SUPPLEMENTARY INFORMATION

The effect of PTC124 on choroideremia fibroblasts and iPSCderived RPE raises considerations for therapy

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Supplementary Figure 1: Western blot analysis to determine the detection threshold of wild-type REP1 expression. Serial dilutions (1:2, 1:5, 1:10, 1:50, 1:100 and 1:500) of wild-type fibroblast cell lysates were analysed by hybridisation with a specific anti-REP1 antibody at short (**A**) and long (**B**) exposure times. REP1 expression was detectable up to a 1:10 dilution. β -actin serves as a loading control.





Supplementary Figure 2: Effect of lower CHX doses and shorter incubation time on the Rab pool in CHM3 fibroblasts. A) *In vitro* prenylation assay showing biotinylated Rab proteins in wild-type (WT), and in non-treated (NT), DMSO-treated or PTC124-treated CHM3 cells. β -actin serves as a loading control. B) Longer exposure time of the western blot shown in (A). Non-treated (NT), DMSO-treated and PTC124-treated CHM3 cells show high levels of biotinylated Rabs. Treatment with CHX reduced this Rab pool in a dose-dependent manner after 4 h incubation. The decrease in biotinylated Rabs was more pronounced after 24 h of CHX treatment. This effect was independent of PTC124.

Window Position				Hur	nan Feb. 2	009 (GRC)	1 <mark>37/h</mark> g	g 19)	chrX:85,213,890-85,2	13,937 (48	bp)				
Scale chrX:	1	85,213,895	85,213,900	85,213,	10 ba 905	ses 85,213,910		85,	213,915 85,213,	19 920	85,213,925	85,3	213,93d	85,213	.935
>	TGC	CAAGA	АТССТ	GGT	ААТ	ATT	TT	T efSec	A A A C T C Genes	TGC	ATA	тсб	ACT	AAC	ATT
CHM/NM_001320959	<<<<<	<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<	««««««««««««««««««««««««««««««««««««««		<<<<<<		<<<<	<<<<				<<<<<<	<<<<<<	<<<<<<	<<<<<<
CHW/NW_000390						Pfan	Dom	ains	in UCSC Genes						
GDI 4.88 _		<<<<<<<			100	vertebrate	s Bas	<<<<	e Conservation by Phy	loP		<<<<<	<u> </u>		<<<<<<
100 Vert. Cons															
-4.5 _						Multiz /	Vienm		of 100 Vortobratos						
Gaps						WUUZ A	aignin	ients	or roo vertebrates						
Human Chimp	A	L	I R I R	T		N N	К	((F E F E	A	Y	R	S S	v	N N
Gorilla	A	L	I R	T		N	K	(FE	A	Y	R	S	V	N
Gibbon	Â	L	I R	Ť		N	K	č	FE	Â	Ý	R	S	v	N
Rhesus Crab-eating macague	A	L	I R I R	T		N	<u>к</u>	((F E F E	A	Y	R	S S	- V	N
Baboon	A	L	I R	Ţ		N	K	(FE	A	Y	R	S	V	N
Marmoset	Â	L	I R	Ť		N	K	<	F E	A	Y	R	S	v	N
Squirrel_monkey Chinese tree shrew	A	L	I R I R	T	V	N	K K	((F E F E	A	Y Y	R	S S		N
Squirrel	A	L	I R	T	1	N	K	<u>(</u>	F E	A	Y	R	S	V	N
Prairie_vole	Â	Ľ	I R	Ť		N	K	č	FE	Â	Ý	R	s	v	N
Chinese_hamster Golden hamster	A V	L	I R I R	Т	V	N	K K	((F E F E	A	Y	R	S S		N
Mouse	A	L	I R	Ţ		N	K	ç	F E	A	Y	R	S	V	N
Hat Naked_mole-rat	A	L	I R	Ť		N	K	(F E	A	Y	R	S	v	N
Guinea_pig Chinchilla	S	L	I R I R	T T		N N	K	(F E	A	Y	R	S S	v	N N
Rabbit	A	L	I R	T	I	N	K	(FE	A	Y	R	S	V	N
Pig	Â	L	I R	Ť	I	N	ĸ	č	FE	A	Ý	R	S	v	N
Alpaca Bactrian camel	A	L	I R I R	T		N	К	((F E F E	A	Y	R	S S	v	N
Dolphin Killor, whole	A	L	I R	T		N	K	<u> </u>	FE	A	Y	R	S	V	N
Tibetan_antelope	Â	Ľ	I R	Ť		N	K	č	FE	Â	Ý	R	s	v	N
Cow Sheep	A	L	I R I R	T T		N N	K K	((F E F E	A A	Y	R R	S S	v	N N
Domestic_goat	A	L	I R	Ţ		N	K	(,	FE	A	Y	R	S	V	N
White_rhinoceros	Â	Ľ	I R	Ť		N	ĸ	Ċ	FE	Â	Ý	R	s	v	N
Cat Dog	A	L	I R I R	T		N	<u>к</u>	((F E F E	A	Y	R	S S	v	N
Ferret_	A	L	I R	T		N	K	(FE	A	Y	R	S	V	N
Pacific_walrus	Â	Ĺ	I R	Ť		N	ĸ	Ì	FE	Â	Ý	R	S	v	N
Weddell_seal Black_flying-fox	A	L	I R I R	- T		N	K	(F E	A	Y	R	S S	v	N
David's_myotis_(bat)	A A	L	I R I B	T		N	K	(F E F F	A	Y	H	S	V	N
Big_brown_bat	A	Ĺ	I R	Ť		N	K	ç.	FE	A	Ý	Н	s	v	N
Star-nosed_mole	A	L	I R	T		N	K	<	F E	A	Y	R	S	v	N
Elephant Manatee	A	L	I R I R	T	V	N	<u>к</u>	(F E F E	A	Y	R	S S	V V	N
Cape_golden_mole	S	Ē.	I R	Ť		N	K	Ċ	FE	A	Ý	R	s	i	N
Aardvark	A	L	I R	T		N	K	<	F E	A	Y	R	S	V	N
Opossum Tasmanian devil	G	L	I R I R	T	V	S N	<u>к</u>	((F E F E	A	Y	R	S S	v	N
Wallaby	G	L	I R	T	V	N	K	(FE	A	Y	R	S	V	S
Saker_falcon	A	L	I R	Ť	A	N	K	Ċ	FE	A	Ý	R	S	v	N
Peregrine_falcon Collared flycatcher	A	L	I R V R	T	A	N	<u>к</u>	((F E F E	A	Y	R	S S		N
White-throated_sparrow	A	L	V R	T	A	N	K	(FE	A	Y	R	S	V	N
Zebra_finch	Â	Ĺ	V R	Ť	Â	N	K	È	FE	Â	Ý	R	S	v	N
Tibetan_ground_jay Budgerigar	A	L	V R I R	T	A	N	K	(F E F E	A	Y	R	S S	v	N
Parrot Scarlet macaw	A	L	I R I R	T	A	N	K	((F E F F	A	Y	R	S	V	N
Mallard_duck	A	Ē.	I R	Ť	A	N	ĸ	ç.	FE	A	Ý	R	s	v	N
Turkey	A	L	I R	T	A	N	K	(F E	A	Y	R	S	v	N
American_alligator	V	L	I R	T	A	N	K	(F E F F	A	Y	R	S	V V	N
Painted_turtle	A	Ē.	I R	Ť	V	N	K	ç.	FE	A	Ý	R	s	v	N
Spiny_softshell_turtle	A	L	I R	T	V	N	K	(FE	A	Y	R	S	v	N
Lizard X tropicalis	А Т	L	I R I B	T T	VV	N N	ĸ	(F E F E	А Т	Y Y	R R	S S	V V	N N
Coelacanth	A	Ē.	I R	Ť	V	N	K	(FE	A	Ŷ	R	S	v	N
r etraodon Fugu	T	L	I R	T	V	N	K	(FE	A	Y	R	S	v	N
Nile_tilapia Princess of Burundi	T T	L	I R I R	T T	V V	N N	ĸ	(F E F E	A A	Y Y	R R	S S	V V	N N
Burton's_mouthbreeder	T	L	I R	T	V	N	K	(F E	A	Y	R	S	V	N
Zebra_mbuha Pundamilia_nyererei	T	L	I R	Ť	V	N	K	(F E	A	Y	R	S	v	N
Medaka Southern platvfish	T T	L	I R I R	T T	V	N N	ĸ	(F E F E	T A	Y Y	R	S S	V V	N N
Stickleback	T	L	I R	Т	V	N	K	(F E	A	Y	R	S	V	N
Atlantic_cod Zebrafish	T	L	I R	G	I	N	K	(F E	A	Y	R	S	v	N
Mexican_tetra_(cavefish) Spotted_gar	T	L	I R	S	L	N	K		F E F F	A	Y	R	S	V	N

Supplementary Figure 3: Conservation of the K258 amino acid residue of human REP1. Sequence alignment showing the conservation of the lysine residue at position 258 (in orange) of human REP1 among 91 vertebrates species. Nine species with undefined sequences have been hidden. Screen shot obtained from the UCSC genome browser, http://genome.ucsc.edu.