Table e-1 Summary of clinical features in the pedigree

Individual	**II-2**	**II-3**
Sex/age (years)	M/8	F/6
Age at onset (years)	1	1
First symptoms	Lower limb muscle weakness	Lower limb muscle weakness
Muscle weakness[a]		
Upper limb, proximal	+	+
Upper limb, distal	+	++
Lower limb, proximal	+	+
Lower limb, distal	++	++
Muscle atrophy[b]		
Upper limb, proximal	+	+
Upper limb, distal	++	+
Lower limb, proximal	+	+
Lower limb, distal	++	++
Sensory loss[c]		
Upper limb	++	+
Lower limb	++	++
Deep tendon reflexes[d]	Abs	Abs
Foot deformity[e]	+	+
Spine deformity[e]	+	+
General stage of disability[f]	Abnormal walking only with crutches	Abnormal walking only with crutches

[a] —= no weakness; + = 4/5 on MRC scale; ++ = <4/5 on MRC scale; +++ = complete paralysis.

[b] —= not affected; + = mild atrophy; ++ = moderate atrophy; +++ = severe atrophy.

[c] —= normal; + = reduced below wrist/ankle; ++ = reduced below knee/elbow; +++ = reduced at or above elbow/knee.

[d] N = normal/present; ++ = brisk; +++ = brisk with extensor plantars; +/—= present with reinforcement; Abs = absent.

[e] —= none; + = mild; ++ = severe; +++ = surgery required.

Table e-2 Electrophysiological features of patients

Patients		II-2	II-3	Normal values
Age at exam (years)		7	6	
Motor nerves				
	Median nerve			
	TL (ms)	3.3	5.1	<4.2
	CMAP (mV)	0.4	0.7	>5
	MNCV (m/s)	29	21	>45
	Ulnar nerve			
	TL (ms)	3.3	3.2	<3
	CMAP (mV)	0.6	0.4	>5
	MNCV (m/s)	24	26	>45
	Peroneal nerve			
	TL (ms)	Abs	5.4	<5.5
	CMAP (mV)	Abs	0.2	>3
	MNCV (m/s)	Abs	29	>40
	Tibial nerve			
	TL (ms)	Abs	Abs	<6.0
	CMAP (mV)	Abs	Abs	>3
	MNCV (m/s)	Abs	Abs	>40
Sensory nerves				
	Median nerve			
	SNAP (μV)	0.5	4	>3
	SNCV (m/s)	33.3	29	>45
	Ulnar nerve			
	SNAP (μV)	2.2	4	>3
	SNCV (m/s)	27.3	29	>44
	Sural nerve			
	SNAP (μV)	Abs	Abs	>3
	SNCV (m/s)	Abs	Abs	>40
Muscle				
	Deltoideus（L/R）			
	ASA	－/－	－/－	
	MUAP (mV)	1.0/0.7	0.9/1.1	0.5-1.6
	Opponens pollicis（L/R）			
	ASA	－/＋	＋/－	
	MUAP (mV)	0.2/0.1	0.1/0.1	0.4-2.0
	Vastus medialis（L/R）			
	ASA	－/－	－/－	
	MUAP (mV)	0.8/0.8	1.1/0.7	0.6-1.6
	Tibialis anterior（L/R）			

	ASA	＋/＋	＋/＋	
	MUAP (mV)	Abs / Abs	Abs / Abs	0.5-1.5

Abs, absent; NT, not tested. TL, terminal latency; CMAP, compound muscle action potential; MNCV, motor nerve conduction velocity; SNAP, sensory nerve action potential; SNCV, sensory nerve conduction velocity; L/R, left/right; ASA, abnormal spontaneous activity (fibrillation potential, positive sharp waves or fasciculation potential); MUAP, motor unit action potential; －, not present; ＋, present;

Table e-3 Exome data-filtering approach to identify mutations with recessive inheritance patterns in the family

Steps	**Data filtering**	**Candidate variants**
	SNP/Indel Calling	124969 variants
Step1	Identify missense, nonsense and splicing variants (SNP+Indel)	10993 variants
Step2	Remove variants found in cg46	1434 variants
Step3	Remove variants with SIFT score > 0.05	345 variants
Step4	Remove variants with PolyPhen2 score(HumanDiv database) < 0.93	161 variants
Step5	Remove variants in the 1000 Genomes Project(ALL) with MAF>0.01	128 variants
Step6	Remove variants in NHLBI-ESP 6500 exomes with MAF>0.01	121 variants
Step7	Compile a list of candidate genes based on diseaes model	16 genes
Step8	Candidate gene links to mendelian disorders	IGHMBP2

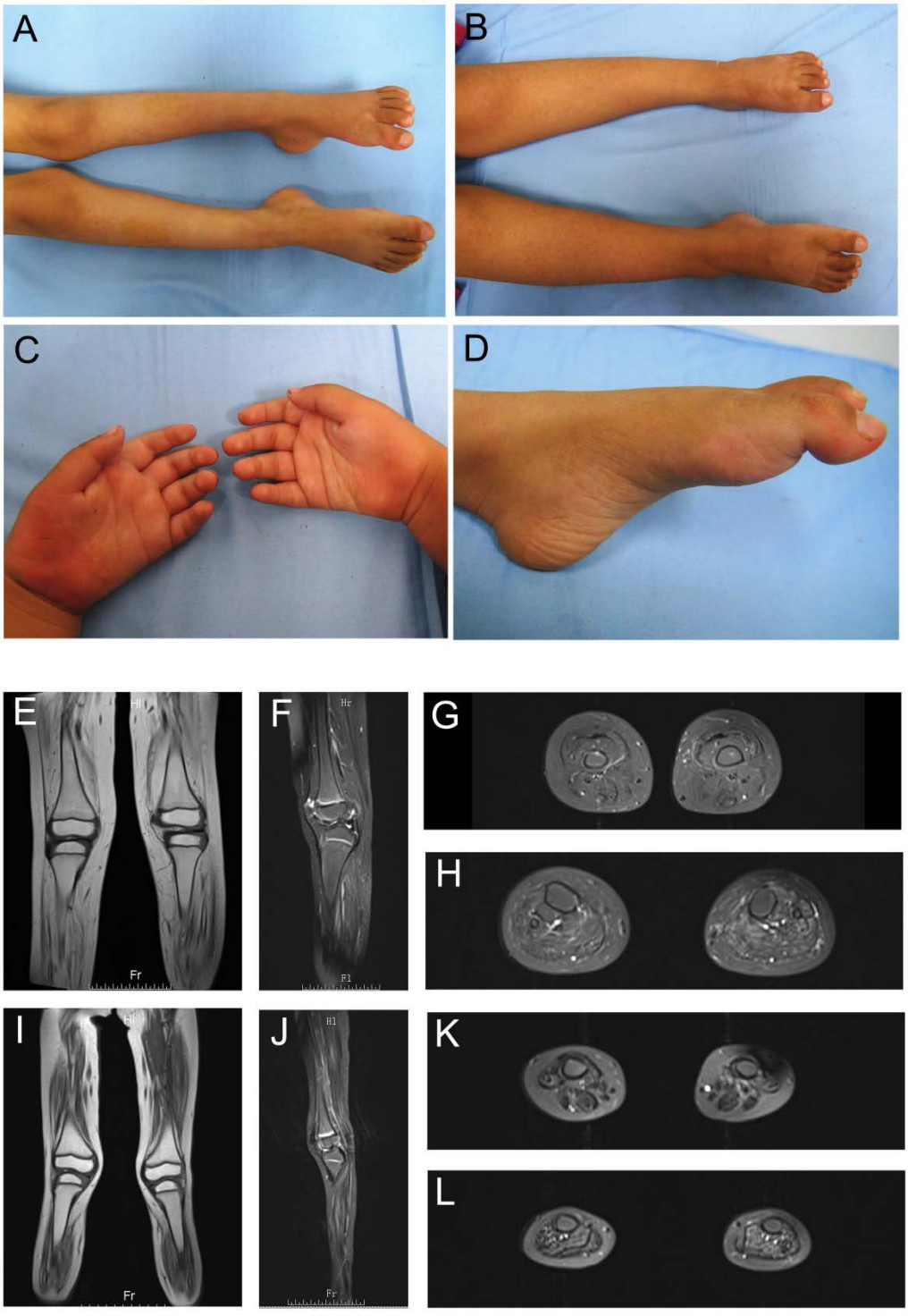

Figure e-1: Photographs and T1-weighted MRI of the individuals with IGHMBP2 mutations.

(A and B) Legs and feet of the patients II-3 and II-2, showing wasting in the lower limbs.(C) Involved hands of individual II-2.(D) Foot deformity of individual II-2. (E-L) T1-weighted MRIs of the thigh and lower leg of the patients. MRIs demonstrated severe muscle atrophied and diffuse fatty hyperintense with signal changes and the lower legs were more severe than the thighs. (E~H),

II-2; (I~L), II-3. (E,I), coronal images;(F,J) sagitta images;(G,H,K,L)Axial images(right).

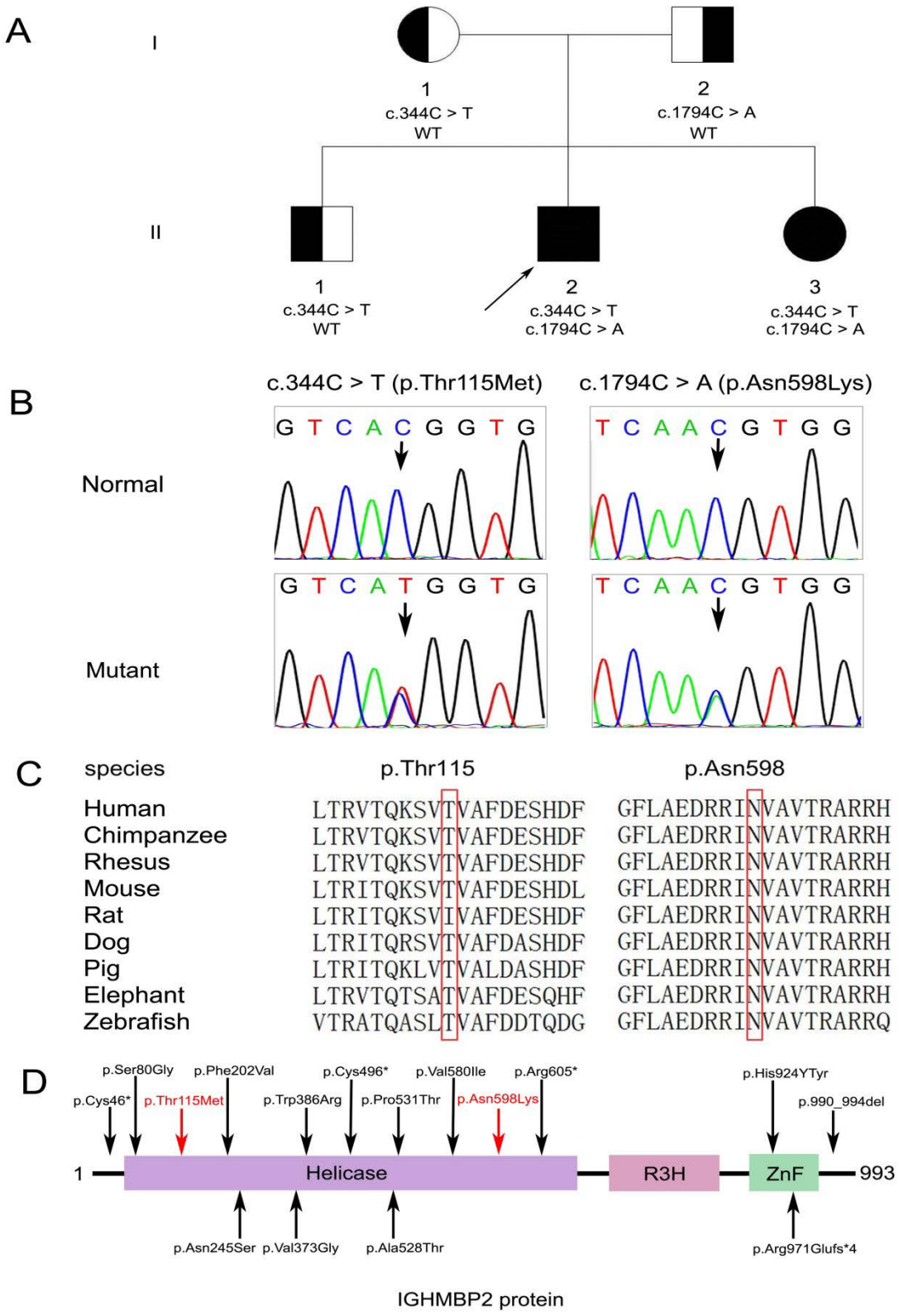

Figure e-2: Pedigree of the family affected by IGHMBP2 mutations .

(A) Pedigree. Open symbols, unaffected ; filled symbol, affected; Half-filled symbols, carriers (possessing one mutant allele); arrow, proband. Genotypes of both IGHMBP2 mutations are indicated at below each individual. (B) Sequencing chromatograms. Vertical arrows indicate the mutation site. (C) Conservation analysis of amino acid sequences. The analysis was conducted using clustalx2.1 software. The amino acids p.Asn598 is fully conserved across species while the amino acids p.Thr115 is partial conserved. Red boxes indicate the location of the amino acid changed due to the mutation. (D) Domain structure of the IGHMBP2 protein. The schematic of IGHMBP2 shows the helicase, R3H, and ZnF domains. The positions of the identified mutations related to HMSN are located and mutations of our family are in red.