filters	Im-MCD_606			CerID-22		
Mean Coverage	151 reads (5x: 99%, 15x: 99%)			148 reads (5x: 99%, 15x: 99%)		
Total substitutions, deletions and insertions	112829			117888		
Frequency<1% in dbSNP, EVS, 1KG, in-house exomes	331			454		
	Familial model			Familial model		
	Autosomic Recessive		Autosomic Dominant and *de novo*	Autosomic Recessive		Autosomic Dominant and *de novo*
	Homozygous	Compound Heterozygous		Homozygous	Compound Heterozygous	
Essential splicing, non synonymous, frameshift and stop mutations	6 variants (6 genes) *NROB1* *HSD17B10* *IL13RA1*	8 variants (2 genes) ***WDR81*** *SIPA1L3*	1 variant (1 gene) *DSPP*	0	6 variants (3genes) *MGA* ***WDR81*** *SNRNP200*	10 variants (10 genes): *ARID1A* *PTPN7* *KLHL42* *RASA3* *ACOT2* *ITGAE* *FASN* *HDAC2* *MUC12* *DMD*

Predicted damaging by polyphen and sift	4 variants (2 genes) *HSD17B10* *IL13RA1*	8 variants (2 genes) ***WDR81*** *SIPA1L3*	0	0	2 variants (1 gene): ***WDR81***	8 variants (8 genes): *ARID1A* *PTPN7* *KLHL42* *RASA3* *ITGAE* *HDAC2* *MUC12* *DMD*

Table S1: WES filtering strategies and variants. Variant filtering strategies following trio based exome sequencing. dbSNP : SNP databases (build 140), EVS: Exome Variant Server (release ESP6500SI-V2), 1KG: 1000 Genomes (release Apr 2015) and over 7500 in-house exomes performed at the Imagine Institute.

ADN	sexe		Brain malformation
Im-MCD_503	F	Fœtus	MLIS
Im-MCD_704	M	Foetus	MLIS
Im-MCD_509	M	Live Patient	MLIS
Im-MCD_613	M	Fœtus	MLIS
Im-MCD_712	M	Live Patient	MIC/MLIS
Im-MCD_436	M	Fœtus	MLIS
Im-MCD_322	M	Live Patient	MIC
Im-MCD_150	F	Live Patient	MIC/MLIS
Im-MCD_084	M	Live Patient	MLIS
Im-MCD_097	M	Fœtus	MLIS
Im_MCD_216	M	Live Patient	MLIS
Im-MCD_437	M	Fœtus	MIC/MLIS
Im-MCD_693	M	Fœtus	MLIS
Im-MCD_322	M	Live patient	MLIS
Im-MCD_598	F	Live Patient	MLIS
Im-MCD_743	M	Live Patient	MLIS
Im-MCD_836	F	Live Patient	MIC

Table S2: Phenotypic characteristics of a replicative cohort consisting of 17 patients and fetuses with microcephaly (MIC) and/or Microlissencephaly (MLIS).

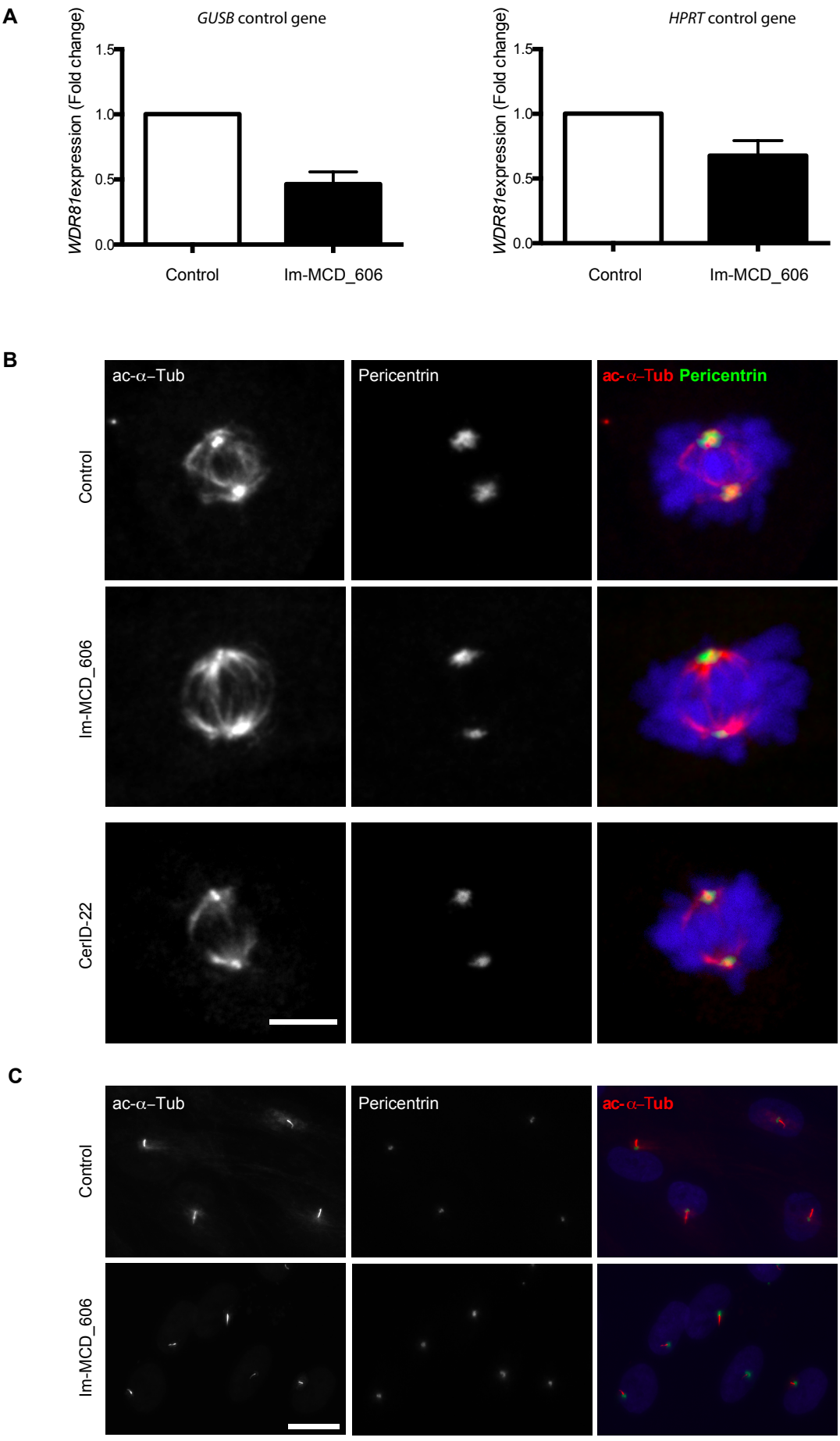

Figure S1: WDR81 mutant cells from patient 1 display reduced WDR81 expression and normal centriole number and primary cilia biogenesis. (A) Real-time RT-PCR analysis on mRNA extracted from patient fibroblasts shows a decreased amount of WDR81 mRNA levels by almost 40% as compared to controls; HPRT and GUSB were used as internal control genes. (B) Staining of mutant and control cells with acetylted alpha-tubulin and pericentrin shows normal centriole number and mitotic spindle morphology in mutant cells as compared to controls. (C). Same staining was performed on confluent serum starved cells for 48 hours to induced ciliogenesis and no alteration in cilia number and morphology has been detected.

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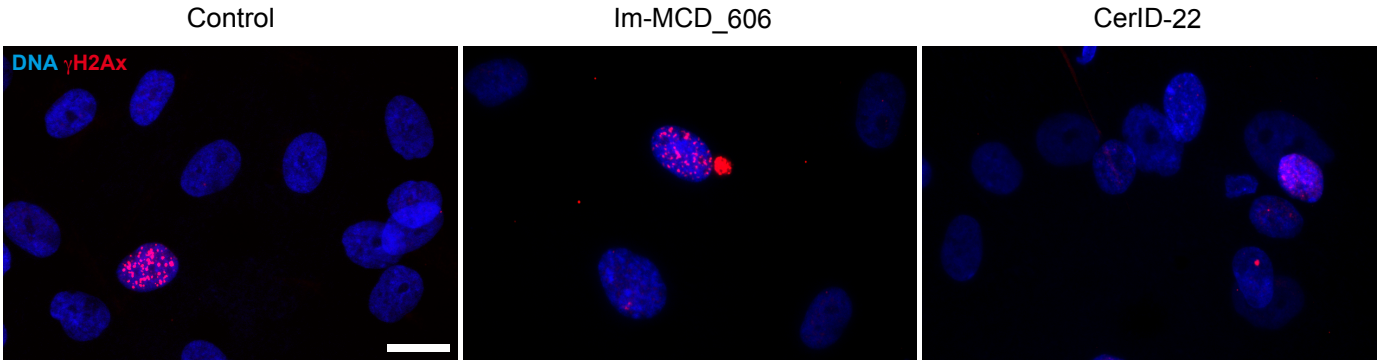

Figure S2: WDR81 mutant cells show normal DNA damage response. Staining with γ-H2AX antibody did not reveal any abnormal DNA damage response in mutant cells as compared to age-matched control cells. Scale bar 5 μm.

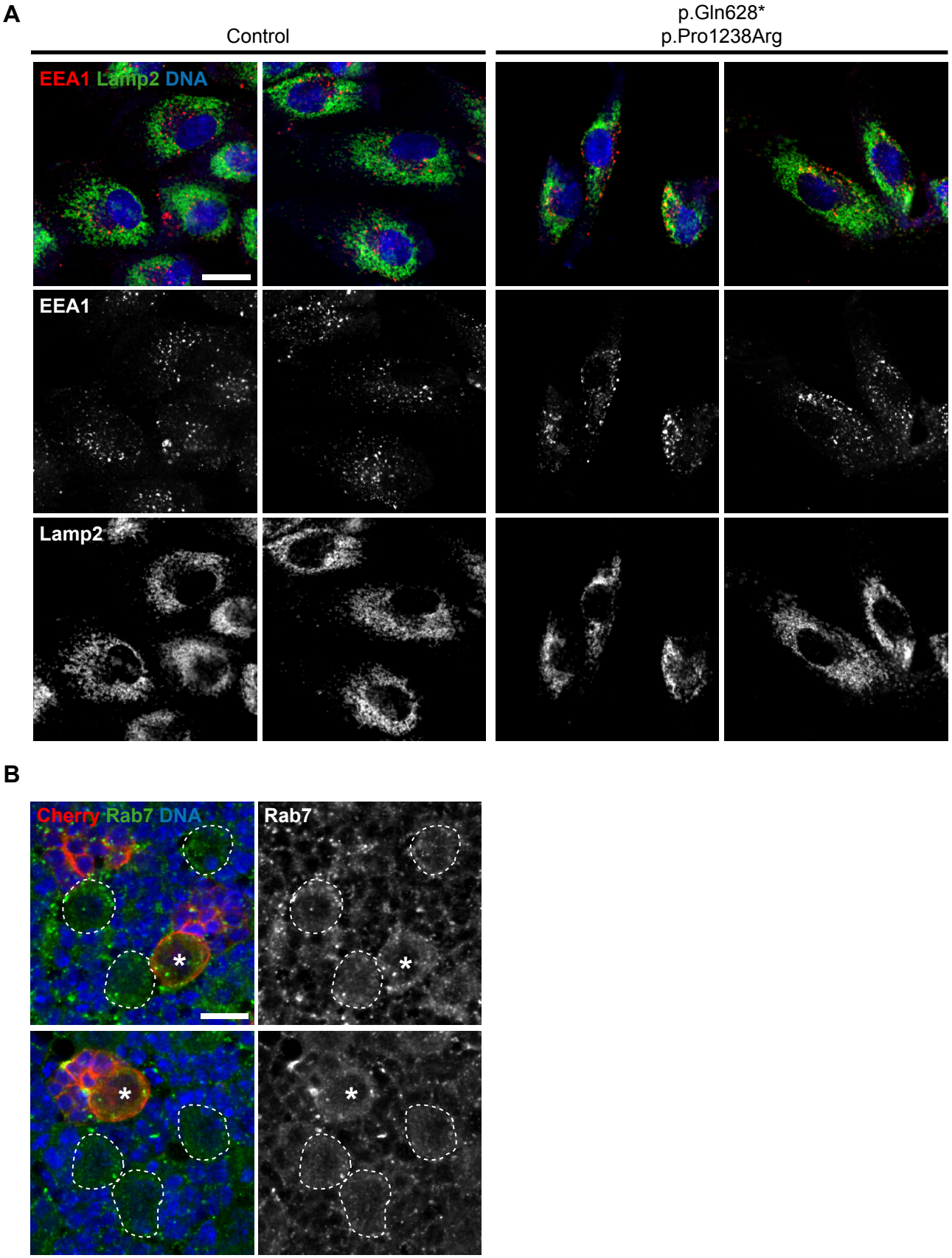

Figure S3. *WDR81* mutant cells and partial knockdown cells in *Drosophila* do not show defects in the morphology of the endolysosomal compartment. (A) Confocal microscopy images of human fibroblasts immunolabelled with EEA1 (red) and Lamp2 (green), markers for endosomes and lysosomes respectively. No differences are observed between control (upper panel) and patient (lower panel) fibroblasts. Scale bar 20 μm. (B) Confocal microscopy images of neuralstem cells within the Drosophila larval brain. Cells expressing Cherry (in red, asterisks) are knockdown for dWDR81 (RNAi). Cells with dashed outlines are wild type no RNAi). Rab7 antibodies were used to label endosomes (green). Similarly to human fibroblasts, we observe no differences between wild type cells and cells with dWDR81 knockdown. Scale bar 10 μm.