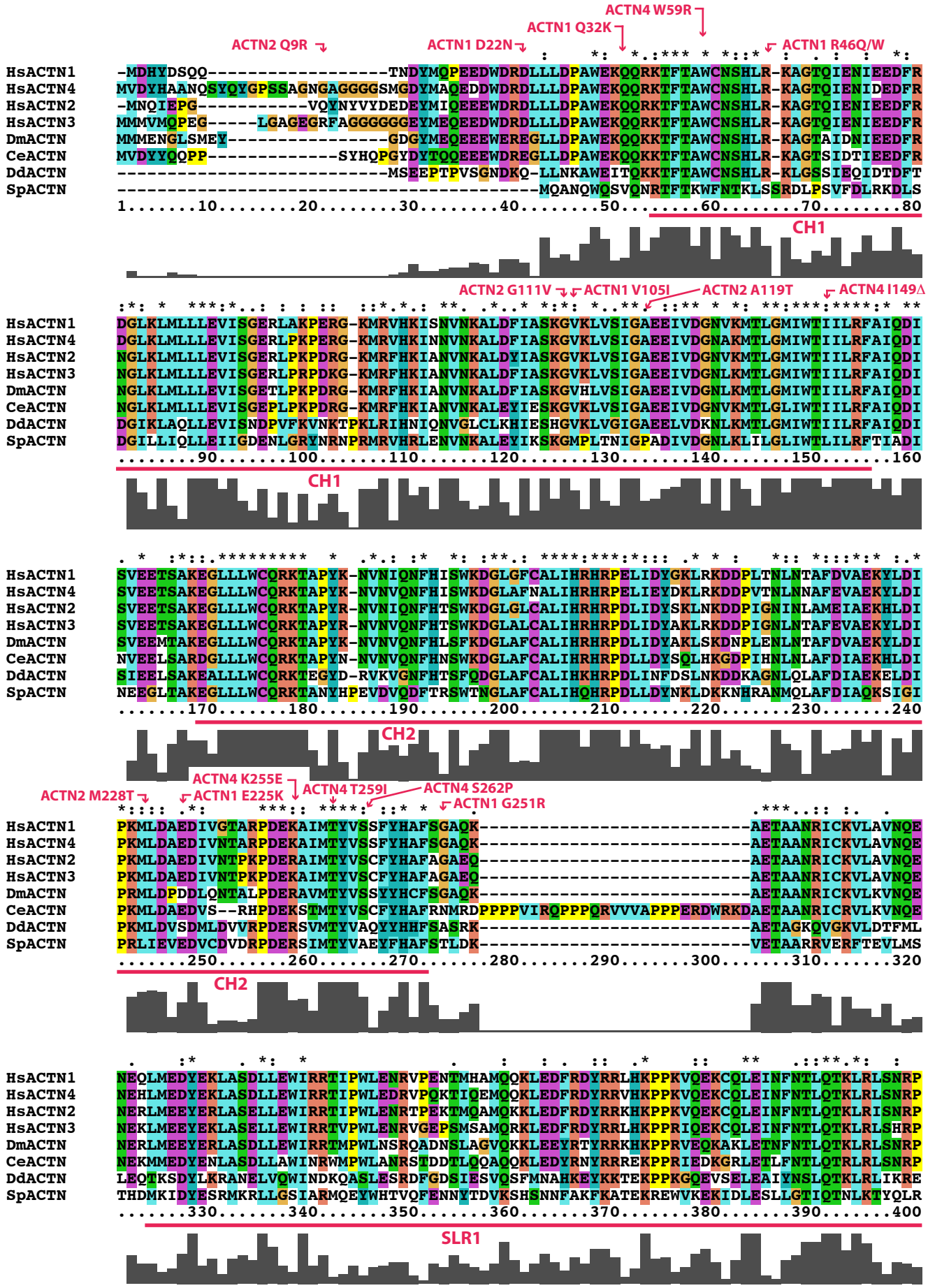
Additional file 1

Multiple sequence alignment of selected actinin protein sequences

An alignment prepared using ClustalX of human actinin-1, -2, -3 and -4, as well as actinin sequences from select model organisms. Sequence conservation is plotted beneath the alignment and conserved residues marked and color-coded according to the default CustalX settings. Locations of PFAM protein domains as identified in the Protein Data Bank for human actinin-2 (PDB ID: 4D1E) are indicated in red below the alignment. Known disease/phenotype associated mutations for the human actinins are identified in red text above the alignment. Accession numbers for sequences are as follows: *Hs*ACTN1 = NP_001093.1; *Hs*ACTN2 = NP_001094.1; *Hs*ACTN3 = NP_001095.2; *Hs*ACTN4 = NP_004915.2; *Dd*ACTN = XP_646979; *DmACTN* = NP_477484; *Ce*ACTN = NP_506127; *Sp*ACTN = NP_594295. Hs = *Homo sapiens;* Dm = *Drosophila melanogaster;* Ce = *Caenorhabditis elegans;* Dd = *Dictyostelium discoideum;* Sp = *Schizosaccharomyces pombe*


ACTN4 W59R
ACTN1 Q32K
ACTN2 Q9R
ACTN1 D22N
ACTN1 R46Q/W
CH1
ACTN2 G111V
ACTN1 V105I
ACTN2 A119T
ACTN4 I149Δ
CH1
CH2
ACTN4 K255E
ACTN2 M228T
ACTN1 E225K
ACTN4 T259I
ACTN4 S262P
ACTN1 G251R
CH2
SLR1
HsACTN1
HsACTN4
HsACTN2
HsACTN3
DmACTN
CeACTN
DdACTN
SpACTN

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                 : .  *    ::   *  :   *    . :  .
HsACTN1    AFMPSEGRMVSDINNAWGCLEQVEKGYEEWLLNEIRRLERLDHLAEKFRQKASIHEAWTDGKEAMLRQKDYETATLSEIK   431
HsACTN4    AFMPSEGKMVSDINNGWQHLEQAEKGYEEWLLNEIRRLERLDHLAEKFRQKASIHEAWTDGKEAMLKHRDYETATLSDIK   450
HsACTN2    AFMPSEGKMVSDIAGAWQRLEQAEKGYEEWLLNEIRRLERLEHLAEKFRQKASTHETWAYGKEQILLQKDYESASLTEVR   438
HsACTN3    AFMPSEGKLVSDIANAWRGLEQVEKGYEDWLLSEIRRLQRLQHLAEKFRQKASLHEAWTRGKEEMLSQRDYDSALLQEVR   445
DmACTN     AYLPTEGKTVSDISNSWKGLELAEKAFEEWLLAETMRLERLEHLAQKFKHKADAHEDWTRGKEEMLQSQDFRQCKLNELK   434
CeACTN     AFLPRDGHLIKDINAAWAGLEDSEKGFEEWLLSEIMRLERLEHLAEKFRRKCALHEEWAHGKEDALRSNDWRSCGLYKIK   462
DdACTN     PFVAPAGLTPNEIDSTWSALEKAEQEHAEALRIELKRQKKIAVLLQKYNRILKKLENWATTKSVYLGSNETGDS-ITAVQ   422
SpACTN     KYEPPAGLKIVDLERQWKDFLSEEANQSKLINTHMR-------------------------------------------   367
           .......410.......420.......430.......440.......450.......460.......470.......480
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                                                                ACTN2 T495M ↴                  :  :
HsACTN1    ALLKKHEAFESDLAAHQDR-VEQIAAIAQELNELDYYDSPSVNAR-CQKICDQWDNLGALTQKRREALERTEKLLETIDQ   509
HsACTN4    ALIRKHEAFESDLAAHQDR-VEQIAAIAQELNELDYYDSHNVNTR-CQKICDQWDALGSLTHSRREALEKTEKQLEAIDQ   528
HsACTN2    ALLRKHEAFESDLAAHQDR-VEQIAAIAQELNELDYHDAVNVNDR-CQKICDQWDRLGTLTQKRREALERMEKLLETIDQ   516
HsACTN3    ALLRRHEAFESDLAAHQDR-VEHIAALAQELNELDYHEAASVNSR-CQAICDQWDNLGTLTQKRRDALERMEKLLETIDQ   523
DmACTN     ALKKKHEAFESDLAAHQDR-VEQIAAIAQELNTLEYHDCVSVNAR-CQRICDQWDRLGALTQRRRTALDEAERILEKIDI   512
CeACTN     ALRKRHEAFESDLGAHQDR-VEQIAAIARELNNLRYPDIGPINAR-CQAICSQWDRLGQLSSKRRETLEDAERIAERLDS   540
DdACTN     AKLKNLEAFDGECQSLEGQSNSDLLSILAQLTELNYNGVPELTERKDTFFAQQWTGVKSSAETYKNTLLAELERLQKIED   502
SpACTN     ---------------------------------------------------------------------------EIKES   372
           .......490.......500.......510.......520.......530.......540.......550.......560
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                 : :* **  :.  :.   :.: :                ACTN3 R577X ↴   ACTN2 E583A ↴
HsACTN1    LYLEYAKRAAPFNNWMEGAMEDLQDTFIVHTIEEIQGLTTAHEQFKATLPDADKERLAILGIHNEVSKIVQTYHVNMAGT   589
HsACTN4    LHLEYAKRAAPFNNWMESAMEDLQDMFIVHTIEEIEGLISAHDQFKSTLPDADREREAILAIHKEAQRIAESNHIKLSGS   608
HsACTN2    LHLEFAKRAAPFNNWMEGAMEDLQDMFIVHSIEEIQSLITAHEQFKATLPEADGERQSIMAIQNEVEKVIQSYNIRISSS   596
HsACTN3    LQLEFARRAAPFNNWLDGAVEDLQDVWLVHSVEETQSLLTAHDQFKATLPEADRERGAIMGIQGEIQKICQTYGLRPCST   603
DmACTN     LHLEFAKRAAPFNNWLDGTREDLVDMFIVHTMEEIQGLIQAHDQFKATLGEADKEFNLIVNLVREVESIVKQHQIPGGLE   592
CeACTN     LYLDFAKRAAPFNNWLDGAREDLADLVIVHEMREIEELVNAHDQFKSTLGDADREFSSINQIEHEVEHLVTSHGLDRELL   620
DdACTN     SLVEFAKRAAQLNVWIEAADDHVFDPINVDSVQGVQEIQEKFDAFLHDQSQQFAELEALAALTQQLRELGRSE-------   575
SpACTN     MRIAFADRANSFSKMLSTISNEITN-------------------------------------------------------   397
           .......570.......580.......590.......600.......610.......620.......630.......640
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                                ACTN2 E628G ↴                                          .  .: :
HsACTN1    -NPYTTITPQEINGKWDHVRQLVPRRDQALTEEHARQQHNERLRKQFGAQANVIGPWIQTKMEEIGRISIEMHGTLEDQL   668
HsACTN4    -NPYTTVTPQIINSKWEKVQQLVPKRDHALLEEQSKQQSNEHLRRQFASQANVVGPWIQTKMEEIGRISIEMNGTLEDQL   687
HsACTN2    -NPYSTVTMDELRTKWDKVKQLVPIRDQSLQEELARQHANERLRRQFAAQANAIGPWIQNKMEEIARSSIQITGALEDQM   675
HsACTN3    -NPYITLSPQDINTKWDMVRKLVPSRDQTLQEELARQQVNERLRRQFAAQANAIGPWIQAKVEEVGRLAAGLAGSLEEQM   682
DmACTN     -NPYTTLTANDMTRKWSDVRQLVPQRDQTLANELRKQQNNEMLRRQFAEKANIVGPWIERQMDAVTAIGMGLQGSLEDQL   671
CeACTN     RNPYTDLSASDIRRKWGEVQNSVPRRDSQLQAELKRQQNNERLRTIFAEKANQVGPWLERELEQVLAIGLGGRGRLEDAI   700
DdACTN     -NDYSVISYDELSAKWNNLLAGIEERKVQLANELTTQTNNDVLCQSFSVKANEISDYVRVTLDAISQN---TSSDPQEQL   651
SpACTN     ----------------------------------------------------------------------LQGDWRDQL   406
           .......650.......660.......670.......680.......690.......700.......710.......720
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                                                                ACTN1 T737N ↴↳ ↲ ACTN1 R738W
                 :.          : ::  :    .   :  : :*  : .: * :.  :    .    .. : .* ::* ::   :: ::
HsACTN1    SHLRQYEKSIVNYKPKIDQLEGDHQLIQEALIFDNKHTNYTMEHIRVGWEQLLTTIARTINEVENQILTRDAKGISQEQM   748
HsACTN4    SHLKQYERSIVDYKPNLDLLEQQHQLIQEALIFDNKHTNYTMEHIRVGWEQLLTTIARTINEVENQILTRDAKGISQEQM   767
HsACTN2    NQLKQYEHNIINYKNNIDKLEGDHQLIQEALVFDNKHTNYTMEHIRVGWELLLTTIARTINEVETQILTRDAKGITQEQM   755
HsACTN3    AGLRQQEQNIINYKTNIDRLEGDHQLLQESLVFDNKHTVYSMEHIRVGWEQLLTSIARTINEVENQVLTRDAKGLSQEQL   762
DmACTN     HRLKEYEQAVYAYKPNIEELEKIHQAVQESMIFENRYTNYTMETLRVGWEQLLTSINRNINEVENQILTRDSKGISQEQL   751
CeACTN     QQLRSIQRNVLGYKPNLDELERVHQEMQENFVFENRKSRYSMESLRVGWETLLTSINKTINEFENQVLLRDSKGISEEQI   780
DdACTN     NNIRAIITAHAEKKPELDELYTIASQLEEAQVVDNKHTQHSLESIKLKWDKLNTLAKKNEQVVEGEILAKQLTGVTAEEL   731
SpACTN     DHVEFLQEHLGPLEVELASVKVLYDNCFQAGIEENDYTMFSYEDLEHEFGITANIIANKIKYLENELLEREKRTLSKQEL   486
           .......730.......740.......750.......760.......770.......780.......790.......800
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ACTN2 R759T
ACTN1 R752Q
ACTN1 G764S
ACTN1 E769K

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                 :    * **:: . . :    :: :.* *:*            :    :    .:    : :: * : :  .    *:. .
HsACTN1     NEFRASFNHFDRDHSGTLGPEEFKACLISLGYDIGNDPQGEAEFARIMSIVDPNRLGVVTFQAFIDFMSRETADTDTADQ   828
HsACTN4     QEFRASFNHFDKDHGGALGPEEFKACLISLGYDVENDRQGEAEFNRIMSLVDPNHSGLVTFQAFIDFMSRETTDTDTADQ   847
HsACTN2     NEFRASFNHFDRRKNGLMDHEDFRACLISMGYDLG-----EAEFARIMTLVDPNGQGTVTFQSFIDFMTRETADTDTAEQ   830
HsACTN3     NEFRASFNHFDRKRNGMMEPDDFRACLISMGYDLG-----EVEFARIMTMVDPNAAGVVTFQAFIDFMTRETAETDTTEQ   837
DmACTN      NEFRSSFNHFDKNRTGRLSPEEFKSCLVSLGYSIGKDRQGDLDFQRILAVVDPNNTGYVHFDAFLDFMTRESTDTDTAEQ   831
CeACTN      AEFRASFSHFDKERAG-LDPEQLRSCLISVGYTIRPGREGDAELHRVLAHVDPNRMGRVPFEAFLDFMTKENSDQDTVEQ   859
DdACTN      SEFKACFSHFDKDNDNKLNRLEFSSCLKSIGDELT-----EEQLNQVISKIDTDGNGTISFEEFIDYMVSSRKGTDSVES   806
SpACTN      DGITKVFRHFEKKKSNMLNEVEFYAALASLGLVYD------TEEGTALFHRAANSEEGVTYERFTEIVMEELEDRDSARQ   560
            .......810.......820.......830.......840.......850.......860.......870.......880
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EF1/2 EF3/4

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               :*  :* .* ::   ::       .   :    *          .:** ::   *
HsACTN1     VMASFKILAGDKNYITMDELRRELP-PDQAEYCIARMAPYTGPDSVPGALDYMSFSTALYGESDL--   892
HsACTN4     VIASFKVLAGDKNFITAEELRRELP-PDQAEYCIARMAPYQGPDAVPGALDYKSFSTALYGESDL--   911
HsACTN2     VIASFRILASDKPYILAEELRRELP-PDQAQYCIKRMPAYSGPGSVPGALDYAAFSSALYGESDL--   894
HsACTN3     VVASFKILAGDKNYITPEELRRELP-AKQAEYCIRRMVPYKGSGAPAGALDYVAFSSALYGESDL--   901
DmACTN      VIDSFRILAADKPYILPDELRRELP-PDQAEYCIQRMPPYKGPNGVPGALDYMSFSTALYGETDL--   895
CeACTN      MIDSFRILASGKTFITADELERELP-RDQAAYCMARMAPSREPGAPPRSFDYVTFSRSLYSQ-----   920
DdACTN      TKAAFKVMAEDKDFITEAQIRAAISDSKQIDYLLASMP------AVEGGFDYNSFAEKLYQ------   861
SpACTN      VLYAFCDVADGKSYVTSDDLLRSQVRPNIVKFLECNMN------KHSEGLDYLTWIKQLLAEDKEIV   621
            .......890.......900.......910.......920.......930.......940.......
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EF3/4