Supplemental Table 1 Genotype of patients with MSP-related variants (N=29)

Gene	Patients	Age /sex	Phenotypes	DNA nucleotide change	Protein change	Pathogenicity classification	ACMG evidence codes
VCP	P1	37/m	IBM	c.705A>G	p.R155H	Pathogenic	PM1+PM2+PP2+PP3+PP5
	P2	52/m	IBM, PDB, PD	c.593T>G	p.L198W	VUS, novel	PM1+PM2+PP5
	P3	48/m	IBM	c.1106T>C	p.I369T	Likely pathogenic	PM1+PM2+PP2+PP3
	P4	35/m	ALS	c.463C>T	p.R155C	Pathogenic	PM1+PM2+PP2+PP3+PP5
	P5	49/m	ALS, FTD	c.464G>A	p.R155H	Pathogenic	PM1+PM2+PP2+PP3+PP5
	P6	51/m	ALS, FTD	c.464G>A	p.R155H	Pathogenic	PM1+PM2+PP2+PP3+PP5
HNRNPA1	P7	42/m	IBM	c.644A>G	p.N215S	VUS	PM1+PM2+BP3
	P8	12/m	IBM	c.961T>G	p.*321Eext*6	VUS	PM2+PM4+PP3
				c.1117T>G	p.X373E	VUS	PM2+PM4+PP3
SQSTM1	P9	27/f	IBM	c.5C>T	p.A2V	VUS	PM1
	P10[a]	45/f	IBM	c.295A>C	p.I15L	VUS	PM1+PP3
	P11	71/m	ALS	c.1210A>C	p.M404L	VUS	PM2+PM5+PP3
MATR3	P12	41/m	IBM	c. 254 C >G	p.S85C	Pathogenic	PM1+PM2+PP3+PP5
	P13	43/m	IBM	c.254C>G	p.S85C	Pathogenic	PM1+PM2+PP3+PP5
	P14[b]	26/f	ALS	c.1141A>G	p.K381E	VUS, novel	PM1
OPTN	P15	65/f	ALS, FTD	c.1546G>C	p.E516Q	Likely Pathogenic	PM1+PM2+PP3+PP5+BP1
	P16	44/m	ALS, FTD	c.531del	p.F178Lfs*15	VUS, novel	PM1
	P17[c]	76/f	ALS	c.407C>T	p.A136V	VUS	PM1+PM2+PP5
	P18	70/m	ALS	c.1634G>A	p.R545Q	VUS	PM1+PP5

	P19	68/m	ALS	c.1634G>A	p.R545Q	VUS	PM1+PP5
ANXA11	P20	55/m	IBM, ALS, FTD	c.118G>T	p.D40Y	Pathogenic	PS3+ PM1+PM2+PP2+PP5
	P21	66/m	ALS, FTD	c.119A>G	p.D40G	Pathogenic	PS3+ PM1+PM2+PP2+PP5
	P22	33/f	ALS	c.119A>G	p.D40G	Pathogenic	PS3+ PM1+PM2+PP2+PP5
	P23	61/f	ALS	c.1156C>T	p.R386W	VUS	PM1+PP2
	P24	33/m	ALS	c.1156C>T	p.R386W	VUS	PM1+PP2
	P25	53/f	ALS	c.1471G>A	p.G491R	VUS	PM2+PP2
	P26	52/m	ALS	c.962C>A	p.T321N	VUS	PM6+PP2
	P27[d]	36/m	ALS	c..962C>A	p.T321N	VUS	PM6+PP2
	P28	66/m	ALS, FTD	c.107C>G	p.P36R	VUS	PM1+PM2+PP2
	P29	36/m	ALS	c.289C>T	p.Q97X	VUS, novel	PSV1+PP3

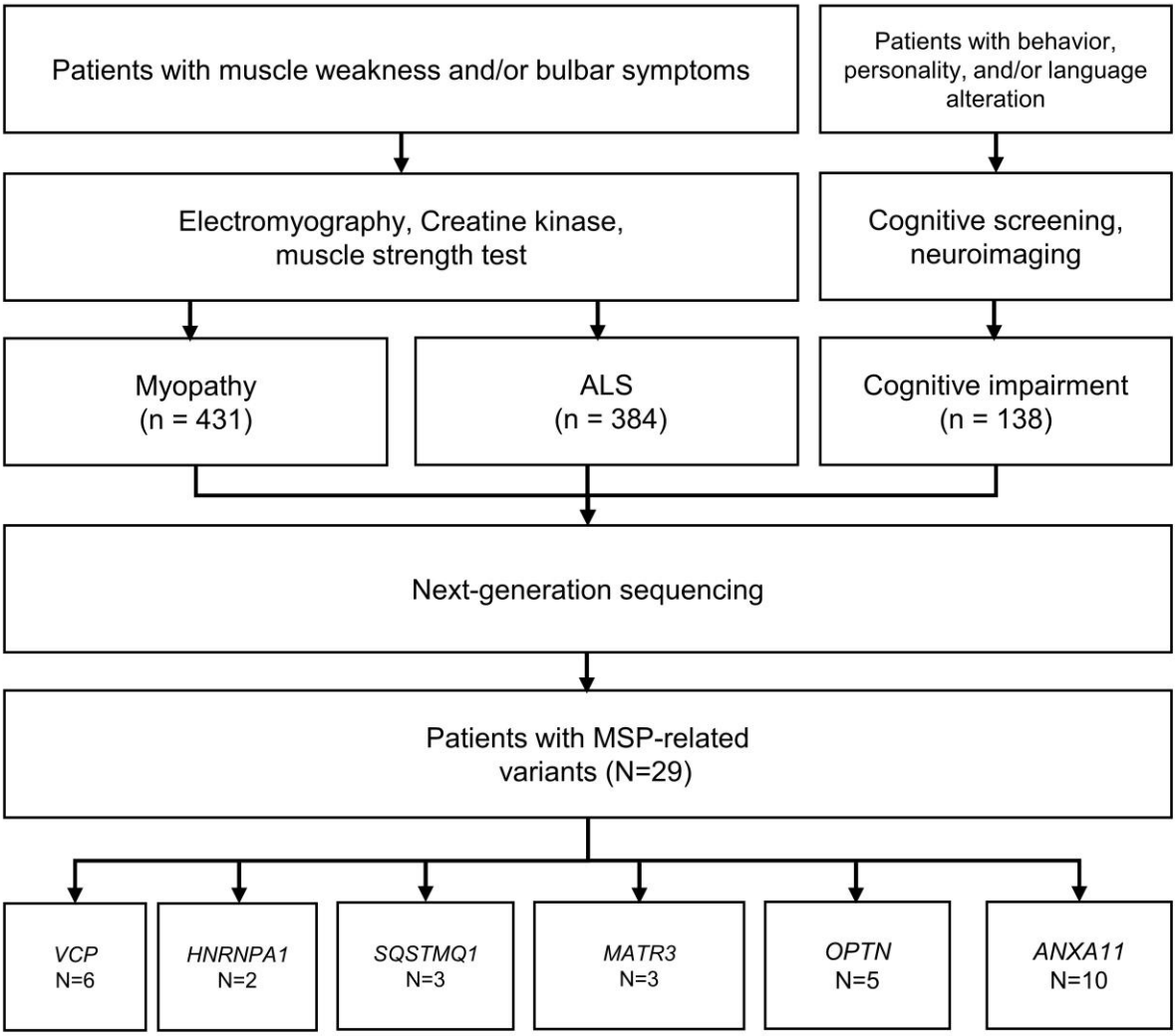
Abbreviations: ALS, amyotrophic lateral sclerosis; IBM, inclusion body myopathy; PDB, Paget disease of the bone; FTD, frontotemporal dementia; VCP, valosin-containing protein; hnRNPA1, heterogeneous nuclear ribonucleoprotein A1; MATR3, matrin 3; MSP, multisystem proteinopathy; SQSTM1, sequestosome 1; ANXA11, annexin A11; OPTN, Optineurin; MAPT, Microtubule Associated Protein Tau; FTD, frontotemporal dementia; IBM, inclusion body myopathy; VUS, variant of uncertain significant; ACMG guideline,

a The patient also presented with mild cognitive impairment with Montreal Cognitive Assessment (MoCA, 22/30).

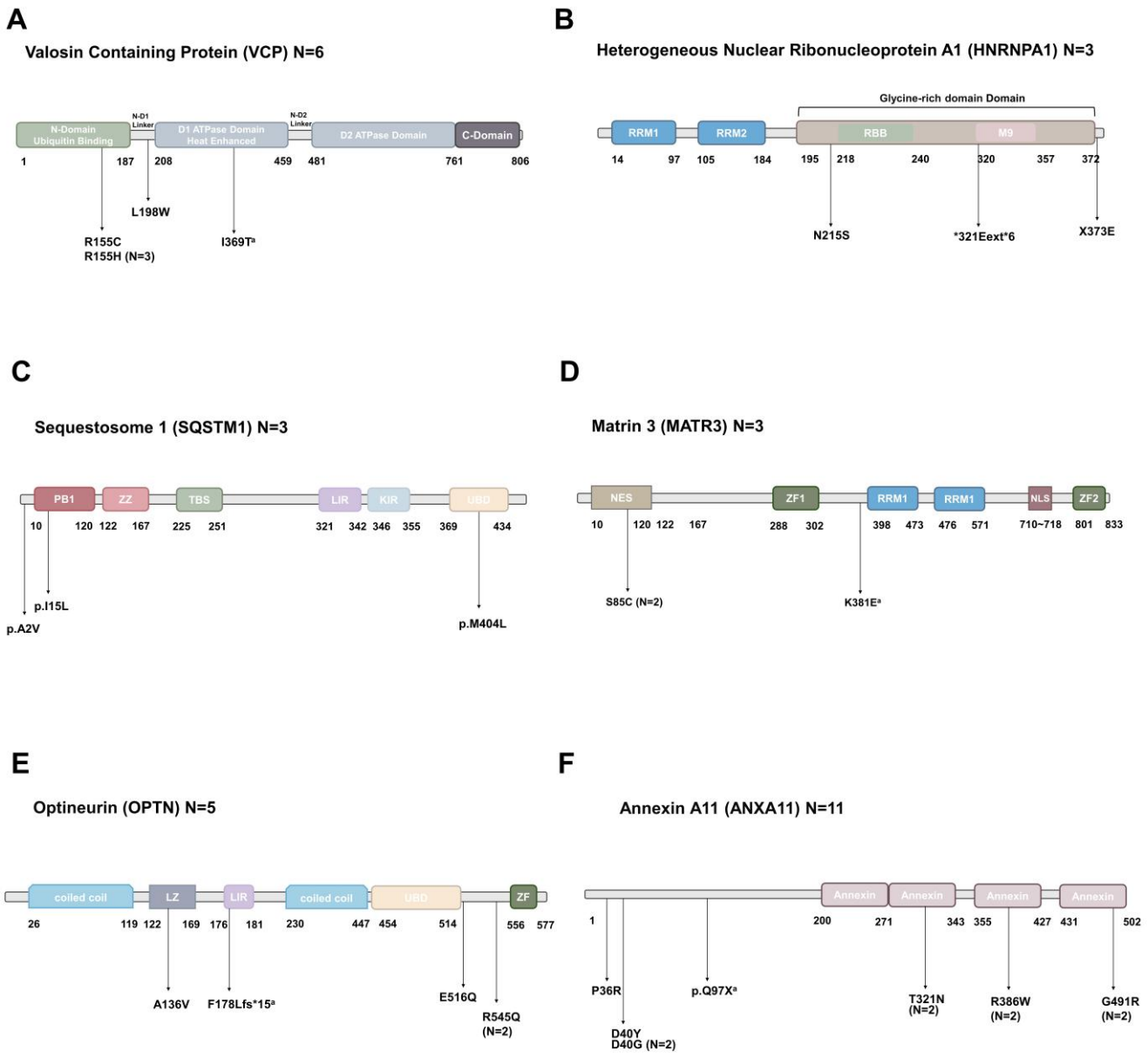
b The patient also carried mutation of ANXA11, c.1454G>A, p.G491R; VUS; FUS, NM_004960.4, c.1454delG, p.R485fs, VUS.

c The patient also carried mutation of MAPT, c.2086G>A, p.G696S, VUS.

d The patient also carried mutation of FUS, NM_004960.4, c.1561C>G, p.R521G, likely pathogenic.



Supplemental Figure 1. Study workflow. This retrospective study enrolled 29 patients with MSP-related variants by next-generation sequencing.



Supplemental Figure 2. Diagram of the protein structures and variants sites of six MSP-related-genes in this study (A-F). Two RNA recognition motifs (RRM 1 and 2); RNA-binding box, RBB; nuclear localization signal M9; The Phox and Bem1 (PB1) domain; The ZZ-type zinc finger (ZZ); the tumor necrosis factor receptor-associated factor 6 (TRAF6)-binding domain (TBS); the LC3-interacting region (LIR) domain; KEAP1 interacting region (KIR) domain; The ubiquitin (UB)-associated (UBA) domain, UBD; Nuclear export signal (NES); Zinc finger domains (ZF), nuclear localization signal (NLS); CC, coiled coil; LIR, LC3 interacting region; LZ, leucine zipper; a, The variants were novel.