**Supplementary Material**

to

A homozygous *AKNA* frameshift variant is associated with primary microcephaly in a Pakistani family

by

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The supporting information contains three supplementary figures and one supplementary table.


**Figure S1.** Map displaying the home area of the MCPH family. It belongs to the Pashtun population of North-West Pakistan (Adopted from: https://www.dw.com/en/women-defy-local-traditions-in-pakistans-swat-valley/a-38609291).

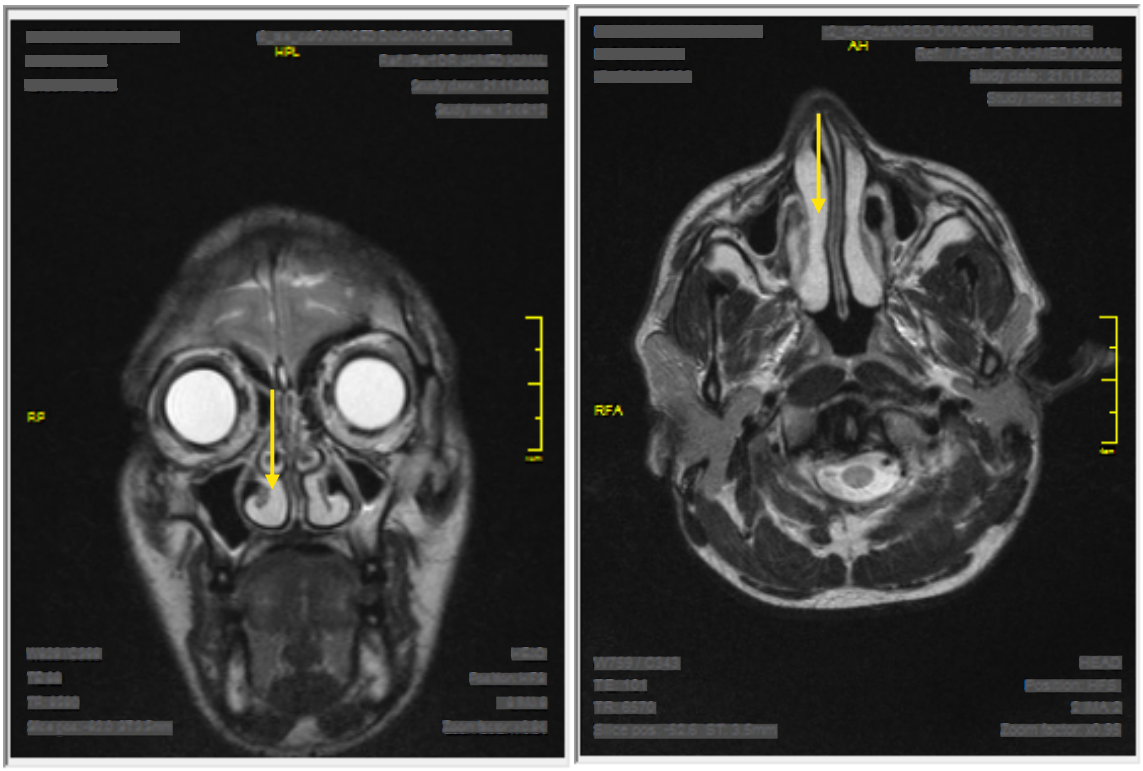

**Figure S2.** MRI images of individual IV-3 to document signs of PCD. In the left panel, the yellow arrow points to thick nasal mucosae as a sign of mild manifestation of PCD. However, the sinuses of the patient are free (yellow arrow in the right panel).

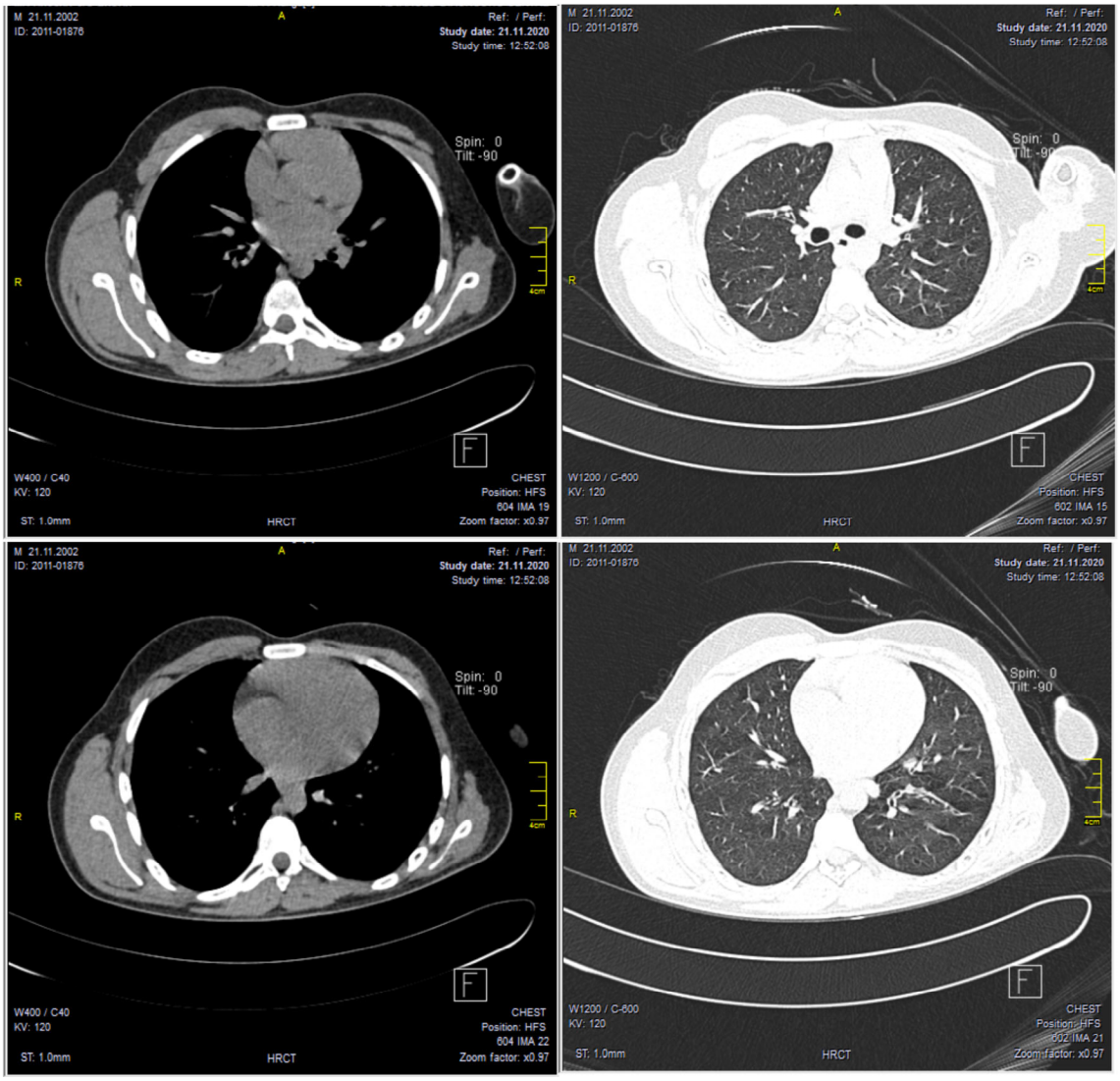


**Figure S3.** Thoracic CT scan of individual IV-3. The lungs appear clear and normal, no honey combing, nodule, collapse or mass lesion. Heart, abdomen and osseous structures are normal. Mediastinal adenopathy and pleural or pericardial effusion are not present.

**Table S1.** Highest ranking homozygous, X-linked and compound heterozygous variants detected by WES.

| Chr. | Gene | Variant | Mutation Taster | CADD PHRED | Polyphen-2 HDIV(v2.2,2) | dbSNP | ClinVar | gnomAD v2.1.1 allele frequency | Variant nature | Conclusion |
|---|---|---|---|---|---|---|---|---|---|---|
| 9 | *AKNA* | NM_030767.4: c.2737delG p.(Glu913Argfs*42) homozygous | Disease causing | 26.5 | NA | rs368704395 | Absent | 0.00003416 9 heterozygotes of African ethnicity 0 homozygotes | LOF | Plausible candidate |
| X | *TSPYL2* | NM_022117.3: c.2033A>C p.(Gln678Pro) hemizygous | Polymorphism (76) | 5.122 | 0.01 | rs781788384 | Absent | 0.0002235 21 heterozygotes 20 hemizygotes | Missense | Excluded |
| 15 | *C15orf40* | NM_001160115.1: c.82A>C, p.(Met28Leu) compound heterozygous | Polymorphism (32) | 22.2 | 0.012 | rs140417286 | Absent | 0.0003486 96 heterozygotes 0 homozygotes | Missense | Excluded |
| | | NM_001160115.1: c.73T>C, (p.Cys25Arg) compound heterozygous | Polymorphism (NA) | 8.391 | NA | rs4842860 | Absent | 0.6244 170578 heterozygotes 54701 homozygotes | Missense | Excluded |

**Note:** NA, Not Available, LOF, Loss-of-function