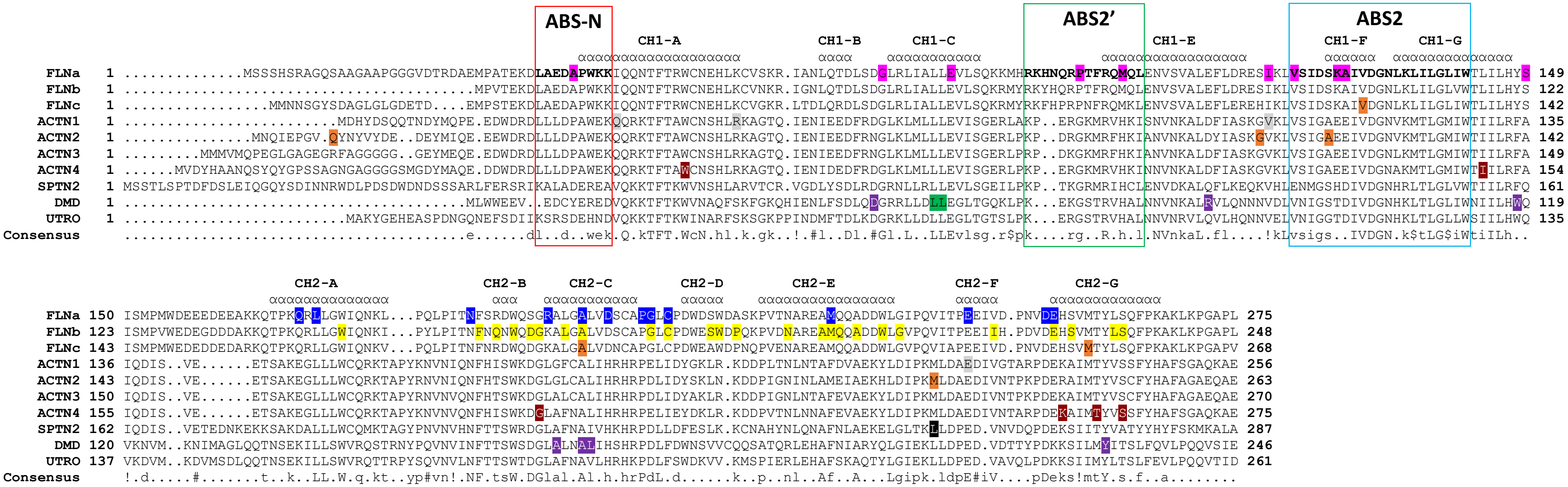

```
                                                               ABS-N                                                        ABS2’                            ABS2
                                                                         CH1-A                 CH1-B      CH1-C                       CH1-E               CH1-F      CH1-G
                                                                   ααααααααααααααααααα         αααα    ααααααααααα              αααααααααααααααααα        ααααααα αααααααααααααα
     FLNa   1 ..............MSSSHSRAGQSAAGAAPGGGVDTRDAEMPATEKDLAEDAPWKKIQQNTFTRWCNEHLKCVSKR.IANLQTDLSDGLRLIALLEVLSQKKMHRKHNQRPTFRQMQLENVSVALEFLDRESIKLVSIDSKAIVDGNLKLILGLIWTLILHYS 149
     FLNb   1 .........................................MPVTEKDLAEDAPWKKIQQNTFTRWCNEHLKCVNKR.IGNLQTDLSDGLRLIALLEVLSQKRMYRKYHQRPTFRQMQLENVSVALEFLDRESIKLVSIDSKAIVDGNLKLILGLVWTLILHYS 122
     FLNc   1 .................MMNNSGYSDAGLGLGDETD....EMPSTEKDLAEDAPWKKIQQNTFTRWCNEHLKCVGKR.LTDLQRDLSDGLRLIALLEVLSQKRMYRKFHPRPNFRQMKLENVSVALEFLEREHIKLVSIDSKAIVDGNLKLILGLIWTLILHYS 142
    ACTN1   1 .........................MDHYDSQQTNDYMQPE.EDWDRDLLLDPAWEKQQRKTFTAWCNSHLRKAGTQ.IENIEEDFRDGLKLMLLLEVISGERLAKP..ERGKMRVHKISNVNKALDFIASKGVKLVSIGAEEIVDGNVKMTLGMIWTIILRFA 135
    ACTN2   1 ...............MNQIEPGV.QYNYVYDE..DEYMIQE.EEWDRDLLLDPAWEKQQRKTFTAWCNSHLRKAGTQ.IENIEEDFRNGLKLMLLLEVISGERLPKP..DRGKMRFHKIANVNKALDYIASKGVKLVSIGAEEIVDGNVKMTLGMIWTIILRFA 142
    ACTN3   1 .........MMMVMQPEGLGAGEGRFAGGGGG..GEYMEQE.EDWDRDLLLDPAWEKQQRKTFTAWCNSHLRKAGTQ.IENIEEDFRNGLKLMLLLEVISGERLPRP..DKGKMRFHKIANVNKALDFIASKGVKLVSIGAEEIVDGNLKMTLGMIWTIILRFA 149
    ACTN4   1 ......MVDYHAANQSYQYGPSSAGNGAGGGGSMGDYMAQE.DDWDRDLLLDPAWEKQQRKTFTAWCNSHLRKAGTQ.IENIDEDFRDGLKLMLLLEVISGERLPKP..ERGKMRVHKINNVNKALDFIASKGVKLVSIGAEEIVDGNAKMTLGMIWTIILRFA 154
    SPTN2   1 MSSTLSPTDFDSLEIQGQYSDINNRWDLPDSDWDNDSSSARLFERSRIKALADEREAVQKKTFTKWVNSHLARVTCR.VGDLYSDLRDGRNLLRLLEVLSGEILPKP..TKGRMRIHCLENVDKALQFLKEQKVHLENMGSHDIVDGNHRLTLGLVWTIILRFQ 161
      DMD   1 ........................................MLWWEEV..EDCYEREDVQKKTFTKWVNAQFSKFGKQHIENLFSDLQDGRRLLDLLEGLTGQKLPK...EKGSTRVHALNNVNKALRVLQNNNVDLVNIGSTDIVDGNHKLTLGLIWNIILHWQ 119
     UTRO   1 ..........................MAKYGEHEASPDNGQNEFSDIIKSRSDEHNDVQKKTFTKWINARFSKSGKPPINDMFTDLKDGRKLLDLLEGLTGTSLPK...ERGSTRVHALNNVNRVLQVLHQNNVELVNIGGTDIVDGNHKLTLGLLWSIILHWQ 135
Consensus     ........................................e......dl..d..wek.Q.kTFT.WcN.hl.k.gk..!.#l..Dl.#Gl.L..LLEvlsg.r$pk....rg..R.h.l.NVnkaL.fl....!kLvsigs..IVDGN.k$tLG$iWtiILh..

                                  CH2-A                 CH2-B     CH2-C        CH2-D        CH2-E              CH2-F         CH2-G
                               αααααααααααααα            ααα   ααααααααααα     ααααα    ααααααααααααααααα      ααααα      αααααααααααααα
     FLNa 150 ISMPMWDEEEDEEAKKQTPKQRLLGWIQNKL...PQLPITNFSRDWQSGRALGALVDSCAPGLCPDWDSWDASKPVTNAREAMQQADDWLGIPQVITPEEIVD.PNVDEHSVMTYLSQFPKAKLKPGAPL 275
     FLNb 123 ISMPVWEDEGDDDAKKQTPKQRLLGWIQNKI...PYLPITNFNQNWQDGKALGALVDSCAPGLCPDWESWDPQKPVDNAREAMQQADDWLGVPQVITPEEIIH.PDVDEHSVMTYLSQFPKAKLKPGAPL 248
     FLNc 143 ISMPMWEDEDDEDARKQTPKQRLLGWIQNKV...PQLPITNFNRDWQDGKALGALVDNCAPGLCPDWEAWDPNQPVENAREAMQQADDWLGVPQVIAPEEIVD.PNVDEHSVMTYLSQFPKAKLKPGAPV 268
    ACTN1 136 IQDIS..VE......ETSAKEGLLLWCQRKTAPYKNVNIQNFHISWKDGLGFCALIHRHRPELIDYGKLR.KDDPLTNLNTAFDVAEKYLDIPKMLDAEDIVGTARPDEKAIMTYVSSFYHAFSGAQKAE 256
    ACTN2 143 IQDIS..VE......ETSAKEGLLLWCQRKTAPYRNVNIQNFHTSWKDGLGLCALIHRHRPDLIDYSKLN.KDDPIGNINLAMEIAEKHLDIPKMLDAEDIVNTPKPDERAIMTYVSCFYHAFAGAEQAE 263
    ACTN3 150 IQDIS..VE......ETSAKEGLLLWCQRKTAPYRNVNVQNFHTSWKDGLALCALIHRHRPDLIDYAKLR.KDDPIGNLNTAFEVAEKYLDIPKMLDAEDIVNTPKPDEKAIMTYVSCFYHAFAGAEQAE 270
    ACTN4 155 IQDIS..VE......ETSAKEGLLLWCQRKTAPYKNVNVQNFHISWKDGLAFNALIHRHRPELIEYDKLR.KDDPVTNLNNAFEVAEKYLDIPKMLDAEDIVNTARPDEKAIMTYVSSFYHAFSGAQKAE 275
    SPTN2 162 IQDIS..VETEDNKEKKSAKDALLLWCQMKTAGYPNVNVHNFTTSWRDGLAFNAIVHKHRPDLLDFESLK.KCNAHYNLQNAFNLAEKELGLTKLLDPED.VNVDQPDEKSIITYVATYYHYFSKMKALA 287
      DMD 120 VKNVM..KNIMAGLQQTNSEKILLSWVRQSTRNYPQVNVINFTTSWSDGLALNALIHSHRPDLFDWNSVVCQQSATQRLEHAFNIARYQLGIEKLLDPED.VDTTYPDKKSILMYITSLFQVLPQQVSIE 246
     UTRO 137 VKDVM..KDVMSDLQQTNSEKILLSWVRQTTRPYSQVNVLNFTTSWTDGLAFNAVLHRHKPDLFSWDKVV.KMSPIERLEHAFSKAQTYLGIEKLLDPED.VAVQLPDKKSIIMYLTSLFEVLPQQVTID 261
Consensus     !.d.....#.......t..k..LL.W.q.kt..yp#vn!.NF.tsW.DGlal.Al.h.hrPdL.d......k..p..nl..Af..A...Lgipk.ldpE#iV....pDeks!mtY.s.f..a........
```

Supplementary Note. Protein sequence alignment of selected human ABDs.

ABDs of FLNa (UniProt Accession Code O21333), FLNb (O75369), FLNc (Q14315), α-actinin 1 (ACTN1 P12814), ACTN2 (P35609), ACTN3 (Q08043), ACTN4 (O43707), β-III-spectrin (SPTN2 O15020), dystrophin (DMD P11532), utrophin (UTRO P46939) were aligned using MultAlin[1]. F-actin-interacting regions in FLNa are bolded and boxed (red = ABS-N, green = ABS2’, blue = ABS2). Secondary structure α-helical elements from FLNa are shown above the alignment as α’s and are labeled with the corresponding CH domain and helix letter identifier. The consensus sequence indicates high conservation (>90%, upper-case amino acid code abbreviation), low conservation (50-90%, lower-case abbreviation), or molecular group conservation (! = I or V, $ = L or M, % = F or Y, # = N, D, Q, or E). Highlighted residues indicate disease-associated point mutations at this position: magenta = PVNH[2–11], blue = OPDSD[12–17], yellow = Larsen syndrome, atelosteogenesis I and III and Boomerang dysplasia disorders[18–23], orange = distal and cardiomyopathies[24–29], grey = macrothrombocytopenia[30], maroon = focal segmental glomerulosclerosis[31–33], black = spinocerebellar ataxia type 5[34], green = Duchenne’s muscular dystrophy[35,36], purple = Becker muscular dystrophy[37–41].

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