

	RRM zf-RanBP mutations	
HsFUSa	MASNDYTQQAATQSYGAYPTQPGQGYSSQSSQPYGQQSYSGYQSTDTSGYGGSSYS-SYG	59
BtFUS	MASNDYTQQAATQSYGAYPTQPGQGYSSQSSQPYGQQSYSGYQSTDTSGYGGSSYS-SYG	60
MmFUS	MASNDYTQQAATQSYGAYPTQPGQGYSSQSSQPYGQQSYSGYQSSADTSGYGGSSYS-SYG	60
RnFUS	MASNDYTQQAATQSYGAYPTQPGQGYSSQSSQPYGQQSYSGYQSSADTSGYGGSSYS-SYG	60
DmCaz	-----MERGGY-----	7
CeC27H5.3	-----MAAYDQSQPDYSTPEGQQAAYWAYYYQQQQQGGQPDQ-----	38
HsFUSa	QSQNTGYGTQSTPQGYGSGTGGYSSSSQSSSYGQQSSYPGYGQQPAPSS TSG SYG SSSQS	119
BtFUS	QTQNS-YSTQSA PQGYGSA GGYSSSSQSSSYGQQSSYPGYGQQPAPSS TSG SYG SSSQS	119
MmFUS	QTQNTGYGTQSA PQGYGSGTGGYSSSSQSSSYGQQSSYPGYGQQPAPSS TSG SYG SSSQS	120
RnFUS	QTQNTGYGTQSA PQGYGSGTGGYSSSSQSSSYGQQSSYPGYGQQPAPSS TSG SYG SSSQS	120
DmCaz	-----GGSGQYNNFAVPPPNYQMPNKTGNYNEPPN-----	40
CeC27H5.3	-----DPYAAAAYGGHDQAQQPQNPYAPPPPGADPYGGSGGQSGG-----	80
HsFUSa	SSYQGPQSGSYSQPQSYGCGQQSYGQQSS-YNPPQGYGQQNQYNSSSGCGGGGGGNYG	178
BtFUS	SGYQGPQGGYGGQSSYGGQQSSYGGQQSS-YNPPQGYGQQSQYNSSS-GGGGGGGG-SYG	176
MmFUS	SSYQGPQSGGYGQQSSYGGCGQQSYGQQSSYNPPQGYGQQNQYNSSSGCGGGGGG-NYG	179
RnFUS	SSYQGPQSGGYGQQSSYGGCGQQSYGQQSSYNPPQGYGQQNQYNSSSGCGGGGGG-NYG	179
DmCaz	-----YGK-QGGYD SGSGHRG-----SGG S GNGGGGG-----	68
CeC27H5.3	DPYGGSRGGGGGFGGSRG-----GGGYDGGRRGSRGYDG	116
HsFUSa	QDQSSMSGGGGGGYGNQDQSGGGGS-GGYGQQDRGGRGRGGSGGGGGGGGYNRSSG	237
BtFUS	QDQP S MS S G G G - G G G Y G N Q D Q S G G - - - - - Y G G G Q D R G G R G R G - - - - - G G G Y N R S S G	223
MmFUS	QDQSSMSGGGG-GGGYGNQDQSGGGGGYGGQQDRGGRGRGG-----GGGYNRSSG	230
RnFUS	QDQSSMSGGGG-GGGYGNQDQSGGGGGYGGQQDRGGRGRGG-----GGGYNRSSG	230
DmCaz	-----SWNDRGG-NSYGN-----GGASKD-----SYNKGHG	93
CeC27H5.3	GRGGYGGDRGGRRGGGGYDGERGGRSRWDDGMSDRQGGPPGG-----RGGYQDRGP	168
HsFUSa	G Y E P R G R G G R G G R G M G S D R G G F N K F G G P R D Q G S R H D S E Q D N S D N N I F W Q L G E N V T	297
BtFUS	G Y E P R G R G G R G G R G M G S D R G G F N K F G G P R D Q G S R H D S E Q D N S D N N I F W Q L G E N V T	283
MmFUS	G Y E P R G R G G R G G R G M G S D R G G F N K F G G P R D Q G S R H D S E Q D N S D N N I F W Q L G E N V T	290
RnFUS	G Y E P R G R G G R G G R G M G S D R G G F N K F G G P R D Q G S R H D S E Q D N S D N N I F W Q L G E N V T	290
DmCaz	G Y S G G G G G G G G G G S G G N D - - - - - M I T Q E D I I F W S G M D P S T T	132
CeC27H5.3	R R D G P P S G G G Y G G G G A A S C N R E F G - - - - - S D G R V E L K E I V F W G G I S T I A N	213
HsFUSa	I E S V A D Y F K Q I G I I K T N K K T G Q P M I N L Y T D R E T G K L K G E A T V S F D D P P S A K A A I D W F D G K	357
BtFUS	I E S V A D Y F K Q I G I I K T N K K T G Q P M I N L Y T D R E T G K L K G E A T V S F D D P P S A K A A I D W F D G K	343
MmFUS	I E S V A D Y F K Q I G I I K T N K K T G Q P M I N L Y T D R E T G K L K G E A T V S F D D P P S A K A A I D W F D G K	350
RnFUS	I E S V A D Y F K Q I G I I K T N K K T G Q P M I N L Y T D R E T G K L K G E A T V S F D D P P S A K A A I D W F D G K	350
DmCaz	E Q D I E T H F G A I G I I K K D K R T M K P K I W L Y K N K E T G A S K G E A T V T Y D D T N A A Q S A I E W F D G R	192
CeC27H5.3	B A Y I A D V P S T G C D I A K N D R G - - P R I K I Y T D R N T G E P K G C E M I T F V D A S A A Q Q A I T M T Y N G Q	271
HsFUSa	E F S G - - N P I K V S F A T R R A D F N - - R G G G N R G - - G R G R G G P M G - R G G Y G G - - G G S G G G G R G	408
BtFUS	E F S G - - N P I K V S F A T R R A D F N - - R G G G N R G - - G R G R G G P M G - R G G Y G G - - G G S G G G G R G	394
MmFUS	E F S G - - N P I K V S F A T R R A D F N - - R G G G N R G - - G R G R G G P M G - R G G Y G G - - G G S G G G G R G	401
RnFUS	E F S G - - N P I K V S F A T R R A D F N - - R G G G N R G - - G R G R G G P M G - R G G Y G G - - G G S G G G G R G	401
DmCaz	D F N G - - N A I K V S L A Q R G N N W N - - K G G G G G G - - G G R G G F G G - R R G G G - - G G G G G G G G	243
CeC27H5.3	P F P G G S S P M S I S L A K F R A D A G G E R G G R G G R G F G G G R G G P M G R G G F G G D R G G Y G G G G R	331
HsFUSa	G - F P S G G G G G G - - - - - Q Q R A G D W K C P N P T C E N M N F S W R N E C N Q C K A P	450
BtFUS	G - F P S G G G G G G - - - - - Q Q R A G D W K C P N P T C E N M N F S W R N E C N Q C K A P	436
MmFUS	G - F P S G G G G G G - - - - - Q Q R A G D W K C P N P T C E N M N F S W R N E C N Q C K A P	443
RnFUS	G - F P S G G G G G G - - - - - Q Q R A G D W K C P N P T C E N M N F S W R N E C N Q C K A P	443
DmCaz	G R F D R G G G G G G R Y D R G G G G G G G G N V Q P R D G D W K C N - - S C N N T N F A W R N E C N R C K T P	301
CeC27H5.3	G G F D G R G G G G - - - - - F R G G D R G G F R G G D R G G F R G G D R G G F R G G D	372
HsFUSa	K P D - - - - - G P G G G P G G S H M G G N Y - - G D D R R G G R G G Y D - - R G G Y R G R G G D R G G F R G G R	498
BtFUS	K P D - - - - - G P G G G P G G S H M G G N Y - - G D D R R G G R G G Y D - - R G G Y R G R G G D R G G F R G G R	484
MmFUS	K P D - - - - - G P G G G P G G S H M G G N Y - - G D D R R G - R G G Y D - - R G G Y R G R G G D R G G F R G G R	490
RnFUS	K P D - - - - - G P G G G P G G S H M G G N Y - - G D D R R G - R G G Y D - - R G G Y R G R G G D R G G F R G G R	490
DmCaz	K G D D E G S S G G G G G Y G G G G G G Y D R G N D R G S G G G Y H N R D R G G N S Q G G G G G G G G G Y	361
CeC27H5.3	R G G - - - - - D R G G F R G G R G V G G G N A N M E Q R K N D W P C E Q - - - - - C G N S N F A F R E C N Q C Q A	421
HsFUSa	G - - - - - G G D R G G F G P G K M D S R - - G E H R Q D R - - R E R P Y	526
BtFUS	G - - - - - G G D R G G F G P G K M D S R - - G E H R Q D R - - R E R P Y	512
MmFUS	G - - - - - G G D R G G F G P G K M D S R - - G E H R Q D R - - R E R P Y	518
RnFUS	G - - - - - G G D R G G F G P G K M D S R - - G E H R Q D R - - R E R P Y	518
DmCaz	S R F N D N N G G G R G G R G G G G N R D G G P M R N D G G M R S R P Y	399
CeC27H5.3	P - - - - - R P D G G S G G G G E R R - G G P P G G D R - - Y R P Y	448

Figure S1. Peptide sequence alignments of FUS proteins from different species, including human (Hs), bovine (Bt), mouse (Mm), rat (Rn), fly (Dm) and worm (Ce). The amino acid residues that are identical across all species are in red (\*). RNA recognition motif (RRM) and zinc finger (zf-) Ran-BP domain are highlighted in yellow and blue, respectively.

**Table S1.** Published ALS cases with FUS mutations: the age of onset and duration

	Subject	Age of onset (years)	Duration (months)	Reference	
	1	13	20	Huang et al., 2010	
Sporadic	2	22	10	Baumer et al., 2010	
	3	18	11		
P525L	1	21	<12	Chiò et al., 2009	
	2	32	<12		
Familial	3	16	<12		
	4	27	<24		
	5	22	6	Kwiatkowski et al., 2009	
R524S	Familial	1	34	39	Kwiatkowski et al., 2009

ALS, amyotrophic lateral sclerosis.

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