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Supplemental Data

Exome Sequencing Identifies a *DYNC1H1* Mutation in a Large Pedigree with Dominant Axonal Charcot-Marie-Tooth Disease

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Table S1. Exome sequence alignment and coverage data. CCDS bases refer to the exonic bases from the September 2008 CCDS release and the cumulative number of these target bases that were covered with increasing read depth is presented.

Individual	**IV-2**	**IV-7**	**IV-14**
Total reads	78,538,784	84,024,940	80,266,112
Total sequence (bases)	5,968,947,584	6,385,895,440	6,100,224,512
Aligned Reads	68,551,918	71,239,522	69,352,229
Uniquely Aligned Reads	64,008,530	66,630,886	64,675,318
Total bait bases	37,792,908	37,792,908	37,792,908
Total CCDS target bases	27,484,507	27,484,507	27,484,507
CCDS bases covered >=1X	26,604,824	26,496,548	26,526,222
CCDS bases covered >=4X	25,459,911	25,278,509	25,329,116
CCDS bases covered >=10X	23,583,984	23,416,289	23,463,106
CCDS bases covered >=20X	20,992,799	20,940,420	21,024,746
Bait bases covered >=20X	28,200,599	28,203,872	28,368,627
Average bait base coverage	64	66	65
Average CCDS base coverage	69	71	70

Table S2. Breakdown of variants identified. Only bases covered >=4X were included. Ti/Tv refers to the transition/transversion ratio. Target bases refer to the exonic bases from the September 2008 CCDS release.

Individual	**IV-2**	**IV-7**	**IV-14**
Total Variants	24,208	24,237	24,484
Total Variants in target region	14,997	14,930	15,170
Ti/Tv ratio of total coding region variants	3.37	3.46	3.39
Novel variants in coding region after dbSNP131, 1000 genomes and 11 "in house" control exome filtering (het/hom)	177/6	192/7	199/8
Ti/Tv of novel coding variants	2.77	2.25	2.00
Novel missense	168	183	197
Novel nonsense	4	8	2
Novel frameshift	9	8	7
Novel splice site	2	0	1

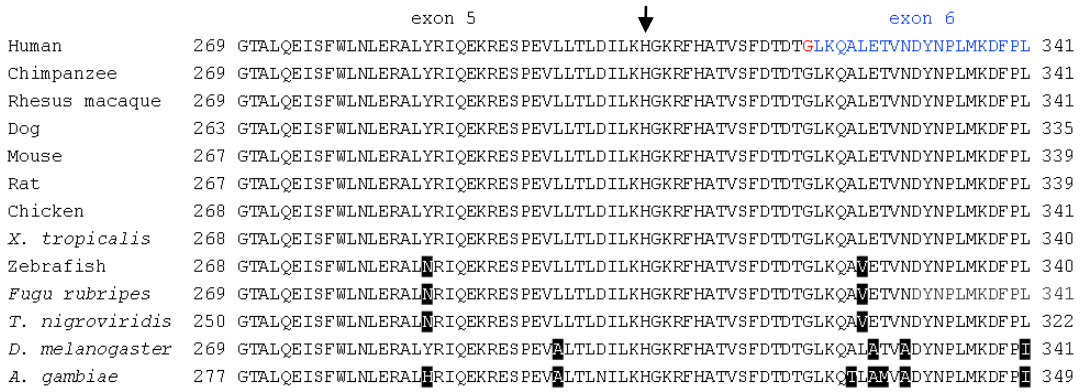

Figure S1. Sequence Conservation in DYNC1H1 Stem Region
The sequence of human DYNC1H1 amino acids 269-341 is shown aligned to orthologues from other species. For the human sequence, residues encoded by exons 5 and 6 are shown in black and blue font respectively; Gly321, the codon for which lies across the exon junction, is shown in red. The position of His306 is shown by an arrow above the sequence. Positions of non-identity with the human sequence are shown by inverted type in orthologous sequences. The *in silico* tools SIFT[1], PolyPhen2[2] and Mutation Taster[3] all predict that the p.His306Arg mutation is likely to be pathogenic.

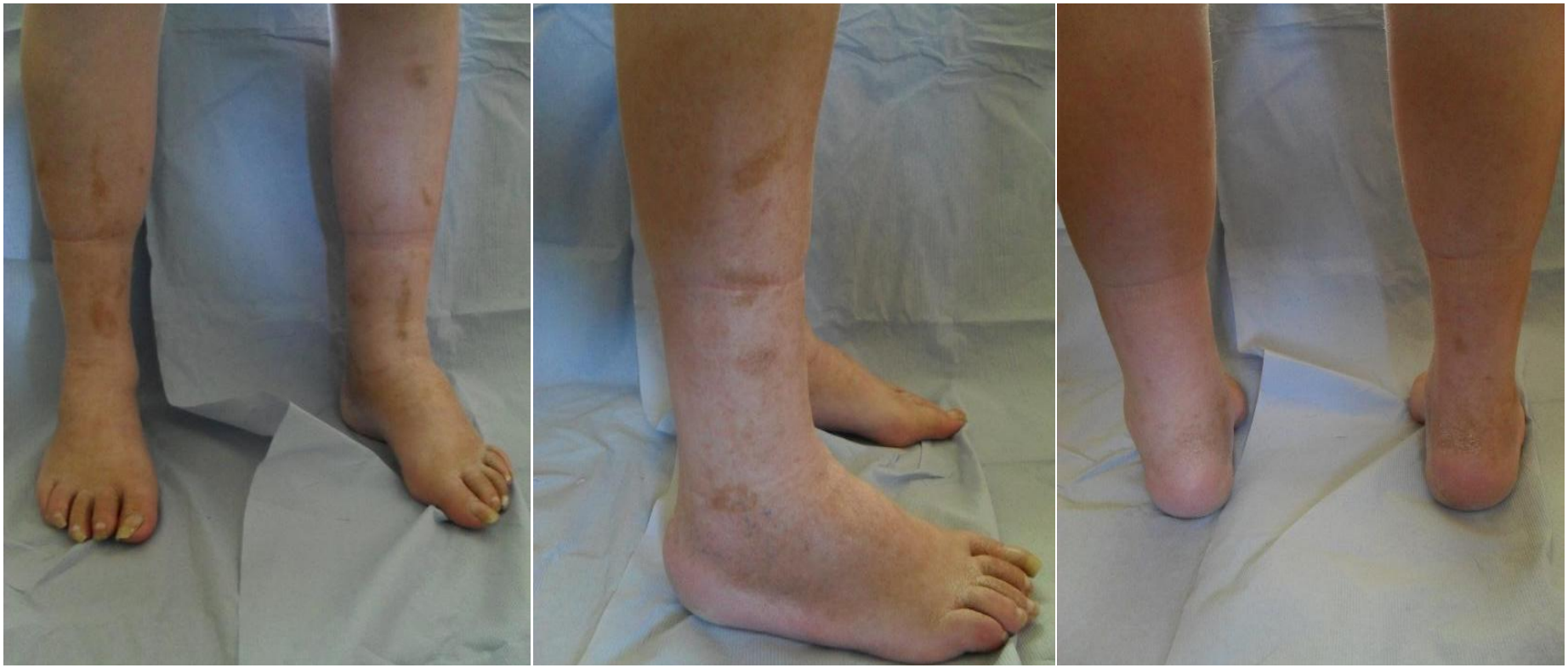

Figure S2. Lower legs of patient II 13 at age 58 Demonstrating Calf Atrophy and Hair Loss

Supplementary References

1. Kumar, P., Henikoff, S. & Ng, P.C. Predicting the effects of coding non-synonymous variants on protein function using the SIFT algorithm. *Nat Protoc* **4**, 1073-81 (2009).
2. Adzhubei, I.A. et al. A method and server for predicting damaging missense mutations. *Nat Methods* **7**, 248-9 (2010).
3. Schwarz, J.M., Rodelsperger, C., Schuelke, M. & Seelow, D. MutationTaster evaluates disease-causing potential of sequence alterations. *Nat Methods* **7**, 575-6 (2010).