Supplementary Material

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Supplementary Table 1 Primer pairs used to amplify the FBLN5 gene coding region.

Name		Primer	
FBLN5-1F	5´	CCTCTGGAATAAAACACCCG	3´
FBLN5-1rv	5´	AGGAATGAAGCGCTGAGAAT	3´
FBLN5-2F	5´	GTCTGGAACCACCATGACCT	3´
FBLN5-2R	5´	ACTGTAAAGCCACTCCCACC	3´
FBLN5-3fw	5´	AAACCCTGAAACCTGTCTGC	3´
FBLN5-3rv	5´	CCCCTCTCAGTGCTTAGCTC	3´
FBLN5-4fw	5´	CCCACCACTCAATATTGCAA	3′
FBLN5-4rv	5´	GGTGCATTGAATGGCAACTA	3´
FBLN5-5F	5´	TAGGATGGCAGAAGGATTCC	3´
FBLN5-5R	5´	CTTACTACCCTCAGGCAGCC	3´
FBLN5-6F	5´	GCCTTGTATTCGAGACAGCA	3´
FBLN5-6R	5´	CACAAACATAAGCTGCCAGG	3´
FBLN5-7F	5´	AGATCATGCTCCCAAAGGTC	3´
FBLN5-7R	5´	TCCCAAACTGGACATGTGTC	3′
FBLN5-8F	5´	TCCATTGCTAGAAGTGCTGG	3´
FBLN5-8R	5´	GAGCTGCCACTATGAGAGCC	3´
FBLN5-9F	5´	CTGTTGCTGCCATATTGGAT	3´
FBLN5-9R	5´	CATGACGTAGGTAGTAGGCCAG	3´
FBLN5-10F	5´	GCCAGGAGCAGAGACATTCT	3´
FBLN5-10R	5´	GGCTCAGGAGGAGAAGCAT	3´
FBLN5-11F	5´	GAAAGAGCATGGCACAGTTG	3´
FBLN5-11R	5´	AATGCCTAACGTCTGTGTCG	3´

Supplementary Table 2 Normal values of nerve conductions (range in brackets), amplitudes of

motor nerves are peak-peak.

NCVs: nerve conduction studies; NCV: nerve conduction velocity in meter per second (m/sec);

NE: not examined; NR: no response

Motor median nerve: DL: 3.4-4.3 msec; AM: 4.8-10.0 mV; NCV: 48.0-60.0 m/sec

Sensory median nerve: AM: 10.0-30.0µV; NCV: 45.0-56.0 m/sec

Motor peroneal nerve: DL: 4.5-5.8 msec; AM: 4.5-9.0 mV; NCV: 44.0-50.0 m/sec

Sural nerve: AM: 8.0-20.0µV; NCV: 44.0-52.0 m/sec

FAMILY AND MEMBER	FBLN5 SEQUENCE	NCVs peroneal motor/	NCVS MEDIAN MOTOR/	
	VARIATION		SENSORY NERVE	
		NCV-DL-AM//NCV	NCV-DL-AM//NCV	
Family A				
A11	p.R373C	NR // NR	NR // NR	
A14	p.R373C	NE // NE	22.0-8.4-1.1 // NR	
A16	p.R373C	20.7-9.0-0.2 // NR	NE//NE	
A17	p.R373C	21.0-6.4-5.0 // NR	28.0-7.0-11.0 // NR	
A22	p.R373C	NE // NE	37.5-8.1-11.5 // NE	
A23	p.R373C	24.0-6.5-2.4 // NE	35.0-7.2-5.1 // 29.0	
Family B				
B5	p.R373C	NE // NE	NE // NE	
B9	p.R373C	NR // NR	23.8-7.4-8.4 // 27.9	
Family C				
C1	p.G90S	35.5-8.2-0.1 // 51.6	52.6-3.8-1.6 // 65.1	
C2	p.G90S	NR // NE	NE-3.9-4.1 // 50.0	
C3	p.G90S	48.0-3.0-5.7 // NE	54.0-3.5-22.0 // 39.0	
C4	p.G90S	40.6-6.8-2.6 // NE	56.3-4.2-9.3 // NE	
C5	p.G90S	47.4-4.4-3.1 // NE	55.9-3.3-7.8 // 44.4	
Family D				
D1	p.V126M	51.0-5.4-5.2 // 44.0	59.0-4.0-4.2 // 53.0	
D2	p.V126M	40.4-5.6-1.5 // NE	53.6-5.1-13.7 // NE	
AMD-Pat				
E	p.V126M	NE // NE	NE // NE	
F	p.V126M	43.8-4.8-4.1 // NE	NE // NE	
G	p.G90S	34.2-5.0-0.8 // NE	46.2-4.0-3.6 // NE	
Н	p.T48I	44.0-4.5-5.3 // NE	58.0-4.8-4.6 // NE	
Κ	p.G267S	NE	NE	
L	p.G267S	40.3-5.6-0.9 // NR	56.7-4.5-9.0 // 50.7	
Controls				
Ι	p.V126M	NR // NE	52.4-5.4-3.7 // NE	
J	p.V126M	41.4-4.9-1.4 // NE	50.0-3.8-4.4 // NE	

Supplementary Table 3 Sequencing statistics and list of the observed High Confidence

Differences.

Variations are sorted based on their variation types; ns (non-synonymous) and s (synonymous).

Supplementary Table 3A

Total sequence information	72.263Mb
Capture Array Target Region	695.5kb
Disease linked exome size	120.4kb
Target bp with a coverage >10-fold	>91%
Total nr. of variants	82
Variants in coding sequence	30
synonymous	18
novel synonymous	1
non- synonymous	12
novel non- synonymous	1

Supplementary Table 3B

Reference			Ref	Var	Total	Var	Ref	Var	Region		Variation
Accno	Start Pos	End Pos	Nuc	Nuc	Depth	Freq	AA	AA	Name	Known SNP's	Туре
chr14	87470966	87470966	Т	С	55	100%	Т	А	GALC	rs421262	ns
chr14	87477641	87477641	А	G	30	37%	I	Т	GALC	rs398607	ns
chr14	87932282	87932282	G	А	35	60%	V	М	SPATA7	rs3179969	ns
chr14	88008405	88008405	А	G	60	58%	V	А	PTPN21	rs2274736	ns
chr14	88016375	88016375	G	А	14	50%	L	F	PTPN21	rs2401751	ns
chr14	88275018	88275018	Т	С	51	57%	I	V	EML5	rs17188228	ns
chr14	90712148	90712148	G	А	26	58%	S	N	C14orf159	rs34302825	ns
chr14	90808834	90808834	А	G	12	50%	L	Р	CCDC88C	rs941920	ns
chr14	91338368	91338368	Т	G	37	100%	К	Т	TC2N	rs2402073	ns
chr14	91413652	91413652	G	А	25	48%	R	С	FBLN5	novel	ns
chr14	91510819	91510819	С	Т	30	43%	G	S	TRIP11	rs1051340	ns
chr14	91575668	91575668	Т	А	35	40%	М	L	TRIP11	rs17127898	ns
chr14	87477628	87477628	Т	А	31	97%	V	V	GALC	rs421466	S
chr14	87481700	87481700	Т	С	48	100%	Т	Т	GALC	rs367327	S
chr14	87501651	87501651	С	Т	38	37%	Q	Q	GALC	rs12888666	S
chr14	87547166	87547166	С	Т	74	100%	Т	Т	GPR65	rs6574978	s
chr14	87722142	87722142	С	Т	23	65%	А	А	KCNK10	rs3742692	S
chr14	87763478	87763478	G	С	65	58%	V	V	KCNK10	rs2277524	s
chr14	88005678	88005678	А	G	57	58%	Т	Т	PTPN21	rs2297129	S
chr14	88015344	88015344	А	G	13	38%	Р	Р	PTPN21	rs879932	s
chr14	89799824	89799824	С	Т	59	100%	I	I	PSMC1	rs11554757,rs4811	s
chr14	90193328	90193328	Т	С	18	100%	Р	Р	TTC7B	rs3742660	S
chr14	90231615	90231615	С	Т	27	63%	Т	Т	TTC7B	rs10146731	S
chr14	91017796	91017796	Т	С	81	64%	Т	Т	SMEK1	rs17127374	S
chr14	91153757	91153757	С	G	42	55%	V	V	CATSPERB	rs1620238	S
chr14	91157769	91157769	G	А	36	47%	I	I	CATSPERB	rs1296082	S
chr14	91321340	91321340	А	G	44	48%	L	L	TC2N	novel	s
chr14	91417433	91417433	А	G	20	45%	1	I	FBLN5	rs2430347	S
chr14	91862008	91862008	G	А	45	100%	Т	Т	SLC24A4	rs941646	S
chr14	91978826	91978826	Т	С	4	100%	Н	Н	SLC24A4	rs941650	S

Supplementary Figure 1 Sequence coverage of the disease linked interval (chr.14: bp 87,435,655 – 91,913,433).

The x-axis indicates the calculated coverage per target nucleotide and the y-axis represents the percentage of sequenced target nucleotides. Bars in bold highlight the observed sequencing depth of 25-, 20-, 10-, 5- and 1-fold. >91% of the target nucleotides were sequenced to a minimum depth of 10-fold.



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Supplementary Figure 2 Sequence traces from the 37 unique reads covering the FBLN5 c.1117

C>T (p.R373C) mutation (obtained from patient A16).

The mutated nucleotide at position 91413652 was covered by 37 unique sequence reads, in 22 of the reads the reference allele (G on the anti-sense strand) and in the other 17 reads the mutant allele (A on the antisense strand) was detected indicating that the mutation is present in a heterozygous state. The *FBLN5* gene is transcribed from the minus-strand of chromosome 14; therefore the substitution of a cytosine by a thymidine is represented by a guanine (reference allele) and an adenine (mutant allele) nucleotide in mapping diagram.

chr14 contiq01644 F6TGQCJ01B7R7E F6TGQCJ01B1R7E F6TGQCJ01B1R5E F6TGQCJ01B1ASE F6TGQCJ01B1ASE F6TGQCJ01AICFH F6TGQCJ01B8012 F6TGQCJ01B8012 F6TGQCJ01B87AH F6TGQCJ01B87AH F6TGQCJ01B87AH F6TGQCJ01B87AH F6TGQCJ01B87AH F6TGQCJ01B87AH F6TGQCJ01B87B1 F6TGQCJ01B87B4 F6TGQCJ01B87B4 F6TGQCJ01A3WQX F6TGQCJ01A9G14 F6TGQCJ01A9G54 F6TGQCJ01B95VY F6TGQCJ01B87V F6TGQCJ01A8725 F6TGQCJ

CENENTIT CATELOGNANATETNATAGECCCCAGGETA GE	COTCO TOCOTTOC ATTT COANCATOTOA O C COCAACOOAG
CCAGAIII-GAICIG <mark>-</mark> AAA <mark>-</mark> IG <mark>-</mark> AAIAGGCCCCAGGGIA-GC-	GGICG-IGGCIIGC-AIII-GGAAGAIGICA-G-C-GGGAACGGAG
CCAGATTT-GATCTGGAAAATGTAATAGGCCCCAGGGTA-GC-	<u>ומסדכמ-דממכדד</u>
CCAGATTT-GATCTGGAAAATGTAATAGGCCCCAGG <mark>-</mark> TA-GC <mark>A</mark>	G - TCG - TGGCTTGC - ATTT - GGAAGATGTCA - G - C - GGGAACGGAG
CCAGATTT-GATCTGGAAAATGTAATAGGCCC <mark>-</mark> AGGGTA-GC-	GGTCG-TGGCTTGC-ATTT-GGAAGATGTCA-G-C-GGGAACGGAG
CCAGATTT-GATCTGGAAAATGTAATAGGCCCCAGGGTA-GC-	GGTCG-TGGCTTGC-ATTT-GGAAGATGTCA-G-C-GGGAACGGAG
CCAGATTT-GATCTGGAAAATGTAATAGGCCCCAGGGTA-GC-	GGTCG-TGGCTTGC <mark>T</mark> ATTT-GGAAGATGTCA-G <mark>G</mark> C-GGGAACGGAG
CCAGATTT-GATCTGGAAAATGTAATAGGCCCCAGGGTA-GCA	G - TCG - TGGCTTGC - ATTT - GGAAGATGTCA - G - C - GGGAACGGAG
CCAGATTT-GATCTGGAAAATGTAATAGGCCCCAGGGTA-GCA	G <mark>-</mark> TCG-TGGCTTG
CCAGATTT-GATCTGGAAAATGTAATAGGCCCCAGGGTA-GC-	GGTCG-T
CCAGATTT-GATCTGGAAAATGTAATAGGCCCCAGGGTA-GCA	G-TCG-TGGCTTGC-ATTT-GGAAGATGTCA-G-C-GGGAACGGAG
CCAGATTT-GATCTGGAAAATGTAATAGGCCCCAGGGTA-GCA	G-TCG-TGGCTTGC-ATTT-GGAAGATGTCA-G-C-GGGAACGGAG
	COTCO TOCCTTOC ATTT COARGATOTCA C C COCAACCOAC
	C TEC TECETTEC ATTL COMMONTATION C C CECANCECAG
	0 - I C G - I G G C I I G C - A I I I - G G A A G A I G I C A - G - C - G G G A A C G G A G
	GGICG-IGGCIIGC-AIII-GGAAGAIGICA-G-C-GGGAACGGAG
CCAGATTT-GATCTGGAAAATGTAATAGGCCCCAGGGTA-GC-	GGTCG-TGGCTTGC-ATTT-GGAAGATGTCA-G-C-GGGAACGGAG
CCAGATTT <u>-</u> GATCTGGAAAATGTAATAGGCCCCAGGGTA-GC <mark>A</mark>	G <mark>-</mark> TCG-TGGCTTGC-ATTT-GGAAGATGTCA-G-C-GGGAACGGAG
CCAGATTT <mark>T</mark> GATCTGGAAAATGTAATAGGCCCCAGGGTA-GC <mark>A</mark>	G <mark>-</mark> TCG-TGGCTTGC-ATTT-GGAAGATGTCA-G-C-GGGAACGGAG
CCAGATTT-GATCTGGAAAATGTAATAGGCCCCAGGGTA-GC <mark>A</mark>	G <mark>-</mark> TCG-TGGCTTGC-ATTT-GGAAGATGTCA-G-C-GGGAACGGAG
CCAGATTT-GATCTGGAAAATGTAATAGGCCCCAGGGTA-GC <mark>A</mark>	G - TCG - TGGCTTGC - ATTT - GGAAGATGTCA - G - C - GGGAACGGAG
CCAGATTT-GATCTGGAAAATGTAATAGGCCCCAGGGTA-GC-	GGTCG-TGGCTTGC-ATTT-GGAAGATGTCA-G-C-GGGAACGGAG
CCAGATTT-GATCTGGAAAATGTAATAGGCCCCAGGGTA-GC <mark>A</mark>	G - TCG - TGGCTTGC - ATTT - GGAAGATGTCA - G - C - GGGAACGGAG
CCAGATTT-GATCTGGAAAATGTAATAGGCCCCAGGGTA-GC-C	GGTCG-TGGCTTGC-ATTT-GGAAGATGTCA-G-C-GGGAACGGAG
CCAGATTT-GATCTGGAAAATGTAATAGGCCCCAGGGTA-GC-	GGTCG-TGGCTTGC-ATTT-GGAAGATGTCA-G-C-GGGAACGGAG
T <mark>-</mark> T G G A A A A T G T A A T A G G C C C C A G G G T A - G C - <mark>(</mark>	GGTCG-TGGCTTGC-ATTT-GGAAGATGTCAN-C-GGGAACGGAG
T <mark>-</mark> TGGAAAATGTAATAGGCCCCAGGGTA - GC - <mark>C</mark>	GGTCG-TGGCTTGC-ATTT-GGAAGATGTCA-G-C-GGGAACGGAG
T <mark>-</mark> T G G A A A A T G T A A T A G G C C C C A G G G T A - G C - C	GGTCG-TGGCTTGC-ATTT-GGAAGATGTCA-G-C-GGGAACGGAG
CTGGAAAATGTAATAGGCCCCAGGGTA-GC-	GGTCG-TGGCTTGC-ATTT-GGAAGATGTCA-G-C-GGGAACGGAG
A – G C <mark>A</mark>	G-TCG-TGGCTTGC-ATTT-GGAAGATGTCA-G-C-GGGAACGGAG
C - (GGTCGGTGGCTTGC-ATT-GGAAGATGTCA-G-C-GGGAACGGAG
	TCG-TGGCTTGC-ATTT-GGAAGATGTCA-G-C-GGGAACGGAG
	GGAAGATGTCA-G-C-GGGAACGGAG
	GATGTCA-G-C-GGGA-CGGAG
	CGGAG
	G

Supplementary Figure 3 Evolutionary conservation of the FBLN5 protein.

The FBLN5 sequence was compared to its orthologues and paralogues with VectorNTI software.

Human (NP_006320.2), Orangutan (NP_001125375.1), Chimpanzee (XP_001145383.1), White-

tufted-ear marmoset (XP_002754249.1), Rhesus monkey (XP_001092011.1), Dog

(XP_537350.2), Bovine (NP_001014946.1), Rat (NP_062026.2), Mouse (NP_035942.1), Chicken

(XP_421323.1), Xenopus (NP_001025619.1), Danio (NP_001005979.1), FBLN1 (NP_006477.2),

FBLN2 (NP_001004019.1), FBLN3 (NP_001034438.1), FBLN4 (NP_058634.3), FBLN6

(NP_114141.2), FBLN7 (NP_694946.2). The arrows indicate mutation sites found in exons 4, 8

and 10.

	T48I		G90 S		V126M
	. ↓	Insertion	4		ł
F8LN5_human	44 DECRTIPEACRGDMMCVNQ	NGGYLCIPRTNPVYRGPYSNP	YS TP YSGP YPAAAP		PLSAPNYPTISR-PLICRFGYQN-DESNQCVDVDECA
FBLN5_orangutan	44 DECRTIPEACRGDMMCVNQ	NGRYLCIPRTNPVYRGPYSNP	YSTPYSGPYPAAAP		PLSAPNYPTISR-PLICRFGYQN-DESNQCVDVDECA
FRINS comment	43 DECRITPEACRODMECTING	NGGYLCIPR	VETRYSCRYPARAP		PLSRPNIPTISE PLICEFORM DESNOCUDUECA
FBLN5 thesus markey	44 DECRTIPEACRODNHCVNO	VGGYLCIPRTNPVYRGPYSNP	YSTPYSGPYPAAAP		PLSAPNYPTISR-PLICEFGYON-DEGNOCUDUDECA
FBLN5_dog	23 DECRTIPEACRGDMHCVNG	VGGYLCIPRTNPVYRGPYSNP	YSNPYTGPYPAAAP		PLSAPNYPTISR-PLICEFGYON-DESNOCVDVDECA
FBLN5_bovine	44 DECRTIPEACRGDMHCVNQ	MGGYLCIPRTNPVYRGPY5NP	YSNP YSASYPAAAP		PLSAPNYPTISR-PLICRFGYQN-DESNQCVDVDECA
FBLN5_rat	44 DECRTIPEACRGDMMCVNQ	NGGYLCIPRTNPVYRGPYSNP	YSTSYSGPYPAAAP		PVPASNYPTISR-PLVCRFGYQM-DEGNQCVDVDECA
F8LN5_mouse	44 DECRTIPEACRGDNHCVNQ	ACCATCIBE	VSTS YSGPYPAAAP		PWPASNYPTISR-PLWCRFGYQN-DEGNQCVDVDECA
FBLN5_chicken	44 DECRTIPEACRGDHVCVNQ	NGGYLCVPRTNPVYRSPYLNP	YSNIYPPPPA		PGPVPNYPTVTR-PLICRFGYQL-DENNQCADIDECA
FBLND_xenopus FBLN5_dario	43 DECRILDACRGDMHCVNQ	ACCAL CAPPER YEOSYCRIMERI RAPEASARTERAR	DEL CUETTE ADUADUA DEDE	an	PPNFPSPPR-PLICRFGYQL-DED-QCVDIDECA
F9LN1_human	284 DECESSIENCLEDETCONT	LGSEBCRPKLOCKSGFTODALGNCIDIN	ECLSTSAPCPIG		CINTEGSVICOKNUPNCGRGVHLNEGTECUDUDECA
F8LN2_human	813 DECAMOTHICOPOFLCONT	KGSFYCOARORCHDGFLODPEGNCVDIN	ECTSLSEPCRPG		CINTVGSYTCORNPLICARGYHASDDGTRCVDVNECE
F8LN3_human	46 DECDIVPBACKGGHKCVNH	YGGYLCLPKTAQIIVNNEQPQQETQPAEGTSGATTO	SVVAASSHATSGVLPGGGFVASAAA	VAGPEMQTGRNNFVIRRN	PADPORIPSNPSHRIQCAAGYEQ-SEHNVCQDIDECT
F8LN4_human	56 NECLTIPEACKGENKCINH	YGGYLCLPRSAAVINDLHG	E-GPPP		PVPPAQHPNPCPPGYEP-DDQDSCVDVDECA
F8LN6_human	5149 DECALGRHTCHAGQDCDNT	IGSYRCVVRCGSGFRRTSDGLSCQDINECQESSPCI	IQRCFNAIGSFHCGCEPGYQLK	GRKCMDVNECRQNVCR	PDQHCKNTRGGYKCIDLCPNGNTKAENGTCIDIDECK
P8LIV7_numen	3 PSSPRALFLLLL ILACPEP	RASQNCUSEQQLLSAIRQLQQLLKGQ	ETRFAEGIRHNKSR	LA	ALQNSVGRVGPDALP <u>V</u> SCPALNTPADGRKFGSKYLVD
	G267S				
	*				
FBLN5_human	260 HECVNQPGTYFCSCP-PGY1	LLDDNRSCOD INECEHRNHTCNLOQTC YNLOGGF KC	IDPIRCEEPYLRISDNRCMCPAEN-	PGC	
FBLN5_orangutan	260 HECVNQPGTYFCSCP-PGY1	LLDDNRS <mark>CQDINECEHRNHTCNLQQTCYNLQG</mark> GFKC	IDPIRCEEPYLRISDNRCMCPAEN-	PGC	
FBLN5_chimp	265 HECVNQPGTYFCSCP-PGY1	LLDDNRSCQD INECEHRNHTCNLQQTC YNLQGGF KC	IDPIRCEEPYLRISDNRCMCPAEN-	PGC	
FBLN5_marmoset	260 HECVNQPGTYFCSCP-PGY1	LLDDNRSCQD INECEHRNHTCNLQQTCYNLQGGFKC	IDPIRCEEPYLRISDNRCMCPAEN-	PGC	
FBLN5_mesus monkey	239 HECKNOPGTYECSCP-PGY	LIEDNRSCODINECEHRNHICNLOOTCYNLOGGER	IDPIRCEEPILRISDNRCHCPAEN-	PGC	
FBLN5 bovine	260 HECVNOPGTYFCSCP-AGY	LLDDNRSCOD INECEHRNHTC ILOOTCYNLOGGFKC	IDPIRCEEPVLRISDNRCMCPAEN-	PGC	
FBLN5_rat	260 HECVNQPGSYFCSCP-PGYN	LLEDNRSCOD INECEHRNHTCTPLQTCYNLQGGFKC	IDPIVCEEPYLL IGDNRCMCPAEN-	TGC	
FBLN5_mouse	260 HECVNQPGSYFCSCP-PGYV	LLDDNRS <mark>CQD INECEHRNHTCTSLQTC YNLQG</mark> GFKC	IDPISCEEPYLL IGENRCMCPAEH-	TSC	
FBLN5_chicken	256 HECVNGPGSYYCVCP-SGYN	LLDDSRSCQD INECE IRNFTCTLQQTCFN IPGEYKC	LDPVRCEEPVIQINENRCMCPAEN-	PGC	
FBLN5_xenopus	251 HDCVNEPGSYYCRCP-EGY	LLDDSRTCQDIDECDTGNNTCTLQQLCFNIPGSYRC	LDTVRCEDPYIQINDNRCMCPVEN-	TAC	
FBLIND_Ganio EPI N1	496 MDCTNTDCSFSCACP-SGY	VYEDGRSCEDENECESGNNTCTTEQUCENEQGYTC	LNPLRCDPPYIELSDNQCMCSAEN-	PCIN	
FBLN2	1043 FRCLNVPGSVOCACPFOGV	MTANGRSCKDUDECALGTHNCSINEICFNIGGSER	LR-FECPENTRRSARIEQUERIDIV	FLFC	
FBLN3	307 YOCVNEPGKESCHCP-QGYC	AVRS-RTCODINECET-TNECREDEMCWNYHGGFR	YPRNPCODPYILTPENRCVCPVSN-	ANC	
FBLN4	256 YRCVNEPGRESCHCP-QGYC	LLAT-RLCODIDECESGAHQCSEAQTCVNFHGGYRC	VDTNRCVEPYIQVSENRCLCPASN-	PLC	
FBLN6	5444 HECKNTFGSYQCICP-PGYC	LTHNGKTCODIDECLEONVHCGPNRMCFNMRGSYOC	ID TPCPPNYQRDPVSGFCLKNCPPN	JDLEC	
FBLN7	242 HACVNTPGSYRCTCP-GGYF	TLADGKSCEDVDECVGLQPVCPQGTTCINTGGSFQC	VSPECPEGSGNVSYVKTSPFQCERN	IPCPMDSRP <mark>C</mark>	
			F	R373C	
			Charles Redis Barles Barris	1	
FBLN5 human	299 CNLOOTCYNLOGGEKCIDP	IRCEEPYLRISDNRCMCPAENPGCRDOP	TILYRDNDVVSGRSVPADIFONOA	TTRYPGATYIFOIKSONE	GREFYNROTGPISATLVNT
FBLN5_orangutan	299 CNLOOTCYNLOGGERCIDP	IRCEEPYLRISDNRCMCPAENPGCRDQP	TILYRDNDVVSGRSVPADIFONQA	TTRYPGAYYIFQIKSGNE	GREFYMRQTGPISATLVNT
FBLN5_chimp	304 CNLQQTCYNLQGGFKCIDP	IRCEEPYLRISDNRCHCPAENPGCRDQP	TILYRDNDVVSGRSVPADIFQNQA	TTRYPGAYYIFQIKSGNE	GREFYHRQTGP ISATLVNT
FBLN5_marmoset	299 CNLOOTCYNLOGGERCIDP	IRCEEPYLRISDNRCMCPAENPGCRDQPI	TILYRDNDVVSGRSVPADIFOROA	TTRYPGAYYIFQIKSGNE	GREFYMRQTGPISATLVNT
FBLN5_rhesus mankey	299 CNLQQTCYNLQGGFKCIDP	IRCEEPYLRISDNRCMCPAENPGCRDQP	TILYRDNDVVSGRSVPADIFQNQA	TTRYPGAYYIFQIKSGNE	GREFYMRQTGPISATLVNT
FBLND_dog	2/8 CNLOQTCYNLOGGFRCIDP	IRCEEPYLRISDNRCMCPAENPGCRDQP	TILYRD HDVVSGRSVPADIFQHQA	TTRYPGAYYIFQIKSCNE	GREFYHRQTGPISATLVNT
FBLIND_DOWNE	299 CTDL OTCANLOGGERCIDP	INCERPTERISONRCMCPAENPGCRDQP	TILTED NDVVSGRSVPADIF QRQA	TTRYPGAYYIFQIKSGND	GREFTARQIGPISATLVAT
FBI N5 mouse	299 CTSLOTCANLOGGERCIDE	ISCEPTILICENCOCPACTION TO COLORI	TIL VERNOVVSCRSVPADIFOROM	TTDVDCIVVIEOTVSCNE	COF
FBLN5_chicken	295 CTLOOTCENIPGEYKCLDP	RCEEPYIOINENRCMCPAENPGCRDOP	TILYRVNDVLSGRSVPSDIFONOA	TTRYPGAYYIFOIKSONE	GREFYMROTGPISATLVNT
FBLN5_xenopus	290 CTLOOLCFNIPGSYRCLDT	RCEDPYIQINDNRCMCPVENTACRDOP	TIVHRHMDLLSTRSVPTDIFONQA	TTREPGATYLEQIKSONE	GREFYNROTGPISATLVLT
FBLN5_danio	328 CTTEQVCENFQGGYTCLNP	RCDPPYIELSDNOCMCSAENPACRDRP	TVLYRHNDLSSGRSVPADIFQNQA	TTRYPGAFYIFQIKSGNE	GREFYHROTSNHSATLVLA
FBLN1_human	536 CSINETCENIQGOERCLA-	ECPENYRRSAATLQQEKTDTVRCIKSCRP	IDVICVF DPVHTISHTVISLPTFRE	FTRPEEIIFLRAITPPHP	ASQANIIFD ITEGNLRDSFDIIKRYMDGHTVGVVRQV
F8LN2_human	1083 CSEAETCHNIQGSFRCLR-	FECPPNYVQVSKTRCERTTCHDFLECONSPI	RITHYQLNFQTGLLVPAHIFRIGP	APAFTGDTIALNIIKGN-	EEGYFGTRRLNAYTGVVYLQ
FBLN3_human	344 CREDENCUNYHGGFRCYPR	VPCQDPYILTPENRCVCPVSNAMCRELPC	SIVYKYNSIRSDRSVPSDIFQIQA	TTIYANTINTFRIKSGNE.	NGEFYLRQT3PVSAMLVLV
F8LN4_human	254 CSEAQTCVNFHGGYRCVDT	VRCVEPYTQVSENRCLCPASNPLCREOPS	SIVHRYNTITSERSVPADUFQIQA	ISVYPGAYNAFQIRAGNS	COPFYIRQINNVSAHLVLA
F9LN6_human	281 CROCTTC INTOCS OCIDI	CPPONTQRDPVSGFCUKNCPPNDLECALSP	ADDIAL VSLPYGIAINODLIRLVA	A DODA CONSI DECTIC	LUIVFFALRDENLKGVVYTT
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Supplementary Figure 4 Simplified and schematic model of elastic fiber assembly.

A. Pericellular assembly of tropoelastin into globules and stabilizing through cross-linking by LOX. FBLN4 and LOX form together with tropoelastin a ternary complex. The binding of FBLN4 with LOX facilitates the cross-linking of tropoelastin. *B.* FBLN5 associates with elastin globules. *C.* FBLN5 facilitates direct high affinity binding of elastin on microfibrils. This is mutually inhibitory to the interaction of FBLN5 and tropoelastin due to the same or overlapping binding site. Fibrillin also disrupts FBLN4 binding to LOX and tropoelastin. FBLN4 and FBLN5 thus do not have compensatory roles in this process. Active LOX cross-links by coalescing elastin globules on microfibrils. *D.* LOX, FBLN4 and FBLN5 may remain associated with microfibrils or dissociate to begin a new cycle of assembly.

