI2 HYDIN MCIDAS ODAD1 ODAD2 ODAD4 RSPH1 RSPH4A SPAG1 ZMYND10	CFAP43 DNAH1 DNAH17
Strong	FOXJ1	DNAH8
Limited	CFAP57 DNAH1 DNAL1 GAS2L2	CFAP47

These efforts provide a basis for future classifications of gene-disease relationships. The goal of the GCEP is to leverage emerging research to enhance the reliability of genetic testing for improved clinical detection and diagnosis of motile ciliopathies.

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