Supplementary Table 1: Variant filtration

High-confidence variants discovered in family	105,815 (63,994 on target)				
Variant genotype shared II.2 and III.3	62,798 (37,977)				
Variant ALT allele <0.01 in global 'healthy' populations and rare in-house	850 (524)				
Variant likely to affect protein sequence	142 (139)				
Genotype not shared with II.1 or III.2	94 (91)				
Interpreted for causality under genetic model	DOM	CR+DOM	CR	HOM REC	DE NOVO
	77	8	9	0	0
Variants selected for family-wide genotyping	9	0	0	0	0
Variants co-segregating with disease severity	1	0	0	0	0

DOM	variant interpreted under dominant genetic model
CR+DOM	variant interpreted under compound recessive and dominant genetic models
CR	variant interpreted under compound recessive model
HOM REC	variant interpreted under homozygous and hemizygous genetic models
DE NOVO	variant interpreted under *de novo* genetic model
on-target	site is directly targeted by the exome enrichment kit