

Figure S1 Multiple alignments of Txnip homologs. (A) Alignment of the three most closely related mouse homologs of Txnip demonstrated that the Txnip cysteine 267 is the only conserved cysteine. (B) Alignment of predicted *C. elegans* and *D. melanogaster* sequences in the arrestin-domain-containing family proteins demonstrated that Txnip cysteine 267 is conserved through evolution. All alignments were generated with the ClustalW algorithm.

Figure S1

A Multiple alignment of mouse Txnip homologs

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Txnip      -----MVMFKKIKSFEVVFND-----PEKVYGSGEKVAGRVIVEVCEVTRVKAVRILAC 49
Arrdc4    MGGEAGADGPRGRVKS LGLVFEDESKG---CYSSGETVAGHVLL EAAEPVALRGLRLEAQ 57
Arrdc3    -----MVLGKVKSLTISFDCLNDSNVPVYSSGDTVSGRVNLEVTGEIRVKSLKIHAR 52
Arrdc2    -----MLFDKVKAFVVEIDGARTGTEPVFHGGQAVAGRVLLELAGAARVGALRLRAR 52
           ::*:: : : : : : . * : * : * : * : * : : : : *

Txnip      GVAKVLWMQG-----SQQCKQTL DYLR YEDTLL LLEE QPTGENE--MVIMRPGNKY 97
Arrdc4    GRATSAWGPSAGARVCIGGGSPAASSEVEYLNLR LSLLEAPAGEG-----VTLLQPG-KH 111
Arrdc3    GHAKVRWTESRNAGSNT-AYTQNYT EEEVYFNHKDILIGHERDDD NSEEGFHTIHSG-RH 110
Arrdc2    GRARAHWTESRSAGSST-AYTQSYSERVEV VNRATLLAPDSGD-----IATLPAG-RH 104
           * * * . : .. :: .. . * : . : .* ::

Txnip      EYKFGFELPQGPLGTSFKGKYGCVDYVWKAF LDRPSQPTQEAKNFEVMDLVDVNTPDLM 157
Arrdc4    EFPFRFQLPSEPLATSFTGKYGSIQYCVRAVLERPQVPDQSVRRELQV VSHVDVNTPELL 171
Arrdc3    EYAFS FELPQTPLATSFEGRHGSVRYVWKAELHRPWLLPVK LKKEFTVFEHIDINTPSLL 170
Arrdc2    EFPFSFQLPIS-LVTSFEKGHGSVRYSIKATLHRPWV PARCARKVFTVIEPVDINTPALL 163
           *: * * : * * * * * : * : * * * * * : : : * . . : * : * * * * *

Txnip      APVSAKKEKKVSCMFI PDGRVSVSARIDRKGFC EGDDISIHADFENTCSRI VVPKAAIIVA 217
Arrdc4    TPMLKTQEKMVG CWF LFTSGPVSLSVKIERKGYCNGEAIPIYAEIENCSSRLVVPKAAIFQ 231
Arrdc3    SPQAGTKEKTLCCWFCTSGPISLSAKIERKGYTPGESIQIFAEIENCSSRMVVPKAAIYQ 230
Arrdc2    EPQAGAREKVARSWYCTRGLVLSAKIDRKG YTPGEVPIPIFAEIDNGSTRAVQPRAALVQ 223
           * : * * . . * : * : * : * : * : * : * * * * * : * * * * *

Txnip      RHTYLANGQTKVFTQKLSSVRGNHII SGT CASWRGKSLRVQKIRPSILG CNILKVEYSLL 277
Arrdc4    TQTYLASGKTKTVRHMVANVRGNHIGSGSTDTWNGKMLKIPPVTPSILD CCIIRVDYSLA 291
Arrdc3    TQAFYAKGKMKEVKQLVANLRGESLSSGKTETWNGKLLKIPPVSPSILD C SIIRVEYSLM 290
Arrdc2    TQTFMARGARKQKRAVVASVDGEPVGP NRRALWPGRALRIPPVGPSILQ CRVLSVDYSLK 283
           : : : * * * : : : * : : . . * * : * : : : * * * * * * : : * : * * * *

Txnip      IYVSVPGSKKVILDPLVIGSR--SGLSSRTFSMASRTSSEM SWIDLNIPDTPEAPPCYM 335
Arrdc4    VYIHIPGAKRLMLELPLVIGTI PYSGFGRN SSVASQFSMDMCWLALALPEQPEAPPNYA 351
Arrdc3    VYVDIPGAMDLLL SLPLVIGTIPLHPFGSRTSSVSSQCSMSMNWLALALPERPEAPPSYA 350
Arrdc2    VFVDIPGSSKLLLELPLVIGTVPLHPLGSR SASVGSRASFLQDWGLCTMMDRPEAPPEYS 343
           : : : * * : : * . * * * * * : . . * . * : * : * : * : * : * * * *

Txnip      DIIPEDHRLES--PTTPLLDDVDDSDSPI FMYAPEFQFMPPPTYTEVDPCVLNNNNNNN 393
Arrdc4    DVVSEEEFSRH-VPPYPQPSDCDGEACYSMFACIQEFRFQPPPLYSEVDPHPGDAQETQP 410
Arrdc3    EVVTEEQRRNN-LAPVGACDDFERALQGPLFAYIQEFRFLPPPLYSEIDPNPDQSSEDRP 409
Arrdc2    EVVRESQLVCASPGPSSLLHDLGVTTEGPYFACLQEFRYCPPPLYSEEDPNP-PSEAVRP 402
           : : : * . . . * . * * : : * * * * * * * . .

Txnip      NVQ-- 396
Arrdc4    VSFIL 415
Arrdc3    SCPSR 414
Arrdc2    RCMTC 407

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B Multiple alignment of D. melanogaster and C. elegans Txnip homologs

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Human Txnip      MVMFKKIKSFEVVFND-PEKVYGSGERVAGRIVIVEVCEVTRVKAVRILACGVAKVLWMQG 59
C ele T12D8.4    ---MVQLDRFEILFNN-PEQAYFAGQEISGKVI I ENKEPKKVNEILLELKGARTYWTKH 56
D mel CG1105     ----MGLKGCELQLDN-PWNTYYAGQTVNGQVKFTFDSPKKVRGII I RFLGEANTEWSEE 55
D mel CG18745    -----MTVTC EIDFDNMPHGTYFGGEVLTGRVTLKLDKMKLVKAITL NITGYAETR WIER 55
C ele Y17G7B.11  -----MDDLRIEYDA-PNDVYFPGQAVTGKVI I QNREWIKARFLKICIHGGAHTHWSES 53
D mel CG7047     --MPRKLKFLIIFDN-TSLLYFPGQFLSGRVLI ELQDETPALGLHFHVVGEGVVRNGRR 57
C ele F40F8.8    ---MDYISSFDIRL NK---DVYYAGETISG SVLLENTENIKIRGIRVLLR GKVHATLKVV 54
                : : . * *: : * * . . : . * .

Human Txnip      SQQCKQT-----SEYLR YEDTLLEDQPTGENEMVIMRPGNKY EYKFGFELP 106
C ele T12D8.4    SGKSRKHCSHSEPYFLEQFNPGYTHKFTVVKDGKEKER-----ILPAGIHQVFPFSYTL P 110
D mel CG1105     KSVTTSEGKTENEVTQLKGHEEYFKIQYYLLGGKNSSE-----TELPPGHTY PFTCALP 110
D mel CG18745    --VTNRRRRR---RTFCGREDIASKTFLVGSNLSSQ-----VSI EAGIHTYNFVCLIP 105
C ele Y17G7B.11  --RSTYRTNTRGERERFTENVNYNATINYL TGESIAWQSRDGTDRLPAGTNVFPFAFNLP 111
D mel CG7047     QERTYDK-----ENYIDFRMRL LGDVDQGGP----AILSPGIHSFPFKLGLP 100
C ele F40F8.8    KSGERRTLK-----DDQYVLDEKQLLW GKDKSDES DSVPI LARGVHQFSFNFDLP 104
                . * : . . * : *

Human Txnip      QGPLGTSFKGKYGCVDYVWKAFLDRPSQPTQETKKNFEVVDLVDVNT P--DLMAPVSAKK 164
C ele T12D8.4    KS-LPSSFEGEFGHIRYTCKAICERPWFDFI VSRKAFTVVGIEDINSDPKLNEPATCVES 169
D mel CG1105     PN-LPSSFEGEFGHVRYTIKVT LDRPWKFDQDMKMAFTVIAPVDLNLN-PRVKEPFKLEL 168
D mel CG18745    TE-CPSSFEGSHGRVRYMATVTLVRPWKFDQSYTRCF TVLVKVMDLNFDSPLLRVP AHSET 164
C ele Y17G7B.11  IN-CAPSFEGCHGHIRYDVHVELDRPWKFNKKS RKCFSVIPVFDL NITPTAINPMVNTAS 170
D mel CG7047     LG-LPSTFLGRYGIWQFYCKAALRENNGI I HKNHQVFIVMNPIDL NLEKPI LAQPFTCEV 159
C ele F40F8.8    QSSLPCSLESRHCTIRYFFKVI IDIPYASSPQGIKYFTIIG-PHIDSMEEKYLSPLSAQD 163
                . : : . : : . * : : . : :

Human Txnip      EKKVSCMFIPDGRVSVSARIDRKGFCGDEISIHADFENTC-SRIVVPKAAIVARHTYLA 223
C ele T12D8.4    NHAVTFCCRSAGSVTGEIRISKCGYTPGEKIDVSFKVINLS-SKTRTTALRFVQQTTYKA 228
D mel CG1105     EKSFFCCCRSGPLAVITNIPQTGFVSGQVLPITCEVDNTSNVNL TAVKFELRKLVTFHT 228
D mel CG18745    SKTYCCWPCRS DPLALQLTVPQTGFVPGQNVPLSVLVTNDSHIPVEQLLISFVMLV TYHS 224
C ele Y17G7B.11  KN--TGLILKGLVTITVNLPKRGYVAGEIMPITVNI DNNGSKVAVSEVS AKMTQLSHFHA 228
D mel CG7047     EHKLGVVCGVGGQIKCRVSLDRGGYVPGENILVTA F I SNYSNVSIKRTKASLTETIEYLA 219
C ele F40F8.8    RKNVCCWCCQRGALALRIILERTAYVCGENIRVRAQIENRQSTAQSLVIRLVQHVEVFVE 223
                : : . : : : * : : . * :

Human Txnip      NG-----QTKVLTQKLSSVRGNHII SGTCASWRGKSLRVQKIRPS-ILGCN ILRV 272
C ele T12D8.4    KT-----FAGHEHIKNVVRVISKIDKGEVPGGSTE WQEESITIPSLPPK-LGCKKILSV 282
D mel CG1105     NQ-----PRSEKRESKVI IANLSVG-PVNGGESRTFTQOMEIPALPPTNLLNCGI IAL 280
D mel CG18745    KP-----PSPMNTT SERLVVNTFKGDAVQRNCKKLF SYEIRVPATPPTCFNLCGI IQI 277
C ele Y17G7B.11  SHGNMIGVTAHTHNRNDEKLVAESRRVADVPAKSRGQMVLSMKIPAI VPS--FNCPI IAV 286
D mel CG7047     RG-----KVVQTEKRELAVLVRGKIRPGAKDEWHN-ELYV PPLPPTNLHGCHLIKI 269
C ele F40F8.8    KG----LLGENKMMSCVVF EHKSPAIAANSQ GK YDSTLEQPIRLPVV PPTLVGVCRLIQI 279
                : : * . * : :

Human Txnip      EYSLLIYVSVPGSKK--VILD LPLVIGSRSGLSRT-----SSMARTSSEM SW 319
C ele T12D8.4    TYSVELEVEQT-----LTVPCPIVIGSIPQLS QLL----IHSKQSVQSAGNGSLPKSSI 332
D mel CG1105     DYDLHVECEVSGPHRN-LTGKVPITLGTIPLAGVRPPTQFTDAPS AVQSEDPSLAP TQPV 339
D mel CG18745    AYQVEVEARVKGCHNN-EVVTIPLTIGSVPLAQHVP----IQPRGFVPQLNVNELAVEEV 332
C ele Y17G7B.11  DYCLTVKVSTQQIFGGGLKCEFPLIIGTIPIRQMNQ----AAPGAMP T M P S V S A P P Y P V 341
D mel CG7047     SYDVFFVIEPKSMEKE-IKLQLPIVLATYPFR-----HSGDAVNANTWPE 313
C ele F40F8.8    YYALRVCMEDEKGN EC-LHIDFPLTVATIPYRIPNAPPPV D YDFCSNHVEGGKYVSP EF 338
                * : . * : : .

Human Txnip      VDLNIP-----DTPEAPPCYMDVIPEDHRL ESPTTPLLDDMDGS----- 358
C ele T12D8.4    KDSPPK-----WDESECVQTTITDESGQLVEELGNEMEALLSARKR----- 373
D mel CG1105     SPASPPGGDGVGGALGWNVADSTGGGSLYPNIPPPQFVETQYRAPT IAGRDD----- 391
D mel CG18745    ATAP-----NSSSPWSVDASIPPPNYQEAVHMRSTAATRSDDLLDDPEPV 376

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C ele Y17G7B.11	VAGAS-----ASQAVYPTAPSAPPASPGGEAPPSYEEVHGAG-----	379
D mel CG7047	SVLKP-----DTHTHYPTLP IFRPWLHEKPIEA-----	342
C ele F40F8.8	RLGQVYDG-----EGEEINKEEEIVLYRPVYVKLADRRIGSPHVSKDFRSGS--	385
Human Txnip	----QDSPIFMYAPEFKFMPPPTYTEVDPCILNINVQ-----	391
C ele T12D8.4	----VRMPSSILSELYPTMPSPYYKESFFGASDISE-EKEQAQFGEASFAPKYPFYTD-	426
D mel CG1105	SEHTQMIGDGAFAPRYPTFQFN--NATAPPASQ-----	422
D mel CG18745	PPNTLSLDGGAYKPLYPVFDIP--SPSAPPPTDYTONYMAERAFVNPAMDVDKDKGTWL	433
C ele Y17G7B.11	----KVEDAEAFAPRYPVYNNLPQQQNSQLPPEYAPPLPAKSGF-----	419
D mel CG7047	-----	
C ele F40F8.8	FTRIADSSSLALVTEPNGSRRRSILVASNPCLAMRDESMDEKLMMTNGCNSEGDPPLVA--	442