Figure S1: **Examples of ciliary ultrastructure for the five main ultrastructural phenotypes of PCD**, as shown by transmission electron microscopy. A: combined outer and inner dynein arm defect (2DA group). B: outer dynein arm defect (ODA group). C: inner dynein arm defect with microtubular disorganization (IDA/MTD group). D: central complex defect (CC group). E: no detectable ultrastructural defect (nEM group). Scale bar: 0.1µm.

Table S2: **Ciliary beating analysis in a disease control group** (n=15), previously published by Papon et al.[25] Results are presented either as median [range] regarding data analyzed per patient (i.e. percentage of beating cilia, qualitative evaluation and maximal ciliary beat frequency (CBF)), or as mean (standard error) regarding data analyzed per cilia after pooling all cilia (i.e. quantitative analysis).

| | | |
|---|---|---|
| **Percentage of beating cilia** *median [range]* | 95% | [75-100] |
| **Qualitative evaluation** *median [range]* | | |
| Normal beating | 90% | [75-100] |
| Virtually immotile cilia | 0% | [0-20] |
| Stiff beating with reduced amplitude | 5% | [0-25] |
| Circular gyrating motion | 0% | [0-0] |
| **Maximal CBF (Hz)** *median [range]* | 13.16 | [8.93-18.18] |
| **Quantitative analysis** *mean (standard error)* | | |
| Beat frequency (Hz) | 8.83 | (0.26) |
| Power stroke duration (s) | 0.036 | (0.001) |
| Recovery stroke duration (s) | 0.046 | (0.002) |
| Total pause (s) | 0.049 | (0.003) |
| Pause after stroke (s) | 0.037 | (0.003) |
| Pause after recovery (s) | 0.013 | (0.001) |
| Angle (°) | 72.23 | (1.53) |
| Distance/beat (µm) | 7.62 | (0.19) |
| Area/beat (µm²) | 23.74 | (0.85) |
| Distance/second (µm) | 66.99 | (2.57) |
| Area/second (µm²) | 209.71 | (10.12) |
| Weighted distance/second (µm) | 60.80 | (2.49) |

Table S3: **Detailed genotypes of the 72 patients with available DNA**. Pathogenic classification refers to ACMG standards and guidelines.[30]

| Phenotypic group | Patient | Gene | Allele 1 | Allele 2 | Variation type (pathogenic classification) | | Potential production of full-length protein |
|---|---|---|---|---|---|---|---|
| | | | | | Allele 1 | Allele 2 | |
| **2DA** | DCP1534 | *DNAAF1* | **c.280C>T, p.(Gln94*)** | **c.280C>T, p.(Gln94*)** | nonsense (5) | nonsense (5) | N |
| | DCP818 | *DNAAF1* | **c.508_509ins321,p.(Glu170Glyfs*32)** | **c.508_509ins321, p.(Glu170Glyfs*32)** | frameshift (5) | frameshift (5) | N |
| | DCP1580 | *DNAAF1* | **c.1022_1023del, p.(Gln344Argfs*10)** | **c.1022_1023del, p.(Gln344Argfs*10)** | frameshift (5) | frameshift (5) | N |
| | DCP1284 | *ZMYND10* | c.47T>G, p.(Val16Gly) | **c.934_935del, p.(Ser312Phefs*9)** | missense (4) | frameshift (5) | Y |
| | DCP1285 | *ZMYND10* | c.47T>G, p.(Val16Gly) | **c.934_935del, p.(Ser312Phefs*9)** | missense (4) | frameshift (5) | Y |
| | DCP841 | *ZMYND10* | c.1038_1039del, p.(Gly347Glnfs*30) | c.1038_1039del, p.(Gly347Glnfs*30) | frameshift (5) | frameshift (5) | N |
| | DCP181 | *LRRC6* | c.574C>T, p.(Gln192*) | c.576dup, p.(Glu192Argfs*4) | nonsense (5) | frameshift (5) | N |
| | DCP1499 | *LRRC6* | c.630del, p.(Trp210Cysfs*12) | c.630del, p.(Trp210Cysfs*12) | frameshift (5) | frameshift (5) | N |
| | DCP855 | *PIH1D3*† | arr[hg19]Xq22.2q22.3(103,077,143-106,814,443)X0 | - | whole gene deletion (5) | - | N |
| | DCP894 | *PIH1D3*† | c.263_268delinsG, p.(Ile88Argfs*12) | - | frameshift (5) | - | N |
| | DCP998 | *CCDC114* | **c.337C>T, p.(Arg113*)** | **c.337C>T, p.(Arg113*)** | nonsense (5) | nonsense (5) | N |
| | DCP1172 | *CCDC114* | **c.337C>T, p.(Arg113*)** | **c.337C>T, p.(Arg113*)** | nonsense (5) | nonsense (5) | N |
| | DCP1275 | *DNAAF2* | **c.564dup, p.(Lys189Glufs*5)** | **c.564dup, p.(Lys189Glufs*5)** | frameshift (5) | frameshift (5) | N |
| | DCP1308 | *DNAAF3* | **c.896A>G, p.(Asn299Ser)** | c.896A>G, p.(Asn299Ser) | missense (3) | missense (3) | Y |
| | DCP1413 | *DYX1C1* | **c.(-256+1_-255-1)_(271+1_272-1), p.?** | **c.(-256+1_-255-1)_(271+1_272-1), p.?** | deletion (5) | deletion (5) | N |
| **ODA** | DCP188 | *DNAI1* | c.48+2dup, p.(Ser17Valfs*9) | c.48+2dup, p.(Ser17Valfs*9) | splice (5) | splice (5) | N |
| | DCP761 | *DNAI1* | c.48+2dup, p.(Ser17Valfs*9) | c.48+2dup, p.(Ser17Valfs*9) | splice (5) | splice (5) | N |
| | DCP1315 | *DNAI1* | **c.180G>A, p.?** | **c.885_886dup, p.(Asp296Valfs*64)** | splice (5) | frameshift (5) | Y‡ |
| | DCP498 | *DNAI1* | **c.735dup, p.(Glu246Argfs*11)** | **c.735dup, p.(Glu246Argfs*11)** | frameshift (5) | frameshift (5) | N |
| | DCP368 | *DNAI1* | c.1019+5G>C, p.(Asp301Glyfs*19) | c.1019+5G>C, p.(Asp301Glyfs*19) | splice (5) | splice (5) | Y§ |
| | DCP369 | *DNAI1* | c.1019+5G>C, p.(Asp301Glyfs*19) | c.1019+5G>C, p.(Asp301Glyfs*19) | splice (5) | splice (5) | Y§ |
| | DCP617 | *DNAI1* | c.1019+5G>C, p.(Asp301Glyfs*19) | c.1019+5G>C, p.(Asp301Glyfs*19) | splice (5) | splice (5) | Y§ |
| | DCP898 | *DNAI1* | c.1019+5G>C, p.(Asp301Glyfs*19) | c.1019+5G>C, p.(Asp301Glyfs*19) | splice (5) | splice (5) | Y§ |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | DCP1212 | *DNAH5* | **c.2710G>T, p.(Glu904*)** | **c.9106-1G>A, p.?** | nonsense (5) | splice (5) | N |
| | DCP1166 | *DNAH5* | c.5563dup, p.(Ile1855Asnfs*6) | c.5563dup, p.(Ile1855Asnfs*6) | frameshift (5) | frameshift (5) | N |
| | DCP268 | *DNAH5* | **c.7753-2A>G, p.?** | **c.7753-2A>G, p.?** | splice (5) | splice (5) | N |
| | DCP1240 | *DNAH5* | **c.7753-1G>T, p.?** | c.13486C>T, p.(Arg4496*) | splice (5) | nonsense (5) | N |
| | DCP154 | *DNAH5* | **c.8311C>T, p.(Arg2771Cys)** | **c.11589dup, p.(Thr3864Tyrfs*7)** | missense (4) | frameshift (5) | Y |
| | DCP486 | *DNAH5* | **c.10815del, p.(Pro3606Hisfs*23)** | c.13486C>T, p.(Arg4496*) | frameshift (5) | nonsense (5) | N |
| **IDA/MTD** | DCP1390 | *CCDC39* | c.357+1G>C, p.? | c.2190del, p.(Glu731Asnfs*31) | splice (5) | frameshift (5) | N |
| | DCP1391 | *CCDC39* | c.357+1G>C, p.? | c.2190del, p.(Glu731Asnfs*31) | splice (5) | frameshift (5) | N |
| | DCP692 | *CCDC39* | c.610-2A>G, p.? | c.2483_2484del, p.(Leu828Profs*2) | splice (5) | frameshift (5) | N |
| | DCP554 | *CCDC39* | c.1072del, p.(Thr358Glnfs*3) | c.1072del, p.(Thr358Glnfs*3) | frameshift (5) | frameshift (5) | N |
| | DCP181 | *CCDC39* | c.1714C>T, p.(Arg562*) | c.1714C>T, p.(Arg562*) | nonsense (5) | nonsense (5) | N |
| | DCP1059 | *CCDC39* | **c.1939_1940del, p.(Val647Cysfs*6)** | **c.1939_1940del, p.(Val647Cysfs*6)** | frameshift (5) | frameshift (5) | N |
| | DCP863 | *CCDC39* | c.2190del, p.(Glu731Asnfs*31) | c.2190del, p.(Glu731Asnfs*31) | frameshift (5) | frameshift (5) | N |
| | DCP1156 | *CCDC39* | c.2190del, p.(Glu731Asnfs*31) | c.2190del, p.(Glu731Asnfs*31) | frameshift (5) | frameshift (5) | N |
| | DCP1540 | *CCDC39* | c.2190del, p.(Glu731Asnfs*31) | c.2190del, p.(Glu731Asnfs*31) | frameshift (5) | frameshift (5) | N |
| | DCP1245 | *CCDC39* | c.2347_2351del, p.(Phe783Thrfs*3) | c.2347_2351del, p.(Phe783Thrfs*3) | frameshift (5) | frameshift (5) | N |
| | DCP903 | *CCDC40* | c.248del, p.(Ala83Valfs*84) | c.2824_2825insCTGT, p.(Arg942Thrfs*57) | frameshift (5) | frameshift (5) | N |
| | DCP1068 | *CCDC40* | **c.2711+24C>G, p.?** | **c.2712-1G>T, p.?** | splice (5) | splice (5) | Y‖ |
| | DCP128 | *CCDC40* | c.3097A>T, p.(Lys1033*) | c.3097A>T, p.(Lys1033*) | nonsense (5) | nonsense (5) | N |
| **CC** | DCP729 | *RSPH1* | c.85G>T, p.(Glu29*) | c.308G>A, p.(Gly103Asp) | nonsense (5) | missense (4) | Y |
| | DCP1064 | *RSPH1* | c.85G>T, p.(Glu29*) | c.366G>A, p.(Arg122=) | nonsense (5) | splice (5) | Y |
| | DCP1057 | *RSPH1* | c.275-2A>C, p.? | c.727+5G>A, p.? | splice (5) | splice (5) | Y†† |
| | DCP1153 | *RSPH1* | c.275-2A>C, p.? | c.275-2A>C, p.? | splice (5) | splice (5) | Y†† |
| | DCP1154 | *RSPH1* | c.275-2A>C, p.? | c.275-2A>C, p.? | splice (5) | splice (5) | Y†† |
| | DCP781 | *RSPH1* | c.366-3C>A, p.? | c.407_410del, p.(Lys136Metfs*6) | splice (5) | frameshift (5) | Y |
| | DCP1276 | *RSPH9* | **c.19del, p.(Leu7Cysfs*57)** | **c.19del, p.(Leu7Cysfs*57)** | frameshift (5) | frameshift (5) | N |
| | DCP518 | *RSPH9* | c.52C>T, p.(Gln18*) | c.52C>T, p.(Gln18*) | nonsense (5) | nonsense (5) | N |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | DCP519 | *RSPH9* | c.52C>T, p.(Gln18*) | c.52C>T, p.(Gln18*) | nonsense (5) | nonsense (5) | N |
| | DCP1280 | *RSPH9* | c.804_806del, p.(Lys268del) | c.804_806del, p.(Lys268del) | amino acid deletion (5) | amino acid deletion (5) | Y |
| | DCP812 | *DNAJB13* | c.833T>G, p.(Met278Arg) | c.833T>G, p.(Met278Arg) | missense (5) | missense (5) | N |
| | DCP813 | *DNAJB13* | c.833T>G, p.(Met278Arg) | c.833T>G, p.(Met278Arg) | missense (5) | missense (5) | N |
| | DCP837 | *HYDIN* | **c.1330C>T, p.(Arg444*)** | **c.1330C>T, p.(Arg444*)** | nonsense (5) | nonsense (5) | N |
| | DCP358 | NI | - | - | - | - | - |
| | DCP501 | NI | - | - | - | - | - |
| **nEM** | DCP1106 | *DNAH11* | **c.496-2A>G, p.?** | **c.5845C>T, p.(Arg1949*)** | splice (5) | nonsense (5) | N |
| | DCP505 | *DNAH11* | **c.1145C>G, p.(Ala382Gly)** | **c.5692G>A, p.(Gly1898Arg)** | splice (3) | missense (4) | Y |
| | DCP1567 | *DNAH11* | **c.1459del, p.(Leu487Trpfs*14)** | **c.6317del, p.(Val2106Glyfs*67)** | frameshift (5) | frameshift (5) | N |
| | DCP641 | *DNAH11* | c.2569C>T, p.(Arg857*) | **c.13475G>A, p.(Trp4492*)** | nonsense (5) | nonsense (5) | Y‡‡ |
| | DCP1397 | *DNAH11* | **c.3911del, p.(Arg1304Leufs*13)** | **c.3911del, p.(Arg1304Leufs*13)** | frameshift (5) | frameshift (5) | N |
| | DCP563 | *DNAH11* | **c.4425C>A, p.(Tyr1475*)** | **c.4880G>A, p.(Arg1627His)** | nonsense (5) | missense (3) | Y |
| | DCP1072 | *DNAH11* | **c.6017C>T, p.(Pro2006Leu)** | **c.12970C>T, p.(Gln4324*)** | missense (4) | nonsense (5) | Y |
| | DCP1420 | *DNAH11* | **c.7134+1G>A, p.?** | **c.7134+1G>A, p.?** | splice (5) | splice (5) | N |
| | DCP514 | *DNAH11* | **c.11203-2A>G, p.?** | **c.11203-2A>G, p.?** | splice (5) | splice (5) | N |
| | DCP974 | *DNAH11* | **c.11327T>C, p.(Leu3776Pro)** | **c.12970C>T, p.(Gln4324*)** | missense (4) | nonsense (5) | Y |
| | DCP1259 | *DNAH11* | c.12980T>G, p.(Leu4327Trp) | c.12980T>G, p.(Leu4327Trp) | missense (3) | missense (3) | Y |
| | DCP878 | *DNAH11* | **c.13223C>A, p.(Ala4408Asp)** | **c.13223C>A, p.(Ala4408Asp)** | missense (3) | missense (3) | Y |
| | DCP1344 | *DNAH11* | **c.13435C>A, p.(Pro4479Thr)** | **c.13435C>A, p.(Pro4479Thr)** | missense (4) | missense (4) | Y |
| | DCP521 | NI | - | - | - | - | - |
| | DCP1058 | NI | - | - | - | - | - |

M: male, F: female, Y: yes, N: no, NI: no identified, **in bold**: newly described mutation, †*PIH1D3* is on the X chromosome: DCP855 and DCP894 are males hemizygous for a mutation. ‡c.180G>A alters the 5'-splice site of intron 3 (MaxEntScan score of 7.39 vs. 10.49 for the regular 5'-splice site). §c.1019+5G>C alters the 5'-splice site of intron 11 (MaxEntScan score 5.45 vs. 10.65 for the regular 5'-splice site). ‖c.2711+24C>G creates a new 5'-splice site (MaxEntScan score 8.56 vs. 4.46 for the regular intron 7 5'-splice site). ††c.275-2A>C transcript analysis (epithelial nasal cells) showed a small proportion of transcripts corresponding to a single-amino acid deletion (p.(Gly92del)). ‡‡c.13475G>A may drive to the production of a protein lacking the last 25 amino acids (out of 4516).

Table S4: **Results of the statistical analyses (Kruskal-Wallis test) of the qualitative evaluation of ciliary beating**: comparison of the percentage per patient of ciliated edges with each beat pattern (as described by Chilvers et al.,[13] according to the ultrastructural phenotype. Significant differences between ultrastructural phenotypes (p value < 0.05) are in bold.

Pattern "normal beating"

| | ODA | IDA/MTD | CC | nEM |
|---|---|---|---|---|
| **2DA** | 1.000000 | 1.000000 | **0.000002** | **0.000325** |
| **ODA** | | 1.000000 | **0.002598** | 0.092930 |
| **IDA/MTD** | | | **0.000015** | **0.001690** |
| **CC** | | | | 1.000000 |

Pattern "virtually immotile"

| | ODA | IDA/MTD | CC | nEM |
|---|---|---|---|---|
| **2DA** | **0.027841** | **0.006815** | **0.000000** | **0.000004** |
| **ODA** | | 1.000000 | **0.000107** | 0.377540 |
| **IDA/MTD** | | | **0.000645** | 0.946768 |
| **CC** | | | | 0.200913 |

Pattern "stiff beating with reduce amplitude"

| | ODA | IDA/MTD | CC | nEM |
|---|---|---|---|---|
| **2DA** | **0.046948** | **0.000027** | **0.000000** | **0.000026** |
| **ODA** | | 0.617497 | **0.005002** | 0.605914 |
| **IDA/MTD** | | | 1.000000 | 1.000000 |
| **CC** | | | | 1.000000 |

Pattern "circular gyrating motion"

| | ODA | IDA/MTD | CC | nEM |
|---|---|---|---|---|
| **2DA** | 1.000000 | 1.000000 | **0.005753** | 1.000000 |
| **ODA** | | 1.000000 | **0.005753** | 1.000000 |
| **IDA/MTD** | | | **0.005753** | 1.000000 |
| **CC** | | | | 0.128467 |

Video S5: **Video of ciliary beating from a PCD patient with combined outer/ inner dynein arms defect in 100% of cilia and bi-allelic mutations in *LRRC6* (DCP181, 2DA group)**, captured by high-speed video-microscopy. All cilia are strictly immotile. Magnification x1000.

Video S6: **Video of ciliary beating from a PCD patient with outer dynein arms defect in 100% of cilia and bi-allelic mutations in *DNAI1* (DCP498, ODA group)**, captured by high-speed video-microscopy. Cilia are mainly immotile and motile cilia exhibits slow motion, long pauses but normal angle. Mean beat frequency: 2.1Hz, weighted distance travelled by the cilium tip: 0.06µm. Magnification x1000.

Video S7: **Video of ciliary beating from a PCD patient with inner dynein arms defect in 100% of cilia with microtubular disorganization and bi-allelic mutations in *CCDC39* (DCP1540, IDA/MTD group)**, captured by high-speed video-microscopy. Cilia are mainly motile with stiff beating, reduced angle but relatively conserved beat frequency and pauses. Mean beat frequency: 5.2Hz (max 15.7Hz), mean weighted distance travelled by the cilium tip: 12µm. Magnification x1000.

Video S8: **Video of ciliary beating from a PCD patient with central complex defect in 42% of cilia and bi-allelic mutations in *RSPH9* (DCP1280, CC group)**, captured by high-speed video-microscopy. All cilia are beating, with nearly normal parameters. Mean beat frequency: 6.7Hz, mean weighted distance travelled by the cilium tip: 51µm). Magnification x1000.

Video S9: **Video of ciliary beating from a PCD patient with normal ultrastructure in 94% of cilia but without identified molecular defect (DCP1058, nEM group)**, captured by high-speed video-microscopy. All cilia are beating with a coordinated and hyperkinetic motion. Mean beat frequency: 16.7Hz, mean weighted distance travelled by the cilium tip: 42µm. Magnification x1000.