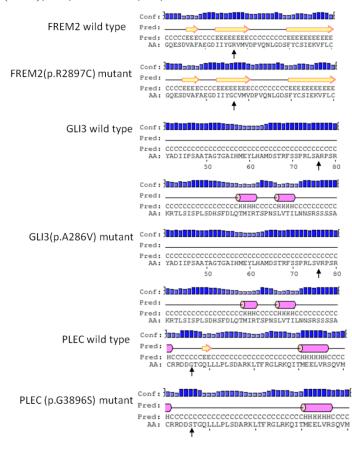
**Supplementary Fig. 3** Predicted secondary structures of the wild and mutant protein sequences flanking the remaining candidate rare mutations. The diagrams show the protein sequences with their secondary structures and their confidence values at the aligned positions. The secondary structure is annotated as follows: pink cylinder (alpha-helix); yellow arrow (beta-sheet); black line (coil); Conf, confidence; Pred, predict; H in Pred line (Helix); C in Pred line (coil); E in Pred line (sheet); AA, amino acid; **↑**, mutant amino acid.



PLEC wild type	Conf: <b>}000000000000000000000000000000000000</b>	
	Pred: CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC	
PLEC (p.S39G) mutant	Conf: ]01002222222222222200000000000000000000	
	Pred: CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC	
USH2A wild type	Conf:]000000000000000000000000000000000000	
	Pred: CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC	
USH2A (p.N336S) mutant	Conf: 1001000000000000000000000000000000000	
	AA: RVSRLSPEAHPLSFVNDNDVGTSWVSNVFTNITOLNOGVT	
GBA wild type	Conf: Confice Content	
	AA: INLLYHVVGWIDWNLALNPEGGPNWVRNFVDSPIIVDIIK	
GBA (p.N344S) mutant	Conf: 100-100 - 00	
	AA: TNLLYHVVGWTDWNLALNPEGGPSWVRNFVDSPIIVDITK	
PLEC wild type	Conf;; <b>);;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;</b>	
	AA: MEVLLASKARAEEESRSTSEKSKORLEAEAGRFRELAEEA	
PLEC (p.A1799V) mutant	Pred: Pred: никиникиникиникиникиникиникиникиникиник	
	<b>†</b>	
GLI3 wild type		
	Pred: CCCCCCCCCCCCCKHHHCCCCCCCCCCCCCCCCC AA: VPRFSSLSSCNPPAMATSAEKRSLVLQNYTRPEGGQSRNF	
GLI3 (p.A1036V) mutant Conf: 3033300000000000000000000000000000000		
	Pred: CCCCCCCCCCCCCHHHHCCCCCCCCCCCCCCCCC AA: VPRFSSLSSCNPPAMVTSAEKRSLVLONYTRPEGGSSRNF	
POMT1 wild type		
Pred: HHXXHHHXXHHHXXHCCCCCCHHXXHHHXXHHXXHHXXH		
POMT1 (p.L476F) mutant Conf: JUILING		
	Pred: HHXKHHHXKHHHXKHCCCCCCHHXKHHKKHHHXKHHKKH AA: YALLSFWYLLRRRRNVHDLPODAMLRWVLAGALCAGGWAV	
USH2A wild type prod.		
	Pred: Pred: CCCEEEEEEEECCCEEEEEEECCCCCCCCCCCCCCCC	
	T Conf: 3000000000000000000000000000000000000	
USH2A (p.N1797D) mu	Pred: CCCEEEEEEECCEEEEEECCCCCEEEEEECCCCCCCCC	
AA: GPDFLAMELKSGILTFRLNTSLAFTQVDLLLGLSYCDGKW		
	Pred: EECEEEEEECCCCCCCCCEEEEEEEECCCCCCCCCCC	
	AA: VTSAVLSQKVTHLIPFTNYSVTIVACSGGNGYLGGCTESL	
USH2A (p.T2807I) mut	Pred:	
USH2A (p.T2807I) mut	all	

USH2A wild typ	e Conf: ]]]]]]]]]]]]]]]]]]]]]]]]]]]]]]]]]]]]
USH2A (p.Q3624R) muta	nt Conf: DDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDD
USH2A wild ty	<pre>/pe Conf: ]]]]]]]]]]]]]]]]]]]]]]]]]]]]]]]]]]]]</pre>
USH2A p.N3653S mut	ant Conf: ]]]]]]]]]]]]]]]]]]]]]]]]]]]]]]]]]]]]
USH2A wild ty	/pe Conf: }
USH2A (p.P3708L) muta	Int Conf: ]]]]]]]]]]]]]]]]]]]]]]]]]]]]]]]]]]]]
USH2A wild type	Conf:
USH2A (p.R4115H) mutant	Conf: DISSINGLAS
USH2A wild type	Conf: 3333344444444444444444444444444444444
USH2A (p.I4386T) mutant	Conf: ]=DDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDDD