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Supplementary Table 1 Proteins reported to bind directly to 14-3-3s with relevant interaction sites indicated A. Mammalian proteins; B. Non-mammalian animal proteins; C. Fungal proteins; D. Plant proteins; E. Bacterial and viral proteins that interact with 14-3-3s inside eukaryotic host cells.

The abstracts of 2969 papers listed with the keyword '14-3-3' in PubMed (11 Jan 2010) were searched for reports of direct interactions between 14-3-3 and a target protein, and where possible relevant sites were identified in the manuscript. Often residue numbers were given with no species or amino acid sequence context, in which case these details were requested from corresponding authors, and/or deduced from the sequences of oligonucleotides used for site-directed mutagenesis of 14-3-3-binding sites. Where the precise form of a mammalian protein that had been studied in a publication was not specified, we assigned a sequence that contained the relevant site, choosing a human sequence where the species studied was unclear. Any sites that still could not be placed in a sequence context were omitted. 14-3-3-binding sites are indicated as lower case letters highlighted in yellow, and where more than two sites are implicated in 14-3-3 binding of a protein, these are highlighted in turquoise and not included in the Weblogo analysis in Supplementary Table 2 and Fig 1 (except for MAPT, see notes). **Caveat emptor:** The data collected may include assignments that are incorrect, due to inaccuracies in the original assignments, or our interpretation of authors' intentions for which we apologise. To aid future improvements in the dataset, we ask authors to report any corrections to c.mackintosh@dundee.ac.uk.

A. Mammalian proteins reported to interact directly with 14-3-3

Human AANAT Serotonin N-acetyltransferase; arylalkylamine *N*-acetyltransferase, melatonin-synthesizing enzyme. (Swissprot = Q16613)

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       1 MSTQSTHPLK PEAPRLPPGI PESPSCQRRH tLPASEFRCL TPEDAVSAFE IEREAFISVL
      61 GVCPLYLDEI RHFLTLCPEL SLGWFEEGCL VAFIIGSLWD KERLMQESLT LHRSGGHIAH
     121 LHVLAVHRAF RQQGRGPILL WRYLHHLGSQ PAVRRAALMC EDALVPFYER FSFHAVGPCA
     181 ITVGSLTFME LHCSLRGHPF LRRNsGC
>gi|11387096|sp|Q16613.1|SNAT_HUMAN RecName: Full=Serotonin N-
acetyltransferase; Short=Serotonin acetylase; AltName: Full=Aralkylamine N-
acetyltransferase; Short=AA-NAT
MSTQSTHPLKPEAPRLPPGIPESPSCQRRHTLPASEFRCLTPEDAVSAFEIEREAFISVLGVCPLYLDEI
RHFLTLCPELSLGWFEEGCLVAFIIGSLWDKERLMQESLTLHRSGGHIAHLHVLAVHRAFRQQGRGPILL
WRYLHHLGSQPAVRRAALMCEDALVPFYERFSFHAVGPCAITVGSLTFMELHCSLRGHPFLRRNSGC
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Notes

14-3-3 binding to phosphoThr31 and phosphoSer205, phosphorylated by PKA in response to light in pineal gland, activates AANAT and protects it from proteolytic degradation.

References to 14-3-3-binding to AANAT

Obsil T, Ghirlando R, Klein DC, Ganguly S, Dyda F (2001) Crystal structure of the 14-3-3zeta:serotonin N-acetyltransferase complex. A role for scaffolding in enzyme regulation. Cell 105:257–267

Pozdeyev N, Taylor C, Haque R, Chaurasia SS, Visser A, Thazyeen A, Du Y, Fu H, Weller J, Klein DC, Iuvone PM. Photic Regulation of Arylalkylamine N-Acetyltransferase Binding to 14-3-3 Proteins in Retinal Photoreceptor Cells. J Neurosci. 2006 Sep 6;26(36):9153-61.

Ganguly S, Weller JL, Ho A, Chemineau P, Malpaux B, Klein DC (2005) Melatonin synthesis: 14-3-3-dependent activation and inhibition of arylalkylamine N-acetyltransferase mediated by phosphoserine-205. Proc Natl Acad Sci USA 102:1222–1227

Human Abl1 Abelson murine leukemia viral oncogene homolog 1 (Tyrosine kinase) (Swissprot = P00519)

```
       1 MLEICLKLVG CKSKKGLSSS SSCYLEEALQ RPVASDFEPQ GLSEAARWNS KENLLAGPSE
      61 NDPNLFVALY DFVASGDNTL SITKGEKLRV LGYNHNGEWC EAQTKNGQGW VPSNYITPVN
     121 SLEKHSWYHG PVSRNAAEYL LSSGINGSFL VRESESSPGQ RSISLRYEGR VYHYRINTAS
     181 DGKLYVSSES RFNTLAELVH HHSTVADGLI TTLHYPAPKR NKPTVYGVSP NYDKWEMERT
     241 DITMKHKLGG GQYGEVYEGV WKKYSLTVAV KTLKEDTMEV EEFLKEAAVM KEIKHPNLVQ
     301 LLGVCTREPP FYIITEFMTY GNLLDYLREC NRQEVNAVVL LYMATQISSA MEYLEKKNFI
     361 HRDLAARNCL VGENHLVKVA DFGLSRLMTG DTYTAHAGAK FPIKWTAPES LAYNKFSIKS
     421 DVWAFGVLLW EIATYGMSPY PGIDLSQVYE LLEKDYRMER PEGCPEKVYE LMRACWQWNP
     481 SDRPSFAEIH QAFETMFQES SISDEVEKEL GKQGVRGAVS TLLQAPELPT KTRTSRRAAE
     541 HRDTTDVPEM PHSKGQGESD PLDHEPAVSP LLPRKERGPP EGGLNEDERL LPKDKKTNLF
     601 SALIKKKKKT APTPPKRSSS FREMDGQPER RGAGEEEGRD ISNGALAFTP LDTADPAKSP
     661 KPSNGAGVPN GALRESGGSG FRSPHLWKKS STLTSSRLAT GEEEGGGSSS KRFLRSCSAS
     721 CVPHGAKDTE WRSVtLPRDL QSTGRQFDSS TFGGHKSEKP ALPRKRAGEN RSDQVTRGTV
     781 TPPPRLVKKN EEAADEVFKD IMESSPGSSP PNLTPKPLRR QVTVAPASGL PHKEEAGKGS
     841 ALGTPAAAEP VTPTSKAGSG APGGTSKGPA EESRVRRHKH SSESPGRDKG KLSRLKPAPP
     901 PPPAASAGKA GGKPSQSPSQ EAAGEAVLGA KTKATSLVDA VNSDAAKPSQ PGEGLKKPVL
     961 PATPKPQSAK PSGTPISPAP VPSTLPSASS ALAGDQPSST AFIPLISTRV SLRKTRQPPE
    1021 RIASGAITKG VVLDSTEALC LAISRNSEQM ASHSAVLEAG KNLYTFCVSY VDSIQQMRNK
    1081 FAFREAINKL ENNLRELQIC PATAGSGPAA TQDFSKLLSS VKEISDIVQR
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>gi|85681908|sp|P00519.4|ABL1_HUMAN RecName: Full=Proto-oncogene tyrosine-
protein kinase ABL1; AltName: Full=Abelson murine leukemia viral oncogene
homolog 1; AltName: Full=c-ABL; AltName: Full=p150
MLEICLKLVGCKSKKGLSSSSSCYLEEALQRPVASDFEPQGLSEAARWNSKENLLAGPSENDPNLFVALY
DFVASGDNTLSITKGEKLRVLGYNHNGEWCEAQTKNGQGWVPSNYITPVNSLEKHSWYHGPVSRNAAEYL
LSSGINGSFLVRESESSPGQRSISLRYEGRVYHYRINTASDGKLYVSSESRFNTLAELVHHHSTVADGLI
TTLHYPAPKRNKPTVYGVSPNYDKWEMERTDITMKHKLGGGQYGEVYEGVWKKYSLTVAVKTLKEDTMEV
EEFLKEAAVMKEIKHPNLVQLLGVCTREPPFYIITEFMTYGNLLDYLRECNRQEVNAVVLLYMATQISSA
MEYLEKKNFIHRDLAARNCLVGENHLVKVADFGLSRLMTGDTYTAHAGAKFPIKWTAPESLAYNKFSIKS
DVWAFGVLLWEIATYGMSPYPGIDLSQVYELLEKDYRMERPEGCPEKVYELMRACWQWNPSDRPSFAEIH
QAFETMFQESSISDEVEKELGKQGVRGAVSTLLQAPELPTKTRTSRRAAEHRDTTDVPEMPHSKGQGESD
PLDHEPAVSPLLPRKERGPPEGGLNEDERLLPKDKKTNLFSALIKKKKKTAPTPPKRSSSFREMDGQPER
RGAGEEEGRDISNGALAFTPLDTADPAKSPKPSNGAGVPNGALRESGGSGFRSPHLWKKSSTLTSSRLAT
GEEEGGGSSSKRFLRSCSASCVPHGAKDTEWRSVTLPRDLQSTGRQFDSSTFGGHKSEKPALPRKRAGEN
RSDQVTRGTVTPPPRLVKKNEEAADEVFKDIMESSPGSSPPNLTPKPLRRQVTVAPASGLPHKEEAGKGS
ALGTPAAAEPVTPTSKAGSGAPGGTSKGPAEESRVRRHKHSSESPGRDKGKLSRLKPAPPPPPAASAGKA
GGKPSQSPSQEAAGEAVLGAKTKATSLVDAVNSDAAKPSQPGEGLKKPVLPATPKPQSAKPSGTPISPAP
VPSTLPSASSALAGDQPSSTAFIPLISTRVSLRKTRQPPERIASGAITKGVVLDSTEALCLAISRNSEQM
ASHSAVLEAGKNLYTFCVSYVDSIQQMRNKFAFREAINKLENNLRELQICPATAGSGPAATQDFSKLLSS
VKEISDIVQR
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Notes

Regulates cytoskeleton remodeling during cell differentiation, cell division and cell adhesion. Localizes to dynamic actin structures, and phosphorylates CRK and CRKL, DOK1, and other proteins controlling cytoskeleton dynamics. Regulates DNA repair potentially by activating the proapoptotic pathway when the DNA damage is too severe to be repaired. Contains both SH2 and SH3 domains and a nuclear localization signals. Expression of Abl in the cytoplasm results in cell proliferation and survival. In contrast, nuclear Abl is activated and induces apoptosis after genotoxic stress. Phosphorylated cABL binds 14-3-3, which sequesters ABL in the cytoplasm. Upon DNA damage 14-3-3 is phosphorylated by JNK leading to dissociation from Abl and Abl translocation to the mucleus inducing apoptosis. TTK (also known as Mps1) phosphorylates c-Abl at Thr735 and that this phosphorylation is of importance to the cytoplasmic sequestration of c-Abl. 14-3-3 also binds to Abl in the context of the Bcr-Abl tyrosine kinase fusion of Philadelphia chromosome (Ph1)-positive human leukemias.

References to 14-3-3 binding to Abl1

Mancini M, Corradi V, Petta S, Martinelli G, Barbieri E, Santucci MA. mTOR inhibitor RAD001 (Everolimus) enhances the effects of imatinib in chronic myeloid leukemia by raising the nuclear expression of c-ABL protein. Leuk Res. 2009 Jul 28.

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Mancini M, Veljkovic N, Corradi V, Zuffa E, Corrado P, Pagnotta E, Martinelli G, Barbieri E, Santucci MA. 14-3-3 ligand prevents nuclear import of c-ABL protein in chronic myeloid leukemia. Traffic. 2009 Jun;10(6):637-47.

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Pendergast AM. Stress and death: breaking up the c-Abl/14-3-3 complex in apoptosis. Nat Cell Biol. 2005 Mar;7(3):213-4.

Yoshida K, Yamaguchi T, Natsume T, Kufe D, Miki Y. JNK phosphorylation of 14-3-3 proteins regulates nuclear targeting of c-Abl in the apoptotic response to DNA damage. Nat Cell Biol. 2005 Mar;7(3):278-85.

Reuther GW, Fu H, Cripe LD, Collier RJ, Pendergast AM. Association of the protein kinases c-Bcr and Bcr-Abl with proteins of the 14-3-3 family. Science. 1994 Oct 7;266(5182):129-33.

Human ADAM22 Disintegrin and metalloproteinase domain-containing protein 22 (Swissprot = Q9P0K1)

```
        1 MQAAVAVSVP FLLLCVLGTC PPARCGQAGD ASLMELEKRK ENRFVERQSI VPLRLIYRSG
       61 GEDESRHDAL DTRVRGDLGG PQLTHVDQAS FQVDAFGTSF ILDVVLNHDL LSSEYIERHI
      121 EHGGKTVEVK GGEHCYYQGH IRGNPDSFVA LSTCHGLHGM FYDGNHTYLI EPEENDTTQE
      181 DFHFHSVYKS RLFEFSLDDL PSEFQQVNIT PSKFILKPRP KRSKRQLRRY PRNVEEETKY
      241 IELMIVNDHL MFKKHRLSVV HTNTYAKSVV NMADLIYKDQ LKTRIVLVAM ETWATDNKFA
      301 ISENPLITLR EFMKYRRDFI KEKSDAVHLF SGSQFESSRS GAAYIGGICS LLKGGGVNEF
      361 GKTDLMAVTL AQSLAHNIGI ISDKRKLASG ECKCEDTWSG CIMGDTGYYL PKKFTQCNIE
      421 EYHDFLNSGG GACLFNKPSK LLDPPECGNG FIETGEECDC GTPAECVLEG AECCKKCTLT
      481 QDSQCSDGLC CKKCKFQPMG TVCREAVNDC DIRETCSGNS SQCAPNIHKM DGYSCDGVQG
      541 ICFGGRCKTR DRQCKYIWGQ KVTASDKYCY EKLNIEGTEK GNCGKDKDTW IQCNKRDVLC
      601 GYLLCTNIGN IPRLGELDGE ITSTLVVQQG RTLNCSGGHV KLEEDVDLGY VEDGTPCGPQ
      661 MMCLEHRCLP VASFNFSTCL SSKEGTICSG NGVCSNELKC VCNRHWIGSD CNTYFPHNDD
      721 AKTGITLSGN GVAGTNIIIG IIAGTILVLA LILGITAWGY KNYREQRQLP QGDYVKKPGD
      781 GDSFYSDIPP GVSTNSASSS KKRSNGLSHS WSERIPDTKH ISDICENGRP RSNsWQGNLG
      841 GNKKKIRGKR FRPRSNsTET LSPAKSPSSS TGSIASSRKY PYPMPPLPDE DKKVNRQSAR
      901 LWETSI
>gi|14423634|sp|Q9P0K1.1|ADA22_HUMAN RecName: Full=Disintegrin and
metalloproteinase domain-containing protein 22; Short=ADAM 22; AltName:
Full=Metalloproteinase-like, disintegrin-like, and cysteine-rich protein 2;
AltName: Full=Metalloproteinase-disintegrin ADAM22-3; Flags: Precursor
MQAAVAVSVPFLLLCVLGTCPPARCGQAGDASLMELEKRKENRFVERQSIVPLRLIYRSGGEDESRHDAL
DTRVRGDLGGPQLTHVDQASFQVDAFGTSFILDVVLNHDLLSSEYIERHIEHGGKTVEVKGGEHCYYQGH
IRGNPDSFVALSTCHGLHGMFYDGNHTYLIEPEENDTTQEDFHFHSVYKSRLFEFSLDDLPSEFQQVNIT
PSKFILKPRPKRSKRQLRRYPRNVEEETKYIELMIVNDHLMFKKHRLSVVHTNTYAKSVVNMADLIYKDQ
LKTRIVLVAMETWATDNKFAISENPLITLREFMKYRRDFIKEKSDAVHLFSGSQFESSRSGAAYIGGICS
LLKGGGVNEFGKTDLMAVTLAQSLAHNIGIISDKRKLASGECKCEDTWSGCIMGDTGYYLPKKFTQCNIE
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EYHDFLNSGGGACLFNKPSKLLDPPECGNGFIETGEECDCGTPAECVLEGAECCKKCTLTQDSQCSDGLC
CKKCKFQPMGTVCREAVNDCDIRETCSGNSSQCAPNIHKMDGYSCDGVQGICFGGRCKTRDRQCKYIWGQ
KVTASDKYCYEKLNIEGTEKGNCGKDKDTWIQCNKRDVLCGYLLCTNIGNIPRLGELDGEITSTLVVQQG
RTLNCSGGHVKLEEDVDLGYVEDGTPCGPQMMCLEHRCLPVASFNFSTCLSSKEGTICSGNGVCSNELKC
VCNRHWIGSDCNTYFPHNDDAKTGITLSGNGVAGTNIIIGIIAGTILVLALILGITAWGYKNYREQRQLP
QGDYVKKPGDGDSFYSDIPPGVSTNSASSSKKRSNGLSHSWSERIPDTKHISDICENGRPRSNSWQGNLG
GNKKKIRGKRFRPRSNSTETLSPAKSPSSSTGSIASSRKYPYPMPPLPDEDKKVNRQSARLWETSI
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Notes

Transmembrane protein, thought to be an adhesion molecule or a receptorADAM22 variant 1 (ADAM22v1) has the largest cytoplasmic domain. The cytoplasmic tail has two RSNS 14-3-3 protein consensus binding sites RSNSWQ [amino acids (aa)831-836] and RSNSTE (aa854-859) and mutation of both 14-3-3 consensus sites is needed to abolish interaction with 14-3-3 proteins.

References to 14-3-3 binding to Adam22

Zhu P, Sun Y, Xu R, Sang Y, Zhao J, Liu G, Cai L, Li C, Zhao S. The interaction between ADAM 22 and 14-3-3zeta: regulation of cell adhesion and spreading. Biochem Biophys Res Commun. 2003 Feb 21;301(4):991-9.

Zhu P, Sang Y, Xu R, Zhao J, Li C, Zhao S. The interaction between ADAM22 and 14-3-3beta.Sci China C Life Sci. 2002 Dec;45(6):577-82.

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Human AKAP13 AKAP-Lbc**,** guanine nucleotide exchange factor (GEF) for RhoA (Swissprot = Q12802)

```
        1 MKLNPQQAPL YGDCVVTVLL AEEDKAEDDV VFYLVFLGST LRHCTSTRKV SSDTLETIAP
       61 GHDCCETVKV QLCASKEGLP VFVVAEEDFH FVQDEAYDAA QFLATSAGNQ QALNFTRFLD
      121 QSGPPSGDVN SLDKKLVLAF RHLKLPTEWN VLGTDQSLHD AGPRETLMHF AVRLGLLRLT
      181 WFLLQKPGGR GALSIHNQEG ATPVSLALER GYHKLHQLLT EENAGEPDSW SSLSYEIPYG
      241 DCSVRHHREL DIYTLTSESD SHHEHPFPGD GCTGPIFKLM NIQQQLMKTN LKQMDSLMPL
      301 MMTAQDPSSA PETDGQFLPC APEPTDPQRL SSSEETESTQ CCPGSPVAQT ESPCDLSSIV
      361 EEENTDRSCR KKNKGVERKG EEVEPAPIVD SGTVSDQDSC LQSLPDCGVK GTEGLSSCGN
      421 RNEETGTKSS GMPTDQESLS SGDAVLQRDL VMEPGTAQYS SGGELGGIST TNVSTPDTAG
      481 EMEHGLMNPD ATVWKNVLQG GESTKERFEN SNIGTAGASD VHVTSKPVDK ISVPNCAPAA
      541 SSLDGNKPAE SSLAFSNEET STEKTAETET SRSREESADA PVDQNSVVIP AAAKDKISDG
      601 LEPYTLLAAG IGEAMSPSDL ALLGLEEDVM PHQNSETNSS HAQSQKGKSS PICSTTGDDK
      661 LCADSACQQN TVTSSGDLVA KLCDNIVSES ESTTARQPSS QDPPDASHCE DPQAHTVTSD
      721 PVRDTQERAD FCPFKVVDNK GQRKDVKLDK PLTNMLEVVS HPHPVVPKME KELVPDQAVI
      781 SDSTFSLANS PGSESVTKDD ALSFVPSQKE KGTATPELHT ATDYRDGPDG NSNEPDTRPL
      841 EDRAVGLSTS STAAELQHGM GNTSLTGLGG EHEGPAPPAI PEALNIKGNT DSSLQSVGKA
      901 TLALDSVLTE EGKLLVVSES SAAQEQDKDK AVTCSSIKEN ALSSGTLQEE QRTPPPGQDT
      961 QQFHEKSISA DCAKDKALQL SNSPGASSAF LKAETEHNKE VAPQVSLLTQ GGAAQSLVPP
     1021 GASLATESRQ EALGAEHNSS ALLPCLLPDG SDGSDALNCS QPSPLDVGVK NTQSQGKTSA
     1081 CEVSGDVTVD VTGVNALQGM AEPRRENISH NTQDILIPNV LLSQEKNAVL GLPVALQDKA
     1141 VTDPQGVGTP EMIPLDWEKG KLEGADHSCT MGDAEEAQID DEAHPVLLQP VAKELPTDME
     1201 LSAHDDGAPA GVREVMRAPP SGRERSTPSL PCMVSAQDAP LPKGADLIEE AASRIVDAVI
     1261 EQVKAAGALL TEGEACHMSL SSPELGPLTK GLESAFTEKV STFPPGESLP MGSTPEEATG
     1321 SLAGCFAGRE EPEKIILPVQ GPEPAAEMPD VKAEDEVDFR ASSISEEVAV GSIAATLKMK
     1381 QGPMTQAINR ENWCTIEPCP DAASLLASKQ SPECENFLDV GLGRECTSKQ GVLKRESGSD
     1441 SDLFHSPSDD MDSIIFPKPE EEHLACDITG SSSSTDDTAS LDRHSSHGSD VSLSQILKPN
     1501 RSRDRQSLDG FYSHGMGAEG RESESEPADP GDVEEEEMDS ITEVPANCSV LRSSMRSLSP
     1561 FRRHsWGPGK NAASDAEMNH RSSMRVLGDV VRRPPIHRRS FSLEGLTGGA GVGNKPSSSL
     1621 EVSSANAEEL RHPFSGEERV DSLVSLSEED LESDQREHRM FDQQICHRSK QQGFNYCTSA
     1681 ISSPLTKSIS LMTISHPGLD NSRPFHSTFH NTSANLTESI TEENYNFLPH SPSKKDSEWK
     1741 SGTKVSRTFS YIKNKMSSSK KSKEKEKEKD KIKEKEKDSK DKEKDKKTVN GHTFSSIPVV
     1801 GPISCSQCMK PFTNKDAYTC ANCSAFVHKG CRESLASCAK VKMKQPKGSL QAHDTSSLPT
     1861 VIMRNKPSQP KERPRSAVLL VDETATTPIF ANRRSQQSVS LSKSVSIQNI TGVGNDENMS
     1921 NTWKFLSHST DSLNKISKVN ESTESLTDEG VGTDMNEGQL LGDFEIESKQ LEAESWSRII
     1981 DSKFLKQQKK DVVKRQEVIY ELMQTEFHHV RTLKIMSGVY SQGMMADLLF EQQMVEKLFP
     2041 CLDELISIHS QFFQRILERK KESLVDKSEK NFLIKRIGDV LVNQFSGENA ERLKKTYGKF
     2101 CGQHNQSVNY FKDLYAKDKR FQAFVKKKMS SSVVRRLGIP ECILLVTQRI TKYPVLFQRI
     2161 LQCTKDNEVE QEDLAQSLSL VKDVIGAVDS KVASYEKKVR LNEIYTKTDS KSIMRMKSGQ
     2221 MFAKEDLKRK KLVRDGSVFL KNAAGRLKEV QAVLLTDILV FLQEKDQKYI FASLDQKSTV
     2281 ISLKKLIVRE VAHEEKGLFL ISMGMTDPEM VEVHASSKEE RNSWIQIIQD TINTLNRDED
     2341 EGIPSENEEE KKMLDTRARE LKEQLHQKDQ KILLLLEEKE MIFRDMAECS TPLPEDCSPT
     2401 HSPRVLFRSN TEEALKGGPL MKSAINEVEI LQGLVSGNLG GTLGPTVSSP IEQDVVGPVS
     2461 LPRRAETFGG FDSHQMNASK GGEKEEGDDG QDLRRTESDS GLKKGGNANL VFMLKRNSEQ
     2521 VVQSVVHLYE LLSALQGVVL QQDSYIEDQK LVLSERALTR SLSRPSSLIE QEKQRSLEKQ
     2581 RQDLANLQKQ QAQYLEEKRR REREWEARER ELREREALLA QREEEVQQGQ QDLEKEREEL
     2641 QQKKGTYQYD LERLRAAQKQ LEREQEQLRR EAERLSQRQT ERDLCQVSHP HTKLMRIPSF
     2701 FPSPEEPPSP SAPSIAKSGS LDSELSVSPK RNSISRTHKD KGPFHILSST SQTNKGPEGQ
     2761 SQAPASTSAS TRLFGLTKPK EKKEKKKKNK TSRSQPGDGP ASEVSAEGEE IFC
>gi|134048676|sp|Q12802.2|AKP13_HUMAN RecName: Full=A-kinase anchor protein
13; Short=AKAP 13; AltName: Full=Protein kinase A-anchoring protein 13;
AltName: Full=Breast cancer nuclear receptor-binding auxiliary protein;
AltName: Full=Human thyroid-anchoring protein 31; AltName: Full=Guanine
nucleotide exchange factor Lbc; AltName: Full=AKAP-Lbc; AltName: Full=P47;
AltName: Full=Lymphoid blast crisis oncogene; Short=LBC oncogene; AltName:
Full=Non-oncogenic Rho GTPase-specific GTP exchange factor
MKLNPQQAPLYGDCVVTVLLAEEDKAEDDVVFYLVFLGSTLRHCTSTRKVSSDTLETIAPGHDCCETVKV
QLCASKEGLPVFVVAEEDFHFVQDEAYDAAQFLATSAGNQQALNFTRFLDQSGPPSGDVNSLDKKLVLAF
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RHLKLPTEWNVLGTDQSLHDAGPRETLMHFAVRLGLLRLTWFLLQKPGGRGALSIHNQEGATPVSLALER
GYHKLHQLLTEENAGEPDSWSSLSYEIPYGDCSVRHHRELDIYTLTSESDSHHEHPFPGDGCTGPIFKLM
NIQQQLMKTNLKQMDSLMPLMMTAQDPSSAPETDGQFLPCAPEPTDPQRLSSSEETESTQCCPGSPVAQT
ESPCDLSSIVEEENTDRSCRKKNKGVERKGEEVEPAPIVDSGTVSDQDSCLQSLPDCGVKGTEGLSSCGN
RNEETGTKSSGMPTDQESLSSGDAVLQRDLVMEPGTAQYSSGGELGGISTTNVSTPDTAGEMEHGLMNPD
ATVWKNVLQGGESTKERFENSNIGTAGASDVHVTSKPVDKISVPNCAPAASSLDGNKPAESSLAFSNEET
STEKTAETETSRSREESADAPVDQNSVVIPAAAKDKISDGLEPYTLLAAGIGEAMSPSDLALLGLEEDVM
PHQNSETNSSHAQSQKGKSSPICSTTGDDKLCADSACQQNTVTSSGDLVAKLCDNIVSESESTTARQPSS
QDPPDASHCEDPQAHTVTSDPVRDTQERADFCPFKVVDNKGQRKDVKLDKPLTNMLEVVSHPHPVVPKME
KELVPDQAVISDSTFSLANSPGSESVTKDDALSFVPSQKEKGTATPELHTATDYRDGPDGNSNEPDTRPL
EDRAVGLSTSSTAAELQHGMGNTSLTGLGGEHEGPAPPAIPEALNIKGNTDSSLQSVGKATLALDSVLTE
EGKLLVVSESSAAQEQDKDKAVTCSSIKENALSSGTLQEEQRTPPPGQDTQQFHEKSISADCAKDKALQL
SNSPGASSAFLKAETEHNKEVAPQVSLLTQGGAAQSLVPPGASLATESRQEALGAEHNSSALLPCLLPDG
SDGSDALNCSQPSPLDVGVKNTQSQGKTSACEVSGDVTVDVTGVNALQGMAEPRRENISHNTQDILIPNV
LLSQEKNAVLGLPVALQDKAVTDPQGVGTPEMIPLDWEKGKLEGADHSCTMGDAEEAQIDDEAHPVLLQP
VAKELPTDMELSAHDDGAPAGVREVMRAPPSGRERSTPSLPCMVSAQDAPLPKGADLIEEAASRIVDAVI
EQVKAAGALLTEGEACHMSLSSPELGPLTKGLESAFTEKVSTFPPGESLPMGSTPEEATGSLAGCFAGRE
EPEKIILPVQGPEPAAEMPDVKAEDEVDFRASSISEEVAVGSIAATLKMKQGPMTQAINRENWCTIEPCP
DAASLLASKQSPECENFLDVGLGRECTSKQGVLKRESGSDSDLFHSPSDDMDSIIFPKPEEEHLACDITG
SSSSTDDTASLDRHSSHGSDVSLSQILKPNRSRDRQSLDGFYSHGMGAEGRESESEPADPGDVEEEEMDS
ITEVPANCSVLRSSMRSLSPFRRHSWGPGKNAASDAEMNHRSSMRVLGDVVRRPPIHRRSFSLEGLTGGA
GVGNKPSSSLEVSSANAEELRHPFSGEERVDSLVSLSEEDLESDQREHRMFDQQICHRSKQQGFNYCTSA
ISSPLTKSISLMTISHPGLDNSRPFHSTFHNTSANLTESITEENYNFLPHSPSKKDSEWKSGTKVSRTFS
YIKNKMSSSKKSKEKEKEKDKIKEKEKDSKDKEKDKKTVNGHTFSSIPVVGPISCSQCMKPFTNKDAYTC
ANCSAFVHKGCRESLASCAKVKMKQPKGSLQAHDTSSLPTVIMRNKPSQPKERPRSAVLLVDETATTPIF
ANRRSQQSVSLSKSVSIQNITGVGNDENMSNTWKFLSHSTDSLNKISKVNESTESLTDEGVGTDMNEGQL
LGDFEIESKQLEAESWSRIIDSKFLKQQKKDVVKRQEVIYELMQTEFHHVRTLKIMSGVYSQGMMADLLF
EQQMVEKLFPCLDELISIHSQFFQRILERKKESLVDKSEKNFLIKRIGDVLVNQFSGENAERLKKTYGKF
CGQHNQSVNYFKDLYAKDKRFQAFVKKKMSSSVVRRLGIPECILLVTQRITKYPVLFQRILQCTKDNEVE
QEDLAQSLSLVKDVIGAVDSKVASYEKKVRLNEIYTKTDSKSIMRMKSGQMFAKEDLKRKKLVRDGSVFL
KNAAGRLKEVQAVLLTDILVFLQEKDQKYIFASLDQKSTVISLKKLIVREVAHEEKGLFLISMGMTDPEM
VEVHASSKEERNSWIQIIQDTINTLNRDEDEGIPSENEEEKKMLDTRARELKEQLHQKDQKILLLLEEKE
MIFRDMAECSTPLPEDCSPTHSPRVLFRSNTEEALKGGPLMKSAINEVEILQGLVSGNLGGTLGPTVSSP
IEQDVVGPVSLPRRAETFGGFDSHQMNASKGGEKEEGDDGQDLRRTESDSGLKKGGNANLVFMLKRNSEQ
VVQSVVHLYELLSALQGVVLQQDSYIEDQKLVLSERALTRSLSRPSSLIEQEKQRSLEKQRQDLANLQKQ
QAQYLEEKRRREREWEARERELREREALLAQREEEVQQGQQDLEKEREELQQKKGTYQYDLERLRAAQKQ
LEREQEQLRREAERLSQRQTERDLCQVSHPHTKLMRIPSFFPSPEEPPSPSAPSIAKSGSLDSELSVSPK
RNSISRTHKDKGPFHILSSTSQTNKGPEGQSQAPASTSASTRLFGLTKPKEKKEKKKKNKTSRSQPGDGP
ASEVSAEGEEIFC
```

Notes

14-3-3-binding site = pSer1565
PKA dependant binding to 14-3-3,

References to 14-3-3 binding to AKAP13

Diviani D, Abuin L, Cotecchia S, Pansier L (2004) Anchoring of both PKA and 14-3-3 inhibits the Rho-GEF activity of the AKAP-Lbc signaling complex. EMBO J 23, 2811-20

Baisamy L, Jurisch N, Diviani D. Leucine zipper-mediated homo-oligomerization regulates the Rho-GEF activity of AKAP-Lbc. J Biol Chem. 2005 Apr 15;280(15):15405-12.

Jin J, Smith FD, Stark C, Wells CD, Fawcett JP, Kulkarni S, Metalnikov P, O'Donnell P, Taylor P, Taylor L, Zougman A, Woodgett JR, Langeberg LK, Scott JD, Pawson T. Proteomic, functional, and domain-based analysis of in vivo 14-3-3 binding proteins involved in cytoskeletal regulation and cellular organization. Curr Biol. 2004 Aug 24;14(16):1436-50.

Human Akirin2 (aka fourteen-three-three beta interactant 1 FBI1 (C6orf166)) NP_060534 (Swissprot = Q53H80)

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        1 MACGATLKRT LDFDPLLSPA SPKRRRCAPL sAPTSAAASP LSAAAATAAS FSAAAASPQK
       61 YLRMEPSPFG DVSSRLTTEQ ILYNIKQEYK RMQKRRHLET SFQQtDPCCT SDAQPHAFLL
      121 sGPASPGTSS AAsSPLKKEQ PLFTLRQVGM ICERLLKERE EKVREEYEEI LNTKLAEQYD
      181 AFVKFTHDQI MRRYGEQPAS YVS
>gi|71152385|sp|Q53H80.2|AKIR2_HUMAN RecName: Full=Akirin-2
MACGATLKRTLDFDPLLSPASPKRRRCAPLSAPTSAAASPLSAAAATAASFSAAAASPQKYLRMEPSPFG
DVSSRLTTEQILYNIKQEYKRMQKRRHLETSFQQTDPCCTSDAQPHAFLLSGPASPGTSSAASSPLKKEQ
PLFTLRQVGMICERLLKEREEKVREEYEEILNTKLAEQYDAFVKFTHDQIMRRYGEQPASYVS
```

Notes

“Putative 14-3-3-binding sites were converted to Ala and designated as S31A, T103A, S111A, S119A, and S131A, respectively. These mutants were inserted into pACT2, and the interaction with 14-3-3β was analyzed using the yeast two-hybrid system. All mutants did not bind to 14-3-3β (Fig. 2C), suggesting that multiple 14-3-3β-binding motifs of FBI1 are required for the interaction with 14-3-3β. (Komiva et al 2008).” Note that Komiva et al studied the rat protein, and here the human sequence is shown. Note that Rat Ser103 is Ala in the mouse sequence and Ser111 is Ala113 in the human sequence. There is a related protein Akirin 1 (Mighty) whose expression is regulated by myostatin. Akirin2, is required for NF-kappaB-mediated gene transcription.

Sasaki S, Yamada T, Sukegawa S, Miyake T, Fujita T, Morita M, Ohta T, Takahagi Y, Murakami H, Morimatsu F, Sasaki Y. Association of a single nucleotide polymorphism in akirin 2 gene with marbling in Japanese Black beef cattle. BMC Res Notes. 2009 Jul 14;2:131.

References to 14-3-3 binding to human Akirin2

Macqueen DJ, Johnston IA. Evolution of the multifaceted eukaryotic akirin gene family. BMC Evol Biol. 2009 Feb 6;9:34.

Komiya Y, Kurabe N, Katagiri K, Ogawa M, Sugiyama A, Kawasaki Y, Tashiro F. A novel binding factor of 14-3-3beta functions as a transcriptional repressor and promotes anchorage-independent growth, tumorigenicity, and

SITES NOT ALL CONSERVED AND NOT CERTAIN TO BE PHOSPHORYLATED, NOT IN WEBLOGO metastasis. J Biol Chem. 2008 Jul 4;283(27):18753-64.

Human AKT1S1 (PRAS40) (Swissprot = Q96B36)

```
        1 MASGRPEELW EAVVGAAERF RARTGTELVL LTAAPPPPPR PGPCAYAAHG RGALAEAARR
       61 CLHDIALAHR AATAARPPAP PPAPQPPSPT PSPPRPTLAR EDNEEDEDEP TETETSGEQL
      121 GISDNGGLFV MDEDATLQDL PPFCESDPES TDDGSLSEET PAGPPTCSVP PASALPTQQY
      181 AKsLPVSVPV WGFKEKRTEA RSSDEENGPP SSPDLDRIAA SMRALVLREA EDTQVFGDLP
      241 RPRLNtSDFQ KLKRKY
>gi|74731194|sp|Q96B36.1|AKTS1_HUMAN RecName: Full=Proline-rich AKT1
substrate 1; AltName: Full=40 kDa proline-rich AKT substrate
MASGRPEELWEAVVGAAERFRARTGTELVLLTAAPPPPPRPGPCAYAAHGRGALAEAARRCLHDIALAHR
AATAARPPAPPPAPQPPSPTPSPPRPTLAREDNEEDEDEPTETETSGEQLGISDNGGLFVMDEDATLQDL
PPFCESDPESTDDGSLSEETPAGPPTCSVPPASALPTQQYAKSLPVSVPVWGFKEKRTEARSSDEENGPP
SSPDLDRIAASMRALVLREAEDTQVFGDLPRPRLNTSDFQKLKRKY
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Notes

Akt1S1 plays a role in phosphatidylinositol 3-kinase (PI3K)/AKT survival signaling. PRAS40 is a physiological target of in vivo insulin action. Hyperinsulinemia increased its phosphorylation in human skeletal muscle biopsies. Phosphorylated PRAS40 is predominantly localized to the nucleus. In rats fed a high-fat diet (HFD), phosphorylation of PRAS40 was markedly reduced when compared with low-fat diet-fed animals in all tissues examined. A novel mTOR binding partner that mediates Akt signals to mTOR. Binding of PRAS40 inhibits mTOR activity and suppresses constitutive activation of mTOR in cells lacking TSC2. Phosphorylation by Akt and perhaps related kinases leads to its binding to 14-3-3. Two alternatively spliced isoforms have been described. PRAS40 is a novel substrate of Akt, the phosphorylation of which leads to the binding of this protein to 14-3-3. PRAS40 phosphorylation by Akt and association with 14-3-3, a cytosolic anchor protein, are crucial for insulin to stimulate mTOR. PRAS40^{T246E} and PRAS40^{T246D} could not bind 14-3-3, further indicating that PRAS40–14-3-3 interaction is important for mTOR activation. The 14-3-3 binding may lead to facilitated release of PRAS40 from mTOR, or loose association of PRAS40 with mTOR, to activate mTOR and to inactivate IRS-1 through the negative feedback regulation.

activation of mTORC1 signalling by phorbol esters does not require PRAS40 to be phosphorylated at Thr(246), bind to 14-3-3 or be released from mTORC1. It is conceivable that phorbol esters activate mTORC1 by a distinct mechanism not involving PRAS40. Indeed, our results suggest that PRAS40 may not actually be involved in controlling mTORC1, but rather be a downstream target of mTORC1 that is regulated in response only to specific stimuli, such as insulin.

mutation of Ser-221 to Ala reduces the interaction with 14-3-3 to the same extent as mutation of Thr-246, the Akt/protein kinase B-phosphorylated site. We also find that mutation of Ser-221 to Ala increases the inhibitory activity of PRAS40 toward mTORC1. We propose that after mTORC1 kinase activation by upstream regulators, PRAS40 is phosphorylated directly by mTOR, thus contributing to the relief of PRAS40-mediated substrate competition.

References to 14-3-3 binding to PRAS40

Kovacina KS, Park GY, Bae SS, Guzzetta AW, Schaefer E, Birnbaum MJ, Roth RA. Identification of a proline-rich Akt substrate as a 14-3-3 binding partner. J Biol Chem. 2003 Mar 21;278(12):10189-94

Vander Haar E, Lee SI, Bandhakavi S, Griffin TJ, Kim DH. Insulin signalling to mTOR mediated by the Akt/PKB substrate PRAS40. Nat Cell Biol. 2007 Mar;9(3):316-23

Fonseca BD, Lee VH, Proud CG. The binding of PRAS40 to 14-3-3 proteins is not required for activation of mTORC1 signalling by phorbol esters/ERK. Biochem J. 2008 Apr 1;411(1):141-9.

Fonseca BD, Smith EM, Lee VH, MacKintosh C, Proud CG. PRAS40 is a target for mammalian target of rapamycin complex 1 and is required for signaling downstream of this complex. J Biol Chem. 2007 Aug 24;282(34):24514-24.

Wang L, Harris TE, Lawrence JC Jr.Regulation of proline-rich Akt substrate of 40 kDa (PRAS40) function by mammalian target of rapamycin
complex 1 (mTORC1)-mediated phosphorylation. J Biol Chem. 2008 Jun 6;283(23):15619-27.

Dubois F, Vandermoere F, Gernez A, Murphy J, Toth R, Chen S, Geraghty KM, Morrice NA, Mackintosh C. Differential 14-3-3-affinity capture reveals new downstream targets of PI 3-kinase signaling. Mol Cell Proteomics. 2009 Aug 1.

Zhang F, Beharry ZM, Harris TE, Lilly MB, Smith CD, Mahajan S, Kraft AS. PIM1 protein kinase regulates PRAS40 phosphorylation and mTOR activity in FDCP1 cells. Cancer Biol Ther. 2009 May;8(9):846-53.

Sancak Y, Thoreen CC, Peterson TR, Lindquist RA, Kang SA, Spooner E, Carr SA, Sabatini DM. PRAS40 is an insulin-regulated inhibitor of the mTORC1 protein kinase. Mol Cell. 2007 Mar 23;25(6):903-15.

Harthill JE, Pozuelo Rubio M, Milne FC, MacKintosh C. Regulation of the 14-3-3-binding protein p39 by growth factors and nutrients in rat PC12 pheochromocytoma cells. Biochem J. 2002 Dec 1;368(Pt 2):565-72.

Human ARaf1 (ARAF) (Swissprot = P10398)

```
        1 MEPPRGPPAN GAEPSRAVGT VKVYLPNKQR TVVTVRDGMS VYDSLDKALK VRGLNQDCCV
       61 VYRLIKGRKT VTAWDTAIAP LDGEELIVEV LEDVPLTMHN FVRKTFFSLA FCDFCLKFLF
      121 HGFRCQTCGY KFHQHCSSKV PTVCVDMSTN RQQFYHSVQD LSGGSRQHEA PSNRPLNELL
      181 TPQGPSPRTQ HCDPEHFPFP APANAPLQRI RSTsTPNVHM VSTTAPMDSN LIQLTGQSFS
      241 TDAAGSRGGS DGTPRGSPSP ASVSSGRKSP HSKSPAEQRE RKSLADDKKK VKNLGYRDSG
      301 YYWEVPPSEV QLLKRIGTGS FGTVFRGRWH GDVAVKVLKV SQPTAEQAQA FKNEMQVLRK
      361 TRHVNILLFM GFMTRPGFAI ITQWCEGSSL YHHLHVADTR FDMVQLIDVA RQTAQGMDYL
      421 HAKNIIHRDL KSNNIFLHEG LTVKIGDFGL ATVKTRWSGA QPLEQPSGSV LWMAAEVIRM
      481 QDPNPYSFQS DVYAYGVVLY ELMTGSLPYS HIGCRDQIIF MVGRGYLSPD LSKISSNCPK
      541 AMRRLLSDCL KFQREERPLF PQILATIELL QRSLPKIERS AsEPSLHRTQ ADELPACLLS
      601 AARLVP
>gi|1730068|sp|P10398.2|ARAF_HUMAN RecName: Full=A-Raf proto-oncogene
serine/threonine-protein kinase; AltName: Full=A-raf-1; AltName: Full=Proto-
oncogene Pks
MEPPRGPPANGAEPSRAVGTVKVYLPNKQRTVVTVRDGMSVYDSLDKALKVRGLNQDCCVVYRLIKGRKT
VTAWDTAIAPLDGEELIVEVLEDVPLTMHNFVRKTFFSLAFCDFCLKFLFHGFRCQTCGYKFHQHCSSKV
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PTVCVDMSTNRQQFYHSVQDLSGGSRQHEAPSNRPLNELLTPQGPSPRTQHCDPEHFPFPAPANAPLQRI RSTSTPNVHMVSTTAPMDSNLIQLTGQSFSTDAAGSRGGSDGTPRGSPSPASVSSGRKSPHSKSPAEQRE RKSLADDKKKVKNLGYRDSGYYWEVPPSEVQLLKRIGTGSFGTVFRGRWHGDVAVKVLKVSQPTAEQAQA FKNEMQVLRKTRHVNILLFMGFMTRPGFAIITQWCEGSSLYHHLHVADTRFDMVQLIDVARQTAQGMDYL HAKNIIHRDLKSNNIFLHEGLTVKIGDFGLATVKTRWSGAQPLEQPSGSVLWMAAEVIRMQDPNPYSFQS DVYAYGVVLYELMTGSLPYSHIGCRDQIIFMVGRGYLSPDLSKISSNCPKAMRRLLSDCLKFQREERPLF PQILATIELLQRSLPKIERSASEPSLHRTQADELPACLLSAARLVP **Notes** **References to 14-3-3-binding to ARaf1** (Also see references for BRaf and CRaf.) Kobayashi T, Aoki Y, Niihori T, Cavé H, Verloes A, Okamoto N, Kawame H, Fujiwara I, Takada F, Ohata T, Sakazume S, Ando T, Nakagawa N, Lapunzina P, Meneses AG, Gillessen-Kaesbach G, Wieczorek D, Kurosawa K, Mizuno S, Ohashi H, David A, Philip N, Guliyeva A, Narumi Y, Kure S, Tsuchiya S, Matsubara Y. Molecular and clinical analysis of RAF1 in Noonan syndrome and related disorders: dephosphorylation of serine 259 as the essential mechanism for mutant activation. Hum Mutat. 2010 Jan 5. [Epub ahead of print]	
Human ARHGEF2 GEF-H1 microtubule-localized Rho exchange factor (Swissprot = Q92974) 1 MSRIESLTRA RIDRSRELAS KTREKEKMKE AKDARYTNGH LFTTISVSGM TMCYACNKSI 61 TAKEALICPT CNVTIHNRCK DTLANCTKVK QKQQKAALLK NNTALQSVSL RSKTTIRERP 121 SSAIYPSDSF RQSLLGSRRG RSSLSLAKSV STTNIAGHFN DESPLGLRRI LSQSTDSLNM 181 RNRTLSVESL IDEAEVIYSE LMSDFEMDEK DFAADSWSLA VDSSFLQQHK KEVMKQQDVI 241 YELIQTELHH VRTLKIMTRL FRTGMLEELH LEPGVVQGLF PCVDELSDIH TRFLSQLLER 301 RRQALCPGST RNFVIHRLGD LLISQFSGPS AEQMCKTYSE FCSRHSKALK LYKELYARDK 361 RFQQFIRKVT RPAVLKRHGV QECILLVTQR ITKYPLLISR ILQHSHGIEE ERQDLTTALG 421 LVKELLSNVD EGIYQLEKGA RLQEIYNRMD PRAQTPVPGK GPFGREELLR RKLIHDGCLL 481 WKTATGRFKD VLVLLMTDVL VFLQEKDQKY IFPTLDKPSV VSLQNLIVRD IANQEKGMFL 541 ISAAPPEMYE VHTASRDDRS TWIRVIQQSV RTCPSREDFP LIETEDEAYL RRIKMELQQK 601 DRALVELLRE KVGLFAEMTH FQAEEDGGSG MALPTLPRGL FRSESLESPR GERLLQDAIR 661 EVEGLKDLLV GPGVELLLTP REPALPLEPD SGGNTSPGVT ANGEARTFNG SIELCRADSD 721 SSQRDRNGNQ LRSPQEEALQ RLVNLYGLLH GLQAAVAQQD TLMEARFPEG PERREKLCRA 781 NSRDGEAGRA GAAPVAPEKQ ATELALLQRQ HALLQEELRR CRRLGEERAT EAGSLEARLR 841 ESEQARALLE REAEEARRQL AALGQTEPLP AEAPWARRPV DPRRRsLPAG DALYLSFNPP 901 QPSRGTDRLD LPVTTRSVHR NFEDRERQEL GSPEERLQDS SDPDTGSEEE GSSRLSPPHS 961 PRDFTRMQDI PEETESRDGE AVASES >gi|205830906|sp|Q92974.4|ARHG2_HUMAN RecName: Full=Rho guanine nucleotide exchange factor 2; AltName: Full=Guanine nucleotide exchange factor H1; Short=GEF-H1; AltName: Full=Microtubule-regulated Rho-GEF; AltName: Full=Proliferating cell nucleolar antigen p40 MSRIESLTRARIDRSRELASKTREKEKMKEAKDARYTNGHLFTTISVSGMTMCYACNKSITAKEALICPT CNVTIHNRCKDTLANCTKVKQKQQKAALLKNNTALQSVSLRSKTTIRERPSSAIYPSDSFRQSLLGSRRG RSSLSLAKSVSTTNIAGHFNDESPLGLRRILSQSTDSLNMRNRTLSVESLIDEAEVIYSELMSDFEMDEK DFAADSWSLAVDSSFLQQHKKEVMKQQDVIYELIQTELHHVRTLKIMTRLFRTGMLEELHLEPGVVQGLF PCVDELSDIHTRFLSQLLERRRQALCPGSTRNFVIHRLGDLLISQFSGPSAEQMCKTYSEFCSRHSKALK LYKELYARDKRFQQFIRKVTRPAVLKRHGVQECILLVTQRITKYPLLISRILQHSHGIEEERQDLTTALG LVKELLSNVDEGIYQLEKGARLQEIYNRMDPRAQTPVPGKGPFGREELLRRKLIHDGCLLWKTATGRFKD VLVLLMTDVLVFLQEKDQKYIFPTLDKPSVVSLQNLIVRDIANQEKGMFLISAAPPEMYEVHTASRDDRS TWIRVIQQSVRTCPSREDFPLIETEDEAYLRRIKMELQQKDRALVELLREKVGLFAEMTHFQAEEDGGSG MALPTLPRGLFRSESLESPRGERLLQDAIREVEGLKDLLVGPGVELLLTPREPALPLEPDSGGNTSPGVT ANGEARTFNGSIELCRADSDSSQRDRNGNQLRSPQEEALQRLVNLYGLLHGLQAAVAQQDTLMEARFPEG PERREKLCRANSRDGEAGRAGAAPVAPEKQATELALLQRQHALLQEELRRCRRLGEERATEAGSLEARLR ESEQARALLEREAEEARRQLAALGQTEPLPAEAPWARRPVDPRRRSLPAGDALYLSFNPPQPSRGTDRLD LPVTTRSVHRNFEDRERQELGSPEERLQDSSDPDTGSEEEGSSRLSPPHSPRDFTRMQDIPEETESRDGE AVASES **Notes** Phosphorylation of GEF-H1 at Ser(885) by PAK1 induces 14-3-3 binding to the exchange factor and relocation of 14-3-3 to microtubules (= Ser 886 in Q92974) **References to 14-3-3-binding to ARHGEF2 (GEF-H1)** Zenke FT, Krendel M, DerMardirossian C, King CC, Bohl BP, Bokoch GM. p21-activated kinase 1 phosphorylates and regulates 14-3-3 binding to GEF-H1, a microtubule-localized Rho exchange factor. J Biol Chem. 2004 Apr 30;279(18):18392-400.	
Human ARHGEF7 (beta-Pix, COOL-1) (Swissprot = Q14155) 1 MNSAEQTVTW LITLGVLESP KKTISDPEGF LQASLKDGVV LCRLLERLLP GTIEKVYPEP 61 RSESECLSNI REFLRGCGAS LRLELLFPPS QPPQHLVTTI LLSASTFDAN DLYQGQNFNK 121 VLSSLVTLNK VTADIGLGSD SVCARPSSHR IKSFDSLGSQ SLHTRTSKLF QGQYRSLDMT 181 DNSNNQLVVR AKFNFQQTNE DELSFSKGDV IHVTRVEEGG WWEGTLNGRT GWFPSNYVRE 241 VKASEKPVSP KSGTLKSPPK GFDTTAINKS YYNVVLQNIL ETENEYSKEL QTVLSTYLRP 301 LQTSEKLSSA NISYLMGNLE EICSFQQMLV QSLEECTKLP EAQQRVGGCF LNLMPQMKTL 361 YLTYCANHPS AVNVLTEHSE ELGEFMETKG ASSPGILVLT TGLSKPFMRL DKYPTLLKEL 421 ERHMEDYHTD RQDIQKSMAA FKNLSAQCQE VRKRKELELQ ILTEAIRNWE GDDIKTLGNV 481 TYMSQVLIQC AGSEEKNERY LLLFPNVLLM LSASPRMSGF IYQGKLPTTG MTITKLEDSE 541 NHRNAFEISG SMIERILVSC NNQQDLQEWV EHLQKQTKVT SVGNPTIKPH SVPSHTLPSH 601 PVTPSSKHAD SKPAPLTPAY HTLPHPSHHG TPHTTINWGP LEPPKTPKPW SLSCLRPAPP 661 LRPSAALCYK EDLSKSPKTM KKLLPKRKPE RKPSDEEFAS RKSTAALEED AQILKVIEAY 721 CTSAKTRQTL NSTWQGTDLM HNHVLADDDQ PSLDSLGRRS SLSRLEPSDL SEDSDYDSIW 781 TAHSYRMGST SRKSCCSYIS HQN >gi|50403776|sp|Q14155.2|ARHG7_HUMAN RecName: Full=Rho guanine nucleotide exchange factor 7; AltName: Full=PAK-interacting exchange factor beta; AltName: Full=Beta-Pix; AltName: Full=COOL-1; AltName: Full=p85	DATA INDICATE DIRECT INTERACTION BETWEEN ARHGEF7 PROTEIN AND 14-3-3-, BUT SITE(S) NOT IDENTIFIED. NOT IN WEBLOGO.

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MNSAEQTVTWLITLGVLESPKKTISDPEGFLQASLKDGVVLCRLLERLLPGTIEKVYPEPRSESECLSNI
REFLRGCGASLRLELLFPPSQPPQHLVTTILLSASTFDANDLYQGQNFNKVLSSLVTLNKVTADIGLGSD
SVCARPSSHRIKSFDSLGSQSLHTRTSKLFQGQYRSLDMTDNSNNQLVVRAKFNFQQTNEDELSFSKGDV
IHVTRVEEGGWWEGTLNGRTGWFPSNYVREVKASEKPVSPKSGTLKSPPKGFDTTAINKSYYNVVLQNIL
ETENEYSKELQTVLSTYLRPLQTSEKLSSANISYLMGNLEEICSFQQMLVQSLEECTKLPEAQQRVGGCF
LNLMPQMKTLYLTYCANHPSAVNVLTEHSEELGEFMETKGASSPGILVLTTGLSKPFMRLDKYPTLLKEL
ERHMEDYHTDRQDIQKSMAAFKNLSAQCQEVRKRKELELQILTEAIRNWEGDDIKTLGNVTYMSQVLIQC
AGSEEKNERYLLLFPNVLLMLSASPRMSGFIYQGKLPTTGMTITKLEDSENHRNAFEISGSMIERILVSC
NNQQDLQEWVEHLQKQTKVTSVGNPTIKPHSVPSHTLPSHPVTPSSKHADSKPAPLTPAYHTLPHPSHHG
TPHTTINWGPLEPPKTPKPWSLSCLRPAPPLRPSAALCYKEDLSKSPKTMKKLLPKRKPERKPSDEEFAS
RKSTAALEEDAQILKVIEAYCTSAKTRQTLNSTWQGTDLMHNHVLADDDQPSLDSLGRRSSLSRLEPSDL
SEDSDYDSIWTAHSYRMGSTSRKSCCSYISHQN
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Notes

Basal association between endogenous βPix and endogenous 14-3-3β was increased after forskolin stimulation and significantly inhibited by protein kinase A inhibitor. However, forskolin stimulation failed to increase the interaction between 14-3-3β and a β_1Pix mutant that is insensitive to protein kinase A phosphorylation, β_1Pix(S516A, T526A). (Mutating Ser560 has NO effect on 14-3-3 binding, RKE(S560)AP).

Binding of 14-3-3β inhibits dimeric β_1Pix-GEF activity, 14-3-3β binding may either block the interaction between Rac1 and the DH domain of β_1Pix or induce a conformational change of the DH domain that would interfere with GTP binding.

The numbering here seems to relate to MOUSE Rho guanine nucleotide exchange factor (GEF) 7 sequence NM_017402.3:

```
MTDNTNSQLVVRAKFNFQQTNEDELSFSKGDVIHVTRVEEGGWWEGTHNG
RTGWFPSNYVREIKPSEKPVSPKSGTLKSPPKGFDTTAINKSYYNVVLQN
ILETEHEYSKELQSVLSTYLRPLQTSDKLSSANTSYLMGNLEEISSFQQV
LVQSLEECTKSPEAQQRVGGCFLSLMPQMRTLYLAYCANHPSAVSVLTEH
SEDLGEFMETKGASSPGILVLTTGLSKPFMRLDKYPTLLKELERHMEDYH
PDRQDIQKSMTAFKNLSAQCQEVRKRKELELQILTEPIRSWEGDDIKTLG
SVTYMSQVTIQCAGSEEKNERYLLLFPNLLLMLSASPRMSGFIYQGKLPT
TGMTITKLEDSENHRNAFEISGSMIERILVSCTSQQDLHEWVEHLQKQTK
VTSVSNPTIKPHSVPSHTLPSHPLTPSSKHADSKPVALTPAYHTLPHPSH
HGTPHTTISWGPLEPPKTPKPWSLSCLRPAPPLRPSAALCYKEDLSKSPK
TMKKLLPKRKPERKPSDEEFAVRKSTAALEEDAQILKVIEAYCTSAKTRQ
TLNSSSRKESAPQVLLPEEEKIIVEETKSNGQTVIEEKSLVDTVYALKDE
VQELRQDNKKMKKSLEEEQRARKDLEKLVRKVLKNMNDPAWDETNL*
```

(This version has actually been updated to NM_001113517.1 GI:165377084 which is longer)
W43K context is VEEGGkWEGT
L238R/L239S context is KYPTrsKELERHM
S516A context is PERKPaDEEFAV
T526A context is AVRKSaAALEED

References to 14-3-3 binding to ARHGEF7

Chahdi A, Sorokin A. Protein kinase A-dependent phosphorylation modulates beta1Pix guanine nucleotide exchange factor activity through 14-3-3beta binding. Mol Cell Biol. 2008 Mar;28(5):1679-87. Epub 2007 Dec 26
Chahdi A, Miller B, Sorokin A. Endothelin 1 induces beta 1Pix translocation and Cdc42 activation via protein kinase A-dependent pathway. J Biol Chem. 2005 Jan 7;280(1):578-84.
Angrand PO, Segura I, Völkel P, Ghidelli S, Terry R, Brajenovic M, Vintersten K, Klein R, Superti-Furga G, Drewes G, Kuster B, Bouwmeester T, Acker-Palmer A. Transgenic mouse proteomics identifies new 14-3-3-associated proteins involved in cytoskeletal rearrangements and cell signaling. Mol Cell Proteomics. 2006 Dec;5(12):2211-27.

<u>**Human ATXN-1**</u> Ataxin-1. PolyQ mutant in spinocerebellar ataxia 1.   (Swissprot = P54253)

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        1 MKSNQERSNE CLPPKKREIP ATSRSSEEKA PTLPSDNHRV EGTAWLPGNP GGRGHGGGRH
       61 GPAGTSVELG LQQGIGLHKA LSTGLDYSPP SAPRSVPVAT TLPAAYATPQ PGTPVSPVQY
      121 AHLPHTFQFI GSSQYSGTYA SFIPSQLIPP TANPVTSAVA SAAGATTPSQ RSQLEAYSTL
      181 LANMGSLSQT PGHKAEQQQQ QQQQQQQQHQ HQQQQQQQQQ QQQQQHLSRA PGLITPGSPP
      241 PAQQNQYVHI SSSPQNTGRT ASPPAIPVHL HPHQTMIPHT LTLGPPSQVV MQYADSGSHF
      301 VPREATKKAE SSRLQQAIQA KEVLNGEMEK SRRYGAPSSA DLGLGKAGGK SVPHPYESRH
      361 VVVHPSPSDY SSRDPSGVRA SVMVLPNSNT PAADLEVQQA THREASPSTL NDKSGLHLGK
      421 PGHRSYALSP HTVIQTTHSA SEPLPVGLPA TAFYAGTQPP VIGYLSGQQQ AITYAGSLPQ
      481 HLVIPGTQPL LIPVGSTDME ASGAAPAIVT SSPQFAAVPH TFVTTALPKS ENFNPEALVT
      541 QAAYPAMVQA QIHLPVVQSV ASPAAAPPTL PPYFMKGSII QLANGELKKV EDLKTEDFIQ
      601 SAEISNDLKI DSSTVERIED SHSPGVAVIQ FAVGEHRAQV SVEVLVEYPF FVFGQGWSSC
      661 CPERTSQLFD LPCSKLSVGD VCISLTLKNL KNGSVKKGQP VDPASVLLKH SKADGLAGSR
      721 HRYAEQENGI NQGSAQMLSE NGELKFPEKM GLPAAPFLTK IEPSKPAATR KRRWsAPESR
      781 KLEKSEDEPP LTLPKPSLIP QEVKICIEGR SNVGK
>gi|206729854|sp|P54253.2|ATX1_HUMAN RecName: Full=Ataxin-1; AltName:
Full=Spinocerebellar ataxia type 1 protein
MKSNQERSNECLPPKKREIPATSRSSEEKAPTLPSDNHRVEGTAWLPGNPGGRGHGGGRHGPAGTSVELG
LQQGIGLHKALSTGLDYSPPSAPRSVPVATTLPAAYATPQPGTPVSPVQYAHLPHTFQFIGSSQYSGTYA
SFIPSQLIPPTANPVTSAVASAAGATTPSQRSQLEAYSTLLANMGSLSQTPGHKAEQQQQQQQQQQQQHQ
HQQQQQQQQQQQQQQHLSRAPGLITPGSPPPAQQNQYVHISSSPQNTGRTASPPAIPVHLHPHQTMIPHT
LTLGPPSQVVMQYADSGSHFVPREATKKAESSRLQQAIQAKEVLNGEMEKSRRYGAPSSADLGLGKAGGK
SVPHPYESRHVVVHPSPSDYSSRDPSGVRASVMVLPNSNTPAADLEVQQATHREASPSTLNDKSGLHLGK
PGHRSYALSPHTVIQTTHSASEPLPVGLPATAFYAGTQPPVIGYLSGQQQAITYAGSLPQHLVIPGTQPL
LIPVGSTDMEASGAAPAIVTSSPQFAAVPHTFVTTALPKSENFNPEALVTQAAYPAMVQAQIHLPVVQSV
ASPAAAPPTLPPYFMKGSIIQLANGELKKVEDLKTEDFIQSAEISNDLKIDSSTVERIEDSHSPGVAVIQ
FAVGEHRAQVSVEVLVEYPFFVFGQGWSSCCPERTSQLFDLPCSKLSVGDVCISLTLKNLKNGSVKKGQP
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VDPASVLLKHSKADGLAGSRHRYAEQENGINQGSAQMLSENGELKFPEKMGLPAAPFLTKIEPSKPAATR
KRRWSAPESRKLEKSEDEPPLTLPKPSLIPQEVKICIEGRSNVGK
```

Notes

RRWpS^{776}AP (= Ser775 in P54253). Kinase suggested to be PKB/Akt or PKA, but not clear.

References to 14-3-3 binding to ataxin-1

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de Chiara C, Menon RP, Strom M, Gibson TJ, Pastore A. Phosphorylation of s776 and 14-3-3 binding modulate ataxin-1 interaction with splicing factors. PLoS One. 2009 Dec 23;4(12):e8372.

Human BAD (Swissprot = Q92934)

```
        1 MFQIPEFEPS EQEDSSSAER GLGPSPAGDG PSGSGKHHRQ APGLLWDASH QQEQPTSSSH
       61 HGGAGAVEIR SRHSsYPAGT EDDEGMGEEP SPFRGRSRsA PPNLWAAQRY GRELRRMSDE
      121 FVDSFKKGLP RPKSAGTATQ MRQSSSWTRV FQSWWDRNLG RGSSAPSQ
>gi|17371773|sp|Q92934.3|BAD_HUMAN RecName: Full=Bcl2 antagonist of cell
death; Short=BAD; AltName: Full=Bcl-2-binding component 6; AltName: Full=Bcl-
2-like protein 8; Short=Bcl2-L-8; AltName: Full=Bcl-XL/Bcl-2-associated death
promoter
MFQIPEFEPSEQEDSSSAERGLGPSPAGDGPSGSGKHHRQAPGLLWDASHQQEQPTSSSHHGGAGAVEIR
SRHSSYPAGTEDDEGMGEEPSPFRGRSRSAPPNLWAAQRYGRELRRMSDEFVDSFKKGLPRPKSAGTATQ
MRQSSSWTRVFQSWWDRNLGRGSSAPSQ
```

Notes

Phosphorylated Bad is sequestered in the cytoplasm by 14-3-3 thereby preventing its mitochondrial translocation to induce apoptosis. The 14-3-3-binding sites can phosphorlyated by a number of protein kinases, including PKB and PKA. 14-3-3 binding reduces interactions with Bcl-2 & Bcl-xl. The 14-3-3-binding sites are commonly numbered as Ser112 and Ser136 according to the murine BAD (Swissprot = Q61337), which correspond to Ser75 and Ser99 in the human BAD (Q92934). Murine BAD is longer than human BAD.

References to 14-3-3 binding to BAD

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Human BAIP2 (also known as IRSp53) Brain-specific angiogenesis inhibitor 1-associated protein 2 (Swissprot = Q9UQB8)

```
1 MSLSRSEEMH RLTENVYKTI MEQFNPSLRN FIAMGKNYEK ALAGVTYAAK GYFDALVKMG
       61 ELASESQGSK ELGDVLFQMA EVHRQIQNQL EEMLKSFHNE LLTQLEQKVE LDSRYLSAAL
      121 KKYQTEQRSK GDALDKCQAE LKKLRKKSQG SKNPQKYSDK ELQYIDAISN KQGELENYVS
      181 DGYKTALTEE RRRFCFLVEK QCAVAKNSAA YHSKGKELLA QKLPLWQQAC ADPSKIPERA
      241 VQLMQQVASN GATLPSALSA SKSNLVISDP IPGAKPLPVP PELAPFVGRM SAQESTPIMN
      301 GVTGPDGEDY SPWADRKAAQ PKSLSPPQSQ SKLSDSYSNt LPVRKSVTPK NSYATTENKt
      361 LPRSSSMAAG LERNGRMRVK AIFSHAAGDN STLLSFKEGD LITLLVPEAR DGWHYGESEK
      421 TKMRGWFPFS YTRVLDSDGS DRLHMSLQQG KSSSTGNLLD KDDLAIPPPD YGAASRAFPA
      481 QTASGFKQRP YSVAVPAFSQ GLDDYGARSM SRNPFAHVQL KPTVTNDRCD LSAQGPEGRE
      541 HGDGSARTLA GR
```

Notes
MRRS(pS87)LLSR, said to be phosphorylated by Akt/PKB, but not conventional Akt/PKB site.
References to 14-3-3 binding to BAIP2 (IRSp53)
Robens JM, Lee YF, Ng E, Hall C, Manser E. Regulation of IRSp53-dependent filopodial dynamics by antagonism between 14-3-3 binding and SH3-mediated localization. Mol Cell Biol. 2009 Nov 23. [Epub ahead of print]

Human BCL2L11 = Bcl-2-like protein 11 = BimEL =EL isoform of Bim (Swissprot = O43521)

```
        1 MAKQPSDVSS ECDREGRQLQ PAERPPQLRP GAPTSLQTEP QGNPEGNHGG EGDSCPHGSP
       61 QGPLAPPASP GPFATRSPLF IFMRRSsLLS RSSSGYFSFD TDRSPAPMSC DKSTQTPSPP
      121 CQAFNHYLSA MASMRQAEPA DMRPEIWIAQ ELRRIGDEFN AYYARRVFLN NYQAAEDHPR
      181 MVILRLLRYI VRLVWRMH
>gi|18202042|sp|O43521.1|B2L11_HUMAN RecName: Full=Bcl-2-like protein 11;
Short=Bcl2-L-11; AltName: Full=Bcl2-interacting mediator of cell death
MAKQPSDVSSECDREGRQLQPAERPPQLRPGAPTSLQTEPQGNPEGNHGGEGDSCPHGSPQGPLAPPASP
GPFATRSPLFIFMRRSSLLSRSSSGYFSFDTDRSPAPMSCDKSTQTPSPPCQAFNHYLSAMASMRQAEPA
DMRPEIWIAQELRRIGDEFNAYYARRVFLNNYQAAEDHPRMVILRLLRYIVRLVWRMH
```

Notes
MRRS(pS87)LLSR, said to be phosphorylated by Akt/PKB, but not conventional Akt/PKB site.
References to 14-3-3 binding to BimEL
Qi XJ, Wildey GM, Howe PH. Evidence that Ser87 of BimEL is phosphorylated by Akt and regulates BimEL apoptotic function. J Biol Chem. 2006 Jan 13;281(2):813-23.

Human BRaf1 (BRAF) (Swissprot = P15056)

```
        1 MAALSGGGGG GAEPGQALFN GDMEPEAGAG AGAAASSAAD PAIPEEVWNI KQMIKLTQEH
       61 IEALLDKFGG EHNPPSIYLE AYEEYTSKLD ALQQREQQLL ESLGNGTDFS VSSSASMDTV
      121 TSSSSSSLSV LPSSLSVFQN PTDVARSNPK SPQKPIVRVF LPNKQRTVVP ARCGVTVRDS
      181 LKKALMMRGL IPECCAVYRI QDGEKKPIGW DTDISWLTGE ELHVEVLENV PLTTHNFVRK
      241 TFFTLAFCDF CRKLLFQGFR CQTCGYKFHQ RCSTEVPLMC VNYDQLDLLF VSKFFEHHPI
      301 PQEEASLAET ALTSGSSPSA PASDSIGPQI LTSPSPSKSI PIPQPFRPAD EDHRNQFGQR
      361 DRSSsAPNVH INTIEPVNID DLIRDQGFRG DGGSTTGLSA TPPASLPGSL TNVKALQKSP
      421 GPQRERKSSS SSEDRNRMKT LGRRDSSDDW EIPDGQITVG QRIGSGSFGT VYKGKWHGDV
      481 AVKMLNVTAP TPQQLQAFKN EVGVLRKTRH VNILLFMGYS TKPQLAIVTQ WCEGSSLYHH
      541 LHIIETKFEM IKLIDIARQT AQGMDYLHAK SIIHRDLKSN NIFLHEDLTV KIGDFGLATV
      601 KSRWSGSHQF EQLSGSILWM APEVIRMQDK NPYSFQSDVY AFGIVLYELM TGQLPYSNIN
      661 NRDQIIFMVG RGYLSPDLSK VRSNCPKAMK RLMAECLKKK RDERPLFPQI LASIELLARS
      721 LPKIHRSAsE PSLNRAGFQT EDFSLYACAS PKTPIQAGGY GAFPVH
>gi|50403720|sp|P15056.4|BRAF1_HUMAN RecName: Full=B-Raf proto-oncogene
serine/threonine-protein kinase; AltName: Full=p94; AltName: Full=v-Raf
murine sarcoma viral oncogene homolog B1
MAALSGGGGGGAEPGQALFNGDMEPEAGAGAGAAASSAADPAIPEEVWNIKQMIKLTQEHIEALLDKFGG
EHNPPSIYLEAYEEYTSKLDALQQREQQLLESLGNGTDFSVSSSASMDTVTSSSSSSLSVLPSSLSVFQN
PTDVARSNPKSPQKPIVRVFLPNKQRTVVPARCGVTVRDSLKKALMMRGLIPECCAVYRIQDGEKKPIGW
DTDISWLTGEELHVEVLENVPLTTHNFVRKTFFTLAFCDFCRKLLFQGFRCQTCGYKFHQRCSTEVPLMC
VNYDQLDLLFVSKFFEHHPIPQEEASLAETALTSGSSPSAPASDSIGPQILTSPSPSKSIPIPQPFRPAD
EDHRNQFGQRDRSSSAPNVHINTIEPVNIDDLIRDQGFRGDGGSTTGLSATPPASLPGSLTNVKALQKSP
GPQRERKSSSSSEDRNRMKTLGRRDSSDDWEIPDGQITVGQRIGSGSFGTVYKGKWHGDVAVKMLNVTAP
TPQQLQAFKNEVGVLRKTRHVNILLFMGYSTKPQLAIVTQWCEGSSLYHHLHIIETKFEMIKLIDIARQT
AQGMDYLHAKSIIHRDLKSNNIFLHEDLTVKIGDFGLATVKSRWSGSHQFEQLSGSILWMAPEVIRMQDK
NPYSFQSDVYAFGIVLYELMTGQLPYSNINNRDQIIFMVGRGYLSPDLSKVRSNCPKAMKRLMAECLKKK
RDERPLFPQILASIELLARSLPKIHRSASEPSLNRAGFQTEDFSLYACASPKTPIQAGGYGAFPVH
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Notes
References to 14-3-3-binding to BRaf1
See references for ARaf1 and CRaf.

Human Cabin1 (Calcineurin-binding protein cabin-1) (Q9Y6J0)

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        1 MIRIAALNAS STIEDDHEGS FKSHKTQTKE AQEAEAFALY HKALDLQKHD RFEESAKAYH
       61 ELLEASLLRE AVSSGDEKEG LKHPGLILKY STYKNLAQLA AQREDLETAM EFYLEAVMLD
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     121 STDVNLWYKI GHVALRLIRI PLARHAFEEG LRCNPDHWPC LDNLITVLYT LSDYTTCLYF
     181 ICKALEKDCR YSKGLVLKEK IFEEQPCLRK DSLRMFLKCD MSIHDVSVSA AETQAIVDEA
     241 LGLRKKRQAL IVREKEPDLK LVQPIPFFTW KCLGESLLAM YNHLTTCEPP RPSLGKRIDL
     301 SDYQDPSQPL ESSMVVTPVN VIQPSTVSTN PAVAVAEPVV SYTSVATTSF PLHSPGLLET
     361 GAPVGDISGG DKSKKGVKRK KISEESGETA KRRSARVRNT KCKKEEKVDF QELLMKFLPS
     421 RLRKLDPEEE DDSFNNYEVQ SEAKLESFPS IGPQRLSFDS ATFMESEKQD VHEFLLENLT
     481 NGGILELMMR YLKAMGHKFL VRWPPGLAEV VLSVYHSWRR HSTSLPNPLL RDCSNKHIKD
     541 MMLMSLSCME LQLDQWLLTK GRSSAVSPRN CPAGMVNGRF GPDFPGTHCL GDLLQLSFAS
     601 SQRDLFEDGW LEFVVRVYWL KARFLALQGD MEQALENYDI CTEMLQSSTA IQVEAGAERR
     661 DIVIRLPNLH NDSVVSLEEI DKNLKSLERC QSLEEIQRLY EAGDYKAVVH LLRPTLCTSG
     721 FDRAKHLEFM TSIPERPAQL LLLQDSLLRL KDYRQCFECS DVALNEAVQQ MVNSGEAAAK
     781 EEWVATVTQL LMGIEQALSA DSSGSILKVS SSTTGLVRLT NNLIQVIDCS MAVQEEAKEP
     841 HVSSVLPWII LHRIIWQEED TFHSLCHQQQ LQNPAEEGMS ETPMLPSSLM LLNTAHEYLG
     901 RRSWCCNSDG ALLRFYVRVL QKELAASTSE DTHPYKEELE TALEQCFYCL YSFPSKKSKA
     961 RYLEEHSAQQ VDLIWEDALF MFEYFKPKTL PEFDSYKTST VSADLANLLK RIATIVPRTE
    1021 RPALSLDKVS AYIEGTSTEV PCLPEGADPS PPVVNELYYL LADYHFKNKE QSKAIKFYMH
    1081 DICICPNRFD SWAGMALARA SRIQDKLNSN ELKSDGPIWK HATPVLNCFR RALEIDSSNL
    1141 SLWIEYGTMS YALHSFASRQ LKQWRGELPP ELVQQMEGRR DSMLETAKHC FTSAARCEGD
    1201 GDEEEWLIHY MLGKVAEKQQ QPPTVYLLHY RQAGHYLHEE AARYPKKIHY HNPPELAMEA
    1261 LEVYFRLHAS ILKLLGKPDS GVGAEVLVNF MKEAAEGPFA RGEEKNTPKA SEKEKACLVD
    1321 EDSHSSAGTL PGPGASLPSS SGPGLTSPPY TATPIDHDYV KCKKPHQQAT PDDRSQDSTA
    1381 VALSDSSSTQ DFFNEPTSLL EGSRKSYTEK RLPILSSQAG ATGKDLQGAT EERGKNEESL
    1441 ESTEGFRAAE QGVQKPAAET PASACIPGKP SASTPTLWDG KKRGDLPGEP VAFPQGLPAG
    1501 AEEQRQFLTE QCIASFRLCL SRFPQHYKSL YRLAFLYTYS KTHRNLQWAR DVLLGSSIPW
    1561 QQLQHMPAQG LFCERNKTNF FNGIWRIPVD EIDRPGSFAW HMNRSIVLLL KVLAQLRDHS
    1621 TLLKVSSMLQ RTPDQGKKYL RDADRQVLAQ RAFILTVKVL EDTLSELAEG SERPGPKVCG
    1681 LPGARMTTDV SHKASPEDGQ EGLPQPKKPP LADGSGPGPE PGGKVGLLNH RPVAMDAGDS
    1741 ADQSGERKDK ESPRAGPTEP MDTSEATVCH SDLERTPPLL PGRPARDRGP ESRPTELSLE
    1801 ELSISARQQP TPLTPAQPAP APAPATTTGT RAGGHPEEPL SRLSRKRKLL EDTESGKTLL
    1861 LDAYRVWQQG QKGVAYDLGR VERIMSETYM LIKQVDEEAA LEQAVKFCQV HLGAAAQRQA
    1921 SGDTPTTPKH PKDSRENFFP VTVVPTAPDP VPADSVQRPS DAHTKPRPAL AAATTIITCP
    1981 PSASASTLDQ SKDPGPPRPH RPEATPSMAS LGPEGEELAR VAEGTSFPPQ EPRHSPQVKM
    2041 APTSSPAEPH CWPAEAALGT GAEPTCSQEG KLRPEPRRDG EAQEAASETQ PLSSPPTAAS
    2101 SKAPSSGSAQ PPEGHPGKPE PSRAKsRPLP NMPKLVIPSA ATKFPPEITV TPPTPTLLSP
    2161 KGSISEETKQ KLKSAILSAQ SAANVRKESL CQPALEVLET SSQESSLESE TDEDDDYMDI
>gi|6685261|sp|Q9Y6J0.1|CABIN_HUMAN RecName: Full=Calcineurin-binding protein
cabin-1; AltName: Full=Calcineurin inhibitor; Short=CAIN
MIRIAALNASSTIEDDHEGSFKSHKTQTKEAQEAEAFALYHKALDLQKHDRFEESAKAYHELLEASLLRE
AVSSGDEKEGLKHPGLILKYSTYKNLAQLAAQREDLETAMEFYLEAVMLDSTDVNLWYKIGHVALRLIRI
PLARHAFEEGLRCNPDHWPCLDNLITVLYTLSDYTTCLYFICKALEKDCRYSKGLVLKEKIFEEQPCLRK
DSLRMFLKCDMSIHDVSVSAAETQAIVDEALGLRKKRQALIVREKEPDLKLVQPIPFFTWKCLGESLLAM
YNHLTTCEPPRPSLGKRIDLSDYQDPSQPLESSMVVTPVNVIQPSTVSTNPAVAVAEPVVSYTSVATTSF
PLHSPGLLETGAPVGDISGGDKSKKGVKRKKISEESGETAKRRSARVRNTKCKKEEKVDFQELLMKFLPS
RLRKLDPEEEDDSFNNYEVQSEAKLESFPSIGPQRLSFDSATFMESEKQDVHEFLLENLTNGGILELMMR
YLKAMGHKFLVRWPPGLAEVVLSVYHSWRRHSTSLPNPLLRDCSNKHIKDMMLMSLSCMELQLDQWLLTK
GRSSAVSPRNCPAGMVNGRFGPDFPGTHCLGDLLQLSFASSQRDLFEDGWLEFVVRVYWLKARFLALQGD
MEQALENYDICTEMLQSSTAIQVEAGAERRDIVIRLPNLHNDSVVSLEEIDKNLKSLERCQSLEEIQRLY
EAGDYKAVVHLLRPTLCTSGFDRAKHLEFMTSIPERPAQLLLLQDSLLRLKDYRQCFECSDVALNEAVQQ
MVNSGEAAAKEEWVATVTQLLMGIEQALSADSSGSILKVSSSTTGLVRLTNNLIQVIDCSMAVQEEAKEP
HVSSVLPWIILHRIIWQEEDTFHSLCHQQQLQNPAEEGMSETPMLPSSLMLLNTAHEYLGRRSWCCNSDG
ALLRFYVRVLQKELAASTSEDTHPYKEELETALEQCFYCLYSFPSKKSKARYLEEHSAQQVDLIWEDALF
MFEYFKPKTLPEFDSYKTSTVSADLANLLKRIATIVPRTERPALSLDKVSAYIEGTSTEVPCLPEGADPS
PPVVNELYYLLADYHFKNKEQSKAIKFYMHDICICPNRFDSWAGMALARASRIQDKLNSNELKSDGPIWK
HATPVLNCFRRALEIDSSNLSLWIEYGTMSYALHSFASRQLKQWRGELPPELVQQMEGRRDSMLETAKHC
FTSAARCEGDGDEEEWLIHYMLGKVAEKQQQPPTVYLLHYRQAGHYLHEEAARYPKKIHYHNPPELAMEA
LEVYFRLHASILKLLGKPDSGVGAEVLVNFMKEAAEGPFARGEEKNTPKASEKEKACLVDEDSHSSAGTL
PGPGASLPSSSGPGLTSPPYTATPIDHDYVKCKKPHQQATPDDRSQDSTAVALSDSSSTQDFFNEPTSLL
EGSRKSYTEKRLPILSSQAGATGKDLQGATEERGKNEESLESTEGFRAAEQGVQKPAAETPASACIPGKP
SASTPTLWDGKKRGDLPGEPVAFPQGLPAGAEEQRQFLTEQCIASFRLCLSRFPQHYKSLYRLAFLYTYS
KTHRNLQWARDVLLGSSIPWQQLQHMPAQGLFCERNKTNFFNGIWRIPVDEIDRPGSFAWHMNRSIVLLL
KVLAQLRDHSTLLKVSSMLQRTPDQGKKYLRDADRQVLAQRAFILTVKVLEDTLSELAEGSERPGPKVCG
LPGARMTTDVSHKASPEDGQEGLPQPKKPPLADGSGPGPEPGGKVGLLNHRPVAMDAGDSADQSGERKDK
ESPRAGPTEPMDTSEATVCHSDLERTPPLLPGRPARDRGPESRPTELSLEELSISARQQPTPLTPAQPAP
APAPATTTGTRAGGHPEEPLSRLSRKRKLLEDTESGKTLLLDAYRVWQQGQKGVAYDLGRVERIMSETYM
LIKQVDEEAALEQAVKFCQVHLGAAAQRQASGDTPTTPKHPKDSRENFFPVTVVPTAPDPVPADSVQRPS
DAHTKPRPALAAATTIITCPPSASASTLDQSKDPGPPRPHRPEATPSMASLGPEGEELARVAEGTSFPPQ
EPRHSPQVKMAPTSSPAEPHCWPAEAALGTGAEPTCSQEGKLRPEPRRDGEAQEAASETQPLSSPPTAAS
SKAPSSGSAQPPEGHPGKPEPSRAKSRPLPNMPKLVIPSAATKFPPEITVTPPTPTLLSPKGSISEETKQ
KLKSAILSAQSAANVRKESLCQPALEVLETSSQESSLESETDEDDDYMDI
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Notes

(RAKpS^{2126}RP)   Cabin1 is a transcriptional corepressor for myocyte enhancer factor 2

References to 14-3-3 binding to Cabin1

Pan F, Means AR, Liu JO. Calmodulin-dependent protein kinase IV regulates nuclear export of Cabin1 during T-cell activation. EMBO J. 2005 Jun 15;24(12):2104-13.

Choi SJ, Park SY, Han TH. 14-3-3tau associates with and activates the MEF2D transcription factor during muscle cell differentiation. Nucleic Acids Res. 2001 Jul 1;29(13):2836-42.

Human Cbl E3 ubiquitin-protein ligase CBL (swissprot = P22681)

```
      1 MAGNVKKSSG AGGGSGSGGS GSGGLIGLMK DAFQPHHHHH HHLSPHPPGT VDKKMVEKCW
     61 KLMDKVVRLC QNPKLALKNS PPYILDLLPD TYQHLRTILS RYEGKMETLG ENEYFRVFME
    121 NLMKKTKQTI SLFKEGKERM YEENSQPRRN LTKLSLIFSH MLAELKGIFP SGLFQGDTFR
    181 ITKADAAEFW RKAFGEKTIV PWKSFRQALH EVHPISSGLE AMALKSTIDL TCNDYISVFE
    241 FDIFTRLFQP WSSLLRNWNS LAVTHPGYMA FLTYDEVKAR LQKFIHKPGS YIFRLSCTRL
    301 GQWAIGYVTA DGNILQTIPH NKPLFQALID GFREGFYLFP DGRNQNPDLT GLCEPTPQDH
    361 IKVTQEQYEL YCEMGSTFQL CKICAENDKD VKIEPCGHLM CTSCLTSWQE SEGQGCPFCR
    421 CEIKGTEPIV VDPFDPRGSG SLLRQGAEGA PSPNYDDDDD ERADDTLFMM KELAGAKVER
    481 PPSPFSMAPQ ASLPPVPPRL DLLPQRVCVP SSASALGTAS KAASGSLHKD KPLPVPPTLR
    541 DLPPPPPPDR PYSVGAESRP QRRPLPCTPG DCPSRDKLPP VPSSRLGDSW LPRPIPKVPV
    601 SAPSSSDPWT GRELTNRHsL PFsLPSQMEP RPDVPRLGsT FsLDTSMSMN SSPLVGPECD
    661 HPKIKPSSSA NAIYSLAARP LPVPKLPPGE QCEGEEDTEY MTPSSRPLRP LDTSQSSRAC
    721 DCDQQIDSCT YEAMYNIQSQ APSITESSTF GEGNLAAAHA NTGPEESENE DDGYDVPKPP
    781 VPAVLARRTL SDISNASSSF GWLSLDGDPT TNVTEGSQVP ERPPKPFPRR INSERKAGSC
    841 QQGSGPAASA ATASPQLSSE IENLMSQGYS YQDIQKALVI AQNNIEMAKN ILREFVSISS
    901 PAHVAT
```

```
>gi|251757253|sp|P22681.2|CBL_HUMAN RecName: Full=E3 ubiquitin-protein ligase
CBL; AltName: Full=Signal transduction protein CBL; AltName: Full=Proto-
oncogene c-CBL; AltName: Full=Casitas B-lineage lymphoma proto-oncogene;
AltName: Full=RING finger protein 55
MAGNVKKSSGAGGGSGSGGSGSGGLIGLMKDAFQPHHHHHHHLSPHPPGTVDKKMVEKCWKLMDKVVRLC
QNPKLALKNSPPYILDLLPDTYQHLRTILSRYEGKMETLGENEYFRVFMENLMKKTKQTISLFKEGKERM
YEENSQPRRNLTKLSLIFSHMLAELKGIFPSGLFQGDTFRITKADAAEFWRKAFGEKTIVPWKSFRQALH
EVHPISSGLEAMALKSTIDLTCNDYISVFEFDIFTRLFQPWSSLLRNWNSLAVTHPGYMAFLTYDEVKAR
LQKFIHKPGSYIFRLSCTRLGQWAIGYVTADGNILQTIPHNKPLFQALIDGFREGFYLFPDGRNQNPDLT
GLCEPTPQDHIKVTQEQYELYCEMGSTFQLCKICAENDKDVKIEPCGHLMCTSCLTSWQESEGQGCPFCR
CEIKGTEPIVVDPFDPRGSGSLLRQGAEGAPSPNYDDDDDERADDTLFMMKELAGAKVERPPSPFSMAPQ
ASLPPVPPRLDLLPQRVCVPSSASALGTASKAASGSLHKDKPLPVPPTLRDLPPPPPPDRPYSVGAESRP
QRRPLPCTPGDCPSRDKLPPVPSSRLGDSWLPRPIPKVPVSAPSSSDPWTGRELTNRHSLPFSLPSQMEP
RPDVPRLGSTFSLDTSMSMNSSPLVGPECDHPKIKPSSSANAIYSLAARPLPVPKLPPGEQCEGEEDTEY
MTPSSRPLRPLDTSQSSRACDCDQQIDSCTYEAMYNIQSQAPSITESSTFGEGNLAAAHANTGPEESENE
DDGYDVPKPPVPAVLARRTLSDISNASSSFGWLSLDGDPTTNVTEGSQVPERPPKPFPRRINSERKAGSC
QQGSGPAASAATASPQLSSEIENLMSQGYSYQDIQKALVIAQNNIEMAKNILREFVSISSPAHVAT
```

Notes

Mutation of Cbl serine residues 619, 623, 639, and 642 abolished the interaction between Cbl and 14-3-3 (Pedraza-Alva et al 2001). RH(pS619)LPF(pS623), RLG(pS639)TF(pS642) , most likely NRH(S619)LP and RLG(pS639)TF, but not certain?

References to 14-3-3 binding to Cbl

Liu YC, Elly C, Yoshida H, Bonnefoy-Berard N, Altman A. Activation-modulated association of 14-3-3 proteins with Cbl in T cells. J Biol Chem. 1996 Jun 14;271(24):14591-5.

Melander F, Andersson T, Dib K. Engagement of beta2 integrins recruits 14-3-3 proteins to c-Cbl in human neutrophils. Biochem Biophys Res Commun. 2004 May 14;317(4):1000-5.

Subramanian RR, Masters SC, Zhang H, Fu H. Functional conservation of 14-3-3 isoforms in inhibiting bad-induced apoptosis. Exp Cell Res. 2001 Nov 15;271(1):142-51.

Chernock RD, Cherla RP, Ganju RK. SHP2 and cbl participate in alpha-chemokine receptor CXCR4-mediated signaling pathways. Blood. 2001 Feb 1;97(3):608-15.

Pedraza-Alva G, Sawasdikosol S, Liu YC, Mérida LB, Cruz-Muñoz ME, Oceguera-Yañez F, Burakoff SJ, Rosenstein Y. Regulation of Cbl molecular interactions by the co-receptor molecule CD43 in human T cells. J Biol Chem. 2001 Jan 5;276(1):729-37.

Liu Y, Liu YC, Meller N, Giampa L, Elly C, Doyle M, Altman A. Protein kinase C activation inhibits tyrosine phosphorylation of Cbl and its recruitment of Src homology 2 domain-containing proteins. J Immunol. 1999 Jun 15;162(12):7095-101.

Liu YC, Altman A. Cbl: complex formation and functional implications. Cell Signal. 1998 Jun;10(6):377-85.

Wang H, Zhang L, Liddington R, Fu H. Mutations in the hydrophobic surface of an amphipathic groove of 14-3-3zeta disrupt its interaction with Raf-1 kinase. J Biol Chem. 1998 Jun 26;273(26):16297-304.

Robertson H, Langdon WY, Thien CB, Bowtell DD. A c-Cbl yeast two hybrid screen reveals interactions with 14-3-3 isoforms and cytoskeletal components. Biochem Biophys Res Commun. 1997 Nov 7;240(1):46-50.

Liu YC, Liu Y, Elly C, Yoshida H, Lipkowitz S, Altman A. Serine phosphorylation of Cbl induced by phorbol ester enhances its association with 14-3-3 proteins in T cells via a novel serine-rich 14-3-3-binding motif. J Biol Chem. 1997 Apr 11;272(15):9979-85.

SITES NOT DEFINED PRECISELY, NOT INCLUDED IN WEBLOGO ANALYSIS.

Human CBY1 Chibby = antagonist of β –catenin (ARPP-binding protein) (Swissprot = Q9Y3M2)

```
      1 MPFFGNTFSP KKTPPRKSAs LSNLHSLDRS TREVELGLEY GSPTMNLAGQ SLKFENGQWI
     61 AETGVSGGVD RREVQRLRRR NQQLEEENNL LRLKVDILLD MLSESTAESH LMEKELDELR
    121 ISRKRK
```

```
>gi|20454882|sp|Q9Y3M2.1|CBY1_HUMAN RecName: Full=Protein chibby homolog 1;
AltName: Full=PKD2 interactor, Golgi and endoplasmic reticulum-associated 1;
AltName: Full=PIGEA-14; AltName: Full=Cytosolic leucine-rich protein;
AltName: Full=ARPP-binding protein
MPFFGNTFSPKKTPPRKSASLSNLHSLDRSTREVELGLEYGSPTMNLAGQSLKFENGQWIAETGVSGGVD
RREVQRLRRRNQQLEEENNLLRLKVDILLDMLSESTAESHLMEKELDELRISRKRK
```

Notes

Cby is a 14.5kDa protein evolutionarily conserved from fly to human. Cby possibly acts in concert with 14-3-3 proteins to facilitate nuclear export of beta-catenin, thereby antagonizing beta-catenin signaling. Said to be phosphorylated by AKt/PKB, but not a convnentional site for this kinase.

"14-3-3 proteins specifically recognize serine 20 (RKSASLS) within the 14-3-3–binding motif of Cby when phosphorylated by Akt kinase. Notably, 14-3-3 binding results in sequestration of Cby into the cytoplasm. Feng-Qian et al 2008)"

References to 14-3-3 binding to Chibby

Takemaru K, Fischer V, Li FQ. Fine-tuning of nuclear-catenin by Chibby and 14-3-3. Cell Cycle. 2009 Jan 15;8(2):210-3.

Feng-Qian Li, Adaobi Mofunanya, Kimberley Harris, and Ken-Ichi Takemaru. Chibby cooperates with 14-3-3 to regulate β-catenin subcellular distribution and signaling activity. J Cell Biol. 2008 June 30; 181(7): 1141–1154.

Li FQ, Mofunanya A, Fischer V, Hall J, Takemaru KI.Nuclear-Cytoplasmic Shuttling of Chibby Controls {beta}-Catenin Signaling. Mol Biol Cell. 2009 Nov 25. [Epub ahead of print]

Human CD74 Major histocompatibility complex, class II invariant chain (Swissprot = P04233-1 for canonical long isoform)

```
         1 MHRRRSRsCR EDQKPVMDDQ RDLISNNEQL PMLGRRPGAP ESKCSRGALY TGFSILVTLL
        61 LAGQATTAYF LYQQQGRLDK LTVTSQNLQL ENLRMKLPKP PKPVSKMRMA TPLLMQALPM
       121 GALPQGPMQN ATKYGNMTED HVMHLLQNAD PLKVYPPLKG SFPENLRHLK NTMETIDWKV
       181 FESWMHHWLL FEMSRHSLEQ KPTDAPPKES LELEDPSSGL GVTKQDLGPV PM
```

Notes

MHRRRSR(pS8)CREDQKPV in the N-terminal cytoplasmic tail

References to 14-3-3 binding to CD74 (also known as Iip35)

Kuwana T, Peterson PA, Karlsson L. Exit of major histocompatibility complex class II-invariant chain p35 complexes from the endoplasmic reticulum is modulated by phosphorylation. Proc Natl Acad Sci U S A. 1998 Feb 3;95(3):1056-61.

O'Kelly I, Butler MH, Zilberberg N, Goldstein SA. Forward transport. 14-3-3 binding overcomes retention in endoplasmic reticulum by dibasic signals. Cell. 2002 Nov 15;111(4):577-88.

Anderson HA, Bergstralh DT, Kawamura T, Blauvelt A, Roche PA. Phosphorylation of the invariant chain by protein kinase C regulates MHC class II trafficking to antigen-processing compartments. J Immunol. 1999 Nov 15;163(10):5435-43.

Faul, C., S. Huttelmaier, J. Oh, V. Hachet, R. H. Singer, and P. Mundel. 2005. Promotion of importin {alpha}-mediated nuclear import by the phosphorylation-dependent binding of cargo protein to 14-3-3. J. Cell Biol. 169:415-424

Human Cdc25A M-phase inducer phosphatase 1 (Swissprot = P30304)

```
         1 MELGPEPPHR RRLLFACSPP PASQPVVKAL FGASAAGGLS PVTNLTVTMD QLQGLGSDYE
        61 QPLEVKNNSN LQRMGSSEST DSGFCLDSPG PLDSKENLEN PMRRIHSLPQ KLLGCSPALK
       121 RSHSDSLDHD IFQLIDPDEN KENEAFEFKK PVRPVSRGCL HSHGLQEGKD LFTQRQNsAP
       181 ARMLSSNERD SSEPGNFIPL FTPQSPVTAT LSDEDDGFVD LLDGENLKNE EETPSCMASL
       241 WTAPLVMRTT NLDNRCKLFD SPSLCSSSTR SVLKRPERSQ EESPPGSTKR RKSMSGASPK
       301 ESTNPEKAHE TLHQSLSLAS SPKGTIENIL DNDPRDLIGD FSKGYLFHTV AGKHQDLKYI
       361 SPEIMASVLN GKFANLIKEF VIIDCRYPYE YEGGHIKGAV NLHMEEEVED FLLKKPIVPT
       421 DGKRVIVVFH CEFSSERGPR MCRYVRERDR LGNEYPKLHY PELYVLKGGY KEFFMKCQSY
       481 CEPPSYRPMH HEDFKEDLKK FRTKSRTWAG EKSKREMYSR LKKL
>gi|50403734|sp|P30304.2|MPIP1_HUMAN RecName: Full=M-phase inducer
phosphatase 1; AltName: Full=Dual specificity phosphatase Cdc25A
MELGPEPPHRRRLLFACSPPPASQPVVKALFGASAAGGLSPVTNLTVTMDQLQGLGSDYEQPLEVKNNSN
LQRMGSSESTDSGFCLDSPGPLDSKENLENPMRRIHSLPQKLLGCSPALKRSHSDSLDHDIFQLIDPDEN
KENEAFEFKKPVRPVSRGCLHSHGLQEGKDLFTQRQNSAPARMLSSNERDSSEPGNFIPLFTPQSPVTAT
LSDEDDGFVDLLDGENLKNEEETPSCMASLWTAPLVMRTTNLDNRCKLFDSPSLCSSSTRSVLKRPERSQ
EESPPGSTKRRKSMSGASPKESTNPEKAHETLHQSLSLASSPKGTIENILDNDPRDLIGDFSKGYLFHTV
AGKHQDLKYISPEIMASVLNGKFANLIKEFVIIDCRYPYEYEGGHIKGAVNLHMEEEVEDFLLKKPIVPT
DGKRVIVVFHCEFSSERGPRMCRYVRERDRLGNEYPKLHYPELYVLKGGYKEFFMKCQSYCEPPSYRPMH
HEDFKEDLKKFRTKSRTWAGEKSKREMYSRLKKL
```

Notes

Phosphorylated Ser177-Cdc25A that is specific for 14.3.3 binding

References to 14-3-3 binding to Cdc25A

Madlener S, Rosner M, Krieger S, Giessrigl B, Gridling M, Vo TP, Leisser C, Lackner A, Raab I, Grusch M, Hengstschläger M, Dolznig H, Krupitza G. Short 42 degrees C heat shock induces phosphorylation and degradation of Cdc25A which depends on p38MAPK, Chk2 and 14.3.3. Hum Mol Genet. 2009 Jun 1;18(11):1990-2000.

Conklin DS, Galaktionov K, Beach D. 14-3-3 proteins associate with cdc25 phosphatases. Proc Natl Acad Sci U S A. 1995 Aug 15;92(17):7892-6.

Human Cdc25B M-phase inducer phosphatase 2 (Swissprot = P30305)

```
         1 MEVPQPEPAP GSALSPAGVC GGAQRPGHLP GLLLGSHGLL GSPVRAAASS PVTTLTQTMH
        61 DLAGLGSETP KSQVGTLLFR SRSRLTHLSL SRRASESSLS SESSESSDAG LCMDSPSPMD
       121 PHMAEQTFEQ AIQAASRIIR NEQFAIRRFQ SMPVRLLGHS PVLRNITNSQ APDGRRKSEA
       181 GSGAASSSGE DKENDGFVFK MPWKPTHPSS THALAEWASR REAFAQRPSS APDLMCLSPD
       241 RKMEVEELSP LALGRFSLTP AEGDTEEDDG FVDILESDLK DDDAVPPGME SLISAPLVKT
       301 LEKEEEKDLV MYSKCQRLFR SPsMPCSVIR PILKRLERPQ DRDTPVQNKR RRSVTPPEEQ
       361 QEAEEPKARV LRSKSLCHDE IENLLDSDHR ELIGDYSKAF LLQTVDGKHQ DLKYISPETM
       421 VALLTGKFSN IVDKFVIVDC RYPYEYEGGH IKTAVNLPLE RDAESFLLKS PIAPCSLDKR
       481 VILIFHCEFS SERGPRMCRF IRERDRAVND YPSLYYPEMY ILKGGYKEFF PQHPNFCEPQ
       541 DYRPMNHEAF KDELKTFRLK TRSWAGERSR RELCSRLQDQ
>gi|21264471|sp|P30305.2|MPIP2_HUMAN RecName: Full=M-phase inducer
phosphatase 2; AltName: Full=Dual specificity phosphatase Cdc25B
MEVPQPEPAPGSALSPAGVCGGAQRPGHLPGLLLGSHGLLGSPVRAAASSPVTTLTQTMHDLAGLGSETP
KSQVGTLLFRSRSRLTHLSLSRRASESSLSSESSESSDAGLCMDSPSPMDPHMAEQTFEQAIQAASRIIR
NEQFAIRRFQSMPVRLLGHSPVLRNITNSQAPDGRRKSEAGSGAASSSGEDKENDGFVFKMPWKPTHPSS
THALAEWASRREAFAQRPSSAPDLMCLSPDRKMEVEELSPLALGRFSLTPAEGDTEEDDGFVDILESDLK
DDDAVPPGMESLISAPLVKTLEKEEEKDLVMYSKCQRLFRSPSMPCSVIRPILKRLERPQDRDTPVQNKR
```

```
RRSVTPPEEQQEAEEPKARVLRSKSLCHDEIENLLDSDHRELIGDYSKAFLLQTVDGKHQDLKYISPETM
VALLTGKFSNIVDKFVIVDCRYPYEYEGGHIKTAVNLPLERDAESFLLKSPIAPCSLDKRVILIFHCEFS
SERGPRMCRFIRERDRAVNDYPSLYYPEMYILKGGYKEFFPQHPNFCEPQDYRPMNHEAFKDELKTFRLK
TRSWAGERSRRELCSRLQDQ
```

Notes

References to 14-3-3 binding to Cdc25B

Pirino G, Wescott MP, Donovan PJ._Protein kinase A regulates resumption of meiosis by phosphorylation of Cdc25B in mammalian oocytes. Cell Cycle. 2009 Feb 15;8(4):665-70.

Conklin DS, Galaktionov K, Beach D. 14-3-3 proteins associate with cdc25 phosphatases. Proc Natl Acad Sci U S A. 1995 Aug 15;92(17):7892-6.

Bulavin DV, Higashimoto Y, Popoff IJ, Gaarde WA, Basrur V, Potapova O, Appella E, Fornace AJ Jr. Initiation of a G2/M checkpoint after ultraviolet radiation requires p38 kinase. Nature. 2001 May 3;411(6833):102-7.

Uchida S, Kubo A, Kizu R, Nakagama H, Matsunaga T, Ishizaka Y, Yamashita K. Amino acids C-terminal to the 14-3-3 binding motif in CDC25B affect the efficiency of 14-3-3 binding. J Biochem. 2006 Apr;139(4):761-9.

Manke IA, Nguyen A, Lim D, Stewart MQ, Elia AE, Yaffe MB. MAPKAP kinase-2 is a cell cycle checkpoint kinase that regulates the G2/M transition and S phase progression in response to UV irradiation. Mol Cell. 2005 Jan 7;17(1):37-48.

Lindqvist A, Källström H, Karlsson Rosenthal C. Characterisation of Cdc25B localisation and nuclear export during the cell cycle and in response to stress. J Cell Sci. 2004 Oct 1;117(Pt 21):4979-90.

Uchida S, Kuma A, Ohtsubo M, Shimura M, Hirata M, Nakagama H, Matsunaga T, Ishizaka Y, Yamashita K. Binding of 14-3-3beta but not 14-3-3sigma controls the cytoplasmic localization of CDC25B: binding site preferences of 14-3-3 subtypes and the subcellular localization of CDC25B. J Cell Sci. 2004 Jun 15;117(Pt 14):3011-20.

Bulavin DV, Higashimoto Y, Demidenko ZN, Meek S, Graves P, Phillips C, Zhao H, Moody SA, Appella E, Piwnica-Worms H, Fornace AJ Jr. Dual phosphorylation controls Cdc25 phosphatases and mitotic entry. Nat Cell Biol. 2003 Jun;5(6):545-51.

Human Cdc25C M-phase inducer phosphatase 3 (Swissprot = P30307)

```
        1 MSTELFSSTR EEGSSGSGPS FRSNQRKMLN LLLERDTSFT VCPDVPRTPV GKFLGDSANL
       61 SILSGGTPKR CLDLSNLSSG EITATQLTTS ADLDETGHLD SSGLQEVHLA GMNHDQHLMK
      121 CSPAQLLCST PNGLDRGHRK RDAMCSSSAN KENDNGNLVD SEMKYLGSPI TTVPKLDKNP
      181 NLGEDQAEEI SDELMEFSLK DQEAKVSRSG LYRSPsMPEN LNRPRLKQVE KFKDNTIPDK
      241 VKKKYFSGQG KLRKGLCLKK TVSLCDITIT QMLEEDSNQG HLIGDFSKVC ALPTVSGKHQ
      301 DLKYVNPETV AALLSGKFQG LIEKFYVIDC RYPYEYLGGH IQGALNLYSQ EELFNFFLKK
      361 PIVPLDTQKR IIIVFHCEFS SERGPRMCRC LREEDRSLNQ YPALYYPELY ILKGGYRDFF
      421 PEYMELCEPQ SYCPMHHQDH KTELLRCRSQ SKVQEGERQL REQIALLVKD MSP
>gi|116242631|sp|P30307.2|MPIP3_HUMAN RecName: Full=M-phase inducer
phosphatase 3; AltName: Full=Dual specificity phosphatase Cdc25C
MSTELFSSTREEGSSGSGPSFRSNQRKMLNLLLERDTSFTVCPDVPRTPVGKFLGDSANLSILSGGTPKR
CLDLSNLSSGEITATQLTTSADLDETGHLDSSGLQEVHLAGMNHDQHLMKCSPAQLLCSTPNGLDRGHRK
RDAMCSSSANKENDNGNLVDSEMKYLGSPITTVPKLDKNPNLGEDQAEEISDELMEFSLKDQEAKVSRSG
LYRSPSMPENLNRPRLKQVEKFKDNTIPDKVKKKYFSGQGKLRKGLCLKKTVSLCDITITQMLEEDSNQG
HLIGDFSKVCALPTVSGKHQDLKYVNPETVAALLSGKFQGLIEKFYVIDCRYPYEYLGGHIQGALNLYSQ
EELFNFFLKKPIVPLDTQKRIIIVFHCEFSSERGPRMCRCLREEDRSLNQYPALYYPELYILKGGYRDFF
PEYMELCEPQSYCPMHHQDHKTELLRCRSQSKVQEGERQLREQIALLVKDMSP
```

Notes

Phosphorylated by CHK1 on Ser-216. This phosphorylation creates a binding site for 14-3-3 protein and inhibits the phosphatase.

References to 14-3-3 binding to Cdc25C

Telles E, Hosing AS, Kundu ST, Venkatraman P, Dalal SN. A novel pocket in 14-3-3epsilon is required to mediate specific complex formation with cdc25C and to inhibit cell cycle progression upon activation of checkpoint pathways. Exp Cell Res. 2009 May 1;315(8):1448-57.

Bulavin DV, Higashimoto Y, Popoff IJ, Gaarde WA, Basrur V, Potapova O, Appella E, Fornace AJ Jr. Initiation of a G2/M checkpoint after ultraviolet radiation requires p38 kinase. Nature. 2001 May 3;411(6833):102-7.

Graves PR, Lovly CM, Uy GL, Piwnica-Worms H. Localization of human Cdc25C is regulated both by nuclear export and 14-3-3 protein binding. Oncogene. 2001 Apr 5;20(15):1839-51.

Human CDC2L2=CDK11p110 (Cyclin-dependant Kinase 11) (Swissprot = P21127)

```
        1 MGDEKDSWKV KTLDEILQEK KRRKEQEEKA EIKRLKNSDD RDSKRDSLEE GELRDHRMEI
       61 TIRNSPYRRE DSMEDRGEED DSLAIKPPQQ MSRKEKVHHR KDEKRKEKRR HRsHSAEGGK
      121 HARVKEKERE HERRKRHREE QDKARREWER QKRREMAREH SRRERDRLEQ LERKRERERK
      181 MREQQKEQRE QKERERRAEE RRKEREARRE VSAHHRTMRE DYSDKVKASH WSRSPPRPPR
      241 ERFELGDGRK PGEARPARAQ KPAQLKEEKM EERDLLSDLQ DISDSERKTS SAESSSAESG
      301 SGSEEEEEEE EEEEEEGSTS EESEEEEEEE EEEEEETGSN SEEASEQSAE EVSEEEMSED
      361 EERENENHLL VVPESRFDRD SGESEEAEEE VGEGTPQSSA LTEGDYVPDS PALSPIELKQ
      421 ELPKYLPALQ GCRSVEEFQC LNRIEEGTYG VVYRAKDKKT DEIVALKRLK MEKEKEGFPI
      481 TSLREINTIL KAQHPNIVTV REIVVGSNMD KIYIVMNYVE HDLKSLMETM KQPFLPGEVK
      541 TLMIQLLRGV KHLHDNWILH RDLKTSNLLL SHAGILKVGD FGLAREYGSP LKAYTPVVVT
      601 LWYRAPELLL GAKEYSTAVD MWSVGCIFGE LLTQKPLFPG KSEIDQINKV FKDLGTPSEK
      661 IWPGYSELPA VKKMTFSEHP YNNLRKRFGA LLSDQGFDLM NKFLTYFPGR RISAEDGLKH
      721 EYFRETPLPI DPSMFPTWPA KSEQQRVKRG TSPRPPEGGL GYSQLGDDDL KETGFHLTTT
      781 NQGASAAGPG FSLKF
>gi|34978359|sp|P21127.3|CD2L1_HUMAN RecName: Full=PITSLRE serine/threonine-
protein kinase CDC2L1; AltName: Full=Cell division cycle 2-like protein
kinase 1; Short=CLK-1; AltName: Full=p58 CLK-1; AltName:
Full=Galactosyltransferase-associated protein kinase p58/GTA; AltName:
Full=CDK11
MGDEKDSWKVKTLDEILQEKKRRKEQEEKAEIKRLKNSDDRDSKRDSLEEGELRDHRMEITIRNSPYRRE
```

```
DSMEDRGEEDDSLAIKPPQQMSRKEKVHHRKDEKRKEKRRHRSHSAEGGKHARVKEKEREHERRKRHREE
QDKARREWERQKRREMAREHSRRERDRLEQLERKRERERKMREQQKEQREQKERERRAEERRKEREARRE
VSAHHRTMREDYSDKVKASHWSRSPPRPPRERFELGDGRKPGEARPARAQKPAQLKEEKMEERDLLSDLQ
DISDSERKTSSAESSSAESGSGSEEEEEEEEEEEEEEGSTSEESEEEEEEEEEEEEETGSNSEEASEQSAE
EVSEEEMSEDEERENENHLLVVPESRFDRDSGESEEAEEEVGEGTPQSSALTEGDYVPDSPALSPIELKQ
ELPKYLPALQGCRSVEEFQCLNRIEEGTYGVVYRAKDKKTDEIVALKRLKMEKEKEGFPITSLREINTIL
KAQHPNIVTVREIVVGSNMDKIYIVMNYVEHDLKSLMETMKQPFLPGEVKTLMIQLLRGVKHLHDNWILH
RDLKTSNLLLSHAGILKVGDFGLAREYGSPLKAYTPVVVTLWYRAPELLLGAKEYSTAVDMWSVGCIFGE
LLTQKPLFPGKSEIDQINKVFKDLGTPSEKIWPGYSELPAVKKMTFSEHPYNNLRKRFGALLSDQGFDLM
NKFLTYFPGRRISAEDGLKHEYFRETPLPIDPSMFPTWPAKSEQQRVKRGTSPRPPEGGLGYSQLGDDDL
KETGFHLTTTNQGASAAGPGFSLKF
```

Notes

RHRpS^{118}HS = Ser113 in P21127.

References to 14-3-3 binding to CDK11^{p110}

Feng Y, Qi W, Martinez J, Nelson MA. The cyclin-dependent kinase 11 interacts with 14-3-3 proteins. Biochem Biophys Res Commun. 2005 Jun 17;331(4):1503-9.

Wilker EW, van Vugt MA, Artim SA, Huang PH, Petersen CP, Reinhardt HC, Feng Y, Sharp PA, Sonenberg N, White FM, Yaffe MB. 14-3-3sigma controls mitotic translation to facilitate cytokinesis. Nature. 2007 Mar 15;446(7133):329-32.

Human CDKN1B (p27Kip1) Cyclin-dependent kinase inhibitor 1B (Swissprot = P46527)

```
      1 MSNVRVSNGS PSLERMDARQ AEHPKPSACR NLFGPVDHEE LTRDLEKHCR DMEEASQRKW
     61 NFDFQNHKPL EGKYEWQEVE KGSLPEFYYR PPRPPKGACK VPAQESQDVS GSRPAAPLIG
    121 APANSEDTHL VDPKTDPSDS QTGLAEQCAG IRKRPAtDDS STQNKRANRT EENVSDGSPN
    181 AGSVEQTPKK PGLRRRQt
>gi|1168871|sp|P46527.1|CDN1B_HUMAN RecName: Full=Cyclin-dependent kinase
inhibitor 1B; AltName: Full=Cyclin-dependent kinase inhibitor p27; AltName:
Full=p27Kip1
MSNVRVSNGSPSLERMDARQAEHPKPSACRNLFGPVDHEELTRDLEKHCRDMEEASQRKWNFDFQNHKPL
EGKYEWQEVEKGSLPEFYYRPPRPPKGACKVPAQESQDVSGSRPAAPLIGAPANSEDTHLVDPKTDPSDS
QTGLAEQCAGIRKRPATDDSSTQNKRANRTEENVSDGSPNAGSVEQTPKKPGLRRRQT
```

Notes

p27Kip1 a cell-cycle regulatory protein that interacts with cyclin-CDK2 and -CDK4, inhibiting cell cycle progression at G1. May mediate TGF beta-induced g1 arrest. Its degradation is triggered by its CDK dependent phosphorylation and subsequent ubiquitination by SCF complexes, is required for the cellular transition from quiescence to the proliferative state.

Akt bound directly to and phosphorylated p27(Kip1). Screening p27(Kip1) phosphorylation sites identified the COOH-terminal Thr(198) residue as a novel site. Further analysis revealed that 14-3-3 proteins bound to p27(Kip1) through Thr(198) only when it was phosphorylated by Akt. Although Akt also phosphorylated p27(Kip1) at Ser(10) and Thr(187), these two sites were not involved in the binding to 14-3-3 proteins. p27(Kip1) phosphorylated at Thr(198) exists only in the cytoplasm. Therefore, Akt promotes cell-cycle progression through the mechanisms of phosphorylation-dependent 14-3-3 binding to p27(Kip1) and cytoplasmic localization.

p90 ribosomal protein S6 kinases (RSKs) could bind to and directly phosphorylate p27Kip1 at Thr198 in a Ras/Raf/MEK-dependent manner. RSK-dependent phosphorylation promoted the p27Kip1 binding to 14-3-3 and its cytoplasmic localization.

“Consistent with the previous reports, the interaction between 14-3-3 and p27Kip1 was weakened when the T157 or T198 residue in p27Kip1 was converted to Ala (T157A or T198A, respectively).” “14-3-3 proteins preferentially bound to p27Kip1 that was phosphorylated at the T198 residue rather than at the T157 residue. (Morishita et al 2008).”

References to 14-3-3 binding to CDKN1B (p27Kip1)

Fujita N, Sato S, Tsuruo T. Phosphorylation of p27Kip1 at threonine 198 by p90 ribosomal protein S6 kinases promotes its binding to 14-3-3 and cytoplasmic localization. J Biol Chem. 2003 Dec 5;278(49):49254-60.

Morishita D, Katayama R, Sekimizu K, Tsuruo T, Fujita N. Pim kinases promote cell cycle progression by phosphorylating and down-regulating p27Kip1 at the transcriptional and posttranscriptional levels. Cancer Res. 2008 Jul 1;68(13):5076-85.

Fujita N, Sato S, Katayama K, Tsuruo T. Akt-dependent phosphorylation of p27Kip1 promotes binding to 14-3-3 and cytoplasmic localization. J Biol Chem. 2002 Aug 9;277(32):28706-13.

Sekimoto T, Fukumoto M, Yoneda Y. 14-3-3 suppresses the nuclear localization of threonine 157-phosphorylated p27(Kip1). EMBO J. 2004 May 5;23(9):1934-42.

Wang Z, Yu BW, Rahman KM, Ahmad F, Sarkar FH. Induction of growth arrest and apoptosis in human breast cancer cells by 3,3-diindolylmethane is associated with induction and nuclear localization of p27kip. Mol Cancer Ther. 2008 Feb;7(2):341-9.

Rosner M, Freilinger A, Hanneder M, Fujita N, Lubec G, Tsuruo T, Hengstschläger M. p27Kip1 localization depends on the tumor suppressor protein tuberin. Hum Mol Genet. 2007 Jul 1;16(13):1541-56.

Human CENPJ (Centromere protein J) CPAP (Centrosomal Protein 4.1-Associated Protein) (Swissprot = Q9HC77)

```
      1 MFLMPTSSEL NSGQNFLTQW MTNPSRAGVI LNRGFPILEA DKEKRAAVDI STSFPIKGTH
     61 FSDSFSFINE EDSLLEEQKL ESNNPYKPQS DKSETHTAFP CIKKGPQVAA CHSAPGHQEE
    121 NKNDFIPDLA SEFKEGAYKD PLFKKLEQLK EVQQKKQEQL KRQQLEQLQR LMEEQEKLLT
    181 MVSGQCTLPG LSLLPDDQSQ KHRSPGNTTT GERATCCFPS YVYPDPTQEE TYPSNILSHE
    241 QSNFCRTAHG DFVLTSKRAS PNLFSEAQYQ EAPVEKNNLK EENRNHPTGE SILCWEKVTE
    301 QIQEANDKNL QKHDDSSEVA NIEERPIKAA IGERKQTFED YLEEQIQLEE QELKQKQLKE
    361 AEGPLPIKAK PKQPFLKRGE GLARFTNAKS KFQKGKESKL VTNQSTSEDQ PLFKMDRQQL
    421 QRKTALKNKE LCADNPILKK DSKARTKSGS VTLSQKPKML KCSNRKSLSP SGLKIQTGKK
    481 CDGQFRDQIK FENKVTSNNK ENVTECPKPC DTGCTGWNKT QGKDRLPLST GPASRLAAKS
    541 PIRETMKESE SSLDVSLQKK LETWEREKEK ENLELDEFLF LEQAADEISF SSNSSFVLKI
    601 LERDQQICKG HRMSSTPVKA VPQKTNPADP ISHCNRSEDL DHTAREKESE CEVAPKQLHS
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      661 LSSADELREQ PCKIRKAVQK STSENQTEWN ARDDEGVPNS DSSTDSEEQL DVTIKPSTED
      721 RERGISSRED SPQVCDDKGP FKDTRTQEDK RRDVDLDLSD KDYSSDESIM ESIKHKVSEP
      781 SRSSSLSLSK MDFDDERTWT DLEENLCNHD VVLGNESTYG TPQTCYPNNE IGILDKTIKR
      841 KIAPVKRGED LSKSRRSRSP PTSELMMKFF PSLKPKPKSD SHLGNELKLN ISQDQPPGDN
      901 ARSQVLREKI IELETEIEKF KAENASLAKL RIERESALEK LRKEIADFEQ QKAKELARIE
      961 EFKKEEMRKL QKERKVFEKY TTAARTFPDK KEREEIQTLK QQIADLREDL KRKETKWSST
     1021 HSRLRSQIQM LVRENTDLRE EIKVMERFRL DAWKRAEAIE SSLEVEKKDK LANTSVRFQN
     1081 SQISSGTQVE KYKKNYLPMQ GNPPRRSKsA PPRDLGNLDK GQAASPREPL EPLNFPDPEY
     1141 KEEEEDQDIQ GEISHPDGKV EKVYKNGCRV ILFPNGTRKE VSADGKTITV TFFNGDVKQV
     1201 MPDQRVIYYY AAAQTTHTTY PEGLEVLHFS SGQIEKHYPD GRKEITFPDQ TVKNLFPDGQ
     1261 EESIFPDGTI VRVQRDGNKL IEFNNGQREL HTAQFKRREY PDGTVKTVYA NGHQETKYRS
     1321 GRIRVKDKEG NVLMDTEL
>gi|62899891|sp|Q9HC77.2|CENPJ_HUMAN RecName: Full=Centromere protein J;
Short=CENP-J; AltName: Full=Centrosomal P4.1-associated protein; AltName:
Full=LAG-3-associated protein; AltName: Full=LYST-interacting protein 1
MFLMPTSSELNSGQNFLTQWMTNPSRAGVILNRGFPILEADKEKRAAVDISTSFPIKGTHFSDSFSFINE
EDSLLEEQKLESNNPYKPQSDKSETHTAFPCIKKGPQVAACHSAPGHQEENKNDFIPDLASEFKEGAYKD
PLFKKLEQLKEVQQKKQEQLKRQQLEQLQRLMEEQEKLLTMVSGQCTLPGLSLLPDDQSQKHRSPGNTTT
GERATCCFPSYVYPDPTQEETYPSNILSHEQSNFCRTAHGDFVLTSKRASPNLFSEAQYQEAPVEKNNLK
EENRNHPTGESILCWEKVTEQIQEANDKNLQKHDDSSEVANIEERPIKAAIGERKQTFEDYLEEQIQLEE
QELKQKQLKEAEGPLPIKAKPKQPFLKRGEGLARFTNAKSKFQKGKESKLVTNQSTSEDQPLFKMDRQQL
QRKTALKNKELCADNPILKKDSKARTKSGSVTLSQKPKMLKCSNRKSLSPSGLKIQTGKKCDGQFRDQIK
FENKVTSNNKENVTECPKPCDTGCTGWNKTQGKDRLPLSTGPASRLAAKSPIRETMKESESSLDVSLQKK
LETWEREKEKENLELDEFLFLEQAADEISFSSNSSFVLKILERDQQICKGHRMSSTPVKAVPQKTNPADP
ISHCNRSEDLDHTAREKESECEVAPKQLHSLSSADELREQPCKIRKAVQKSTSENQTEWNARDDEGVPNS
DSSTDSEEQLDVTIKPSTEDRERGISSREDSPQVCDDKGPFKDTRTQEDKRRDVDLDLSDKDYSSDESIM
ESIKHKVSEPSRSSSLSLSKMDFDDERTWTDLEENLCNHDVVLGNESTYGTPQTCYPNNEIGILDKTIKR
KIAPVKRGEDLSKSRRSRSPPTSELMMKFFPSLKPKPKSDSHLGNELKLNISQDQPPGDNARSQVLREKI
IELETEIEKFKAENASLAKLRIERESALEKLRKEIADFEQQKAKELARIEEFKKEEMRKLQKERKVFEKY
TTAARTFPDKKEREEIQTLKQQIADLREDLKRKETKWSSTHSRLRSQIQMLVRENTDLREEIKVMERFRL
DAWKRAEAIESSLEVEKKDKLANTSVRFQNSQISSGTQVEKYKKNYLPMQGNPPRRSKSAPPRDLGNLDK
GQAASPREPLEPLNFPDPEYKEEEEDQDIQGEISHPDGKVEKVYKNGCRVILFPNGTRKEVSADGKTITV
TFFNGDVKQVMPDQRVIYYYAAAQTTHTTYPEGLEVLHFSSGQIEKHYPDGRKEITFPDQTVKNLFPDGQ
EESIFPDGTIVRVQRDGNKLIEFNNGQRELHTAQFKRREYPDGTVKTVYANGHQETKYRSGRIRVKDKEG
NVLMDTEL
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Notes

"May play an important role in cell division and centrosome function. Inhibits microtubule nucleation from the centrosome.

Mutation of serine 1109 to alanine (S1109A) in the 14-3-3 binding motif (PRRSKsAP) completely abolished the association of CPAP with 14-3-3. The interaction between CPAP and 14-3-3 was significantly reduced in mitotic cells, suggesting that 14-3-3 binding to CPAP is regulated during cell cycle progression. Another Ser859 located within the first 14-3-3 binding motif (^{856}RSRSPP^{861}) may also participate in 14-3-3 binding. Chen et al (2006)"

References to 14-3-3 binding to CENPJ

Chen CY, Olayioye MA, Lindeman GJ, Tang TK. CPAP interacts with 14-3-3 in a cell cycle-dependent manner. Biochem Biophys Res Commun. 2006 Apr 21;342(4):1203-10.

Human CFL1 Cofilin 1 (Swissprot = P23528)

```
        1 MAsGVAVSDG VIKVFNDMKV RKSsTPEEVK KRKKAVLFCL SEDKKNIILE EGKEILVGDV
       61 GQTVDDPYAT FVKMLPDKDC RYALYDATYE TKESKKEDLV FIFWAPESAP LKSKMIYASS
      121 KDAIKKKLTG IKHELQANCY EEVKDRCTLA EKLGGSAVIS LEGKPL
>gi|116848|sp|P23528.3|COF1_HUMAN RecName: Full=Cofilin-1; AltName:
Full=Cofilin, non-muscle isoform; AltName: Full=18 kDa phosphoprotein;
AltName: Full=p18
MASGVAVSDGVIKVFNDMKVRKSSTPEEVKKRKKAVLFCLSEDKKNIILEEGKEILVGDVGQTVDDPYAT
FVKMLPDKDCRYALYDATYETKESKKEDLVFIFWAPESAPLKSKMIYASSKDAIKKKLTGIKHELQANCY
EEVKDRCTLAEKLGGSAVISLEGKPL
```

Notes

MApS^{3}GVAV, RKSpS^{24}TP

References to 14-3-3 binding to cofilin

Edwards DC, Sanders LC, Bokoch GM, Gill GN. Activation of LIM-kinase by Pak1 couples Rac/Cdc42 GTPase signalling to actin cytoskeletal dynamics. Nat Cell Biol. 1999 Sep;1(5):253-9.

Maekawa M, Ishizaki T, Boku S, Watanabe N, Fujita A, Iwamatsu A, Obinata T, Ohashi K, Mizuno K, Narumiya S. Signaling from Rho to the actin cytoskeleton through protein kinases ROCK and LIM-kinase. Science. 1999 Aug 6;285(5429):895-8.

Gohla A, Bokoch GM. 14-3-3 regulates actin dynamics by stabilizing phosphorylated cofilin. Curr Biol. 2002 Oct 1;12(19):1704-10.

Birkenfeld J, Betz H, Roth D.Identification of cofilin and LIM-domain-containing protein kinase 1 as novel interaction partners of 14-3-3 zeta. Biochem J. 2003 Jan 1;369(Pt 1):45-54.

Human CRTC2 (TORC2) (Swissprot = Q53ET0)

ONLY USE phosphoSER171 FOR WEBLOGO

```
        1 MATSGANGPG SATASASNPR KFSEKIALQK QRQAEETAAF EEVMMDIGST RLQAQKLRLA
       61 YTRSSHYGGs LPNVNQIGSG LAEFQSPLHS PLDSSRSTRH HGLVERVQRD PRRMVSPLRR
      121 YTRHIDSSPY SPAYLSPPPE SSWRRTMAWG NFPAEKGQLF RLPSALNRTS sDSALHTSVM
      181 NPSPQDTYPG PTPPSILPSR RGGILDGEMD PKVPAIEENL LDDKHLLKPW DAKKLSSSSS
      241 RPRSCEVPGI NIFPSPDQPA NVPVLPPAMN TGGsLPDLTN LHFPPPLPTP LDPEETAYPS
      301 LSGGNSTSNL THTMTHLGIS RGMGLGPGYD APGLHSPLSH PSLQSSLSNP NLQASLSSPQ
      361 PQLQGSHSHP SLPASSLARH VLPTTSLGHP SLSAPALSSS SSSSTSSPV LGAPSYPAST
      421 PGASPHHRRV PLSPLSLLAG PADARRSQQQ LPKQFSPTMS PTLSSITQGV PLDTSKLSTD
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```
      481 QRLPPYPYSS PSLVLPTQPH TPKSLQQPGL PSQSCSVQSS GGQPPGRQSH YGTPYPPGPS
      541 GHGQQSYHRP MSDFNLGNLE QFSMESPSAS LVLDPPGFSE GPGFLGGEGP MGGPQDPHT
      601 NHQNLTHCSR HGSGPNIILT GDSSPGFSKE IAAALAGVPG FEVSAAGLEL GLGLEDELRM
      661 EPLGLEGLNM LSDPCALLPD PAVEESFRSD RLQ
>gi|167009135|sp|Q53ET0.2|CRTC2_HUMAN RecName: Full=CREB-regulated
transcription coactivator 2; AltName: Full=Transducer of regulated cAMP
response element-binding protein 2; Short=TORC-2; Short=Transducer of CREB
protein 2
MATSGANGPGSATASASNPRKFSEKIALQKQRQAEETAAFEEVMMDIGSTRLQAQKLRLAYTRSSHYGGS
LPNVNQIGSGLAEFQSPLHSPLDSSRSTRHHGLVERVQRDPRRMVSPLRRYTRHIDSSPYSPAYLSPPPE
SSWRRTMAWGNFPAEKGQLFRLPSALNRTSSDSALHTSVMNPSPQDTYPGPTPPSILPSRRGGILDGEMD
PKVPAIEENLLDDKHLLKPWDAKKLSSSSSRPRSCEVPGINIFPSPDQPANVPVLPPAMNTGGSLPDLTN
LHFPPPLPTPLDPEETAYPSLSGGNSTSNLTHTMTHLGISRGMGLGPGYDAPGLHSPLSHPSLQSSLSNP
NLQASLSSPQPQLQGSHSHPSLPASSLARHVLPTTSLGHPSLSAPALSSSSSSSSTSSPVLGAPSYPAST
PGASPHHRRVPLSPLSLLAGPADARRSQQQLPKQFSPTMSPTLSSITQGVPLDTSKLSTDQRLPPYPYSS
PSLVLPTQPHTPKSLQQPGLPSQSCSVQSSGGQPPGRQSHYGTPYPPGPSGHGQQSYHRPMSDFNLGNLE
QFSMESPSASLVLDPPGFSEGPGFLGGEGPMGGPQDPHTFNHQNLTHCSRHGSGPNIILTGDSSPGFSKE
IAAALAGVPGFEVSAAGLELGLGLEDELRMEPLGLEGLNMLSDPCALLPDPAVEESFRSDRLQ
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Notes

All papers cite phosphoSer171 as a 14-3-3 binding site, but differ in whether phosphoSer71 (Dentin et al 2008), phosphoSer358 and/or phosphoSer275 (Jansson et al 2008) provides a second 14-3-3-binding site. AMP-activated protein kinase (AMPK) and the AMPK family members salt-inducible kinase (SIK)1 and SIK2 can phosphorylate CRTC2 at Ser 171 and thereby inhibit CRTC2 activity (Koo et al, 2005; Dentin et al, 2007). In resting cells, CRTC2 is sequestered in the cytoplasm by 14-3-3 proteins through phosphorylation at Ser70 and Ser171 by members of the AMP-activated protein kinase (AMPK) family of Ser-Thr kinases (Screaton et al 2004). Consistent with the proposed role of O-glycosylation in blocking protein phosphorylation, alanine mutations at Ser70 and Ser171 disrupted the CRTC2:14-3-3 interaction and promoted localization of these mutant CRTC2 proteins to the nucleus (Dentin et al 2008).

TORC2 the transducer of regulated CREB protein 2 (TORC2) is a cAMP responsive coactivator that, in concert with LKB1 and AMPK, controls glucose homeostasis in the liver. Under fasting conditions, cytoplasmic TORC2 is transported to the nucleus where it binds to CREB and stimulates gluconeogenisis. Re-feeding and the ensuing insulin response inhibits gluconeogenic gene expression by promoting the phosphorylation, cytoplasmic export and degradation of TORC2. TORC2 is phosphorylated by the kinase QIK which in turn is activated by phosphorylation at Ser358 [of SIK] by insulin-activated Akt2. Phosphorylated TORC2 is subsequently ubiquitinylated at Lys 628 and degraded by the 26S proteasome. TORC2 protein levels and activity are increased in diabetes owing to a block in TORC2 phosphorylation, implicating this pathway in the pathogenesis of diabetes. The CREB/TORC2 regulatory axis controls the normal pattern of germinal center (GC) B cell gene activation/repression that promotes B cell development and circumvents GC lymphomagenesis.

Ser275 of TORC2 was identified as a 14-3-3 binding site that is phosphorylated under low glucose conditions and which becomes dephosphorylated by calcineurin in response to glucose influx. Dephosphorylation of Ser-275 is essential for both glucose and cAMP-mediated activation of CREB in beta cells and islets (Jansson et al 2008).

References to 14-3-3 binding to CRTC2

Screaton RA, Conkright MD, Katoh Y, Best JL, Canettieri G, Jeffries S, Guzman E, Niessen S, Yates JR 3rd, Takemori H, Okamoto M, Montminy M. The CREB coactivator TORC2 functions as a calcium- and cAMP-sensitive coincidence detector. Cell. 2004 Oct 1;119(1):61-74.

Jansson D, Ng AC, Fu A, Depatie C, Al Azzabi M, Screaton RA. Glucose controls CREB activity in islet cells via regulated phosphorylation of TORC2. Proc Natl Acad Sci U S A. 2008 Jul 22;105(29):10161-6.

Lerner RG, Depatie C, Rutter GA, Screaton RA, Balthasar N. A role for the CREB co-activator CRTC2 in the hypothalamic mechanisms linking glucose sensing with gene regulation. EMBO Rep. 2009 Aug 28. [Epub ahead of print]

Dentin R, Hedrick S, Xie J, Yates J 3rd, Montminy M.Hepatic glucose sensing via the CREB coactivator CRTC2. Science. 2008 Mar 7;319(5868):1402-5.

Human CSF2RB (GM-CSF/IL-3/IL-5 cytokine receptor common beta subunit) (Swissprot = P32927)

```
        1 MVLAQGLLSM ALLALCWERS LAGAEETIPL QTLRCYNDYT SHITCRWADT QDAQRLVNVT
       61 LIRRVNEDLL EPVSCDLSDD MPWSACPHPR CVPRRCVIPC QSFVVTDVDY FSFQPDRPLG
      121 TRLTVTLTQH VQPPEPRDLQ ISTDQDHFLL TWSVALGSPQ SHWLSPGDLE FEVVYKRLQD
      181 SWEDAAILLS NTSQATLGPE HLMPSSTYVA RVRTRLAPGS RLSGRPSKWS PEVCWDSQPG
      241 DEAQPQNLEC FFDGAAVLSC SWEVRKEVAS SVSFGLFYKP SPDAGEEECS PVLREGLGSL
      301 HTRHHCQIPV PDPATHGQYI VSVQPRRAEK HIKSSVNIQM APPSLNVTKD GDSYSLRWET
      361 MKMRYEHIDH TFEIQYRKDT ATWKDSKTET LQNAHSMALP ALEPSTRYWA RVRVRTSRTG
      421 YNGIWSEWSE ARSWDTESVL PMWVLALIVI FLTIAVLLAL RFCGIYGYRL RRKWEEKIPN
      481 PSKSHLFQNG SAELWPPGSM SAFTSGSPPH QGPWGSRFPE LEGVFPVGFG DSEVSPLTIE
      541 DPKHVCDPPS GPDTTPAASD LPTEQPPSPQ PGPPAASHTP EKQASSFDFN GPYLGPPHSR
      601 sLPDILGQPE PPQEGGSQKS PPPGSLEYLC LPAGGQVQLV PLAQAMGPGQ AVEVERRPSQ
      661 GAAGSPSLES GGGPAPPALG PRVGGQDQKD SPVAIPMSSG DTEDPGVASG YVSSADLVFT
      721 PNSGASSVSL VPSLGLPSDQ TPSLCPGLAS GPPGAPGPVK SGFEGYVELP PIEGRSPRSP
      781 RNNPVPPEAK SPVLNPGERP ADVSPTSPQP EGLLVLQQVG DYCFLPGLGP GPLSLRSKPS
      841 SPGPGPEIKN LDQAFQVKKP PGQAVPQVPV IQLFKALKQQ DYLSLPPWEV NKPGEVC
>gi|1345923|sp|P32927.2|IL3RB_HUMAN RecName: Full=Cytokine receptor common
subunit beta; AltName: Full=GM-CSF/IL-3/IL-5 receptor common beta-chain;
AltName: Full=CDw131; AltName: CD_antigen=CD131; Flags: Precursor
MVLAQGLLSMALLALCWERSLAGAEETIPLQTLRCYNDYTSHITCRWADTQDAQRLVNVTLIRRVNEDLL
EPVSCDLSDDMPWSACPHPRCVPRRCVIPCQSFVVTDVDYFSFQPDRPLGTRLTVTLTQHVQPPEPRDLQ
ISTDQDHFLLTWSVALGSPQSHWLSPGDLEFEVVYKRLQDSWEDAAILLSNTSQATLGPEHLMPSSTYVA
RVRTRLAPGSRLSGRPSKWSPEVCWDSQPGDEAQPQNLECFFDGAAVLSCSWEVRKEVASSVSFGLFYKP
SPDAGEEECSPVLREGLGSLHTRHHCQIPVPDPATHGQYIVSVQPRRAEKHIKSSVNIQMAPPSLNVTKD
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GDSYSLRWETMKMRYEHIDHTFEIQYRKDTATWKDSKTETLQNAHSMALPALEPSTRYWARVRVRTSRTG
YNGIWSEWSEARSWDTESVLPMWVLALIVIFLTIAVLLALRFCGIYGYRLRRKWEEKIPNPSKSHLFQNG
SAELWPPGSMSAFTSGSPPHQGPWGSRFPELEGVFPVGFGDSEVSPLTIEDPKHVCDPPSGPDTTPAASD
LPTEQPPSPQPGPPAASHTPEKQASSFDFNGPYLGPPHSRSLPDILGQPEPPQEGGSQKSPPPGSLEYLC
LPAGGQVQLVPLAQAMGPGQAVEVERRPSQGAAGSPSLESGGGPAPPALGPRVGGQDQKDSPVAIPMSSG
DTEDPGVASGYVSSADLVFTPNSGASSVSLVPSLGLPSDQTPSLCPGLASGPPGAPGPVKSGFEGYVELP
PIEGRSPRSPRNNPVPPEAKSPVLNPGERPADVSPTSPQPEGLLVLQQVGDYCFLPGLGPGPLSLRSKPS
SPGPGPEIKNLDQAFQVKKPPGQAVPQVPVIQLFKALKQQDYLSLPPWEVNKPGEVC
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Notes

PPHSRpS^{585}LP (Ser601). Defects in CSF2RB are a cause of congenital pulmonary alveolar proteinosis (PAP) [MIM:265120]. PAP is an autosomal recessive fatal respiratory disease.

References to 14-3-3 binding to β-Chain of GM-CSF/IL-3/IL-5 receptors

Stomski FC, Dottore M, Winnall W, Guthridge MA, Woodcock J, Bagley CJ, Thomas DT, Andrews RK, Berndt MC, Lopez AF. Identification of a 14-3-3 binding sequence in the common beta chain of the granulocyte-macrophage colony-stimulating factor (GM-CSF), interleukin-3 (IL-3), and IL-5 receptors that is serine-phosphorylated by GM-CSF. Blood. 1999 Sep 15;94(6):1933-42.

Human CTNNB1 Catenin beta-1 (Beta-catenin) **(Swissprot =** P35222**)**

```
        1 MATQADLMEL DMAMEPDRKA AVSHWQQQSY LDSGIHSGAT TTAPSLSGKG NPEEEDVDTS
       61 QVLYEWEQGF SQSFTQEQVA DIDGQYAMTR AQRVRAAMFP ETLDEGMQIP STQFDAAHPT
      121 NVQRLAEPSQ MLKHAVVNLI NYQDDAELAT RAIPELTKLL NDEDQVVVNK AAVMVHQLSK
      181 KEASRHAIMR SPQMVSAIVR TMQNTNDVET ARCTAGTLHN LSHHREGLLA IFKSGGIPAL
      241 VKMLGSPVDS VLFYAITTLH NLLLHQEGAK MAVRLAGGLQ KMVALLNKTN VKFLAITTDC
      301 LQILAYGNQE SKLIILASGG PQALVNIMRT YTYEKLLWTT SRVLKVLSVC SSNKPAIVEA
      361 GGMQALGLHL TDPSQRLVQN CLWTLRNLSD AATKQEGMEG LLGTLVQLLG SDDINVVTCA
      421 AGILSNLTCN NYKNKMMVCQ VGGIEALVRT VLRAGDREDI TEPAICALRH LTSRHQEAEM
      481 AQNAVRLHYG LPVVVKLLHP PSHWPLIKAT VGLIRNLALC PANHAPLREQ GAIPRLVQLL
      541 VRAHQDTQRR TsMGGTQQQF VEGVRMEEIV EGCTGALHIL ARDVHNRIVI RGLNTIPLFV
      601 QLLYSPIENI QRVAAGVLCE LAQDKEAAEA IEAEGATAPL TELLHSRNEG VATYAAAVLF
      661 RMSEDKPQDY KKRLSVELTS SLFRTEPMAW NETADLGLDI GAQGEPLGYR QDDPSYRSFH
      721 SGGYGQDALG MDPMMEHEMG GHHPGADYPV DGLPDLGHAQ DLMDGLPPGD SNQLAWFDTD
      781 L
>gi|461854|sp|P35222.1|CTNB1_HUMAN RecName: Full=Catenin beta-1; AltName:
Full=Beta-catenin
MATQADLMELDMAMEPDRKAAVSHWQQQSYLDSGIHSGATTTAPSLSGKGNPEEEDVDTSQVLYEWEQGF
SQSFTQEQVADIDGQYAMTRAQRVRAAMFPETLDEGMQIPSTQFDAAHPTNVQRLAEPSQMLKHAVVNLI
NYQDDAELATRAIPELTKLLNDEDQVVVNKAAVMVHQLSKKEASRHAIMRSPQMVSAIVRTMQNTNDVET
ARCTAGTLHNLSHHREGLLAIFKSGGIPALVKMLGSPVDSVLFYAITTLHNLLLHQEGAKMAVRLAGGLQ
KMVALLNKTNVKFLAITTDCLQILAYGNQESKLIILASGGPQALVNIMRTYTYEKLLWTTSRVLKVLSVC
SSNKPAIVEAGGMQALGLHLTDPSQRLVQNCLWTLRNLSDAATKQEGMEGLLGTLVQLLGSDDINVVTCA
AGILSNLTCNNYKNKMMVCQVGGIEALVRTVLRAGDREDITEPAICALRHLTSRHQEAEMAQNAVRLHYG
LPVVVKLLHPPSHWPLIKATVGLIRNLALCPANHAPLREQGAIPRLVQLLVRAHQDTQRRTSMGGTQQQF
VEGVRMEEIVEGCTGALHILARDVHNRIVIRGLNTIPLFVQLLYSPIENIQRVAAGVLCELAQDKEAAEA
IEAEGATAPLTELLHSRNEGVATYAAAVLFRMSEDKPQDYKKRLSVELTSSLFRTEPMAWNETADLGLDI
GAQGEPLGYRQDDPSYRSFHSGGYGQDALGMDPMMEHEMGGHHPGADYPVDGLPDLGHAQDLMDGLPPGD
SNQLAWFDTDL
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Notes

AKT phosphorylates beta-catenin at Ser552 and enhances its interaction with 14-3-3zeta.

References to 14-3-3-binding to beta-catenin

Fang D, Hawke D, Zheng Y, Xia Y, Meisenhelder J, Nika H, Mills GB, Kobayashi R, Hunter T, Lu Z. Phosphorylation of beta-catenin by AKT promotes beta-catenin transcriptional activity. J Biol Chem. 2007 Apr 13;282(15):11221-9.

Takemaru K, Fischer V, Li FQ. Fine-tuning of nuclear-catenin by Chibby and 14-3-3. Cell Cycle. 2009 Jan 15;8(2):210-3.

Li FQ, Mofunanya A, Harris K, Takemaru K. Chibby cooperates with 14-3-3 to regulate β-catenin subcellular distribution and signaling activity. J Cell Biol. 2008 June 30; 181(7): 1141–1154.

Human Cx43 connexin43 (Swissprot = P17302)

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        1 MGDWSALGKL LDKVQAYSTA GGKVWLSVLF IFRILLLGTA VESAWGDEQS AFRCNTQQPG
       61 CENVCYDKSF PISHVRFWVL QIIFVSVPTL LYLAHVFYVM RKEEKLNKKE EELKVAQTDG
      121 VNVDMHLKQI EIKKFKYGIE EHGKVKMRGG LLRTYIISIL FKSIFEVAFL LIQWYIYGFS
      181 LSAVYTCKRD PCPHQVDCFL SRPTEKTIFI IFMLVVSLVS LALNIIELFY VFFKGVKDRV
      241 KGKSDPYHAT SGALSPAKDC GSQKYAYFNG CSSPTAPLSP MSPPGYKLVT GDRNNSSCRN
      301 YNKQASEQNW ANYSAEQNRM GQAGSTISNS HAQPFDFPDD NQNSKKLAAG HELQPLAIVD
      361 QRPSSRASSR ASsRPRPDDL EI
>gi|117706|sp|P17302.2|CXA1_HUMAN RecName: Full=Gap junction alpha-1 protein;
AltName: Full=Connexin-43; Short=Cx43; AltName: Full=Gap junction 43 kDa
heart protein
MGDWSALGKLLDKVQAYSTAGGKVWLSVLFIFRILLLGTAVESAWGDEQSAFRCNTQQPGCENVCYDKSF
PISHVRFWVLQIIFVSVPTLLYLAHVFYVMRKEEKLNKKEEELKVAQTDGVNVDMHLKQIEIKKFKYGIE
EHGKVKMRGGLLRTYIISILFKSIFEVAFLLIQWYIYGFSLSAVYTCKRDPCPHQVDCFLSRPTEKTIFI
IFMLVVSLVSLALNIIELFYVFFKGVKDRVKGKSDPYHATSGALSPAKDCGSQKYAYFNGCSSPTAPLSP
MSPPGYKLVTGDRNNSSCRNYNKQASEQNWANYSAEQNRMGQAGSTISNSHAQPFDFPDDNQNSKKLAAG
HELQPLAIVDQRPSSRASSRASSRPRPDDLEI
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Notes

Hexamers of connexin-43 form connexons, which form gap junctions. 14-3-3s are reported to bind to Akt-phosphorylated Ser373 in the cytoplasmic tail of Cx43 on Ser373, and GST-14-3-3 binds to Cx43 phosphorylated endogenously in EGF-treated cells (but Ser373 is not a conventional PKB consensus site).

References to 14-3-3 binding to connexin43

Majoul IV, Onichtchouk D, Butkevich E, Wenzel D, Chailakhyan LM, Duden R. Limiting transport steps and novel interactions of Connexin-43 along the secretory pathway. Histochem Cell Biol. 2009 Jul 22.

Park DJ, Wallick CJ, Martyn KD, Lau AF, Jin C, Warn-Cramer BJ. Akt phosphorylates Connexin43 on Ser373, a "mode-1" binding site for 14-3-3. Cell Commun Adhes. 2007 Sep-Oct;14(5):211-26.

Park DJ, Freitas TA, Wallick CJ, Guyette CV, Warn-Cramer BJ. Molecular dynamics and in vitro analysis of Connexin43: A new 14-3-3 mode-1 interacting protein. Protein Sci. 2006 Oct;15(10):2344-55.

Human DAB2IP Disabled homolog 2-interacting protein aka AIP1 ASK1-interacting protein 1 (Ras-GAP) (Swissprot = Q5VWQ8)

```
   1 MSAGGSARKS TGRSSYYYRL LRRPRLQRQR SRSRSRTRPA RESPQERPGS RRSLPGSLSE
  61 KSPSMEPSAA TPFRVTGFLS RRLKGSIKRT KSQPKLDRNH SFRHILPGFR SAAAAAADNE
 121 RSHLMPRLKE SRSHESLLSP SSAVEALDLS MEEEVVIKPV HSSILGQDYC FEVTTSSGSK
 181 CFSCRSAAER DKWMENLRRA VHPNKDNSRR VEHILKLWVI EAKDLPAKKK YLCELCLDDV
 241 LYARTTGKLK TDNVFWGEHF EFHNLPPLRT VTVHLYRETD KKKKKERNSY LGLVSLPAAS
 301 VAGRQFVEKW YPVVTPNPKG GKGPGPMIRI KARYQTITIL PMEMYKEFAE HITNHYLGLC
 361 AALEPILSAK TKEEMASALV HILQSTGKVK DFLTDLMMSE VDRCGDNEHL IFRENTLATK
 421 AIEEYLKLVG QKYLQDALGE FIKALYESDE NCEVDPSKCS AADLPEHQGN LKMCCELAFC
 481 KIINSYCVFP RELKEVFASW RQECSSRGRP DISERLISAS LFLRFLCPAI MSPSLFNLLQ
 541 EYPDDRTART LTLIAKVTQN LANFAKFGSK EEYMSFMNQF LEHEWTNMQR FLLEISNPET
 601 LSNTAGFEGY IDLGRELSSL HSLLWEAVSQ LEQSIVSKLG PLPRILRDVH TALSTPGSGQ
 661 LPGTNDLAST PGSGSSSISA GLQKMVIEND LSGLIDFTRL PSPTPENKDL FFVTRSSGVQ
 721 PSPARSSsYS EANEPDLQMA NGGKSLSMVD LQDARTLDGE AGSPAGPDVL PTDGQAAAAQ
 781 LVAGWPARAT PVNLAGLATV RRAGQTPTTP GTSEGAPGRP QLLAPLSFQN PVYQMAAGLP
 841 LSPRGLGDSG SEGHSSLSSH SNSEELAAAA KLGSFSTAAE ELARRPGELA RRQMSLTEKG
 901 GQPTVPRQNS AGPQRRIDQP PPPPPPPPPA PRGRTPPNLL STLQYPRPSS GTLASASPDW
 961 VGPSTRLRQQ SSSSKGDSPE LKPRAVHKQG PSPVSPNALD RTAAWLLTMN AQLLEDEGLG
1021 PDPPHRDRLR SKDELSQAEK DLAVLQDKLR ISTKKLEEYE TLFKCQEETT QKLVLEYQAR
1081 LEEGEERLRR QQEDKDIQMK GIISRLMSVE EELKKDHAEM QAAVDSKQKI IDAQEKRIAS
1141 LDAANARLMS ALTQLKERYS MQARNGISPT NPTKLQITEN GEFRNSSNC
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>GI|116247768|SP|Q5VWQ8.2|DAB2P_HUMAN RECNAME: FULL=DISABLED HOMOLOG 2-
INTERACTING PROTEIN; SHORT=DAB2-INTERACTING PROTEIN; SHORT=DAB2 INTERACTION
PROTEIN; ALTNAME: FULL=ASK-INTERACTING PROTEIN 1
MSAGGSARKSTGRSSYYYRLLRRPRLQRQRSRSRSRTRPARESPQERPGSRRSLPGSLSEKSPSMEPSAA
TPFRVTGFLSRRLKGSIKRTKSQPKLDRNHSFRHILPGFRSAAAAAADNERSHLMPRLKESRSHESLLSP
SSAVEALDLSMEEEVVIKPVHSSILGQDYCFEVTTSSGSKCFSCRSAAERDKWMENLRRAVHPNKDNSRR
VEHILKLWVIEAKDLPAKKKYLCELCLDDVLYARTTGKLKTDNVFWGEHFEFHNLPPLRTVTVHLYRETD
KKKKKERNSYLGLVSLPAASVAGRQFVEKWYPVVTPNPKGGKGPGPMIRIKARYQTITILPMEMYKEFAE
HITNHYLGLCAALEPILSAKTKEEMASALVHILQSTGKVKDFLTDLMMSEVDRCGDNEHLIFRENTLATK
AIEEYLKLVGQKYLQDALGEFIKALYESDENCEVDPSKCSAADLPEHQGNLKMCCELAFCKIINSYCVFP
RELKEVFASWRQECSSRGRPDISERLISASLFLRFLCPAIMSPSLFNLLQEYPDDRTARTLTLIAKVTQN
LANFAKFGSKEEYMSFMNQFLEHEWTNMQRFLLEISNPETLSNTAGFEGYIDLGRELSSLHSLLWEAVSQ
LEQSIVSKLGPLPRILRDVHTALSTPGSGQLPGTNDLASTPGSGSSSISAGLQKMVIENDLSGLIDFTRL
PSPTPENKDLFFVTRSSGVQPSPARSSSYSEANEPDLQMANGGKSLSMVDLQDARTLDGEAGSPAGPDVL
PTDGQAAAAQLVAGWPARATPVNLAGLATVRRAGQTPTTPGTSEGAPGRPQLLAPLSFQNPVYQMAAGLP
LSPRGLGDSGSEGHSSLSSHSNSEELAAAAKLGSFSTAAEELARRPGELARRQMSLTEKGGQPTVPRQNS
AGPQRRIDQPPPPPPPPPPAPRGRTPPNLLSTLQYPRPSSGTLASASPDWVGPSTRLRQQSSSSKGDSPE
LKPRAVHKQGPSPVSPNALDRTAAWLLTMNAQLLEDEGLGPDPPHRDRLRSKDELSQAEKDLAVLQDKLR
ISTKKLEEYETLFKCQEETTQKLVLEYQARLEEGEERLRRQQEDKDIQMKGIISRLMSVEEELKKDHAEM
QAAVDSKQKIIDAQEKRIASLDAANARLMSALTQLKERYSMQARNGISPTNPTKLQITENGEFRNSSNC
```

Notes

Authors report that mutation of Ser604 in GenBank accession no. AY032952 prevents 14-3-3 binding = Ser728 in Q5VWQ8 as shown.

References to 14-3-3 binding to AIP1

Zhang H, Zhang H, Lin Y, Li J, Pober JS, Min W. RIP1-mediated AIP1 phosphorylation at a 14-3-3-binding site is critical for tumor necrosis factor-induced ASK1-JNK/p38 activation. J Biol Chem. 2007 May 18;282(20):14788-96.

Min W, Lin Y, Tang S, Yu L, Zhang H, Wan T, Luhn T, Fu H, Chen H. AIP1 recruits phosphatase PP2A to ASK1 in tumor necrosis factor-induced ASK1-JNK activation. Circ Res. 2008 Apr 11;102(7):840-8.

Zhang R, He X, Liu W, Lu M, Hsieh JT, Min W. AIP1 mediates TNF-alpha-induced ASK1 activation by facilitating dissociation of ASK1 from its inhibitor 14-3-3. J Clin Invest. 2003 Jun;111(12):1933-43.

Li X, Zhang R, Luo D, Park SJ, Wang Q, Kim Y, Min W. Tumor necrosis factor alpha-induced desumoylation and cytoplasmic translocation of homeodomain-interacting protein kinase 1 are critical for apoptosis signal-regulating kinase 1-JNK/p38 activation. J Biol Chem. 2005 Apr 15;280(15):15061-70.

Human DDIT4 DNA-damage-inducible transcript 4 protein (Redd1) (Swissprot = Q9NX09)

```
  1 MPSLWDRFSS SSTSSSPSSL PRTPTPDRPP RSAWGSATRE EGFDRSTSLE SSDCESLDSS
 61 NSGFGPEEDT AYLDGVSLPD FELLSDPEDE HLCANLMQLL QESLAQARLG SRRPARLLMP
121 SQLVSQVGKE LLRLAYsEPC GLRGALLDVC VEQGKSCHSV GQLALDPSLV PTFQLTLVLR
181 LDSRLWPKIQ GLFSSANSPF LPGFSQSLTL STGFRVIKKK LYSSEQLLIE EC
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>gi|74753036|sp|Q9NX09.1|DDT4_HUMAN RecName: Full=DNA-damage-inducible
transcript 4 protein; AltName: Full=Protein regulated in development and DNA
damage response 1; Short=REDD-1; AltName: Full=HIF-1 responsive protein
RTP801
MPSLWDRFSSSSTSSSPSSLPRTPTPDRPPRSAWGSATREEGFDRSTSLESSDCESLDSSNSGFGPEEDT
AYLDGVSLPDFELLSDPEDEHLCANLMQLLQESLAQARLGSRRPARLLMPSQLVSQVGKELLRLAYSEPC
GLRGALLDVCVEQGKSCHSVGQLALDPSLVPTFQLTLVLRLDSRLWPKIQGLFSSANSPFLPGFSQSLTL
STGFRVIKKKLYSSEQLLIEEC
```

Human DDIT4L DNA-damage-inducible transcript 4-like protein (Redd2) (Swissprot = Q96D03) 1 MVATGSLSSK NPASISELLD CGYHPESLLS DFDYWDYVVP EPNLNEVIFE ESTCQNLVKM 61 LENCLSKSKQ TKLGCSKVLV PEKLTQRIAQ DVLRLSStEP CGLRGCVMHV NLEIENVCKK 121 LDRIVCDSSV VPTFELTLVF KQENCSWTSF RDFFFSRGRF SSGFRRTLIL SSGFRLVKKK 181 LYSLIGTTVI EGS >gi|74731396|sp|Q96D03.1|DDT4L_HUMAN RecName: Full=DNA-damage-inducible transcript 4-like protein; AltName: Full=Protein regulated in development and DNA damage response 2; Short=REDD-2; AltName: Full=HIF-1 responsive protein RTP801-like MVATGSLSSKNPASISELLDCGYHPESLLSDFDYWDYVVPEPNLNEVIFEESTCQNLVKMLENCLSKSKQ TKLGCSKVLVPEKLTQRIAQDVLRLSSTEPCGLRGCVMHVNLEIENVCKKLDRIVCDSSVVPTFELTLVF KQENCSWTSFRDFFFSRGRFSSGFRRTLILSSGFRLVKKKLYSLIGTTVIEGS **Notes** Motif scanning within this domain revealed a consensus Arg-X-X-X-Ser/Thr-X-Pro-binding site for 14–3–3 proteins that is conserved among mammalian orthologs of both REDD1 and the REDD1-related protein REDD2. Of note, both Drosophila REDD1 orthologs harbor a variant of this motif with the serine residue at the +2 position relative to arginine (Arg-X-Ser-X-X-X-Pro). hREDD1 RLAY(S)EP mREDD1 RLAY(S)EP hREDD2 RLSS(T)EP mREDD2 RLSS(T)EP **References to 14-3-3 binding to Redd1** DeYoung MP, Horak P, Sofer A, Sgroi D, Ellisen LW. Hypoxia regulates TSC1/2-mTOR signaling and tumor suppression through REDD1-mediated 14-3-3 shuttling. Genes Dev. 2008 Jan 15;22(2):239-51. **References to 14-3-3 binding to Redd2 (SMHS1/RTP801L/DDIT4L)** Miyazaki M, Esser KA. REDD2 is enriched in skeletal muscle and inhibits mTOR signaling in response to leucine and stretch. Am J Physiol Cell Physiol. 2009 Mar;296(3):C583-	
Human DYRK1A Dual-specificity tyrosine-phosphorylated and regulated kinase (Swissprot = Q13627) 1 MHTGGETSAC KPSSVRLAPS FSFHAAGLQM AGQMPHSHQY SDRRQPNISD QQVSALSYSD 61 QIQQPLTNQV MPDIVMLQRR MPQTFRDPAT APLRKLSVDL IKTYKHINEV YYAKKKRRHQ 121 QGQGDDSSHK KERKVYNDGY DDDNYDYIVK NGEKWMDRYE IDSLIGKGSF GQVVKAYDRV 181 EQEWVAIKII KNKKAFLNQA QIEVRLLELM NKHDTEMKYY IVHLKRHFMF RNHLCLVFEM 241 LSYNLYDLLR NTNFRGVSLN LTRKFAQQMC TALLFLATPE LSIIHCDLKP ENILLCNPKR 301 SAIKIVDFGS SCQLGQRIYQ YIQSRFYRSP EVLLGMPYDL AIDMWSLGCI LVEMHTGEPL 361 FSGANEVDQM NKIVEVLGIP PAHILDQAPK ARKFFEKLPD GTWNLKKTKD GKREYKPPGT 421 RKLHNILGVE TGGPGGRRAG ESGHTVADYL KFKDLILRML DYDPKTRIQP YYALQHSFFK 481 KTADEGTNTS NSVSTSPAME QSQSSGTTSS TSSSSGGSSG TSNSGRARsD PTHQHRHSGG 541 HFTAAVQAMD CETHSPQVRQ QFPAPLGWSG TEAPTQVTVE THPVQETTFH VAPQQNALHH 601 HHGNSSHHHH HHHHHHHHHG QQALGNRTRP RVYNSPTNSS STQDSMEVGH SHHSMTSLSS 661 STTSSSTSSS STGNQGNQAY QNRPVAANTL DFGQNGAMDV NLTVYSNPRQ ETGIAGHPTY 721 QFSANTGPAH YMTEGHLTMR QGADREESPM TGVCVQQSPV ASS >gi|3219996|sp|Q13627.2|DYR1A_HUMAN RecName: Full=Dual specificity tyrosine-phosphorylation-regulated kinase 1A; AltName: Full=Protein kinase minibrain homolog; Short=MNBH; Short=hMNB; AltName: Full=HP86; AltName: Full=Dual specificity YAK1-related kinase MHTGGETSACKPSSVRLAPSFSFHAAGLQMAGQMPHSHQYSDRRQPNISDQQVSALSYSDQIQQPLTNQV MPDIVMLQRRMPQTFRDPATAPLRKLSVDLIKTYKHINEVYYAKKKRRHQQGQGDDSSHKKERKVYNDGY DDDNYDYIVKNGEKWMDRYEIDSLIGKGSFGQVVKAYDRVEQEWVAIKIIKNKKAFLNQAQIEVRLLELM NKHDTEMKYYIVHLKRHFMFRNHLCLVFEMLSYNLYDLLRNTNFRGVSLNLTRKFAQQMCTALLFLATPE LSIIHCDLKPENILLCNPKRSAIKIVDFGSSCQLGQRIYQYIQSRFYRSPEVLLGMPYDLAIDMWSLGCI LVEMHTGEPLFSGANEVDQMNKIVEVLGIPPAHILDQAPKARKFFEKLPDGTWNLKKTKDGKREYKPPGT RKLHNILGVETGGPGGRRAGESGHTVADYLKFKDLILRMLDYDPKTRIQPYYALQHSFFKKTADEGTNTS NSVSTSPAMEQSQSSGTTSSTSSSSGGSSGTSNSGRARSDPTHQHRHSGGHFTAAVQAMDCETHSPQVRQ QFPAPLGWSGTEAPTQVTVETHPVQETTFHVAPQQNALHHHHGNSSHHHHHHHHHHHHGQQALGNRTRP RVYNSPTNSSSTQDSMEVGHSHHSMTSLSSSTTSSSTSSSSTGNQGNQAYQNRPVAANTLDFGQNGAMDV NLTVYSNPRQETGIAGHPTYQFSANTGPAHYMTEGHLTMRQGADREESPMTGVCVQQSPVASS **Notes** DYRK1A autophosphorylates on Ser-520 (RAR(pS520)DP, in the PEST domain of the protein. We also show that phosphorylation of this residue, which we show is subjected to dynamic changes in vivo, mediates the interaction of DYRK1A with 14-3-3beta. A second 14-3-3 binding site is present within the N-terminal of the protein. In the context of the DYRK1A molecule, neither site can act independently of the other. A previous report on 14-3-3 and DYRK1A identified the first 125 amino acids of DYRK1A as the interacting domain, based on the lack of binding of an N-terminal deletion mutant (Kim et al., 2004). **References to 14-3-3 binding to DYRK1A** Alvarez M, Altafaj X, Aranda S, de la Luna S. DYRK1A autophosphorylation on serine residue 520 modulates its kinase activity via 14-3-3 binding. Mol Biol Cell. 2007 Apr;18(4):1167-78. Kim D, Won J, Shin DW, Kang J, Kim YJ, Choi SY, Hwang MK, Jeong BW, Kim GS, Joe CO, Chung SH, Song WJ. Regulation of Dyrk1A kinase activity by 14-3-3. Biochem Biophys Res Commun. 2004 Oct 15;323(2):499-504.	Controversy about site of 14-3-3-binding. NOT IN WEBLOGO.
Human ELAVL1 (Swissprot = Q15717) 1 MSNGYEDHMA EDCRGDIGRT NLIVNYLPQN MTQDELRSLF SSIGEVESAK LIRDKVAGHS 61 LGYGFVNYVT AKDAERAINT LNGLRLQSKT IKVSYARPSS EVIKDANLYI SGLPRTMTQK 121 DVEDMFSRFG RIINSRVLVD QTTGLSRGVA FIRFDKRSEA EEAITSFNGH KPPGSSEPIT 181 VKFAANPNQN KNVALLSQLY HsPARRFGGP VHHQAQRFRF SPMGVDHMSG LSGVNVPGNA 241 SSGWCIFIYN LGQDADEGIL WQMFGPFGAV TNVKVIRDFN TNKCKGFGFV TMTNYEEAAM 301 AIASLNGYRL GDKILQVSFK TNKSHK	Ser202 phophorylated, but not the 14-3-3-binding site. THEREFORE NOT IN WEBLOGO ANALYSIS

<table>
<tr><th></th><th></th></tr>
<tr><td>>gi|20981691|sp|Q15717.2|ELAV1_HUMAN RecName: Full=ELAV-like protein 1; AltName: Full=Hu-antigen R; Short=HuR
MSNGYEDHMAEDCRGDIGRTNLIVNYLPQNMTQDELRSLFSSIGEVESAKLIRDKVAGHSLGYGFVNYVT
AKDAERAINTLNGLRLQSKTIKVSYARPSSEVIKDANLYISGLPRTMTQKDVEDMFSRFGRIINSRVLVD
QTTGLSRGVAFIRFDKRSEAEEAITSFNGHKPPGSSEPITVKFAANPNQNKNVALLSQLYHSPARRFGGP
VHHQAQRFRFSPMGVDHMSGLSGVNVPGNASSGWCIFIYNLGQDADEGILWQMFGPFGAVTNVKVIRDFN
TNKCKGFGFVTMTNYEEAAMAIASLNGYRLGDKILQVSFKTNKSHK
Notes
Ser202 phosphorylation occurred at the same time as 14-3-3 binding, but not functionally linked and ELAVL1 binds avidly to the AU-rich element in FOS and IL3/interleukin-3 mRNAs. In the case of the FOS AU-rich element, HUR binds to a core element of 27 nucleotides that contain AUUUA, AUUUUA, and AUUUUUA motifs. Interacts with ANP32A.
Here, we present evidence that HuR phosphorylation at S202 by the G2-phase kinase Cdk1 influences its subcellular distribution. In keeping with the prominently cytoplasmic location of the nonphosphorylatable point mutant HuR(S202A), phospho-HuR(S202) was shown to be predominantly nuclear using a novel anti-phospho-HuR(S202) antibody. The enhanced cytoplasmic presence of unphosphorylated HuR was linked to its decreased association with 14-3-3 and to its heightened binding to target mRNAs.
References to 14-3-3 binding to ELAVL1
Kim HH, Abdelmohsen K, Lal A, Pullmann R Jr, Yang X, Galban S, Srikantan S, Martindale JL, Blethrow J, Shokat KM, Gorospe M. Nuclear HuR accumulation through phosphorylation by Cdk1. Genes Dev. 2008 Jul 1;22(13):1804-15
Kim HH, Gorospe M. Phosphorylated HuR shuttles in cycles. Cell Cycle. 2008 Oct;7(20):3124-6.</td><td></td></tr>
<tr><td>Human FAM82A2 (PTPIP51) Regulator of microtubule dynamics protein 3 (Protein tyrosine phosphatase-interacting protein 51) (Swissprot = Q96TC7)
1 MSRLGALGGA RAGLGLLLGT AAGLGFLCLL YSQRWKRTQR HGRSQsLPNS LDYTQTSDPG
61 RHVMLLRAVP GGAGDASVLP SLPREGQEKV LDRLDFVLTS LVALRREVEE LRSSLRGLAG
121 EIVGEVRCHM EENQRVARRR RFPFVRERsD sTGSSSVYFT ASSGATFTDA ESEGGYTTAN
181 AESDNERDSD KESEDGEDEV SCETVKMGRK DSLDLEEEAA SGASSALEAG GSSGLEDVLP
241 LLQQADELHR GDEQGKREGF QLLLNNKLVY GSRQDFLWRL ARAYSDMCEL TEEVSEKKSY
301 ALDGKEEAEA ALEKGDESAD CHLWYAVLCG QLAEHESIQR RIQSGFSFKE HVDKAIALQP
361 ENPMAHFLLG RWCYQVSHLS WLEKKTATAL LESPLSATVE DALQSFLKAE ELQPGFSKAG
421 RVYISKCYRE LGKNSEARWW MKLALELPDV TKEDLAIQKD LEELEVILRD
>gi|147643203|sp|Q96TC7.2|RMD3_HUMAN RecName: Full=Regulator of microtubule dynamics protein 3; Short=RMD-3; Short=hRMD-3; AltName: Full=Protein FAM82A2; AltName: Full=Protein FAM82C; AltName: Full=Protein tyrosine phosphatase-interacting protein 51; AltName: Full=TCPTP-interacting protein 51; AltName: Full=Cerebral protein 10
MSRLGALGGARAGLGLLLGTAAGLGFLCLLYSQRWKRTQRHGRSQSLPNSLDYTQTSDPGRHVMLLRAVP
GGAGDASVLPSLPREGQEKVLDRLDFVLTSLVALRREVEELRSSLRGLAGEIVGEVRCHMEENQRVARRR
RFPFVRERSDSTGSSSVYFTASSGATFTDAESEGGYTTANAESDNERDSDKESEDGEDEVSCETVKMGRK
DSLDLEEEAASGASSALEAGGSSGLEDVLPLLQQADELHRGDEQGKREGFQLLLNNKLVYGSRQDFLWRL
ARAYSDMCELTEEVSEKKSYALDGKEEAEAALEKGDESADCHLWYAVLCGQLAEHESIQRRIQSGFSFKE
HVDKAIALQPENPMAHFLLGRWCYQVSHLSWLEKKTATALLESPLSATVEDALQSFLKAEELQPGFSKAG
RVYISKCYRELGKNSEARWWMKLALELPDVTKEDLAIQKDLEELEVILRD
Notes
Said to be a ternary complex of PTPIP51, 14–3–3, and Raf-1 (Yu et al 2008). Proposed sites are 43RSQ(pS46)LP48, and either 146RER(pS149)DS151 or 148RSD(pS151)TG154.
References to 14-3-3 binding to PTPIP51
Yu C, Han W, Shi T, Lv B, He Q, Zhang Y, Li T, Zhang Y, Song Q, Wang L, Ma D. PTPIP51, a novel 14-3-3 binding protein, regulates cell morphology and motility via Raf-ERK pathway. Cell Signal. 2008 Dec;20(12):2208-20.
Stenzinger A, Schreiner D, Koch P, Hofer HW, Wimmer M. Cell and molecular biology of the novel protein tyrosine-phosphatase-interacting protein 51. Int Rev Cell Mol Biol. 2009;275:183-246.</td><td>Only show pSer46 on WEBLOGO. Not sure whether Ser148 or 151 is the potential second site.</td></tr>
<tr><td>Human FGFR2 Fibroblast growth factor receptor 2 (Swissprot = P21802
1 MVSWGRFICL VVVTMATLSL ARPSFSLVED TTLEPEEPPT KYQISQPEVY VAAPGESLEV
61 RCLLKDAAVI SWTKDGVHLG PNNRTVLIGE YLQIKGATPR DSGLYACTAS RTVDSETWYF
121 MVNVTDAISS GDDEDDTDGA EDFVSENSNN KRAPYWTNTE KMEKRLHAVP AANTVKFRCP
181 AGGNPMPTMR WLKNGKEFKQ EHRIGGYKVR NQHWSLIMES VVPSDKGNYT CVVENEYGSI
241 NHTYHLDVVE RSPHRPILQA GLPANASTVV GGDVEFVCKV YSDAQPHIQW IKHVEKNGSK
301 YGPDGLPYLK VLKAAGVNTT DKEIEVLYIR NVTFEDAGEY TCLAGNSIGI SFHSAWLTVL
361 PAPGREKEIT ASPDYLEIAI YCIGVFLIAC MVVTVILCRM KNTTKKPDFS SQPAVHKLTK
421 RIPLRRQVTV SAESSSSMNS NTPLVRITTR LSSTADTPML AGVSEYELPE DPKWEFPRDK
481 LTLGKPLGEG CFGQVVMAEA VGIDKDKPKE AVTVAVKMLK DDATEKDLSD LVSEMEMMKM
541 IGKHKNIINL LGACTQDGPL YVIVEYASKG NLREYLRARR PPGMEYSYDI NRVPEEQMTF
601 KDLVSCTYQL ARGMEYLASQ KCIHRDLAAR NVLVTENNVM KIADFGLARD INNIDYYKKT
661 TNGRLPVKWM APEALFDRVY THQSDVWSFG VLMWEIFTLG GSPYPGIPVE ELFKLLKEGH
721 RMDKPANCTN ELYMMMRDCW HAVPSQRPTF KQLVEDLDRI LTLTTNEEYL DLSQPLEQYS
781 PsYPDTRSSC SSGDDSVFSP DPMPYEPCLP QYPHINGSVK T
>gi|120049|sp|P21802.1|FGFR2_HUMAN RecName: Full=Fibroblast growth factor receptor 2; Short=FGFR-2; AltName: Full=Keratinocyte growth factor receptor 2; AltName: CD_antigen=CD332; Flags: Precursor
MVSWGRFICLVVVTMATLSLARPSFSLVEDTTLEPEEPPTKYQISQPEVYVAAPGESLEVRCLLKDAAVI
SWTKDGVHLGPNNRTVLIGEYLQIKGATPRDSGLYACTASRTVDSETWYFMVNVTDAISSGDDEDDTDGA
EDFVSENSNNKRAPYWTNTEKMEKRLHAVPAANTVKFRCPAGGNPMPTMRWLKNGKEFKQEHRIGGYKVR
NQHWSLIMESVVPSDKGNYTCVVENEYGSINHTYHLDVVERSPHRPILQAGLPANASTVVGGDVEFVCKV
YSDAQPHIQWIKHVEKNGSKYGPDGLPYLKVLKAAGVNTTDKEIEVLYIRNVTFEDAGEYTCLAGNSIGI</td><td></td></tr>
</table>

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SFHSAWLTVLPAPGREKEITASPDYLEIAIYCIGVFLIACMVVTVILCRMKNTTKKPDFSSQPAVHKLTK
RIPLRRQVTVSAESSSSMNSNTPLVRITTRLSSTADTPMLAGVSEYELPEDPKWEFPRDKLTLGKPLGEG
CFGQVVMAEAVGIDKDKPKEAVTVAVKMLKDDATEKDLSDLVSEMEMMKMIGKHKNIINLLGACTQDGPL
YVIVEYASKGNLREYLRARRPPGMEYSYDINRVPEEQMTFKDLVSCTYQLARGMEYLASQKCIHRDLAAR
NVLVTENNVMKIADFGLARDINNIDYYKKTTNGRLPVKWMAPEALFDRVYTHQSDVWSFGVLMWEIFTLG
GSPYPGIPVEELFKLLKEGHRMDKPANCTNELYMMMRDCWHAVPSQRPTFKQLVEDLDRILTLTTNEEYL
DLSQPLEQYSPSYPDTRSSCSSGDDSVFSPDPMPYEPCLPQYPHINGSVKT
```

Notes

"FGFR2 is phosphorylated on serine 779 (KEQYSP(pS779)YPDTRC) in response to FGF2. S779, which lies adjacent to the phospholipase Cgamma binding site at Y766, provides a docking site for the 14-3-3 phosphoserine-binding proteins and is essential for the full activation of the phosphatidylinositol 3-kinase and Ras/mitogen-activated protein kinase pathways" (Lonic et al 2008). Ser779 signaling is essential for promoting cell survival and proliferation in both Ba/F3 cells and BALB/c 3T3 fibroblasts.

Ser776 is conserved across mammalian species in both FGFR2 and FGFR1, and similar sites in other receptors (Lonic et al 2008).

FGFR2 (Bek) 763 NEE**Y**LLSQPLE......................QYSP**S**YP P21802
GM-CSF/IL-3/IL-5 receptor βc subunit c 590 NGP**Y**LGPP..........HSR**S**LP NP_000386
FGFR1(Flg) 763 NQE**Y**LDLSIPLD.....................QYSP**S**FP P11362
ErbB4 1239 NPD**Y**..............................WNH**S**LP NP_005226
Low-density lipoprotein receptor-related protein 1 4470
NPT**Y**KMYEGGEPDDVGGLLDADFALDPD....KPTNF**T**NP Q07954
Low-density lipoprotein receptor 802 NPV**Y**QKTTEDEVHICHN................QDGY**S**YP AAF24515
Very-low-density lipoprotein receptor 834 NPV**Y**LKTTEEDLSIDIG................RHSA**S**VG NP_003374
Integrin beta 1 (fibronectin receptor) 780 NPI**Y**.............KSAVT**T**VV NP_002202
Integrin beta 3 (platelet glycoprotein IIIa) 770 NPL**Y**KEA.........TSTF**T**NI NP_000203
Integrin beta-6 759 NPL**Y**R.......GSTS**T**FK A37057
Integrin beta-7 775 NPL**Y**KS...........................AITT**T**IN P26010
ErbB3 972 PPR**Y**LVI...........................KRE**S**GP P21860
FLT3 receptor tyrosine kinase 916 EEI**Y**IIMQSCWAFDS........RKRP**S**FP CAA81393
Vascular endothelial growth factor receptor 2 1220 ISQ**Y**LQNS..........................KRK**S**RP AAC16450
Granulocyte colony stimulating factor receptor 764 PGH**Y**L.............................RDS**T**QP Q99062
IL-6 receptor beta chain (glycoprotein 130) 764 HSG**Y**RHQVPSVQVFS.....RSES**T**QP P40189
TrkB tyrosine kinase (BDNF/NT-3 receptor) 752 QPW**Y**QLSNNEVIECITQGRVL............QRPR**T**CP Q16620
Platelet-derived growth factor receptor alpha 608 GTA**Y**........GLSR**S**QP P16234
c-Met 1023 QVQ**Y**PLTDMSPILTSG.................DSDI**S**SP P08581
Macrophage-stimulating protein receptor (p185-Ron) 1357
PAT**Y**MNLGPSTSHEMNVRPEQPQFSPMPGNVRRPRPL**S**EP Q04912
IGF-1R 1278 SFY**Y**SEENKLPEPEELDLEPENMESVPLD..PSASSS**S**LP NP_000866

TABLE 1 in Lonic et al (2008) Identification of putative conserved phosphotyrosine/serine motifs in diverse cell surface receptors. The tyrosine and serine residues in boldface in each motif are conserved between at least three species including, human, mouse, and rat.

References to 14-3-3 binding to FGFR2

Lonic A, Barry EF, Quach C, Kobe B, Saunders N, Guthridge MA. Fibroblast Growth Factor Receptor 2 Phosphorylation on Serine 779 Couples to 14-3-3 and Regulates Cell Survival and Proliferation. Mol Cell Biol. 2008 May;28(10):3372-85.

Human FOXO1 Forkhead box protein O1 transcription factor (FKHR) (FOXO1A) (Swissprot = Q12778)

```
        1 MAEAPQVVEI DPDFEPLPRP RSCtWPLPRP EFSQSNSATS SPAPSGSAAA NPDAAAGLPS
       61 ASAAAVSADF MSNLSLLEES EDFPQAPGSV AAAVAAAAAA AATGGLCGDF QGPEAGCLHP
      121 APPQPPPPGP LSQHPPVPPA AAGPLAGQPR KSSSSRRNAW GNLSYADLIT KAIESSAEKR
      181 LTLSQIYEWM VKSVPYFKDK GDSNSSAGWK NSIRHNLSLH SKFIRVQNEG TGKSSWWMLN
      241 PEGGKSGKSP RRRAAsMDNN SKFAKSRSRA AKKKASLQSG QEGAGDSPGS QFSKWPASPG
      301 SHSNDDFDNW STFRPRTSSN ASTISGRLSP IMTEQDDLGE GDVHSMVYPP SAAKMASTLP
      361 SLSEISNPEN MENLLDNLNL LSSPTSLTVS TQSSPGTMMQ QTPCYSFAPP NTSLNSPSPN
      421 YQKYTYGQSS MSPLPQMPIQ TLQDNKSSYG GMSQYNCAPG LLKELLTSDS PPHNDIMTPV
      481 DPGVAQPNSR VLGQNVMMGP NSVMSTYGSQ ASHNKMMNPS SHTHPGHAQQ TSAVNGRPLP
      541 HTVSTMPHTS GMNRLTQVKT PVQVPLPHPM QMSALGGYSS VSSCNGYGRM GLLHQEKLPS
      601 DLDGMFIERL DCDMESIIRN DLMDGDTLDF NFDNVLPNQS FPHSVKTTTH SWVSG
>gi|116241368|sp|Q12778.2|FOXO1_HUMAN RecName: Full=Forkhead box protein O1;
AltName: Full=Forkhead box protein O1A; AltName: Full=Forkhead in
rhabdomyosarcoma
MAEAPQVVEIDPDFEPLPRPRSCTWPLPRPEFSQSNSATSSPAPSGSAAANPDAAAGLPSASAAAVSADF
MSNLSLLEESEDFPQAPGSVAAAVAAAAAAAATGGLCGDFQGPEAGCLHPAPPQPPPPGPLSQHPPVPPA
AAGPLAGQPRKSSSSRRNAWGNLSYADLITKAIESSAEKRLTLSQIYEWMVKSVPYFKDKGDSNSSAGWK
NSIRHNLSLHSKFIRVQNEGTGKSSWWMLNPEGGKSGKSPRRRAASMDNNSKFAKSRSRAAKKKASLQSG
QEGAGDSPGSQFSKWPASPGSHSNDDFDNWSTFRPRTSSNASTISGRLSPIMTEQDDLGEGDVHSMVYPP
SAAKMASTLPSLSEISNPENMENLLDNLNLLSSPTSLTVSTQSSPGTMMQQTPCYSFAPPNTSLNSPSPN
YQKYTYGQSSMSPLPQMPIQTLQDNKSSYGGMSQYNCAPGLLKELLTSDSPPHNDIMTPVDPGVAQPNSR
VLGQNVMMGPNSVMSTYGSQASHNKMMNPSSHTHPGHAQQTSAVNGRPLPHTVSTMPHTSGMNRLTQVKT
PVQVPLPHPMQMSALGGYSSVSSCNGYGRMGLLHQEKLPSDLDGMFIERLDCDMESIIRNDLMDGDTLDF
NFDNVLPNQSFPHSVKTTTHSWVSG
```

Notes

FOXO1A a transcription factors of the forkhead family. Contains 1 fork-head domain. May play a role in myogenic growth and differentiation. Translocation of this gene with PAX3 has been associated with alveolar rhabdomyosarcoma. Phosphorylated FOXO1 binds 14-3-3 proteins, and co-precipitation studies with tagged proteins indicate that 14-3-3 binding involves co-operative interactions with both Thr-24 and Ser-256. Ser-256 is located in the C-terminal region of the DBD, where 14-3-3 proteins may interfere both with DNA-binding and with nuclear-localization functions.

Multiple elements regulate nuclear/cytoplasmic shuttling of FOXO1: characterization of phosphorylation- and 14-3-3-dependent and -independent mechanisms. Zhao X, Gan L, Pan H, Kan D, Majeski M, Adam SA, Unterman TG.

Yuan Z, Lehtinen MK, Merlo P, Villén J, Gygi S, Bonni A. Regulation of neuronal cell death by MST1-FOXO1 signaling. J Biol Chem. 2009 Apr 24;284(17):11285-92.

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Won CK, Ji HH, Koh PO. Estradiol prevents the focal cerebral ischemic injury-induced decrease of forkhead transcription factors phosphorylation. Neurosci Lett. 2006 May 1;398(1-2):39-43.

Woods YL, Rena G. Effect of multiple phosphorylation events on the transcription factors FKHR, FKHRL1 and AFX. Biochem Soc Trans. 2002 Aug;30(4):391-7.

Rena G, Prescott AR, Guo S, Cohen P, Unterman TG. Roles of the forkhead in rhabdomyosarcoma (FKHR) phosphorylation sites in regulating 14-3-3 binding, transactivation and nuclear targetting. Biochem J. 2001 Mar 15;354(Pt 3):605-12.

Morishita D, Katayama R, Sekimizu K, Tsuruo T, Fujita N. Pim kinases promote cell cycle progression by phosphorylating and down-regulating p27Kip1 at the transcriptional and posttranscriptional levels. Cancer Res. 2008 Jul 1;68(13):5076-85.

Yuan Z, Becker EB, Merlo P, Yamada T, DiBacco S, Konishi Y, Schaefer EM, Bonni A. Activation of FOXO1 by Cdk1 in cycling cells and postmitotic neurons. Science. 2008 Mar 21;319(5870):1665-8.

Human FOXO3 Forkhead box protein O3 (FKHRL1) (FOXO3A) (Swissprot = O43524)

```
       1 MAEAPASPAP LSPLEVELDP EFEPQSRPRS CtWPLQRPEL QASPAKPSGE TAADSMIPEE
      61 EDDEDDEDGG GRAGSAMAIG GGGGSGTLGS GLLLEDSARV LAPGGQDPGS GPATAAGGLS
     121 GGTQALLQPQ QPLPPPQPGA AGGSGQPRKC SSRRNAWGNL SYADLITRAI ESSPDKRLTL
     181 SQIYEWMVRC VPYFKDKGDS NSSAGWKNSI RHNLSLHSRF MRVQNEGTGK SSWWIINPDG
     241 GKSGKAPRRR AVsMDNSNKY TKSRGRAAKK KAALQTAPES ADDSPSQLSK WPGSPTSRSS
     301 DELDAWTDFR SRTNSNASTV SGRLSPIMAS TELDEVQDDD APLSPMLYSS SASLSPSVSK
     361 PCTVELPRLT DMAGTMNLND GLTENLMDDL LDNITLPPSQ PSPTGGLMQR SSSFPYTTKG
     421 SGLGSPTSSF NSTVFGPSSL NSLRQSPMQT IQENKPATFS SMSHYGNQTL QDLLTSDSLS
     481 HSDVMMTQSD PLMSQASTAV SAQNSRRNVM LRNDPMMSFA AQPNQGSLVN QNLLHHQHQT
     541 QGALGGSRAL SNSVSNMGLS ESSSLGSAKH QQQSPVSQSM QTLSDSLSGS SLYSTSANLP
     601 VMGHEKFPSD LDLDMFNGSL ECDMESIIRS ELMDADGLDF NFDSLISTQN VVGLNVGNFT
     661 GAKQASSQSW VPG
```

```
>gi|8134467|sp|O43524.1|FOXO3_HUMAN RecName: Full=Forkhead box protein O3;
AltName: Full=Forkhead in rhabdomyosarcoma-like 1; AltName: Full=AF6q21
protein
MAEAPASPAPLSPLEVELDPEFEPQSRPRSCTWPLQRPELQASPAKPSGETAADSMIPEEEDDEDDEDGG
GRAGSAMAIGGGGGSGTLGSGLLLEDSARVLAPGGQDPGSGPATAAGGLSGGTQALLQPQQPLPPPQPGA
AGGSGQPRKCSSRRNAWGNLSYADLITRAIESSPDKRLTLSQIYEWMVRCVPYFKDKGDSNSSAGWKNSI
RHNLSLHSRFMRVQNEGTGKSSWWIINPDGGKSGKAPRRRAVSMDNSNKYTKSRGRAAKKKAALQTAPES
ADDSPSQLSKWPGSPTSRSSDELDAWTDFRSRTNSNASTVSGRLSPIMASTELDEVQDDDAPLSPMLYSS
SASLSPSVSKPCTVELPRLTDMAGTMNLNDGLTENLMDDLLDNITLPPSQPSPTGGLMQRSSSFPYTTKG
SGLGSPTSSFNSTVFGPSSLNSLRQSPMQTIQENKPATFSSMSHYGNQTLQDLLTSDSLSHSDVMMTQSD
PLMSQASTAVSAQNSRRNVMLRNDPMMSFAAQPNQGSLVNQNLLHHQHQTQGALGGSRALSNSVSNMGLS
ESSSLGSAKHQQQSPVSQSMQTLSDSLSGSSLYSTSANLPVMGHEKFPSDLDLDMFNGSLECDMESIIRS
ELMDADGLDFNFDSLISTQNVVGLNVGNFTGAKQASSQSWVPG
```

Notes

Higher levels of FOXO3A in the cytosol correlated with phosphorylation at Ser253, which accounted for its nuclear exclusion.

FOXO4 (together wih FOXO1, FOXO3a and FOXO6) belongs to a small subfamily of the forkhead transcription factors, which is designated as FOXO.

References to 14-3-3 binding to FOXO3A

Shukla S, Shukla M, Maclennan GT, Fu P, Gupta S. Deregulation of FOXO3A during prostate cancer progression. Int J Oncol. 2009 Jun;34(6):1613-20.

Su B, Liu H, Wang X, Chen SG, Siedlak SL, Kondo E, Choi R, Takeda A, Castellani RJ, Perry G, Smith MA, Zhu X, Lee HG. Ectopic localization of FOXO3a protein in Lewy bodies in Lewy body dementia and Parkinson's disease. Mol Neurodegener. 2009 Jul 23;4:32.

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Morishita D, Katayama R, Sekimizu K, Tsuruo T, Fujita N. Pim kinases promote cell cycle progression by phosphorylating and down-regulating p27Kip1 at the transcriptional and posttranscriptional levels. Cancer Res. 2008 Jul 1;68(13):5076-85.

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Muñoz-Fontela C, Marcos-Villar L, Gallego P, Arroyo J, Da Costa M, Pomeranz KM, Lam EW, Rivas C. Latent protein LANA2 from Kaposi's sarcoma-associated herpesvirus interacts with 14-3-3 proteins and inhibits FOXO3a transcription factor. J Virol. 2007 Feb;81(3):1511-6.

Brunet A, Kanai F, Stehn J, Xu J, Sarbassova D, Frangioni JV, Dalal SN, DeCaprio JA, Greenberg ME, Yaffe MB. 14-3-3 transits to the nucleus and participates in dynamic nucleocytoplasmic transport. J Cell Biol. 2002 Mar 4;156(5):817-28. Erratum in: J Cell Biol 2002 Apr 29;157(3):533.

Brunet A, Bonni A, Zigmond MJ, Lin MZ, Juo P, Hu LS, Anderson MJ, Arden KC, Blenis J, Greenberg ME. Akt promotes cell survival by phosphorylating and inhibiting a Forkhead transcription factor. Cell. 1999 Mar 19;96(6):857-68.

Human FOXO4 Forkhead box protein O4 (AFX, AFX1, MLLT7)) (Swissprot = P98177)

```
        1 MDPGNENSAT EAAAIIDLDP DFEPQSRPRS CtWPLPRPEI ANQPSEPPEV EPDLGEKVHT
       61 EGRSEPILLP SRLPEPAGGP QPGILGAVTG PRKGGSRRNA WGNQSYAELI SQAIESAPEK
      121 RLTLAQIYEW MVRTVPYFKD KGDSNSSAGW KNSIRHNLSL HSKFIKVHNE ATGKSSWWML
      181 NPEGGKSGKA PRRRAAsMDS SSKLLRGRSK APKKKPSVLP APPEGATPTS PVGHFAKWSG
      241 SPCSRNREEA DMWTTFRPRS SSNASSVSTR LSPLRPESEV LAEEIPASVS SYAGGVPPTL
      301 NEGLELLDGL NLTSSHSLLS RSGLSGFSLQ HPGVTGPLHT YSSSLFSPAE GPLSAGEGCF
      361 SSSQALEALL TSDTPPPPAD VLMTQVDPIL SQAPTLLLLG GLPSSSKLAT GVGLCPKPLE
      421 APGPSSLVPT LSMIAPPPVM ASAPIPKALG TPVLTPPTEA ASQDRMPQDL DLDMYMENLE
      481 CDMDNIISDL MDEGEGLDFN FEPDP
>gi|110825720|sp|P98177.5|FOXO4_HUMAN RecName: Full=Forkhead box protein O4; AltName: Full=Fork head domain transcription factor AFX1
MDPGNENSATEAAAIIDLDPDFEPQSRPRSCTWPLPRPEIANQPSEPPEVEPDLGEKVHTEGRSEPILLP
SRLPEPAGGPQPGILGAVTGPRKGGSRRNAWGNQSYAELISQAIESAPEKRLTLAQIYEWMVRTVPYFKD
KGDSNSSAGWKNSIRHNLSLHSKFIKVHNEATGKSSWWMLNPEGGKSGKAPRRRAASMDSSSKLLRGRSK
APKKKPSVLPAPPEGATPTSPVGHFAKWSGSPCSRNREEADMWTTFRPRSSSNASSVSTRLSPLRPESEV
LAEEIPASVSSYAGGVPPTLNEGLELLDGLNLTSSHSLLSRSGLSGFSLQHPGVTGPLHTYSSSLFSPAE
GPLSAGEGCFSSSQALEALLTSDTPPPPADVLMTQVDPILSQAPTLLLLGGLPSSSKLATGVGLCPKPLE
APGPSSLVPTLSMIAPPPVMASAPIPKALGTPVLTPPTEAASQDRMPQDLDLDMYMENLECDMDNIISDL
MDEGEGLDFNFEPDP
```

Notes

AKT/PKB phosphorylation site Ser193

References to 14-3-3 binding to FOXO4

Silhan J, Vacha P, Strnadova P, Vecer J, Herman P, Sulc M, Teisinger J, Obsilova V, Obsil T. 14-3-3 protein masks the DNA binding interface of forkhead transcription factor FOXO4. J Biol Chem. 2009 Jul 17;284(29):19349-60.

Boura E, Silhan J, Herman P, Vecer J, Sulc M, Teisinger J, Obsilova V, Obsil T. Both the N-terminal loop and wing W2 of the forkhead domain of transcription factor Foxo4 are important for DNA binding. J Biol Chem. 2007 Mar 16;282(11):8265-75.

Obsilova V, Vecer J, Herman P, Pabianova A, Sulc M, Teisinger J, Boura E, Obsil T. 14-3-3 Protein interacts with nuclear localization sequence of forkhead transcription factor FoxO4. Biochemistry. 2005 Aug 30;44(34):11608-17.

Human GAB2 GRB2-associated binding protein 2 (Swissprot = Q9UQC2)

```
        1 MSGGGDVVCT GWLRKSPPEK KLRRYAWKKR WFILRSGRMS GDPDVLEYYK NDHSKKPLRI
       61 INLNFCEQVD AGLTFNKKEL QDSFVFDIKT SERTFYLVAE TEEDMNKWVQ SICQICGFNQ
      121 AEESTDSLRN VSSAGHGPRS SPAELSSSSQ HLLRERKSSA PSHSSQPTLF TFEPPVSNHM
      181 QPTLSTSAPQ EYLYLHQCIS RRAENARSAs FSQGTRASFL MRSDTAVQKL AQGNGHCVNG
      241 ISGQVHGFYS LPKPSRHNTE FRDSTYDLPR SLASHGHTKG SLTGSETDNE DVYTFKTPSN
      301 TLCREFGDLL VDNMDVPATP LSAYQIPRTF TLDKNHNAMT VATPGDSAIA PPPRPPKPSQ
      361 AETPRWGSPQ QRRPISENSR SVAATIPRRN tLPAMDNSRL HRASSCETYE YPQRGGESAG
      421 RSAESMSDGV GSFLPGKMIV GRSDSTNSED NYVPMNPGSS TLLAMERAGD NSQSVYIPMS
      481 PGAHHFDSLG YPSTTLPVHR GPSRGSEIQP PPVNRNLKPD RKAKPTPLDL RNNTVIDELP
      541 FKSPITKSWS RANHTFNSSS SQYCRPISTQ SITSTDSGDS EENYVPMQNP VSASPVPSGT
      601 NSPAPKKSTG SVDYLALDFQ PSSPSPHRKP STSSVTSDEK VDYVQVDKEK TQALQNTMQE
      661 WTDVRQSSEP SKGAKL
>gi|46396035|sp|Q9UQC2.1|GAB2_HUMAN RecName: Full=GRB2-associated-binding protein 2; AltName: Full=Growth factor receptor bound protein 2-associated protein 2; AltName: Full=GRB2-associated binder 2; AltName: Full=pp100
MSGGGDVVCTGWLRKSPPEKKLRRYAWKKRWFILRSGRMSGDPDVLEYYKNDHSKKPLRIINLNFCEQVD
AGLTFNKKELQDSFVFDIKTSERTFYLVAETEEDMNKWVQSICQICGFNQAEESTDSLRNVSSAGHGPRS
SPAELSSSSQHLLRERKSSAPSHSSQPTLFTFEPPVSNHMQPTLSTSAPQEYLYLHQCISRRAENARSAS
FSQGTRASFLMRSDTAVQKLAQGNGHCVNGISGQVHGFYSLPKPSRHNTEFRDSTYDLPRSLASHGHTKG
SLTGSETDNEDVYTFKTPSNTLCREFGDLLVDNMDVPATPLSAYQIPRTFTLDKNHNAMTVATPGDSAIA
PPPRPPKPSQAETPRWGSPQQRRPISENSRSVAATIPRRNTLPAMDNSRLHRASSCETYEYPQRGGESAG
RSAESMSDGVGSFLPGKMIVGRSDSTNSEDNYVPMNPGSSTLLAMERAGDNSQSVYIPMSPGAHHFDSLG
YPSTTLPVHRGPSRGSEIQPPPVNRNLKPDRKAKPTPLDLRNNTVIDELPFKSPITKSWSRANHTFNSSS
SQYCRPISTQSITSTDSGDSEENYVPMQNPVSASPVPSGTNSPAPKKSTGSVDYLALDFQPSSPSPHRKP
STSSVTSDEKVDYVQVDKEKTQALQNTMQEWTDVRQSSEPSKGAKL
```

Notes

"Growth factor-induced phosphorylation of Gab2 on two residues, S210 and T391, leads to recruitment of 14-3-3 proteins. Together, these events mediate negative-feedback regulation, as Gab2(S210A/T391A) exhibits sustained receptor association and signalling and promotes cell proliferation and transformation." In human Gab2, NARSA(pS210)FSQGT and IPRRN(pT391)LPAM (conserved in Gab2 from mouse, rat, Monodelphis, Gallus, Tetraodon), but not conserved in Gab1 and Gab3. Binding of 14-3-3 proteins attenuate Grb2 binding to Gab2. (Bummer et al 2008)."

References to 14-3-3 binding to Gab2

Brummer T, Larance M, Herrera Abreu MT, Lyons RJ, Timpson P, Emmerich CH, Fleuren ED, Lehrbach GM, Schramek D, Guilhaus M, James DE, Daly RJ. Phosphorylation-dependent binding of 14-3-3 terminates signalling by the Gab2 docking protein. EMBO J. 2008 Sep 3;27(17):2305-16.

Human GEM Kir/Gem, with Rad, Rem and Rem2, is a member of the RGK small GTP-binding protein family (Swissprot = P55040)

```
        1 MTLNNVTMRQ GTVGMQPQQQ RWsIPADGRH LMVQKEPHQY SHRNRHSATP EDHCRRSWSS
       61 DSTDSVISSE SGNTYYRVVL IGEQGVGKST LANIFAGVHD SMDSDCEVLG EDTYERTLMV
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121 DGESATIILL DMWENKGENE WLHDHCMQVG DAYLIVYSIT DRASFEKASE LRIQLRRARQ 181 TEDIPIILVG NKSDLVRCRE VSVSEGRACA VVFDCKFIET SAAVQHNVKE LFEGIVRQVR 241 LRRDSKEKNE RRLAYQKRKE SMPRKARRFW GKIVAKNNKN MAFKLKSKsC HDLSVL >gi|1707896|sp|P55040.1|GEM_HUMAN RecName: Full=GTP-binding protein GEM; AltName: Full=GTP-binding mitogen-induced T-cell protein; AltName: Full=RAS-like protein KIR MTLNNVTMRQGTVGMQPQQQRWSIPADGRHLMVQKEPHQYSHRNRHSATPEDHCRRSWSSDSTDSVISSE SGNTYYRVVLIGEQGVGKSTLANIFAGVHDSMDSDCEVLGEDTYERTLMVDGESATIILLDMWENKGENE WLHDHCMQVGDAYLIVYSITDRASFEKASELRIQLRRARQTEDIPIILVGNKSDLVRCREVSVSEGRACA VVFDCKFIETSAAVQHNVKELFEGIVRQVRLRRDSKEKNERRLAYQKRKESMPRKARRFWGKIVAKNNKN MAFKLKSKSCHDLSVL **Notes** Human - Phosphorylation of serine 289 in conjunction with serine 23 results in bidentate 14-3-3 binding, leading to increased Gem protein half-life (Ward et al 2004). **References to 14-3-3 binding to Kir/Gem** Mahalakshmi RN, Nagashima K, Ng MY, Inagaki N, Hunziker W, Béguin P.Nuclear transport of Kir/Gem requires specific signals and importin alpha5 and is regulated by calmodulin and predicted serine phosphorylations. Traffic. 2007 Sep;8(9):1150-63. Mahalakshmi RN, Ng MY, Guo K, Qi Z, Hunziker W, Béguin P. Nuclear localization of endogenous RGK proteins and modulation of cell shape remodeling by regulated nuclear transport. Traffic. 2007 Sep;8(9):1164-78. Béguin P, Mahalakshmi RN, Nagashima K, Cher DH, Takahashi A, Yamada Y, Seino Y, Hunziker W. 14-3-3 and calmodulin control subcellular distribution of Kir/Gem and its regulation of cell shape and calcium channel activity. J Cell Sci. 2005 May 1;118(Pt 9):1923-34. Ward Y, Spinelli B, Quon MJ, Chen H, Ikeda SR, Kelly K. Phosphorylation of critical serine residues in Gem separates cytoskeletal reorganization from down-regulation of calcium channel activity. Mol Cell Biol. 2004 Jan;24(2):651-61.	
Human GFAP Glial fibrillary acidic protein (Swissprot = P14136) 1 MERRRITsAA RRSYVSSGEM MVGGLAPGRR LGPGTRLSLA RMPPPLPTRV DFSLAGALNA 61 GFKETRASER AEMMELNDRF ASYIEKVRFL EQQNKALAAE LNQLRAKEPT KLADVYQAEL 121 RELRLRLDQL TANSARLEVE RDNLAQDLAT VRQKLQDETN LRLEAENNLA AYRQEADEAT 181 LARLDLERKI ESLEEEIRFL RKIHEEEVRE LQEQLARQQV HVELDVAKPD LTAALKEIRT 241 QYEAMASSNM HEAEEWYRSK FADLTDAAAR NAELLRQAKH EANDYRRQLQ SLTCDLESLR 301 GTNESLERQM REQEERHVRE AASYQEALAR LEEEGQSLKD EMARHLQEYQ DLLNVKLALD 361 IEIATYRKLL EGEENRITIP VQTFSNLQIR ETSLDTKSVS EGHLKRNIVV KTVEMRDGEV 421 IKESKQEHKD VM >gi|121135|sp|P14136.1|GFAP_HUMAN RecName: Full=Glial fibrillary acidic protein; Short=GFAP MERRRITSAARRSYVSSGEMMVGGLAPGRRLGPGTRLSLARMPPPLPTRVDFSLAGALNAGFKETRASER AEMMELNDRFASYIEKVRFLEQQNKALAAELNQLRAKEPTKLADVYQAELRELRLRLDQLTANSARLEVE RDNLAQDLATVRQKLQDETNLRLEAENNLAAYRQEADEATLARLDLERKIESLEEEIRFLRKIHEEEVRE LQEQLARQQVHVELDVAKPDLTAALKEIRTQYEAMASSNMHEAEEWYRSKFADLTDAAARNAELLRQAKH EANDYRRQLQSLTCDLESLRGTNESLERQMREQEERHVREAASYQEALARLEEEGQSLKDEMARHLQEYQ DLLNVKLALDIEIATYRKLLEGEENRITIPVQTFSNLQIRETSLDTKSVSEGHLKRNIVVKTVEMRDGEV IKESKQEHKDVM **Notes** GFAP a class-III intermediate filament protein. A cell-specific marker that, during the development of the central nervous system, distinguishes astrocytes from other glial cells. Mutations in this gene cause Alexander disease, a rare disorder of astrocytes in the central nervous system. An additional transcript variant isoform has been described.14-3-3gamma associates with both soluble and filamentous GFAP in a phosphorylation- and cell-cycle-dependent manner in primary cultured astrocytes. The amount of association increases during G2/M phase due to more phosphorylated GFAP. Serine 8 in the head domain is essential for the direct association of GFAP to 14-3-3gamma. Overexpression of 14-3-3gamma destroyed the integrity and affected the movement of GFAP intermediate filaments. This data demonstrates that 14-3-3gamma contributes to the regulation of dynamics of GFAP filaments, which may contribute to the stability of the cytoskeleton and the mechanisms of central nervous system neurodegenerative disease. **References to 14-3-3 binding to GFAP** Li H, Guo Y, Teng J, Ding M, Yu AC, Chen J. 14-3-3gamma affects dynamics and integrity of glial filaments by binding to phosphorylated GFAP. J Cell Sci. 2006 Nov 1;119(Pt 21):4452-61.	
Human GIT1 (G protein-coupled receptor kinase-interactor 1) **Notes** **References to 14-3-3 binding to GIT1** Angrand PO, Segura I, Völkel P, Ghidelli S, Terry R, Brajenovic M, Vintersten K, Klein R, Superti-Furga G, Drewes G, Kuster B, Bouwmeester T, Acker-Palmer A. Transgenic mouse proteomics identifies new 14-3-3-associated proteins involved in cytoskeletal rearrangements and cell signaling. Mol Cell Proteomics. 2006 Dec;5(12):2211-27.	SITES NOT REPORTED. NOT IN WEBLOGO.
Human Gli1 GLI family zinc finger 1 (Glioma-associated oncogene) transcription factor (Swissprot = P08151) 1 MFNSMTPPPI SSYGEPCCLR PLPSQGAPSV GTEGLSGPPF CHQANLMSGP HSYGPARETN 61 SCTEGPLFSS PRSAVKLTKK RALSISPLSD ASLDLQTVIR TSPSSLVAFI NSRCTSPGGS 121 YGHLSIGTMS PSLGFPAQMN HQKGPSPSFG VQPCGPHDSA RGGMIPHPQS RGPFPTCQLK 181 SELDMLVGKC REEPLEGDMS SPNSTGIQDP LLGMLDGRED LEREEKREPE SVYETDCRWD 241 GCSQEFDSQE QLVHHINSEH IHGERKEFVC HWGGCSRELR PFKAQYMLVV HMRRHTGEKP 301 HKCTFEGCRK SYSRLENLKT HLRSHTGEKP YMCEHEGCSK AFSNASDRAK HQNRTHSNEK 361 PYVCKLPGCT KRYTDPSSLR KHVKTVHGPD AHVTKRHRGD GPLPRAPSIS TVEPKREREG 421 GPIREESRLT VPEGAMKPQP SPGAQSSCSS DHSPAGSAAN TDSGVEMTGN AGGSTEDLSS 481 LDEGPCIAGT GLSTLRRLEN LRLDQLHQLR PIGTRGLKLP SLSHTGTTVS RRVGPPVSLE 541 RRSSSSSSIS SAYTVSRRSS LASPFPPGSP PENGASSLPG LMPAQHYLLR ARYASARGGG	

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      601 TSPTAASSLD RIGGLPMPPW RSRAEYPGYN PNAGVTRRAs DPAQAADRPA PARVQRFKSL
      661 GCVHTPPTVA GGGQNFDPYL PTSVYSPQPP SITENAAMDA RGLQEEPEVG TSMVGSGLNP
      721 YMDFPPTDTL GYGGPEGAAA EPYGARGPGS LPLGPGPPTN YGPNPCPQQA SYPDPTQETW
      781 GEFPSHSGLY PGPKALGGTY SQCPRLEHYG QVQVKPEQGC PVGSDSTGLA PCLNAHPSEG
      841 PPHPQPLFSH YPQPSPPQYL QSGPYTQPPP DYLPSEPRPC LDFDSPTHST GQLKAQLVCN
      901 YVQSQQELLW EGGGREDAPA QEPSYQSPKF LGGSQVSPSR AKAPVNTYGP GFGPNLPNHK
      961 SGSYPTPSPC HENFVVGANR ASHRAAAPPR LLPPLPTCYG PLKVGGTNPS CGHPEVGRLG
     1021 GGPALYPPPE GQVCNPLDSL DLDNTQLDFV AILDEPQGLS PPPSHDQRGS SGHTPPPSGP
     1081 PNMAVGNMSV LLRSLPGETE FLNSSA
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Notes

Similar PKA-phosphorylated sites in Gli1, Gli2 and Gli3 (see other entries).

References to 14-3-3 binding to Gli1

Asaoka Y, Kanai F, Ichimura T, Tateishi K, Tanaka Y, Ohta M, Seto M, Tada M, Ijichi H, Ikenoue T, Kawabe T, Isobe T, Yaffe MB, Omata M. Identification of a suppressive mechanism for hedgehog signaling through a novel interaction of Gli with 14-3-3. J Biol Chem. 2009 Dec 7. [Epub ahead of print]

Human Gli2 GLI family zinc finger 2 (Tax helper protein) transcription factor (Swissprot = P10070)

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1 METSASATAS EKQEAKSGIL EAAGFPDPGK KASPLVVAAA AAAAVAAQGV PQHLLPPFHA
       61 PLPIDMRHQE GRYHYEPHSV HGVHGPPALS GSPVISDISL IRLSPHPAGP GESPFNAPHP
      121 YVNPHMEHYL RSVHSSPTLS MISAARGLSP ADVAQEHLKE RGLFGLPAPG TTPSDYYHQM
      181 TLVAGHPAPY GDLLMQSGGA ASAPHLHDYL NPVDVSRFSS PRVTPRLSRK RALSISPLSD
      241 ASLDLQRMIR TSPNSLVAYI NNSRSSSAAS GSYGHLSAGA LSPAFTFPHP INPVAYQQIL
      301 SQQRGLGSAF GHTPPLIQPS PTFLAQQPMA LTSINATPTQ LSSSSNCLSD TNQNKQSSES
      361 AVSSTVNPVA IHKRSKVKTE PEGLRPASPL ALTQGQVSGH GSCGCALPLS QEQLADLKED
      421 LDRDDCKQEA EVVIYETNCH WEDCTKEYDT QEQLVHHINN EHIHGEKKEF VCRWQACTRE
      481 QKPFKAQYML VVHMRRHTGE KPHKCTFEGC SKAYSRLENL KTHLRSHTGE KPYVCEHEGC
      541 NKAFSNASDR AKHQNRTHSN EKPYICKIPG CTKRYTDPSS LRKHVKTVHG PDAHVTKKQR
      601 NDVHLRTPLL KENGDSEAGT EPGGPESTEA SSTSQAVEDC LHVRAIKTES SGLCQSSPGA
      661 QSSCSSEPSP LGSAPNNDSG VEMPGTGPGS LGDLTALDDT PPGADTSALA APSAGGLQLR
      721 KHMTTMHRFE QLKKEKLKSL KDSCSWAGPT PHTRNTKLPP LPGSGSILEN FSGSGGGGPA
      781 GLLPNPRLSE LSASEVTMLS QLQERRDSST STVSSAYTVS RRSSGISPYF SSRRSSEASP
      841 LGAGRPHNAS SADSYDPIST DASRRSSEAS QCSGGSGLLN LTPAQQYSLR AKYAAATGGP
      901 PPTPLPGLER MSLRTRLALL DAPERTLPAG CPRPLGPRRG SDGPTYGHGH AGAAPAFPHE
      961 APGGGARRAs DPVRRPDALS LPRVQRFHST HNVNPGPLPP CADRRGLRLQ SHPSTDGGLA
     1021 RGAYSPRPPS ISENVAMEAV AAGVDGAGPE ADLGLPEDDL VLPDDVVQYI KAHASGALDE
     1081 GTGQVYPTES TGFSDNPRLP SPGLHGQRRM VAADSNVGPS APMLGGCQLG FGAPSSLNKN
     1141 NMPVQWNEVS SGTVDALASQ VKPPPFPQGN LAVVQQKPAF GQYPGYSPQG LQASPGGLDS
     1201 TQPHLQPRSG APSQGIPRVN YMQQLRQPVA GSQCPGMTTT MSPHACYGQV HPQLSPSTIS
     1261 GALNQFPQSC SNMPAKPGHL GHPQQTEVAP DPTTMGNRHR ELGVPDSALA GVPPPHPVQS
     1321 YPQQSHHLAA SMSQEGYHQV PSLLPARQPG FMEPQTGPMG VATAGFGLVQ PRPPLEPSPT
     1381 GRHRGVRAVQ QQLAYARATG HAMAAMPSSQ ETAEAVPKGA MGNMGSVPPQ PPPQDAGGAP
     1441 DHSMLYYYGQ IHMYEQDGGL ENLGSCQVMR SQPPQPQACQ DSIQPQPLPS PGVNQVSSTV
     1501 DSQLLEAPQI DFDAIMDDGD HSSLFSGALS PSLLHSLSQN SSRLTTPRNS LTLPSIPAGI
     1561 SNMAVGDMSS MLTSLAEESK FLNMMT
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Notes

Similar PKA-phosphorylated sites in Gli1, Gli2 and Gli3 (see other entries). In the form of Gli2 studied by Asaoka et al (2009 prepublication date), the 14-3-3-binding site (Ser970 in the reference sequence above) is at Ser975.

References to 14-3-3 binding to Gli2

Asaoka Y, Kanai F, Ichimura T, Tateishi K, Tanaka Y, Ohta M, Seto M, Tada M, Ijichi H, Ikenoue T, Kawabe T, Isobe T, Yaffe MB, Omata M. Identification of a suppressive mechanism for hedgehog signaling through a novel interaction of Gli with 14-3-3. J Biol Chem. 2009 Dec 7. [Epub ahead of print]

Human Gli3 GLI family zinc finger 3 transcription factor (Swissprot = P10071)

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1 MEAQSHSSTT TEKKKVENSI VKCSTRTDVS EKAVASSTTS NEDESPGQTY HRERRNAITM
       61 QPQNVQGLSK VSEEPSTSSD ERASLIKKEI HGSLPHVAEP SVPYRGTVFA MDPRNGYMEP
      121 HYHPPHLFPA FHPPVPIDAR HHEGRYHYDP SPIPPLHMTS ALSSSPTYPD LPFIRISPHR
      181 NPTAASESPF SPPHPYINPY MDYIRSLHSS PSLSMISATR GLSPTDAPHA GVSPAEYYHQ
      241 MALLTGQRSP YADIIPSAAT AGTGAIHMEY LHAMDSTRFS SPRLSARPSR KRTLSISPLS
      301 DHSFDLQTMI RTSPNSLVTI LNNSRSSSSA SGSYGHLSAS AISPALSFTY SSAPVSLHMH
      361 QQILSRQQSL GSAFGHSPPL IHPAPTFPTQ RPIPGIPTVL NPVQVSSGPS ESSQNKPTSE
      421 SAVSSTGDPM HNKRSKIKPD EDLPSPGARG QQEQPEGTTL VKEEGDKDES KQEPEVIYET
      481 NCHWEGCARE FDTQEQLVHH INNDHIHGEK KEFVCRWLDC SREQKPFKAQ YMLVVHMRRH
      541 TGEKPHKCTF EGCTKAYSRL ENLKTHLRSH TGEKPYVCEH EGCNKAFSNA SDRAKHQNRT
      601 HSNEKPYVCK IPGCTKRYTD PSSLRKHVKT VHGPEAHVTK KQRGDIHPRP PPPRDSGSHS
      661 QSRSPGRPTQ GALGEQQDLS NTTSKREECL QVKTVKAEKP MTSQPSPGGQ SSCSSQQSPI
      721 SNYSNSGLEL PLTDGGSIGD LSAIDETPIM DSTISTATTA LALQARRNPA GTKWMEHVKL
      781 ERLKQVNGMF PRLNPILPPK APAVSPLIGN GTQSNNTCSL GGPMTLLPGR SDLSGVDVTM
      841 LNMLNRRDSS ASTISSAYLS SRRSSGISPC FSSRRSSEAS QAEGRPQNVS VADSYDPIST
      901 DASRRSSEAS QSDGLPSLLS LTPAQQYRLK AKYAAATGGP PPTPLPNMER MSLKTRLALL
      961 GDALEPGVAL PPVHAPRRCS DGGAHGYGRR HLQPHDAPGH GVRRAsDPVR TGSEGLALPR
     1021 VPRFSSLSSC NPPAMATSAE KRSLVLQNYT RPEGGQSRNF HSSPCPPSIT ENVTLESLTM
     1081 DADANLNDED FLPDDVVQYL NSQNQAGYEQ HFPSALPDDS KVPHGPGDFD APGLPDSHAG
     1141 QQFHALEQPC PEGSKTDLPI QWNEVSSGSA DLSSSKLKCG PRPAVPQTRA FGFCNGMVVH
     1201 PQNPLRSGPA GGYQTLGENS NPYGGPEHLM LHNSPGSGTS GNAFHEQPCK APQYGNCLNR
     1261 QPVAPGALDG ACGAGIQASK LKSTPMQGSG GQLNFGLPVA PNESAGSMVN GMQNQDPVGQ
     1321 GYLAHQLLGD SMQHPGAGRP GQQMLGQISA TSHINIYQGP ESCLPGAHGM GSQPSSLAVV
     1381 RGYQPCASFG GSRRQAMPRD SLALQSGQLS DTSQTCRVNG IKMEMKGQPH PLCSNLQNYS
     1441 GQFYDQTVGF SQQDTKAGSF SISDASCLLQ GTSAKNSELL SPGANQVTST VDSLDSHDLE
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     1501 GVQIDFDAII DDGDHSSLMS GALSPSIIQN LSHSSSRLTT PRASLPFPAL SMSTTNMAIG
     1561 DMSSLLTSLA EESKFLAVMQ
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Notes

Similar PKA-phosphorylated sites in Gli1, Gli2 and Gli3 (see other entries). Phosphorylated 14-3-3-binding site is Ser1006.

References to 14-3-3 binding to Gli3

Asaoka Y, Kanai F, Ichimura T, Tateishi K, Tanaka Y, Ohta M, Seto M, Tada M, Ijichi H, Ikenoue T, Kawabe T, Isobe T, Yaffe MB, Omata M. Identification of a suppressive mechanism for hedgehog signaling through a novel interaction of Gli with 14-3-3. J Biol Chem. 2009 Dec 7. [Epub ahead of print]

Human GP1BA Glycocalicin; Platelet glycoprotein Ib alpha chain (GPIb alpha) (Swissprot = P07359)

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        1 MPLLLLLLLL PSPLHPHPIC EVSKVASHLE VNCDKRNLTA LPPDLPKDTT ILHLSENLLY
       61 TFSLATLMPY TRLTQLNLDR CELTKLQVDG TLPVLGTLDL SHNQLQSLPL LGQTLPALTV
      121 LDVSFNRLTS LPLGALRGLG ELQELYLKGN ELKTLPPGLL TPTPKLEKLS LANNNLTELP
      181 AGLLNGLENL DTLLLQENSL YTIPKGFFGS HLLPFAFLHG NPWLCNCEIL YFRRWLQDNA
      241 ENVYVWKQGV DVKAMTSNVA SVQCDNSDKF PVYKYPGKGC PTLGDEGDTD LYDYYPEEDT
      301 EGDKVRATRT VVKFPTKAHT TPWGLFYSWS TASLDSQMPS SLHPTQESTK EQTTFPPRWT
      361 PNFTLHMESI TFSKTPKSTT EPTPSPTTSE PVPEPAPNMT TLEPTPSPTT PEPTSEPAPS
      421 PTTPEPTPIP TIATSPTILV SATSLITPKS TFLTTTKPVS LLESTKKTIP ELDQPPKLRG
      481 VLQGHLESSR NDPFLHPDFC CLLPLGFYVL GLFWLLFASV VLILLLSWVG HVKPQALDSG
      541 QGAALTTATQ TTHLELQRGR QVTVPRAWLL FLRGsLPTFR SSLFLWVRPN GRVGPLVAGR
      601 RPSALsQGRG QDLLSTVSIR YSGHS
>gi|121531|sp|P07359.1|GP1BA_HUMAN RecName: Full=Platelet glycoprotein Ib
alpha chain; Short=Glycoprotein Ibalpha; Short=GP-Ib alpha; Short=GPIb-alpha;
Short=GPIbA; AltName: Full=Antigen CD42b-alpha; AltName: CD_antigen=CD42b;
Contains: RecName: Full=Glycocalicin; Flags: Precursor
MPLLLLLLLLPSPLHPHPICEVSKVASHLEVNCDKRNLTALPPDLPKDTTILHLSENLLYTFSLATLMPY
TRLTQLNLDRCELTKLQVDGTLPVLGTLDLSHNQLQSLPLLGQTLPALTVLDVSFNRLTSLPLGALRGLG
ELQELYLKGNELKTLPPGLLTPTPKLEKLSLANNNLTELPAGLLNGLENLDTLLLQENSLYTIPKGFFGS
HLLPFAFLHGNPWLCNCEILYFRRWLQDNAENVYVWKQGVDVKAMTSNVASVQCDNSDKFPVYKYPGKGC
PTLGDEGDTDLYDYYPEEDTEGDKVRATRTVVKFPTKAHTTPWGLFYSWSTASLDSQMPSSLHPTQESTK
EQTTFPPRWTPNFTLHMESITFSKTPKSTTEPTPSPTTSEPVPEPAPNMTTLEPTPSPTTPEPTSEPAPS
PTTPEPTPIPTIATSPTILVSATSLITPKSTFLTTTKPVSLLESTKKTIPELDQPPKLRGVLQGHLESSR
NDPFLHPDFCCLLPLGFYVLGLFWLLFASVVLILLLSWVGHVKPQALDSGQGAALTTATQTTHLELQRGR
QVTVPRAWLLFLRGSLPTFRSSLFLWVRPNGRVGPLVAGRRPSALSQGRGQDLLSTVSIRYSGHSL
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Notes

Underlined is the signal sequence, papers quote residue numbers that do not include this.

From references in Bialkowska et al (2003) (to Proc Natl Acad Sci U S A. 1987 August; 84(16): 5615–5619. PMCID: PMC298913). Truncation of the last 19 aa prevents 14-3-3 binding although there is no obvious 14-3-3 consensus.

Mangin et al (2009) S609 is phosphorylated in resting platlets (phosphospecific antibody) and so is the 580-590 peptide S590A reduces co-ip of 14-3-3 zeta although S587A also weakens the interaction but to a lesser extent. Dephosphorylation of these sites appears after adherence to a VWF matrix

Inhibitors of PKA and PKG have no effect on S609 phosphoryation

Forskolin does not induce incorporation of 32P in the 580-590 peptide

S590 and S609 are 19 residues apart

"GPIb/VWF signaling leads to the mobilization of intracellular Ca2+, platelet shape change, and activation of integrin {alpha}IIb{beta}3." Filamin binds 570-580

Human platelets were tested for 14-3-3 expression and all isoforms found except sigma.

CHO cells were tested and they found all isoforms except sigma. S587A/S590A double mutant abolished co-ip of endogenous 14-3-3s in CHO cells as did deletion of S605-610.

RLpS^{166}LTDP, RYSGHSL^{610}-$_{\text{COOH}}$

In Yuan et al 92009) the R557GpSLP561 sequence is reported to bind to 14-3-3 (with pS equivalent to pSer575 in P07359.

References to 14-3-3-binding to GPIb α subunit of platelet membrane glycoprotein Ib

Bialkowska K, Zaffran Y, Meyer SC, Fox JE. 14-3-3 zeta mediates integrin-induced activation of Cdc42 and Rac. Platelet glycoprotein Ib-IX regulates integrin-induced signaling by sequestering 14-3-3 zeta. J Biol Chem. **2003** Aug 29;278(35):33342-5

Dai K, Bodnar R, Berndt MC, Du X.A critical role for 14-3-3zeta protein in regulating the VWF binding function of platelet glycoprotein Ib-IX and its therapeutic implications. Blood. 2005 Sep 15;106(6):1975-81.

Mu FT, Andrews RK, Arthur JF, Munday AD, Cranmer SL, Jackson SP, Stomski FC, Lopez AF, Berndt MC. A functional 14-3-3zeta-independent association of PI3-kinase with glycoprotein Ib alpha, the major ligand-binding subunit of the platelet glycoprotein Ib-IX-V complex. Blood. 2008 May 1;111(9):4580-7. Epub 2008 Feb 25.

Mangin PH, Receveur N, Wurtz V, David T, Gachet C, Lanza F. Identification of five novel 14-3-3 isoforms interacting with the GPIb-IX complex in Platelets. J Thromb Haemost. 2009 Jun 24. [Epub ahead of print]

Yuan Y, Zhang W, Yan R, Liao Y, Zhao L, Ruan C, Du X, Dai K. Identification of a Novel 14-3-3{zeta} Binding Site Within the Cytoplasmic Domain of Platelet Glycoprotein Ib{alpha} That Plays a Key Role in Regulating the von Willebrand Factor Binding Function of Glycoprotein Ib-IX. Circ Res. 2009 Oct 29. [Epub ahead of print]

Human Gremlin 1 **14-3-3-binding sites not defined precisely**

Gremlin 1 **14-3-3-binding sites not defined precisely**

References to 14-3-3 binding to Gremlin 1

Namkoong H, Shin SM, Kim HK, Ha SA, Cho GW, Hur SY, Kim TE, Kim JW. The bone morphogenetic protein antagonist gremlin 1 is overexpressed in human cancers and interacts with YWHAH protein. BMC Cancer. 2006 Mar 18;6:74.

SITES NOT REPORTED. NOT IN WEBLOGO.

Human GRIN2C (NMDAR2C) NMDA receptor subunit 2C (Swissprot = Q14957)

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        1 MGGALGPALL LTSLFGAWAG LGPGQGEQGM TVAVVFSSSG PPQAQFRARL TPQSFLDLPL
       61 EIQPLTVGVN TTNPSSLLTQ ICGLLGAAHV HGIVFEDNVD TEAVAQILDF ISSQTHVPIL
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      121 SISGGSAVVL TPKEPGSAFL QLGVSLEQQL QVLFKVLEEY DWSAFAVITS LHPGHALFLE
      181 GVRAVADASH VSWRLLDVVT LELGPGGPRA RTQRLLRQLD APVFVAYCSR EEAEVLFAEA
      241 AQAGLVGPGH VWLVPNLALG STDAPPATFP VGLISVVTES WRLSLRQKVR DGVAILALGA
      301 HSYWRQHGTL PAPAGDCRVH PGPVSPAREA FYRHLLNVTW EGRDFSFSPG GYLVQPTMVV
      361 IALNRHRLWE MVGRWEHGVL YMKYPVWPRY SASLQPVVDS RHLTVATLEE RPFVIVESPD
      421 PGTGGCVPNT VPCRRQSNHT FSSGDVAPYT KLCCKGFCID ILKKLARVVK FSYDLYLVTN
      481 GKHGKRVRGV WNGMIGEVYY KRADMAIGSL TINEERSEIV DFSVPFVETG ISVMVARSNG
      541 TVSPSAFLEP YSPAVWVMMF VMCLTVVAIT VFMFEYFSPV SYNQNLTRGK KSGGPAFTIG
      601 KSVWLLWALV FNNSVPIENP RGTTSKIMVL VWAFFAVIFL ASYTANLAAF MIQEQYIDTV
      661 SGLSDKKFQR PQDQYPPFRF GTVPNGSTER NIRSNYRDMH THMVKFNQRS VEDALTSLKM
      721 GKLDAFIYDA AVLNYMAGKD EGCKLVTIGS GKVFATTGYG IAMQKDSHWK RAIDLALLQF
      781 LGDGETQKLE TVWLSGICQN EKNEVMSSKL DIDNMAGVFY MLLVAMGLAL LVFAWEHLVY
      841 WKLRHSVPNS SQLDFLLAFS RGIYSCFSGV QSLASPPRQA SPDLTASSAQ ASVLKMLQAA
      901 RDMVTTAGVS SSLDRATRTI ENWGGGRRAP PPSPCPTPRS GPSPCLPTPD PPPEPSPTGW
      961 GPPDGGRAAL VRRAPQPPGR PPTPGPPLSD VSRVSRRPAW EARWPVRTGH CGRHLSASER
     1021 PLSPARCHYS SFPRADRSGR PFLPLFPEPP ELEDLPLLGP EQLARREALL HAAWARGSRP
     1081 RHAsLPSSVA EAFARPSSLP AGCTGPACAR PDGHSACRRL AQAQSMCLPI YREACQEGEQ
     1141 AGAPAWQHRQ HVCLHAHAHL PFCWGAVCPH LPPCASHGSW LSGAWGPLGH RGRTLGLGTG
     1201 YRDSGGLDEI SRVARGTQGF PGPCTWRRIS SLESEV
>gi|215274091|sp|Q14957.2|NMDE3_HUMAN RecName: Full=Glutamate [NMDA] receptor
subunit epsilon-3; AltName: Full=N-methyl D-aspartate receptor subtype 2C;
Short=NMDAR2C; Short=NR2C; Flags: Precursor
MGGALGPALLLTSLFGAWAGLGPGQGEQGMTVAVVFSSSGPPQAQFRARLTPQSFLDLPLEIQPLTVGVN
TTNPSSLLTQICGLLGAAHVHGIVFEDNVDTEAVAQILDFISSQTHVPILSISGGSAVVLTPKEPGSAFL
QLGVSLEQQLQVLFKVLEEYDWSAFAVITSLHPGHALFLEGVRAVADASHVSWRLLDVVTLELGPGGPRA
RTQRLLRQLDAPVFVAYCSREEAEVLFAEAAQAGLVGPGHVWLVPNLALGSTDAPPATFPVGLISVVTES
WRLSLRQKVRDGVAILALGAHSYWRQHGTLPAPAGDCRVHPGPVSPAREAFYRHLLNVTWEGRDFSFSPG
GYLVQPTMVVIALNRHRLWEMVGRWEHGVLYMKYPVWPRYSASLQPVVDSRHLTVATLEERPFVIVESPD
PGTGGCVPNTVPCRRQSNHTFSSGDVAPYTKLCCKGFCIDILKKLARVVKFSYDLYLVTNGKHGKRVRGV
WNGMIGEVYYKRADMAIGSLTINEERSEIVDFSVPFVETGISVMVARSNGTVSPSAFLEPYSPAVWVMMF
VMCLTVVAITVFMFEYFSPVSYNQNLTRGKKSGGPAFTIGKSVWLLWALVFNNSVPIENPRGTTSKIMVL
VWAFFAVIFLASYTANLAAFMIQEQYIDTVSGLSDKKFQRPQDQYPPFRFGTVPNGSTERNIRSNYRDMH
THMVKFNQRSVEDALTSLKMGKLDAFIYDAAVLNYMAGKDEGCKLVTIGSGKVFATTGYGIAMQKDSHWK
RAIDLALLQFLGDGETQKLETVWLSGICQNEKNEVMSSKLDIDNMAGVFYMLLVAMGLALLVFAWEHLVY
WKLRHSVPNSSQLDFLLAFSRGIYSCFSGVQSLASPPRQASPDLTASSAQASVLKMLQAARDMVTTAGVS
SSLDRATRTIENWGGGRRAPPPSPCPTPRSGPSPCLPTPDPPPEPSPTGWGPPDGGRAALVRRAPQPPGR
PPTPGPPLSDVSRVSRRPAWEARWPVRTGHCGRHLSASERPLSPARCHYSSFPRADRSGRPFLPLFPEPP
ELEDLPLLGPEQLARREALLHAAWARGSRPRHASLPSSVAEAFARPSSLPAGCTGPACARPDGHSACRRL
AQAQSMCLPIYREACQEGEQAGAPAWQHRQHVCLHAHAHLPFCWGAVCPHLPPCASHGSWLSGAWGPLGH
RGRTLGLGTGYRDSGGLDEISRVARGTQGFPGPCTWRRISSLESEV
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Notes

Chen and Roche (2009) demonstrate that PKB/Akt directly phosphorylates NR2C on serine 1096 (WARGPRPRHA(S1096)LPSSVAEAF). “In addition, we identify 14-3-3epsilon as an NR2C interactor, whose binding is dependent on S1096 phosphorylation.” Ser1096 = Ser1084 in Q14957 (WARGSRPRHA(s1084)LPSSVA).

References to 14-3-3 binding to NR2C

Chen BS, Roche KW. Growth factor-dependent trafficking of cerebellar NMDA receptors via protein kinase B/Akt phosphorylation of NR2C. Neuron. 2009 May 28;62(4):471-8.

<u>Human HDAC4</u> Histone deacetylase 4 (Swissprot = P56524)

```
        1 MSSQSHPDGL SGRDQPVELL NPARVNHMPS TVDVATALPL QVAPSAVPMD LRLDHQFSLP
       61 VAEPALREQQ LQQELLALKQ KQQIQRQILI AEFQRQHEQL SRQHEAQLHE HIKQQQEMLA
      121 MKHQQELLEH QRKLERHRQE QELEKQHREQ KLQQLKNKEK GKESAVASTE VKMKLQEFVL
      181 NKKKALAHRN LNHCISSDPR YWYGKTQHSS LDQSSPPQSG VSTSYNHPVL GMYDAKDDFP
      241 LRKTAsEPNL KLRSRLKQKV AERRSSPLLR RKDGPVVTAL KKRPLDVTDS ACSSAPGSGP
      301 SSPNNSSGSV SAENGIAPAV PSIPAETSLA HRLVAREGSA APLPLYTSPS LPNITLGLPA
      361 TGPSAGTAGQ QDTERLTLPA LQQRLSLFPG THLTPYLSTS PLERDGGAAH SPLLQHMVLL
      421 EQPPAQAPLV TGLGALPLHA QSLVGADRVS PSIHKLRQHR PLGRTQsAPL PQNAQALQHL
      481 VIQQQHQQFL EKHKQQFQQQ QLQMNKIIPK PSEPARQPES HPEETEEELR EHQALLDEPY
      541 LDRLPGQKEA HAQAGVQVKQ EPIESDEEEA EPPREVEPGQ RQPSEQELLF RQQALLEQQ
      601 RIHQLRNYQA SMEAAGIPVS FGGHRPLSRA QSSPASATFP VSVQEPPTKP RFTTGLVYDT
      661 LMLKHQCTCG SSSSHPEHAG RIQSIWSRLQ ETGLRGKCEC IRGRKATLEE LQTVHSEAHT
      721 LLYGTNPLNR QKLDSKKLLG SLASVFVRLP CGGVGVDSDT IWNEVHSAGA ARLAVGCVVE
      781 LVFKVATGEL KNGFAVVRPP GHHAEESTPM GFCYFNSVAV AAKLLQQRLS VSKILIVDWD
      841 VHHGNGTQQA FYSDPSVLYM SLHRYDDGNF FPGSGAPDEV GTGPGVGFNV NMAFTGGLDP
      901 PMGDAEYLAA FRTVVMPIAS EFAPDVVLVS SGFDAVEGHP TPLGGYNLSA RCFGYLTKQL
      961 MGLAGGRIVL ALEGGHDLTA ICDASEACVS ALLGNELDPL PEKVLQQRPN ANAVRSMEKV
     1021 MEIHSKYWRC LQRTTSTAGR SLIEAQTCEN EEAETVTAMA SLSVGVKPAE KRPDEEPMEE
     1081 EPPL
>gi|11182425|sp|P56524.2|HDAC4_HUMAN RecName: Full=Histone deacetylase 4;
Short=HD4
MSSQSHPDGLSGRDQPVELLNPARVNHMPSTVDVATALPLQVAPSAVPMDLRLDHQFSLPVAEPALREQQ
LQQELLALKQKQQIQRQILIAEFQRQHEQLSRQHEAQLHEHIKQQQEMLAMKHQQELLEHQRKLERHRQE
QELEKQHREQKLQQLKNKEKGKESAVASTEVKMKLQEFVLNKKKALAHRNLNHCISSDPRYWYGKTQHSS
LDQSSPPQSGVSTSYNHPVLGMYDAKDDFPLRKTASEPNLKLRSRLKQKVAERRSSPLLRRKDGPVVTAL
KKRPLDVTDSACSSAPGSGPSSPNNSSGSVSAENGIAPAVPSIPAETSLAHRLVAREGSAAPLPLYTSPS
LPNITLGLPATGPSAGTAGQQDTERLTLPALQQRLSLFPGTHLTPYLSTSPLERDGGAAHSPLLQHMVLL
EQPPAQAPLVTGLGALPLHAQSLVGADRVSPSIHKLRQHRPLGRTQSAPLPQNAQALQHLVIQQQHQQFL
```

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EKHKQQFQQQQLQMNKIIPKPSEPARQPESHPEETEEELREHQALLDEPYLDRLPGQKEAHAQAGVQVKQ
EPIESDEEEAEPPREVEPGQRQPSEQELLFRQQALLLEQQRIHQLRNYQASMEAAGIPVSFGGHRPLSRA
QSSPASATFPVSVQEPPTKPRFTTGLVYDTLMLKHQCTCGSSSSHPEHAGRIQSIWSRLQETGLRGKCEC
IRGRKATLEELQTVHSEAHTLLYGTNPLNRQKLDSKKLLGSLASVFVRLPCGGVGVDSDTIWNEVHSAGA
ARLAVGCVVELVFKVATGELKNGFAVVRPPGHHAEESTPMGFCYFNSVAVAAKLLQQRLSVSKILIVDWD
VHHGNGTQQAFYSDPSVLYMSLHRYDDGNFFPGSGAPDEVGTGPGVGFNVNMAFTGGLDPPMGDAEYLAA
FRTVVMPIASEFAPDVVLVSSGFDAVEGHPTPLGGYNLSARCFGYLTKQLMGLAGGRIVLALEGGHDLTA
ICDASEACVSALLGNELDPLPEKVLQQRPNANAVRSMEKVMEIHSKYWRCLQRTTSTAGRSLIEAQTCEN
EEAETVTAMASLSVGVKPAEKRPDEEPMEEEPPL
```

References to 14-3-3-binding (see entry for HDAC9)

<u>Human HDAC5</u> Histone deacetylase 5 (Swissprot = Q9UQL6)

```
        1 MNSPNESDGM SGREPSLEIL PRTSLHSIPV TVEVKPVLPR AMPSSMGGGG GGSPSPVELR
       61 GALVGSVDPT LREQQLQQEL LALKQQQQLQ KQLLFAEFQK QHDHLTRQHE VQLQKHLKQQ
      121 QEMLAAKQQQ EMLAAKRQQE LEQQRQREQQ RQEELEKQRL EQQLLILRNK EKSKESAIAS
      181 TEVKLRLQEF LLSKSKEPTP GGLNHSLPQH PKCWGAHHAS LDQSSPPQSG PPGTPPSYKL
      241 PLPGPYDSRD DFPLRKTAsE PNLKVRSRLK QKVAERRSSP LLRRKDGTVI STFKKRAVEI
      301 TGAGPGASSV CNSAPGSGPS SPNSSHSTIA ENGFTGSVPN IPTEMLPQHR ALPLDSSPNQ
      361 FSLYTSPSLP NISLGLQATV TVTNSHLTAS PKLSTQQEAE RQALQSLRQG GTLTGKFMST
      421 SSIPGCLLGV ALEGDGSPHG HASLLQHVLL LEQARQQSTL IAVPLHGQSP LVTGERVATS
      481 MRTVGKLPRH RPLSRTQsSP LPQSPQALQQ LVMQQQHQQF LEKQKQQQLQ LGKILTKTGE
      541 LPRQPTTHPE ETEEELTEQQ EVLLGEGALT MPREGSTESE STQEDLEEED EEEDGEEEED
      601 CIQVKDEEGE SGAEEGPDLE EPGAGYKKLF SDAQPLQPLQ VYQAPLSLAT VPHQALGRTQ
      661 SSPAAPGGMK SPPDQPVKHL FTTGVVYDTF MLKHQCMCGN THVHPEHAGR IQSIWSRLQE
      721 TGLLSKCERI RGRKATLDEI QTVHSEYHTL LYGTSPLNRQ KLDSKKLLGP ISQKMYAVLP
      781 CGGIGVDSDT VWNEMHSSSA VRMAVGCLLE LAFKVAAGEL KNGFAIIRPP GHHAEESTAM
      841 GFCFFNSVAI TAKLLQQKLN VGKVLIVDWD IHHGNGTQQA FYNDPSVLYI SLHRYDNGNF
      901 FPGSGAPEEV GGGPGVGYNV NVAWTGGVDP PIGDVEYLTA FRTVVMPIAH EFSPDVVLVS
      961 AGFDAVEGHL SPLGGYSVTA RCFGHLTRQL MTLAGGRVVL ALEGGHDLTA ICDASEACVS
     1021 ALLSVELQPL DEAVLQQKPN INAVATLEKV IEIQSKHWSC VQKFAAGLGR SLREAQAGET
     1081 EEAETVSAMA LLSVGAEQAQ AAAAREHSPR PAEEPMEQEP AL
>gi|10720027|sp|Q9UQL6.1|HDAC5_HUMAN RecName: Full=Histone deacetylase 5;
Short=HD5; AltName: Full=Antigen NY-CO-9
MNSPNESDGMSGREPSLEILPRTSLHSIPVTVEVKPVLPRAMPSSMGGGGGGSPSPVELRGALVGSVDPT
LREQQLQQELLALKQQQQLQKQLLFAEFQKQHDHLTRQHEVQLQKHLKQQQEMLAAKQQQEMLAAKRQQE
LEQQRQREQQRQEELEKQRLEQQLLILRNKEKSKESAIASTEVKLRLQEFLLSKSKEPTPGGLNHSLPQH
PKCWGAHHASLDQSSPPQSGPPGTPPSYKLPLPGPYDSRDDFPLRKTASEPNLKVRSRLKQKVAERRSSP
LLRRKDGTVISTFKKRAVEITGAGPGASSVCNSAPGSGPSSPNSSHSTIAENGFTGSVPNIPTEMLPQHR
ALPLDSSPNQFSLYTSPSLPNISLGLQATVTVTNSHLTASPKLSTQQEAERQALQSLRQGGTLTGKFMST
SSIPGCLLGVALEGDGSPHGHASLLQHVLLLEQARQQSTLIAVPLHGQSPLVTGERVATSMRTVGKLPRH
RPLSRTQSSPLPQSPQALQQLVMQQQHQQFLEKQKQQQLQLGKILTKTGELPRQPTTHPEETEEELTEQQ
EVLLGEGALTMPREGSTESESTQEDLEEEDEEEDGEEEEDCIQVKDEEGESGAEEGPDLEEPGAGYKKLF
SDAQPLQPLQVYQAPLSLATVPHQALGRTQSSPAAPGGMKSPPDQPVKHLFTTGVVYDTFMLKHQCMCGN
THVHPEHAGRIQSIWSRLQETGLLSKCERIRGRKATLDEIQTVHSEYHTLLYGTSPLNRQKLDSKKLLGP
ISQKMYAVLPCGGIGVDSDTVWNEMHSSSAVRMAVGCLLELAFKVAAGELKNGFAIIRPPGHHAEESTAM
GFCFFNSVAITAKLLQQKLNVGKVLIVDWDIHHGNGTQQAFYNDPSVLYISLHRYDNGNFFPGSGAPEEV
GGGPGVGYNVNVAWTGGVDPPIGDVEYLTAFRTVVMPIAHEFSPDVVLVSAGFDAVEGHLSPLGGYSVTA
RCFGHLTRQLMTLAGGRVVLALEGGHDLTAICDASEACVSALLSVELQPLDEAVLQQKPNINAVATLEKV
IEIQSKHWSCVQKFAAGLGRSLREAQAGETEEAETVSAMALLSVGAEQAQAAAAREHSPRPAEEPMEQEP
AL
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References to 14-3-3-binding (see entry for HDAC9)

<u>Human HDAC7</u> Histone deacetylase 7 (Swissprot = Q8WUI4)

```
        1 MDLRVGQRPP VEPPPEPTLL ALQRPQRLHH HLFLAGLQQQ RSVEPMRLSM DTPMPELQVG
       61 PQEQELRQLL HKDKSKRSAV ASSVVKQKLA EVILKKQQAA LERTVHPNSP GIPYRTLEPL
      121 ETEGATRSML SSFLPPVPSL PSDPPEHFPL RKTVsEPNLK LRYKPKKSLE RRKNPLLRKE
      181 SAPPSLRRRP AETLGDSSPS SSSTPASGCS SPNDSEHGPN PILGSEALLG QRLRLQETSV
      241 APFALPTVSL LPAITLGLPA PARADSDRRT HPTLGPRGPI LGSPHTPLFL PHGLEPEAGG
      301 TLPSRLQPIL LLDPSGSHAP LLTVPGLGPL PFHFAQSLMT TERLSGSGLH WPLSRTRsEP
      361 LPPSATAPPP PGPMQPRLEQ LKTHVQVIKR SAKPSEKPRL RQIPSAEDLE TDGGGPGQVV
      421 DDGLEHRELG HGQPEARGPA PLQQHPQVLL WEQQRLAGRL PRGSTGDTVL LPLAQGGHRP
      481 LSRAQsSPAA PASLSAPEPA SQARVLSSSE TPARTLPFTT GLIYDSVMLK HQCSCGDNSR
      541 HPEHAGRIQS IWSRLQERGL RSQCECLRGR KASLEELQSV HSERHVLLYG TNPLSRLKLD
      601 NGKLAGLLAQ RMFVMLPCGG VGVDTDTIWN ELHSSNAARW AAGSVTDLAF KVASRELKNG
      661 FAVVRPPGHH ADHSTAMGFC FFNSVAIACR QLQQQSKASK ILIVDWDVHH GNGTQQTFYQ
      721 DPSVLYISLH RHDDGNFFPG SGAVDEVGAG SGEGFNVNVA WAGGLDPPMG DPEYLAAFRI
      781 VVMPIAREFS PDLVLVSAGF DAAEGHPAPL GGYHVSAKCF GYMTQQLMNL AGGAVVLALE
      841 GGHDLTAICD ASEACVAALL GNRVDPLSEE GWKQKPNLNA IRSLEAVIRV HSKYWGCMQR
      901 LASCPDSWVP RVPGADKEEV EAVTALASLS VGILAEDRPS EQLVEEEEPM NL
>gi|30913097|sp|Q8WUI4.2|HDAC7_HUMAN RecName: Full=Histone deacetylase 7;
Short=HD7; AltName: Full=HD7a
MDLRVGQRPPVEPPPEPTLLALQRPQRLHHHLFLAGLQQQRSVEPMRLSMDTPMPELQVGPQEQELRQLL
HKDKSKRSAVASSVVKQKLAEVILKKQQAALERTVHPNSPGIPYRTLEPLETEGATRSMLSSFLPPVPSL
PSDPPEHFPLRKTVSEPNLKLRYKPKKSLERRKNPLLRKESAPPSLRRRPAETLGDSSPSSSSTPASGCS
SPNDSEHGPNPILGSEALLGQRLRLQETSVAPFALPTVSLLPAITLGLPAPARADSDRRTHPTLGPRGPI
LGSPHTPLFLPHGLEPEAGGTLPSRLQPILLLDPSGSHAPLLTVPGLGPLPFHFAQSLMTTERLSGSGLH
WPLSRTRSEPLPPSATAPPPPGPMQPRLEQLKTHVQVIKRSAKPSEKPRLRQIPSAEDLETDGGGPGQVV
DDGLEHRELGHGQPEARGPAPLQQHPQVLLWEQQRLAGRLPRGSTGDTVLLPLAQGGHRPLSRAQSSPAA
PASLSAPEPASQARVLSSSETPARTLPFTTGLIYDSVMLKHQCSCGDNSRHPEHAGRIQSIWSRLQERGL
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RSQCECLRGRKASLEELQSVHSERHVLLYGTNPLSRLKLDNGKLAGLLAQRMFVMLPCGGVGVDTDTIWN
ELHSSNAARWAAGSVTDLAFKVASRELKNGFAVVRPPGHHADHSTAMGFCFFNSVAIACRQLQQQSKASK
ILIVDWDVHHGNGTQQTFYQDPSVLYISLHRHDDGNFFPGSGAVDEVGAGSGEGFNVNVAWAGGLDPPMG
DPEYLAAFRIVVMPIAREFSPDLVLVSAGFDAAEGHPAPLGGYHVSAKCFGYMTQQLMNLAGGAVVLALE
GGHDLTAICDASEACVAALLGNRVDPLSEEGWKQKPNLNAIRSLEAVIRVHSKYWGCMQRLASCPDSWVP
RVPGADKEEVEAVTALASLSVGILAEDRPSEQLVEEEEPMNL
```

References to 14-3-3-binding (see entry for HDAC9)

Human HDAC9 Histone deacetylase 9 (Swissprot = Q9UKV0)

```
        1 MHSMISSVDV KSEVPVGLEP ISPLDLRTDL RMMMPVVDPV VREKQLQQEL LLIQQQQQIQ
       61 KQLLIAEFQK QHENLTRQHQ AQLQEHIKEL LAIKQQQELL EKEQKLEQQR QEQEVERHRR
      121 EQQLPPLRGK DRGRERAVAS TEVKQKLQEF LLSKSATKDT PTNGKNHSVS RHPKLWYTAA
      181 HHTSLDQSSP PLSGTSPSYK YTLPGAQDAK DDFPLRKTAs EPNLKVRSRL KQKVAERRSS
      241 PLLRRKDGNV VTSFKKRMFE VTESSVSSSS PGSGPSSPNN GPTGSVTENE TSVLPPTPHA
      301 EQMVSQQRIL IHEDSMNLLS LYTSPSLPNI TLGLPAVPSQ LNASNSLKEK QKCETQTLRQ
      361 GVPLPGQYGG SIPASSSHPH VTLEGKPPNS SHQALLQHLL LKEQMRQQKL LVAGGVPLHP
      421 QSPLATKERI SPGIRGTHKL PRHRPLNRTQ sAPLPQSTLA QLVIQQQHQQ FLEKQKQYQQ
      481 QIHMNKLLSK SIEQLKQPGS HLEEAEEELQ GDQAMQEDRA PSSGNSTRSD SSACVDDTLG
      541 QVGAVKVKEE PVDSDEDAQI QEMESGEQAA FMQQPFLEPT HTRALSVRQA PLAAVGMDGL
      601 EKHRLVSRTH SSPAASVLPH PAMDRPLQPG SATGIAYDPL MLKHQCVCGN STTHPEHAGR
      661 IQSIWSRLQE TGLLNKCERI QGRKASLEEI QLVHSEHHSL LYGTNPLDGQ KLDPRILLGD
      721 DSQKFFSSLP CGGLGVDSDT IWNELHSSGA ARMAVGCVIE LASKVASGEL KNGFAVVRPP
      781 GHHAEESTAM GFCFFNSVAI TAKYLRDQLN ISKILIVDLD VHHGNGTQQA FYADPSILYI
      841 SLHRYDEGNF FPGSGAPNEV GTGLGEGYNI NIAWTGGLDP PMGDVEYLEA FRTIVKPVAK
      901 EFDPDMVLVS AGFDALEGHT PPLGGYKVTA KCFGHLTKQL MTLADGRVVL ALEGGHDLTA
      961 ICDASEACVN ALLGNELEPL AEDILHQSPN MNAVISLQKI IEIQSMSLKF S
```

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>gi|19865267|sp|Q9UKV0.2|HDAC9_HUMAN RecName: Full=Histone deacetylase 9;
Short=HD9; AltName: Full=HD7B; Short=HD7; AltName: Full=Histone deacetylase-
related protein; AltName: Full=MEF2-interacting transcription repressor MITR
MHSMISSVDVKSEVPVGLEPISPLDLRTDLRMMMPVVDPVVREKQLQQELLLIQQQQQIQKQLLIAEFQK
QHENLTRQHQAQLQEHIKELLAIKQQQELLEKEQKLEQQRQEQEVERHRREQQLPPLRGKDRGRERAVAS
TEVKQKLQEFLLSKSATKDTPTNGKNHSVSRHPKLWYTAAHHTSLDQSSPPLSGTSPSYKYTLPGAQDAK
DDFPLRKTASEPNLKVRSRLKQKVAERRSSPLLRRKDGNVVTSFKKRMFEVTESSVSSSSPGSGPSSPNN
GPTGSVTENETSVLPPTPHAEQMVSQQRILIHEDSMNLLSLYTSPSLPNITLGLPAVPSQLNASNSLKEK
QKCETQTLRQGVPLPGQYGGSIPASSSHPHVTLEGKPPNSSHQALLQHLLLKEQMRQQKLLVAGGVPLHP
QSPLATKERISPGIRGTHKLPRHRPLNRTQSAPLPQSTLAQLVIQQQHQQFLEKQKQYQQQIHMNKLLSK
SIEQLKQPGSHLEEAEEELQGDQAMQEDRAPSSGNSTRSDSSACVDDTLGQVGAVKVKEEPVDSDEDAQI
QEMESGEQAAFMQQPFLEPTHTRALSVRQAPLAAVGMDGLEKHRLVSRTHSSPAASVLPHPAMDRPLQPG
SATGIAYDPLMLKHQCVCGNSTTHPEHAGRIQSIWSRLQETGLLNKCERIQGRKASLEEIQLVHSEHHSL
LYGTNPLDGQKLDPRILLGDDSQKFFSSLPCGGLGVDSDTIWNELHSSGAARMAVGCVIELASKVASGEL
KNGFAVVRPPGHHAEESTAMGFCFFNSVAITAKYLRDQLNISKILIVDLDVHHGNGTQQAFYADPSILYI
SLHRYDEGNFFPGSGAPNEVGTGLGEGYNINIAWTGGLDPPMGDVEYLEAFRTIVKPVAKEFDPDMVLVS
AGFDALEGHTPPLGGYKVTAKCFGHLTKQLMTLADGRVVLALEGGHDLTAICDASEACVNALLGNELEPL
AEDILHQSPNMNAVISLQKIIEIQSMSLKFS
```

Notes

Specifically, phosphorylation of HDAC5 serines 259 and 498 causes HDAC5 to bind to 14-3-3 and dissociate from MEF2.

Histone deacetylase, HDAC5 RKTApS^{259}EP, RTQpS^{498}SP

Histone deacetylase, HDAC7   RKTVpS^{178}EP, RTRpS^{344}EP, RAQpS^{479}S

14-3-3 binding sites on HDAC4 Ser246, Ser467 and Ser632 (Paroni et al 2007)

“The binding of HDAC7 to 14-3-3 appeared to be dependent on the serine residues Ser-178, Ser-344, and Ser-479, since the replacement of these residues by alanine reduced 14-3-3 binding by HDAC7. Interestingly, all three 14-3-3-binding sites within each HDAC are not equivalent. Ser-178 in the 14-3-3-binding site, RKT(A/V)pSEP, was the most critical for 14-3-3 binding in both HDAC4 and HDAC7 (47). Indeed, the inactivation of this site had a stronger effect than that of the two others (Fig. 5, C and D). Sequence comparison revealed that among the three sites, the NH$_2$-terminal one presented the best homology to the consensus binding motif. Nevertheless, other sites also contributed to the binding of 14-3-3 by HDAC7 since the binding of HDAC7 by 14-3-3 was completely abolished only when all three motifs were inactivated. Similar results have also been observed for HDAC4 (47). Taken together, these results suggest that these three serines are the primary regulatory sites for nuclear export of class II HDACs. It is also interesting to note that class II HDACs are the only molecules identified so far that contain more than two 14-3-3-binding sites.” Kao et al 2001

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Human HIST1H3A Histone H3 (Swissprot = P68431)

```
      1 MARTKQTARK sTGGKAPRKQ LATKAARKsA PATGGVKKPH RYRPGTVALR EIRRYQKSTE
     61 LLIRKLPFQR LVREIAQDFK TDLRFQSSAV MALQEACEAY LVGLFEDTNL CAIHAKRVTI
    121 MPKDIQLARR IRGERA
>gi|55977055|sp|P68431.2|H31_HUMAN RecName: Full=Histone H3.1; AltName:
Full=H3/a; AltName: Full=H3/b; AltName: Full=H3/c; AltName: Full=H3/d;
AltName: Full=H3/f; AltName: Full=H3/h; AltName: Full=H3/i; AltName:
Full=H3/j; AltName: Full=H3/k; AltName: Full=H3/l
MARTKQTARKSTGGKAPRKQLATKAARKSAPATGGVKKPHRYRPGTVALREIRRYQKSTELLIRKLPFQR
LVREIAQDFKTDLRFQSSAVMALQEACEAYLVGLFEDTNLCAIHAKRVTIMPKDIQLARRIRGERA
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Notes

H3 Histone H3, along with histone H4, plays a central role in nucleosome formation. Because it is often impossible to distinguish among histone paralogues using the short sequences surrounding post-translational modifications, we have chosen to bundle the proteins of the H3 histone class into a single entry. These do not represent splicing isoforms or polymorphisms but, rather, the products of different genes. Histone H3 sequence is $_{7}$ARKpSTGGK$_{14}$ and ARK$_{Ac}$S$_{p}$TGGK$_{Ac}$, residues 7–14.

"In vitro, the affinity of 14-3-3 for phosphoserine 10 is weak but becomes significantly increased by additional acetylation of either lysine 9 or lysine 14 on the same histone tail. In contrast, the histone H3S28 site matches elements of 14-3-3 high affinity consensus motifs. Winter et al (2008)"

References to 14-3-3 binding to Histone H3

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Human HJURP Holliday junction recognition protein (Swissprot = Q8NCD3)

```
      1 MLGTLRAMEG EDVEDDQLLQ KLRASRRRFQ RRMQRLIEKY NQPFEDTPVV QMATLTYETP
     61 QGLRIWGGRL IKERNKGEIQ DSSMKPADRT DGSVQAAAWG PELPSHRTVL GADSKSGEVD
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121 ATSDQEESVA WALAPAVPQS PLKNELRRKY LTQVDILLQG AEYFECAGNR AGRDVRVTPL 181 PSLASPAVPA PGYCSRISGK SPGDPAKPAS SPREWDPLHP SSTDMALVPR NDSLSLQETS 241 SSSFLSSQPF EDDDICNVTI SDLYAGMLHS MSRLLSTKPS SIISTKTFIM QNWNCRRRHR 301 YKSRMNKTYC KGARRSQRSS KENFIPCSEP VKGTGALRDC KNVLDVSCRK TGLKLEKAFL 361 EVNRPQIHKL DPSWKERKVT PSKYSSLIYF DSSATYNLDE ENRFRTLKWL ISPVKIVSRP 421 TIRQGHGENR QREIEIRFDQ LHREYCLSPR NQPRRMCLPD SWAMNMYRGG PASPGGLQGL 481 ETRRLsLPSS KAKAKSLSEA FENLGKRSLE AGRCLPKSDS SSSLPKTNPT HSATRPQQTS 541 DLHVQGNSSG IFRKSVSPSK TLSVPDKEVP GHGRNRYDEI KEEFDKLHQK YCLKSPGQMT 601 VPLCIGVSTD KASMEVRYQT EGFLGKLNPD PHFQGFQKLP SSPLGCRKSL LGSTAIEAPS 661 STCVARAITR DGTRDHQFPA KRPRLSEPQG SGRQGNSLGA SDGVDNTVRP GDQGSSSQPN 721 SEERGENTSY RMEEKSDFML EKLETKSV >gi|239938642|sp|Q8NCD3.2|HJURP_HUMAN RecName: Full=Holliday junction recognition protein; AltName: Full=14-3-3-associated AKT substrate; AltName: Full=Fetal liver-expressing gene 1 protein; AltName: Full=Up-regulated in lung cancer 9 MLGTLRAMEGEDVEDDQLLQKLRASRRRFQRRMQRLIEKYNQPFEDTPVVQMATLTYETPQGLRIWGGRL IKERNEGEIQDSSMKPADRTDGSVQAAAWGPELPSHRTVLGADSKSGEVDATSDQEESVAWALAPAVPQS PLKNELRRKYLTQVDILLQGAEYFECAGNRAGRDVRVTPLPSLASPAVPAPGYCSRISRKSPGDPAKPAS SPREWDPLHPSSTDMALVPRNDSLSLQETSSSSFLSSQPFEDDDICNVTISDLYAGMLHSMSRLLSTKPS SIISTKTFIMQNWNSRRRHRYKSRMNKTYCKGARRSQRSSKENFIPCSEPVKGTGALRDCKNVLDVSCRK TGLKLEKAFLEVNRPQIHKLDPSWKERKVTPSKYSSLIYFDSSATYNLDEENRFRTLKWLISPVKIVSRP TIRQGHGENRQREIEIRFDQLHREYCLSPRNQPRRMCLPDSWAMNMYRGGPASPGGLQGLETRRLSLPSS KAKAKSLSEAFENLGKRSLEAGRCLPKSDSSSSLPKTNPTHSATRPQQTSDLHVQGNSSGIFRKSVSPSK TLSVPDKEVPGHGRNRYDEIKEEFDKLHQKYCLKSPGQMTVPLCIGVSTDKASMEVRYQTEGFLGKLNPD PHFQGFQKLPSSPLGCRKSLLGSTAIEAPSSTCVARAITRDGTRDHQFPAKRPRLSEPQGSGRQGNSLGA SDGVDNTVRPGDQGSSSQPNSEERGENTSYRMEEKSDFMLEKLETKSV **Notes** "Centromeric protein that plays a central role in the incorporation and maintenance of histone H3-like variant CENPA at centromeres. Acts as a specific chaperone for CENPA and is required for the incorporation of newly synthesized CENPA molecules into nucleosomes at replicated centromeres. Directly binds Holliday junctions" Interacts with 14-3-3 family members in a phosphorylation-dependent manner. Interacts with MSH5 and NBN. Directly binds Holliday junctions. 14-3-3/FAKTS interaction was markedly enhanced by the expression of activated Akt/PKB, suggesting a phosphorylation dependent event. Ser479 as the predominant residue that mediates the association (RRLS479LP). (Ser473= Ser486 in Q8NCD3) (N.B. This is not a conventional Akt/PKB site). **References to 14-3-3 binding to JURP (FAKTS)** Luhn P, Wang H, Marcus AI, Fu H. Identification of FAKTS as a novel 14-3-3-associated nuclear protein. Proteins. 2007 May 1;67(2):479-89	
Human HSF1 Heat-shock transcription factor (Swissprot = Q00613) 1 MDLPVGPGAA GPSNVPAFLT KLWTLVSDPD TDALICWSPS GNSFHVFDQG QFAKEVLPKY 61 FKHNNMASFV RQLNMYGFRK VVHIEQGGLV KPERDDTEFQ HPCFLRGQEQ LLENIKRKVT 121 SVSTLKSEDI KIRQDSVTKL LTDVQLMKGK QECMDSKLLA MKHENEALWR EVASLRQKHA 181 QQQKVVNKLI QFLISLVQSN RILGVKRKIP LMLNDSGSAH SMPKYSRQFS LEHVHGSGPY 241 SAPSPAYSSS SLYAPDAVAS SGPIISDITE LAPASPMASP GGSIDERPLS SSPLVRVKEE 301 PPsPPQsPRV EEASPGRPSS VDTLLSPTAL IDSILRESEP APASVTALTD ARGHTDTEGR 361 PPSPPPTSTP EKCLSVACLD KNELSDHLDA MDSNLDNLQT MLSSHGFSVD TSALLDLFSP 421 SVTVPDMSLP DLDSSLASIQ ELLSPQEPPR PPEAENSSPD SGKQLVHYTA QPLFLLDPGS 481 VDTGSNDLPV LFELGEGSYF SEGDGFAEDP TISLLTGSEP PKAKDPTVS >gi|462333|sp|Q00613.1|HSF1_HUMAN RecName: Full=Heat shock factor protein 1; Short=HSF 1; AltName: Full=Heat shock transcription factor 1; Short=HSTF 1 MDLPVGPGAAGPSNVPAFLTKLWTLVSDPDTDALICWSPSGNSFHVFDQGQFAKEVLPKYFKHNNMASFV RQLNMYGFRKVVHIEQGGLVKPERDDTEFQHPCFLRGQEQLLENIKRKVTSVSTLKSEDIKIRQDSVTKL LTDVQLMKGKQECMDSKLLAMKHENEALWREVASLRQKHAQQQKVVNKLIQFLISLVQSNRILGVKRKIP LMLNDSGSAHSMPKYSRQFSLEHVHGSGPYSAPSPAYSSSSLYAPDAVASSGPIISDITELAPASPMASP GGSIDERPLSSSPLVRVKEEPPSPPQSPRVEEASPGRPSSVDTLLSPTALIDSILRESEPAPASVTALTD ARGHTDTEGRPPSPPPTSTPEKCLSVACLDKNELSDHLDAMDSNLDNLQTMLSSHGFSVDTSALLDLFSP SVTVPDMSLPDLDSSLASIQELLSPQEPPRPPEAENSSPDSGKQLVHYTAQPLFLLDPGSVDTGSNDLPV LFELGEGSYFSEGDGFAEDPTISLLTGSEPPKAKDPTVS **Notes** HSF1 a heat-shock transcription factor. Transcription of heat-shock genes is rapidly induced after temperature stress. Hsp90, by itself and/or associated with multichaperone complexes, is a major repressor of HSF1. Two alternatively spliced isoforms have been described. ERK activation results in the recruitment of the phosphoserine binding protein 14-3-3epsilon in a manner dependent on previous HSF1 phosphorylation by ERK. The effects of 14-3-3epsilon binding on HSF1 were complex, however, depending on extracellular conditions, in that HSF1-14-3-3 binding at 37 degrees C led to the cytoplasmic sequestration and repression of HSF1, whereas heat shock overrode these effects and caused quantitative nuclear localization of HSF1. Although the effects of 14-3-3epsilon binding to HSF1 were overridden acutely by stress, during recovery from heat shock, 14-3-3epsilon association again led to enhanced cytoplasmic localization of HSF1, implicating a role for ERK/14-3-3epsilon in HSF1 deactivation in recovering cells. Association of HSF1 with ERK and 14-3-3epsilon during heat shock may thus modulate the amplitude of the response and lead to efficient termination of HSP expression on resumption of growth conditions. Wild-type HSF1 binds to 14-3-3{epsilon}-GST with markedly greater avidity than the double Ser303Ala/Ser307Ala mutant. However, the HSF1 mutant was observed to bind in repeated experiments, albeit at ~20% of the efficiency of wtHSF1. Our experiments indicate that serines 303 and 307 are required for efficient HSF1 binding to 14-3-3{epsilon}. They also suggest the possibility that 14-3-3{epsilon} can bind with reduced efficiency to the unphosphorylated Ser-303/307 region or to another as-yet uncharacterized site in HSF1. **References to 14-3-3 binding to HSF1**	SITES NOT DEFINED PRECISELY, NOT INCLUDED IN WEBLOGO ANALYSIS

Wang X, Grammatikakis N, Siganou A, Stevenson MA, Calderwood SK. Interactions between extracellular signal-regulated protein kinase 1, 14-3-3epsilon, and heat shock factor 1 during stress. J Biol Chem. 2004 Nov 19;279(47):49460-9.
Wang X, Grammatikakis N, Siganou A, Calderwood SK.
Regulation of molecular chaperone gene transcription involves the serine phosphorylation, 14-3-3 epsilon binding, and cytoplasmic sequestration of heat shock factor 1. Mol Cell Biol. 2003 Sep;23(17):6013-26.
Calderwood SK. Regulatory interfaces between the stress protein response and other gene expression programs in the cell. Methods. 2005 Feb;35(2):139-48.

Human HspB6 (HSP20) (Swissprot = O14558)

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        1 MEIPVPVQPS WLRRAsAPLP GLSAPGRLFD QRFGEGLLEA ELAALCPTTL APYYLRAPSV
       61 ALPVAQVPTD PGHFSVLLDV KHFSPEEIAV KVVGEHVEVH ARHEERPDEH GFVAREFHRR
      121 YRLPPGVDPA AVTSALSPEG VLSIQAAPAS AQAPPPAAAK
>gi|22096351|sp|O14558.2|HSPB6_HUMAN RecName: Full=Heat shock protein beta-6;
Short=HspB6; AltName: Full=Heat shock 20 kDa-like protein p20
MEIPVPVQPSWLRRASAPLPGLSAPGRLFDQRFGEGLLEAELAALCPTTLAPYYLRAPSVALPVAQVPTD
PGHFSVLLDVKHFSPEEIAVKVVGEHVEVHARHEERPDEHGFVAREFHRRYRLPPGVDPAAVTSALSPEG
VLSIQAAPASAQAPPPAAAK
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Notes

WLRRA(pS16)APLPGL

References to 14-3-3 binding to HSP20

Dreiza CM, Brophy CM, Komalavilas P, Furnish EJ, Joshi L, Pallero MA, Murphy-Ullrich JE, von Rechenberg M, Ho YS, Richardson B, Xu N, Zhen Y, Peltier JM, Panitch A.Transducible heat shock protein 20 (HSP20) phosphopeptide alters cytoskeletal dynamics. FASEB J. 2005 Feb;19(2):261-3.
Chernik IS, Seit-Nebi AS, Marston SB, Gusev NB. Small heat shock protein Hsp20 (HspB6) as a partner of 14-3-3gamma. Mol Cell Biochem. 2007 Jan;295(1-2):9-17.
Lopes LB, Furnish EJ, Komalavilas P, Flynn CR, Ashby P, Hansen A, Ly DP, Yang GP, Longaker MT, Panitch A, Brophy CM. Cell permeant peptide analogues of the small heat shock protein, HSP20, reduce TGF-beta1-induced CTGF expression in keloid fibroblasts. J Invest Dermatol. 2009 Mar;129(3):590-8.

Human IGF1R Insulin-like growth factor I receptor (Swissprot = P08069)

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        1 MKSGSGGGSP TSLWGLLFLS AALSLWPTSG EICGPGIDIR NDYQQLKRLE NCTVIEGYLH
       61 ILLISKAEDY RSYRFPKLTV ITEYLLLFRV AGLESLGDLF PNLTVIRGWK LFYNYALVIF
      121 EMTNLKDIGL YNLRNITRGA IRIEKNADLC YLSTVDWSLI LDAVSNNYIV GNKPPKECGD
      181 LCPGTMEEKP MCEKTTINNE YNYRCWTTNR CQKMCPSTCG KRACTENNEC CHPECLGSCS
      241 APDNDTACVA CRHYYYAGVC VPACPPNTYR FEGWRCVDRD FCANILSAES SDSEGFVIHD
      301 GECMQECPSG FIRNGSQSMY CIPCEGPCPK VCEEEKKTKT IDSVTSAQML QGCTIFKGNL
      361 LINIRRGNNI ASELENFMGL IEVVTGYVKI RHSHALVSLS FLKNLRLILG EEQLEGNYSF
      421 YVLDNQNLQQ LWDWDHRNLT IKAGKMYFAF NPKLCVSEIY RMEEVTGTKG RQSKGDINTR
      481 NNGERASCES DVLHFTSTTT SKNRIIITWH RYRPPDYRDL ISFTVYYKEA PFKNVTEYDG
      541 QDACGSNSWN MVDVDLPPNK DVEPGILLHG LKPWTQYAVY VKAVTLTMVE NDHIRGAKSE
      601 ILYIRTNASV PSIPLDVLSA SNSSSQLIVK WNPPSLPNGN LSYYIVRWQR QPQDGYLYRH
      661 NYCSKDKIPI RKYADGTIDI EEVTENPKTE VCGGEKGPCC ACPKTEAEKQ AEKEEAEYRK
      721 VFENFLHNSI FVPRPERKRR DVMQVANTTM SSRSRNTTAA DTYNITDPEE LETEYPFFES
      781 RVDNKERTVI SNLRPFTLYR IDIHSCNHEA EKLGCSASNF VFARTMPAEG ADDIPGPVTW
      841 EPRPENSIFL KWPEPENPNG LILMYEIKYG SQVEDQRECV SRQEYRKYGG AKLNRLNPGN
      901 YTARIQATSL SGNGSWTDPV FFYVQAKTGY ENFIHLIIAL PVAVLLIVGG LVIMLYVFHR
      961 KRNNSRLGNG VLYASVNPEY FSAADVYVPD EWEVAREKIT MSRELGQGSF GMVYEGVAKG
     1021 VVKDEPETRV AIKTVNEAAS MRERIEFLNE ASVMKEFNCH HVVRLLGVVS QGQPTLVIME
     1081 LMTRGDLKSY LRSLRPEMEN NPVLAPPSLS KMIQMAGEIA DGMAYLNANK FVHRDLAARN
     1141 CMVAEDFTVK IGDFGMTRDI YETDYYRKGG KGLLPVRWMS PESLKDGVFT TYSDVWSFGV
     1201 VLWEIATLAE QPYQGLSNEQ VLRFVMEGGL LDKPDNCPDM LFELMRMCWQ YNPKMRPSFL
     1261 EIISSIKEEM EPGFREVSFY YSEENKLPEP EELDLEPENM ESVPLDPSAS SSsLPLPDRH
     1321 SGHKAENGPG PGVLVLRASF DERQPYAHMN GGRKNERALP LPQSSTC
>gi|124240|sp|P08069.1|IGF1R_HUMAN RecName: Full=Insulin-like growth factor 1
receptor; AltName: Full=Insulin-like growth factor I receptor; Short=IGF-I
receptor; AltName: CD_antigen=CD221; Contains: RecName: Full=Insulin-like
growth factor 1 receptor alpha chain; Contains: RecName: Full=Insulin-like
growth factor 1 receptor beta chain; Flags: Precursor
MKSGSGGGSPTSLWGLLFLSAALSLWPTSGEICGPGIDIRNDYQQLKRLENCTVIEGYLHILLISKAEDY
RSYRFPKLTVITEYLLLFRVAGLESLGDLFPNLTVIRGWKLFYNYALVIFEMTNLKDIGLYNLRNITRGA
IRIEKNADLCYLSTVDWSLILDAVSNNYIVGNKPPKECGDLCPGTMEEKPMCEKTTINNEYNYRCWTTNR
CQKMCPSTCGKRACTENNECCHPECLGSCSAPDNDTACVACRHYYYAGVCVPACPPNTYRFEGWRCVDRD
FCANILSAESSDSEGFVIHDGECMQECPSGFIRNGSQSMYCIPCEGPCPKVCEEEKKTKTIDSVTSAQML
QGCTIFKGNLLINIRRGNNIASELENFMGLIEVVTGYVKIRHSHALVSLSFLKNLRLILGEEQLEGNYSF
YVLDNQNLQQLWDWDHRNLTIKAGKMYFAFNPKLCVSEIYRMEEVTGTKGRQSKGDINTRNNGERASCES
DVLHFTSTTTSKNRIIITWHRYRPPDYRDLISFTVYYKEAPFKNVTEYDGQDACGSNSWNMVDVDLPPNK
DVEPGILLHGLKPWTQYAVYVKAVTLTMVENDHIRGAKSEILYIRTNASVPSIPLDVLSASNSSSQLIVK
WNPPSLPNGNLSYYIVRWQRQPQDGYLYRHNYCSKDKIPIRKYADGTIDIEEVTENPKTEVCGGEKGPCC
ACPKTEAEKQAEKEEAEYRKVFENFLHNSIFVPRPERKRRDVMQVANTTMSSRSRNTTAADTYNITDPEE
LETEYPFFESRVDNKERTVISNLRPFTLYRIDIHSCNHEAEKLGCSASNFVFARTMPAEGADDIPGPVTW
EPRPENSIFLKWPEPENPNGLILMYEIKYGSQVEDQRECVSRQEYRKYGGAKLNRLNPGNYTARIQATSL
SGNGSWTDPVFFYVQAKTGYENFIHLIIALPVAVLLIVGGLVIMLYVFHRKRNNSRLGNGVLYASVNPEY
FSAADVYVPDEWEVAREKITMSRELGQGSFGMVYEGVAKGVVKDEPETRVAIKTVNEAASMRERIEFLNE
ASVMKEFNCHHVVRLLGVVSQGQPTLVIMELMTRGDLKSYLRSLRPEMENNPVLAPPSLSKMIQMAGEIA
DGMAYLNANKFVHRDLAARNCMVAEDFTVKIGDFGMTRDIYETDYYRKGGKGLLPVRWMSPESLKDGVFT
TYSDVWSFGVVLWEIATLAEQPYQGLSNEQVLRFVMEGGLLDKPDNCPDMLFELMRMCWQYNPKMRPSFL
EIISSIKEEMEPGFREVSFYYSEENKLPEPEELDLEPENMESVPLDPSASSSSLPLPDRHSGHKAENGPG
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PGVLVLRASFDERQPYAHMNGGRKNERALPLPQSSTC **Notes** Spence et al (2003) report PMA-stimulated phosphorylation and 14-3-3 binding to VPLDPSASSSpS^{1283}LP (=Ser1313 in P08069) **References to 14-3-3 binding to IGF1 receptor** Craparo A, Freund R, Gustafson TA. 14-3-3 (epsilon) interacts with the insulin-like growth factor I receptor and insulin receptor substrate I in a phosphoserine-dependent manner. J Biol Chem. 1997 Apr 25;272(17):11663-9. Spence SL, Dey BR, Terry C, Albert P, Nissley P, Furlanetto RW. Interaction of 14-3-3 proteins with the insulin-like growth factor I receptor (IGFIR): evidence for a role of 14-3-3 proteins in IGFIR signaling. Biochem Biophys Res Commun. 2003 Dec 26;312(4):1060-6. Furlanetto RW, Dey BR, Lopaczynski W, Nissley SP. 14-3-3 proteins interact with the insulin-like growth factor receptor but not the insulin receptor. Biochem J. 1997 Nov 1;327 (Pt 3):765-71.	
Human IL-9R (α-Chain of interleukin 9 receptor) **Notes** KARpS^{519}WpT^{521}F-$_{COOH}$ **References to 14-3-3 binding to α-chain of interleukin 9 receptor (IL-9R)** Sliva D, Gu M, Zhu YX, Chen J, Tsai S, Du X, Yang YC. 14-3-3zeta interacts with the alpha-chain of human interleukin 9 receptor. Biochem J. 2000 Feb 1;345 Pt 3:741-7.	NOT CERTAIN WHETHER SER519 OR THR521 IS THE PHOPHORYLATED 14-3-3-BINDING SITE – NOT IN WEBLOGO
Human ING1 (p33ING1b) Inhibitor of growth protein 1 (Swissprot = Q9UK53) 1 YSSSSDPGPV GRGRGCSSDR LPRPAGPARR QFQAASLLTR GWGRAWPWKQ ILKELDECYE 61 RFSRETDGAQ KRRMLHCVQR ALIRSQELGD EKIQIVSQMV ELVENRTRQV DSHVELFEAQ 121 QELGDTAGNS GKAGADRPKG EAAAQADKPN SKRSRRQRNN ENRENASSNH DHDDGASGTP 181 KEKKAKTSKK KKRSKAKAER EAsPADLPID PNEPTYCLCN QVSYGEMIGC DNDECPIEWF 241 HFSCVGLNHK PKGKWYCPKC RGENEKTMDK ALEKSKKERA YNR >gi|212276438|sp|Q9UK53.2|ING1_HUMAN RecName: Full=Inhibitor of growth protein 1 MSFVECPYHSPAERLVAEADEGGPSAITGMGLCFRCLLFSFSGRSGVEGGRVDLNVFGSLGLQPWIGSSR CWGGPCSSALRCGWFSSWPPPSKSAIPIGGGSRGAGRVSRWPPPHWLEAWRVSPLPLSPLSPATFGRGFI AVAVIPGLWARGRGCSSDRLPRPAGPARRQFQAASLLTRGWGRAWPWKQILKELDECYERFSRETDGAQK RRMLHCVQRALIRSQELGDEKIQIVSQMVELVENRTRQVDSHVELFEAQQELGDTAGNSGKAGADRPKGE AAAQADKPNSKRSRRQRNNENRENASSNHDHDDGASGTPKEKKAKTSKKKKRSKAKAEREASPADLPIDP NEPTYCLCNQVSYGEMIGCDNDECPIEWFHFSCVGLNHKPKGKWYCPKCRGENEKTMDKALEKSKKERAY NR **Notes** The REASPADLP motif, which has homology to 14-3-3 consensus binding sites is located between the NLS and PHD regions. Serine 199 represents a candidate phosphorylation site for regulating 14-3-3 binding. (Gong et al 2006). N.B. This site has a proline at +1. **References to 14-3-3 binding to p33ING1b** Gong W, Russell M, Suzuki K, Riabowol K. Subcellular targeting of p33ING1b by phosphorylation-dependent 14-3-3 binding regulates p21WAF1 expression. Mol Cell Biol. 2006 Apr;26(8):2947-54.	
Human IRS1 Insulin receptor substrate 1 (Swissprot = P35568) 1 MASPPESDGF SDVRKVGYLR KPKSMHKRFF VLRAASEAGG PARLEYYENE KKWRHKSSAP 61 KRSIPLESCF NINKRADSKN KHLVALYTRD EHFAIAADSE AEQDSWYQAL LQLHNRAKGH 121 HDGAAALGAG GGGGSCSGSS GLGEAGEDLS YGDVPPGPAF KEVWQVILKP KGLGQTKNLI 181 GIYRLCLTSK TISFVKLNSE AAAVVLQLMN IRRCGHSENF FFIEVGRSAV TGPGEFWMQV 241 DDSVVAQNMH ETILEAMRAM SDEFRPRSKs QSSSNCSNPI SVPLRRHHLN NPPPSQVGLT 301 RRSRTESITA TSPASMVGGK PGSFRVRASS DGEGTMSRPA SVDGSPVSPS TNRTHAHRHR 361 GSARLHPPLN HSRsIPMPAS RCSPSATSPV SLSSSSTSGH GSTSDCLFPR RSSASVSGSP 421 SDGGFISSDE YGSSPCDFRS SFRSVTPDSL GHTPPARGEE ELSNYICMGG KGPSTLTAPN 481 GHYILSRGGN GHRCTPGTGL GTSPALAGDE AASAADLDNR FRKRTHSAGT SPTITHQKTP 541 SQSSVASIEE YTEMMPAYPP GGGSGGRLPG HRHSAFVPTR SYPEEGLEMH PLERRGGHHR 601 PDSSTLHTDD GYMPMSPGVA PVPSGRKGSG DYMPMSPKSV sAPQQIINPI RRHPQRVDPN 661 GYMMMSPSGG CSPDIGGGPS SSSSSSNAVP SGTSYGKLWT NGVGGHHSHV LPHPKPPVES 721 SGGKLLPCTG DYMNMSPVGD SNTSSPSDCY YGPEDPQHKP VLSYYSLPRS FKHTQRPGEP 781 EEGARHQHLR LSTSSGRLLY AATADDSSSS TSSDSLGGGY CGARLEPSLP HPHHQVLQPH 841 LPRKVDTAAQ TNSRLARPTR LSLGDPKAST LPRAREQQQQ QQPLLHPPEP KSPGEYVNIE 901 FGSDQSGYLS GPVAFHSSPS VRCPSQLQPA PREEETGTEE YMKMDLGPGR RAAWQESTGV 961 EMGRLGPAPP GAASICRPTR AVPSSRGDYM TMQMSCPRQS YVDTSPAAPV SYADMRTGIA 1021 AEEVSLPRAT MAAASSSSAA SASPTGPQGA AELAAHSSLL GGPQGPGGMS AFTRVNLSPN 1081 RNQSAKVIRA DPQGCRRRHS SETFSSTPSA TRVGNTVPFG AGAAVGGGGG SSSSSEDVKR 1141 HSSASFENVW LRPGELGGAP KEPAKLCGAA GGLENGLNYI DLDLVKDFKQ CPQECTPEPQ 1201 PPPPPPPHQP LGSGESSSTR RSSEDLSAYA SISFQKQPED RQ >gi|547738|sp|P35568.1|IRS1_HUMAN RecName: Full=Insulin receptor substrate 1; Short=IRS-1 MASPPESDGFSDVRKVGYLRKPKSMHKRFFVLRAASEAGGPARLEYYENEKKWRHKSSAPKRSIPLESCF NINKRADSKNKHLVALYTRDEHFAIAADSEAEQDSWYQALLQLHNRAKGHHDGAAALGAGGGGGSCSGSS GLGEAGEDLSYGDVPPGPAFKEVWQVILKPKGLGQTKNLIGIYRLCLTSKTISFVKLNSEAAAVVLQLMN IRRCGHSENFFFIEVGRSAVTGPGEFWMQVDDSVVAQNMHETILEAMRAMSDEFRPRSKSQSSSNCSNPI SVPLRRHHLNNPPPSQVGLTRRSRTESITATSPASMVGGKPGSFRVRASSDGEGTMSRPASVDGSPVSPS TNRTHAHRHRGSARLHPPLNHSRSIPMPASRCSPSATSPVSLSSSSTSGHGSTSDCLFPRRSSASVSGSP SDGGFISSDEYGSSPCDFRSSFRSVTPDSLGHTPPARGEEELSNYICMGGKGPSTLTAPNGHYILSRGGN GHRCTPGTGLGTSPALAGDEAASAADLDNRFRKRTHSAGTSPTITHQKTPSQSSVASIEEYTEMMPAYPP GGGSGGRLPGHRHSAFVPTRSYPEEGLEMHPLERRGGHHRPDSSTLHTDDGYMPMSPGVAPVPSGRKGSG DYMPMSPKSVSAPQQIINPIRRHPQRVDPNGYMMMSPSGGCSPDIGGGPSSSSSSSNAVPSGTSYGKLWT NGVGGHHSHVLPHPKPPVESSGGKLLPCTGDYMNMSPVGDSNTSSPSDCYYGPEDPQHKPVLSYYSLPRS FKHTQRPGEPEEGARHQHLRLSTSSGRLLYAATADDSSSSTSSDSLGGGYCGARLEPSLPHPHHQVLQPH	

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LPRKVDTAAQTNSRLARPTRLSLGDPKASTLPRAREQQQQQPLLHPPEPKSPGEYVNIEFGSDQSGYLS
GPVAFHSSPSVRCPSQLQPAPREEETGTEEYMKMDLGPGRRAAWQESTGVEMGRLGPAPPGAASICRPTR
AVPSSRGDYMTMQMSCPRQSYVDTSPAAPVSYADMRTGIAAEEVSLPRATMAAASSSSAASASPTGPQGA
AELAAHSSLLGGPQGPGGMSAFTRVNLSPNRNQSAKVIRADPQGCRRRHSSETFSSTPSATRVGNTVPFG
AGAAVGGGGGSSSSSEDVKRHSSASFENVWLRPGELGGAPKEPAKLCGAAGGLENGLNYIDLDLVKDFKQ
CPQECTPEPQPPPPPPPHQPLGSGESSSTRRSSEDLSAYASISFQKQPEDRQ
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Notes

The following phosphopeptides bound to 14-3-3s and displaced them from IRS-1 in in vitro competiton assays: DEFRPRSK[pS]QSSSNC ([pS] corresponds to Ser-270 in human IRS-1), HPPLNHSR[pS]IPMPAS (Ser-374 in human IRS-1), MPMSPKSV[pS]APQQII (Ser-641 in human IRS-1) (Ogihara et al 1997). Of these sites, only Ser270 and Ser374 have been demonstrated to be phosphorylated in vivo in several studies (http://www.phosphosite.org/). Sequence alignment indicates that IRS-1 contains at least five putative 14-3-3 binding sites. Three of them are within the amino-terminal portion of the molecule that is important for the interaction of IRS-1 with the insulin receptor and PI3K and might contribute to its subcellular localization (Xiang et al 2002).

References to 14-3-3-binding to IRS1

Oriente F, Andreozzi F, Romano C, Perruolo G, Perfetti A, Fiory F, Miele C, Beguinot F, Formisano P. Protein kinase C-alpha regulates insulin action and degradation by interacting with insulin receptor substrate-1 and 14-3-3 epsilon. J Biol Chem. 2005 Dec 9;280(49):40642-9.
Xiang X, Yuan M, Song Y, Ruderman N, Wen R, Luo Z. 14-3-3 facilitates insulin-stimulated intracellular trafficking of insulin receptor substrate 1. Mol Endocrinol. 2002 Mar;16(3):552-62.
Craparo A, Freund R, Gustafson TA. 14-3-3 (epsilon) interacts with the insulin-like growth factor I receptor and insulin receptor substrate I in a phosphoserine-dependent manner. J Biol Chem. 1997 Apr 25;272(17):11663-9.
Ogihara T, Isobe T, Ichimura T, Taoka M, Funaki M, Sakoda H, Onishi Y, Inukai K, Anai M, Fukushima Y, Kikuchi M, Yazaki Y, Oka Y, Asano T. 14-3-3 protein binds to insulin receptor substrate-1, one of the binding sites of which is in the phosphotyrosine binding domain. J Biol Chem. 1997 Oct 3;272(40):25267-74.
Kosaki A, Yamada K, Suga J, Otaka A, Kuzuya H. 14-3-3beta protein associates with insulin receptor substrate 1 and decreases insulin-stimulated phosphatidylinositol 3'-kinase activity in 3T3L1 adipocytes. J Biol Chem. 1998 Jan 9;273(2):940-4.

Human ITGA4 (CD49D) Integrin alpha4 (Swissprot = P13612)

```
         1 MAWEARREPG PRRAAVRETV MLLLCLGVPT GRPYNVDTES ALLYQGPHNT LFGYSVVLHS
        61 HGANRWLLVG APTANWLANA SVINPGAIYR CRIGKNPGQT CEQLQLGSPN GEPCGKTCLE
       121 ERDNQWLGVT LSRQPGENGS IVTCGHRWKN IFYIKNENKL PTGGCYGVPP DLRTELSKRI
       181 APCYQDYVKK FGENFASCQA GISSFYTKDL IVMGAPGSSY WTGSLFVYNI TTNKYKAFLD
       241 KQNQVKFGSY LGYSVGAGHF RSQHTTEVVG GAPQHEQIGK AYIFSIDEKE LNILHEMKGK
       301 KLGSYFGASV CAVDLNADGF SDLLVGAPMQ STIREEGRVF VYINSGSGAV MNAMETNLVG
       361 SDKYAARFGE SIVNLGDIDN DGFEDVAIGA PQEDDLQGAI YIYNGRADGI SSTFSQRIEG
       421 LQISKSLSMF GQSISGQIDA DNNGYVDVAV GAFRSDSAVL LRTRPVVIVD ASLSHPESVN
       481 RTKFDCVENG WPSVCIDLTL CFSYKGKEVP GYIVLFYNMS LDVNRKAESP PRFYFSSNGT
       541 SDVITGSIQV SSREANCRTH QAFMRKDVRD ILTPIQIEAA YHLGPHVISK RSTEEFPPLQ
       601 PILQQKKEKD IMKKTINFAR FCAHENCSAD LQVSAKIGFL KPHENKTYLA VGSMKTLMLN
       661 VSLFNAGDDA YETTLHVKLP VGLYFIKILE LEEKQINCEV TDNSGVVQLD CSIGYIYVDH
       721 LSRIDISFLL DVSSLSRAEE DLSITVHATC ENEEEMDNLK HSRVTVAIPL KYEVKLTVHG
       781 FVNPTSFVYG SNDENEPETC MVEKMNLTFH VINTGNSMAP NVSVEIMVPN SFSPQTDKLF
       841 NILDVQTTTG ECHFENYQRV CALEQQKSAM QTLKGIVQFL SKTDKRLLYC IKADPHCLNF
       901 LCNFGKMESG KEASVHIQLE GRPSILEMDE TSALKFEIRA TGFPEPNPRV IELNKDENVA
       961 HVLLEGLHHQ RPKRYFTIVI ISSSLLLGLI VLLLISYVMW KAGFFKRQYK sILQEENRRD
      1021 SWSYINSKSN DD
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>gi|215274002|sp|P13612.2|ITA4_HUMAN RecName: Full=Integrin alpha-4; AltName:
Full=Integrin alpha-IV; AltName: Full=VLA-4; AltName: Full=CD49 antigen-like
family member D; AltName: CD_antigen=CD49d; Flags: Precursor
MAWEARREPGPRRAAVRETVMLLLCLGVPTGRPYNVDTESALLYQGPHNTLFGYSVVLHSHGANRWLLVG
APTANWLANASVINPGAIYRCRIGKNPGQTCEQLQLGSPNGEPCGKTCLEERDNQWLGVTLSRQPGENGS
IVTCGHRWKNIFYIKNENKLPTGGCYGVPPDLRTELSKRIAPCYQDYVKKFGENFASCQAGISSFYTKDL
IVMGAPGSSYWTGSLFVYNITTNKYKAFLDKQNQVKFGSYLGYSVGAGHFRSQHTTEVVGGAPQHEQIGK
AYIFSIDEKELNILHEMKGKKLGSYFGASVCAVDLNADGFSDLLVGAPMQSTIREEGRVFVYINSGSGAV
MNAMETNLVGSDKYAARFGESIVNLGDIDNDGFEDVAIGAPQEDDLQGAIYIYNGRADGISSTFSQRIEG
LQISKSLSMFGQSISGQIDADNNGYVDVAVGAFRSDSAVLLRTRPVVIVDASLSHPESVNRTKFDCVENG
WPSVCIDLTLCFSYKGKEVPGYIVLFYNMSLDVNRKAESPPRFYFSSNGTSDVITGSIQVSSREANCRTH
QAFMRKDVRDILTPIQIEAAYHLGPHVISKRSTEEFPPLQPILQQKKEKDIMKKTINFARFCAHENCSAD
LQVSAKIGFLKPHENKTYLAVGSMKTLMLNVSLFNAGDDAYETTLHVKLPVGLYFIKILELEEKQINCEV
TDNSGVVQLDCSIGYIYVDHLSRIDISFLLDVSSLSRAEEDLSITVHATCENEEEMDNLKHSRVTVAIPL
KYEVKLTVHGFVNPTSFVYGSNDENEPETCMVEKMNLTFHVINTGNSMAPNVSVEIMVPNSFSPQTDKLF
NILDVQTTTGECHFENYQRVCALEQQKSAMQTLKGIVQFLSKTDKRLLYCIKADPHCLNFLCNFGKMESG
KEASVHIQLEGRPSILEMDETSALKFEIRATGFPEPNPRVIELNKDENVAHVLLEGLHHQRPKRYFTIVI
ISSSLLLGLIVLLLISYVMWKAGFFKRQYKSILQEENRRDSWSYINSKSNDD
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Notes

Deakin et al (2009) used a different version because residue numbers don’t match although sequence around 14-3-3 binding motif is the same. Y991 in paper (Y1024 here)
RQYKSIL – 14-3-3 binding motif with pS978 in paper (S1011 here)
ENRRDSWSY – paxillin binding region with S988 a known PKA phosphorylation site (S1021 here).
S978A decreases metabolic labeling of integrin alpha 4 with 32P-orthophosphate
FRET analysis found an interaction between 14-3-3 zeta and integrin α4“The interaction between α4 integrin and 14-3-3ζ is enhanced by the direct association between 14-3-3ζ and paxillin, resulting in the formation of a ternary complex that stabilizes the recruitment of each component. The ternary complex focuses Cdc42 activity at

lamellipodial leading edge".

"Here, we show that MSP-mediated PI3K pathway activation induces Ron serine phosphorylation at residue 1394 as well as α6β4 phosphorylation in the connecting sequence to generate 14-3-3 binding sites on both molecules. Thus, dimeric 14-3-3 proteins mediate the MSP-dependent formation of a Ron/α6β4 complex that in turn induces disassembly of HDs and α6β4 relocation at lamellipodia. Further, α3β1 integrin activation and keratinocyte spreading/migration on laminin-5 takes place. All these findings suggest a role for Ron and 14-3-3 in epidermal reepithelization processes". (Santoro et al 2003)

References to 14-3-3 binding to integrin alpha4

Deakin NO, Bass MD, Warwood S, Schoelermann J, Mostafavi-Pour Z, Knight D, Ballestrem C, Humphries MJ. An integrin-alpha4-14-3-3zeta-paxillin ternary complex mediates localised Cdc42 activity and accelerates cell migration. J Cell Sci. 2009 May 15;122(Pt 10):1654-64.

Santoro MM, Gaudino G, Marchisio PC. The MSP receptor regulates alpha6beta4 and alpha3beta1 integrins via 14-3-3 proteins in keratinocyte migration. Dev Cell. 2003 Aug;5(2):257-71.

Human ITGB1 Integrin beta 1 subunit (fibronectin receptor) (Swissprot = P05556)

```
      1 MNLQPIFWIG LISSVCCVFA QTDENRCLKA NAKSCGECIQ AGPNCGWCTN STFLQEGMPT
     61 SARCDDLEAL KKKGCPPDDI ENPRGSKDIK KNKNVTNRSK GTAEKLKPED ITQIQPQQLV
    121 LRLRSGEPQT FTLKFKRAED YPIDLYYLMD LSYSMKDDLE NVKSLGTDLM NEMRRITSDF
    181 RIGFGSFVEK TVMPYISTTP AKLRNPCTSE QNCTSPFSYK NVLSLTNKGE VFNELVGKQR
    241 ISGNLDSPEG GFDAIMQVAV CGSLIGWRNV TRLLVFSTDA GFHFAGDGKL GGIVLPNDGQ
    301 CHLENNMYTM SHYYDYPSIA HLVQKLSENN IQTIFAVTEE FQPVYKELKN LIPKSAVGTL
    361 SANSSNVIQL IIDAYNSLSS EVILENGKLS EGVTISYKSY CKNGVNGTGE NGRKCSNISI
    421 GDEVQFEISI TSNKCPKKDS DSFKIRPLGF TEEVEVILQY ICECECQSEG IPESPKCHEG
    481 NGTFECGACR CNEGRVGRHC ECSTDEVNSE DMDAYCRKEN SSEICSNNGE CVCGQCVCRK
    541 RDNTNEIYSG KFCECDNFNC DRSNGLICGG NGVCKCRVCE CNPNYTGSAC DCSLDTSTCE
    601 ASNGQICNGR GICECGVCKC TDPKFQGQTC EMCQTCLGVC AEHKECVQCR AFNKGEKKDT
    661 CTQECSYFNI TKVESRDKLP QPVQPDPVSH CKEKDVDDCW FYFTYSVNGN NEVMVHVVEN
    721 PECPTGPDII PIVAGVVAGI VLIGLALLLI WKLLMIIHDR REFAKFEKEK MNAKWDTGEN
    781 PIYKSAVtTV VNPKYEGK
>gi|218563324|sp|P05556.2|ITB1_HUMAN RecName: Full=Integrin beta-1; AltName:
Full=Fibronectin receptor subunit beta; AltName: Full=Integrin VLA-4 subunit
beta; AltName: CD_antigen=CD29; Flags: Precursor
MNLQPIFWIGLISSVCCVFAQTDENRCLKANAKSCGECIQAGPNCGWCTNSTFLQEGMPTSARCDDLEAL
KKKGCPPDDIENPRGSKDIKKNKNVTNRSKGTAEKLKPEDITQIQPQQLVLRLRSGEPQTFTLKFKRAED
YPIDLYYLMDLSYSMKDDLENVKSLGTDLMNEMRRITSDFRIGFGSFVEKTVMPYISTTPAKLRNPCTSE
QNCTSPFSYKNVLSLTNKGEVFNELVGKQRISGNLDSPEGGFDAIMQVAVCGSLIGWRNVTRLLVFSTDA
GFHFAGDGKLGGIVLPNDGQCHLENNMYTMSHYYDYPSIAHLVQKLSENNIQTIFAVTEEFQPVYKELKN
LIPKSAVGTLSANSSNVIQLIIDAYNSLSSEVILENGKLSEGVTISYKSYCKNGVNGTGENGRKCSNISI
GDEVQFEISITSNKCPKKDSDSFKIRPLGFTEEVEVILQYICECECQSEGIPESPKCHEGNGTFECGACR
CNEGRVGRHCECSTDEVNSEDMDAYCRKENSSEICSNNGECVCGQCVCRKRDNTNEIYSGKFCECDNFNC
DRSNGLICGGNGVCKCRVCECNPNYTGSACDCSLDTSTCEASNGQICNGRGICECGVCKCTDPKFQGQTC
EMCQTCLGVCAEHKECVQCRAFNKGEKKDTCTQECSYFNITKVESRDKLPQPVQPDPVSHCKEKDVDDCW
FYFTYSVNGNNEVMVHVVENPECPTGPDIIPIVAGVVAGIVLIGLALLLIWKLLMIIHDRREFAKFEKEK
MNAKWDTGENPIYKSAVTTVVNPKYEGK
```

Notes

Reported to be a phosphorylation-independent interaction between 14-3-3 and integrin beta1

References to 14-3-3 binding to integrin beta1

Han DC, Rodriguez LG, Guan JL. Identification of a novel interaction between integrin beta1 and 14-3-3beta. Oncog 2001 Jan 18;20(3):346-57

Human ITGB2 Integrin beta 2 subunit. (Swissprot = P05107)

Thr758 only for WEBLOGO

```
      1 MLGLRPPLLA LVGLLSLGCV LSQECTKFKV SSCRECIESG PGCTWCQKLN FTGPGDPDSI
     61 RCDTRPQLLM RGCAADDIMD PTSLAETQED HNGGQKQLSP QKVTLYLRPG QAAAFNVTFR
    121 RAKGYPIDLY YLMDLSYSML DDLRNVKKLG GDLLRALNEI TESGRIGFGS FVDKTVLPFV
    181 NTHPDKLRNP CPNKEKECQP PFAFRHVLKL TNNSNQFQTE VGKQLISGNL DAPEGGLDAM
    241 MQVAACPEEI GWRNVTRLLV FATDDGFHFA GDGKLGAILT PNDGRCHLED NLYKRSNEFD
    301 YPSVGQLAHK LAENNIQPIF AVTSRMVKTY EKLTEIIPKS AVGELSEDSS NVVQLIKNAY
    361 NKLSSRVFLD HNALPDTLKV TYDSFCSNGV THRNQPRGDC DGVQINVPIT FQVKVTATEC
    421 IQEQSFVIRA LGFTDIVTVQ VLPQCECRCR DQSRDRSLCH GKGFLECGIC RCDTGYIGKN
    481 CECQTQGRSS QELEGSCRKD NNSIICSGLG DCVCGQCLCH TSDVPGKLIY GQYCECDTIN
    541 CERYNGQVCG GPGRGLCFCG KCRCHPGFEG SACQCERTTE GCLNPRRVEC SGRGRCRCNV
    601 CECHSGYQLP LCQECPGCPS PCGKYISCAE CLKFEKGPFG KNCSAACPGL QLSNNPVKGR
    661 TCKERDSEGC WVAYTLEQQD GMDRYLIYVD ESRECVAGPN IAAIVGGTVA GIVLIGILLL
    721 VIWKALIHLS DLREYRRFEK EKLKSQWNND NPLFKSAtTT VMNPKFAES
>gi|124056465|sp|P05107.2|ITB2_HUMAN RecName: Full=Integrin beta-2; AltName:
Full=Cell surface adhesion glycoproteins LFA-1/CR3/p150,95 subunit beta;
AltName: Full=Complement receptor C3 subunit beta; AltName: CD_antigen=CD18;
Flags: Precursor
MLGLRPPLLALVGLLSLGCVLSQECTKFKVSSCRECIESGPGCTWCQKLNFTGPGDPDSIRCDTRPQLLM
RGCAADDIMDPTSLAETQEDHNGGQKQLSPQKVTLYLRPGQAAAFNVTFRRAKGYPIDLYYLMDLSYSML
DDLRNVKKLGGDLLRALNEITESGRIGFGSFVDKTVLPFVNTHPDKLRNPCPNKEKECQPPFAFRHVLKL
TNNSNQFQTEVGKQLISGNLDAPEGGLDAMMQVAACPEEIGWRNVTRLLVFATDDGFHFAGDGKLGAILT
PNDGRCHLEDNLYKRSNEFDYPSVGQLAHKLAENNIQPIFAVTSRMVKTYEKLTEIIPKSAVGELSEDSS
NVVQLIKNAYNKLSSRVFLDHNALPDTLKVTYDSFCSNGVTHRNQPRGDCDGVQINVPITFQVKVTATEC
IQEQSFVIRALGFTDIVTVQVLPQCECRCRDQSRDRSLCHGKGFLECGICRCDTGYIGKNCECQTQGRSS
QELEGSCRKDNNSIICSGLGDCVCGQCLCHTSDVPGKLIYGQYCECDTINCERYNGQVCGGPGRGLCFCG
KCRCHPGFEGSACQCERTTEGCLNPRRVECSGRGRCRCNVCECHSGYQLPLCQECPGCPSPCGKYISCAE
CLKFEKGPFGKNCSAACPGLQLSNNPVKGRTCKERDSEGCWVAYTLEQQDGMDRYLIYVDESRECVAGPN
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IAAIVGGTVAGIVLIGILLLVIWKALIHLSDLREYRRFEKEKLKSQWNNDNPLFKSATTTVMNPKFAES
>gi|124056465|sp|P05107.2|ITB2_HUMAN RecName: Full=Integrin beta-2; AltName:
Full=Cell surface adhesion glycoproteins LFA-1/CR3/p150,95 subunit beta;
AltName: Full=Complement receptor C3 subunit beta; AltName: CD_antigen=CD18;
Flags: Precursor
MLGLRPPLLALVGLLSLGCVLSQECTKFKVSSCRECIESGPGCTWCQKLNFTGPGDPDSIRCDTRPQLLM
RGCAADDIMDPTSLAETQEDHNGGQKQLSPQKVTLYLRPGQAAAFNVTFRRAKGYPIDLYYLMDLSYSML
DDLRNVKKLGGDLLRALNEITESGRIGFGSFVDKTVLPFVNTHPDKLRNPCPNKEKECQPPFAFRHVLKL
TNNSNQFQTEVGKQLISGNLDAPEGGLDAMMQVAACPEEIGWRNVTRLLVFATDDGFHFAGDGKLGAILT
PNDGRCHLEDNLYKRSNEFDYPSVGQLAHKLAENNIQPIFAVTSRMVKTYEKLTEIIPKSAVGELSEDSS
NVVQLIKNAYNKLSSRVFLDHNALPDTLKVTYDSFCSNGVTHRNQPRGDCDGVQINVPITFQVKVTATEC
IQEQSFVIRALGFTDIVTVQVLPQCECRCRDQSRDRSLCHGKGFLECGICRCDTGYIGKNCECQTQGRSS
QELEGSCRKDNNSIICSGLGDCVCGQCLCHTSDVPGKLIYGQYCECDTINCERYNGQVCGGPGRGLCFCG
KCRCHPGFEGSACQCERTTEGCLNPRRVECSGRGRCRCNVCECHSGYQLPLCQECPGCPSPCGKYISCAE
CLKFEKGPFGKNCSAACPGLQLSNNPVKGRTCKERDSEGCWVAYTLEQQDGMDRYLIYVDESRECVAGPN
IAAIVGGTVAGIVLIGILLLVIWKALIHLSDLREYRRFEKEKLKSQWNNDNPLFKSATTTVMNPKFAES
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Notes

ITGB2 the integrin beta 2 subunit. Can combine with multiple partners resulting in different integrins. For example, beta 2 combines with the alpha L chain to form the integrin LFA-1, and combines with the alpha M chain to form the integrin Mac-1. Participates in cell adhesion as well as cell-surface mediated signaling. Defects are the cause of leukocyte adhesion deficiency type I (LAD1).

From Fagerholmet al (2002)

S745 and T758 are phosphorylated by PKC βδη in vitro using an integrin peptide as substrate (RRFEK EKLKSQWNND NPLFKSAtTT VMNPKFAES)

Endogenous 14-3-3s from human leukocyte lysate was specifically pulled down on an agarose column that had been covalently coupled with phospho-T758 peptide but not unphosphorylated peptide or phospho-S756.

Endogenous 14-3-3 from cytoplasmic and cytoskeletal fractions bound to phospho-T758 column but not unphosphorylated column – most of the phosphorylated integrins reside in the cytoskeleton fraction.

Mass fingerprint of the endogenous 14-3-3s identified 14-3-3 βand ζ

S756 is an in vivo phosphorylation site induced by phorbol ester stimulation.

From Takala et al (2008)

Phorbol ester treatment (PDBu) of T cells leads to T758 phosphorylation, seen with a phosphospecific antibody. Peptide affinity columns corresponding to phospho-T758 and non-phospho-T758 were used to pulldown proteins from T cell lysates. 14-3-3 only interacted with phosphoryated peptide column while filamin showed preference for the non-phosphorylated column. When T758 is phosphorylated, 14-3-3s bind while filamin cannot bind so phosphorylation acts as a switch. Phosphorylation of T758 may lead to detachment of talin from the integrin tail.

Notes

ITGB2 the integrin beta 2 subunit. Can combine with multiple partners resulting in different integrins. For example, beta 2 combines with the alpha L chain to form the integrin LFA-1, and combines with the alpha M chain to form the integrin Mac-1. Participates in cell adhesion as well as cell-surface mediated signaling. Defects are the cause of leukocyte adhesion deficiency type I (LAD1).

Integrin beta 1 (fibronectin receptor)	780 NPI**Y**...........................KSAVT**T**VV	NP_002202
Integrin beta 3 (platelet glycoprotein IIIa)	770 NPL**Y**KEA..........................TSTF**T**NI	NP_000203
Integrin beta-6	759 NPL**Y**R............................GSTS**T**FK	A37057
Integrin beta-7	775 NPL**Y**KS..........................AITT**T**IN	P26010

References to 14-3-3 binding to integrin beta2

Fagerholm S, Morrice N, Gahmberg CG, Cohen P. Phosphorylation of the cytoplasmic domain of the integrin CD18 chain by protein kinase C isoforms in leukocytes. J Biol Chem. 2002 Jan 18;277(3):1728-38.

Takala H, Nurminen E, Nurmi SM, Aatonen M, Strandin T, Takatalo M, Kiema T, Gahmberg CG, Ylänne J, Fagerholm SC. Beta2 integrin phosphorylation on Thr758 acts as a molecular switch to regulate 14-3-3 and filamin binding. Blood. 2008 Sep 1;112(5):1853-62.

Nurmi SM, Gahmberg CG, Fagerholm SC. 14-3-3 proteins bind both filamin and alphaLbeta2 integrin in activated T cells. Ann N Y Acad Sci. 2006 Dec;1090:318-25.

The focus of the paper below was not on integrin beta2 but on c-Cbl

Co-ip of 14-3-3 with c-Cbl was enhanced after cells were allowed to adhere to fibrinogen in the presence of TNF when compared to control cells. It was reduced after pretreatment of cells with a PKC inhibitor. GF-109203X

Melander F, Andersson T, Dib K. Engagement of beta2 integrins recruits 14-3-3 proteins to c-Cbl in human neutrophils. Biochem Biophys Res Commun. 2004 May 14;317(4):1000-5.

Legate KR, Fässler R. Mechanisms that regulate adaptor binding to beta-integrin cytoplasmic tails. J Cell Sci. 2009 Jan 15;122(Pt 2):187-98.

Human KANK1 kidney ankyrin repeat–containing protein 1 (aka ANKRD15) (Swissprot = Q14678)

```
         1 MAHTTKVNGS ASGKAGDILS GDQDKEQKDP YFVETPYGYQ LDLDFLKYVD DIQKGNTIKR
        61 LNIQKRRKPS VPCPEPRTTS GQQGIWTSTE SLSSSNSDDN KQCPNFLIAR SQVTSTPISK
       121 PPPPLETSLP FLTIPENRQL PPPSPQLPKH NLHVTKTLME TRRRLEQERA TMQMTPGEFR
       181 RPRLASFGGM GTTSSLPSFV GSGNHNPAKH QLQNGYQGNG DYGSYAPAAP TTSSMGSSIR
       241 HSPLSSGIST PVTNVSPMHL QHIREQMAIA LKRLKELEEQ VRTIPVLQVK ISVLQEEKRQ
       301 LVSQLKNQRA ASQINVCGVR KRSYsAGNAS QLEQLSRARR SGGELYIDYE EEEMETVEQS
       361 TQRIKEFRQL TADMQALEQK IQDSSCEASS ELRENGECRS VAVGAEENMN DIVVYHRGSR
       421 SCKDAAVGTL VEMRNCGVSV TEAMLGVMTE ADKEIELQQQ TIESLKEKIY RLEVQLRETT
       481 HDREMTKLKQ ELQAAGSRKK VDKATMAQPL VFSKVVEAVV QTRDQMVGSH MDLVDTCVGT
       541 SVETNSVGIS CQPECKNKVV GPELPMNWWI VKERVEMHDR CAGRSVEMCD KSVSVEVSVC
       601 ETGSNTEESV NDLTLLKTNL NLKEVRSIGC GDCSVDVTVC SPKECASRGV NTEAVSQVEA
       661 AVMAVPRTAD QDTSTDLEQV HQFTNTETAT LIESCTNTCL STLDKQTSTQ TVETRTVAVG
       721 EGRVKDINSS TKTRSIGVGT LLSGHSGFDR PSAVKTKESG VGQININDNY LVGLKMRTIA
       781 CGPPQLTVGL TASRRSVGVG DDPVGESLEN PQPQAPLGMM TGLDHYIERI QKLLAEQQTL
       841 LAENYSELAE AFGEPHSQMG SLNSQLISTL SSINSVMKSA STEELRNPDF QKTSLGKITG
```

```
      901 NYLGYTCKCG GLQSGSPLSS QTSQPEQEVG TSEGKPISSL DAFPTQEGTL SPVNLTDDQI
      961 AAGLYACTNN ESTLKSIMKK KDGNKDSNGA KKNLQFVGIN GGYETTSSDD SSSDESSSSE
     1021 SDDECDVIEY PLEEEEEEED EDTRGMAEGH HAVNIEGLKS ARVEDEMQVQ ECEPEKVEIR
     1081 ERYELSEKML SACNLLKNTI NDPKALTSKD MRFCLNTLQH EWFRVSSQKS AIPAMVGDYI
     1141 AAFEAISPDV LRYVINLADG NGNTALHYSV SHSNFEIVKL LLDADVCNVD HQNKAGYTPI
     1201 MLAALAAVEA EKDMRIVEEL FGCGDVNAKA SQAGQTALML AVSHGRIDMV KGLLACGADV
     1261 NIQDDEGSTA LMCASEHGHV EIVKLLLAQP GCNGHLEDND GSTALSIALE AGHKDIAVLL
     1321 YAHVNFAKAQ SPGTPRLGRK TSPGPTHRGS FD
>gi|73920184|sp|Q14678.3|KANK1_HUMAN RecName: Full=KN motif and ankyrin
repeat domain-containing protein 1; AltName: Full=Ankyrin repeat domain-
containing protein 15; AltName: Full=Kidney ankyrin repeat-containing protein
MAHTTKVNGSASGKAGDILSGDQDKEQKDPYFVETPYGYQLDLDFLKYVDDIQKGNTIKRLNIQKRRKPS
VPCPEPRTTSGQQGIWTSTESLSSSNSDDNKQCPNFLIARSQVTSTPISKPPPPLETSLPFLTIPENRQL
PPPSPQLPKHNLHVTKTLMETRRRLEQERATMQMTPGEFRRPRLASFGGMGTTSSLPSFVGSGNHNPAKH
QLQNGYQGNGDYGSYAPAAPTTSSMGSSIRHSPLSSGISTPVTNVSPMHLQHIREQMAIALKRLKELEEQ
VRTIPVLQVKISVLQEEKRQLVSQLKNQRAASQINVCGVRKRSYSAGNASQLEQLSRARRSGGELYIDYE
EEEMETVEQSTQRIKEFRQLTADMQALEQKIQDSSCEASSELRENGECRSVAVGAEENMNDIVVYHRGSR
SCKDAAVGTLVEMRNCGVSVTEAMLGVMTEADKEIELQQQTIESLKEKIYRLEVQLRETTHDREMTKLKQ
ELQAAGSRKKVDKATMAQPLVFSKVVEAVVQTRDQMVGSHMDLVDTCVGTSVETNSVGISCQPECKNKVV
GPELPMNWWIVKERVEMHDRCAGRSVEMCDKSVSVEVSVCETGSNTEESVNDLTLLKTNLNLKEVRSIGC
GDCSVDVTVCSPKECASRGVNTEAVSQVEAAVMAVPRTADQDTSTDLEQVHQFTNTETATLIESCTNTCL
STLDKQTSTQTVETRTVAVGEGRVKDINSSTKTRSIGVGTLLSGHSGFDRPSAVKTKESGVGQININDNY
LVGLKMRTIACGPPQLTVGLTASRRSVGVGDDPVGESLENPQPQAPLGMMTGLDHYIERIQKLLAEQQTL
LAENYSELAEAFGEPHSQMGSLNSQLISTLSSINSVMKSASTEELRNPDFQKTSLGKITGNYLGYTCKCG
GLQSGSPLSSQTSQPEQEVGTSEGKPISSLDAFPTQEGTLSPVNLTDDQIAAGLYACTNNESTLKSIMKK
KDGNKDSNGAKKNLQFVGINGGYETTSSDDSSSDESSSSESDDECDVIEYPLEEEEEEEDEDTRGMAEGH
HAVNIEGLKSARVEDEMQVQECEPEKVEIRERYELSEKMLSACNLLKNTINDPKALTSKDMRFCLNTLQH
EWFRVSSQKSAIPAMVGDYIAAFEAISPDVLRYVINLADGNGNTALHYSVSHSNFEIVKLLLDADVCNVD
HQNKAGYTPIMLAALAAVEAEKDMRIVEELFGCGDVNAKASQAGQTALMLAVSHGRIDMVKGLLACGADV
NIQDDEGSTALMCASEHGHVEIVKLLLAQPGCNGHLEDNDGSTALSIALEAGHKDIAVLLYAHVNFAKAQ
SPGTPRLGRKTSPGPTHRGSFD
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Notes

Deletion of the ANKRD15 gene at 9p24.3 causes parent-of-origin-dependent inheritance of familial cerebral palsy. The Kank family of proteins, Kank1–Kank4, are characterized by their unique structure, coiled-coil motifs in the N-terminal region, and ankyrin-repeats in the C-terminal region, with an additional motif, the KN motif, at the N-terminus. Kank is KANK potential tumour suppressor for renal cell carcinoma and an Akt substrate located downstream of PI3K and a 14-3-3-binding protein. The interaction between Kank and 14-3-3 is regulated by insulin and EGF and is mediated through phosphorylation of Kank by Akt. Q14678 is the KANK-L (long isoform), whereas Kakinuma et al (2008) must have studied the KANK-S form, which lacks the N-terminal 158 amino acids, because they report the phosphorylated residue to be Ser167 (NVCGVRKRSYsAGNASQLEQL). (Variants described in Wang Y, Onishi Y, Kakinuma N, Roy BC, Aoyagi T, Kiyama R. Alternative splicing of the human Kank gene produces two types of Kank protein. Biochem Biophys Res Commun. 2005 May 20;330(4):1247-53.)

References to 14-3-3 binding to KANK1

Kakinuma N, Roy BC, Zhu Y, Wang Y, Kiyama R. (2008) Kank regulates RhoA-dependent formation of actin stress fibers and cell migration via 14-3-3 in PI3K-Akt signaling. J Cell Biol. 181(3):537-49

Kakinuma N, Zhu Y, Wang Y, Roy BC, Kiyama R. Kank proteins: structure, functions and diseases. Cell Mol Life Sci. 2009 Aug;66(16):2651-9.

Human KCNK3 Two-pore-domain potassium channel TASK-1 (Swissprot = O14649)

```
        1 MKRQNVRTLA LIVCTFTYLL VGAAVFDALE SEPELIERQR LELRQQELRA RYNLSQGGYE
       61 ELERVVLRLK PHKAGVQWRF AGSFYFAITV ITTIGYGHAA PSTDGGKVFC MFYALLGIPL
      121 TLVMFQSLGE RINTLVRYLL HRAKKGLGMR RADVSMANMV LIGFFSCIST LCIGAAAFSH
      181 YEHWTFFQAY YYCFITLTTI GFGDYVALQK DQALQTQPQY VAFSFVYILT GLTVIGAFLN
      241 LVVLRFMTMN AEDEKRDAEH RALLTRNGQA GGGGGGGSAH TTDTASSTAA AGGGGFRNVY
      301 AEVLHFQSMC SCLWYKSREK LQYSIPMIIP RDLSTSDTCV EQSHSSPGGG GRYSDTPSRR
      361 CLCSGAPRSA ISSVSTGLHS LSTFRGLMKR RSsV
>gi|13124040|sp|O14649.1|KCNK3_HUMAN RecName: Full=Potassium channel
subfamily K member 3; AltName: Full=Acid-sensitive potassium channel protein
TASK-1; AltName: Full=TWIK-related acid-sensitive K(+) channel 1; AltName:
Full=Two pore potassium channel KT3.1
MKRQNVRTLALIVCTFTYLLVGAAVFDALESEPELIERQRLELRQQELRARYNLSQGGYEELERVVLRLK
PHKAGVQWRFAGSFYFAITVITTIGYGHAAPSTDGGKVFCMFYALLGIPLTLVMFQSLGERINTLVRYLL
HRAKKGLGMRRADVSMANMVLIGFFSCISTLCIGAAAFSHYEHWTFFQAYYYCFITLTTIGFGDYVALQK
DQALQTQPQYVAFSFVYILTGLTVIGAFLNLVVLRFMTMNAEDEKRDAEHRALLTRNGQAGGGGGGGSAH
TTDTASSTAAAGGGGFRNVYAEVLHFQSMCSCLWYKSREKLQYSIPMIIPRDLSTSDTCVEQSHSSPGGG
GRYSDTPSRRCLCSGAPRSAISSVSTGLHSLSTFRGLMKRRSSV
```

Notes

$\mathrm{RRSpS}^{393}\mathrm{V}\text{-}_{\mathrm{COOH}}$

References to 14-3-3 binding to KCNK3

O'Kelly I, Butler MH, Zilberberg N, Goldstein SA. Forward transport. 14-3-3 binding overcomes retention in endoplasmic reticulum by dibasic signals. Cell. 2002 Nov 15;111(4):577-88.

Zuzarte M, Heusser K, Renigunta V, Schlichthörl G, Rinné S, Wischmeyer E, Daut J, Schwappach B, Preisig-Müller R. Intracellular traffic of the K+ channels TASK-1 and TASK-3: role of N- and C-terminal sorting signals and interaction with 14-3-3 proteins. J Physiol. 2009 Mar 1;587(Pt 5):929-52.

Human KCNK9 Two-pore-domain potassium channel TASK-3 (Swissprot = Q9NPC2)

```
        1 MKRQNVRTLS LIVCTFTYLL VGAAVFDALE SDHEMREEEK LKAEEIRIKG KYNISSEDYR
       61 QLELVILQSE PHRAGVQWKF AGSFYFAITV ITTIGYGHAA PGTDAGKAFC MFYAVLGIPL
```

```
      121 TLVMFQSLGE RMNTFVRYLL KRIKKCCGMR NTDVSMENMV TVGFFSCMGT LCIGAAAFSQ
      181 CEEWSFFHAY YYCFITLTTI GFGDYVALQT KGALQKKPLY VAFSFMYILV GLTVIGAFLN
      241 LVVLRFLTMN SEDERRDAEE RASLAGNRNS MVIHIPEEPR PSRPRYKADV PDLQSVCSCT
      301 CYRSQDYGGR SVAPQNSFSA KLAPHYFHSI SYKIEEISPS TLKNSLFPSP ISSISPGLHS
      361 FTDHQRLMKR RKsV
>gi|13431426|sp|Q9NPC2.1|KCNK9_HUMAN RecName: Full=Potassium channel
subfamily K member 9; AltName: Full=Acid-sensitive potassium channel protein
TASK-3; AltName: Full=TWIK-related acid-sensitive K(+) channel 3; AltName:
Full=Two pore potassium channel KT3.2
MKRQNVRTLSLIVCTFTYLLVGAAVFDALESDHEMREEEKLKAEEIRIKGKYNISSEDYRQLELVILQSE
PHRAGVQWKFAGSFYFAITVITTIGYGHAAPGTDAGKAFCMFYAVLGIPLTLVMFQSLGERMNTFVRYLL
KRIKKCCGMRNTDVSMENMVTVGFFSCMGTLCIGAAAFSQCEEWSFFHAYYYCFITLTTIGFGDYVALQT
KGALQKKPLYVAFSFMYILVGLTVIGAFLNLVVLRFLTMNSEDERRDAEERASLAGNRNSMVIHIPEEPR
PSRPRYKADVPDLQSVCSCTCYRSQDYGGRSVAPQNSFSAKLAPHYFHSISYKIEEISPSTLKNSLFPSP
ISSISPGLHSFTDHQRLMKRRKSV
```

Notes

RRKpS^{373}V-$_{\mathrm{COOH}}$

References to 14-3-3 binding to KCNK9

Zuzarte M, Heusser K, Renigunta V, Schlichthörl G, Rinné S, Wischmeyer E, Daut J, Schwappach B, Preisig-Müller R. Intracellular traffic of the K+ channels TASK-1 and TASK-3: role of N- and C-terminal sorting signals and interaction with 14-3-3 proteins. J Physiol. 2009 Mar 1;587(Pt 5):929-52.

Human KIF1C (Kinesin-like protein KIF1C) (Swissprot = O43896)

```
        1 MAGASVKVAV RVRPFNARET SQDAKCVVSM QGNTTSIINP KQSKDAPKSF TFDYSYWSHT
       61 STEDPQFASQ QQVYRDIGEE MLLHAFEGYN VCIFAYGQTG AGKSYTMMGR QEPGQQGIVP
      121 QLCEDLFSRV SENQSAQLSY SVEVSYMEIY CERVRDLLNP KSRGSLRVRE HPILGPYVQD
      181 LSKLAVTSYA DIADLMDCGN KARTVAATNM NETSSRSHAV FTIVFTQRCH DQLTGLDSEK
      241 VSKISLVDLA GSERADSSGA RGMRLKEGAN INKSLTTLGK VISALADMQS KKRKSDFIPY
      301 RDSVLTWLLK ENLGGNSRTA MIAALSPADI NYEETLSTLR YADRTKQIRC NAIINEDPNA
      361 RLIRELQEEV ARLRELLMAQ GLSASALEGL KTEEGSVRGA LPAVSSPPAP VSPSSPTTHN
      421 GELEPSFSPN TESQIGPEEA MERLQETEKI IAELNETWEE KLRKTEALRM EREALLAEMG
      481 VAVREDGGTV GVFSPKKTPH LVNLNEDPLM SECLLYHIKD GVTRVGQVDM DIKLTGQFIR
      541 EQHCLFRSIP QPDGEVVVTL EPCEGAETYV NGKLVTEPLV LKSGNRIVMG KNHVFRFNHP
      601 EQARLERERG VPPPPGPPSE PVDWNFAQKE LLEQQGIDIK LEMEKRLQDL ENQYRKEKEE
      661 ADLLLEQQRL YADSDSGDDS DKRSCEESWR LISSLREQLP PTTVQTIVKR CGLPSSGKRR
      721 APRRVYQIPQ RRRLQGKDPR WATMADLKMQ AVKEICYEVA LADFRHGRAE IEALAALKMR
      781 ELCRTYGKPD GPGDAWRAVA RDVWDTVGEE EGGGAGSGGG SEEGARGAEV EDLRAHIDKL
      841 TGILQEVKLQ NSSKDRELQA LRDRMLRMER VIPLAQDHED ENEEGGEVPW APPEGSEAAE
      901 EAAPSDRMPS ARPPSPPLSS WERVSRLMEE DPAFRRGRLR WLKQEQLRLQ GLQGSGGRGG
      961 GLRRPPARFV PPHDCKLRFP FKSNPQHRES WPGMGSGEAP TPLQPPEEVT PHPATPARRP
     1021 PSPRRSHHPR RNSLDGGGRS RGAGSAQPEP QHFQPKKHNS YPQPPQPYPA QRPPGPRYPP
     1081 YTTPPRMRRQ RsAPDLKESG AAV
>gi|116242606|sp|O43896.3|KIF1C_HUMAN RecName: Full=Kinesin-like protein
KIF1C
MAGASVKVAVRVRPFNARETSQDAKCVVSMQGNTTSIINPKQSKDAPKSFTFDYSYWSHTSTEDPQFASQ
QQVYRDIGEEMLLHAFEGYNVCIFAYGQTGAGKSYTMMGRQEPGQQGIVPQLCEDLFSRVSENQSAQLSY
SVEVSYMEIYCERVRDLLNPKSRGSLRVREHPILGPYVQDLSKLAVTSYADIADLMDCGNKARTVAATNM
NETSSRSHAVFTIVFTQRCHDQLTGLDSEKVSKISLVDLAGSERADSSGARGMRLKEGANINKSLTTLGK
VISALADMQSKKRKSDFIPYRDSVLTWLLKENLGGNSRTAMIAALSPADINYEETLSTLRYADRTKQIRC
NAIINEDPNARLIRELQEEVARLRELLMAQGLSASALEGLKTEEGSVRGALPAVSSPPAPVSPSSPTTHN
GELEPSFSPNTESQIGPEEAMERLQETEKIIAELNETWEEKLRKTEALRMEREALLAEMGVAVREDGGTV
GVFSPKKTPHLVNLNEDPLMSECLLYHIKDGVTRVGQVDMDIKLTGQFIREQHCLFRSIPQPDGEVVVTL
EPCEGAETYVNGKLVTEPLVLKSGNRIVMGKNHVFRFNHPEQARLERERGVPPPPGPPSEPVDWNFAQKE
LLEQQGIDIKLEMEKRLQDLENQYRKEKEEADLLLEQQRLYADSDSGDDSDKRSCEESWRLISSLREQLP
PTTVQTIVKRCGLPSSGKRRAPRRVYQIPQRRRLQGKDPRWATMADLKMQAVKEICYEVALADFRHGRAE
IEALAALKMRELCRTYGKPDGPGDAWRAVARDVWDTVGEEEGGGAGSGGGSEEGARGAEVEDLRAHIDKL
TGILQEVKLQNSSKDRELQALRDRMLRMERVIPLAQDHEDENEEGGEVPWAPPEGSEAAEEAAPSDRMPS
ARPPSPPLSSWERVSRLMEEDPAFRRGRLRWLKQEQLRLQGLQGSGGRGGGLRRPPARFVPPHDCKLRFP
FKSNPQHRESWPGMGSGEAPTPLQPPEEVTPHPATPARRPPSPRRSHHPRRNSLDGGGRSRGAGSAQPEP
QHFQPKKHNSYPQPPQPYPAQRPPGPRYPPYTTPPRMRRQRSAPDLKESGAAV
```

Notes

RRQRS^{1092}AP

References to 14-3-3 binding to KIF1C

Dorner C, Ullrich A, Häring HU, Lammers R. The kinesin-like motor protein KIF1C occurs in intact cells as a dimer and associates with proteins of the 14-3-3 family. J Biol Chem. 1999 Nov 19;274(47):33654-60.

Human KLC2 (Swissprot = Q9H0B6)

```
        1 MAMMVFPREE KLSQDEIVLG TKAVIQGLET LRGEHRALLA PLVAPEAGEA EPGSQERCIL
       61 LRRSLEAIEL GLGEAQVILA LSSHLGAVES EKQKLRAQVR RLVQENQWLR EELAGTQQKL
      121 QRSEQAVAQL EEEKQHLLFM SQIRKLDEDA SPNEEKGDVP KDTLDDLFPN EDEQSPAPSP
      181 GGGDVSGQHG GYEIPARLRT LHNLVIQYAS QGRYEVAVPL CKQALEDLEK TSGHDHPDVA
      241 TMLNILALVY RDQNKYKEAA HLLNDALAIR EKTLGKDHPA VAATLNNLAV LYGKRGKYKE
      301 AEPLCKRALE IREKVLGKFH PDVAKQLSNL ALLCQNQGKA EEVEYYYRRA LEIYATRLGP
      361 DDPNVAKTKN NLASCYLKQG KYQDAETLYK EILTRAHEKE FGSVNGDNKP IWMHAEEREE
      421 SKDKRRDSAP YGEYGSWYKA CKVDSPTVNT TLRSLGALYR RQGKLEAAHT LEDCASRNRK
      481 QGLDPASQTK VVELLKDGSG RRGDRRSSRD MAGGAGPRSE SDLEDVGPTA EWNGDGSGSL
      541 RRSGSFGKLR DALRRSSEML VKKLQGGTPQ EPPNPRMKRA SsLNFLNKSV EEPTQPGGTG
      601 LSDSRTLSSS SMDLSRRSSL VG
```

```
>gi|13878553|sp|Q9H0B6.1|KLC2_HUMAN RecName: Full=Kinesin light chain 2;
Short=KLC 2
MAMMVFPREEKLSQDEIVLGTKAVIQGLETLRGEHRALLAPLVAPEAGEAEPGSQERCILLRRSLEAIEL
GLGEAQVILALSSHLGAVESEKQKLRAQVRRLVQENQWLREELAGTQQKLQRSEQAVAQLEEEKQHLLFM
SQIRKLDEDASPNEEKGDVPKDTLDDLFPNEDEQSPAPSPGGGDVSGQHGGYEIPARLRTLHNLVIQYAS
QGRYEVAVPLCKQALEDLEKTSGHDHPDVATMLNILALVYRDQNKYKEAAHLLNDALAIREKTLGKDHPA
VAATLNNLAVLYGKRGKYKEAEPLCKRALEIREKVLGKFHPDVAKQLSNLALLCQNQGKAEEVEYYYRRA
LEIYATRLGPDDPNVAKTKNNLASCYLKQGKYQDAETLYKEILTRAHEKEFGSVNGDNKPIWMHAEERE
SKDKRRDSAPYGEYGSWYKACKVDSPTVNTTLRSLGALYRRQGKLEAAHTLEDCASRNRKQGLDPASQTK
VVELLKDGSGRRGDRRSSRDMAGGAGPRSESDLEDVGPTAEWNGDGSGSLRRSGSFGKLRDALRRSSEML
VKKLQGGTPQEPPNPRMKRASSLNFLNKSVEEPTQPGGTGLSDSRTLSSSSMDLSRRSSLVG
```

Notes

KLC2 Kinesin is a microtubule-associated force-producing protein that may play a role in organelle transport. The light chain may function in coupling of cargo to the heavy chain or in the modulation of its ATPase activity. Subsequent analysis showed that 14-3-3 directly binds to kinesin heterodimers through interaction with KLC2 and that this interaction is dependent on the phosphorylation of KLC2. Studies on the interaction between 14-3-3 and KLC2 variants expressed in cultured cells coupled with mass spectrometric analysis proved that Ser575 (RAS(pS575)LNFL) in mouse KLC2 (6680578) is the site of phosphorylation in KLC2 that is responsible for the in vivo interaction with the 14-3-3 protein (= Ser582 in human KLC2 Q9H0B6).

References to 14-3-3 binding to kinesin light chain 2

Ichimura T, Wakamiya-Tsuruta A, Itagaki C, Taoka M, Hayano T, Natsume T, Isobe T. Phosphorylation-dependent interaction of kinesin light chain 2 and the 14-3-3 protein. Biochemistry. 2002 Apr 30;41(17):5566-72

Pozuelo Rubio M, Geraghty KM, Wong BH, Wood NT, Campbell DG, Morrice N, Mackintosh C. 14-3-3-affinity purification of over 200 human phosphoproteins reveals new links to regulation of cellular metabolism, proliferation and trafficking. Biochem J. 2004 Apr 15;379(Pt 2):395-408.

Human KRT18 Keratin 18 (Swissprot = P05783)

```
        1 MSFTTRSTFS TNYRSLGSVQ APSYGARPVS SAAsVYAGAG GSGSRISVSR STSFRGGMGS
       61 GGLATGIAGG LAGMGGIQNE KETMQSLNDR LASYLDRVRS LETENRRLES KIREHLEKKG
      121 PQVRDWSHYF KIIEDLRAQI FANTVDNARI VLQIDNARLA ADDFRVKYET ELAMRQSVEN
      181 DIHGLRKVID DTNITRLQLE TEIEALKEEL LFMKKNHEEE VKGLQAQIAS SGLTVEVDAP
      241 KSQDLAKIMA DIRAQYDELA RKNREELDKY WSQQIEESTT VVTTQSAEVG AAETTLTELR
      301 RTVQSLEIDL DSMRNLKASL ENSLREVEAR YALQMEQLNG ILLHLESELA QTRAEGQRQA
      361 QEYEALLNIK VKLEAEIATY RRLLEDGEDF NLGDALDSSN SMQTIQKTTT RRIVDGKVVS
      421 ETNDTKVLRH
>gi|125083|sp|P05783.2|K1C18_HUMAN RecName: Full=Keratin, type I cytoskeletal
18; AltName: Full=Cytokeratin-18; Short=CK-18; AltName: Full=Keratin-18;
Short=K18; AltName: Full=Cell proliferation-inducing gene 46 protein
MSFTTRSTFSTNYRSLGSVQAPSYGARPVSSAASVYAGAGGSGSRISVSRSTSFRGGMGSGGLATGIAGG
LAGMGGIQNEKETMQSLNDRLASYLDRVRSLETENRRLESKIREHLEKKGPQVRDWSHYFKIIEDLRAQI
FANTVDNARIVLQIDNARLAADDFRVKYETELAMRQSVENDIHGLRKVIDDTNITRLQLETEIEALKEEL
LFMKKNHEEEVKGLQAQIASSGLTVEVDAPKSQDLAKIMADIRAQYDELARKNREELDKYWSQQIEESTT
VVTTQSAEVGAAETTLTELRRTVQSLEIDLDSMRNLKASLENSLREVEARYALQMEQLNGILLHLESELA
QTRAEGQRQAQEYEALLNIKVKLEAEIATYRRLLEDGEDFNLGDALDSSNSMQTIQKTTTRRIVDGKVVS
ETNDTKVLRH
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Notes

Shear stress activates PKC {zeta}, which then phosphorylates K18pSer33 and promotes the interaction of 14-3-3 with KIFs (Ser33 = Ser34 in P05783)

References to 14-3-3 binding to keratin 18

Sivaramakrishnan S, Schneider JL, Sitikov A, Goldman RD, Ridge KM.Shear stress induced reorganization of the keratin intermediate filament network requires phosphorylation by protein kinase C zeta. Mol Biol Cell. 2009 Jun;20(11):2755-65.

Liao J, Omary MB.14-3-3 proteins associate with phosphorylated simple epithelial keratins during cell cycle progression and act as a solubility cofactor. J Cell Biol. 1996 Apr;133(2):345-57.

Ku NO, Michie S, Resurreccion EZ, Broome RL, Omary MB. Keratin binding to 14-3-3 proteins modulates keratin filaments and hepatocyte mitotic progression. Proc Natl Acad Sci U S A. 2002 Apr 2;99(7):4373-8.

Ku NO, Liao J, Omary MB. Phosphorylation of human keratin 18 serine 33 regulates binding to 14-3-3 proteins. EMBO J. 1998 Apr 1;17(7):1892-906.

Human KSR1 (kinase suppressor of Ras) (Swissprot = Q8IVT5)

```
        1 MDRAALRAAA MGEKKEGGGG GDAAEGGAGA AASRALQQCG QLQKLIDISI GSLRGLRTKC
       61 AVSNDLTQQE IRTLEAKLVR YICKQRQCKL SVAPGERTPE LNSYPRFSDW LYTFNVRPEV
      121 VQEIPRDLTL DALLEMNEAK VKETLRRCGA SGDECGRLQY ALTCLRKVTG LGGEHKEDSS
      181 WSSLDARRES GSGPSTDTLS AASLPWPPGS SQLGRAGNSA QGPRSISVSA LPASDSPTPS
      241 FSEGLSDTCI PLHASGRLTP RALHSFITPP TTPQLRRHTK LKPPRTPPPP SRKVFQLLPS
      301 FPTLTRSKsH ESQLGNRIDD VSSMRFDLSH GSPQMVRRDI GLSVTHRFST KSWLSQVCHV
      361 CQKSMIFGVK CKHCRLKCHN KCTKEAPACR ISFLPLTRLR RTEsVPSDIN NPVDRAAEPH
      421 FGTLPKALTK KEHPPAMNHL DSSSNPSSTT SSTPSSPAPF PTSSNPSSAT TPPNPSPGQR
      481 DSRFNFPAAY FIHHRQQFIF PVPSAGHCWK CLLIAESLKE NAFNISAFAH AAPLPEAADG
      541 TRLDDQPKAD VLEAHEAEAE EPEAGKSEAE DDEDEVDDLP SSRRPWRGPI SRKASQTSVY
      601 LQEWDIPFEQ VELGEPIGQG RWGRVHRGRW HGEVAIRLLE MDGHNQDHLK LFKKEVMNYR
      661 QTRHENVVLF MGACMNPPHL AIITSFCKGR TLHSFVRDPK TSLDINKTRQ IAQEIIKGMG
      721 YLHAKGIVHK DLKSKNVFYD NGKVVITDFG LFGISGVVRE GRRENQLKLS HDWLCYLAPE
      781 IVREMTPGKD EDQLPFSKAA DVYAFGTVWY ELQARDWPLK NQAAEASIWQ IGSGEGMKRV
      841 LTSVSLGKEV SEILSACWAF DLQERPSFSL LMDMLEKLPK LNRRLSHPGH FWKSAEINSS
      901 KVVPRFERFG LGVLESSNPK M
>gi|56749095|sp|Q8IVT5.2|KSR1_HUMAN RecName: Full=Kinase suppressor of Ras 1
MDRAALRAAAMGEKKEGGGGGDAAEGGAGAAASRALQQCGQLQKLIDISIGSLRGLRTKCAVSNDLTQQE
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IRTLEAKLVRYICKQRQCKLSVAPGERTPELNSYPRFSDWLYTFNVRPEVVQEIPRDLTLDALLEMNEAK
VKETLRRCGASGDECGRLQYALTCLRKVTGLGGEHKEDSSWSSLDARRESGSGPSTDTLSAASLPWPPGS
SQLGRAGNSAQGPRSISVSALPASDSPTPSFSEGLSDTCIPLHASGRLTPRALHSFITPPTTPQLRRHTK
LKPPRTPPPPSRKVFQLLPSFPTLTRSKSHESQLGNRIDDVSSMRFDLSHGSPQMVRRDIGLSVTHRFST
KSWLSQVCHVCQKSMIFGVKCKHCRLKCHNKCTKEAPACRISFLPLTRLRRTESVPSDINNPVDRAAEPH
FGTLPKALTKKEHPPAMNHLDSSSNPSSTTSSTPSSPAPFPTSSNPSSATTPPNPSPGQRDSRFNFPAAY
FIHHRQQFIFPVPSAGHCWKCLLIAESLKENAFNISAFAHAAPLPEAADGTRLDDQPKADVLEAHEAEAE
EPEAGKSEAEDDEDEVDDLPSSRRPWRGPISRKASQTSVYLQEWDIPFEQVELGEPIGQGRWGRVHRGRW
HGEVAIRLLEMDGHNQDHLKLFKKEVMNYRQTRHENVVLFMGACMNPPHLAIITSFCKGRTLHSFVRDPK
TSLDINKTRQIAQEIIKGMGYLHAKGIVHKDLKSKNVFYDNGKVVITDFGLFGISGVVREGRRENQLKLS
HDWLCYLAPEIVREMTPGKDEDQLPFSKAADVYAFGTVWYELQARDWPLKNQAAEASIWQIGSGEGMKRV
LTSVSLGKEVSEILSACWAFDLQERPSFSLLMDMLEKLPKLNRRLSHPGHFWKSAEINSSKVVPRFERFG
LGVLESSNPKM
```

Notes

Two 14-3-3 binding sites are RSKpS^{297}HE (=S309 in Q81VT5) and RTEpS^{392}VP (= Ser404 in Q8IVT5)
KSR a serine/threonine kinase of the Raf family with no demonstrated kinase activity. KSR, 14-3-3 and Raf form an oligomeric signaling complex and that KSR positively regulates the Ras signaling pathway in vertebrate organisms.

References to 14-3-3 binding to KSR1

Xing H, Kornfeld K, Muslin AJ.The protein kinase KSR interacts with 14-3-3 protein and Raf. Curr Biol. 1997 May 1;7(5):294-300

Jagemann LR, Pérez-Rivas LG, Ruiz EJ, Ranea JA, Sánchez-Jiménez F, Nebreda AR, Alba E, Lozano J. The functional interaction of 14-3-3 proteins with the ERK1/2 scaffold KSR1 occurs in an isoform-specific manner. J Biol Chem. 2008 Jun 20;283(25):17450-62.

Ory S, Zhou M, Conrads TP, Veenstra TD, Morrison DK. Protein phosphatase 2A positively regulates Ras signaling by dephosphorylating KSR1 and Raf-1 on critical 14-3-3 binding sites. Curr Biol. 2003 Aug 19;13(16):1356-64.

Müller J, Ory S, Copeland T, Piwnica-Worms H, Morrison DK. C-TAK1 regulates Ras signaling by phosphorylating the MAPK scaffold, KSR1. Mol Cell. 2001 Nov;8(5):983-93.

Cacace AM, Michaud NR, Therrien M, Mathes K, Copeland T, Rubin GM, Morrison DK. Identification of constitutive and ras-inducible phosphorylation sites of KSR: implications for 14-3-3 binding, mitogen-activated protein kinase binding, and KSR overexpression. Mol Cell Biol. 1999 Jan;19(1):229-40.

Human LCP2(SLP-76) (Lymphocyte cytosolic protein 2, aka SLP-76) (Swissprot = Q13094)

```
        1 MALRNVPFRS EVLGWDPDSL ADYFKKLNYK DCEKAVKKYH IDGARFLNLT ENDIQKFPKL
       61 RVPILSKLSQ EINKNEERRS IFTRKPQVPR FPEETESHEE DNGGWSSFEE DDYESPNDDQ
      121 DGEDDGDYES PNEEEEAPVE DDADYEPPPS NDEEALQNSI LPAKPFPNSN SMYIDRPPSG
      181 KTPQQPPVPP QRPMAALPPP PAGRNHSPLP PPQTNHEEPS RSRNHKTAKL PAPSIDRSTK
      241 PPLDRSLAPF DREPFTLGKK PPFSDKPSIP AGRSLGEHLP KIQKPPLPPT TERHERSSPL
      301 PGKKPPVPKH GWGPDRREND EDDVHQRPLP QPALLPMSSN TFPSRSTKPS PMNPLPSSHM
      361 PGAFSESNSS FPQSAsLPPY FSQGPSNRPP IRAEGRNFPL PLPNKPRPPS PAEEENSLNE
      421 EWYVSYITRP EAEAALRKIN QDGTFLVRDS SKKTTTNPYV LMVLYKDKVY NIQIRYQKES
      481 QVYLLGTGLR GKEDFLSVSD IIDYFRKMPL LLIDGKNRGS RYQCTLTHAA GYP
>gi|10720065|sp|Q13094.1|LCP2_HUMAN RecName: Full=Lymphocyte cytosolic
protein 2; AltName: Full=SH2 domain-containing leukocyte protein of 76 kDa;
AltName: Full=SLP-76 tyrosine phosphoprotein; Short=SLP76
MALRNVPFRSEVLGWDPDSLADYFKKLNYKDCEKAVKKYHIDGARFLNLTENDIQKFPKLRVPILSKLSQ
EINKNEERRSIFTRKPQVPRFPEETESHEEDNGGWSSFEEDDYESPNDDQDGEDDGDYESPNEEEEAPVE
DDADYEPPPSNDEEALQNSILPAKPFPNSNSMYIDRPPSGKTPQQPPVPPQRPMAALPPPPAGRNHSPLP
PPQTNHEEPSRSRNHKTAKLPAPSIDRSTKPPLDRSLAPFDREPFTLGKKPPFSDKPSIPAGRSLGEHLP
KIQKPPLPPTTERHERSSPLPGKKPPVPKHGWGPDRRENDEDDVHQRPLPQPALLPMSSNTFPSRSTKPS
PMNPLPSSHMPGAFSESNSSFPQSASLPPYFSQGPSNRPPIRAEGRNFPLPLPNKPRPPSPAEEENSLNE
EWYVSYITRPEAEAALRKINQDGTFLVRDSSKKTTTNPYVLMVLYKDKVYNIQIRYQKESQVYLLGTGLR
GKEDFLSVSDIIDYFRKMPLLLIDGKNRGSRYQCTLTHAAGYP
```

Notes

"Here, we identify 14-3-3epsilon and zeta proteins as SLP-76 binding partners. This interaction was induced by TCR ligation and required phosphorylation of SLP-76 at serine 376."

References to 14-3-3 binding to SLP-76

Di Bartolo V, Montagne B, Salek M, Jungwirth B, Carrette F, Fourtane J, Sol-Foulon N, Michel F, Schwartz O, Lehmann WD, Acuto O. A novel pathway down-modulating T cell activation involves HPK-1-dependent recruitment of 14-3-3 proteins on SLP-76. J Exp Med. 2007 Mar 19;204(3):681-91

Human LSR **Isoform 2 of lipolysis-stimulated lipoprotein receptor** (Swissprot = Q86X29)

```
        1 MQQDGLGVGT RNGSGKGRSV HPSWPWCAPR PLRYFGRDAR ARRAQTAAMA LLAGGLSRGL
       61 GSHPAAAGRD AVVFVWLLLS TWCTAPARAI QVTVSNPYHV VILFQPVTLP CTYQMTSTPT
      121 QPIVIWKYKS FCRDRIADAF SPASVDNQLN AQLAAGNPGY NPYVECQDSV RTVRVVATKQ
      181 GNAVTLGDYY QGRRITITGN ADLTFDQTAW GDSGVYYCSV VSAQDLQGNN EAYAELIVLG
      241 RTSGVAELLP GFQAGPIEDW LFVVVVCLAA FLIFLLLGIC WCQCCPHTCC CYVRCPCCPD
      301 KCCCPEALYA AGKAATSGVP SIYAPSTYAH LSPAKTPPPP AMIPMGPAYN GYPGGYPGDV
      361 DRSSSAGGQG SYVPLLRDTD SSVASEVRSG YRIQASQQDD SMRVLYYMEK ELANFDPSRP
      421 GPPSGRVERA MSEVTSLHED DWRSRPSRGP ALTPIRDEEW GGHSPRSPRG WDQEPAREQA
      481 GGGWRARRPR ARsVDALDDL TPPSTAESGS RSPTSNGGRS RAYMPPRSRS RDDLYDQDDS
      541 RDFPRSRDPH YDDFRSRERP PADPRSHHHR TRDPRDNGSR SGDLPYDGRL LEEAVRKKGS
      601 EERRRPHKEE EEEAYYPPAP PPYSETDSQA SRERRLKKNL ALSRESLVV
>gi|116242622|sp|Q86X29.4|LSR_HUMAN RecName: Full=Lipolysis-stimulated
lipoprotein receptor
MQQDGLGVGTRNGSGKGRSVHPSWPWCAPRPLRYFGRDARARRAQTAAMALLAGGLSRGLGSHPAAAGRD
AVVFVWLLLSTWCTAPARAIQVTVSNPYHVVILFQPVTLPCTYQMTSTPTQPIVIWKYKSFCRDRIADAF
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SPASVDNQLNAQLAAGNPGYNPYVECQDSVRTVRVVATKQGNAVTLGDYYQGRRITITGNADLTFDQTAW
GDSGVYYCSVVSAQDLQGNNEAYAELIVLGRTSGVAELLPGFQAGPIEDWLFVVVVCLAAFLIFLLLGIC
WCQCCPHTCCCYVRCPCCPDKCCCPEALYAAGKAATSGVPSIYAPSTYAHLSPAKTPPPPAMIPMGPAYN
GYPGGYPGDVDRSSSAGGQGSYVPLLRDTDSSVASEVRSGYRIQASQQDDSMRVLYYMEKELANFDPSRP
GPPSGRVERAMSEVTSLHEDDWRSRPSRGPALTPIRDEEWGGHSPRSPRGWDQEPAREQAGGGWRARRPR
ARSVDALDDLTPPSTAESGSRSPTSNGGRSRAYMPPRSRSRDDLYDQDDSRDFPRSRDPHYDDFRSRERP
PADPRSHHHRTRDPRDNGSRSGDLPYDGRLLEEAVRKKGSEERRRPHKEEEEEAYYPPAPPPYSETDSQA
SRERRLKKNLALSRESLVV
```

Notes

Dubois et al (2009) reports that phosphoSer493 of LSR (RPRAR(pS493)LD provides one of the 14-3-3-binding sites on this protein, and this site was identified on the endogenous protein from HEK293 cells. In the reference sequence (Q86X29) the L at +1 is a V.

References to 14-3-3 binding to LSR

Dubois F, Vandermoere F, Gernez A, Murphy J, Toth R, Chen S, Geraghty KM, Morrice NA and MacKintosh C (2009) Differential 14-3-3-affinity capture reveals new downstream targets of PI 3-kinase signaling (Epub 2009 Aug 1)

Human MAP3K3 (MEKK3) Protein kinase of the STE11 family (Swissprot = Q99759)

```
        1 MDEQEALNSI MNDLVALQMN RRHRMPGYET MKNKDTGHSN RQSDVRIKFE HNGERRIIAF
       61 SRPVKYEDVE HKVTTVFGQP LDLHYMNNEL SILLKNQDDL DKAIDILDRS SSMKSLRILL
      121 LSQDRNHNSS SPHSGVSRQV RIKASQSAGD INTIYQPPEP RSRHLSVSSQ NPGRSSPPPG
      181 YVPERQQHIA RQGSYTSINS EGEFIPETSE QCMLDPLSSA ENSLSGSCQS LDRSADSPSF
      241 RKSRMSRAQS FPDNRQEYSD RETQLYDKGV KGGTYPRRYH VSVHHKDYSD GRRtFPRIRR
      301 HQGNLFTLVP SSRSLSTNGE NMGLAVQYLD PRGRLRSADS ENALSVQERN VPTKSPSAPI
      361 NWRRGKLLGQ GAFGRVYLCY DVDTGRELAS KQVQFDPDSP ETSKEVSALE CEIQLLKNLQ
      421 HERIVQYYGC LRDRAEKTLT IFMEYMPGGS VKDQLKAYGA LTESVTRKYT RQILEGMSYL
      481 HSNMIVHRDI KGANILRDSA GNVKLGDFGA SKRLQTICMS GTGMRSVTGT PYWMSPEVIS
      541 GEGYGRKADV WSLGCTVVEM LTEKPPWAEY EAMAAIFKIA TQPTNPQLPS HISEHGRDFL
      601 RRIFVEARQR PSAEELLTHH FAQLMY
>gi|160332306|sp|Q99759.2|M3K3_HUMAN RecName: Full=Mitogen-activated protein
kinase kinase kinase 3; AltName: Full=MAPK/ERK kinase kinase 3; Short=MEK
kinase 3; Short=MEKK 3
MDEQEALNSIMNDLVALQMNRRHRMPGYETMKNKDTGHSNRQSDVRIKFEHNGERRIIAFSRPVKYEDVE
HKVTTVFGQPLDLHYMNNELSILLKNQDDLDKAIDILDRSSSMKSLRILLLSQDRNHNSSSPHSGVSRQV
RIKASQSAGDINTIYQPPEPRSRHLSVSSQNPGRSSPPPGYVPERQQHIARQGSYTSINSEGEFIPETSE
QCMLDPLSSAENSLSGSCQSLDRSADSPSFRKSRMSRAQSFPDNRQEYSDRETQLYDKGVKGGTYPRRYH
VSVHHKDYSDGRRTFPRIRRHQGNLFTLVPSSRSLSTNGENMGLAVQYLDPRGRLRSADSENALSVQERN
VPTKSPSAPINWRRGKLLGQGAFGRVYLCYDVDTGRELASKQVQFDPDSPETSKEVSALECEIQLLKNLQ
HERIVQYYGCLRDRAEKTLTIFMEYMPGGSVKDQLKAYGALTESVTRKYTRQILEGMSYLHSNMIVHRDI
KGANILRDSAGNVKLGDFGASKRLQTICMSGTGMRSVTGTPYWMSPEVISGEGYGRKADVWSLGCTVVEM
LTEKPPWAEYEAMAAIFKIATQPTNPQLPSHISEHGRDFLRRIFVEARQRPSAEELLTHHFAQLMY
```

Notes

MEKK3 a protein kinase of the STE11 family. Phosphorylated and activated by MLK3 and TAK1. Phosphorylates and activates MEK5.

Endogenous MEKK3 was phosphorylated on Ser526 in response to osmotic stress. In addition, phosphorylation of Ser526 was required for MKK6 phosphorylation in vitro, whereas dephosphorylation of Ser526 was mediated by protein phosphatase 2A and sensitive to okadaic acid and sodium fluoride. Finally, the association between MEKK3 and 14-3-3 was dependent on Ser526 and prevented dephosphorylation of Ser526.

Phosphorylation of MEKK3 at threonine 294 promotes 14-3-3 association to inhibit nuclear factor kappaB activation (Matitau et al 2008).

We identified two phosphorylated amino acids at Ser166 and Ser337 RSRHLsVSSQ However, neither of these phosphorylated amino acids is required for association with 14-3-3 protein or regulation of MEKK3-dependent ERK and JNK activity. Nonetheless, these results suggest that MEKK3 is a convergence point of multiple upstream signaling pathways. (Adams et al 2002).

References to 14-3-3 binding to MAP3K3

Matitau AE, Scheid MP. Phosphorylation of MEKK3 at threonine 294 promotes 14-3-3 association to inhibit nuclear factor kappaB activation. J Biol Chem. 2008 May 9;283(19):13261-8.

Adams DG, Sachs NA, Vaillancourt RR. Phosphorylation of the stress-activated protein kinase, MEKK3, at serine 166. Arch Biochem Biophys. 2002 Nov 1;407(1):103-16

Fritz A, Brayer KJ, McCormick N, Adams DG, Wadzinski BE, Vaillancourt RR. Phosphorylation of serine 526 is required for MEKK3 activity, and association with 14-3-3 blocks dephosphorylation. J Biol Chem. 2006 Mar 10;281(10):6236-45.

Fanger GR, Widmann C, Porter AC, Sather S, Johnson GL, Vaillancourt RR. 14-3-3 proteins interact with specific MEK kinases. J Biol Chem. 1998 Feb 6;273(6):3476-83.

Abbasi S, Lee JD, Su B, Chen X, Alcon JL, Yang J, Kellems RE, Xia Y. Protein kinase-mediated regulation of calcineurin through the phosphorylation of modulatory calcineurin-interacting protein 1. J Biol Chem. 2006 Mar 24;281(12):7717-26.

Human MAP3K5 (ASK1, MEKK5) Mitogen-activated protein kinase kinase kinase 5 also known as Apoptosis signal-regulating kinase 1 (Swissprot = Q99683)

```
        1 MSTEADEGIT FSVPPFAPSG FCTIPEGGIC RRGGAAAVGE GEEHQLPPPP PGSFWNVESA
       61 AAPGIGCPAA TSSSSATRGR GSSVGGGSRR TTVAYVINEA SQGQLVVAES EALQSLREAC
      121 ETVGATLETL HFGKLDFGET TVLDRFYNAD IAVVEMSDAF RQPSLFYHLG VRESFSMANN
      181 IILYCDTNSD SLQSLKEIIC QKNTMCTGNY TFVPYMITPH NKVYCCDSSF MKGLTELMQP
      241 NFELLLGPIC LPLVDRFIQL LKVAQASSSQ YFRESILNDI RKARNLYTGK ELAAELARIR
      301 QRVDNIEVLT ADIVINLLLS YRDIQDYDSI VKLVETLEKL PTFDLASHHH VKFHYAFALN
      361 RRNLPGDRAK ALDIMIPMVQ SEGQVASDMY CLVGRIYKDM FLDSNFTDTE SRDHGASWFK
      421 KAFESEPTLQ SGINYAVLLL AAGHQFESSF ELRKVGVKLS SLLGKKGNLE KLQSYWEVGF
      481 FLGASVLAND HMRVIQASEK LFKLKTPAWY LKSIVETILI YKHFVKLTTE QPVAKQELVD
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```
      541 FWMDFLVEAT KTDVTVVRFP VLILEPTKIY QPSYLSINNE VEEKTISIWH VLPDDKKGIH
      601 EWNFSASSVR GVSISKFEER CCFLYVLHNS DDFQIYFCTE LHCKKFFEMV NTITEEKGRS
      661 TEEGDCESDL LEYDYEYDEN GDRVVLGKGT YGIVYAGRDL SNQVRIAIKE IPERDSRYSQ
      721 PLHEEIALHK HLKHKNIVQY LGSFSENGFI KIFMEQVPGG SLSALLRSKW GPLKDNEQTI
      781 GFYTKQILEG LKYLHDNQIV HRDIKGDNVL INTYSGVLKI SDFGTSKRLA GINPCTETFT
      841 GTLQYMAPEI IDKGPRGYGK AADIWSLGCT IIEMATGKPP FYELGEPQAA MFKVGMFKVH
      901 PEIPESMSAE AKAFILKCFE PDPDKRACAN DLLVDEFLKV SSKKKKTQPK LSALSAGSNE
      961 YLRSIsLPVP VLVEDTSSSS EYGSVSPDTE LKVDPFSFKT RAKSCGERDV KGIRTLFLGI
     1021 PDENFEDHSA PPSPEEKDSG FFMLRKDSER RATLHRILTE DQDKIVRNLM ESLAQGAEEP
     1081 KLKWEHITTL IASLREFVRS TDRKIIATTL SKLKLELDFD SHGISQVQVV LFGFQDAVNK
     1141 VLRNHNIKPH WMFALDSIIR KAVQTAITIL VPELRPHFSL ASESDTADQE DLDVEDDHEE
     1201 QPSNQTVRRP QAVIEDAVAT SGVSTLSSTV SHDSQSAHRS LNVQLGRMKI ETNRLLEELV
     1261 RKEKELQALL HRAIEEKDQE IKHLKLKSQP IEIPELPVFH LNSSGTNTED SELTDWLRVN
     1321 GADEDTISRF LAEDYTLLDV LYYVTRDDLK CLRLRGGMLC TLWKAIIDFR NKQT
>gi|6685617|sp|Q99683.1|M3K5_HUMAN RecName: Full=Mitogen-activated protein
kinase kinase kinase 5; AltName: Full=MAPK/ERK kinase kinase 5; Short=MEK
kinase 5; Short=MEKK 5; AltName: Full=Apoptosis signal-regulating kinase 1;
Short=ASK-1
MSTEADEGITFSVPPFAPSGFCTIPEGGICRRGGAAAVGEGEEHQLPPPPPGSFWNVESAAAPGIGCPAA
TSSSSATRGRGSSVGGGSRRTTVAYVINEASQGQLVVAESEALQSLREACETVGATLETLHFGKLDFGET
TVLDRFYNADIAVVEMSDAFRQPSLFYHLGVRESFSMANNIILYCDTNSDSLQSLKEIICQKNTMCTGNY
TFVPYMITPHNKVYCCDSSFMKGLTELMQPNFELLLGPICLPLVDRFIQLLKVAQASSSQYFRESILNDI
RKARNLYTGKELAAELARIRQRVDNIEVLTADIVINLLLSYRDIQDYDSIVKLVETLEKLPTFDLASHHH
VKFHYAFALNRRNLPGDRAKALDIMIPMVQSEGQVASDMYCLVGRIYKDMFLDSNFTDTESRDHGASWFK
KAFESEPTLQSGINYAVLLLAAGHQFESSFELRKVGVKLSSLLGKKGNLEKLQSYWEVGFFLGASVLAND
HMRVIQASEKLFKLKTPAWYLKSIVETILIYKHFVKLTTEQPVAKQELVDFWMDFLVEATKTDVTVVRFP
VLILEPTKIYQPSYLSINNEVEEKTISIWHVLPDDKKGIHEWNFSASSVRGVSISKFEERCCFLYVLHNS
DDFQIYFCTELHCKKFFEMVNTITEEKGRSTEEGDCESDLLEYDYEYDENGDRVVLGKGTYGIVYAGRDL
SNQVRIAIKEIPERDSRYSQPLHEEIALHKHLKHKNIVQYLGSFSENGFIKIFMEQVPGGSLSALLRSKW
GPLKDNEQTIGFYTKQILEGLKYLHDNQIVHRDIKGDNVLINTYSGVLKISDFGTSKRLAGINPCTETFT
GTLQYMAPEIIDKGPRGYGKAADIWSLGCTIIEMATGKPPFYELGEPQAAMFKVGMFKVHPEIPESMSAE
AKAFILKCFEPDPDKRACANDLLVDEFLKVSSKKKKTQPKLSALSAGSNEYLRSISLPVPVLVEDTSSSS
EYGSVSPDTELKVDPFSFKTRAKSCGERDVKGIRTLFLGIPDENFEDHSAPPSPEEKDSGFFMLRKDSER
RATLHRILTEDQDKIVRNLMESLAQGAEEPKLKWEHITTLIASLREFVRSTDRKIIATTLSKLKLELDFD
SHGISQVQVVLFGFQDAVNKVLRNHNIKPHWMFALDSIIRKAVQTAITILVPELRPHFSLASESDTADQE
DLDVEDDHEEQPSNQTVRRPQAVIEDAVATSGVSTLSSTVSHDSQSAHRSLNVQLGRMKIETNRLLEELV
RKEKELQALLHRAIEEKDQEIKHLKLKSQPIEIPELPVFHLNSSGTNTEDSELTDWLRVNGADEDTISRF
LAEDYTLLDVLYYVTRDDLKCLRLRGGMLCTLWKAIIDFRNKQT
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Notes

H_2O_2 triggers dephosphorylation of Ser967 resulting in dissociation of the ASK1·14-3-3 complex with concomitant increase of ASK1 catalytic activity and ASK1-mediated activation of JNK and p38 pathways.

The N-terminus of ASK1-interacting protein (AIP1) (Ras GTPase-activating protein) containing the C2 and GAP domains constitutively binds to ASK1 and facilitates the release of 14-3-3 from ASK1.

Antioxidants EUK8 and N-acetyl cystenine significantly decreased apoptosis by inhibiting the ASK1 dephosphorylation at Ser(967) (= Ser966 in Q99683) and subsequently increased the interaction of ASK1 with thioredoxin or 14-3-3 proteins (Kuo et al 2007).

References to 14-3-3 binding to ASK1

Kuo PL, Chen CY, Hsu YL.Isoobtusilactone A induces cell cycle arrest and apoptosis through reactive oxygen species/apoptosis signal-regulating kinase 1 signaling pathway in human breast cancer cells. Cancer Res. 2007 Aug 1;67(15):7406-20.

Hsieh CC, Papaconstantinou J. Thioredoxin-ASK1 complex levels regulate ROS-mediated p38 MAPK pathway activity in livers of aged and long-lived Snell dwarf mice. FASEB J 2006;20:259–68.

Goldman EH, Chen L, Fu H. Activation of apoptosis signal-regulating kinase 1 by reactive oxygen species through dephosphorylation at serine 967 and 14–3-3 dissociation. J Biol Chem 2004;279:10442–9.

Yingmei Liu, Guoyong Yin, James Surapisitchat, Bradford C. Berk, and Wang Min (2001) Laminar flow inhibits TNF-induced ASK1 activation by preventing dissociation of ASK1 from its inhibitor 14-3-3. J Clin Invest. 2001 April 1; 107(7): 917–923.

Zhang R, He X, Liu W, Lu M, Hsieh JT, Min W (2003)AIP1 mediates TNF-alpha-induced ASK1 activation by facilitating dissociation of ASK1 from its inhibitor 14-3-3. J Clin Invest. 2003 Jun;111(12):1933-43.

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Lee JA, Park JE, Lee DH, Park SG, Myung PK, Park BC, Cho S. G1 to S phase transition protein 1 induces apoptosis signal-regulating kinase 1 activation by dissociating 14-3-3 from ASK1. Oncogene. 2008 Feb 21;27(9):1297-305.

Liu Y, Yin G, Surapisitchat J, Berk BC, Min W. Laminar flow inhibits TNF-induced ASK1 activation by preventing dissociation of ASK1 from its inhibitor 14-3-3. J Clin Invest. 2001 Apr; 107(7):917-23.

Jung H, Seong HA, Manoharan R, Ha H. Serine-threonine kinase receptor-associated protein (STRAP) inhibits apoptosis signal-regulating kinase 1 function through direct interaction. J Biol Chem. 2009 Oct 30. [Epub ahead of print]

Cockrell LM, Puckett MC, Goldman EH, Khuri FR, Fu H. Dual engagement of 14-3-3 proteins controls signal relay from ASK2 to the ASK1 signalosome. Oncogene. 2009 Nov 23. [Epub ahead of print]

Seong HA, Jung H, Ichijo H, Ha H. Reciprocal negative regulation of 3-phosphoinositide-dependent protein kinase-1 (PDK1) and apoptosis signal-regulating kinase 1 (ASK1) signaling by direct interaction and phosphorylation. J Biol Chem. 2009 Nov 17. [Epub ahead of print]

Human MAP3K6 (ASK2, MAPKKK6, MEKK6) Apoptosis signal-regulating kinase 2 (Swissprot = O95382)

<table>
<tr><td>1 MAGPCPRSGA ERAGSCWQDP LAVALSRGRQ LAAPPGRGCA RSRPLSVVYV LTREPQPGLE
61 PREGTEAEPL PLRCLREACA QVPRPRPPPQ LRSLPFGTLE LGDTAALDAF YNADVVVLEV
121 SSSLVQPSLF YHLGVRESFS MTNNVLLCSQ ADLPDLQALR EDVFQKNSDC VGSYTLIPYV
181 VTATGRVLCG DAGLLRGLAD GLVQAGVGTE ALLTPLVGRL ARLLEATPTD SCGYFRETIR
241 RDIRQARERF SGPQLRQELA RLQRRLDSVE LLSPDIIMNL LLSYRDVQDY SAIIELVETL
301 QALPTCDVAE QHNVCFHYTF ALNRRNRPGD RAKALSVLLP LVQLEGSVAP DLYCMCGRIY
361 KDMFFSSGFQ DAGHREQAYH WYRKAFDVEP SLHSGINAAV LLIAAGQHFE DSKELRLIGM
421 KLGCLLARKG CVEKMQYYWD VGFYLGAQIL ANDPTQVVLA AEQLYKLNAP IWYLVSVMET
481 FLLYQHFRPT PEPPGGPPRR AHFWLHFLLQ SCQPFKTACA QGDQCLVLVL EMNKVLLPAK
541 LEVRGTDPVS TVTLSLLEPE TQDIPSSWTF PVASICGVSA SKRDERCCFL YALPPAQDVQ
601 LCFPSVGHCQ WFCGLIQAWV TNPDSTAPAE EAEGAGEMLE FDYEYTETGE RLVLGKGTYG
661 VVYAGRDRHT RVRIAIKEIP ERDSRFSQPL HEEIALHRRL RHKNIVRYLG SASQGGYLKI
721 FMEEVPGGSL SSLLRSVWGP LKDNESTISF YTRQILQGLG YLHDNHIVHR DIKGDNVLIN
781 TFSGLLKISD FGTSKRLAGI TPCTETFTGT LQYMAPEIID QGPRGYGKAA DIWSLGCTVI
841 EMATGRPPFH ELGSPQAAMF QVGMYKVHPP MPSSLSAEAQ AFLLRTFEPD PRLRASAQTL
901 LGDPFLQPGK RSRSPSSPRH APRPSDAPSA SPTPSANSTT QSQTFPCPQA PSQHPPSPPK
961 RCLsYGGTSQ LRVPEEPAAE EPASPEESSG LSLLHQESKR RAMLAAVLEQ ELPALAENLH
1021 QEQKQEQGAR LGRNHVEELL RCLGAHIHTP NRRQLAQELR ALQGRLRAQG LGPALLHRPL
1081 FAFPDAVKQI LRKRQIRPHW MFVLDSLLSR AVRAALGVLG PEVEKEAVSP RSEELSNEGD
1141 SQQSPGQQSP LPVEPEQGPA PLMVQLSLLR AETDRLREIL AGKEREYQAL VQRALQRLNE
1201 EARTYVLAPE PPTALSTDQG LVQWLQELNV DSGTIQMLLN HSFTLHTLLT YATRDDLIYT
1261 RIRGGMVCRI WRAILAQRAG STPVTSGP
Notes
"We show that ASK2 specifically interacts with 14-3-3 proteins through phosphorylated S964. Although a 14-3-3-binding defective mutant of ASK1 (S967A) has no effect on the ASK2/14-3-3 interaction, both overexpression of the analogous ASK2 (S964A) mutant and knockdown of ASK2 dramatically reduced the amount of ASK1 complexed with 14-3-3. These data suggest a dominant role of ASK2 in 14-3-3 control of ASK1 function. Indeed, ASK2 S964A-induced dissociation of 14-3-3 from ASK1 correlated with enhanced phosphorylation of ASK1 at T838 and increased c-Jun N-terminal kinase phosphorylation, the two biological readouts of ASK1 activation. Our results suggest a model in which upstream signals couple ASK2 S964 phosphorylation to the ASK1 signalosome through dual engagement of 14-3-3." (Cockrell et al 2009 prepublication date).
References to 14-3-3 binding to ASK2
Cockrell LM, Puckett MC, Goldman EH, Khuri FR, Fu H. Dual engagement of 14-3-3 proteins controls signal relay from ASK2 to the ASK1 signalosome. Oncogene. 2009 Nov 23. [Epub ahead of print]</td><td></td></tr>
<tr><td>**Human MAPK7** (ERK5, BMK1) (Swissprot = Q13164)
1 MAEPLKEEDG EDGSAEPPGP VKAEPAHTAA SVAAKNLALL KARSFDVTFD VGDEYEIIET
61 IGNGAYGVVS SARRRLTGQQ VAIKKIPNAF DVVTNAKRTL RELKILKHFK HDNIIAIKDI
121 LRPTVPYGEF KSVYVVLDLM ESDLHQIIHS SQPLTLEHVR YFLYQLLRGL KYMHSAQVIH
181 RDLKPSNLLV NENCELKIGD FGMARGLCTS PAEHQYFMTE YVATRWYRAP ELMLSLHEYT
241 QAIDLWSVGC IFGEMLARRQ LFPGKNYVHQ LQLIMMVLGT PSPAVIQAVG AERVRAYIQS
301 LPPRQPVPWE TVYPGADRQA LSLLGRMLRF EPSARISAAA ALRHPFLAKY HDPDDEPDCA
361 PPFDFAFDRE ALTRERIKEA IVAEIEDFHA RREGIRQQIR FQPSLQPVAS EPGCPDVEMP
421 SPWAPSGDCA MESPPPAPPP CPGPAPDTID LTLQPPPPVS EPAPPKKDGA ISDNTKAALK
481 AALLKsLRSR LRDGPSAPLE APEPRKPVTA QERQREREEK RRRRQERAKE REKRRQERER
541 KERGAGASGG PSTDPLAGLV LSDNDRSLLE RWTRMARPAA PALTSVPAPA PAPTPTPTPV
601 QPTSPPPGPV AQPTGPQPQS AGSTSGPVPQ PACPPPGPAP HPTGPPGPIP VPAPPQIATS
661 TSLLAAQSLV PPPGLPGSST PGVLPYFPPG LPPPDAGGAP QSSMSESPDV NLVTQQLSKS
721 QVEDPLPPVF SGTPKGSGAG YGVGFDLEEF LNQSFDMGVA DGPQDGQADS ASLSASLLAD
781 WLEGHGMNPA DIESLQREIQ MDSPMLLADL PDLQDP
>gi|205371766|sp|Q13164.2|MK07_HUMAN RecName: Full=Mitogen-activated protein kinase 7; AltName: Full=Extracellular signal-regulated kinase 5; Short=ERK-5; AltName: Full=ERK4; AltName: Full=Big MAP kinase 1; Short=BMK1 kinase
MAEPLKEEDGEDGSAEPPGPVKAEPAHTAASVAAKNLALLKARSFDVTFDVGDEYEIIETIGNGAYGVVS
SARRRLTGQQVAIKKIPNAFDVVTNAKRTLRELKILKHFKHDNIIAIKDILRPTVPYGEFKSVYVVLDLM
ESDLHQIIHSSQPLTLEHVRYFLYQLLRGLKYMHSAQVIHRDLKPSNLLVNENCELKIGDFGMARGLCTS
PAEHQYFMTEYVATRWYRAPELMLSLHEYTQAIDLWSVGCIFGEMLARRQLFPGKNYVHQLQLIMMVLGT
PSPAVIQAVGAERVRAYIQSLPPRQPVPWETVYPGADRQALSLLGRMLRFEPSARISAAAALRHPFLAKY
HDPDDEPDCAPPFDFAFDREALTRERIKEAIVAEIEDFHARREGIRQQIRFQPSLQPVASEPGCPDVEMP
SPWAPSGDCAMESPPPAPPPCPGPAPDTIDLTLQPPPPVSEPAPPKKDGAISDNTKAALKAALLKSLRSR
LRDGPSAPLEAPEPRKPVTAQERQREREEKRRRRQERAKEREKRRQERERKERGAGASGGPSTDPLAGLV
LSDNDRSLLERWTRMARPAAPALTSVPAPAPAPTPTPTPVQPTSPPPGPVAQPTGPQPQSAGSTSGPVPQ
PACPPPGPAPHPTGPPGPIPVPAPPQIATSTSLLAAQSLVPPPGLPGSSTPGVLPYFPPGLPPPDAGGAP
QSSMSESPDVNLVTQQLSKSQVEDPLPPVFSGTPKGSGAGYGVGFDLEEFLNQSFDMGVADGPQDGQADS
ASLSASLLADWLEGHGMNPADIESLQREIQMDSPMLLADLPDLQDP
Notes
Big mitogen-activated kinase 1 (BMK1/ERK5) is a member of the MAPK family activated by growth factors that mediates cell growth and survival. Previous data show that BMK1 can be activated by steady laminar flow and is atheroprotective by preventing endothelial cells from undergoing apoptosis. Mutation of serine 486 (BMK1-S486A) prevented the interaction with 14-3-3beta and enhanced BMK1 activity upon epidermal growth factor stimulation. 14-3-3beta binding to BMK1 has an inhibitory function. 14-3-3beta binds to big mitogen-activated protein kinase 1 (BMK1/ERK5) and regulates BMK1 function.
References to 14-3-3 binding to MAPK7
Zheng Q, Yin G, Yan C, Cavet M, Berk BC. 14-3-3beta binds to big mitogen-activated protein kinase 1 (BMK1/ERK5) and regulates BMK1 function. J Biol Chem. 2004 Mar 5;279(10):8787-91.</td><td></td></tr>
<tr><td>**Human MAPT** Microtubule-associated protein tau) (Swissprot =P10636)
1 MAEPRQEFEV MEDHAGTYGL GDRKDQGGYT MHQDQEGDTD AGLKESPLQT PTEDGSEEPG</td><td>THREE SITES IMPICATED IN 14-</td></tr>
</table>

<table>
<tr>
<td>61 SETSDAKSTP TAEDVTAPLV DEGAPGKQAA AQPHTEIPEG TTAEEAGIGD TPSLEDEAAG
121 HVTQEPESGK VVQEGFLREP GPPGLSHQLM SGMPGAPLLP EGPREATRQP SGTGPEDTEG
181 GRHAPELLKH QLLGDLHQEG PPLKGAGGKE RPGSKEEVDE DRDVDESSPQ DSPPSKASPA
241 QDGRPPQTAA REATSIPGFP AEGAIPLPVD FLSKVSTEIP ASEPDGPSVG RAKGQDAPLE
301 FTFHVEITPN VQKEQAHSEE HLGRAAFPGA PGEGPEARGP SLGEDTKEAD LPEPSEKQPA
361 AAPRGKPVSR VPQLKARMVS KSKDGTGSDD KKAKTSTRSS AKTLKNRPCL SPKLPTPGSS
421 DPLIQPSSPA VCPEPPSSPK HVSSVTSRTG SSGAKEMKLK GADGKTKIAT PRGAAPPGQK
481 GQANATRIPA KTPPAPKTPP SSGEPPKSGD RSGYSSPGSP GTPGSRSRTP sLPTPPTREP
541 KKVAVVRTPP KSPSSAKSRL QTAPVPMPDL KNVKSKIGST ENLKHQPGGG KVQIINKKLD
601 LSNVQSKCGS KDNIKHVPGG GSVQIVYKPV DLSKVTSKCG sLGNIHHKPG GGQVEVKSEK
661 LDFKDRVQSK IGsLDNITHV PGGGNKKIET HKLTFRENAK AKTDHGAEIV YKSPVVSGDT
721 SPRHLSNVSS TGSIDMVDSP QLATLADEVS ASLAKQGL
>gi|13124806|sp|P10636.4|TAU_HUMAN RecName: Full=Microtubule-associated protein tau; AltName: Full=Neurofibrillary tangle protein; AltName: Full=Paired helical filament-tau; Short=PHF-tau
MAEPRQEFEVMEDHAGTYGLGDRKDQGGYTMHQDQEGDTDAGLKESPLQTPTEDGSEEPGSETSDAKSTP
TAEDVTAPLVDEGAPGKQAAAQPHTEIPEGTTAEEAGIGDTPSLEDEAAGHVTQEPESGKVVQEGFLREP
GPPGLSHQLMSGMPGAPLLPEGPREATRQPSGTGPEDTEGGRHAPELLKHQLLGDLHQEGPPLKGAGGKE
RPGSKEEVDEDRDVDESSPQDSPPSKASPAQDGRPPQTAAREATSIPGFPAEGAIPLPVDFLSKVSTEIP
ASEPDGPSVGRAKGQDAPLEFTFHVEITPNVQKEQAHSEEHLGRAAFPGAPGEGPEARGPSLGEDTKEAD
LPEPSEKQPAAAPRGKPVSRVPQLKARMVSKSKDGTGSDDKKAKTSTRSSAKTLKNRPCLSPKLPTPGSS
DPLIQPSSPAVCPEPPSSPKHVSSVTSRTGSSGAKEMKLKGADGKTKIATPRGAAPPGQKGQANATRIPA
KTPPAPKTPPSSGEPPKSGDRSGYSSPGSPGTPGSRSRTPSLPTPPTREPKKVAVVRTPPKSPSSAKSRL
QTAPVPMPDLKNVKSKIGSTENLKHQPGGGKVQIINKKLDLSNVQSKCGSKDNIKHVPGGGSVQIVYKPV
DLSKVTSKCGSLGNIHHKPGGGQVEVKSEKLDFKDRVQSKIGSLDNITHVPGGGNKKIETHKLTFRENAK
AKTDHGAEIVYKSPVVSGDTSPRHLSNVSSTGSIDMVDSPQLATLADEVSASLAKQGL
Notes
Six isoforms of human tau generated by alternate splicing, of which tau 3 (P10636-2) is the shortest.
This is the sequence sent by Nikolai B. Gusev. He says “We were working with the shortest isoform of human tau protein (SwissProt #P10636-2), fetal-tau isoform. The sites that were mutated and/or phosphorylated by cAMP-dependent protein kinase and that seem to be important for interaction with 14-3-3 are Ser156, Ser 235 and Ser 267. I am sending you the primary structure of this isoform with phosphorylation sites marked in red as an attachment.”
MAEPRQEFEV MEDHAGTYGL GDRKDQGGYT MHQDQEGDTD AGLKAEEAGI GDTPSLEDEA
AGHVTQARMV SKSKDGTGSD DKKAKGADGK TKIATPRGAA PPGQKGQANA TRIPAKTPPA
PKTPPSSGEP PKSGDRSGYS SPGSPGTPGS RSRTPsLPTP PTREPKKVAV VRTPPKSPSS
AKSRLQTAPV PMPDLKNVKS KIGSTENLKH QPGGGKVQIV YKPVDLSKVT SKCGsLGNIH
HKPGGGQVEV KSEKLDFKDR VQSKIGsLDN ITHVPGGGNK KIETHKLTFR ENAKAKTDHG
AEIVYKSPVV SGDTSPRHLS NVSSTGSIDM VDSPQLATLA DEVSASLAKQ GL
As the phosphorylation at Ser214 is up-regulated in fetal brain, tau's interaction with 14-3-3 may have a significant role in the organization of the microtubule cytoskeleton in development. Also as the phosphorylation at Ser214 is up-regulated in Alzheimer's disease brain, tau's interaction with 14-3-3 might be involved in the pathology of this disease.
References to 14-3-3 binding to Tau
Chun J, Kwon T, Lee EJ, Kim CH, Han YS, Hong SK, Hyun S, Kang SS. 14-3-3 Protein mediates phosphorylation of microtubule-associated protein tau by serum- and glucocorticoid-induced protein kinase 1. Mol Cells. 2004 Dec 31;18(3):360-8
Sadik G, Tanaka T, Kato K, Yanagi K, Kudo T, Takeda M. Phosphorylation of tau at Ser214 mediates its interaction with 14-3-3 protein: implications for the mechanism of tau aggregation. J Neurochem. 2009 Jan;108(1):33-43
Sluchanko NN, Seit-Nebi AS, Gusev NB. Effect of phosphorylation on interaction of human tau protein with 14-3-3zeta. Biochem Biophys Res Commun. 2009 Feb 20;379(4):990-4. Epub 2009 Jan 10.
Sluchanko NN, Seit-Nebi AS, Gusev NB. Phosphorylation of more than one site is required for tight interaction of human tau protein with 14-3-3zeta. FEBS Lett. 2009 Aug 1. [Epub ahead of print] Serine residues phosphorylated by protein kinase A (PKA) in the shortest isoform of human tau protein (tau3)</td>
<td>3-3-BINDING, BUT THE SECOND TWO SHARE SEQUENCE SIMILARITIES (AS SEEN IN SUPPLEMENTARY TABLE 2). WE THEREFORE MADE THE ARBITRARY CHOICE TO INCLUDE SER156 AND SER235 IN WEBLOGO ANALYSIS, AND SUGGEST THAT FURTHER EXPERIMENTAL DISSECTION OF WHETHER ONE OR OTHER OR BOTH OF THE SER235 AND SER267 SITES IS RELEVANT WOULD BE INTERESTING.</td>
</tr>
<tr>
<td>Human MARK2 (aka Par-1b/EMK) (Swissprot = Q7KZI7)
1 MSSARTPLPT LNERDTEQPT LGHLDSKPSS KSNMIRGRNS ATSADEQPHI GNYRLLKTIG
61 KGNFAKVKLA RHILTGKEVA VKIIDKTQLN SSSLQKLFRE VRIMKVLNHP NIVKLFEVIE
121 TEKTLYLVME YASGGEVFDY LVAHGRMKEK EARAKFRQIV SAVQYCHQKF IVHRDLKAEN
181 LLLDADMNIK IADFGFSNEF TFGNKLDTFC GSPPYAAPEL FQGKKYDGPE VDVWSLGVIL
241 YTLVSGSLPF DGQNLKELRE RVLRGKYRIP FYMSTDCENL LKKFLILNPS KRGTLEQIMK
301 DRWMNVGHED DELKPYVEPL PDYKDPRRTE LMVSMGYTRE EIQDSLVGQR YNEVMATYLL
361 LGYKSSELEG DTITLKPRPS ADLTNSSAPS PSHKVQRSVs ANPKQRRFSD QAAGPAIPTS
421 NSYSKKTQSN NAENKRPEED RESGRKASST AKVPASPLPG LERKKTTPTP STNSVLSTST
481 NRSRNSPLLE RASLGQASIQ NGKDSLTMPG SRASTASASA AVSAARPRQH QKSMSASVHP
541 NKASGLPPTE SNCEVPRPST APQRVPVASP SAHNISSSGG APDRTNFPRG VSSRStFHAG
601 QLRQVRDQQN LPYGVTPASP SGHSQGRRGA SGSIFSKFTS KFVRRNLSFR FARRNLNEPE
661 SKDRVETLRP HVVGSGGNDK EKEEFREAKP RSLRFTWSMK TTSSMEPNEM MREIRKVLDA
721 NSCQSELHEK YMLLCMHGTP GHEDFVQWEM EVCKLPRLSL NGVRFKRISG TSMAFKNIAS
781 KIANELKL
>gi|62510922|sp|Q7KZI7.2|MARK2_HUMAN RecName: Full=Serine/threonine-protein kinase MARK2; AltName: Full=MAP/microtubule affinity-regulating kinase 2; AltName: Full=ELKL motif kinase; AltName: Full=EMK1; AltName: Full=PAR1 homolog
MSSARTPLPTLNERDTEQPTLGHLDSKPSSKSNMIRGRNSATSADEQPHIGNYRLLKTIGKGNFAKVKLA
RHILTGKEVAVKIIDKTQLNSSSLQKLFREVRIMKVLNHPNIVKLFEVIETEKTLYLVMEYASGGEVFDY</td>
<td></td>
</tr>
</table>

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LVAHGRMKEKEARAKFRQIVSAVQYCHQKFIVHRDLKAENLLLDADMNIKIADFGFSNEFTFGNKLDTFC
GSPPYAAPELFQGKKYDGPEVDVWSLGVILYTLVSGSLPFDGQNLKELRERVLRGKYRIPFYMSTDCENL
LKKFLILNPSKRGTLEQIMKDRWMNVGHEDDELKPYVEPLPDYKDPRRTELMVSMGYTREEIQDSLVGQR
YNEVMATYLLLGYKSSELEGDTITLKPRPSADLTNSSAPSPSHKVQRSVSANPKQRRFSDQAAGPAIPTS
NSYSKKTQSNNAENKRPEEDRESGRKASSTAKVPASPLPGLERKKTTPTPSTNSVLSTSTNRSRNSPLLE
RASLGQASIQNGKDSLTMPGSRASTASASAAVSAARPRQHQKSMSASVHPNKASGLPPTESNCEVPRPST
APQRVPVASPSAHNISSSGGAPDRTNFPRGVSSRSTFHAGQLRQVRDQQNLPYGVTPASPSGHSQGRRGA
SGSIFSKFTSKFVRRNLSFRFARRNLNEPESKDRVETLRPHVVGSGGNDKEKEEFREAKPRSLRFTWSMK
TTSSMEPNEMMREIRKVLDANSCQSELHEKYMLLCMHGTPGHEDFVQWEMEVCKLPRLSLNGVRFKRISG
TSMAFKNIASKIANELKL
```

Notes

Phosphorylation of human Par1b is mediated by PKCs at Ser400 (not sure but think it is RSVsANP) and Thr595 (SRStFHAGQ). Thr595 is conserved. Serine 400 (S400) is conserved in all 4 mammalian Par-1 kinases as well as the fly ortholog. 2 arms of the PKC pathway regulate interactions between Par-1b and 14-3-3 proteins: one involving aPKC and the other nPKC/PKD.

References to 14-3-3 binding to MARK2

Lin J, Hou KK, Piwnica-Worms H, Shaw AS. The polarity protein Par1b/EMK/MARK2 regulates T cell receptor-induced microtubule-organizing center polarization. J Immunol. 2009 Jul 15;183(2):1215-21.

Watkins JL, Lewandowski KT, Meek SE, Storz P, Toker A, Piwnica-Worms H. Phosphorylation of the Par-1 polarity kinase by protein kinase D regulates 14-3-3 binding and membrane association. Proc Natl Acad Sci U S A. 2008 Nov 25;105(47):18378-83.

Human Mdm2 (Swissprot = Q00987)

```
        1 MCNTNMSVPT DGAVTTSQIP ASEQETLVRP KPLLLKLLKS VGAQKDTYTM KEVLFYLGQY
       61 IMTKRLYDEK QQHIVYCSND LLGDLFGVPS FSVKEHRKIY TMIYRNLVVV NQQESSDSGT
      121 SVSENRCHLE GGSDQKDLVQ ELQEEKPSSS HLVSRPSTSS RRRAIsETEE NSDELSGERQ
      181 RKRHKsDSIS LSFDESLALC VIREICCERS SSSESTGTPS NPDLDAGVSE HSGDWLDQDS
      241 VSDQFSVEFE VESLDSEDYS LSEEGQELSD EDDEVYQVTV YQAGESDTDS FEEDPEISLA
      301 DYWKCTSCNE MNPPLPSHCN RCWALRENWL PEDKGKDKGE ISEKAKLENS TQAEEGFDVP
      361 DCKKTIVNDS RESCVEENDD KITQASQSQE SEDYSQPSTS SSIIYSSQED VKEFEREETQ
      421 DKEESVESSL PLNAIEPCVI CQGRPKNGCI VHGKTGHLMA CFTCAKKLKK RNKPCPVCRQ
      481 PIQMIVLTYF P
>gi|266516|sp|Q00987.1|MDM2_HUMAN RecName: Full=E3 ubiquitin-protein ligase
Mdm2; AltName: Full=p53-binding protein Mdm2; AltName: Full=Oncoprotein Mdm2;
AltName: Full=Double minute 2 protein; AltName: Full=Hdm2
MCNTNMSVPTDGAVTTSQIPASEQETLVRPKPLLLKLLKSVGAQKDTYTMKEVLFYLGQYIMTKRLYDEK
QQHIVYCSNDLLGDLFGVPSFSVKEHRKIYTMIYRNLVVVNQQESSDSGTSVSENRCHLEGGSDQKDLVQ
ELQEEKPSSSHLVSRPSTSSRRRAISETEENSDELSGERQRKRHKSDSISLSFDESLALCVIREICCERS
SSSESTGTPSNPDLDAGVSEHSGDWLDQDSVSDQFSVEFEVESLDSEDYSLSEEGQELSDEDDEVYQVTV
YQAGESDTDSFEEDPEISLADYWKCTSCNEMNPPLPSHCNRCWALRENWLPEDKGKDKGEISEKAKLENS
TQAEEGFDVPDCKKTIVNDSRESCVEENDDKITQASQSQESEDYSQPSTSSSIIYSSQEDVKEFEREETQ
DKEESVESSLPLNAIEPCVICQGRPKNGCIVHGKTGHLMACFTCAKKLKKRNKPCPVCRQPIQMIVLTYF
P
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Notes

14-3-3 proteins bind to Pim kinase-phosphorylated Ser166 and Ser186 on the human E3 ubiquitin ligase mouse double minute 2 (Mdm2), but not protein kinase B (PKB)/Akt-phosphorylated Ser166 and Ser188 (Wood et al 2009). In addition, 14-3-3sigma is reported to bind to the C-terminal RING domain of mdm2, but the precise sites have not been defined (Yang et al 2007).

References to 14-3-3 binding to Mdm2

Wood NT, Meek DW, MacKintosh C. 14-3-3 Binding to Pim-phosphorylated Ser166 and Ser186 of human Mdm2--Potential interplay with the PKB/Akt pathway and p14(ARF). FEBS Lett. 2009 Feb 18;583(4):615-20.

Yang HY, Wen YY, Lin YI, Pham L, Su CH, Yang H, Chen J, Lee MH. Roles for negative cell regulator 14-3-3sigma in control of MDM2 activities. Oncogene. 2007 Nov 15;26(52):7355-62.

Human Mdm4 (MdmX) (Swissprot = O15151)

```
        1 MTSFSTSAQC STSDSACRIS PGQINQVRPK LPLLKILHAA GAQGEMFTVK EVMHYLGQYI
       61 MVKQLYDQQE QHMVYCGGDL LGELLGRQSF SVKDPSPLYD MLRKNLVTLA TATTDAAQTL
      121 ALAQDHSMDI PSQDQLKQSA EESSTSRKRT TEDDIPTLPT SEHKCIHSRE DEDLIENLAQ
      181 DETSRLDLGF EEWDVAGLPW WFLGNLRSNY TPRSNGSTDL QTNQDVGTAI VSDTTDDLWF
      241 LNESVSEQLG VGIKVEAADT EQTSEEVGKV SDKKVIEVGK NDDLEDSKSL SDDTDVEVTS
      301 EDEWQCTECK KFNSPSKRYC FRCWALRKDW YSDCSKLTHS LSTSDITAIP EKENEGNDVP
      361 DCRRTIsAPV VRPKDAYIKK ENSKLFDPCN SVEFLDLAHS SESQETISSM GEQLDNLSEQ
      421 RTDTENMEDC QNLLKPCSLC EKRPRDGNII HGRTGHLVTC FHCARRLKKA GASCPICKKE
      481 IQLVIKVFIA
>gi|76803799|sp|O15151.2|MDM4_HUMAN RecName: Full=Protein Mdm4; AltName:
Full=p53-binding protein Mdm4; AltName: Full=Mdm2-like p53-binding protein;
AltName: Full=Protein Mdmx; AltName: Full=Double minute 4 protein
MTSFSTSAQCSTSDSACRISPGQINQVRPKLPLLKILHAAGAQGEMFTVKEVMHYLGQYIMVKQLYDQQE
QHMVYCGGDLLGELLGRQSFSVKDPSPLYDMLRKNLVTLATATTDAAQTLALAQDHSMDIPSQDQLKQSA
EESSTSRKRTTEDDIPTLPTSEHKCIHSREDEDLIENLAQDETSRLDLGFEEWDVAGLPWWFLGNLRSNY
TPRSNGSTDLQTNQDVGTAIVSDTTDDLWFLNESVSEQLGVGIKVEAADTEQTSEEVGKVSDKKVIEVGK
NDDLEDSKSLSDDTDVEVTSEDEWQCTECKKFNSPSKRYCFRCWALRKDWYSDCSKLTHSLSTSDITAIP
EKENEGNDVPDCRRTISAPVVRPKDAYIKKENSKLFDPCNSVEFLDLAHSSESQETISSMGEQLDNLSEQ
RTDTENMEDCQNLLKPCSLCEKRPRDGNIIHGRTGHLVTCFHCARRLKKAGASCPICKKEIQLVIKVFIA
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Notes

“Serine 367 (S367) is located within the putative binding sequence for 14-3-3, and its substitution with alanine (S367A) abolishes binding of Mdmx to 14-3-3. Transfection assays indicated that the S367A mutation, in cooperation with Mdm2, enhances the ability of Mdmx to repress the transcriptional activity of p53. The S367A mutant is more resistant to Mdm2-dependent ubiquitination and degradation than wild-type Mdmx, and Mdmx phosphorylated at S367 is preferentially degraded by Mdm2. "

Chk2-mediated phosphorylation of MDMX on S367 is important for stimulating 14-3-3 binding, MDMX nuclear import by a cryptic nuclear import signal, and degradation by MDM2.

"Serine/threonine kinase Akt mediates phosphorylation of MDMX at Ser367 (Lopez-Pajares et al 2008).

References to 14-3-3-binding to mdm4 (MdmX)

Okamoto K, Kashima K, Pereg Y, Ishida M, Yamazaki S, Nota A, Teunisse A, Migliorini D, Kitabayashi I, Marine JC, Prives C, Shiloh Y, Jochemsen AG, Taya Y. DNA damage-induced phosphorylation of MdmX at serine 367 activates p53 by targeting MdmX for Mdm2-dependent degradation. Mol Cell Biol. 2005 Nov;25(21):9608-20

LeBron C, Chen L, Gilkes DM, Chen J. Regulation of MDMX nuclear import and degradation by Chk2 and 14-3-3. EMBO J. 2006 Mar 22;25(6):1196-206.

Jin Y, Dai MS, Lu SZ, Xu Y, Luo Z, Zhao Y, Lu H.14-3-3gamma binds to MDMX that is phosphorylated by UV-activated Chk1, resulting in p53 activation. EMBO J. 2006 Mar 22;25(6):1207-18

Lopez-Pajares V, Kim MM, Yuan ZM. Phosphorylation of MDMX mediated by Akt leads to stabilization and induces 14-3-3 binding. J Biol Chem. 2008 May 16;283(20):13707-13. Epub 2008 Mar 20

<u>Human MEFV</u> Pyrin (Swissprot = O15553)

```
        1 MAKTPSDHLL STLEELVPYD FEKFKFKLQN TSVQKEHSRI PRSQIQRARP VKMATLLVTY
       61 YGEEYAVQLT LQVLRAINQR LLAEELHRAA IQEYSTQENG TDDSAASSSL GENKPRSLKT
      121 PDHPEGNEGN GPRPYGGGAA SLRCSQPEAG RGLSRKPLSK RREKASEGLD AQGKPRTRSP
      181 ALPGGRSPGP CRALEGGQAE VRLRRNAssA GRLQGLAGGA PGQKECRPFE VYLPSGKMRP
      241 RsLEVTISTG EKAPANPEIL LTLEEKTAAN LDSATEPRAR PTPDGGASAD LKEGPGNPEH
      301 SVTGRPPDTA ASPRCHAQEG DPVDGTCVRD SCSFPEAVSG HPQASGSRSP GCPRCQDSHE
      361 RKSPGSLSPQ PLPQCKRHLK QVQLLFCEDH DEPICLICSL SQEHQGHRVR PIEEVALEHK
      421 KKIQKQLEHL KKLRKSGEEQ RSYGEEKAVS FLKQTEALKQ RVQRKLEQVY YFLEQQEHFF
      481 VASLEDVGQM VGQIRKAYDT RVSQDIALLD ALIGELEAKE CQSEWELLQD IGDILHRAKT
      541 VPVPEKWTTP QEIKQKIQLL HQKSEFVEKS TKYFSETLRS EMEMFNVPEL IGAQAHAVNV
      601 ILDAETAYPN LIFSDDLKSV RLGNKWERLP DGPQRFDSCI IVLGSPSFLS GRRYWEVEVG
      661 DKTAWILGAC KTSISRKGNM TLSPENGYWV VIMMKENEYQ ASSVPPTRLL IKEPPKRVGI
      721 FVDYRVGSIS FYNVTARSHI YTFASCSFSG PLQPIFSPGT RDGGKNTAPL TICPVGGQGP
      781 D
```

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>gi|8928170|sp|O15553.1|MEFV_HUMAN RecName: Full=Pyrin; AltName:
Full=Marenostrin
MAKTPSDHLLSTLEELVPYDFEKFKFKLQNTSVQKEHSRIPRSQIQRARPVKMATLLVTYYGEEYAVQLT
LQVLRAINQRLLAEELHRAAIQEYSTQENGTDDSAASSSLGENKPRSLKTPDHPEGNEGNGPRPYGGGAA
SLRCSQPEAGRGLSRKPLSKRREKASEGLDAQGKPRTRSPALPGGRSPGPCRALEGGQAEVRLRRNASSA
GRLQGLAGGAPGQKECRPFEVYLPSGKMRPRSLEVTISTGEKAPANPEILLTLEEKTAANLDSATEPRAR
PTPDGGASADLKEGPGNPEHSVTGRPPDTAASPRCHAQEGDPVDGTCVRDSCSFPEAVSGHPQASGSRSP
GCPRCQDSHERKSPGSLSPQPLPQCKRHLKQVQLLFCEDHDEPICLICSLSQEHQGHRVRPIEEVALEHK
KKIQKQLEHLKKLRKSGEEQRSYGEEKAVSFLKQTEALKQRVQRKLEQVYYFLEQQEHFFVASLEDVGQM
VGQIRKAYDTRVSQDIALLDALIGELEAKECQSEWELLQDIGDILHRAKTVPVPEKWTTPQEIKQKIQLL
HQKSEFVEKSTKYFSETLRSEMEMFNVPELIGAQAHAVNVILDAETAYPNLIFSDDLKSVRLGNKWERLP
DGPQRFDSCIIVLGSPSFLSGRRYWEVEVGDKTAWILGACKTSISRKGNMTLSPENGYWVVIMMKENEYQ
ASSVPPTRLLIKEPPKRVGIFVDYRVGSISFYNVTARSHIYTFASCSFSGPLQPIFSPGTRDGGKNTAPL
TICPVGGQGPD
```

Notes

Pyrin probably controls the inflammatory response in myelomonocytic cells at the level of the cytoskeleton organization. Pyrin.fl was phosphorylated, and this modification mediated 14.3.3 binding. Serines 208, 209, and 242, within exon 2, acted as critical residues in the interaction between pyrin.fl and 14.3.3, and pSer208 thought more likely than 209 to be the phosphorylation responsible for binding to 14-3-3. When an S208-S209-S242A pyrin.fl triple mutant or wild-type pyrin.fl in the presence of an inhibitor of 14.3.3-ligand interactions was used, promotion of nuclear translocation of pyrin was observed.

References to 14-3-3 binding to pyrin

Jéru I, Papin S, L'hoste S, Duquesnoy P, Cazeneuve C, Camonis J, Amselem S. Interaction of pyrin with 14.3.3 in an isoform-specific and phosphorylation-dependent manner regulates its translocation to the nucleus. Arthritis Rheum. 2005 Jun;52(6):1848-57

<u>Human MITF</u> MITF Microphthalmia-associated transcription factor (Swissprot = O75030)

```
        1 MQSESGIVPD FEVGEEFHEE PKTYYELKSQ PLKSSSSAEH PGASKPPISS SSMTSRILLR
       61 QQLMREQMQE QERREQQQKL QAAQFMQQRV PVSQTPAINV SVPTTLPSAT QVPMEVLKVQ
      121 THLENPTKYH IQQAQRQQVK QYLSTTLANK HANQVLSLPC PNQPGDHVMP PVPGSSAPNS
      181 PMAMLTLNSN CEKEGFYKFE EQNRAESECP GMNTHSRASC MQMDDVIDDI ISLESSYNEE
      241 ILGLMDPALQ MANTLPVSGN LIDLYGNQGL PPPGLTISNs CPANLPNIKR ELTACIFPTE
      301 SEARALAKER QKKDNHNLIE RRRRFNINDR IKELGTLIPK SNDPDMRWNK GTILKASVDY
      361 IRKLQREQQR AKELENRQKK LEHANRHLLL RIQELEMQAR AHGLSLIPST GLCSPDLVNR
      421 IIKQEPVLEN CSQDLLQHHA DLTCTTTLDL TDGTITFNNN LGTGTEANQA YSVPTKMGSK
      481 LEDILMDDTL SPVGVTDPLL SSVSPGASKT SSRRSSMSME ETEHTC
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>gi|13124344|sp|O75030.2|MITF_HUMAN RecName: Full=Microphthalmia-associated
transcription factor
MQSESGIVPDFEVGEEFHEEPKTYYELKSQPLKSSSSAEHPGASKPPISSSSMTSRILLRQQLMREQMQE
QERREQQQKLQAAQFMQQRVPVSQTPAINVSVPTTLPSATQVPMEVLKVQTHLENPTKYHIQQAQRQQVK
QYLSTTLANKHANQVLSLPCPNQPGDHVMPPVPGSSAPNSPMAMLTLNSNCEKEGFYKFEEQNRAESECP
GMNTHSRASCMQMDDVIDDIISLESSYNEEILGLMDPALQMANTLPVSGNLIDLYGNQGLPPPGLTISNS
CPANLPNIKRELTACIFPTESEARALAKERQKKDNHNLIERRRRFNINDRIKELGTLIPKSNDPDMRWNK
GTILKASVDYIRKLQREQQRAKELENRQKKLEHANRHLLLRIQELEMQARAHGLSLIPSTGLCSPDLVNR
IIKQEPVLENCSQDLLQHHADLTCTTTLDLTDGTITFNNNLGTGTEANQAYSVPTKMGSKLEDILMDDTL
SPVGVTDPLLSSVSPGASKTSSRRSSMSMEETEHTC
```

Notes

Microphthalmia-associated transcription factor that contains both basic helix-loop-helix and leucine zipper structural features. Plays a critical role in the differentiation of various cell types including neural crest- derived melanocytes, mast cells, osteoclasts and optic cup-derived retinal pigment epithelium. Two isoforms are known: the M-isoform is expressed exclusively in melanocytes, while the A-isoform has a much broader range of expression. Mutations in MITF can lead to Waardenburg syndrome. Ten alternatively spliced isoforms have been described.

C-TAK1 increased MITF/14-3-3 complex formation and thus promoted cytoplasmic localization of MITF. C-TAK1 interaction was disrupted by RANKL/CSF-1 treatment. 14-3-3-binding site is Ser173 (PGLTISNsCPANLPN (Bronisz et al 2006, supplementary, which is equivalent to Ser280 in the canonical O75030.

MITF is highly related to the bHLH-Zip transcription factor TFE3 that was identified as 14-3-3 binding partner by mass spectrometry analysis (Jin et al Curr Biol. 2004 Aug 24;14(16):1436-50). TFE3 has a site similar to Ser173 in MITF, which is a potential 14-3-3-binding site in TFE3 (PAITVSNsCPAELPN).

References to 14-3-3 binding to MITF

Bronisz A, Sharma SM, Hu R, Godlewski J, Tzivion G, Mansky KC, Ostrowski MC. Microphthalmia-associated transcription factor interactions with 14-3-3 modulate differentiation of committed myeloid precursors. Mol Biol Cell. 2006 Sep;17(9):3897-906.

Human Mlf1 Myeloid leukemia factor 1 isoform 1 (Swissprot = P58340)

```
        1 MFRMLNSSFE DDPFFSESIL AHRENMRQMI RSFsEPFGRD LLSISDGRGR AHNRRGHNDG
       61 EDSLTHTDVS SFQTMDQMVS NMRNYMQKLE RNFGQLSVDP NGHSFCSSSV MTYSKIGDEP
      121 PKVFQASTQT RRAPGGIKET RKAMRDSDSG LEKMAIGHHI HDRAHVIKKS KNKKTGDEEV
      181 NQEFINMNES DAHAFDEEWQ SEVLKYKPGR HNLGNTRMRS VGHENPGSRE LKRREKPQQS
      241 PAIEHGRRSN VLGDKLHIKG SSVKSNKK
```

>gi|17368170|sp|P58340.1|MLF1_HUMAN RecName: Full=Myeloid leukemia factor 1; AltName: Full=Myelodysplasia-myeloid leukemia factor 1

MFRMLNSSFEDDPFFSESILAHRENMRQMIRSFSEPFGRDLLSISDGRGRAHNRRGHNDGEDSLTHTDVS
SFQTMDQMVSNMRNYMQKLERNFGQLSVDPNGHSFCSSSVMTYSKIGDEPPKVFQASTQTRRAPGGIKET
RKAMRDSDSGLEKMAIGHHIHDRAHVIKKSKNKKTGDEEVNQEFINMNESDAHAFDEEWQSEVLKYKPGR
HNLGNTRMRSVGHENPGSRELKRREKPQQSPAIEHGRRSNVLGDKLHIKGSSVKSNKK

Notes

MRQMIR(pS34)FSEPFGRDL = 14-3-3-binding site on Mlf1 (protein kinase unknown, tagetted by NRBP1 ? (pseudokinase in WNK branch of kinome)

88KLERNFGQLSVDP = NES human (Yoneda-Kato and Kato 2008)

Ala50 to Gln125 = Interaction with CSN3/COPS3 (Yoneda-Kato and Kato 2008)

Klinken et al (2002) Studies the MOUSE form of Mlf1; 88ELQRNFGQLSMD100 = NES DIFFERENT ISOFORM?

References to 14-3-3 binding to Mlf1

Winteringham LN, Endersby R, Kobelke S, McCulloch RK, Williams JH, Stillitano J, Cornwall SM, Ingley E, Klinken SP. Myeloid leukemia factor 1 associates with a novel heterogeneous nuclear ribonucleoprotein U-like molecule. J Biol Chem. 2006 Dec 15;281(50):38791-800.

Lim R, Winteringham LN, Williams JH, McCulloch RK, Ingley E, Tiao JY, Lalonde JP, Tsai S, Tilbrook PA, Sun Y, Wu X, Morris SW, Klinken SP. MADM, a novel adaptor protein that mediates phosphorylation of the 14-3-3 binding site of myeloid leukemia factor 1. J Biol Chem. 2002 Oct 25;277(43):40997-1008

Yoneda-Kato N, Kato JY. Shuttling imbalance of MLF1 results in p53 instability and increases susceptibility to oncogenic transformation. Mol Cell Biol. 2008 Jan;28(1):422-34 (NES)

Human MLK3 (Swissprot = Q16584)

SITES NOT KNOWN.
NOT IN WEBLOGO.

```
        1 MEPLKSLFLK SPLGSWNGSG SGGGGGGGGG RPEGSPKAAG YANPVWTALF DYEPSGQDEL
       61 ALRKGDRVEV LSRDAAISGD EGWWAGQVGG QVGIFPSNYV SRGGGPPPCE VASFQELRLE
      121 EVIGIGGFGK VYRGSWRGEL VAVKAARQDP DEDISVTAES VRQEARLFAM LAHPNIIALK
      181 AVCLEEPNLC LVMEYAAGGP LSRALAGRRV PPHVLVNWAV QIARGMHYLH CEALVPVIHR
      241 DLKSNNILLL QPIESDDMEH KTLKITDFGL AREWHKTTQM SAAGTYAWMA PEVIKASTFS
      301 KGSDVWSFGV LLWELLTGEV PYRGIDCLAV AYGVAVNKLT LPIPSTCPEP FAQLMADCWA
      361 QDPHRRPDFA SILQQLEALE AQVLREMPRD SFHSMQEGWK REIQGLFDEL RAKEKELLSR
      421 EEELTRAARE QRSQAEQLRR REHLLAQWEL EVFERELTLL LQQVDRERPH VRRRRGTFKR
      481 SKLRARDGGE RISMPLDFKH RITVQASPGL DRRRNVFEVG PGDSPTFPRF RAIQLEPAEP
      541 GQAWGRQSPR RLEDSSNGER RACWAWGPSS PKPGEAQNGR RRSRMDEATW YLDSDDSSPL
      601 GSPSTPPALN GNPPRPSLEP EEPKRPVPAE RGSSSGTPKL IQRALLRGTA LLASLGLGRD
      661 LQPPGGPGRE RGESPTTPPT PTPAPCPTEP PPSPLICFSL KTPDSPPTPA PLLLDLGIPV
      721 GQRSAKSPRR EEEPRGGTVS PPPGTSRSAP GTPGTPRSPP LGLISRPRPS PLRSRIDPWS
      781 FVSAGPRPSP LPSPQPAPRR APWTLFPDSD PFWDSPPANP FQGGPQDCRA QTKDMGAQAP
      841 WVPEAGP
```

>gi|71153819|sp|Q16584.1|M3K11_HUMAN RecName: Full=Mitogen-activated protein kinase kinase kinase 11; AltName: Full=Mixed lineage kinase 3; AltName: Full=Src-homology 3 domain-containing proline-rich kinase

MEPLKSLFLKSPLGSWNGSGSGGGGGGGGGRPEGSPKAAGYANPVWTALFDYEPSGQDELALRKGDRVEV
LSRDAAISGDEGWWAGQVGGQVGIFPSNYVSRGGGPPPCEVASFQELRLEEVIGIGGFGKVYRGSWRGEL
VAVKAARQDPDEDISVTAESVRQEARLFAMLAHPNIIALKAVCLEEPNLCLVMEYAAGGPLSRALAGRRV
PPHVLVNWAVQIARGMHYLHCEALVPVIHRDLKSNNILLLQPIESDDMEHKTLKITDFGLAREWHKTTQM
SAAGTYAWMAPEVIKASTFSKGSDVWSFGVLLWELLTGEVPYRGIDCLAVAYGVAVNKLTLPIPSTCPEP
FAQLMADCWAQDPHRRPDFASILQQLEALEAQVLREMPRDSFHSMQEGWKREIQGLFDELRAKEKELLSR
EEELTRAAREQRSQAEQLRRREHLLAQWELEVFERELTLLLQQVDRERPHVRRRRGTFKRSKLRARDGGE
RISMPLDFKHRITVQASPGLDRRRNVFEVGPGDSPTFPRFRAIQLEPAEPGQAWGRQSPRRLEDSSNGER
RACWAWGPSSPKPGEAQNGRRRSRMDEATWYLDSDDSSPLGSPSTPPALNGNPPRPSLEPEEPKRPVPAE
RGSSSGTPKLIQRALLRGTALLASLGLGRDLQPPGGPGRERGESPTTPPTPTPAPCPTEPPPSPLICFSL
KTPDSPPTPAPLLLDLGIPVGQRSAKSPRREEEPRGGTVSPPPGTSRSAPGTPGTPRSPPLGLISRPRPS
PLRSRIDPWSFVSAGPRPSPLPSPQPAPRRAPWTLFPDSDPFWDSPPANPFQGGPQDCRAQTKDMGAQAP
WVPEAGP

Notes

Could not find papers characterizing an interaction between MLK3 and 14-3-3. Papers do however mention phosphorylation of 14-3-3 affecting Bax localization. MLK3 a TKL kinase of the MLK family. Has an amino-terminal SH3 domain followed by the kinase domain, two leucine zipper domains, a cdc42/Rac1 binding (CRIB) domain and several other domains/motifs at the carboxy-terminal region. Phosphorylates IkappaB and activates SEK1 and MKK7.

Zhang QG, Akt inhibits MLK3/JNK3 signaling by inactivating Rac1: a protective mechanism against ischemic brain injury. J Neurochem. 2006 Sep;98(6):1886-98.

<u>Human MST1R</u> (Ron) Tyrosine kinase receptor for MSP (macrophage-stimulating protein receptor) (Swissprot = Q04912)

```
   1 MELLPPLPQS FLLLLLLPAK PAAGEDWQCP RTPYAASRDF DVKYVVPSFS AGGLVQAMVT
  61 YEGDRNESAV FVAIRNRLHV LGPDLKSVQS LATGPAGDPG CQTCAACGPG PHGPPGDTDT
 121 KVLVLDPALP ALVSCGSSLQ GRCFLHDLEP QGTAVHLAAP ACLFSAHHNR PDDCPDCVAS
 181 PLGTRVTVVE QGQASYFYVA SSLDAAVAGS FSPRSVSIRR LKADASGFAP GFVALSVLPK
 241 HLVSYSIEYV HSFHTGAFVY FLTVQPASVT DDPSALHTRL ARLSATEPEL GDYRELVLDC
 301 RFAPKRRRRG APEGGQPYPV LQVAHSAPVG AQLATELSIA EGQEVLFGVF VTGKDGGPGV
 361 GPNSVVCAFP IDLLDTLIDE GVERCCESPV HPGLRRGLDF FQSPSFCPNP PGLEALSPNT
 421 SCRHFPLLVS SSFSRVDLFN GLLGPVQVTA LYVTRLDNVT VAHMGTMDGR ILQVELVRSL
 481 NYLLYVSNFS LGDSGQPVQR DVSRLGDHLL FASGDQVFQV PIRGPGCRHF LTCGRCLRAW
 541 HFMGCGWCGN MCGQQKECPG SWQQDHCPPK LTEFHPHSGP LRGSTRLTLC GSNFYLHPSG
 601 LVPEGTHQVT VGQSPCRPLP KDSSKLRPVP RKDFVEEFEC ELEPLGTQAV GPTNVSLTVT
 661 NMPPGKHFRV DGTSVLRGFS FMEPVLIAVQ PLFGPRAGGT CLTLEGQSLS VGTSRAVLVN
 721 GTECLLARVS EGQLLCATPP GATVASVPLS LQVGGAQVPG SWTFQYREDP VVLSISPNCG
 781 YINSHITICG QHLTSAWHLV LSFHDGLRAV ESRCERQLPE QQLCRLPEYV VRDPQGWVAG
 841 NLSARGDGAA GFTLPGFRFL PPPHPPSANL VPLKPEEHAI KFEYIGLGAV ADCVGINVTV
 901 GGESCQHEFR GDMVVCPLPP SLQLGQDGAP LQVCVDGECH ILGRVVRPGP DGVPQSTLLG
 961 ILLPLLLLVA ALATALVFSY WWRRKQLVLP PNLNDLASLD QTAGATPLPI LYSGSDYRSG
1021 LALPAIDGLD STTCVHGASF SDSEDESCVP LLRKESIQLR DLDSALLAEV KDVLIPHERV
1081 VTHSDRVIGK GHFGVVYHGE YIDQAQNRIQ CAIKSLSRIT EMQQVEAFLR EGLLMRGLNH
1141 PNVLALIGIM LPPEGLPHVL LPYMCHGDLL QFIRSPQRNP TVKDLISFGL QVARGMEYLA
1201 EQKFVHRDLA ARNCMLDESF TVKVADFGLA RDILDREYYS VQQHRHARLP VKWMALESLQ
1261 TYRFTTKSDV WSFGVLLWEL LTRGAPPYRH IDPFDLTHFL AQGRRLPQPE YCPDSLYQVM
1321 QQCWEADPAV RPTFRVLVGE VEQIVSALLG DHYVQLPATY MNLGPSTSHE MNVRPEQPQF
1381 SPMPGNVRRP RPLsEPPRPT
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>gi|585912|sp|Q04912.1|RON_HUMAN RecName: Full=Macrophage-stimulating protein
receptor; Short=MSP receptor; AltName: Full=p185-Ron; AltName: Full=CDw136;
AltName: CD_antigen=CD136; Contains: RecName: Full=Macrophage-stimulating
protein receptor alpha chain; Contains: RecName: Full=Macrophage-stimulating
protein receptor beta chain; Flags: Precursor
MELLPPLPQSFLLLLLLPAKPAAGEDWQCPRTPYAASRDFDVKYVVPSFSAGGLVQAMVTYEGDRNESAV
FVAIRNRLHVLGPDLKSVQSLATGPAGDPGCQTCAACGPGPHGPPGDTDTKVLVLDPALPALVSCGSSLQ
GRCFLHDLEPQGTAVHLAAPACLFSAHHNRPDDCPDCVASPLGTRVTVVEQGQASYFYVASSLDAAVAGS
FSPRSVSIRRLKADASGFAPGFVALSVLPKHLVSYSIEYVHSFHTGAFVYFLTVQPASVTDDPSALHTRL
ARLSATEPELGDYRELVLDCRFAPKRRRRGAPEGGQPYPVLQVAHSAPVGAQLATELSIAEGQEVLFGVF
VTGKDGGPGVGPNSVVCAFPIDLLDTLIDEGVERCCESPVHPGLRRGLDFFQSPSFCPNPPGLEALSPNT
SCRHFPLLVSSSFSRVDLFNGLLGPVQVTALYVTRLDNVTVAHMGTMDGRILQVELVRSLNYLLYVSNFS
LGDSGQPVQRDVSRLGDHLLFASGDQVFQVPIRGPGCRHFLTCGRCLRAWHFMGCGWCGNMCGQQKECPG
SWQQDHCPPKLTEFHPHSGPLRGSTRLTLCGSNFYLHPSGLVPEGTHQVTVGQSPCRPLPKDSSKLRPVP
RKDFVEEFECELEPLGTQAVGPTNVSLTVTNMPPGKHFRVDGTSVLRGFSFMEPVLIAVQPLFGPRAGGT
CLTLEGQSLSVGTSRAVLVNGTECLLARVSEGQLLCATPPGATVASVPLSLQVGGAQVPGSWTFQYREDP
VVLSISPNCGYINSHITICGQHLTSAWHLVLSFHDGLRAVESRCERQLPEQQLCRLPEYVVRDPQGWVAG
NLSARGDGAAGFTLPGFRFLPPPHPPSANLVPLKPEEHAIKFEYIGLGAVADCVGINVTVGGESCQHEFR
GDMVVCPLPPSLQLGQDGAPLQVCVDGECHILGRVVRPGPDGVPQSTLLGILLPLLLLVAALATALVFSY
WWRRKQLVLPPNLNDLASLDQTAGATPLPILYSGSDYRSGLALPAIDGLDSTTCVHGASFSDSEDESCVP
LLRKESIQLRDLDSALLAEVKDVLIPHERVVTHSDRVIGKGHFGVVYHGEYIDQAQNRIQCAIKSLSRIT
EMQQVEAFLREGLLMRGLNHPNVLALIGIMLPPEGLPHVLLPYMCHGDLLQFIRSPQRNPTVKDLISFGL
QVARGMEYLAEQKFVHRDLAARNCMLDESFTVKVADFGLARDILDREYYSVQQHRHARLPVKWMALESLQ
TYRFTTKSDVWSFGVLLWELLTRGAPPYRHIDPFDLTHFLAQGRRLPQPEYCPDSLYQVMQQCWEADPAV
RPTFRVLVGEVEQIVSALLGDHYVQLPATYMNLGPSTSHEMNVRPEQPQFSPMPGNVRRPRPLSEPPRPT
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Notes

RPL(pS1394)EP

References to 14-3-3 binding to MST1R (Ron)

Santoro MM, Gaudino G, Villa-Moruzzi E. Protein phosphatase 1 binds to phospho-Ser-1394 of the macrophage-stimulating protein receptor. Biochem J. 2003 Dec 15;376(Pt 3):587-94.

Santoro MM, Gaudino G, Marchisio PC. The MSP receptor regulates alpha6beta4 and alpha3beta1 integrins via 14-3-3 proteins in keratinocyte migration. Dev Cell. 2003 Aug;5(2):257-71.

<u>Human NCOR1</u> Transcriptional corepressor (Swissprot = O75376) , related to SMRT, which also binds 14-3-3

```
   1 MSSSGYPPNQ GAFSTEQSRY PPHSVQYTFP NTRHQQEFAV PDYRSSHLEV SQASQLLQQQ
  61 QQQQLRRRPS LLSEFHPGSD RPQERRTSYE PFHPGPSPVD HDSLESKRPR LEQVSDSHFQ
 121 RVSAAVLPLV HPLPEGLRAS ADAKKDPAFG GKHEAPSSPI SGQPCGDDQN ASPSKLSKEE
 181 LIQSMDRVDR EIAKVEQQIL KLKKKQQQLE EEAAKPPEPE KPVSPPPVEQ KHRSIVQIIY
 241 DENRKKAEEA HKIFEGLGPK VELPLYNQPS DTKVYHENIK TNQVMRKKLI LFFKRRNHAR
 301 KQREQKICQR YDQLMEAWEK KVDRIENNPR RKAKESKTRE YYEKQFPEIR KQREQQERFQ
 361 RVGQRGAGLS ATIARSEHEI SEIIDGLSEQ ENNEKQMRQL SVIPPMMFDA EQRRVKFINM
 421 NGLMEDPMKV YKDRQFMNVW TDHEKEIFKD KFIQHPKNFG LIASYLERKS VPDCVLYYYL
 481 TKKNENYKAL VRRNYGKRRG RNQQIARPSQ EEKVEEKEED KAEKTEKKEE EKKDEEEKDE
 541 KEDSKENTKE KDKIDGTAEE TEEREQATPR GRKTANSQGR RKGRITRSMT NEAAAASAAA
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     601 AAATEEPPPP LPPPPEPIST EPVETSRWTE EEMEVAKKGL VEHGRNWAAI AKMVGTKSEA
     661 QCKNFYFNYK RRHNLDNLLQ QHKQKTSRKP REERDVSQCE SVASTVSAQE DEDIEASNEE
     721 ENPEDSEVEA VKPSEDSPEN ATSRGNTEPA VELEPTTETA PSTSPSLAVP STKPAEDESV
     781 ETQVNDSISA ETAEQMDVDQ QEHSAEEGSV CDPPPATKAD SVDVEVRVPE NHASKVEGDN
     841 TKERDLDRAS EKVEPRDEDL VVAQQINAQR PEPQSDNDSS ATCSADEDVD GEPERQRMFP
     901 MDSKPSLLNP TGSILVSSPL KPNPLDLPQL QHRAAVIPPM VSCTPCNIPI GTPVSGYALY
     961 QRHIKAMHES ALLEEQRQRQ EQIDLECRSS TSPCGTSKSP NREWEVLQPA PHQVITNLPE
    1021 GVRLPTTRPT RPPPPLIPSS KTTVASEKPS FIMGGSISQG TPGTYLTSHN QASYTQETPK
    1081 PSVGSISLGL PRQQESAKSA TLPYIKQEEF SPRSQNSQPE GLLVRAQHEG VVRGTAGAIQ
    1141 EGSITRGTPT SKISVESIPS LRGSITQGTP ALPQTGIPTE ALVKGSISRM PIEDSSPEKG
    1201 REEAASKGHV IYEGKSGHIL SYDNIKNARE GTRSPRTAHE ISLKRSYESV EGNIKQGMSM
    1261 RESPVSAPLE GLICRALPRG SPHSDLKERT VLSGSIMQGT PRATTESFED GLKYPKQIKR
    1321 ESPPIRAFEG AITKGKPYDG ITTIKEMGRS IHEIPRQDIL TQESRKTPEV VQSTRPIIEG
    1381 SISQGTPIKF DNNSGQSAIK HNVKSLITGP SKLSRGMPPL EIVPENIKVV ERGKYEDVKA
    1441 GETVRSRHTS VVSSGPSVLR STLHEAPKAQ LSPGIYDDTS ARRTPVSYQN TMSRGSPMMN
    1501 RTSDVTISSN KSTNHERKST LTPTQRESIP AKSPVPGVDP VVSHSPFDPH HRGSTAGEVY
    1561 RSHLPTHLDP AMPFHRALDP AAAAYLFQRQ LSPTPGYPSQ YQLYAMENTR QTILNDYITS
    1621 QQMQVNLRPD VARGLSPREQ PLGLPYPATR GIIDLTNMPP TILVPHPGGT STPPMDRITY
    1681 IPGTQITFPP RPYNSASMSP GHPTHLAAAA SAERERERER EKERERERIA AASSDLYLRP
    1741 GSEQPGRPGS HGYVRSPSPS VRTQETMLQQ RPSVFQGTNG TSVITPLDPT AQLRIMPLPA
    1801 GGPSISQGLP ASRYNTAADA LAALVDAAAS APQMDVSKTK ESKHEAARLE ENLRSRSAAV
    1861 SEQQQLEQKT LEVEKRSVQC LYTSSAFPSG KPQPHSSVVY SEAGKDKGPP PKSRYEEELR
    1921 TRGKTTITAA NFIDVIITRQ IASDKDARER GSQSSDSSSS LSSHRYETPS DAIEVISPAS
    1981 SPAPPQEKLQ TYQPEVVKAN QAENDPTRQY EGPLHHYRPQ QESPSPQQQL PPSSQAEGMG
    2041 QVPRTHRLIT LADHICQIIT QDFARNQVSS QTPQQPPTST FQNSPSALVS TPVRTKTSNR
    2101 YSPESQAQSV HHQRPGSRVS PENLVDKSRG SRPGKSPERS HVSSEPYEPI SPPQVPVVHE
    2161 KQDSLLLLSQ RGAEPAEQRN DARSPGSISY LPSFFTKLEN TSPMVKSKKQ EIFRKLNSSG
    2221 GGDSDMAAAQ PGTEIFNLPA VTTSGSVSSR GHSFADPASN LGLEDIIRKA LMGSFDDKVE
    2281 DHGVVMSQPM GVVPGTANTS VVTSGETRRE EGDPSPHSGG VCKPKLISKS NSRKsKSPIP
    2341 GQGYLGTERP SSVSSVHSEG DYHRQTPGWA WEDRPSSTGS TQFPYNPLTM RMLSSTPPTP
    2401 IACAPSAVNQ AAPHQQNRIW EREPAPLLSA QYETLSDSDD
>gi|47117817|sp|O75376.2|NCOR1_HUMAN RecName: Full=Nuclear receptor
corepressor 1; Short=N-CoR1; Short=N-CoR
MSSSGYPPNQGAFSTEQSRYPPHSVQYTFPNTRHQQEFAVPDYRSSHLEVSQASQLLQQQQQQLRRRPS
LLSEFHPGSDRPQERRTSYEPFHPGPSPVDHDSLESKRPRLEQVSDSHFQRVSAAVLPLVHPLPEGLRAS
ADAKKDPAFGGKHEAPSSPISGQPCGDDQNASPSKLSKEELIQSMDRVDREIAKVEQQILKLKKKQQQLE
EEAAKPPEPEKPVSPPPVEQKHRSIVQIIYDENRKKAEEAHKIFEGLGPKVELPLYNQPSDTKVYHENIK
TNQVMRKKLILFFKRRNHARKQREQKICQRYDQLMEAWEKKVDRIENNPRRKAKESKTREYYEKQFPEIR
KQREQQERFQRVGQRGAGLSATIARSEHEISEIIDGLSEQENNEKQMRQLSVIPPMMFDAEQRRVKFINM
NGLMEDPMKVYKDRQFMNVWTDHEKEIFKDKFIQHPKNFGLIASYLERKSVPDCVLYYYLTKKNENYKAL
VRRNYGKRRGRNQQIARPSQEEKVEEKEEDKAEKTEKKEEEKKDEEEKDEKEDSKENTKEKDKIDGTAEE
TEEREQATPRGRKTANSQGRRKGRITRSMTNEAAAASAAAAAATEEPPPPLPPPPEPISTEPVETSRWTE
EEMEVAKKGLVEHGRNWAAIAKMVGTKSEAQCKNFYFNYKRRHNLDNLLQQHKQKTSRKPREERDVSQCE
SVASTVSAQEDEDIEASNEEENPEDSEVEAVKPSEDSPENATSRGNTEPAVELEPTTETAPSTSPSLAVP
STKPAEDESVETQVNDSISAETAEQMDVDQQEHSAEEGSVCDPPPATKADSVDVEVRVPENHASKVEGDN
TKERDLDRASEKVEPRDEDLVVAQQINAQRPEPQSDNDSSATCSADEDVDGEPERQRMFPMDSKPSLLNP
TGSILVSSPLKPNPLDLPQLQHRAAVIPPMVSCTPCNIPIGTPVSGYALYQRHIKAMHESALLEEQRQRQ
EQIDLECRSSTSPCGTSKSPNREWEVLQPAPHQVITNLPEGVRLPTTRPTRPPPPLIPSSKTTVASEKPS
FIMGGSISQGTPGTYLTSHNQASYTQETPKPSVGSISLGLPRQQESAKSATLPYIKQEEFSPRSQNSQPE
GLLVRAQHEGVVRGTAGAIQEGSITRGTPTSKISVESIPSLRGSITQGTPALPQTGIPTEALVKGSISRM
PIEDSSPEKGREEAASKGHVIYEGKSGHILSYDNIKNAREGTRSPRTAHEISLKRSYESVEGNIKQGMSM
RESPVSAPLEGLICRALPRGSPHSDLKERTVLSGSIMQGTPRATTESFEDGLKYPKQIKRESPPIRAFEG
AITKGKPYDGITTIKEMGRSIHEIPRQDILTQESRKTPEVVQSTRPIIEGSISQGTPIKFDNNSGQSAIK
HNVKSLITGPSKLSRGMPPLEIVPENIKVVERGKYEDVKAGETVRSRHTSVVSSGPSVLRSTLHEAPKAQ
LSPGIYDDTSARRTPVSYQNTMSRGSPMMNRTSDVTISSNKSTNHERKSTLTPTQRESIPAKSPVPGVDP
VVSHSPFDPHHRGSTAGEVYRSHLPTHLDPAMPFHRALDPAAAAYLFQRQLSPTPGYPSQYQLYAMENTR
QTILNDYITSQQMQVNLRPDVARGLSPREQPLGLPYPATRGIIDLTNMPPTILVPHPGGTSTPPMDRITY
IPGTQITFPPRPYNSASMSPGHPTHLAAAASAERERERERERERERERIAAASSDLYLRPGSEQPGRPGS
HGYVRSPSPSVRTQETMLQQRPSVFQGTNGTSVITPLDPTAQLRIMPLPAGGPSISQGLPASRYNTAADA
LAALVDAAAASAPQMDVSKTKESKHEAARLEENLRSRSAAVSEQQQLEQKTLEVEKRSVQCLYTSSAFPSG
KPQPHSSVVYSEAGKDKGPPPKSRYEEELRTRGKTTITAANFIDVIITRQIASDKDARERGSQSSDSSSS
LSSHRYETPSDAIEVISPASSPAPPQEKLQTYQPEVVKANQAENDPTRQYEGPLHHYRPQQESPSPQQQL
PPSSQAEGMGQVPRTHRLITLADHICQIITQDFARNQVSSQTPQQPPTSTFQNSPSALVSTPVRTKTSNR
YSPESQAQSVHHQRPGSRVSPENLVDKSRGSRPGKSPERSHVSSEPYEPISPPQVPVVHEKQDSLLLLSQ
RGAEPAEQRNDARSPGSISYLPSFFTKLENTSPMVKSKKQEIFRKLNSSGGGDSDMAAAQPGTEIFNLPA
VTTSGSVSSRGHSFADPASNLGLEDIIRKALMGSFDDKVEDHGVVMSQPMGVVPGTANTSVVTSGETRRE
EGDPSPHSGGVCKPKLISKSNSRKSKSPIPGQGYLGTERPSSVSSVHSEGDYHRQTPGWAWEDRPSSTGS
TQFPYNPLTMRMLSSTPPTPIACAPSAVNQAAPHQQNRIWEREPAPLLSAQYETLSDSDD
```

Notes

Phosphorylation of Ser2345 and Ser2348 (by IKKalpha) creates a functional 14-3-3-binding domain (SRK(pS2348)KSPIPGQ) (Fernández-Majada et al 2007). N-CoR1 is a protein that regulates the activity of some transcription factors, including nuclear receptors, by promoting histone deacetylation and chromatin condensation, thereby altering the accessibility of various genes to the transcriptional machinery. Is known to play a role genetic programming including that for myogenesis. Is a component of a large corepressor complex that contains SIN3A/B and histone deacetylases HDAC1 and HDAC2. This complex associates with the thyroid and the retinoic acid receptors in the absence of ligand. Interacts with the catalytic domain of HDAC9. Increased expression correlates with the loss of vitamin D responsiveness in aggressive androgen-independent prostate cancer cells. Its gene tends

to be overexpressed in multiple-myeloma cell lines. **References to 14-3-3 binding to N-CoR** Fernández-Majada V, Pujadas J, Vilardell F, Capella G, Mayo MW, Bigas A, Espinosa L. Aberrant cytoplasmic localization of N-CoR in colorectal tumors. Cell Cycle. 2007 Jul 15;6(14):1748-52.	

Human Ndel1 (Swissprot = Q9GZM8)
`1 MDGEDIPDFS SLKEETAYWK ELSLKYKQSF QEARDELVEF QEGSRELEAE LEAQLVQAEQ`
`61 RNRDLQADNQ RLKYEVEALK EKLEHQYAQS YKQVSVLEDD LSQTRAIKEQ LHKYVRELEQ`
`121 ANDDLERAKR ATIVSLEDFE QRLNQAIERN AFLESELDEK ESLLVSVQRL KDEARDLRQE`
`181 LAVRERQQEV TRKSAPSsPT LDCEKMDSAV QASLSLPAtP VGKGTENTFP sPKAIPNGFG`
`241 TSPLTPSARI sALNIVGDLL RKVGALESKL AACRNFAKDQ ASRKSYISGN VNCGVLNGNG`
`301 TKFSRSGHTS FFDKGAVNGF DPAPPPPGLG SSRPSsAPGM LPLSV`
`>gi|74725006|sp|Q9GZM8.1|NDEL1_HUMAN RecName: Full=Nuclear distribution protein nudE-like 1; Short=Protein Nudel; AltName: Full=Mitosin-associated protein 1`
`MDGEDIPDFSSLKEETAYWKELSLKYKQSFQEARDELVEFQEGSRELEAELEAQLVQAEQRNRDLQADNQ`
`RLKYEVEALKEKLEHQYAQSYKQVSVLEDDLSQTRAIKEQLHKYVRELEQANDDLERAKRATIVSLEDFE`
`QRLNQAIERNAFLESELDEKESLLVSVQRLKDEARDLRQELAVRERQQEVTRKSAPSSPTLDCEKMDSAV`
`QASLSLPATPVGKGTENTFPSPKAIPNGFGTSPLTPSARISALNIVGDLLRKVGALESKLAACRNFAKDQ`
`ASRKSYISGNVNCGVLNGNGTKFSRSGHTSFFDKGAVNGFDPAPPPPGLGSSRPSSAPGMLPLSV`
Notes
"14-3-3ε binds to CDK5/p35-phosphorylated NUDEL and this binding maintains NUDEL phosphorylation. Similar to LIS1, deficiency of 14-3-3 results in mislocalization of NUDEL and LIS1, consistent with reduction of cytoplasmic dynein function. We produced substitution mutants for each of the CDK5 sites of NUDEL: S198A, T219A and S231A. Each single or double mutant compromised, and the triple mutant completely eliminated, interaction with 14-3-3ε. These Ser/Thr mutants had no effect on the interaction of LIS1 and NUDEL in yeast or as recombinant proteins. Mutation of two other phosphorylation sites (Ser242, Thr245) located outside of the binding region had only mild effects on interaction." (Toyo-oka et al 2003)
References to 14-3-3 binding to Ndel1
Toyo-oka K, Shionoya A, Gambello MJ, Cardoso C, Leventer R, Ward HL, Ayala R, Tsai LH, Dobyns W, Ledbetter D, Hirotsune S, Wynshaw-Boris A. 14-3-3epsilon is important for neuronal migration by binding to NUDEL: a molecular explanation for Miller-Dieker syndrome. Nat Genet. 2003 Jul;34(3):274-85.
	`THREE phosphoSER-PRO SITES - NOT LIKE ANY OTHER 14-3-3-BINDING SITES-NOT IN WEBLOGO (IN YELLOW ARE TWO 14-3-3-BINDING SITES IDENTIFIED HERE, SEE MAIN TEXT (NEW NOT IN WEBLOGO)`

Human NEDD4L E3 ubiquitin ligase Nedd4.2 (Swissprot = Q7Z5N3)
`1 MATGLGEPVY GLSEDEGESR ILRVKVVSGI DLAKKDIFGA SDPYVKLSLY VADENRELAL`
`61 VQTKTIKKTL NPKWNEEFYF RVNPSNHRLL FEVFDENRLT RDDFLGQVDV PLSHLPTEDP`
`121 TMERPYTFKD FLLRPRSHKS RVKGFLRLKM AYMPKNGGQD EENSDQRDDM EHGWEVVDSN`
`181 DSASQHQKEL PPPPLPPGWE EKVDNLGRTY YVNHNNRTTQ WHRPSLMDVS SESDNNIRQI`
`241 NQEAAHRRFR SRRHISEDLE PEPSEGGDVP EPWETISEEV NIAGDSLGLA LPPPPASPGS`
`301 RTSPQELSEE LSRRLQITPD SNGEQFSSLI QREPSSRLRS CsVTDAVAEQ GHLPPPSAPA`
`361 GRARSSTVTG GEEPTPSVAY VHTTPGLPSG WEERKDAKGR TYYVNHNNRT TTWTRPIMQL`
`421 AEDGASGSAT NSNNHLIEPQ IRRPRSLsSP TVTLSAPLEG AKDSPVRRAV KDTLSNPQSP`
`481 QPSPYNSPKP QHKVTQSFLP PGWEMRIAPN GRPFFIDHNT KTTTWEDPRL KFPVHMRSKT`
`541 SLNPNDLGPL PPGWEERIHL DGRTFYIDHN SKITQWEDPR LQNPAITGPA VPYSREFKQK`
`601 YDYFRKKLKK PADIPNRFEM KLHRNNIFEE SYRRIMSVKR PDVLKARLWI EFESEKGLDY`
`661 GGVAREWFFL LSKEMFNPYY GLFEYSATDN YTLQINPNSG LCNEDHLSYF TFIGRVAGLA`
`721 VFHGKLLDGF FIRPFYKMML GKQITLNDME SVDSEYYNSL KWILENDPTE LDLMFCIDEE`
`781 NFGQTYQVDL KPNGSEIMVT NENKREYIDL VIQWRFVNRV QKQMNAFLEG FTELLPIDLI`
`841 KIFDENELEL LMCGLGDVDV NDWRQHSIYK NGYCPNHPVI QWFWKAVLLM DAEKRIRLLQ`
`901 FVTGTSRVPM NGFAELYGSN GPQLFTIEQW GSPEKLPRAH TCFNRLDLPP YETFEDLREK`
`961 LLMAVENAQG FEGVD`
`>gi|74713674|sp|Q7Z5N3|Q7Z5N3_HUMAN NEDD4.2`
`MATGLGEPVYGLSEDEGESRILRVKVVSGIDLAKKDIFGASDPYVKLSLYVADENRELALVQTKTIKKTL`
`NPKWNEEFYFRVNPSNHRLLFEVFDENRLTRDDFLGQVDVPLSHLPTEDPTMERPYTFKDFLLRPRSHKS`
`RVKGFLRLKMAYMPKNGGQDEENSDQRDDMEHGWEVVDSNDSASQHQKELPPPPLPPGWEEKVDNLGRTY`
`YVNHNNRTTQWHRPSLMDVSSESDNNIRQINQEAAHRRFRSRRHISEDLEPEPSEGGDVPEPWETISEEV`
`NIAGDSLGLALPPPPASPGSRTSPQELSEELSRRLQITPDSNGEQFSSLIQREPSSRLRSCSVTDAVAEQ`
`GHLPPPSAPAGRARSSTVTGGEEPTPSVAYVHTTPGLPSGWEERKDAKGRTYYVNHNNRTTTWTRPIMQL`
`AEDGASGSATNSNNHLIEPQIRRPRSLSSPTVTLSAPLEGAKDSPVRRAVKDTLSNPQSPQPSPYNSPKP`
`QHKVTQSFLPPGWEMRIAPNGRPFFIDHNTKTTTWEDPRLKFPVHMRSKTSLNPNDLGPLPPGWEERIHL`
`DGRTFYIDHNSKITQWEDPRLQNPAITGPAVPYSREFKQKYDYFRKKLKKPADIPNRFEMKLHRNNIFEE`
`SYRRIMSVKRPDVLKARLWIEFESEKGLDYGGVAREWFFLLSKEMFNPYYGLFEYSATDNYTLQINPNSG`
`LCNEDHLSYFTFIGRVAGLAVFHGKLLDGFFIRPFYKMMLGKQITLNDMESVDSEYYNSLKWILENDPTE`
`LDLMFCIDEENFGQTYQVDLKPNGSEIMVTNENKREYIDLVIQWRFVNRVQKQMNAFLEGFTELLPIDLI`
`KIFDENELELLMCGLGDVDVNDWRQHSIYKNGYCPNHPVIQWFWKAVLLMDAEKRIRLLQFVTGTSRVPM`
`NGFAELYGSNGPQLFTIEQWGSPEKLPRAHTCFNRLDLPPYETFEDLREKLLMAVENAQGFEGVD`
Notes
NEDD4L E3 ubiquitin-protein ligase which accepts ubiquitin from an E2 ubiquitin-conjugating enzyme in the form of a thioester and then directly transfers the ubiquitin to targeted substrates. Inhibits TGF-beta signaling by triggering SMAD2 and TGFR1 ubiquitination and proteasome-dependent degradation. Promotes ubiquitination and internalization of various plasma membrane channels such as ENaC, Nav1.2, Nav1.3, Nav1.5, Nav1.7, Nav1.8, Kv1.3, EAAT1 or CLC5. Promotes ubiquitination and degradation of SGK. Interacts with NDFIP2 and UBE2E3.Interacts via its WW domains with SCNN1A, SCNN1B, SCNN1G, SCN1A, SCN2A, SCN3A, SCN5A, SCN8A, SCN9A, SCN10A and CLCN5.Interacts with SMAD2, SMAD3, SMAD6 and SMAD7. The phosphorylated form interacts with 14-3-3 proteins.Interacts with Epstein-Barr virus LMP2A.Interacts with NDFIP1 in vitro. 8 isoforms of the human protein are produced by alternative splicing.
References to 14-3-3 binding to Nedd4.2
Liang X, Butterworth MB, Peters KW, Walker WH, Frizzell RA. An obligatory heterodimer of 14-3-3beta and 14-3-3epsilon is required for aldosterone regulation of the epithelial sodium channel.J Biol Chem. 2008 Oct	

10;283(41):27418-25

Lee IH, Campbell CR, Cook DI, Dinudom A. Regulation of epithelial Na+ channels by aldosterone: role of Sgk1. Clin Exp Pharmacol Physiol. 2008 Feb;35(2):235-41.

Nagaki K, Yamamura H, Shimada S, Saito T, Hisanaga S, Taoka M, Isobe T, Ichimura T. 14-3-3 Mediates phosphorylation-dependent inhibition of the interaction between the ubiquitin E3 ligase Nedd4-2 and epithelial Na+ channels. Biochemistry. 2006 May 30;45(21):6733-40.

Bhalla V, Daidié D, Li H, Pao AC, LaGrange LP, Wang J, Vandewalle A, Stockand JD, Staub O, Pearce D. Serum- and glucocorticoid-regulated kinase 1 regulates ubiquitin ligase neural precursor cell-expressed, developmentally down-regulated protein 4-2 by inducing interaction with 14-3-3. Mol Endocrinol. 2005 Dec;19(12):3073-84

Liang X, Peters KW, Butterworth MB, Frizzell RA. 14-3-3 isoforms are induced by aldosterone and participate in its regulation of epithelial sodium channels. J Biol Chem. 2006 Jun 16;281(24):16323-32.

Ichimura T, Yamamura H, Sasamoto K, Tominaga Y, Taoka M, Kakiuchi K, Shinkawa T, Takahashi N, Shimada S, Isobe T. 14-3-3 proteins modulate the expression of epithelial Na+ channels by phosphorylation-dependent interaction with Nedd4-2 ubiquitin ligase. J Biol Chem. 2005 Apr 1;280(13):13187-94

Human NFATC4 (NFAT3) Nuclear factor of activated T-cells (Swissprot = Q14934)

```
      1 MGAASCEDEE LEFKLVFGEE KEAPPLGAGG LGEELDSEDA PPCCRLALGE PPPYGAAPIG
     61 IPRPPPPRPG MHSPPPRPAP SPGTWESQPA RSVRLGGPGG GAGGAGGGRV LECPSIRITS
    121 ISPTPEPPAA LEDNPDAWGD GSPRDYPPPE GFGGYREAGG QGGGAFFSPS PGSSSLSSWS
    181 FFSDASDEAA LYAACDEVES ELNEAASRFG LGSPLPSPRA SPRPWTPEDP WSLYGPSPGG
    241 RGPEDSWLLL SAPGPTPASP RPASPCGKRR YsSSGTPSSA SPALSRRGsL GEEGSEPPPP
    301 PPLPLARDPG SPGPFDYVGA PPAESIPQKT RRTSSEQAVA LPRSEEPASC NGKLPLGAEE
    361 SVAPPGGSRK EVAGMDYLAV PSPLAWSKAR IGGHSPIFRT SALPPLDWPL PSQYEQLELR
    421 IEVQPRAHHR AHYETEGSRG AVKAAPGGHP VVKLLGYSEK PLTLQMFIGT ADERNLRPHA
    481 FYQVHRITGK MVATASYEAV VSGTKVLEMT LLPENNMAAN IDCAGILKLR NSDIELRKGE
    541 TDIGRKNTRV RLVFRVHVPQ GGGKVVSVQA ASVPIECSQR SAQELPQVEA YSPSACSVRG
    601 GEELVLTGSN FLPDSKVVFI ERGPDGKLQW EEEATVNRLQ SNEVTLTLTV PEYSNKRVSR
    661 PVQVYFYVSN GRRKRSPTQS FRFLPVICKE EPLPDSSLRG FPSASATPFG TDMDFSPPRP
    721 PYPSYPHEDP ACETPYLSEG FGYGMPPLYP QTGPPPSYRP GLRMFPETRG TTGCAQPPAV
    781 SFLPRPFPSD PYGGRGSSFS LGLPFSPPAP FRPPPLPASP PLEGPFPSQS DVHPLPAEGY
    841 NKVGPGYGPG EGAPEQEKSR GGYSSGFRDS VPIQGITLEE VSEIIGRDLS GFPAPPGEEP
    901 PA
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>gi|215274090|sp|Q14934.2|NFAC4_HUMAN RecName: Full=Nuclear factor of
activated T-cells, cytoplasmic 4; Short=NF-ATc4; Short=NFATc4; AltName:
Full=T-cell transcription factor NFAT3; Short=NF-AT3
MGAASCEDEELEFKLVFGEEKEAPPLGAGGLGEELDSEDAPPCCRLALGEPPPYGAAPIGIPRPPPPRPG
MHSPPPRPAPSPGTWESQPARSVRLGGPGGGAGGAGGGRVLECPSIRITSISPTPEPPAALEDNPDAWGD
GSPRDYPPPEGFGGYREAGGQGGGAFFSPSPGSSSLSSWSFFSDASDEAALYAACDEVESELNEAASRFG
LGSPLPSPRASPRPWTPEDPWSLYGPSPGGRGPEDSWLLLSAPGPTPASPRPASPCGKRRYSSSGTPSSA
SPALSRRGSLGEEGSEPPPPPPLPLARDPGSPGPFDYVGAPPAESIPQKTRRTSSEQAVALPRSEEPASC
NGKLPLGAEESVAPPGGSRKEVAGMDYLAVPSPLAWSKARIGGHSPIFRTSALPPLDWPLPSQYEQLELR
IEVQPRAHHRAHYETEGSRGAVKAAPGGHPVVKLLGYSEKPLTLQMFIGTADERNLRPHAFYQVHRITGK
MVATASYEAVVSGTKVLEMTLLPENNMAANIDCAGILKLRNSDIELRKGETDIGRKNTRVRLVFRVHVPQ
GGGKVVSVQAASVPIECSQRSAQELPQVEAYSPSACSVRGGEELVLTGSNFLPDSKVVFIERGPDGKLQW
EEEATVNRLQSNEVTLTLTVPEYSNKRVSRPVQVYFYVSNGRRKRSPTQSFRFLPVICKEEPLPDSSLRG
FPSASATPFGTDMDFSPPRPPYPSYPHEDPACETPYLSEGFGYGMPPLYPQTGPPPSYRPGLRMFPETRG
TTGCAQPPAVSFLPRPFPSDPYGGRGSSFSLGLPFSPPAPFRPPPLPASPPLEGPFPSQSDVHPLPAEGY
NKVGPGYGPGEGAPEQEKSRGGYSSGFRDSVPIQGITLEEVSEIIGRDLSGFPAPPGEEPPA
```

Notes

SPRPASPCGKRRYpS^{272}SSGTPSSASPALS RRGpS^{289}LGEEGSEPPPPPPL

Ser272 and Ser289 are conserved in other members of the NFAT family

References to 14-3-3 binding to NFATC4 (NFAT3)

Chow CW, Davis RJ. Integration of calcium and cyclic AMP signaling pathways by 14-3-3. Mol Cell Biol. 2000 Jan;20(2):702-12.

Human NOXA1 activator of NOX1, a superoxide- producing NADPH oxidase (Swissprot = Q86UR1)

```
      1 MASLGDLVRA WHLGAQAVDR GDWARALHLF SGVPAPPARL CFNAGCVHLL AGDPEAALRA
     61 FDQAVTKDTC MAVGFFQRGV ANFQLARFQE ALSDFWLALE QLRGHAAIDY TQLGLRFKLQ
    121 AWEVLHNVAS AQCQLGLWTE AASSLREAMS KWPEGSLNGL DSALDQVQRR GsLPPRQVPR
    181 GEVFRPHRWH LKHLEPVDFL GKAKVVASAI PDDQGWGVRP QQPQGPGANH DARSLIMDSP
    241 RAGTHQGPLD AETEVGADRC TSTAYQEQRP QVEQVGKQAP LSPGLPAMGG PGPGPCEDPA
    301 GAGGAGAGGS EPLVTVTVQC AFTVALRARR GADLSSLRAL LGQALPHQAQ LGQLSYLAPG
    361 EDGHWVPIPE EESLQRAWQD AAACPRGLQL QCRGAGGRPV LYQVVAQHSY SAQGPEDLGF
    421 RQGDTVDVLC EVDQAWLEGH RDGRIGIFPK CFVVPAGPRM sGAPGRLPRS QQGDQP
```

```
>gi|74759404|sp|Q86UR1.1|NOXA1_HUMAN RecName: Full=NADPH oxidase activator 1;
Short=NOX activator 1; AltName: Full=P67phox-like factor; AltName: Full=p51-
nox; AltName: Full=NCF2-like protein; AltName: Full=Antigen NY-CO-31
MASLGDLVRAWHLGAQAVDRGDWARALHLFSGVPAPPARLCFNAGCVHLLAGDPEAALRAFDQAVTKDTC
MAVGFFQRGVANFQLARFQEALSDFWLALEQLRGHAAIDYTQLGLRFKLQAWEVLHNVASAQCQLGLWTE
AASSLREAMSKWPEGSLNGLDSALDQVQRRGSLPPRQVPRGEVFRPHRWHLKHLEPVDFLGKAKVVASAI
PDDQGWGVRPQQPQGPGANHDARSLIMDSPRAGTHQGPLDAETEVGADRCTSTAYQEQRPQVEQVGKQAP
LSPGLPAMGGPGPGPCEDPAGAGGAGAGGSEPLVTVTVQCAFTVALRARRGADLSSLRALLGQALPHQAQ
LGQLSYLAPGEDGHWVPIPEEESLQRAWQDAAACPRGLQLQCRGAGGRPVLYQVVAQHSYSAQGPEDLGF
RQGDTVDVLCEVDQAWLEGHCDGRIGIFPKCFVVPAGPRMSGAPGRLPRSQQGDQP
```

Notes

NOXA1 is as an activator of NOX1, a superoxide- producing NADPH oxidase in the production of reactive oxygen species (ROS) which participate in a variety of biological processes including host defense, hormone biosynthesis, oxygen sensing and signal transduction. May also activate CYBB/gp91phox and NOX3. NOX1, NOXA1, NOXO1, RAC1 and CYBA forms a functional multimeric complex supporting ROS production. Interaction with 14-3-3 prevents the interaction of NOXA1 with NOXO1 and RAC1 and its targeting to membranes, hence reducing its ability to activate NOX1. Belongs to the NCF2/NOXA1 family. Three isoforms of the human protein are produced by alternative splicing. Ser(172) and Ser(461) of NoxA1 as phosphorylation sites for protein kinase A (PKA). A consequence of this phosphorylation was the enhancement of NoxA1 complex formation with 14-3-3 proteins. 14-3-3 binding induce the dissociation of NoxA1 from the Nox1 complex at the plasma membrane, suggesting a mechanism for the inhibitory effect on Nox1 activity. GST-NoxA1 deletion mutants were amplified by PCR using pGEX4T3-NoxA1 as a template, and the following oligonucleotides as primers: The sequence (AAI10841) and phosphorylated 14-3-3-binding sites were confirmed in an email from the authors.

References to 14-3-3 binding to human NOXA1

Kim JS, Diebold BA, Babior BM, Knaus UG, Bokoch GM. Regulation of Nox1 activity via protein kinase A-mediated phosphorylation of NoxA1 and 14-3-3 binding. J Biol Chem. 2007 Nov 30;282(48):34787-800

Human NRIP1 (RIP140) Receptor interacting protein of 140 kDa (Swissprot = P48552)

```
       1 MTHGEELGSD VHQDSIVLTY LEGLLMHQAA GGSGTAVDKK SAGHNEEDQN FNISGSAFPT
      61 CQSNGPVLNT HTYQGSGMLH LKKARLLQSS EDWNAAKRKR LsDSIMNLNV KKEALLAGMV
     121 DSVPKGKQDS TLLASLLQSF SSRLQTVALS QQIRQSLKEQ GYALSHDSLK VEKDLRCYGV
     181 ASSHLKTLLK KSKVKDQKPD TNLPDVTKNL IRDRFAESPH HVGQSGTKVM SEPLSCAARL
     241 QAVASMVEKR ASPATSPKPS VACSQLALLL SSEAHLQQYS REHALKTQNA NQAASERLAA
     301 MARLQENGQK DVGSYQLPKG MSSHLNGQAR TSSSKLMASK SSATVFQNPM GIIPSSPKNA
     361 GYKNSLERNN IKQAANNSLL LHLLKSQTIP KPMNGHSHSE RGSIFEESST PTTIDEYSDN
     421 NPSFTDDSSG DESSYSNCVP IDLSCKHRTE KSESDQPVSL DNFTQSLLNT WDPKVPDVDI
     481 KEDQDTSKNS KLNSHQKVTL LQLLLGHKNE ENVEKNTSPQ GVHNDVSKFN TQNYARTSVI
     541 ESPSTNRTTP VSTPPLLTSS KAGSPINLSQ HSLVIKWNSP PYVCSTQSEK LTNTASNHSM
     601 DLTKSKDPPG EKPAQNEGAQ NSATFSASKL LQNLAQCGMQ SSMSVEEQRP SKQLLTGNTD
     661 KPIGMIDRLN SPLLSNKTNA VEENKAFSSQ PTGPEPGLSG SEIENLLERR TVLQLLLGNP
     721 NKGKSEKKEK TPLRDESTQE HSERALSEQI LMVKIKSEPC DDLQIPNTNV HLSHDAKSAP
     781 FLGMAPAVQR SAPALPVSED FKSEPVSPQD FSFSKNGLLS RLLRQNQDSY LADDSDRSHR
     841 NNEMALLESK NLCMVPKKRK LYTEPLENPF KKMKNNIVDA ANNHSAPEVL YGSLLNQEEL
     901 KFSRNDLEFK YPAGHGSASE SEHRSWARES KSFNVLKQLL LSENCVRDLS PHRSNSVADS
     961 KKKGHKNNVT NSKPEFSISS LNGLMYSSTQ PSSCMDNRTF sYPGVVKTPV SPTFPEHLGC
    1021 AGSRPESGLL NGCSMPSEKG PIKWVITDAE KNEYEKDSPR LTKTNPILYY MLQKGGNSVT
    1081 SRETQDKDIW REASSAESVS QVTAKEELLP TAETKASFFN LRSPYNSHMG NNASRPHSAN
    1141 GEVYGLLGSV LTIKKESE
```

```
>gi|9988061|sp|P48552.2|NRIP1_HUMAN RecName: Full=Nuclear receptor-
interacting protein 1; AltName: Full=Nuclear factor RIP140; AltName:
Full=Receptor-interacting protein 140
MTHGEELGSDVHQDSIVLTYLEGLLMHQAAGGSGTAVDKKSAGHNEEDQNFNISGSAFPTCQSNGPVLNT
HTYQGSGMLHLKKARLLQSSEDWNAAKRKRLSDSIMNLNVKKEALLAGMVDSVPKGKQDSTLLASLLQSF
SSRLQTVALSQQIRQSLKEQGYALSHDSLKVEKDLRCYGVASSHLKTLLKKSKVKDQKPDTNLPDVTKNL
IRDRFAESPHHVGQSGTKVMSEPLSCAARLQAVASMVEKRASPATSPKPSVACSQLALLLSSEAHLQQYS
REHALKTQNANQAASERLAAMARLQENGQKDVGSYQLPKGMSSHLNGQARTSSSKLMASKSSATVFQNPM
GIIPSSPKNAGYKNSLERNNIKQAANNSLLLHLLKSQTIPKPMNGHSHSERGSIFEESSTPTTIDEYSDN
NPSFTDDSSGDESSYSNCVPIDLSCKHRTEKSESDQPVSLDNFTQSLLNTWDPKVPDVDIKEDQDTSKNS
KLNSHQKVTLLQLLLGHKNEENVEKNTSPQGVHNDVSKFNTQNYARTSVIESPSTNRTTPVSTPPLLTSS
KAGSPINLSQHSLVIKWNSPPYVCSTQSEKLTNTASNHSMDLTKSKDPPGEKPAQNEGAQNSATFSASKL
LQNLAQCGMQSSMSVEEQRPSKQLLTGNTDKPIGMIDRLNSPLLSNKTNAVEENKAFSSQPTGPEPGLSG
SEIENLLERRTVLQLLLGNPNKGKSEKKEKTPLRDESTQEHSERALSEQILMVKIKSEPCDDLQIPNTNV
HLSHDAKSAPFLGMAPAVQRSAPALPVSEDFKSEPVSPQDFSFSKNGLLSRLLRQNQDSYLADDSDRSHR
NNEMALLESKNLCMVPKKRKLYTEPLENPFKKMKNNIVDAANNHSAPEVLYGSLLNQEELKFSRNDLEFK
YPAGHGSASESEHRSWARESKSFNVLKQLLLSENCVRDLSPHRSNSVADSKKKGHKNNVTNSKPEFSISS
LNGLMYSSTQPSSCMDNRTFSYPGVVKTPVSPTFPEHLGCAGSRPESGLLNGCSMPSEKGPIKWVITDAE
KNEYEKDSPRLTKTNPILYYMLQKGGNSVTSRETQDKDIWREASSAESVSQVTAKEELLPTAETKASFFN
LRSPYNSHMGNNASRPHSANGEVYGLLGSVLTIKKESE
```

Notes

KRKRL(p**S102)**DSIVN pSer102 PKC, 14-3-3 (species?) and DHRTF(p**S1003)**YPGMV pSer1003 PKC, 14-3-3 (species?) Ser1003 = Ser1001 in P48552.

RIP140 modulates transcriptional activation by steroid receptors such as NR3C1, NR3C2 and ESR1. Also modulates transcriptional repression by nuclear hormone receptors. Interacts with the ligand binding domain (LBD) of NR2C1 in the absence of ligand. Interacts with RARA and RXRB homodimers and RARA/RXRB heterodimers in the presence of ligand. Interacts with HDAC1 and HDAC3 via its N-terminal domain. Found in a complex with both NR3C1 and YWHAH.

References to 14-3-3-binding to NRIP1 (RIP140)

Gupta P, Ho PC, Huq MD, Khan AA, Tsai NP, Wei LN. PKCepsilon stimulated arginine methylation of RIP140 for its nuclear-cytoplasmic export in adipocyte differentiation. PLoS ONE. 2008 Jul 16;3(7):e2658.

Zilliacus J, Holter E, Wakui H, Tazawa H, Treuter E, Gustafsson JA. Regulation of glucocorticoid receptor activity by 14-3-3-dependent intracellular relocalization of the corepressor RIP140. Mol Endocrinol. 2001 Apr;15(4):501-11.

Human PACS2 phosphofurin acidic cluster sorting protein 2 (Swissprot = Q86VP3)

```
       1 MAERGRLGLP GAPGALNTPV PMNLFATWEV DGSSPSCVPR LCSLTLKKLV VFKELEKELI
      61 SVVIAVKMQG SKRILRSHEI VLPPSGQVET DLALTFSLQY PHFLKREGNK LQIMLQRRKR
     121 YKNRTILGYK TLAAGSISMA EVMQHPSEGG QVLSLCSSIK EAPVKAAEIW IASLSSQPID
     181 HEDSTMQAGP KAKSTDNYSE EEYESFSSEQ EASDDAVQGQ DLDEDDFDVG KPKKQRRSIV
     241 RTTSMTRQQN FKQKVVALLR RFKVSDEVLD SEQDPAEHIP EAEEDLDLLY DTLDMEHPSD
     301 SGPDMEDDDS VLSTPKPKLR PYFEGLSHSS SQTEIGSIHS ARSHKEPPSP ADVPEKTRSL
     361 GGRQPSDSVS DTVALGVPGP REHPGQPEDS PEAEASTLDV FTERLPPSGR ITKTESLVIP
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421 STRSEGKQAG RRGRSTsLKE RQAARPQNER ANSLDNERCP DARSQLQIPR KTVYDQLNHI 481 LISDDQLPEN IILVNTSDWQ GQFLSDVLQR HTLPVVCTCS PADVQAAFST IVSRIQRYCN 541 CNSQPPTPVK IAVAGAQHYL SAILRLFVEQ LSHKTPDWLG YMRFLVIPLG SHPVARYLGS 601 VDYRYNNFFQ DLAWRDLFNK LEAQSAVQDT PDIVSRITQY IAGANCAHQL PIAEAMLTYK 661 QKSPDEESSQ KFIPFVGVVK VGIVEPSSAT SGDSDDAAPS GSGTLSSTPP SASPAAKEAS 721 PTPPSSPSVS GGLSSPSQGV GAELMGLQVD YWTAAQPADR KRDAEKKDLP VTKNTLKCTF 781 RSLQVSRLPS SGEAAATPTM SMTVVTKEKN KKVMFLPKKA KDKDVESKSQ CIEGISRLIC 841 TARQQQNMLR VLIDGVECSD VKFFQLAAQW SSHVKHFPIC IFGHSKATF >gi|117949768|sp|Q86VP3.3|PACS2_HUMAN RecName: Full=Phosphofurin acidic cluster sorting protein 2; Short=PACS-2; AltName: Full=PACS1-like protein MAERGRLGLPGAPGALNTPVPMNLFATWEVDGSSPSCVPRLCSLTLKKLVVFKELEKELISVVIAVKMQG SKRILRSHEIVLPPSGQVETDLALTFSLQYPHFLKREGNKLQIMLQRRKRYKNRTILGYKTLAAGSISMA EVMQHPSEGGQVLSLCSSIKEAPVKAAEIWIASLSSQPIDHEDSTMQAGPKAKSTDNYSEEEYESFSSEQ EASDDAVQGQDLDEDDFDVGKPKKQRRSIVRTTSMTRQQNFKQKVVALLRRFKVSDEVLDSEQDPAEHIP EAEEDLDLLYDTLDMEHPSDSGPDMEDDDSVLSTPKPKLRPYFEGLSHSSSQTEIGSIHSARSHKEPPSP ADVPEKTRSLGGRQPSDSVSDTVALGVPGPREHPGQPEDSPEAEASTLDVFTERLPPSGRITKTESLVIP STRSEGKQAGRRGRSTSLKERQAARPQNERANSLDNERCPDARSQLQIPRKTVYDQLNHILISDDQLPEN IILVNTSDWQGQFLSDVLQRHTLPVVCTCSPADVQAAFSTIVSRIQRYCNCNSQPPTPVKIAVAGAQHYL SAILRLFVEQLSHKTPDWLGYMRFLVIPLGSHPVARYLGSVDYRYNNFFQDLAWRDLFNKLEAQSAVQDT PDIVSRITQYIAGANCAHQLPIAEAMLTYKQKSPDEESSQKFIPFVGVVKVGIVEPSSATSGDSDDAAPS GSGTLSSTPPSASPAAKEASPTPPSSPSVSGGLSSPSQGVGAELMGLQVDYWTAAQPADRKRDAEKKDLP VTKNTLKCTFRSLQVSRLPSSGEAAATPTMSMTVVTKEKNKKVMFLPKKAKDKDVESKSQCIEGISRLIC TARQQQNMLRVLIDGVECSDVKFFQLAAQWSSHVKHFPICIFGHSKATF **Notes** "PKB/Akt-phosphorylated Ser437 binds 14-3-3 with high affinity" **References to 14-3-3 binding to PACS2** Aslan JE, You H, Williamson DM, Endig J, Youker RT, Thomas L, Shu H, Du Y, Milewski RL, Brush MH, Possemato A, Sprott K, Fu H, Greis KD, Runckel DN, Vogel A, Thomas G. Akt and 14-3-3 control a PACS-2 homeostatic switch that integrates membrane traffic with TRAIL-induced apoptosis. Mol Cell. 2009 May 14;34(4):497-509.	
Human PCTK1 PCTAIRE protein kinase 1 [Homo sapiens] (Swissprot = Q00536) 1 MDRMKKIKRQ LSMTLRGGRG IDKTNGAPEQ IGLDESGGGG GSDPGEAPTR AAPGELRSAR 61 GPLSSAPEIV HEDLKMGSDG ESDQASATSS DEVQSPVRVR MRNHPPRKIS TEDINKRLsL 121 PADIRLPEGY LEKLTLNSPI FDKPLSRRLR RVSLSEIGFG KLETYIKLDK LGEGTYATVY 181 KGKSKLTDNL VALKEIRLEH EEGAPCTAIR EVSLLKDLKH ANIVTLHDII HTEKSLTLVF 241 EYLDKDLKQY LDDCGNIINM HNVKLFLFQL LRGLAYCHRQ KVLHRDLKPQ NLLINERGEL 301 KLADFGLARA KSIPTKTYSN EVVTLWYRPP DILLGSTDYS TQIDMWGVGC IFYEMATGRP 361 LFPGSTVEEQ LHFIFRILGT PTEETWPGIL SNEEFKTYNY PKYRAEALLS HAPRLDSDGA 421 DLLTKLLQFE GRNRISAEDA MKHPFFLSLG ERIHKLPDTT SIFALKEIQL QKEASLRSSS 481 MPDSGRPAFR VVDTEF >gi|266425|sp|Q00536.1|PCTK1_HUMAN RecName: Full=Serine/threonine-protein kinase PCTAIRE-1; AltName: Full=PCTAIRE-motif protein kinase 1 MDRMKKIKRQLSMTLRGGRGIDKTNGAPEQIGLDESGGGGGSDPGEAPTRAAPGELRSARGPLSSAPEIV HEDLKMGSDGESDQASATSSDEVQSPVRVRMRNHPPRKISTEDINKRLSLPADIRLPEGYLEKLTLNSPI FDKPLSRRLRRVSLSEIGFGKLETYIKLDKLGEGTYATVYKGKSKLTDNLVALKEIRLEHEEGAPCTAIR EVSLLKDLKHANIVTLHDIIHTEKSLTLVFEYLDKDLKQYLDDCGNIINMHNVKLFLFQLLRGLAYCHRQ KVLHRDLKPQNLLINERGELKLADFGLARAKSIPTKTYSNEVVTLWYRPPDILLGSTDYSTQIDMWGVGC IFYEMATGRPLFPGSTVEEQLHFIFRILGTPTEETWPGILSNEEFKTYNYPKYRAEALLSHAPRLDSDGA DLLTKLLQFEGRNRISAEDAMKHPFFLSLGERIHKLPDTTSIFALKEIQLQKEASLRSSSMPDSGRPAFR VVDTEF **Notes** 14-3-3s bind to phosphoSer119 (NKRL(pS$^{119)}$LP) , one of the PKA sites on this protein. **References to 14-3-3 binding to PCTAIRE-1** Graeser R, Gannon J, Poon RY, Dubois T, Aitken A, Hunt T. Regulation of the CDK-related protein kinase PCTAIRE-1 and its possible role in neurite outgrowth in Neuro-2A cells. J Cell Sci. 2002 Sep 1;115(Pt 17):3479-90. Le Bouffant F, Capdevielle J, Guillemot JC, Sladeczek F. Characterization of brain PCTAIRE-1 kinase immunoreactivity and its interactions with p11 and 14-3-3 proteins. Eur J Biochem. 1998 Oct 1;257(1):112-20. Sladeczek F, Camonis JH, Burnol AF, Le Bouffant F. The Cdk-like protein PCTAIRE-1 from mouse brain associates with p11 and 14-3-3 proteins. Mol Gen Genet. 1997 May 20;254(5):571-7.	
Human PDC Phosducin (Swissprot = P20941) 1 MEEAKSQSLE EDFEGQATHT GPKGVINDWR KFKLESQDSD SIPPSKKEIL RQMsSPQSRN 61 GKDSKERVSR KMsIQEYELI HKEKEDENCL RKYRRQCMQD MHQKLSFGPR YGFVYELETG 121 KQFLETIEKE LKITTIVVHI YEDGIKGCDA LNSSLTCLAA EYPIVKFCKI KASNTGAGDR 181 FSLDVLPTLL IYKGGELISN FISVAEQFAE EFFAGDVESF LNEYGLLPER EVHVLEHTKI 241 EEEDVE >gi|130134|sp|P20941.1|PHOS_HUMAN RecName: Full=Phosducin; Short=PHD; AltName: Full=33 kDa phototransducing protein; AltName: Full=MEKA protein MEEAKSQSLEEDFEGQATHTGPKGVINDWRKFKLESQDSDSIPPSKKEILRQMSSPQSRNGKDSKERVSR KMSIQEYELIHKEKEDENCLRKYRRQCMQDMHQKLSFGPRYGFVYELETGKQFLETIEKELKITTIVVHI YEDGIKGCDALNSSLTCLAAEYPIVKFCKIKASNTGAGDRFSLDVLPTLLIYKGGELISNFISVAEQFAE EFFAGDVESFLNEYGLLPEREVHVLEHTKIEEEDVE **Notes** Phosducin may participate in the regulation of visual phototransduction or in the integration of photoreceptor metabolism. phospho-Pd is found to interact with 14-3-3 in material from dark-adapted retina, and this interaction is markedly	

diminished by light, which dephosphorylates Pd. Pd phosphorylation by Ca(2+)/calmodulin-dependent kinase II at Ser-54 and Ser-73 led to binding of the phosphoserine-binding protein 14-3-3 (Thulin et al 2001).

References to 14-3-3 binding to phosducin

Nakano K, Chen J, Tarr GE, Yoshida T, Flynn JM, Bitensky MW.Rethinking the role of phosducin: light-regulated binding of phosducin to 14-3-3 in rod inner segments. Proc Natl Acad Sci U S A. 2001 Apr 10;98(8):4693-8. Epub 2001 Apr 3

Thulin CD, Savage JR, McLaughlin JN, Truscott SM, Old WM, Ahn NG, Resing KA, Hamm HE, Bitensky MW, Willardson BM.Modulation of the G protein regulator phosducin by Ca2+/calmodulin-dependent protein kinase II phosphorylation and 14-3-3 protein binding. J Biol Chem. 2001 Jun 29;276(26):23805-15.

Human PDE3A Phosphodiesterase 3A (Swissprot = Q14432)

```
        1 MAVPGDAARV RDKPVHSGVS QAPTAGRDCH HRADPASPRD SGCRGCWGDL VLQPLRSSRK
       61 LSSALCAGSL SFLLALLVRL VRGEVGCDLE QCKEAAAAEE EEAAPGAEGG VFPGPRGGAP
      121 GGGARLSPWL QPSALLFSLL CAFFWMGLYL LRAGVRLPLA VALLAACCGG EALVQIGLGV
      181 GEDHLLSLPA AGVVLSCLAA ATWLVLRLRL GVLMIALTSA VRTVSLISLE RFKVAWRPYL
      241 AYLAGVLGIL LARYVEQILP QSAEAAPREH LGSQLIAGTK EDIPVFKRRR RSSSVVSAEM
      301 SGCSSKSHRR TSLPCIPREQ LMGHSEWDHK RGPRGSQSSG TSITVDIAVM GEAHGLITDL
      361 LADPSLPPNV CTSLRAVSNL LSTQLTFQAI HKPRVNPVTS LSENYTCSDS EESSEKDKLA
      421 IPKRLRRsLP PGLLRRVSST WTTTTSATGL PTLEPAPVRR DRSTSIKLQE APSSSPDSWN
      481 NPVMMTLTKS RSFTSSYAIS AANHVKAKKQ SRPGALAKIS PLSSPCSSPL QGTPASSLVS
      541 KISAVQFPES ADTTAKQSLG SHRALTYTQS APDLSPQILT PPVICSSCGR PYSQGNPADE
      601 PLERSGVATR TPSRTDDTAQ VTSDYETNNN SDSSDIVQNE DETECLREPL RKASACSTYA
      661 PETMMFLDKP ILAPEPLVMD NLDSIMEQLN TWNFPIFDLV ENIGRKCGRI LSQVSYRLFE
      721 DMGLFEAFKI PIREFMNYFH ALEIGYRDIP YHNRIHATDV LHAVWYLTTQ PIPGLSTVIN
      781 DHGSTSDSDS DSGFTHGHMG YVFSKTYNVT DDKYGCLSGN IPALELMALY VAAAMHDYDH
      841 PGRTNAFLVA TSAPQAVLYN DRSVLENHHA AAAWNLFMSR PEYNFLINLD HVEFKHFRFL
      901 VIEAILATDL KKHFDFVAKF NGKVNDDVGI DWTNENDRLL VCQMCIKLAD INGPAKCKEL
      961 HLQWTDGIVN EFYEQGDEEA SLGLPISPFM DRSAPQLANL QESFISHIVG PLCNSYDSAG
     1021 LMPGKWVEDS DESGDTDDPE EEEEEAPAPN EEETCENNES PKKKTFKRRK IYCQITQHLL
     1081 QNHKMWKKVI EEEQRLAGIE NQSLDQTPQS HSSEQIQAIK EEEEEKGKPR GEEIPTQKPD
     1141 Q
>gi|47117888|sp|Q14432.3|PDE3A_HUMAN RecName: Full=cGMP-inhibited 3',5'-
cyclic phosphodiesterase A; AltName: Full=Cyclic GMP-inhibited
phosphodiesterase A; Short=CGI-PDE A
MAVPGDAARVRDKPVHSGVSQAPTAGRDCHHRADPASPRDSGCRGCWGDLVLQPLRSSRKLSSALCAGSL
SFLLALLVRLVRGEVGCDLEQCKEAAAAEEEEAAPGAEGGVFPGPRGGAPGGGARLSPWLQPSALLFSLL
CAFFWMGLYLLRAGVRLPLAVALLAACCGGEALVQIGLGVGEDHLLSLPAAGVVLSCLAAATWLVLRLRL
GVLMIALTSAVRTVSLISLERFKVAWRPYLAYLAGVLGILLARYVEQILPQSAEAAPREHLGSQLIAGTK
EDIPVFKRRRRSSSVVSAEMSGCSSKSHRRTSLPCIPREQLMGHSEWDHKRGPRGSQSSGTSITVDIAVM
GEAHGLITDLLADPSLPPNVCTSLRAVSNLLSTQLTFQAIHKPRVNPVTSLSENYTCSDSEESSEKDKLA
IPKRLRRSLPPGLLRRVSSTWTTTTSATGLPTLEPAPVRRDRSTSIKLQEAPSSSPDSWNNPVMMTLTKS
RSFTSSYAISAANHVKAKKQSRPGALAKISPLSSPCSSPLQGTPASSLVSKISAVQFPESADTTAKQSLG
SHRALTYTQSAPDLSPQILTPPVICSSCGRPYSQGNPADEPLERSGVATRTPSRTDDTAQVTSDYETNNN
SDSSDIVQNEDETECLREPLRKASACSTYAPETMMFLDKPILAPEPLVMDNLDSIMEQLNTWNFPIFDLV
ENIGRKCGRILSQVSYRLFEDMGLFEAFKIPIREFMNYFHALEIGYRDIPYHNRIHATDVLHAVWYLTTQ
PIPGLSTVINDHGSTSDSDSDSGFTHGHMGYVFSKTYNVTDDKYGCLSGNIPALELMALYVAAAMHDYDH
PGRTNAFLVATSAPQAVLYNDRSVLENHHAAAAWNLFMSRPEYNFLINLDHVEFKHFRFLVIEAILATDL
KKHFDFVAKFNGKVNDDVGIDWTNENDRLLVCQMCIKLADINGPAKCKELHLQWTDGIVNEFYEQGDEEA
SLGLPISPFMDRSAPQLANLQESFISHIVGPLCNSYDSAGLMPGKWVEDSDESGDTDDPEEEEEEAPAPN
EEETCENNESPKKKTFKRRKIYCQITQHLLQNHKMWKKVIEEEQRLAGIENQSLDQTPQSHSSEQIQAIK
EEEEEKGKPRGEEIPTQKPDQ
```

Notes

PDE3A hydrolyzes both cyclic AMP (cAMP) and is inhibited by cyclic GMP (cGMP).

Ser428 was selectively phosphorylated in response to PMA and dephosphorylated in cells treated with aphidicolin and mimosine. Phosphorylation of Ser428 therefore correlated with 14-3-3 binding to PDE3A (Pozuelo Rubio et al 2005).

Platelet activation also led to a PKC-dependent association between PDE3A and 14-3-3 proteins. In contrast, cAMP-elevating agents such as PGE(1) and forskolin-induced phosphorylation of Ser(312) and increased PDE3A activity, but did not stimulate 14-3-3 binding (Hunter et al 2009).

References to 14-3-3 binding to PRAS40

Pozuelo Rubio M, phosphodiesterase 3A binds to 14-3-3 proteins in response to PMA-induced phosphorylation of Ser428. Biochem J. 2005 Nov 15;392(Pt 1):163-72

Hunter RW, Protein kinase C-mediated phosphorylation and activation of PDE3A regulate cAMP levels in human platelets. J Biol Chem. 2009 May 1;284(18):12339-48. Epub 2009 Mar 4

Human PFKFB2 cardiac PFK-2 6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 2 (Swissprot = O60825)

```
1 MSGASSSEQN NNSYETKTPN LRMSEKKCSW ASYMTNSPTL IVMIGLPARG KTYVSKKLTR
       61 YLNWIGVPTK VFNLGVYRRE AVKSYKSYDF FRHDNEEAMK IRKQCALVAL EDVKAYLTEE
      121 NGQIAVFDAT NTTRERRDMI LNFAEQNSFK VFFVESVCDD PDVIAANILE VKVSSPDYPE
      181 RNRENVMEDF LKRIECYKVT YRPLDPDNYD KDLSFIKVIN VGQRFLVNRV QDYIQSKIVY
      241 YLMNIHVQPR TIYLCRHGES EFNLLGKIGG DSGLSVRGKQ FAQALRKFLE EQEITDLKVW
      301 TSQLKRTIQT AESLGVPYEQ WKILNEIDAG VCEEMTYAEI EKRYPEEFAL RDQEKYLYRY
      361 PGGESYQDLV QRLEPVIMEL ERQGNVLVIS HQAVMRCLLA YFLDKGADEL PYLRCPLHTI
      421 FKLTPVAYGC KVETIKLNVE AVNTHRDKPT NNFPKNQTPV RMRRNsFTPL SSSNTIRRPR
      481 NYsVGSRPLK PLSPLRAQDM QEGAD
>gi|12643333|sp|O60825.2|F262_HUMAN RecName: Full=6-phosphofructo-2-
kinase/fructose-2,6-biphosphatase 2; AltName: Full=PFK-2/FBPase-2; AltName:
Full=6PF-2-K/Fru-2,6-P2ASE heart-type isozyme; Includes: RecName: Full=6-
phosphofructo-2-kinase; Includes: RecName: Full=Fructose-2,6-bisphosphatase
```

<table>
<tr><td>MSGASSSEQNNNSYETKTPNLRMSEKKCSWASYMTNSPTLIVMIGLPARGKTYVSKKLTRYLNWIGVPTK
VFNLGVYRREAVKSYKSYDFFRHDNEEAMKIRKQCALVALEDVKAYLTEENGQIAVFDATNTTRERRDMI
LNFAEQNSFKVFFVESVCDDPDVIAANILEVKVSSPDYPERNRENVMEDFLKRIECYKVTYRPLDPDNYD
KDLSFIKVINVGQRFLVNRVQDYIQSKIVYYLMNIHVQPRTIYLCRHGESEFNLLGKIGGDSGLSVRGKQ
FAQALRKFLEEQEITDLKVWTSQLKRTIQTAESLGVPYEQWKILNEIDAGVCEEMTYAEIEKRYPEEFAL
RDQEKYLYRYPGGESYQDLVQRLEPVIMELERQGNVLVISHQAVMRCLLAYFLDKGADELPYLRCPLHTI
FKLTPVAYGCKVETIKLNVEAVNTHRDKPTNNFPKNQTPVRMRRNSFTPLSSSNTIRRPRNYSVGSRPLK
PLSPLRAQDMQEGAD
Notes
PKB-dependent binding of 14-3-3s to phospho-Ser483 of cardiac PFK-2 mediates the stimulation of glycolysis by growth factor.
References to 14-3-3 binding to cardiac PFK-2
Pozuelo Rubio M, Peggie M, Wong BH, Morrice N, MacKintosh C. 14-3-3s regulate fructose-2,6-bisphosphate levels by binding to PKB-phosphorylated cardiac fructose-2,6-bisphosphate kinase/phosphatase. EMBO J. 2003 Jul 15;22(14):3514-23.</td><td></td></tr>
<tr><td>**Human PHB** Prohibitin (Swissprot = P35232)
1 MAAKVFESIG KFGLALAVAG GVVNSALYNV DAGHRAVIFD RFRGVQDIVV GEGTHFLIPW
61 VQKPIIFDCR SRPRNVPVIT GSKDLQNVNI TLRILFRPVA SQLPRIFTSI GEDYDERVLP
121 SITTEILKSV VARFDAGELI TQRELVSRQV SDDLTERAAT FGLILDDVSL THLTFGKEFT
181 EAVEAKQVAQ QEAERARFVV EKAEQQKKAA IISAEGDSKA AELIANSLAT AGDGLIELRK
241 LEAAEDIAYQ LSRSRNITYL PAGQSVLLQL PQ
>gi|464371|sp|P35232.1|PHB_HUMAN RecName: Full=Prohibitin
MAAKVFESIGKFGLALAVAGGVVNSALYNVDAGHRAVIFDRFRGVQDIVVGEGTHFLIPWVQKPIIFDCR
SRPRNVPVITGSKDLQNVNITLRILFRPVASQLPRIFTSIGEDYDERVLPSITTEILKSVVARFDAGELI
TQRELVSRQVSDDLTERAATFGLILDDVSLTHLTFGKEFTEAVEAKQVAQQEAERARFVVEKAEQQKKAA
IISAEGDSKAAELIANSLATAGDGLIELRKLEAAEDIAYQLSRSRNITYLPAGQSVLLQLPQ
Notes
References to 14-3-3 binding to prohibitin
Zhu B, Zhai J, Zhu H, Kyprianou N. Prohibitin regulates TGF-beta induced apoptosis as a downstream effector of smad-dependent and -independent signaling. Prostate. 2009 Sep 1. [Epub ahead of print]</td><td>BINDING SITES
UNKNOWN
NOT IN WEBLOGO.</td></tr>
<tr><td>**Human PI4KB (PI4KIIIbeta)** phosphatidylinositol 4-kinase III beta (Swissprot = Q9UBF8)
1 MGDTVVEPAP LKPTSEPTSG PPGNNGGSLL SVITEGVGEL SVIDPEVAQK ACQEVLEKVK
61 LLHGGVAVSS RGTPLELVNG DGVDSEIRCL DDPPAQIREE EDEMGAAVAS GTAKGARRRR
121 QNNSAKQSWL LRLFESKLFD ISMAISYLYN SKEPGVQAYI GNRLFCFRNE DVDFYLPQLL
181 NMYIHMDEDV GDAIKPYIVH RCRQSINFSL QCALLLGAYS SDMHISTQRH SRGTKLRKLI
241 LSDELKPAHR KRELPSLSPA PDTGLSPSKR THQRSKSDAT ASISLSSNLK RTAsNPKVEN
301 EDEELSSSTE SIDNSFSSPV RLAPEREFIK SLMAIGKRLA TLPTKEQKTQ RLISELSLLN
361 HKLPARVWLP TAGFDHHVVR VPHTQAVVLN SKDKAPYLIY VEVLECENFD TTSVPARIPE
421 NRIRSTRSVE NLPECGITHE QRAGSFSTVP NYDNDDEAWS VDDIGELQVE LPEVHTNSCD
481 NISQFSVDSI TSQESKEPVF IAAGDIRRRL SEQLAHTPTA FKRDPEDPSA VALKEPWQEK
541 VRRIREGSPY GHLPNWRLLS VIVKCGDDLR QELLAFQVLK QLQSIWEQER VPLWIKPYKI
601 LVISADSGMI EPVVNAVSIH QVKKQSQLSL LDYFLQEHGS YTTEAFLSAQ RNFVQSCAGY
661 CLVCYLLQVK DRHNGNILLD AEGHIIHIDF GFILSSSPRN LGFETSAFKL TTEFVDVMGG
721 LDGDMFNYYK MLMLQGLIAA RKHMDKVVQI VEIMQQGSQL PCFHGSSTIR NLKERFHMSM
781 TEEQLQLLVE QMVDGSMRSI TTKLYDGFQY LTNGIM
>gi|38372507|sp|Q9UBF8.1|PI4KB_HUMAN RecName: Full=Phosphatidylinositol 4-kinase beta; Short=PtdIns 4-kinase beta; Short=PI4K-beta; Short=PI4Kbeta; AltName: Full=NPIK; AltName: Full=PI4K92
MGDTVVEPAPLKPTSEPTSGPPGNNGGSLLSVITEGVGELSVIDPEVAQKACQEVLEKVKLLHGGVAVSS
RGTPLELVNGDGVDSEIRCLDDPPAQIREEEDEMGAAVASGTAKGARRRRQNNSAKQSWLLRLFESKLFD
ISMAISYLYNSKEPGVQAYIGNRLFCFRNEDVDFYLPQLLNMYIHMDEDVGDAIKPYIVHRCRQSINFSL
QCALLLGAYSSDMHISTQRHSRGTKLRKLILSDELKPAHRKRELPSLSPAPDTGLSPSKRTHQRSKSDAT
ASISLSSNLKRTASNPKVENEDEELSSSTESIDNSFSSPVRLAPEREFIKSLMAIGKRLATLPTKEQKTQ
RLISELSLLNHKLPARVWLPTAGFDHHVVRVPHTQAVVLNSKDKAPYLIYVEVLECENFDTTSVPARIPE
NRIRSTRSVENLPECGITHEQRAGSFSTVPNYDNDDEAWSVDDIGELQVELPEVHTNSCDNISQFSVDSI
TSQESKEPVFIAAGDIRRRLSEQLAHTPTAFKRDPEDPSAVALKEPWQEKVRRIREGSPYGHLPNWRLLS
VIVKCGDDLRQELLAFQVLKQLQSIWEQERVPLWIKPYKILVISADSGMIEPVVNAVSIHQVKKQSQLSL
LDYFLQEHGSYTTEAFLSAQRNFVQSCAGYCLVCYLLQVKDRHNGNILLDAEGHIIHIDFGFILSSSPRN
LGFETSAFKLTTEFVDVMGGLDGDMFNYYKMLMLQGLIAARKHMDKVVQIVEIMQQGSQLPCFHGSSTIR
NLKERFHMSMTEEQLQLLVEQMVDGSMRSITTKLYDGFQYLTNGIM
Notes
Human PI4Kbeta 288 – LKRTA(pS)NP-297 (Ser294)
References to 14-3-3 binding to PI4KIIIbeta
Hausser A, Link G, Hoene M, Russo C, Selchow O, Pfizenmaier K. Phospho-specific binding of 14-3-3 proteins to phosphatidylinositol 4-kinase III beta protects from dephosphorylation and stabilizes lipid kinase activity. J Cell Sci. 2006 Sep 1;119(Pt 17):3613-21.</td><td></td></tr>
<tr><td>**Human PKP2** Plakophilin 2 (Swissprot = Q99959)
1 MAAPGAPAEY GYIRTVLGQQ ILGQLDSSSL ALPSEAKLKL AGSSGRGGQT VKSLRIQEQV
61 QQTLARKGRS SVGNGNLHRT SsVPEYVYNL HLVENDFVGG RSPVPKTYDM LKAGTTATYE
121 GRWGRGTAQY SSQKSVEERS LRHPLRRLEI SPDSSPERAH YTHSDYQYSQ RSQAGHTLHH
181 QESRRAALLV PPRYARSEIV GVSRAGTTSR QRHFDTYHRQ YQHGSVSDTV FDSIPANPAL
241 LTYPRPGTSR SMGNLLEKEN YLTAGLTVGQ VRPLVPLQPV TQNRASRSSW HQSSFHSTRT
301 LREAGPSVAV DSSGRRAHLT VGQAAAGGSG NLLTERSTFT DSQLGNADME MTLERAVSML
361 EADHMPPSRI SAAATFIQHE CFQKSEARKR VNQLRGILKL LQLLKVQNED VQRAVCGALR
421 NLVFEDNDNK LEVAELNGVP RLLQVLKQTR DLETKKQITD HTVNLRSRNG WPGAVAHACN
481 PSTLGGQGGR ITRSGVRDQP DQHGLLWNLS SNDKLKNLMI TEALLTLTEN IIIPFSGWPE</td><td></td></tr>
</table>

541 GDYPKANGLL DFDIFYNVTG CLRNMSSAGA DGRKAMRRCD GLIDSLVHYV RGTIADYQPD 601 DKATENCVCI LHNLSYQLEA ELPEKYSQNI YIQNRNIQTD NNKSIGCFGS RSRKVKEQYQ 661 DVPMPEEKSN PKGVEWLWHS IVIRMYLSLI AKSVRNYTQE ASLGALQNLT AGSGPMPTSV 721 AQTVVQKESG LQHTRKMLHV GDPSVKKTAI SLLRNLSRNL SLQNEIAKET LPDLVSIIPD 781 TVPSTDLLIE TTASACYTLN NIIQNSYQNA RDLLNTGGIQ KIMAISAGDA YASNKASKAA 841 SVLLYSLWAH TELHHAYKKA QFKKTDFVNS RTAKAYHSLK D >gi|20139105|sp|Q99959.1|PKP2_HUMAN RecName: Full=Plakophilin-2 MAAPGAPAEYGYIRTVLGQQILGQLDSSSLALPSEAKLKLAGSSGRGGQTVKSLRIQEQVQQTLARKGRS SVGNGNLHRTSSVPEYVYNLHLVENDFVGGRSPVPKTYDMLKAGTTATYEGRWGRGTAQYSSQKSVEERS LRHPLRRLEISPDSSPERAHYTHSDYQYSQRSQAGHTLHHQESRRAALLVPPRYARSEIVGVSRAGTTSR QRHFDTYHRQYQHGSVSDTVFDSIPANPALLTYPRPGTSRSMGNLLEKENYLTAGLTVGQVRPLVPLQPV TQNRASRSSWHQSSFHSTRTLREAGPSVAVDSSGRRAHLTVGQAAAGGSGNLLTERSTFTDSQLGNADME MTLERAVSMLEADHMPPSRISAAATFIQHECFQKSEARKRVNQLRGILKLLQLLKVQNEDVQRAVCGALR NLVFEDNDNKLEVAELNGVPRLLQVLKQTRDLETKKQITDHTVNLRSRNGWPGAVAHACNPSTLGGQGGR ITRSGVRDQPDQHGLLWNLSSNDKLKNLMITEALLTLTENIIIPFSGWPEGDYPKANGLLDFDIFYNVTG CLRNMSSAGADGRKAMRRCDGLIDSLVHYVRGTIADYQPDDKATENCVCILHNLSYQLEAELPEKYSQNI YIQNRNIQTDNNKSIGCFGSRSRKVKEQYQDVPMPEEKSNPKGVEWLWHSIVIRMYLSLIAKSVRNYTQE ASLGALQNLTAGSGPMPTSVAQTVVQKESGLQHTRKMLHVGDPSVKKTAISLLRNLSRNLSLQNEIAKET LPDLVSIIPDTVPSTDLLIETTASACYTLNNIIQNSYQNARDLLNTGGIQKIMAISAGDAYASNKASKAA SVLLYSLWAHTELHHAYKKAQFKKTDFVNSRTAKAYHSLKD **Notes** Belongs to the beta-catenin family and contains 8 armadillo repeats. May play a role in junctional plaques. Phosphorylation of PKP2 by C-TAK1 also generates a 14-3-3-binding site that influences PKP2 localization. These findings underscore the importance of C-TAK1 as a regulator of 14-3-3 binding and protein localization. this interaction could be disrupted by mutations that either destroy the S82 site (S82A) or severely reduce its phosphorylation (V87A), confirming that S82 is a functional 14-3-3-binding site. Defects in PKP2 are the cause of familial arrhythmogenic right ventricular dysplasia 9 (ARVD9) [MIM:609040]; also known as arrhythmogenic right ventricular cardiomyopathy 9 (ARVC9). **References to 14-3-3 binding to plakophilin 2** Müller J, Ritt DA, Copeland TD, Morrison DK. Functional analysis of C-TAK1 substrate binding and identification of PKP2 as a new C-TAK1 substrate. EMBO J. 2003 Sep 1;22(17):4431-42.	
Human PMCA1, 3 and 4 (Plasma membrane Ca2+-ATPases) **Notes** TKLKTSPNEGL in PMCA1 (J04027) RRLKTSPVEGL in PMCA2 (M97260) but this isoform did not bind to 14-3-3 RRLKTSPTEGL in PMCA3 (Q16720) SRLKTSPVEGL in PMCA4 (M25874) **References to 14-3-3 binding to PMCA1, PMCA3 and PMCA4** Linde CI, Di Leva F, Domi T, Tosatto SC, Brini M, Carafoli E. Inhibitory interaction of the 14-3-3 proteins with ubiquitous (PMCA1) and tissue-specific (PMCA3) isoforms of the plasma membrane Ca2+ pump. Cell Calcium. 2008 Jun;43(6):550-61. Rimessi A, Coletto L, Pinton P, Rizzuto R, Brini M, Carafoli E. Inhibitory interaction of the 14-3-3{epsilon} protein with isoform 4 of the plasma membrane Ca(2+)-ATPase pump. J Biol Chem. 2005 Nov 4;280(44):37195-203. Domi T, Di Leva F, Fedrizzi L, Rimessi A, Brini M. Functional specificity of PMCA isoforms? Ann N Y Acad Sci. 2007 Mar;1099:237-46.	NOT IN WEBLOGO.
Human PPP1R12A (Swissprot = O14974) 1 MKMADAKQKR NEQLKRWIGS ETDLEPPVVK RQKTKVKFDD GAVFLAACSS GDTDEVLKLL 61 HRGADINYAN VDGLTALHQA CIDDNVDMVK FLVENGANIN QPDNEGWIPL HAAASCGYLD 121 IAEFLIGQGA HVGAVNSEGD TPLDIAEEEA MEELLQNEVN RQGVDIEAAR KEEERIMLRD 181 ARQWLNSGHI NDVRHAKSGG TALHVAAAKG YTEVLKLLIQ AGYDVNIKDY DGWTPLHAAA 241 HWGKEEACRI LVDNLCDMEM VNKVGQTAFD VADEDILGYL EELQKKQNLL HSEKRDKKSP 301 LIESTANMDN NQSQKTFKNK ETLIIEPEKN ASRIESLEQE KVDEEEEGKK DESSCSSEED 361 EEDDSESEAE TDKTKPLASV TNANTSSTQA APVAVTTPTV SSGQATPTSP IKKFPTTATK 421 ISPKEEERKD ESPATWRLGL RKTGSYGALA EITASKEGQK EKDTAGVTRS AsSPRLSSSL 481 DNKEKEKDSK GTRLAYVAPT IPRRLASTSD IEEKENRDSS SLRTSSSYTR RKWEDDLKKN 541 SSVNEGSTYH KSCSFGRRQD DLISSSVPST TSTPTVTSAA GLQKSLLSST STTTKITTGS 601 SSAGTQSSTS NRLWAEDSTE KEKDSVPTAV TIPVAPTVVN AAASTTTLTT TTAGTVSSTT 661 EVRERRRSYL TPVRDEESES QRKARSRQAR QSRRSTQGVT LTDLQEAEKT IGRSRSTRTR 721 EQENEEKEKE EKEKQDKEKQ EEKKESETSR EDEYKQKYSR TYDETYQRYR PVSTSSSTTP 781 SSSLSTMSSS LYASSQLNRP NSLVGITSAY SRGITKENER EGEKREEEKE GEDKSQPKSI 841 RERRRPREKR RSTGVSFWTQ DSDENEQEQQ SDTEEGSNKK ETQTDSISRY ETSSTSAGDR 901 YDSLLGRSGS YSYLEERKPY SSRLEKDDST DFKKLYEQIL AENEKLKAQL HDTNMELTDL 961 KLQLEKATQR QERFADRSLL EMEKRERRAL ERRISEMEEE LKMLPDLKAD NQRLKDENGA 1021 LIRVISKLSK >gi|41017262|sp|O14974.1|MYPT1_HUMAN RecName: Full=Protein phosphatase 1 regulatory subunit 12A; AltName: Full=Myosin phosphatase-targeting subunit 1; AltName: Full=Myosin phosphatase target subunit 1; AltName: Full=Protein phosphatase myosin-binding subunit MKMADAKQKRNEQLKRWIGSETDLEPPVVKRQKTKVKFDDGAVFLAACSSGDTDEVLKLLHRGADINYAN VDGLTALHQACIDDNVDMVKFLVENGANINQPDNEGWIPLHAAASCGYLDIAEFLIGQGAHVGAVNSEGD TPLDIAEEEAMEELLQNEVNRQGVDIEAARKEEERIMLRDARQWLNSGHINDVRHAKSGGTALHVAAAKG YTEVLKLLIQAGYDVNIKDYDGWTPLHAAAHWGKEEACRILVDNLCDMEMVNKVGQTAFDVADEDILGYL EELQKKQNLLHSEKRDKKSPLIESTANMDNNQSQKTFKNKETLIIEPEKNASRIESLEQEKVDEEEEGKK DESSCSSEEDEEDDSESEAETDKTKPLASVTNANTSSTQAAPVAVTTPTVSSGQATPTSPIKKFPTTATK ISPKEEERKDESPATWRLGLRKTGSYGALAEITASKEGQKEKDTAGVTRSASSPRLSSSLDNKEKEKDSK	

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GTRLAYVAPTIPRRLASTSDIEEKENRDSSSLRTSSSYTRRKWEDDLKKNSSVNEGSTYHKSCSFGRRQD
DLISSSVPSTTSTPTVTSAAGLQKSLLSSTSTTTKITTGSSSAGTQSSTSNRLWAEDSTEKEKDSVPTAV
TIPVAPTVVNAAASTTTLTTTTAGTVSSTTEVRERRRSYLTPVRDEESESQRKARSRQARQSRRSTQGVT
LTDLQEAEKTIGRSRSTRTREQENEEKEKEEKEKQDKEKQEEKKESETSREDEYKQKYSRTYDETYQRYR
PVSTSSSTTPSSSLSTMSSSLYASSQLNRPNSLVGITSAYSRGITKENEREGEKREEEKEGEDKSQPKSI
RERRRPREKRRSTGVSFWTQDSDENEQEQQSDTEEGSNKKETQTDSISRYETSSTSAGDRYDSLLGRSGS
YSYLEERKPYSSRLEKDDSTDFKKLYEQILAENEKLKAQLHDTNMELTDLKLQLEKATQRQERFADRSLL
EMEKRERRALERRISEMEEELKMLPDLKADNQRLKDENGALIRVISKLSK
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Notes

MYPT1 myosin phosphatase target subunit 1, a regulatory subunit of protein phosphatase 1. Also called the myosin-binding subunit of myosin phosphatase. Myosin phosphatase regulates the interaction of actin and myosin downstream of the guanosine triphosphatase Rho. Four splice-variant isoforms have been described.

The binding of 14-3-3beta to MYPT1 diminished the direct binding between MYPT1 and myosin II, and 14-3-3beta overexpression abolished MYPT1 localization at stress fiber. Furthermore, 14-3-3beta inhibited MLCP holoenzyme activity via the interaction with MYPT1.# Epidermal growth factor (EGF) stimulation increased both Ser472 phosphorylation and the binding of MYPT1-14-3-3. Rho-kinase inhibitor inhibited the EGF-induced Ser472 phosphorylation and the binding of MYPT1-14-3-3.

References to 14-3-3 binding to PPP1R12A

Koga Y, Ikebe M. A novel regulatory mechanism of myosin light chain phosphorylation via binding of 14-3-3 to myosin phosphatase. Mol Biol Cell. 2008 Mar;19(3):1062-71.

Human PRKCE (PKCE) Protein kinase Cepsilon (Swissprot = Q02156)

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      1 MVVFNGLLKI KICEAVSLKP TAWSLRHAVG PRPQTFLLDP YIALNVDDSR IGQTATKQKT
     61 NSPAWHDEFV TDVCNGRKIE LAVFHDAPIG YDDFVANCTI QFEELLQNGS RHFEDWIDLE
    121 PEGRVYVIID LSGSSGEAPK DNEERVFRER MRPRKRQGAV RRRVHQVNGH KFMATYLRQP
    181 TYCSHCRDFI WGVIGKQGYQ CQVCTCVVHK RCHELIITKC AGLKKQETPD QVGSQRFSVN
    241 MPHKFGIHNY KVPTFCDHCG SLLWGLLRQG LQCKVCKMNV HRRCETNVAP NCGVDARGIA
    301 KVLADLGVTP DKITNSGQRR KKLIAGAESP QPASGSSPSE EDRSKsAPTS PCDQEIKELE
    361 NNIRKALsFD NRGEEHRAAS SPDGQLMSPG ENGEVRQGQA KRLGLDEFNF IKVLGKGSFG
    421 KVMLAELKGK DEVYAVKVLK KDVILQDDDV DCTMTEKRIL ALARKHPYLT QLYCCFQTKD
    481 RLFFVMEYVN GGDLMFQIQR SRKFDEPRSR FYAAEVTSAL MFLHQHGVIY RDLKLDNILL
    541 DAEGHCKLAD FGMCKEGILN GVTTTTFCGT PDYIAPEILQ ELEYGPSVDW WALGVLMYEM
    601 MAGQPPFEAD NEDDLFESIL HDDVLYPVWL SKEAVSILKA FMTKNPHKRL GCVASQNGED
    661 AIKQHPFFKE IDWVLLEQKK IKPPFKPRIK TKRDVNNFDQ DFTREEPVLT LVDEAIVKQI
    721 NQEEFKGFSY FGEDLMP
>gi|400135|sp|Q02156.1|KPCE_HUMAN RecName: Full=Protein kinase C epsilon
type; AltName: Full=nPKC-epsilon
MVVFNGLLKIKICEAVSLKPTAWSLRHAVGPRPQTFLLDPYIALNVDDSRIGQTATKQKTNSPAWHDEFV
TDVCNGRKIELAVFHDAPIGYDDFVANCTIQFEELLQNGSRHFEDWIDLEPEGRVYVIIDLSGSSGEAPK
DNEERVFRERMRPRKRQGAVRRRVHQVNGHKFMATYLRQPTYCSHCRDFIWGVIGKQGYQCQVCTCVVHK
RCHELIITKCAGLKKQETPDQVGSQRFSVNMPHKFGIHNYKVPTFCDHCGSLLWGLLRQGLQCKVCKMNV
HRRCETNVAPNCGVDARGIAKVLADLGVTPDKITNSGQRRKKLIAGAESPQPASGSSPSEEDRSKSAPTS
PCDQEIKELENNIRKALSFDNRGEEHRAASSPDGQLMSPGENGEVRQGQAKRLGLDEFNFIKVLGKGSFG
KVMLAELKGKDEVYAVKVLKKDVILQDDDVDCTMTEKRILALARKHPYLTQLYCCFQTKDRLFFVMEYVN
GGDLMFQIQRSRKFDEPRSRFYAAEVTSALMFLHQHGVIYRDLKLDNILLDAEGHCKLADFGMCKEGILN
GVTTTTFCGTPDYIAPEILQELEYGPSVDWWALGVLMYEMMAGQPPFEADNEDDLFESILHDDVLYPVWL
SKEAVSILKAFMTKNPHKRLGCVASQNGEDAIKQHPFFKEIDWVLLEQKKIKPPFKPRIKTKRDVNNFDQ
DFTREEPVLTLVDEAIVKQINQEEFKGFSYFGEDLMP
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Notes

Phosphoserines 346(RSK(pS346)AP) and 368 (RKAL(pS)FD) interacting with 14-3-3. These sites are unique for PKCepsilon and are conserved through evolution. he actions of p38 and glycogen synthase kinase-3beta (GSK3beta) produce a mode 1 motif at residues 343–348 (RSKpSAP) of PKCalt epsilon and autophosphorylation produces a divergent mode 2 motif at residues 364–370 (RKALpSFD) lacking proline at +2 and an aromatic residue at the -2 position (Durgan et al, 2008; Saurin et al, 2008; Fig 1A). The 14-3-3 interaction mediated by these motifs is crucial for the exit from cytokinesis, as shown by PKCalt epsilon mutants S346A/S368A or R343A, which prevent the ability of PKCalt epsilon to recover cytokinesis defects after PKCalt epsilon knockout or knockdown (Saurin et al 2008).

References to 14-3-3 binding to PKCepsilon

Saurin AT, Durgan J, Cameron AJ, Faisal A, Marber MS, Parker PJ. The regulated assembly of a PKCepsilon complex controls the completion of cytokinesis. Nat Cell Biol. 2008 Aug;10(8):891-901.

Durgan J, Cameron AJ, Saurin AT, Hanrahan S, Totty N, Messing RO, Parker PJ. The identification and characterization of novel PKCepsilon phosphorylation sites provide evidence for functional cross-talk within the PKC superfamily. Biochem J. 2008 Apr 15;411(2):319-31.

Diouf B, Collazos A, Labesse G, Macari F, Choquet A, Clair P, Gauthier-Rouvière C, Guérineau NC, Jay P, Hollande F, Joubert D.A 20-Amino Acid Module of Protein Kinase C{epsilon} Involved in Translocation and Selective Targeting at Cell-Cell Contacts. J Biol Chem. 2009 Jul 10;284(28):18808-15.

Kostelecky B, Saurin AT, Purkiss A, Parker PJ, McDonald NQ. Recognition of an intra-chain tandem 14-3-3 binding site within PKCvarepsilon. EMBO Rep. 2009 Aug 7. [Epub ahead of print]

Human PRLR prolactin receptor 1 (PrlR) (Swissprot = P16471)

```
      1 MKENVASATV FTLLLFLNTC LLNGQLPPGK PEIFKCRSPN KETFTCWWRP GTDGGLPTNY
     61 SLTYHREGET LMHECPDYIT GGPNSCHFGK QYTSMWRTYI MMVNATNQMG SSFSDELYVD
    121 VTYIVQPDPP LELAVEVKQP EDRKPYLWIK WSPPTLIDLK TGWFTLLYEI RLKPEKAAEW
    181 EIHFAGQQTE FKILSLHPGQ KYLVQVRCKP DHGYWSAWSP ATFIQIPSDF TMNDTTVWIS
    241 VAVLSAVICL IIVWAVALKG YSMVTCIFPP VPGPKIKGFD AHLLEKGKSE ELLSALGCQD
    301 FPPTSDYEDL LVEYLEVDDS EDQHLMSVHS KEHPSQGMKP TYLDPDTDSG RGSCDSPSLL
    361 SEKCEEPQAN PSTFYDPEVI EKPENPETTH TWDPQCISME GKIPYFHAGG SKCStWPLPQ
    421 PSQHNPRSSY HNITDVCELA VGPAGAPATL LNEAGKDALK SSQTIKSREE GKATQQREVE
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      481 SFHSETDQDT PWLLPQEKTP FGSAKPLDYV EIHKVNKDGA LSLLPKQREN SGKPKKPGTP
      541 ENNKEYAKVS GVMDNNILVL VPDPHAKNVA CFEESAKEAP PSLEQNQAEK ALANFTATSS
      601 KCRLQLGGLD YLDPACFTHS FH
>gi|130321|sp|P16471.1|PRLR_HUMAN RecName: Full=Prolactin receptor;
Short=PRL-R; Flags: Precursor
MKENVASATVFTLLLFLNTCLLNGQLPPGKPEIFKCRSPNKETFTCWWRPGTDGGLPTNYSLTYHREGET
LMHECPDYITGGPNSCHFGKQYTSMWRTYIMMVNATNQMGSSFSDELYVDVTYIVQPDPPLELAVEVKQP
EDRKPYLWIKWSPPTLIDLKTGWFTLLYEIRLKPEKAAEWEIHFAGQQTEFKILSLHPGQKYLVQVRCKP
DHGYWSAWSPATFIQIPSDFTMNDTTVWISVAVLSAVICLIIVWAVALKGYSMVTCIFPPVPGPKIKGFD
AHLLEKGKSEELLSALGCQDFPPTSDYEDLLVEYLEVDDSEDQHLMSVHSKEHPSQGMKPTYLDPDTDSG
RGSCDSPSLLSEKCEEPQANPSTFYDPEVIEKPENPETTHTWDPQCISMEGKIPYFHAGGSKCSTWPLPQ
PSQHNPRSSYHNITDVCELAVGPAGAPATLLNEAGKDALKSSQTIKSREEGKATQQREVESFHSETDQDT
PWLLPQEKTPFGSAKPLDYVEIHKVNKDGALSLLPKQRENSGKPKKPGTPENNKEYAKVSGVMDNNILVL
VPDPHAKNVACFEESAKEAPPSLEQNQAEKALANFTATSSKCRLQLGGLDYLDPACFTHSFH
```

Notes

Motif (KCSpT^{391}WP) in the long form of the human PrlR is conserved among a wide variety of species.

References to 14-3-3 binding to prolactin receptor

Olayioye MA, Guthridge MA, Stomski FC, Lopez AF, Visvader JE, Lindeman GJ. Threonine 391 phosphorylation of the human prolactin receptor mediates a novel interaction with 14-3-3 proteins. J Biol Chem. 2003 Aug 29;278(35):32929-35.

Fiol DF, Sanmarti E, Sacchi R, Kültz D. A novel tilapia prolactin receptor is functionally distinct from its paralog. J Exp Biol. 2009 Jul;212(Pt 13):2007-15. (two fish prolactin receptors of which only isoform 1 contains the 14-3-3-binding site)

Human PTPN3 Tyrosine-protein phosphatase non-receptor type 3 (aka Protein-tyrosine phosphatase H1 (PTPH1)) (Swissprot = P26045)

```
        1 MTSRLRALGG RINNIRTSEL PKEKTRSEVI CSIHFLDGVV QTFKVTKQDT GQVLLDMVHN
       61 HLGVTEKEYF GLQHDDDSVD SPRWLEASKA IRKQLKGGFP CTLHFRVRFF IPDPNTLQQE
      121 QTRHLYFLQL KMDICEGRLT CPLNSAVVLA SYAVQSHFGD YNSSIHHPGY LSDSHFIPDQ
      181 NEDFLTKVES LHEQHSGLKQ SEAESCYINI ARTLDFYGVE LHSGRDLHNL DLMIGIASAG
      241 VAVYRKYICT SFYPWVNILK ISFKRKKFFI HQRQKQAESR EHIVAFNMLN YRSCKNLWKS
      301 CVEHHTFFQA KKLLPQEKNV LSQYWTMGSR NTKKSVNNQY CKKVIGGMVW NPAMRRSLsV
      361 EHLETKSLPS RSPPITPNWR SPRLRHEIRK PRHSSADNLA NEMTYITETE DVFYTYKGSL
      421 APQDSDSEVS QNRSPHQESL SENNPAQSYL TQKSSSSVSP SSNAPGSCSP DGVDQQLLDD
      481 FHRVTKGGST EDASQYYCDK NDNGDSYLVL IRITPDEDGK FGFNLKGGVD QKMPLVVSRI
      541 NPESPADTCI PKLNEGDQIV LINGRDISEH THDQVVMFIK ASRESHSREL ALVIRRRAVR
      601 SFADFKSEDE LNQLFPEAIF PMCPEGGDTL EGSMAQLKKG LESGTVLIQF EQLYRKKPGL
      661 AITFAKLPQN LDKNRYKDVL PYDTTRVLLQ GNEDYINASY VNMEIPAANL VNKYIATQGP
      721 LPHTCAQFWQ VVWDQKLSLI VMLTTLTERG RTKCHQYWPD PPDVMNHGGF HIQCQSEDCT
      781 IAYVSREMLV TNTQTGEEHT VTHLQYVAWP DHGVPDDSSD FLEFVNYVRS LRVDsEPVLV
      841 HCSAGIGRTG VLVTMETAMC LTERNLPIYP LDIVRKMRDQ RAMMVQTSSQ YKFVCEAILR
      901 VYEEGLVQML DPS
>gi|229462761|sp|P26045.2|PTN3_HUMAN RecName: Full=Tyrosine-protein
phosphatase non-receptor type 3; AltName: Full=Protein-tyrosine phosphatase
H1; Short=PTP-H1
MTSRLRALGGRINNIRTSELPKEKTRSEVICSIHFLDGVVQTFKVTKQDTGQVLLDMVHNHLGVTEKEYF
GLQHDDDSVDSPRWLEASKAIRKQLKGGFPCTLHFRVRFFIPDPNTLQQEQTRHLYFLQLKMDICEGRLT
CPLNSAVVLASYAVQSHFGDYNSSIHHPGYLSDSHFIPDQNEDFLTKVESLHEQHSGLKQSEAESCYINI
ARTLDFYGVELHSGRDLHNLDLMIGIASAGVAVYRKYICTSFYPWVNILKISFKRKKFFIHQRQKQAESR
EHIVAFNMLNYRSCKNLWKSCVEHHTFFQAKKLLPQEKNVLSQYWTMGSRNTKKSVNNQYCKKVIGGMVW
NPAMRRSLSVEHLETKSLPSRSPPITPNWRSPRLRHEIRKPRHSSADNLANEMTYITETEDVFYTYKGSL
APQDSDSEVSQNRSPHQESLSENNPAQSYLTQKSSSSVSPSSNAPGSCSPDGVDQQLLDDFHRVTKGGST
EDASQYYCDKNDNGDSYLVLIRITPDEDGKFGFNLKGGVDQKMPLVVSRINPESPADTCIPKLNEGDQIV
LINGRDISEHTHDQVVMFIKASRESHSRELALVIRRRAVRSFADFKSEDELNQLFPEAIFPMCPEGGDTL
EGSMAQLKKGLESGTVLIQFEQLYRKKPGLAITFAKLPQNLDKNRYKDVLPYDTTRVLLQGNEDYINASY
VNMEIPAANLVNKYIATQGPLPHTCAQFWQVVWDQKLSLIVMLTTLTERGRTKCHQYWPDPPDVMNHGGF
HIQCQSEDCTIAYVSREMLVTNTQTGEEHTVTHLQYVAWPDHGVPDDSSDFLEFVNYVRSLRVDSEPVLV
HCSAGIGRTGVLVTMETAMCLTERNLPIYPLDIVRKMRDQRAMMVQTSSQYKFVCEAILRVYEEGLVQML
DPS
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Notes

“Protein tyrosine phosphatase) non-receptor type 3; protein-tyrosine phosphatase H1 PTPH1) that may act at junctions between the membrane and the cytoskeleton. Two novel motifs RSLS359VE and RVDS853EP in PTPH1 were identified as major 14-3-3beta-binding sites, both of which are distinct from the consensus binding motif RSXSXP recently found in Raf-1. Mutation of Ser359 and Ser853 to alanine significantly reduced the association between 14-3-3beta and PTPH1. Furthermore, association of PTPH1 and 14-3-3beta was detected in several cell lines and was regulated in response to extracellular signals. (Zhang et al 1997)”

Two 14-3-3 binding phosphorylated sites are RSLpS^{359}VE and RVDpS^{853}EP (=Ser835 in Swissprot = P26045)

References to 14-3-3 binding to PTPN3 (PTPH1)

S. H. Zhang, R. Kobayashi, P. R. Graves, H. Piwnica-Worms, and N. K. Tonks, Serine phosphorylation-dependent association of the band 4.1-related protein-tyrosine phosphatase PTPH1 with 14-3-3beta protein, J Biol Chem 272 (1997) 27281-27287.

Human Raf1 (CRAF) (Swissprot = P04049)

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        1 MEHIQGAWKT ISNGFGFKDA VFDGSSCISP TIVQQFGYQR RASDDGKLTD PSKTSNTIRV
       61 FLPNKQRTVV NVRNGMSLHD CLMKALKVRG LQPECCAVFR LLHEHKGKKA RLDWNTDAAS
      121 LIGEELQVDF LDHVPLTTHN FARKTFLKLA FCDICQKFLL NGFRCQTCGY KFHEHCSTKV
      181 PTMCVDWSNI RQLLLFPNST IGDSGVPALP SLTMRRMRES VSRMPVSSQH RYSTPHAFTF
      241 NTSSPSSEGS lsqrqrstst PNVHMVSTTL PVDSRMIEDA IRSHSESASP SALSSSPNNL
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      301 SPTGWSQPKT PVPAQRERAP VSGTQEKNKI RPRGQRDSSY YWEIEASEVM LSTRIGSGSF
      361 GTVYKGKWHG DVAVKILKVV DPTPEQFQAF RNEVAVLRKT RHVNILLFMG YMTKDNLAIV
      421 TQWCEGSSLY KHLHVQETKF QMFQLIDIAR QTAQGMDYLH AKNIIHRDMK SNNIFLHEGL
      481 TVKIGDFGLA TVKSRWSGSQ QVEQPTGSVL WMAPEVIRMQ DNNPFSFQSD VYSYGIVLYE
      541 LMTGELPYSH INNRDQIIFM VGRGYASPDL SKLYKNCPKA MKRLVADCVK KVKEERPLFP
      601 QILSSIELLQ HSLPKINRSA sEPSLHRAAH TEDINACTLT TSPRLPVF
>gi|125651|sp|P04049.1|RAF1_HUMAN RecName: Full=RAF proto-oncogene
serine/threonine-protein kinase; AltName: Full=C-RAF; Short=cRaf; AltName:
Full=Raf-1
MEHIQGAWKTISNGFGFKDAVFDGSSCISPTIVQQFGYQRRASDDGKLTDPSKTSNTIRVFLPNKQRTVV
NVRNGMSLHDCLMKALKVRGLQPECCAVFRLLHEHKGKKARLDWNTDAASLIGEELQVDFLDHVPLTTHN
FARKTFLKLAFCDICQKFLLNGFRCQTCGYKFHEHCSTKVPTMCVDWSNIRQLLLFPNSTIGDSGVPALP
SLTMRRMRESVSRMPVSSQHRYSTPHAFTFNTSSPSSEGSLSQRQRSTSTPNVHMVSTTLPVDSRMIEDA
IRSHSESASPSALSSSPNNLSPTGWSQPKTPVPAQRERAPVSGTQEKNKIRPRGQRDSSYYWEIEASEVM
LSTRIGSGSFGTVYKGKWHGDVAVKILKVVDPTPEQFQAFRNEVAVLRKTRHVNILLFMGYMTKDNLAIV
TQWCEGSSLYKHLHVQETKFQMFQLIDIARQTAQGMDYLHAKNIIHRDMKSNNIFLHEGLTVKIGDFGLA
TVKSRWSGSQQVEQPTGSVLWMAPEVIRMQDNNPFSFQSDVYSYGIVLYELMTGELPYSHINNRDQIIFM
VGRGYASPDLSKLYKNCPKAMKRLVADCVKKVKEERPLFPQILSSIELLQHSLPKINRSASEPSLHRAAH
TEDINACTLTTSPRLPVF
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Notes

References to 14-3-3 binding to Raf

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Positive regulation of A-RAF by phosphorylation of isoform-specific hinge segment and identification of novel phosphorylation sites. J Biol Chem. 2008 Oct 3;283(40):27239-54.

Ory S, Zhou M, Conrads TP, Veenstra TD, Morrison DK. Protein phosphatase 2A positively regulates Ras signaling by dephosphorylating KSR1 and Raf-1 on critical 14-3-3 binding sites. Curr Biol. 2003 Aug 19;13(16):1356-64.

Human Raptor Regulatory-associated protein of mTOR (Swissprot = Q8N122)

```
        1 MESEMLQSPL LGLGEEDEAD LTDWNLPLAF MKKRHCEKIE GSKSLAQSWR MKDRMKTVSV
       61 ALVLCLNVGV DPPDVVKTTP CARLECWIDP LSMGPQKALE TIGANLQKQY ENWQPRARYK
      121 QSLDPTVDEV KKLCTSLRRN AKEERVLFHY NGHGVPRPTV NGEVWVFNKN YTQYIPLSIY
      181 DLQTWMGSPS IFVYDCSNAG LIVKSFKQFA LQREQELEVA AINPNHPLAQ MPLPPSMKNC
      241 IQLAACEATE LLPMIPDLPA DLFTSCLTTP IKIALRWFCM QKCVSLVPGV TLDLIEKIPG
      301 RLNDRRTPLG ELNWIFTAIT DTIAWNVLPR DLFQKLFRQD LLVASLFRNF LLAERIMRSY
      361 NCTPVSSPRL PPTYMHAMWQ AWDLAVDICL SQLPTIIEEG TAFRHSPFFA EQLTAFQVWL
      421 TMGVENRNPP EQLPIVLQVL LSQVHRLRAL DLLGRFLDLG PWAVSLALSV GIFPYVLKLL
      481 QSSARELRPL LVFIWAKILA VDSSCQADLV KDNGHKYFLS VLADPYMPAE HRTMTAFILA
      541 VIVNSYHTGQ EACLQGNLIA ICLEQLNDPH PLLRQWVAIC LGRIWQNFDS ARWCGVRDSA
      601 HEKLYSLLSD PIPEVRCAAV FALGTFVGNS AERTDHSTTI DHNVAMMLAQ LVSDGSPMVR
      661 KELVVALSHL VVQYESNFCT VALQFIEEEK NYALPSPATT EGGSLTPVRD SPCTPRLRSV
      721 SsYGNIRAVA TARSLNKSLQ NLSLTEESGG AVAFSPGNLS TSSSASSTLG SPENEEHILS
      781 FETIDKMRRA SsYSSLNSLI GVSFNSVYTQ IWRVLLHLAA DPYPEVSDVA MKVLNSIAYK
      841 ATVNARPQRV LDTSSLTQSA PASPTNKGVH IHQAGGSPPA SSTSSSSLTN DVAKQPVSRD
      901 LPSGRPGTTG PAGAQYTPHS HQFPRTRKMF DKGPEQTADD ADDAAGHKSF ISATVQTGFC
      961 DWSARYFAQP VMKIPEEHDL ESQIRKEREW RFLRNSRVRR QAQQVIQKGI TRLDDQIFLN
     1021 RNPGVPSVVK FHPFTPCIAV ADKDSICFWD WEKGEKLDYF HNGNPRYTRV TAMEYLNGQD
     1081 CSLLLTATDD GAIRVWKNFA DLEKNPEMVT AWQGLSDMLP TTRGAGMVVD WEQETGLLMS
     1141 SGDVRIVRIW DTDREMKVQD IPTGADSCVT SLSCDSHRSL IVAGLGDGSI RVYDRRMALS
     1201 ECRVMTYREH TAWVVKASLQ KRPDGHIVSV SVNGDVRIFD PRMPESVNVL QIVKGLTALD
     1261 IHPQADLIAC GSVNQFTAIY NSSGELINNI KYYDGFMGQR VGAISCLAFH PHWPHLAVGS
     1321 NDYYISVYSV EKRVR
>gi|46577501|sp|Q8N122.1|RPTOR_HUMAN RecName: Full=Regulatory-associated
protein of mTOR; Short=Raptor; AltName: Full=P150 target of rapamycin (TOR)-
scaffold protein
MESEMLQSPLLGLGEEDEADLTDWNLPLAFMKKRHCEKIEGSKSLAQSWRMKDRMKTVSVALVLCLNVGV
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DPPDVVKTTPCARLECWIDPLSMGPQKALETIGANLQKQYENWQPRARYKQSLDPTVDEVKKLCTSLRRN
AKEERVLFHYNGHGVPRPTVNGEVWVFNKNYTQYIPLSIYDLQTWMGSPSIFVYDCSNAGLIVKSFKQFA
LQREQELEVAAINPNHPLAQMPLPPSMKNCIQLAACEATELLPMIPDLPADLFTSCLTTPIKIALRWFCM
QKCVSLVPGVTLDLIEKIPGRLNDRRTPLGELNWIFTAITDTIAWNVLPRDLFQKLFRQDLLVASLFRNF
LLAERIMRSYNCTPVSSPRLPPTYMHAMWQAWDLAVDICLSQLPTIIEEGTAFRHSPFFAEQLTAFQVWL
TMGVENRNPPEQLPIVLQVLLSQVHRLRALDLLGRFLDLGPWAVSLALSVGIFPYVLKLLQSSARELRPL
LVFIWAKILAVDSSCQADLVKDNGHKYFLSVLADPYMPAEHRTMTAFILAVIVNSYHTGQEACLQGNLIA
ICLEQLNDPHPLLRQWVAICLGRIWQNFDSARWCGVRDSAHEKLYSLLSDPIPEVRCAAVFALGTFVGNS
AERTDHSTTIDHNVAMMLAQLVSDGSPMVRKELVVALSHLVVQYESNFCTVALQFIEEEKNYALPSPATT
EGGSLTPVRDSPCTPRLRSVSSYGNIRAVATARSLNKSLQNLSLTEESGGAVAFSPGNLSTSSSASSTLG
SPENEEHILSFETIDKMRRASSYSSLNSLIGVSFNSVYTQIWRVLLHLAADPYPEVSDVAMKVLNSIAYK
ATVNARPQRVLDTSSLTQSAPASPTNKGVHIHQAGGSPPASSTSSSSLTNDVAKQPVSRDLPSGRPGTTG
PAGAQYTPHSHQFPRTRKMFDKGPEQTADDADDAAGHKSFISATVQTGFCDWSARYFAQPVMKIPEEHDL
ESQIRKEREWRFLRNSRVRRQAQQVIQKGITRLDDQIFLNRNPGVPSVVKFHPFTPCIAVADKDSICFWD
WEKGEKLDYFHNGNPRYTRVTAMEYLNGQDCSLLLTATDDGAIRVWKNFADLEKNPEMVTAWQGLSDMLP
TTRGAGMVVDWEQETGLLMSSGDVRIVRIWDTDREMKVQDIPTGADSCVTSLSCDSHRSLIVAGLGDGSI
RVYDRRMALSECRVMTYREHTAWVVKASLQKRPDGHIVSVSVNGDVRIFDPRMPESVNVLQIVKGLTALD
IHPQADLIACGSVNQFTAIYNSSGELINNIKYYDGFMGQRVGAISCLAFHPHWPHLAVGSNDYYISVYSV
EKRVR
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Notes

Raptor is a regulatory component of the TORC1 complex (with mTOR) by which cells coordinate the rate of cell growth and maintenance of cell size with different environmental conditions. AMPK directly phosphorylates the mTOR binding partner raptor on two well-conserved serine residues, and this phosphorylation induces 14-3-3 binding to raptor.

References to 14-3-3 binding to Raptor

Gwinn DM, Shackelford DB, Egan DF, Mihaylova MM, Mery A, Vasquez DS, Turk BE, Shaw RJ.AMPK phosphorylation of raptor mediates a metabolic checkpoint. Mol Cell. 2008 Apr 25;30(2):214-26.

Human Rem2 RAS (RAD and GEM)-like GTP binding 2 (Swissprot = Q8IYK8-1)

```
        1 MDTETTALCP SGSRRASPPG TPTPEADATL LKKSEKLLAE LDRSGLPSAP GAPRRRGsMP
       61 VPYKHQLRRA QAVDELDWPP QASSSGSSDS LGSGEAAPAQ KDGIFKVMLV GESGVGKSTL
      121 AGTFGGLQGD SAHEPENPED TYERRIMVDK EEVTLVVYDI WEQGDAGGWL RDHCLQTGDA
      181 FLIVFSVTDR RSFSKVPETL LRLRAGRPHH DLPVILVGNK SDLARSREVS LEEGRHLAGT
      241 LSCKHIETSA ALHHNTRELF EGAVRQIRLR RGRNHAGGQR PDPGSPEGPA PPARRESLTK
      301 KAKRFLANLV PRNAKFFKQR SRsCHDLSVL
>gi|51316478|sp|Q8IYK8.1|REM2_HUMAN RecName: Full=GTP-binding protein REM 2;
AltName: Full=Rad and Gem-like GTP-binding protein 2
MDTETTALCPSGSRRASPPGTPTPEADATLLKKSEKLLAELDRSGLPSAPGAPRRRGSMPVPYKHQLRRA
QAVDELDWPPQASSSGSSDSLGSGEAAPAQKDGIFKVMLVGESGVGKSTLAGTFGGLQGDSAHEPENPED
TYERRIMVDKEEVTLVVYDIWEQGDAGGWLRDHCLQTGDAFLIVFSVTDRRSFSKVPETLLRLRAGRPHH
DLPVILVGNKSDLARSREVSLEEGRHLAGTLSCKHIETSAALHHNTRELFEGAVRQIRLRRGRNHAGGQR
PDPGSPEGPAPPARRESLTKKAKRFLANLVPRNAKFFKQRSRSCHDLSVL
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Notes

Fig 1 in Béguin et al (2005) shows that the 14-3-3-binding sites are conserved in Rem2 and Gem, but that a truncated form of Rem2 studied by Finlin and Andres (1999) lacks the first 14-3-3 binding site. “Although kir/Gem, Rad and Rem bind 14-3-3 in a phosphorylation-dependent manner (Ward et al 2004; Finlin and Andres 1999), Rem2 has been reported not to associate with 14-3-3 (Finlin et al 2000). In the present study, we re-evaluate the functions of Rem2 and its interaction with 14-3-3 and CaM. We show that Rem2 does associate with 14-3-3 and CaM and induces changes in cell morphology (sites = RRGpS^{69}M, QRSRpS^{334}C). 14-3-3, in co-operation with CaM, also regulates the subcellular distribution of Rem2. Rem2 interacts with the b-subunits in a GTP-dependent fashion and thereby blocks cell-surface expression of VDCCs. Thus Rem2 shares many previously unrecognized similarities with the other members of the RGK family.”

References to 14-3-3 binding to Rem2

Béguin P, Mahalakshmi RN, Nagashima K, Cher DH, Kuwamura N, Yamada Y, Seino Y, Hunziker W. Roles of 14-3-3 and calmodulin binding in subcellular localization and function of the small G-protein Rem2. Biochem J. 2005 Aug 15;390(Pt 1):67-75. Erratum in: Biochem J. 2005 Nov 1;391(Pt 3):712. (Rat Rem2 AF084464)

Béguin P, Mahalakshmi RN, Nagashima K, Cher DH, Ikeda H, Yamada Y, Seino Y, Hunziker W. Nuclear sequestration of beta-subunits by Rad and Rem is controlled by 14-3-3 and calmodulin and reveals a novel mechanism for Ca2+ channel regulation. J Mol Biol. 2006 Jan 6;355(1):34-46.

Finlin BS, Andres DA. Phosphorylation-dependent association of the Ras-related GTP-binding protein Rem with 14-3-3 proteins. Arch Biochem Biophys. 1999 Aug 15;368(2):401-12.

Finlin, B. S., Shao, H., Kadono-Okuda, K., Guo, N. and Andres, D. A. (2000) Rem2, a new member of the Rem/Rad/Gem/Kir family of Ras-related GTPases. Biochem. J. 347, 223–231

Bierings R, Beato M, Edel MJ.An endothelial cell genetic screen identifies the GTPase Rem2 as a suppressor of p19ARF expression that promotes endothelial cell proliferation and angiogenesis. J Biol Chem. 2008 Feb 15;283(7):4408-16.

Human RGS3 Regulator of G-protein signaling 3 (Swissprot = P49796)

```
        1 MPVIPALWEV EMGRSQGQEI ETILANRSHS DSTPLPNFLS GSHRPECCTC RLLTASGAQD
       61 SLPFGRRLYS GPWRSCEEVC HVSVLSVLST SCGLSLSLPI FPGWMEWLSP DIALPRRDEW
      121 TQTSPARKRI THAKVQGAGQ LRLSIDAQDR VLLLHIIEGK GLISKQPGTC DPYVKISLIP
      181 EDSRLRHQKT QTVPDCRDPA FHEHFFFPVQ EEDDQKRLLV TVWNRASQSR QSGLIGCMSF
      241 GVKSLLTPDK EISGWYYLLG EHLGRTKHLK VARRRLRPLR DPLLRMPGGG DTENGKKLKI
      301 TIPRGKDGFG FTICCDSPVR VQAVDSGGPA ERAGLQQLDT VLQLNERPVE HWKCVELAHE
      361 IRSCPSEIIL LVWRMVPQVK PGPDGGVLRR ASCKSTHDLQ SPPNKREKNC THGVQARPEQ
      421 RHSCHLVCDS SDGLLLGGWE RYTEVAKRGG QHTLPALSRA TAPTDPNYII LAPLNPGSQL
      481 LRPVYQEDTI PEESGSPSKG KSYTGLGKKS RLMKTVQTMK GHGNYQNCPV VRPHATHSSY
      541 GTYVTLAPKV LVFPVFVQPL DLCNPARTLL LSEELLLYEG RNKAAEVTLF AYSDLLLFTK
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     601 EDEPGRCDVL RNPLYLQSVK LQEGSSEDLK FCVLYLAEKA ECLFTLEAHS QEQKKRVCWC
     661 LSENIAKQQQ LAASPPDSKM FETEADEKRE MALEEGKGPG AEDSPPSKEP SPGQELPPGQ
     721 DLPPNKDSPS GQEPAPSQEP LSSKDSATSE GSPPGPDAPP SKDVPPCQEP PPAQDLSPCQ
     781 DLPAGQEPLP HQDPLLTKDL PAIQESPTRD LPPCQDLPPS QVSLPAKALT EDTMSSGDLL
     841 AATGDPPAAP RPAFVIPEVR LDSTYSQKAG AEQGCSGDEE DAEEAEEVEE GEEGEEDEDE
     901 DTSDDNYGER SEAKRSSMIE TGQGAEGGLS LRVQNSLRRR THsEGSLLQE PRGPCFASDT
     961 TLHCSDGEGA ASTWGMPSPS TLKKELGRNG GSMHHLSLFF TGHRKMSGAD TVGDDDEASR
    1021 KRKSKNLAKD MKNKLGIFRR RNESPGAPPA GKADKMMKSF KPTSEEALKW GESLEKLLVH
    1081 KYGLAVFQAF LRTEFSEENL EFWLACEDFK KVKSQSKMAS KAKKIFAEYI AIQACKEVNL
    1141 DSYTREHTKD NLQSVTRGCF DLAQKRIFGL MEKDSYPRFL RSDLYLDLIN QKKMSPPL
>gi|67477383|sp|P49796.2|RGS3_HUMAN RecName: Full=Regulator of G-protein
signaling 3; Short=RGS3; Short=RGP3
MPVIPALWEVEMGRSQGQEIETILANRSHSDSTPLPNFLSGSHRPECCTCRLLTASGAQDSLPFGRRLYS
GPWRSCEEVCHVSVLSVLSTSCGLSLSLPIFPGWMEWLSPDIALPRRDEWTQTSPARKRITHAKVQGAGQ
LRLSIDAQDRVLLLHIIEGKGLISKQPGTCDPYVKISLIPEDSRLRHQKTQTVPDCRDPAFHEHFFFPVQ
EEDDQKRLLVTVWNRASQSRQSGLIGCMSFGVKSLLTPDKEISGWYYLLGEHLGRTKHLKVARRRLRPLR
DPLLRMPGGGDTENGKKLKITIPRGKDGFGFTICCDSPVRVQAVDSGGPAERAGLQQLDTVLQLNERPVE
HWKCVELAHEIRSCPSEIILLVWRMVPQVKPGPDGGVLRRASCKSTHDLQSPPNKREKNCTHGVQARPEQ
RHSCHLVCDSSDGLLLGGWERYTEVAKRGGQHTLPALSRATAPTDPNYIILAPLNPGSQLLRPVYQEDTI
PEESGSPSKGKSYTGLGKKSRLMKTVQTMKGHGNYQNCPVVRPHATHSSYGTYVTLAPKVLVFPVFVQPL
DLCNPARTLLLSEELLLYEGRNKAAEVTLFAYSDLLLFTKEDEPGRCDVLRNPLYLQSVKLQEGSSEDLK
FCVLYLAEKAECLFTLEAHSQEQKKRVCWCLSENIAKQQQLAASPPDSKMFETEADEKREMALEEGKGPG
AEDSPPSKEPSPGQELPPGQDLPPNKDSPSGQEPAPSQEPLSSKDSATSEGSPPGPDAPPSKDVPPCQEP
PPAQDLSPCQDLPAGQEPLPHQDPLLTKDLPAIQESPTRDLPPCQDLPPSQVSLPAKALTEDTMSSGDLL
AATGDPPAAPRPAFVIPEVRLDSTYSQKAGAEQGCSGDEEDAEEAEEVEEGEEGEEDEDEDTSDDNYGER
SEAKRSSMIETGQGAEGGLSLRVQNSLRRRTHSEGSLLQEPRGPCFASDTTLHCSDGEGAASTWGMPSPS
TLKKELGRNGGSMHHLSLFFTGHRKMSGADTVGDDDEASRKRKSKNLAKDMKNKLGIFRRRNESPGAPPA
GKADKMMKSFKPTSEEALKWGESLEKLLVHKYGLAVFQAFLRTEFSEENLEFWLACEDFKKVKSQSKMAS
KAKKIFAEYIAIQACKEVNLDSYTREHTKDNLQSVTRGCFDLAQKRIFGLMEKDSYPRFLRSDLYLDLIN
QKKMSPPL
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Notes

RGS3 is a GTPase activating protein that down-regulates signaling from heterotrimeric G-proteins by increasing the GTPase activity of the alpha subunits, thereby driving them into their inactive GDP-bound form. Down-regulates G- protein-mediated release of inositol phosphates and activation of MAP kinases. Binds EFNB1 and EFNB2. Binds the GNB1- GNG2 heterodimer. 6 isoforms of the human protein are produced by alternative splicing. In a confirmation of the Niu et al (2002) study, Ward et al (2005) report that Ser264 is the 14-3-3-binding site of RGS3, and not the previously-reported Ser496 in RSG3 (the latter being equivalent to Ser 434 in RGS7) (Benzing et al 2000). The S(264)A mutation resulted in the loss of RGS3 binding to 14-3-3, without affecting its ability to bind G alpha(q). Signalling studies showed that the S(264)A mutant was more potent than the wild-type RGS3 in inhibition of G-protein-mediated signalling. Note that the form studies by Ward et al (2005) was 519 amino acids long (isoform 1), and missing 679 amino acids compared with the longer canonical sequence shown here (isoform 3). Ser264 in isoform 1 is equivalent to Ser943 in isoform 3 (shown here).

References to 14-3-3 binding to RGS3

Niu J, Scheschonka A, Druey KM, Davis A, Reed E, Kolenko V, Bodnar R, Voyno-Yasenetskaya T, Du X, Kehrl J, Dulin NO. RGS3 interacts with 14-3-3 via the N-terminal region distinct from the RGS (regulator of G-protein signalling) domain. Biochem J. 2002 Aug 1;365(Pt 3):677-84

Ward RJ, Milligan G. A key serine for the GTPase-activating protein function of regulator of G protein signaling proteins is not a general target for 14-3-3 interactions. Mol Pharmacol. 2005 Dec;68(6):1821-30

Benzing, T., Yaffe, M.B., Arnould, T., Sellin, L., Schermer, B., Schilling, B., Schreiber, R., Kunzelmann, K., Leparc, G.G., Kim, E. and Walz, G. (2000) 14-3-3 interacts with regulator of G protein signaling proteins and modulates their activity. J. Biol. Chem. 275, 28167–28172

<u>Human rictor (AAS79796)</u>

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       1 MAAIGRGRSL KNLRVRGRND SGEENVPLDL TREPSDNLRE ILQNVARLQG VSNMRKLGHL
      61 NNFTKLLCDI GHSEEKLGFH YEDIIICLRL ALLNEAKEVR AAGLRALRYL IQDSSILQKV
     121 LKLKVDYLIA RCIDIQQSNE VERTQALRLV RKMITVNASL FPSSVTNSLI AVGNDGLQER
     181 DRMVRACIAI ICELALQNPE VVALRGGLNT ILKNVIDCQL SRINEALITT ILHLLNHPKT
     241 RQYVRADVEL ERILAPYTDF HYRHSPDTAE GQLKEDREAR FLASKMGIIA TFRSWAGIIN
     301 LCKPGNSGIQ SLIGVLCIPN MEIRRGLLEV LYDIFRLPLP VVTEEFIEAL LSVDPGRFQD
     361 SWRLSDGFVA AEAKTILPHR ARSRPDLMDN YLALILSAFI RNGLLEGLVE VITNSDDHIS
     421 VRATILLGEL LHMANTILPH SHSHHLHCLP TLMNMAASFD IPKEKRLRAS AALNCLKRFH
     481 EMKKRGPKPY SLHLDHIIQK AIATHQKRDQ YLRVQKDIFI LKDTEEALLI NLRDSQVLQH
     541 KENLEWNWNL IGTILKWPNV NLRNYKDEQL HRFVRRLLYF YKPSSKLYAN LDLDFAKAKQ
     601 LTVVGCQFTE FLLESEEDGQ GYLEDLVKDI VQWLNASSGM KPERSLQNNG LLTTLSQHYF
     661 LFIGTLSCHP HGVKMLEKCS VFQCLLNLCS LKNQDHLLKL TVSSLDYSRD GLARVILSKI
     721 LTAATDACRL YATKHLRVLL RANVEFFNNW GIELLVTQLH DKNKTISSEA LDILDEACED
     781 KANLHALIQM KPALSHLGDK GLLLLLRFLS IPKGFSYLNE RGYVAKQLEK WHREYNSKYV
     841 DLIEEQLNEA LTTYRKPVDG DNYVRRSNQR LQRPHVYLPI HLYGQLVHHK TGCHLLEVQN
     901 IITELCRNVR TPDLDKWEEI KKLKASLWAL GNIGSSNWGL NLLQEENVIP DILKLAKQCE
     961 VLSIRGTCVY VLGLIAKTKQ GCDILKCHNW DAVRHSRKHL WPVVPDDVEQ LCNELSSIPS
    1021 TLSLNSESTS SRHNSESESV PSSMFILEDD RFGSSSTSTF FLDINEDTEP TFYDRSGPIK
    1081 DKNSFPFFAS SKLVKNRILN SLTLPNKKHR SSSDPKGGKL SSESKTSNRR IRTLtEPSVD
    1141 FNHSDDFTPI STVQKTLQLE TSFMGNKHIE DTGSTPSIGE NDLKFTKNFG TENHRENTSR
    1201 ERLVVESSTS SHMKIRSQSF NTDTTTSGIS SMSSSPSRET VGVDATTMDT DCGSMSTVVS
    1261 TKTIKTSHYL TPQSNHLSLS KSNSVSLVPP GSSHTLPRRA QSLKAPSIAT IKSLADCNFS
    1321 YTSSRDAFGY ATLKRLQQQR MHPSLSHSEA LASPAKDVLF TDTITMKANS FESRLTPSRF
    1381 MKALSYASLD KEDLLSPINQ NTLQRSSSVR SMVSSATYGG SDDYIGLALP VDINDIFQVK
    1441 DIPYFQTKNI PPHDDRGARA FAHDAGGLPS GTGGLVKNSF HLLRQQMSLT EIMNSIHSDA
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    1501 SLFLESTEDT GLQEHTDDNC LYCVCIEILG FQPSNQLSAI CSHSDFQDIP YSDWCEQTIH
    1561 NPLEVVPSKF SGISGCSDGV SQEGSASSTK STELLLGVKT IPDDTPMCRI LLRKEVLRLV
    1621 INLSSSVSTK CHETGLLTIK EKYPQTFDDI CLYSEVSHLL SHCTFRLPCR RFIQELFQDV
    1681 QFLQMHEEAE AVLATPPKQP IVDTSAES
>gi|46093886|gb|AAS79796.1| rapamycin insensitive companion of mTOR; rictor
[Homo sapiens]
MAAIGRGRSLKNLRVRGRNDSGEENVPLDLTREPSDNLREILQNVARLQGVSNMRKLGHLNNFTKLLCDI
GHSEEKLGFHYEDIIICLRLALLNEAKEVRAAGLRALRYLIQDSSILQKVLKLKVDYLIARCIDIQQSNE
VERTQALRLVRKMITVNASLFPSSVTNSLIAVGNDGLQERDRMVRACIAIICELALQNPEVVALRGGLNT
ILKNVIDCQLSRINEALITTILHLLNHPKTRQYVRADVELERILAPYTDFHYRHSPDTAEGQLKEDREAR
FLASKMGIIATFRSWAGIINLCKPGNSGIQSLIGVLCIPNMEIRRGLLEVLYDIFRLPLPVVTEEFIEAL
LSVDPGRFQDSWRLSDGFVAAEAKTILPHRARSRPDLMDNYLALILSAFIRNGLLEGLVEVITNSDDHIS
VRATILLGELLHMANTILPHSHSHHLHCLPTLMNMAASFDIPKEKRLRASAALNCLKRFHEMKKRGPKPY
SLHLDHIIQKAIATHQKRDQYLRVQKDIFILKDTEEALLINLRDSQVLQHKENLEWNWNLIGTILKWPNV
NLRNYKDEQLHRFVRRLLYFYKPSSKLYANLDLDFAKAKQLTVVGCQFTEFLLESEEDGQGYLEDLVKDI
VQWLNASSGMKPERSLQNNGLLTTLSQHYFLFIGTLSCHPHGVKMLEKCSVFQCLLNLCSLKNQDHLLKL
TVSSLDYSRDGLARVILSKILTAATDACRLYATKHLRVLLRANVEFFNNWGIELLVTQLHDKNKTISSEA
LDILDEACEDKANLHALIQMKPALSHLGDKGLLLLLRFLSIPKGFSYLNERGYVAKQLEKWHREYNSKYV
DLIEEQLNEALTTYRKPVDGDNYVRRSNQRLQRPHVYLPIHLYGQLVHHKTGCHLLEVQNIITELCRNVR
TPDLDKWEEIKKLKASLWALGNIGSSNWGLNLLQEENVIPDILKLAKQCEVLSIRGTCVYVLGLIAKTKQ
GCDILKCHNWDAVRHSRKHLWPVVPDDVEQLCNELSSIPSTLSLNSESTSSRHNSESESVPSSMFILEDD
RFGSSSTSTFFLDINEDTEPTFYDRSGPIKDKNSFPFFASSKLVKNRILNSLTLPNKKHRSSSDPKGGKL
SSESKTSNRRIRTLTEPSVDFNHSDDFTPISTVQKTLQLETSFMGNKHIEDTGSTPSIGENDLKFTKNFG
TENHRENTSRERLVVESSTSSHMKIRSQSFNTDTTTSGISSMSSSPSRETVGVDATTMDTDCGSMSTVVS
TKTIKTSHYLTPQSNHLSLSKSNSVSLVPPGSSHTLPRRAQSLKAPSIATIKSLADCNFSYTSSRDAFGY
ATLKRLQQQRMHPSLSHSEALASPAKDVLFTDTITMKANSFESRLTPSRFMKALSYASLDKEDLLSPINQ
NTLQRSSSVRSMVSSATYGGSDDYIGLALPVDINDIFQVKDIPYFQTKNIPPHDDRGARAFAHDAGGLPS
GTGGLVKNSFHLLRQQMSLTEIMNSIHSDASLFLESTEDTGLQEHTDDNCLYCVCIEILGFQPSNQLSAI
CSHSDFQDIPYSDWCEQTIHNPLEVVPSKFSGISGCSDGVSQEGSASSTKSTELLLGVKTIPDDTPMCRI
LLRKEVLRLVINLSSSVSTKCHETGLLTIKEKYPQTFDDICLYSEVSHLLSHCTFRLPCRRFIQELFQDV
QFLQMHEEAEAVLATPPKQPIVDTSAES
```

Notes

Thr1135 RIRTL(pT)EPSVD (numbering for full-length human rictor)

References to 14-3-3 binding to rictor

Dibble CC, Asara JM, Manning BD. Characterization of Rictor phosphorylation sites reveals direct regulation of mTOR complex 2 by S6K1. Mol Cell Biol. 2009 Aug 31. [Epub ahead of print]

Treins C, Warne PH, Magnuson MA, Pende M, Downward J. Rictor is a novel target of p70 S6 kinase-1.Oncogene. 2009 Nov 23. [Epub ahead of print]

<u>Human RIMS1</u> Rim1 alpha (Swissprot = Q86UR5)

```
       1 MSSAVGPRGP RPPTVPPPMQ ELPDLSHLTE EERNIIMAVM DRQKEEEEKE EAMLKCVVRD
      61 MAKPAACKTP RNAENQPHQP SPRLHQQFES YKEQVRKIGE EARRYQGEHK DDAPTCGICH
     121 KTKFADGCGH LCSYCRTKFC ARCGGRVSLR SNNEDKVVMW VCNLCRKQQE ILTKSGAWFF
     181 GSGPQQTSQD GTLSDTATGA GSEVPREKKA RLQERSRSQT PLSTAAASSQ DAAPPSAPPD
     241 RSKGAEPSQQ ALGPEQKQAS SRSRsEPPRE RKKTPGLSEQ NGKGALKSER KRVPKTSAQP
     301 VEGAVEERER KERRESRRLE KGRSQDYPDT PEKRDEGKAA DEEKQRKEED YQTRYRsDPN
     361 LARYPVKPPP EEQQMRMHAR VSRARHERRH sDVALPRTEA GAALPEGKAG KRAPAAARAS
     421 PPDSPRAYSA ERTAETRAPG AKQLTNHSPP APRHGPVPAE APELKAQEPL RKQSRLDPSS
     481 AVLMRKAKRE KVETMLRNDS LSSDQSESVR PSPPKPHRSK RGGKKRQMSV SSSEEEGVST
     541 PEYTSCEDVE LESESVSEKG DLDYYWLDPA TWHSRETSPI SSHPVTWQPS KEGDRLIGRV
     601 ILNKRTTMPK DSGALLGLKV VGGKMTDLGR LGAFITKVKK GSLADVVGHL RAGDEVLEWN
     661 GKPLPGATNE EVYNIILESK SEPQVEIIVS RPIGDIPRIP ESSHPPLESS SSSFESQKME
     721 RPSISVISPT SPGALKDAPQ VLPGQLSVKL WYDKVGHQLI VNVLQATDLP ARVDGRPRNP
     781 YVKMYFLPDR SDKSKRRTKT VKKILEPKWN QTFVYSHVHR RDFRERMLEI TVWDQPRVQE
     841 EESEFLGEIL IELETALLDD EPHWYKLQTH DESSLPLPQP SPFMPRRHIH GESSSKKLQR
     901 SQRISDSDIS DYEVDDGIGV VPPVGYRSSA RESKSTTLTV PEQQRTTHHR SRSVSPHRGN
     961 DQGKPRSRLP NVPLQRSLDE IHPTRRSRSP TRHHDASRSP VDHRTRDVDS QYLSEQDSEL
    1021 LMLPRAKRGR SAECLHTTRH LVRHYKTLPP KMPLLQSSSH WNIYSSILPA HTKTKSVTRQ
    1081 DISLHHECFN STVLRFTDEI LVSELQPFLD RARSASTNCL RPDTSLHSPE RERGRWSPSL
    1141 DRRRPPSPRI QIQHASPEND RHSRKSERSS IQKQTRKGTA SDAERVLPTC LSRRGHAAPR
    1201 ATDQPVIRGK HPARSRSSEH SSIRTLCSMH HLVPGGSAPP SPLLTRMHRQ RSPTQSPPAD
    1261 TSFSSRRGRQ LPQVPVRSGS IEQASLVVEE RTRQMKMKVH RFKQTTGSGS SQELDREQYS
    1321 KYNIHKDQYR SCDNVSAKSS DSDVSDVSAI SRTSSASRLS STSFMSEQSE RPRGRISSFT
    1381 PKMQGRRMGT SGRSIMKSTS VSGEMYTLEH NDGSQSDTAV GTVGAGGKKR RSSLSAKVVA
    1441 IVSRRSRSTS QLSQTESGHK KLKSTIQRST ETGMAAEMRK MVRQPSREST DGSINSYSSE
    1501 GNLIFPGVRL GADSQFSDFL DGLGPAQLVG RQTLATPAMG DIQIGMEDKK GQLEVEVIRA
    1561 RSLTQKPGSK STPAPYVKVY LLENGACIAK KKTRIARKTL DPLYQQSLVF DESPQGKVLQ
    1621 VIVWGDYGRM DHKCFMGVAQ ILLEELDLSS MVIGWYKLFP PSSLVDPTLT PLTRRASQSS
    1681 LESSTGPPCI RS
>gi|34395763|sp|Q86UR5.1|RIMS1_HUMAN RecName: Full=Regulating synaptic
membrane exocytosis protein 1; AltName: Full=Rab3-interacting molecule 1;
Short=RIM 1
MSSAVGPRGPRPPTVPPPMQELPDLSHLTEEERNIIMAVMDRQKEEEEKEEAMLKCVVRDMAKPAACKTP
RNAENQPHQPSPRLHQQFESYKEQVRKIGEEARRYQGEHKDDAPTCGICHKTKFADGCGHLCSYCRTKFC
ARCGGRVSLRSNNEDKVVMWVCNLCRKQQEILTKSGAWFFGSGPQQTSQDGTLSDTATGAGSEVPREKKA
RLQERSRSQTPLSTAAASSQDAAPPSAPPDRSKGAEPSQQALGPEQKQASSRSRSEPPRERKKTPGLSEQ
NGKGALKSERKRVPKTSAQPVEGAVEERERKERRESRRLEKGRSQDYPDTPEKRDEGKAADEEKQRKEED
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YQTRYRSDPNLARYPVKPPPEEQQMRMHARVSRARHERRHSDVALPRTEAGAALPEGKAGKRAPAAARAS
PPDSPRAYSAERTAETRAPGAKQLTNHSPPAPRHGPVPAEAPELKAQEPLRKQSRLDPSSAVLMRKAKRE
KVETMLRNDSLSSDQSESVRPSPPKPHRSKRGGKKRQMSVSSSEEEGVSTPEYTSCEDVELESESVSEKG
DLDYYWLDPATWHSRETSPISSHPVTWQPSKEGDRLIGRVILNKRTTMPKDSGALLGLKVVGGKMTDLGR
LGAFITKVKKGSLADVVGHLRAGDEVLEWNGKPLPGATNEEVYNIILESKSEPQVEIIVSRPIGDIPRIP
ESSHPPLESSSSSFESQKMERPSISVISPTSPGALKDAPQVLPGQLSVKLWYDKVGHQLIVNVLQATDLP
ARVDGRPRNPYVKMYFLPDRSDKSKRRTKTVKKILEPKWNQTFVYSHVHRRDFRERMLEITVWDQPRVQE
EESEFLGEILIELETALLDDEPHWYKLQTHDESSLPLPQPSPFMPRRHIHGESSSKKLQRSQRISDSDIS
DYEVDDGIGVVPPVGYRSSARESKSTTLTVPEQQRTTHHRSRSVSPHRGNDQGKPRSRLPNVPLQRSLDE
IHPTRRSRSPTRHHDASRSPVDHRTRDVDSQYLSEQDSELLMLPRAKRGRSAECLHTTRHLVRHYKTLPP
KMPLLQSSSHWNIYSSILPAHTKTKSVTRQDISLHHECFNSTVLRFTDEILVSELQPFLDRARSASTNCL
RPDTSLHSPERERGRWSPSLDRRRPPSPRIQIQHASPENDRHSRKSERSSIQKQTRKGTASDAERVLPTC
LSRRGHAAPRATDQPVIRGKHPARSRSSEHSSIRTLCSMHHLVPGGSAPPSPLLTRMHRQRSPTQSPPAD
TSFSSRRGRQLPQVPVRSGSIEQASLVVEERTRQMKMKVHRFKQTTGSGSSQELDREQYSKYNIHKDQYR
SCDNVSAKSSDSDVSDVSAISRTSSASRLSSTSFMSEQSERPRGRISSFTPKMQGRRMGTSGRSIMKSTS
VSGEMYTLEHNDGSQSDTAVGTVGAGGKKRRSSLSAKVVAIVSRRSRSTSQLSQTESGHKKLKSTIQRST
ETGMAAEMRKMVRQPSRESTDGSINSYSSEGNLIFPGVRLGADSQFSDFLDGLGPAQLVGRQTLATPAMG
DIQIGMEDKKGQLEVEVIRARSLTQKPGSKSTPAPYVKVYLLENGACIAKKKTRIARKTLDPLYQQSLVF
DESPQGKVLQVIVWGDYGRMDHKCFMGVAQILLEELDLSSMVIGWYKLFPPSSLVDPTLTPLTRRASQSS
LESSTGPPCIRS
```

References to 14-3-3 binding (see RIMS2)

Human RIMS2 Regulating synaptic membrane exocytosis protein 2 (Rab3-interacting molecule 2) (RIM 2)
Swissprot = Q9UQ26)

```
       1 MSAPVGPRGR LAPIPAASQP PLQPEMPDLS HLTEEERKII LAVMDRQKKK VKEEHKPQLT
      61 QWFPFSGITE LVNNVLQPQQ KQQNEKEPQT KLHQQFEMYK EQVKKMGEES QQQQEQKGDA
     121 PTCGICHKTK FADGCGHNCS YCQTKFCARC GGRVSLRSNK VMWVCNLCRK QQEILTKSGA
     181 WFYNSGSNTP QQPDQKVLRG LRNEEAPQEK KPKLHEQTQF QGPSGDLSVP AVEKSRSHGL
     241 TRQHSIKNGS GVKHHIASDI ASDRKRSPSV SRDQNRRYDQ REEREEYSQY ATSDTAMPRS
     301 PSDYADRRSQ HEPQFYEDSD HLSYRDSNRR SHRHSKEYIV DDEDVESRDE YERQRREEEY
     361 QSRYRsDPNL ARYPVKPQPY EEQMRIHAEV SRARHERRHS DVSLANADLE DSRISMLRMD
     421 RPSRQRSISE RRAAMENQRS YSMERTREAQ GPSSYAQRTT NHSPPTPRRS PLPIDRPDLR
     481 RTDSLRKQHH LDPSSAVRKT KREKMETMLR NDSLSSDQSE SVRPPPPKPH KSKKGGKMRQ
     541 ISLSSSEEEL ASTPEYTSCD DVEIESESVS EKGDSQKGKR KTSEQAVLSD SNTRSERQKE
     601 MMYFGGHSLE EDLEWSEPQI KDSGVDTCSS TTLNEEHSHS DKHPVTWQPS KDGDRLIGRI
     661 LLNKRLKDGS VPRDSGAMLG LKVVGGKMTE SGRLCAFITK VKKGSLADTV GHLRPGDEVL
     721 EWNGRLLQGA TFEEVYNIIL ESKPEPQVEL VVSRPIGDIP RIPDSTHAQL ESSSSSFESQ
     781 KMDRPSISVT SPMSPGMLRD VPQFLSGQLS IKLWFDKVGH QLIVTILGAK DLPSREDGRP
     841 RNPYVKIYFL PDRSDKNKRR TKTVKKTLEP KWNQTFIYSP VHRREFRERM LEITLWDQAR
     901 VREEESEFLG EILIELETAL LDDEPHWYKL QTHDVSSLPL PHPSPYMPRR QLHGESPTRR
     961 LQRSKRISDS EVSDYDCDDG IGVVSDYRHD GRDLQSSTLS VPEQVMSSNH CSPSGSPHRV
    1021 DVIGRTRSWS PSVPPPQSRN VEQGLRGTRT MTGHYNTISR MDRHRVMDDH YSPDRDRDCE
    1081 AADRQPYHRS RSTEQRPLLE RTTTRSRSTE RPDTNLMRSM PSLMTGRSAP PSPALSRSHP
    1141 RTGSVQTSPS STPVAGRRGR QLPQLPPKGT LDRKAGGKKL RSTVQRSTET GLAVEMRNWM
    1201 TRQASRESTD GSMNSYSSEG NLIFPGVRLA SDSQFSDFLD GLGPAQLVGR QTLATPAMGD
    1261 IQVGMMDKKG QLEVEIIRAR GLVVKPGSKT LPAPYVKVYL LDNGVCIAKK KTKVARKTLE
    1321 PLYQQLLSFE ESPQGKVLQI IVWGDYGRMD HKSFMGVAQI LLDELELSNM VIGWFKLFPP
    1381 SSLVDPTLAP LTRRASQSSL ESSTGPSYSR S
```

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>gi|41019522|sp|Q9UQ26.2|RIMS2_HUMAN RecName: Full=Regulating synaptic
membrane exocytosis protein 2; AltName: Full=Rab3-interacting molecule 2;
Short=RIM 2
MSAPVGPRGRLAPIPAASQPPLQPEMPDLSHLTEEERKIILAVMDRQKKKVKEEHKPQLTQWFPFSGITE
LVNNVLQPQQKQQNEKEPQTKLHQQFEMYKEQVKKMGEESQQQQEQKGDAPTCGICHKTKFADGCGHNCS
YCQTKFCARCGGRVSLRSNKVMWVCNLCRKQQEILTKSGAWFYNSGSNTPQQPDQKVLRGLRNEEAPQEK
KPKLHEQTQFQGPSGDLSVPAVEKSRSHGLTRQHSIKNGSGVKHHIASDIASDRKRSPSVSRDQNRRYDQ
REEREEYSQYATSDTAMPRSPSDYADRRSQHEPQFYEDSDHLSYRDSNRRSHRHSKEYIVDDEDVESRDE
YERQRREEEYQSRYRSDPNLARYPVKPQPYEEQMRIHAEVSRARHERRHSDVSLANADLEDSRISMLRMD
RPSRQRSISERRAAMENQRSYSMERTREAQGPSSYAQRTTNHSPPTPRRSPLPIDRPDLRRTDSLRKQHH
LDPSSAVRKTKREKMETMLRNDSLSSDQSESVRPPPPKPHKSKKGGKMRQISLSSSEEELASTPEYTSCD
DVEIESESVSEKGDSQKGKRKTSEQAVLSDSNTRSERQKEMMYFGGHSLEEDLEWSEPQIKDSGVDTCSS
TTLNEEHSHSDKHPVTWQPSKDGDRLIGRILLNKRLKDGSVPRDSGAMLGLKVVGGKMTESGRLCAFITK
VKKGSLADTVGHLRPGDEVLEWNGRLLQGATFEEVYNIILESKPEPQVELVVSRPIGDIPRIPDSTHAQL
ESSSSSFESQKMDRPSISVTSPMSPGMLRDVPQFLSGQLSIKLWFDKVGHQLIVTILGAKDLPSREDGRP
RNPYVKIYFLPDRSDKNKRRTKTVKKTLEPKWNQTFIYSPVHRREFRERMLEITLWDQARVREEESEFLG
EILIELETALLDDEPHWYKLQTHDVSSLPLPHPSPYMPRRQLHGESPTRRLQRSKRISDSEVSDYDCDDG
IGVVSDYRHDGRDLQSSTLSVPEQVMSSNHCSPSGSPHRVDVIGRTRSWSPSVPPPQSRNVEQGLRGTRT
MTGHYNTISRMDRHRVMDDHYSPDRDRDCEAADRQPYHRSRSTEQRPLLERTTTRSRSTERPDTNLMRSM
PSLMTGRSAPPSPALSRSHPRTGSVQTSPSSTPVAGRRGRQLPQLPPKGTLDRKAGGKKLRSTVQRSTET
GLAVEMRNWMTRQASRESTDGSMNSYSSEGNLIFPGVRLASDSQFSDFLDGLGPAQLVGRQTLATPAMGD
IQVGMMDKKGQLEVEIIRARGLVVKPGSKTLPAPYVKVYLLDNGVCIAKKKTKVARKTLEPLYQQLLSFE
ESPQGKVLQIIVWGDYGRMDHKSFMGVAQILLDELELSNMVIGWFKLFPPSSLVDPTLAPLTRRASQSSL
ESSTGPSYSRS
```

Notes

Two groups have found that forms of RIM1 bind to 14-3-3 (Simsek-Duran et al 2004 and Kaeser et al 2008). Also see a separate entry for RIM2, encoded by a different gene, which has been reported to be a 14-3-3 binding protein by Sun et al (2003).

Kaeser et al (2008) report the 14-3-3-binding site to be RRHpS^{413}DVAL (Ser391 in Q86UR5), which is a site

phosphorylated by PKA, and 14-3-3 binding was tested by mutagenesis and with truncation mutants. They also say that the serine-413 phosphorylation site of RIM1α is conserved in RIM2α.
The S287A (RSR(pS287)EP), but not the S379A (RYR(pS379)DP) mutation reduced the Rim1–14-3-3 interaction, and RSR(pS241)QTP mutation further reduced the 14-3-3 binding. These findings indicate that 14-3-3 interacts with N-terminal Rim1 through two phosphorylated serines, Ser241 and Ser287 (Sun et al 2003).
Defects in RIMS1 may be a cause of cone-rod dystrophy type 7 (CORD7) [MIM:603649].

Rim2 is encoded by a different gene from RIM1, and contains a potential consensus site for 14-3-3 binding, RYRS335DP, and another site that has similarities to a consensus site, RSPS238VS. Binding to 14-3-3 was strongly reduced by the S335A mutation, whereas no change swas observed for the S238A mutation (Sun et al 2003). The Ser335 in Sun et al (2003) is equivalent to Ser366 in Q9UQ26.

References to 14-3-3 binding to RIMS1 and RIMS2

Kaeser PS, Kwon HB, Blundell J, Chevaleyre V, Morishita W, Malenka RC, Powell CM, Castillo PE, Südhof TC. RIM1alpha phosphorylation at serine-413 by protein kinase A is not required for presynaptic long-term plasticity or learning. Proc Natl Acad Sci U S A. 2008 Sep 23;105(38):14680-5.

Simsek-Duran F, Linden DJ, Lonart G. Adapter protein 14-3-3 is required for a presynaptic form of LTP in the cerebellum. Nat Neurosci. 2004 Dec;7(12):1296-8

Sun L, Bittner MA, Holz RW. Rim, a component of the presynaptic active zone and modulator of exocytosis, binds 14-3-3 through its N terminus. J Biol Chem. 2003 Oct 3;278(40):38301-9.

Human Rin1 Ras and Rab interactor 1 (RAS effector/interference protein 1) (Swissprot = Q13671)

```
        1 MESPGESGAG SPGAPSPSSF TTGHLAREKP AQDPLYDVPN ASGGQAGGPQ RPGRVVSLRE
       61 RLLLTRPVWL QLQANAAAAL HMLRTEPPGT FLVRKSNTRQ CQALCMRLPE ASGPSFVSSH
      121 YILESPGGVS LEGSELMFPD LVQLICAYCH TRDILLLPLQ LPRAIHHAAT HKELEAISHL
      181 GIEFWSSSLN IKAQRGPAGG PVLPQLKARS PQELDQGTGA ALCFFNPLFP GDLGPTKREK
      241 FKRSFKVRVS TETSSPLSPP AVPPPPVPVL PGAVPSQTER LPPCQLLRRE SSVGYRVPAG
      301 SGPSLPPMPS LQEVDCGSPS SSEEEGVPGS RGSPATSPHL GRRRPLLRSM sAAFCSLLAP
      361 ERQVGRAAAA LMQDRHTAAG QLVQDLLTQV RAGPEPQELQ GIRQALSRAR AMLSAELGPE
      421 KLLSPKRLEH VLEKSLHCSV LKPLRPILAA RLRRRLAADG SLGRLAEGLR LARAQGPGAF
      481 GSHLSLPSPV ELEQVRQKLL QLLRTYSPSA QVKRLLQACK LLYMALRTQE GEGAGADEFL
      541 PLLSLVLAHC DLPELLLEAE YMSELLEPSL LTGEGGYYLT SLSASLALLS GLGQAHTLPL
      601 SPVQELRRSL SLWEQRRLPA THCFQHLLRV AYQDPSSGCT SKTLAVPPEA SIATLNQLCA
      661 TKFRVTQPNT FGLFLYKEQG YHRLPPGALA HRLPTTGYLV YRRAEWPETQ GAVTEEEGSG
      721 QSEARSRGEE QGCQGDGDAG VKASPRDIRE QSETTAEGGQ GQAQEGPAQP GEPEAEGSRA
      781 AEE
>gi|116242760|sp|Q13671.4|RIN1_HUMAN RecName: Full=Ras and Rab interactor 1;
AltName: Full=Ras interaction/interference protein 1; AltName: Full=Ras
inhibitor JC99
MESPGESGAGSPGAPSPSSFTTGHLAREKPAQDPLYDVPNASGGQAGGPQRPGRVVSLRERLLLTRPVWL
QLQANAAAALHMLRTEPPGTFLVRKSNTRQCQALCMRLPEASGPSFVSSHYILESPGGVSLEGSELMFPD
LVQLICAYCHTRDILLLPLQLPRAIHHAATHKELEAISHLGIEFWSSSLNIKAQRGPAGGPVLPQLKARS
PQELDQGTGAALCFFNPLFPGDLGPTKREKFKRSFKVRVSTETSSPLSPPAVPPPPVPVLPGAVPSQTER
LPPCQLLRRESSVGYRVPAGSGPSLPPMPSLQEVDCGSPSSSEEEGVPGSRGSPATSPHLGRRRPLLRSM
SAAFCSLLAPERQVGRAAAALMQDRHTAAGQLVQDLLTQVRAGPEPQELQGIRQALSRARAMLSAELGPE
KLLSPKRLEHVLEKSLHCSVLKPLRPILAARLRRRLAADGSLGRLAEGLRLARAQGPGAFGSHLSLPSPV
ELEQVRQKLLQLLRTYSPSAQVKRLLQACKLLYMALRTQEGEGAGADEFLPLLSLVLAHCDLPELLLEAE
YMSELLEPSLLTGEGGYYLTSLSASLALLSGLGQAHTLPLSPVQELRRSLSLWEQRRLPATHCFQHLLRV
AYQDPSSGCTSKTLAVPPEASIATLNQLCATKFRVTQPNTFGLFLYKEQGYHRLPPGALAHRLPTTGYLV
YRRAEWPETQGAVTEEEGSGQSEARSRGEEQGCQGDGDAGVKASPRDIREQSETTAEGGQGQAQEGPAQP
GEPEAEGSRAAEE
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Notes

RSM(pS351)AA

References to 14-3-3 binding to RIN1

Wang Y, Waldron RT, Dhaka A, Patel A, Riley MM, Rozengurt E, Colicelli J. The RAS effector RIN1 directly competes with RAF and is regulated by 14-3-3 proteins. Mol Cell Biol. 2002 Feb;22(3):916-26.

Senda K, Goi T, Hirono Y, Katayama K, Yamaguchi A. Analysis of RIN1 gene expression in colorectal cancer. Oncol Rep. 2007 May;17(5):1171-5.

Tall GG, Barbieri MA, Stahl PD, Horazdovsky BF. Ras-activated endocytosis is mediated by the Rab5 guanine nucleotide exchange activity of RIN1. Dev Cell. 2001 Jul;1(1):73-82.

Han L, Wong D, Dhaka A, Afar D, White M, Xie W, Herschman H, Witte O, Colicelli J. Protein binding and signaling properties of RIN1 suggest a unique effector function. Proc Natl Acad Sci U S A. 1997 May 13;94(10):4954-9.

Fujioka M, Goi T, Hirono Y, Katayama K, Yamaguchi A. Cloning of a novel splicing variant of RIN1 and its expression in gastric and colon cancer. Oncol Res. 2009;17(11-12):593-9.

Human RNF11 RING finger protein 11 (Swissprot = Q9Y3C5)

```
        1 MGNCLKSPTS DDISLLHESQ SDRASFGEGT EPDQEPPPPY QEQVPVPVYH PTPSQTRLAT
       61 QLTEEEQIRI AQRIGLIQHL PKGVYDPGRD GSEKKIRECV ICMMDFVYGD PIRFLPCMHI
      121 YHLDCIDDWL MRSFtCPSCM EPVDAALLSS YETN
>gi|21362884|sp|Q9Y3C5.1|RNF11_HUMAN RecName: Full=RING finger protein 11;
AltName: Full=Sid 1669
MGNCLKSPTSDDISLLHESQSDRASFGEGTEPDQEPPPPYQEQVPVPVYHPTPSQTRLATQLTEEEQIRI
AQRIGLIQHLPKGVYDPGRDGSEKKIRECVICMMDFVYGDPIRFLPCMHIYHLDCIDDWLMRSFTCPSCM
EPVDAALLSSYETN
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Notes

Component of a biquitin-editing protein complex, comprising also TNFAIP3, ITCH and TAX1BP1, that ensures the transient nature of inflammatory signaling pathways. Interacts with several E2 and E3 ubiquitin ligases.
“RNF11 contains an (AKT) phosphorylation site (T135) that is situated within a 14-3-3 binding domain.”
phosphorylation of RNF11 by AKT either causes its nuclear localization or induces degradation of cytoplasmic

RNF11. In addition, T135E RNF11, which does not bind 14-3-3 and is not phosphorylated by AKT, causes a greater enhancement of transforming growth factor-beta signaling than wild-type RNF11.

References to 14-3-3 binding to RNF11

Connor MK, Azmi PB, Subramaniam V, Li H, Seth A. Molecular characterization of ring finger protein 11. Mol Cancer Res. 2005 Aug;3(8):453-61

Azmi P, Seth A. RNF11 is a multifunctional modulator of growth factor receptor signalling and transcriptional regulation. Eur J Cancer. 2005 Nov;41(16):2549-60

Human RPH3A Rabphilin3 (Swissprot = Q9Y2J0)

```
        1 MTDTVFSNSS NRWMYPSDRP LQSNDKEQLQ AGWSVHPGGQ PDRQRKQEEL TDEEKEIINR
       61 VIARAEKMEE MEQERIGRLV DRLENMRKNV AGDGVNRCIL CGEQLGMLGS ACVVCEDCKK
      121 NVCTKCGVET NNRLHSVWLC KICIEQREVW KRSGAWFFKG FPKQVLPQPM PIKKTKPQQP
      181 VSEPAAPEQP APEPKHPARA PARGDSEDRR GPGQKTGPDP ASAPGRGNYG PPVRRASEAR
      241 MSSSSRDSES WDHSGGAGDS SRSPAGLRRA NsVQASRPAP GSVQSPAPPQ PGQPGTPGGS
      301 RPGPGPAGRF PDQKPEVAPS DPGTTAPPRE ERTGGVGGYP AVGAREDRMS HPSGPYSQAS
      361 AAAPQPAAAR QPPPPEEEEE EANSYDSDEA TTLGALEFSL LYDQDNSSLQ CTIIKAKGLK
      421 PMDSNGLADP YVKLHLLPGA SKSNKLRTKT LRNTRNPIWN ETLVYHGITD EDMQRKTLRI
      481 SVCDEDKFGH NEFIGETRFS LKKLKPNQRK NFNICLERVI PMKRAGTTGS ARGMALYEEE
      541 QVERVGDIEE RGKILVSLMY STQQGGLIVG IIRCVHLAAM DANGYSDPFV KLWLKPDMGK
      601 KAKHKTQIKK KTLNPEFNEE FFYDIKHSDL AKKSLDISVW DYDIGKSNDY IGGCQLGISA
      661 KGERLKHWYE CLKNKDKKIE RWHQLQNENH VSSD
>gi|13878745|sp|Q9Y2J0.1|RP3A_HUMAN RecName: Full=Rabphilin-3A; AltName:
Full=Exophilin-1
MTDTVFSNSSNRWMYPSDRPLQSNDKEQLQAGWSVHPGGQPDRQRKQEELTDEEKEIINRVIARAEKMEE
MEQERIGRLVDRLENMRKNVAGDGVNRCILCGEQLGMLGSACVVCEDCKKNVCTKCGVETNNRLHSVWLC
KICIEQREVWKRSGAWFFKGFPKQVLPQPMPIKKTKPQQPVSEPAAPEQPAPEPKHPARAPARGDSEDRR
GPGQKTGPDPASAPGRGNYGPPVRRASEARMSSSSRDSESWDHSGGAGDSSRSPAGLRRANSVQASRPAP
GSVQSPAPPQPGQPGTPGGSRPGPGPAGRFPDQKPEVAPSDPGTTAPPREERTGGVGGYPAVGAREDRMS
HPSGPYSQASAAAPQPAAARQPPPPEEEEEEANSYDSDEATTLGALEFSLLYDQDNSSLQCTIIKAKGLK
PMDSNGLADPYVKLHLLPGASKSNKLRTKTLRNTRNPIWNETLVYHGITDEDMQRKTLRISVCDEDKFGH
NEFIGETRFSLKKLKPNQRKNFNICLERVIPMKRAGTTGSARGMALYEEEQVERVGDIEERGKILVSLMY
STQQGGLIVGIIRCVHLAAMDANGYSDPFVKLWLKPDMGKKAKHKTQIKKKTLNPEFNEEFFYDIKHSDL
AKKSLDISVWDYDIGKSNDYIGGCQLGISAKGERLKHWYECLKNKDKKIERWHQLQNENHVSSD
```

Notes

"Ser-234 and Ser-274 in Rabphilin3 are residues whose phosphorylation and dephosphorylation have been demonstrated to be dynamically regulated during high K+-induced membrane depolarization. Neither site (RRAS234EA and RANS274VQ, respectively) is a typical 14-3-3 binding motif. Mutant constructs with Ser->Ala mutations were tested for their ability to bind 14-3-3 in vitro. The S274A mutation but not the S234A mutation disrupted the interaction. (Sun et al 2003). The Ser274 pinpointed by Sun et al (2003) (species?) corresponds to Ser272 in Q9Y2J0.

References to 14-3-3 binding to Rabphilin3

Sun L, Bittner MA, Holz RW. Rim, a component of the presynaptic active zone and modulator of exocytosis, binds 14-3-3 through its N terminus. J Biol Chem. 2003 Oct 3;278(40):38301-9.

Human SASH1 Sterile alpha motif and SH3 domain containing 1 (Swissprot = O94885)

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        1 MEDAGAAGPG PEPEPEPEPE PEPAPEPEPE PKPGAGTSEA FSRLWTDVMG ILDGSLGNID
       61 DLAQQYADYY NTCFSDVCER MEELRKKRRVs QDLEVEKPDA SPTSLQLRSQ IEESLGFCSA
      121 VSTPEVERKN PLHKSNSEDS SVGKGDWKKK NKYFWQNFRK NQKGIMRQTS KGEDVGYVAS
      181 EITMSDEERI QLMMMVKEKM ITIEEALARL KEYEAQHRQS AALDPADWPD GSYPTFDGSS
      241 NCNSREQSDD ETEESVKFKR LHKLVNSTRR VRKKLIRVEE MKKPSTEGGE EHVFENSPVL
      301 DERSALYSGV HKKPLFFDGS PEKPPEDDSD SLTTSPSSSS LDTWGAGRKL VKTFSKGESR
      361 GLIKPPKKMG TFFSYPEEEK AQKVSRSLTE GEMKKGLGSL SHGRTCSFGG FDLTNRSLHV
      421 GSNNSDPMGK EGDFVYKEVI KSPTASRISL GKKVKSVKET MRKRMSKKYS SSVSEQDSGL
      481 DGMPGSPPPS QPDPEHLDKP KLKAGGSVES LRSSLSGQSS MSGQTVSTTD SSTSNRESVK
      541 SEDGDDEEPP YRGPFCGRAR VHTDFTPSPY DTDSLKLKKG DIIDIISKPP MGTWMGLLNN
      601 KVGTFKFIYV DVLSEDEEKP KRPTRRRRKG RPPQPKSVED LLDRINLKEH MPTFLFNGYE
      661 DLDTFKLLEE EDLDELNIRD PEHRAVLLTA VELLQEYDSN SDQSGSQEKL LVDSQGLSGC
      721 SPRDSGCYES SENLENGKTR KASLLSAKSS TEPSLKSFSR NQLGNYPTLP LMKSGDALKQ
      781 GQEEGRLGGG LAPDTSKSCD PPGVTGLNKN RRSLPVSICR SCETLEGPQT VDTWPRSHSL
      841 DDLQVEPGAE QDVPTEVTEP PPQIVPEVPQ KTTASSTKAQ PLEQDSAVDN ALLLTQSKRF
      901 SEPQKLTTKK LEGSIAASGR GLSPPQCLPR NYDAQPPGAK HGLARTPLEG HRKGHEFEGT
      961 HHPLGTKEGV DAEQRMQPKI PSQPPPVPAK KSRERLANGL HPVPMGPSGA LPSPDAPCLP
     1021 VKRGSPASPT SPSDCPPALA PRPLSGQAPG SPPSTRPPPW LSELPENTSL QEHGVKLGPA
     1081 LTRKVSCARG VDLETLTENK LHAEGIDLTE EPYSDKHGRC GIPEALVQRY AEDLDQPERD
     1141 VAANMDQIRV KQLRKQHRMA IPSGGLTEIC RKPVSPGCIS SVSDWLISIG LPMYAGTLST
     1201 AGFSTLSQVP SLSHTCLQEA GITEERHIRK LLSAARLFKL PPGPEAM
>gi|145559526|sp|O94885.3|SASH1_HUMAN RecName: Full=SAM and SH3 domain-
containing protein 1; AltName: Full=Proline-glutamate repeat-containing
protein
MEDAGAAGPGPEPEPEPEPEPEPAPEPEPEPKPGAGTSEAFSRLWTDVMGILDGSLGNIDDLAQQYADYY
NTCFSDVCERMEELRKKRRVSQDLEVEKPDASPTSLQLRSQIEESLGFCSAVSTPEVERKNPLHKSNSEDS
SVGKGDWKKKNKYFWQNFRKNQKGIMRQTSKGEDVGYVASEITMSDEERIQLMMMVKEKMITIEEALARL
KEYEAQHRQSAALDPADWPDGSYPTFDGSSNCNSREQSDDETEESVKFKRLHKLVNSTRRVRKKLIRVEE
MKKPSTEGGEEHVFENSPVLDERSALYSGVHKKPLFFDGSPEKPPEDDSDSLTTSPSSSSLDTWGAGRKL
VKTFSKGESRGLIKPPKKMGTFFSYPEEEKAQKVSRSLTEGEMKKGLGSLSHGRTCSFGGFDLTNRSLHV
GSNNSDPMGKEGDFVYKEVIKSPTASRISLGKKVKSVKETMRKRMSKKYSSSVSEQDSGLDGMPGSPPPS
QPDPEHLDKPKLKAGGSVESLRSSLSGQSSMSGQTVSTTDSSTSNRESVKSEDGDDEEPPYRGPFCGRAR
VHTDFTPSPYDTDSLKLKKGDIIDIISKPPMGTWMGLLNNKVGTFKFIYVDVLSEDEEKPKRPTRRRRKG
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RPPQPKSVEDLLDRINLKEHMPTFLFNGYEDLDTFKLLEEEDLDELNIRDPEHRAVLLTAVELLQEYDSN SDQSGSQEKLLVDSQGLSGCSPRDSGCYESSENLENGKTRKASLLSAKSSTEPSLKSFSRNQLGNYPTLP LMKSGDALKQGQEEGRLGGGLAPDTSKSCDPPGVTGLNKNRRSLPVSICRSCETLEGPQTVDTWPRSHSL DDLQVEPGAEQDVPTEVTEPPPQIVPEVPQKTTASSTKAQPLEQDSAVDNALLLTQSKRFSEPQKLTTKK LEGSIAASGRGLSPPQCLPRNYDAQPPGAKHGLARTPLEGHRKGHEFEGTHHPLGTKEGVDAEQRMQPKI PSQPPPVPAKKSRERLANGLHPVPMGPSGALPSPDAPCLPVKRGSPASPTSPSDCPPALAPRPLSGQAPG SPPSTRPPPWLSELPENTSLQEHGVKLGPALTRKVSCARGVDLETLTENKLHAEGIDLTEEPYSDKHGRC GIPEALVQRYAEDLDQPERDVAANMDQIRVKQLRKQHRMAIPSGGLTEICRKPVSPGCISSVSDWLISIG LPMYAGTLSTAGFSTLSQVPSLSHTCLQEAGITEERHIRKLLSAARLFKLPPGPEAM **Notes** RKRRV(PS90)QD provides on of the 14-3-3-binding sites on this protein. **References to 14-3-3 binding to SASH1** Dubois F, Vandermoere F, Gernez A, Murphy J, Toth R, Chen S, Geraghty KM, Morrice NA and MacKintosh C (2009) Differential 14-3-3-affinity capture reveals new downstream targets of PI 3-kinase signaling (Epub 2009 Aug 1)	
Human SH3BP2 SH3-domain binding protein 2 (Swissprot = P78314) 1 MAAEEMHWPV PMKAIGAQNL LTMPGGVAKA GYLHKKGGTQ LQLLKWPLRF VIIHKRCVYY 61 FKSSTSASPQ GAFSLSGYNR VMRAAEETTS NNVFPFKIIH ISKKHRTWFF SASSEEERKS 121 WMALLRREIG HFHEKKDLPL DTSDSSSDTD SFYGAVERPV DISLSPYPTD NEDYEHDDED 181 DSYLEPDSPE PGRLEDALMH PPAYPPPPVP TPRKPAFSDM PRAHsFTSKG PGPLLPPPPP 241 KHGLPDVGLA AEDSKRDPLC PRRAEPCPRV PATPRRMsDP PLSTMPTAPG LRKPPCFRES 301 ASPSPEPWTP GHGACSTSSA AIMATATSRN CDKLKSFHLS PRGPPTSEPP PVPANKPKFL 361 KIAEEDPPRE AAMPGLFVPP VAPRPPALKL PVPEAMARPA VLPRPEKPQL PHLQRSPPDG 421 QSFRSFSFEK PRQPSQADTG GDDSDEDYEK VPLPNSVFVN TTESCEVERL FKATSPRGEP 481 QDGLYCIRNS STKSGKVLVV WDETSNKVRN YRIFEKDSKF YLEGEVLFVS VGSMVEHYHT 541 HVLPSHQSLL LRHPYGYTGP R >gi|3023207|sp|P78314.2|3BP2_HUMAN RecName: Full=SH3 domain-binding protein 2; Short=3BP-2 MAAEEMHWPVPMKAIGAQNLLTMPGGVAKAGYLHKKGGTQLQLLKWPLRFVIIHKRCVYYFKSSTSASPQ GAFSLSGYNRVMRAAEETTSNNVFPFKIIHISKKHRTWFFSASSEEERKSWMALLRREIGHFHEKKDLPL DTSDSSSDTDSFYGAVERPVDISLSPYPTDNEDYEHDDEDDSYLEPDSPEPGRLEDALMHPPAYPPPPVP TPRKPAFSDMPRAHSFTSKGPGPLLPPPPPKHGLPDVGLAAEDSKRDPLCPRRAEPCPRVPATPRRMSDP PLSTMPTAPGLRKPPCFRESASPSPEPWTPGHGACSTSSAAIMATATSRNCDKLKSFHLSPRGPPTSEPP PVPANKPKFLKIAEEDPPREAAMPGLFVPPVAPRPPALKLPVPEAMARPAVLPRPEKPQLPHLQRSPPDG QSFRSFSFEKPRQPSQADTGGDDSDEDYEKVPLPNSVFVNTTESCEVERLFKATSPRGEPQDGLYCIRNS STKSGKVLVVWDETSNKVRNYRIFEKDSKFYLEGEVLFVSVGSMVEHYHTHVLPSHQSLLLRHPYGYTGP R **Notes** "3BP2 an adaptor protein that binds differentially to the SH3 domains of certain proteins. Links the hemopoietic tyrosine kinase Fes to the cytoplasmic membrane in a phosphorylation dependent manner. Regulates FC-epsilon RI -mediated degranulation in rat basophilic leukemia RBL-2H3 cells. Expressed in a variety of tissues including lung, liver, skeletal muscle, kidney and pancreas. Defects in 3BP2 are the cause of cherubism, an autosomal dominant inherited syndrome characterized by excessive bone degradation of the upper and lower jaws, which often begins around three years of age. It is followed by development of fibrous tissue masses, which causes a characteristic facial swelling. Two differentially spliced isoforms have been described. "Cherubism mice", which carry a gain-of-function mutation in SH3-domain binding protein 2 (Sh3bp2), develop osteoporosis and widespread inflammation dependent on the proinflammatory cytokine, TNF-alpha " PMA and cAMP-elevating agents (PKC and PKA in vitro) lead to phosphorylation of pSer225 and pSer277 (Mutation of Ser277 causes greater loss of 14-3-3 binding) **References to 14-3-3 binding to SH3BP2** Miah SM, Hatani T, Qu X, Yamamura H, Sada K. Point mutations of 3BP2 identified in human-inherited disease cherubism result in the loss of function. Genes Cells. 2004 Nov;9(11):993-1004. Foucault I, Liu YC, Bernard A, Deckert M. The chaperone protein 14-3-3 interacts with 3BP2/SH3BP2 and regulates its adapter function. J Biol Chem. 2003 Feb 28;278(9):7146-53	
Human Shc (p66 form) **Notes** Endogenous 14-3-3 is tyrosine-phosphorylated can interact with the SH2 domain of Shc following cytokine (GM-CSF) stimulation (Barry et al 2009). Endothelin-1 induced phosphorylation and 14-3-3-binding is blocked by PD 98059. The sites were not defined. **References to tyrosine-phosphorylated 14-3-3 binding to p66Shc** Foschi M, Franchi F, Han J, La Villa G, Sorokin A. Endothelin-1 induces serine phosphorylation of the adaptor protein p66Shc and its association with 14-3-3 protein in glomerular mesangial cells. J Biol Chem. 2001 Jul 13;276(28):26640-7. Barry EF, Felquer FA, Powell JA, Biggs L, Stomski FC, Urbani A, Ramshaw H, Hoffmann P, Wilce MC, Grimbaldeston MA, Lopez AF, Guthridge MA. 14-3-3:Shc scaffolds integrate phosphoserine and phosphotyrosine signaling to regulate phosphatidylinositol 3-kinase activation and cell survival. J Biol Chem. 2009 May 1;284(18):12080-90.	NOT IN WEBLOGO.
Human Skp2 S-phase kinase associated protein-2 (Swissprot = Q13309) 1 MHRKHLQEIP DLSSNVATSF TWGWDSSKTS ELLSGMGVSA LEKEEPDSEN IPQELLSNLG 61 HPESPPRKRL KsKGSDKDFV IVRRPKLNRE NFPGVSWDSL PDELLLGIFS CLCLPELLKV 121 SGVCKRWYRL ASDESLWQTL DLTGKNLHPD VTGRLLSQGV IAFRCPRSFM DQPLAEHFSP 181 FRVQHMDLSN SVIEVSTLHG ILSQCSKLQN LSLEGLRLSD PIVNTLAKNS NLVRLNLSGC 241 SGFSEFALQT LLSSCSRLDE LNLSWCFDFT EKHVQVAVAH VSETITQLNL SGYRKNLQKS 301 DLSTLVRRCP NLVHLDLSDS VMLKNDCFQE FFQLNYLQHL SLSRCYDIIP ETLLELGEIP 361 TLKTLQVFGI VPDGTLQLLK EALPHLQINC SHFTTIARPT IGNKKNQEIW GIKCRLTLQK 421 PSCL	

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>gi|37537922|sp|Q13309.2|SKP2_HUMAN RecName: Full=S-phase kinase-associated
protein 2; AltName: Full=F-box protein Skp2; AltName: Full=Cyclin A/CDK2-
associated protein p45; AltName: Full=p45skp2; AltName: Full=F-box/LRR-repeat
protein 1
MHRKHLQEIPDLSSNVATSFTWGWDSSKTSELLSGMGVSALEKEEPDSENIPQELLSNLGHPESPPRKRL
KSKGSDKDFVIVRRPKLNRENFPGVSWDSLPDELLLGIFSCLCLPELLKVSGVCKRWYRLASDESLWQTL
DLTGKNLHPDVTGRLLSQGVIAFRCPRSFMDQPLAEHFSPFRVQHMDLSNSVIEVSTLHGILSQCSKLQN
LSLEGLRLSDPIVNTLAKNSNLVRLNLSGCSGFSEFALQTLLSSCSRLDELNLSWCFDFTEKHVQVAVAH
VSETITQLNLSGYRKNLQKSDLSTLVRRCPNLVHLDLSDSVMLKNDCFQEFFQLNYLQHLSLSRCYDIIP
ETLLELGEIPTLKTLQVFGIVPDGTLQLLKEALPHLQINCSHFTTIARPTIGNKKNQEIWGIKCRLTLQK
PSCL
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Notes

Skp2 is an F-box protein that forms the SCF complex with Skp1 and Cullin-1 to constitute an E3 ligase for ubiquitylation

Lin et al (2009) and Gao et al (2009) found that Ser 72 phosphorylation (SPPRKRLK(pS72)KGSKGS) facilitates Skp2 binding to 14-3-3 proteins. Skp2 cytoplasmic localization required 14-3-3beta2. "It is interesting that although mouse Skp2 lacks Ser 72, most molecular consequences of Akt phosphorylation are also observed in mice, suggesting that the Akt–Skp2 axis is functionally conserved but may use distinct mechanisms."

References to 14-3-3 binding to Skp2

Lin HK, Wang G, Chen Z, Teruya-Feldstein J, Liu Y, Chan CH, Yang WL, Erdjument-Bromage H, Nakayama KI, Nimer S, Tempst P, Pandolfi PP. Phosphorylation-dependent regulation of cytosolic localization and oncogenic function of Skp2 by Akt/PKB. Nat Cell Biol. 2009 Apr;11(4):420-32.

Ecker K, Hengst L. Skp2: caught in the Akt. Nat Cell Biol. 2009 Apr;11(4):377-9.

Gao D, Inuzuka H, Tseng A, Chin RY, Toker A, Wei W. Phosphorylation by Akt1 promotes cytoplasmic localization of Skp2 and impairs APCCdh1-mediated Skp2 destruction. Nat Cell Biol. 2009 Apr;11(4):397-408.

Human SLC9A1(NHE1) NHE1 sodium/hydrogen exchanger 1. (Swissprot = P19634)

```
        1 MVLRSGICGL SPHRIFPSLL VVVALVGLLP VLRSHGLQLS PTASTIRSSE PPRERSIGDV
       61 TTAPPEVTPE SRPVNHSVTD HGMKPRKAFP VLGIDYTHVR TPFEISLWIL LACLMKIGFH
      121 VIPTISSIVP ESCLLIVVGL LVGGLIKGVG ETPPFLQSDV FFLFLLPPII LDAGYFLPLR
      181 QFTENLGTIL IFAVVGTLWN AFFLGGLMYA VCLVGGEQIN NIGLLDNLLF GSIISAVDPV
      241 AVLAVFEEIH INELLHILVF GESLLNDAVT VVLYHLFEEF ANYEHVGIVD IFLGFLSFFV
      301 VALGGVLVGV VYGVIAAFTS RFTSHIRVIE PLFVFLYSYM AYLSAELFHL SGIMALIASG
      361 VVMRPYVEAN ISHKSHTTIK YFLKMWSSVS ETLIFIFLGV STVAGSHHWN WTFVISTLLF
      421 CLIARVLGVL GLTWFINKFR IVKLTPKDQF IIAYGGLRGA IAFSLGYLLD KKHFPMCDLF
      481 LTAIITVIFF TVFVQGMTIR PLVDLLAVKK KQETKRSINE EIHTQFLDHL LTGIEDICGH
      541 YGHHHWKDKL NRFNKKYVKK CLIAGERSKE PQLIAFYHKM EMKQAIELVE SGGMGKIPSA
      601 VSTVSMQNIH PKSLPSERIL PALSKDKEEE IRKILRNNLQ KTRQRLRSYN RHTLVADPYE
      661 EAWNQMLLRR QKARQLEQKI NNYLTVPAHK LDSPTMSRAR IGsDPLAYEP KEDLPVITID
      721 PASPQSPESV DLVNEELKGK VLGLSRDPAK VAEEDEDDDG GIMMRSKETS SPGTDDVFTP
      781 APSDSPSSQR IQRCLSDPGP HPEPGEGEPF FPKGQ
>gi|127809|sp|P19634.2|SL9A1_HUMAN RecName: Full=Sodium/hydrogen exchanger 1;
AltName: Full=Na(+)/H(+) exchanger 1; Short=NHE-1; AltName: Full=Solute
carrier family 9 member 1; AltName: Full=Na(+)/H(+) antiporter, amiloride-
sensitive; AltName: Full=APNH
MVLRSGICGLSPHRIFPSLLVVVALVGLLPVLRSHGLQLSPTASTIRSSEPPRERSIGDVTTAPPEVTPE
SRPVNHSVTDHGMKPRKAFPVLGIDYTHVRTPFEISLWILLACLMKIGFHVIPTISSIVPESCLLIVVGL
LVGGLIKGVGETPPFLQSDVFFLFLLPPIILDAGYFLPLRQFTENLGTILIFAVVGTLWNAFFLGGLMYA
VCLVGGEQINNIGLLDNLLFGSIISAVDPVAVLAVFEEIHINELLHILVFGESLLNDAVTVVLYHLFEEF
ANYEHVGIVDIFLGFLSFFVVALGGVLVGVVYGVIAAFTSRFTSHIRVIEPLFVFLYSYMAYLSAELFHL
SGIMALIASGVVMRPYVEANISHKSHTTIKYFLKMWSSVSETLIFIFLGVSTVAGSHHWNWTFVISTLLF
CLIARVLGVLGLTWFINKFRIVKLTPKDQFIIAYGGLRGAIAFSLGYLLDKKHFPMCDLFLTAIITVIFF
TVFVQGMTIRPLVDLLAVKKKQETKRSINEEIHTQFLDHLLTGIEDICGHYGHHHWKDKLNRFNKKYVKK
CLIAGERSKEPQLIAFYHKMEMKQAIELVESGGMGKIPSAVSTVSMQNIHPKSLPSERILPALSKDKEEE
IRKILRNNLQKTRQRLRSYNRHTLVADPYEEAWNQMLLRRQKARQLEQKINNYLTVPAHKLDSPTMSRAR
IGSDPLAYEPKEDLPVITIDPASPQSPESVDLVNEELKGKVLGLSRDPAKVAEEDEDDDGGIMMRSKETS
SPGTDDVFTPAPSDSPSSQRIQRCLSDPGPHPEPGEGEPFFPKGQ
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Notes

RSK phosphorylated S703 on the C-terminus of NHE1 and the adapter protein 14–3–3 bound to phospho-S703, which increased NHE1 activity.

References to 14-3-3 binding to NHE1

Lehoux S, Abe Ji, Florian JA, Berk BC.14-3-3 Binding to Na+/H+ exchanger isoform-1 is associated with serum-dependent activation of Na+/H+ exchange. J Biol Chem. 2001 May 11;276(19):15794-800.

Maekawa N, Abe J, Shishido T, Itoh S, Ding B, Sharma VK, Sheu SS, Blaxall BC, Berk BC.Inhibiting p90 ribosomal S6 kinase prevents (Na+)-H+ exchanger-mediated cardiac ischemia-reperfusion injury. Circulation. 2006 May 30;113(21):2516-23

Human SLITRK1_HUMAN SLIT- and TRK-like family, member 1 (Swiss-Prot=Q96PX8)

```
        1 MLLWILLLET SLCFAAGNVT GDVCKEKICS CNEIEGDLHV DCEKKGFTSL QRFTAPTSQF
       61 YHLFLHGNSL TRLFPNEFAN FYNAVSLHME NNGLHEIVPG AFLGLQLVKR LHINNNKIKS
      121 FRKQTFLGLD DLEYLQADFN LLRDIDPGAF QDLNKLEVLI LNDNLISTLP ANVFQYVPIT
      181 HLDLRGNRLK TLPYEEVLEQ IPGIAEILLE DNPWDCTCDL LSLKEWLENI PKNALIGRVV
      241 CEAPTRLQGK DLNETTEQDL CPLKNRVDSS LPAPPAQEET FAPGPLPTPF KTNGQEDHAT
      301 PGSAPNGGTK IPGNWQIKIR PTAAIATGSS RNKPLANSLP CPGGCSCDHI PGSGLKMNCN
      361 NRNVSSLADL KPKLSNVQEL FLRDNKIHSI RKSHFVDYKN LILLDLGNNN IATVENNTFK
      421 NLLDLRWLYM DSNYLDTLSR EKFAGLQNLE YLNVEYNAIQ LILPGTFNAM PKLRILILNN
      481 NLLRSLPVDV FAGVSLSKLS LHNNYFMYLP VAGVLDQLTS IIQIDLHGNP WECSCTIVPF
      541 KQWAERLGSE VLMSDLKCET PVNFFRKDFM LLSNDEICPQ LYARISPTLT SHSKNSTGLA
      601 ETGTHSNSYL DTSRVSISVL VPGLLLVFVT SAFTVVGMLV FILRNRKRSK RRDANSSASE
```

661 INSLQTVCDS SYWHNGPYNA DGAHRVYDCG SHSLsD
>gi|46396997|sp|Q96PX8.2|SLIK1_HUMAN RecName: Full=SLIT and NTRK-like protein 1; AltName: Full=Leucine-rich repeat-containing protein 12; Flags: Precursor
MLLWILLLETSLCFAAGNVTGDVCKEKICSCNEIEGDLHVDCEKKGFTSLQRFTAPTSQFYHLFLHGNSL
TRLFPNEFANFYNAVSLHMENNGLHEIVPGAFLGLQLVKRLHINNNKIKSFRKQTFLGLDDLEYLQADFN
LLRDIDPGAFQDLNKLEVLILNDNLISTLPANVFQYVPITHLDLRGNRLKTLPYEEVLEQIPGIAEILLE
DNPWDCTCDLLSLKEWLENIPKNALIGRVVCEAPTRLQGKDLNETTEQDLCPLKNRVDSSLPAPPAQEET
FAPGPLPTPFKTNGQEDHATPGSAPNGGTKIPGNWQIKIRPTAAIATGSSRNKPLANSLPCPGGCSCDHI
PGSGLKMNCNNRNVSSLADLKPKLSNVQELFLRDNKIHSIRKSHFVDYKNLILLDLGNNNIATVENNTFK
NLLDLRWLYMDSNYLDTLSREKFAGLQNLEYLNVEYNAIQLILPGTFNAMPKLRILILNNNLLRSLPVDV
FAGVSLSKLSLHNNYFMYLPVAGVLDQLTSIIQIDLHGNPWECSCTIVPFKQWAERLGSEVLMSDLKCET
PVNFFRKDFMLLSNDEICPQLYARISPTLTSHSKNSTGLAETGTHSNSYLDTSRVSISVLVPGLLLVFVT
SAFTVVGMLVFILRNRKRSKRRDANSSASEINSLQTVCDSSYWHNGPYNADGAHRVYDCGSHSLSD

Notes

A type-I transmembrane protein with an extracellular leucine-rich repeat (LRR) domain homologous to SLIT. Recent studies identified alterations at the SLITRK1 locus in subjects with Tourette syndrome (TS), attention-deficit/hyperactivity disorder (ADHD), and obsessive-compulsive disorder (OCD) symptoms.
Phosphorylation site at serine 695 (Ser695) of SLITRK1, which is phosphorylated by casein kinase II (CK2) and regulates the interaction between SLITRK1 and 14-3-3 proteins. Because Ser695 is both a CK2 substrate and corresponds to a mode 3 motif. Deletion of the six terminal amino acid residues resulted in the complete abolishment of the interaction between purified recombinant 14-3-3 β and SLITRK1. A motif in the carboxyl terminus of the intracellular domain of SLITRK1 (SHSLpSD-COOH) meets criteria for the mode 3 motif. This tail is different in the other gene products (SLITRKs 2 to 6). The tail is conserved in the mouse sequence (Q810C1. Mouse…….DGSHRVYDCG SHSLSD).
Carol note: Direct phosphorylation-dependent interaction of GST-SICD) (form of SLITRK1 with longer cytoplasmic domain) with 14-3-3 demonstrated in vitro.

References to 14-3-3 binding to SLITRK1

Kajiwara Y, Buxbaum JD, Grice DE. SLITRK1 Binds 14-3-3 and Regulates Neurite Outgrowth in a Phosphorylation-Dependent Manner. Biol Psychiatry. 2009 Jul 27. [Epub ahead of print]

Human Snn (Stannin) (Swissprot = O75324)

1 MSIMDHSPTT GVVTVIVILI AIAALGALIL GCWCYLRLQR ISQsEDEESI VGDGETKEPF
61 LLVQYSAKGP CVERKAKLMT PNGPEVHG
>gi|6094313|sp|O75324.1|SNN_HUMAN RecName: Full=Stannin; AltName: Full=AG8_1
MSIMDHSPTTGVVTVIVILIAIAALGALILGCWCYLRLQRISQSEDEESIVGDGETKEPFLLVQYSAKGP
CVERKAKLMTPNGPEVHG

Notes

In all species examined, the putative 14-3-3-binding motif (amino acid residues 39–45 within Snn) is conserved. Stannin and 14-3-3 co-immunoprecipitation was demonstrated, but no experiments reported to determine whether Ser45 is phosphorylated or responsible for binding to 14-3-3. RISQpS^{45}ED (= Ser44 in O75324)

References to 14-3-3 binding to stannin

Davidson CE, Reese BE, Billingsley ML, Yun JK. The protein stannin binds 14-3-3zeta and modulates mitogen-activated protein kinase signaling. Brain Res Mol Brain Res. 2005 Aug 18;138(2):256-63.

Human SRPK2 Serine/arginine-rich protein-specific kinase 2 (Swiss-Prot = P78362)

1 MSVNSEKSSS SERPEPQQKA PLVPPPPPPP PPPPPPLPDP TPPEPEEEIL GSDDEEQEDP
61 ADYCKGGYHP VKIGDLFNGR YHVIRKLGWG HFSTVWLCWD MQGKRFVAMK VVKSAQHYTE
121 TALDEIKLLK CVRESDPSDP NKDMVVQLID DFKISGMNGI HVCMVFEVLG HHLLKWIIKS
181 NYQGLPVRCV KSIIRQVLQG LDYLHSKCKI IHTDIKPENI LMCVDDAYVR RMAAEATEWQ
241 KAGAPPPSGS AVSTAPQQKP IGKISKNKKK KLKKKQKRQA ELLEKRLQEI EELEREAERK
301 IIEENITSAA PSNDQDGEYC PEVKLKTTGL EEAAEAETAK DNGEAEDQEE KEDAEKENIE
361 KDEDDVDQEL ANIDPTWIES PKTNGHIENG PFSLEQQLDD EDDDEEDCPN PEEYNLDEPN
421 AESDYTYSSS YEQFNGELPN GRHKIPESQF PEFSTSLFSG SLEPVACGSV LSEGSPLTEQ
481 EESSPSHDRS RtVSASSTGD LPKAKTRAAD LLVNPLDPRA RDKIRVKIAD LGNACWVHKH
541 FTEDIQTRQY RSIEVLIGAG YSTPADIWST ACMAFELATG DYLFEPHSGE DYSRDEDHIA
601 HIIELLGSIP RHFALSGKYS REFFNRRGEL RHITKLKPWS LFDVLVEKYG WPHEDAAQFT
661 DFLIPMLEMV PEKRASAGCL CRHPWLNS
>gi|68566065|sp|P78362.2|SRPK2_HUMAN RecName: Full=Serine/threonine-protein kinase SRPK2; AltName: Full=Serine/arginine-rich protein-specific kinase 2; Short=SR-protein-specific kinase 2; AltName: Full=SFRS protein kinase 2
MSVNSEKSSSSERPEPQQKAPLVPPPPPPPPPPPPLPDPTPPEPEEEILGSDDEEQEDPADYCKGGYHP
VKIGDLFNGRYHVIRKLGWGHFSTVWLCWDMQGKRFVAMKVVKSAQHYTETALDEIKLLKCVRESDPSDP
NKDMVVQLIDDFKISGMNGIHVCMVFEVLGHHLLKWIIKSNYQGLPVRCVKSIIRQVLQGLDYLHSKCKI
IHTDIKPENILMCVDDAYVRRMAAEATEWQKAGAPPPSGSAVSTAPQQKPIGKISKNKKKKLKKKQKRQA
ELLEKRLQEIEELEREAERKIIEENITSAAPSNDQDGEYCPEVKLKTTGLEEAAEAETAKDNGEAEDQEE
KEDAEKENIEKDEDDVDQELANIDPTWIESPKTNGHIENGPFSLEQQLDDEDDDEEDCPNPEEYNLDEPN
AESDYTYSSSYEQFNGELPNGRHKIPESQFPEFSTSLFSGSLEPVACGSVLSEGSPLTEQEESSPSHDRS
RTVSASSTGDLPKAKTRAADLLVNPLDPRARDKIRVKIADLGNACWVHKHFTEDIQTRQYRSIEVLIGAG
YSTPADIWSTACMAFELATGDYLFEPHSGEDYSRDEDHIAHIIELLGSIPRHFALSGKYSREFFNRRGEL
RHITKLKPWSLFDVLVEKYGWPHEDAAQFTDFLIPMLEMVPEKRASAGCLCRHPWLNS

Notes

Akt reported to phosphorylate SRPK2 on T492. (This motif (HDRSRtVSAS) is not a conventional RxRxx(pS/T) phosphorylation site for PKB/Akt.)

References to 14-3-3 binding to SPRK2

Jang SW, Liu X, Fu H, Rees H, Yepes M, Levey A, Ye K. Interaction of Akt-phosphorylated SRPK2 with 14-3-3 mediates cell cycle and cell death in neurons. J Biol Chem. 2009 Jul 10. [Epub ahead of print]

Human SSH1L The phosphatase Slingshot 1-like, which dephosphorylates cofilin. (isoform 1, Swissprot = Q8WYL5)

```
         1 MALVTLQRSP TPSAASSSAS NSELEAGSEE DRKLNLSLSE SFFMVKGAAL FLQQGSSPQG
        61 QRSLQHPHKH AGDLPQHLQV MINLLRCEDR IKLAVRLESA WADRVRYMVV VYSSGRQDTE
       121 ENILLGVDFS SKESKSCTIG MVLRLWSDTK IHLDGDGGFS VSTAGRMHIF KPVSVQAMWS
       181 ALQVLHKACE VARRHNYFPG GVALIWATYY ESCISSEQSC INEWNAMQDL ESTRPDSPAL
       241 FVDKPTEGER TERLIKAKLR SIMMSQDLEN VTSKEIRNEL EKQMNCNLKE LKEFIDNEML
       301 LILGQMDKPS LIFDHLYLGS EWNASNLEEL QGSGVDYILN VTREIDNFFP GLFAYHNIRV
       361 YDEETTDLLA HWNEAYHFIN KAKRNHSKCL VHCKMGVSRS ASTVIAYAMK EFGWPLEKAY
       421 NYVKQKRSIT RPNAGFMRQL SEYEGILDAS KQRHNKLWRQ QTDSSLQQPV DDPAGPGDFL
       481 PETPDGTPES QLPFLDDAAQ PGLGPPLPCC FRRLSDPLLP SPEDETGSLV HLEDPEREAL
       541 LEEAAPPAEV HRPARQPQQG SGLCEKDVKK KLEFGSPKGR SGSLLQVEET EREEGLGAGR
       601 WGQLPTQLDQ NLLNSENLNN NSKRSCPNGM EDDAIFGILN KVKPSYKSCA DCMYPTASGA
       661 PEASRERCED PNAPAICTQP AFLPHITSSP VAHLASRSRV PEKPASGPTE PPPFLPPAGS
       721 RRADTSGPGA GAALEPPASL LEPSRETPKV LPKSLLLKNS HCDKNPPSTE VVIKEESSPK
       781 KDMKPAKDLR LLFSNESEKP TTNSYLMQHQ ESIIQLQKAG LVRKHTKELE RLKSVPADPA
       841 PPSRDGPASR LEASIPEESQ DPAALHELGP LVMPSQAGSD EKSEAAPASL EGGSLKSPPP
       901 FFYRLDHTSS FSKDFLKTIC YTPTSSSMSS NLTRSSsSDS IHSVRGKPGL VKQRTQEIET
       961 RLRLAGLTVS SPLKRSHsLA KLGSLTFSTE DLSSEADPST VADSQDTTLS ESSFLHEPQG
      1021 TPRDPAATSK PSGKPAPENL KSPSWMSKS
>gi|82582267|sp|Q8WYL5.2|SSH1_HUMAN RecName: Full=Protein phosphatase
Slingshot homolog 1; AltName: Full=SSH-1L; AltName: Full=hSSH-1L
MALVTLQRSPTPSAASSSASNSELEAGSEEDRKLNLSLSESFFMVKGAALFLQQGSSPQGQRSLQHPHKH
AGDLPQHLQVMINLLRCEDRIKLAVRLESAWADRVRYMVVVYSSGRQDTEENILLGVDFSSKESKSCTIG
MVLRLWSDTKIHLDGDGGFSVSTAGRMHIFKPVSVQAMWSALQVLHKACEVARRHNYFPGGVALIWATYY
ESCISSEQSCINEWNAMQDLESTRPDSPALFVDKPTEGERTERLIKAKLRSIMMSQDLENVTSKEIRNEL
EKQMNCNLKELKEFIDNEMLLILGQMDKPSLIFDHLYLGSEWNASNLEELQGSGVDYILNVTREIDNFFP
GLFAYHNIRVYDEETTDLLAHWNEAYHFINKAKRNHSKCLVHCKMGVSRSASTVIAYAMKEFGWPLEKAY
NYVKQKRSITRPNAGFMRQLSEYEGILDASKQRHNKLWRQQTDSSLQQPVDDPAGPGDFLPETPDGTPES
QLPFLDDAAQPGLGPPLPCCFRRLSDPLLPSPEDETGSLVHLEDPEREALLEEAAPPAEVHRPARQPQQG
SGLCEKDVKKKLEFGSPKGRSGSLLQVEETEREEGLGAGRWGQLPTQLDQNLLNSENLNNNSKRSCPNGM
EDDAIFGILNKVKPSYKSCADCMYPTASGAPEASRERCEDPNAPAICTQPAFLPHITSSPVAHLASRSRV
PEKPASGPTEPPPFLPPAGSRRADTSGPGAGAALEPPASLLEPSRETPKVLPKSLLLKNSHCDKNPPSTE
VVIKEESSPKKDMKPAKDLRLLFSNESEKPTTNSYLMQHQESIIQLQKAGLVRKHTKELERLKSVPADPA
PPSRDGPASRLEASIPEESQDPAALHELGPLVMPSQAGSDEKSEAAPASLEGGSLKSPPPFFYRLDHTSS
FSKDFLKTICYTPTSSSMSSNLTRSSSSDSIHSVRGKPGLVKQRTQEIETRLRLAGLTVSSPLKRSHSLA
KLGSLTFSTEDLSSEADPSTVADSQDTTLSESSFLHEPQGTPRDPAATSKPSGKPAPENLKSPSWMSKS
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Notes

14-3-3 proteins associate with SSH1L when phosphorylated at serines 937 and 978, thereby sequestering SSH1L in the cytoplasm and preventing translocation of the phosphatase to F-actin–rich membrane protrusions (Nagata-Ohashi et al 2004). PKD1 and PKD2 directly phosphorylate SSH1L at these residues, thereby controlling SSH1L localization and thus cofilin dephosphorylation and activation at membrane protrusions and migration of breast cancer cells (Peterburs et al 2009).

14-3-3 also binds to the C-terminal region of the related slingshot protein (Eiseler et al 2009)

References to 14-3-3 binding to SSH1L

Nagata-Ohashi K, Ohta Y, Goto K, et al. A pathway of neuregulin-induced activation of cofilin-phosphatase Slingshot and cofilin in lamellipodia. J Cell Biol 2004;165:465–71

Peterburs P, Heering J, Link G, Pfizenmaier K, Olayioye MA, Hausser A. Protein kinase D regulates cell migration by direct phosphorylation of the cofilin phosphatase slingshot 1 like. Cancer Res. 2009 Jul 15;69(14):5634-8.

Kligys, K., Yao, J., Yu, D. and Jones, J.C.14-3-3zeta/tau heterodimers regulate Slingshot activity in migrating keratinocytes. Biochem. Biophys. Res. Commun. (2009) 383 (4), 450-454.

Eiseler T, Döppler H, Yan IK, Kitatani K, Mizuno K, Storz P. Protein kinase D1 regulates cofilin-mediated F-actin reorganization and cell motility through slingshot. Nat Cell Biol. 2009 May;11(5):545-56.

Human TBC1D1 (SwissProt=Q86TI0)

```
         1 MEPITFTARK HLLSNEVSVD FGLQLVGSLP VHSLTTMPML PWVVAEVRRL SRQSTRKEPV
        61 TKQVRLCVSP SGLRCEPEPG RSQQWDPLIY SSIFECKPQR VHKLIHNSHD PSYFACLIKE
       121 DAVHRQSICY VFKADDQTKV PEIISSIRQA GKIARQEELH CPSEFDDTFS KKFEVLFCGR
       181 VTVAHKKAPP ALIDECIEKF NHVSGSRGSE SPRPNPPHAA PTGSQEPVRR PMRKSFsQPG
       241 LRSLAFRKEL QDGGLRSSGF FSSFEESDIE NHLISGHNIV QPTDIEENRT MLFTIGQSEV
       301 YLISPDTKKI ALEKNFKEIS FCSQGIRHVD HFGFICRESS GGGGFHFVCY VFQCTNEALV
       361 DEIMMTLKQA FTVAAVQQTA KAPAQLCEGC PLQSLHKLCE RIEGMNSSKT KLELQKHLTT
       421 LTNQEQATIF EEVQKLRPRN EQRENELIIS FLRCLYEEKQ KEHIHIGEMK QTSQMAAENI
       481 GSELPPSATR FRLDMLKNKA KRSLTESLES ILSRGNKARG LQEHSISVDL DSSLSSTLSN
       541 TSKEPSVCEK EALPISESSF KLLGSSEDLS SDSESHLPEE PAPLSPQQAF RRRANtLSHF
       601 PIECQEPPQP ARGSPGVSQR KLMRYHSVST ETPHERKDFE SKANHLGDSG GTPVKTRRHS
       661 WRQQIFLRVA TPQKACDSSS RYEDYSELGE LPPRSPLEPV CEDGPFGPPP EEKKRTSREL
       721 RELWQKAILQ QILLLRMEKE NQKLQASEND LLNKRLKLDY EEITPCLKEV TTVWEKMLST
       781 PGRSKIKFDM EKMHSAVGQG VPRHHRGEIW KFLAEQFHLK HQFPSKQQPK DVPYKELLKQ
       841 LTSQQHAILI DLGRTFPTHP YFSAQLGAGQ LSLYNILKAY SLLDQEVGYC QGLSFVAGIL
       901 LLHMSEEEAF KMLKFLMFDM GLRKQYRPDM IILQIQMYQL SRLLHDYHRD LYNHLEEHEI
       961 GPSLYAAPWF LTMFASQFPL GFVARVFDMI FLQGTEVIFK VALSLLGSHK PLILQHENLE
      1021 TIVDFIKSTL PNLGLVQMEK TINQVFEMDI AKQLQAYEVE YHVLQEELID SSPLSDNQRM
      1081 DKLEKTNSSL RKQNLDLLEQ LQVANGRIQS LEATIEKLLS SESKLKQAML TLELERSALL
      1141 QTVEELRRRS AEPSDREPEC TQPEPTGD
>gi|116242816|sp|Q86TI0.2|TBCD1_HUMAN RecName: Full=TBC1 domain family member
1
MEPITFTARKHLLSNEVSVDFGLQLVGSLPVHSLTTMPMLPWVVAEVRRLSRQSTRKEPVTKQVRLCVSP
SGLRCEPEPGRSQQWDPLIYSSIFECKPQRVHKLIHNSHDPSYFACLIKEDAVHRQSICYVFKADDQTKV
PEIISSIRQAGKIARQEELHCPSEFDDTFSKKFEVLFCGRVTVAHKKAPPALIDECIEKFNHVSGSRGSE
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SPRPNPPHAAPTGSQEPVRRPMRKSFSQPGLRSLAFRKELQDGGLRSSGFFSSFEESDIENHLISGHNIV
QPTDIEENRTMLFTIGQSEVYLISPDTKKIALEKNFKEISFCSQGIRHVDHFGFICRESSGGGGFHFVCY
VFQCTNEALVDEIMMTLKQAFTVAAVQQTAKAPAQLCEGCPLQSLHKLCERIEGMNSSKTKLELQKHLTT
LTNQEQATIFEEVQKLRPRNEQRENELIISFLRCLYEEKQKEHIHIGEMKQTSQMAAENIGSELPPSATR
FRLDMLKNKAKRSLTESLESILSRGNKARGLQEHSISVDLDSSLSSTLSNTSKEPSVCEKEALPISESSF
KLLGSSEDLSSDSESHLPEEPAPLSPQQAFRRRANTLSHFPIECQEPPQPARGSPGVSQRKLMRYHSVST
ETPHERKDFESKANHLGDSGGTPVKTRRHSWRQQIFLRVATPQKACDSSSRYEDYSELGELPPRSPLEPV
CEDGPFGPPPEEKKRTSRELRELWQKAILQQILLLRMEKENQKLQASENDLLNKRLKLDYEEITPCLKEV
TTVWEKMLSTPGRSKIKFDMEKMHSAVGQGVPRHHRGEIWKFLAEQFHLKHQFPSKQQPKDVPYKELLKQ
LTSQQHAILIDLGRTFPTHPYFSAQLGAGQLSLYNILKAYSLLDQEVGYCQGLSFVAGILLLHMSEEEAF
KMLKFLMFDMGLRKQYRPDMIILQIQMYQLSRLLHDYHRDLYNHLEEHEIGPSLYAAPWFLTMFASQFPL
GFVARVFDMIFLQGTEVIFKVALSLLGSHKPLILQHENLETIVDFIKSTLPNLGLVQMEKTINQVFEMDI
AKQLQAYEVEYHVLQEELIDSSPLSDNQRMDKLEKTNSSLRKQNLDLLEQLQVANGRIQSLEATIEKLLS
SESKLKQAMLTLELERSALLQTVEELRRRSAEPSDREPECTQPEPTGD
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Notes

TBC1D1 (related to AS160/TBC1D4) a putative GTPase activating protein for Rab family protein(s). May play a rol
cell cycle and differentiation of various tissues.

When AMPK (AMP-activated protein kinase) is activated in HEK (human embryonic kidney)-293 cells, 14-3-3s bind primarily to pSer237 (where pSer is phosphorylated serine) in TBC1D1, whereas 14-3-3 binding depends primarily on pThr596 (where pThr is phosphorylated threonine) in cells stimulated with IGF-1 (insulin-like growth factor 1), EGF (epidermal growth factor) and PMA; and both pSer237 and pThr596 contribute to 14-3-3 binding in cells stimulated with forskolin. In HEK-293 cells, LY294002 inhibits phosphorylation of Thr596 of TBC1D1, and promotes phosphorylation of AMPK and Ser237 of TBC1D1.

TBC1D1 is strongly phosphorylated on Ser237 and binds to 14-3-3s in response to the AMPK activators AICAR (5-aminoimidazole-4-carboxamide-1-b-D-ribofuranoside), phenformin and A-769662, whereas insulin promotes phosphorylation of Thr596 but not 14-3-3 binding. In contrast, AS160 is phosphorylated on its 14-3-3-binding sites (Ser341 and Thr642) and binds to 14-3-3s in response to insulin, but not A-769662, in L6 cells.

References to 14-3-3 binding to TBC1D1

Chen S, Murphy J, Toth R, Campbell DG, Morrice NA, Mackintosh C. Complementary regulation of TBC1D1 and AS160 by growth factors, insulin and AMPK activators. Biochem J. 2008 Jan 15;409(2):449-59

Pehmøller C, Treebak JT, Birk JB, Chen S, Mackintosh C, Hardie DG, Richter EA, Wojtaszewski JF. Genetic disruption of AMPK signaling abolishes both contration- and insulin-stimulated TBC1D1 phosphorylation and 14-3-3 bidning in mouse skeletal muscle. Am J. Physiol. Endocrinol Metab 2009 Jun 16.

Human TBC1D4 (AS160)   RabGAP TBC1D4 = AS160 (Swissprot = O60343 (longer variant))

```
        1 MEPPSCIQDE PFPHPLEPEP GVSAQPGPGK PSDKRFRLWY VGGSCLDHRT TLPMLPWLMA
       61 EIRRRSQKPE AGGCGAPAAR EVILVLSAPF LRCVPAPGAG ASGGTSPSAT QPNPAVFIFE
      121 HKAQHISRFI HNSHDLTYFA YLIKAQPDDP ESQMACHVFR ATDPSQVPDV ISSIRQLSKA
      181 AMKEDAKPSK DNEDAFYNSQ KFEVLYCGKV TVTHKKAPSS LIDDCMEKFS LHEQQRLKIQ
      241 GEQRGPDPGE DLADLEVVVP GSPGDCLPEE ADGTDTHLGL PAGASQPALT SSRVCFPERI
      301 LEDSGFDEQQ EFRSRCSSVT GVQRRVHEGS QKSQPRRRHA sAPSHVQPSD SEKNRTMLFQ
      361 VGRFEINLIS PDTKSVVLEK NFKDISSCSQ GIKHVDHFGF ICRESPEPGL SQYICYVFQC
      421 ASESLVDEVM LTLKQAFSTA AALQSAKTQI KLCEACPMHS LHKLCERIEG LYPPRAKLVI
      481 QRHLSSLTDN EQADIFERVQ KMKPVSDQEE NELVILHLRQ LCEAKQKTHV HIGEGPSTIS
      541 NSTIPENATS SGRFKLDILK NKAKRSLTSS LENIFSRGAN RMRGRLGSVD SFERSNSLAS
      601 EKDYSPGDSP PGTPPASPPS SAWQTFPEED SDSPQFRRRA HtFSHPPSST KRKLNLQDGR
      661 AQGVRSPLLR QSSSEQCSNL SSVRRMYKES NSSSSLPSLH TSFSAPSFTA PSFLKSFYQN
      721 SGRLSPQYEN EIRQDTASES SDGEGRKRTS STCSNESLSV GGTSVTPRRI SWRQRIFLRV
      781 ASPMNKSPSA MQQQDGLDRN ELLPLSPLSP TMEEEPLVVF LSGEDDPEKI EERKKSKELR
      841 SLWRKAIHQQ ILLLRMEKEN QKLEASRDEL QSRKVKLDYE EVGACQKEVL ITWDKKLLNC
      901 RAKIRCDMED IHTLLKEGVP KSRRGEIWQF LALQYRLRHR LPNKQQPPDI SYKELLKQLT
      961 AQQHAILVDL GRTFPTHPYF SVQLGPGQLS LFNLLKAYSL LDKEVGYCQG ISFVAGVLLL
     1021 HMSEEQAFEM LKFLMYDLGF RKQYRPDMMS LQIQMYQLSR LLHDYHRDLY NHLEENEISP
     1081 SLYAAPWFLT LFASQFSLGF VARVFDIIFL QGTEVIFKVA LSLLSSQETL IMECESFENI
     1141 VEFLKNTLPD MNTSEMEKII TQVFEMDISK QLHAYEVEYH VLQDELQESS YSCEDSETLE
     1201 KLERANSQLK RQNMDLLEKL QVAHTKIQAL ESNLENLLTR ETKMKSLIRT LEQEKMAYQK
     1261 TVEQLRKLLP ADALVNCDLL LRDLNCNPNN KAKIGNKP
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>gi|67473227|sp|O60343.2|TBCD4_HUMAN RecName: Full=TBC1 domain family member
4; AltName: Full=Akt substrate of 160 kDa; Short=AS160
MEPPSCIQDEPFPHPLEPEPGVSAQPGPGKPSDKRFRLWYVGGSCLDHRTTLPMLPWLMAEIRRRSQKPE
AGGCGAPAAREVILVLSAPFLRCVPAPGAGASGGTSPSATQPNPAVFIFEHKAQHISRFIHNSHDLTYFA
YLIKAQPDDPESQMACHVFRATDPSQVPDVISSIRQLSKAAMKEDAKPSKDNEDAFYNSQKFEVLYCGKV
TVTHKKAPSSLIDDCMEKFSLHEQQRLKIQGEQRGPDPGEDLADLEVVVPGSPGDCLPEEADGTDTHLGL
PAGASQPALTSSRVCFPERILEDSGFDEQQEFRSRCSSVTGVQRRVHEGSQKSQPRRRHASAPSHVQPSD
SEKNRTMLFQVGRFEINLISPDTKSVVLEKNFKDISSCSQGIKHVDHFGFICRESPEPGLSQYICYVFQC
ASESLVDEVMLTLKQAFSTAAALQSAKTQIKLCEACPMHSLHKLCERIEGLYPPRAKLVIQRHLSSLTDN
EQADIFERVQKMKPVSDQEENELVILHLRQLCEAKQKTHVHIGEGPSTISNSTIPENATSSGRFKLDILK
NKAKRSLTSSLENIFSRGANRMRGRLGSVDSFERSNSLASEKDYSPGDSPPGTPPASPPSSAWQTFPEED
SDSPQFRRRAHTFSHPPSSTKRKLNLQDGRAQGVRSPLLRQSSSEQCSNLSSVRRMYKESNSSSSLPSLH
TSFSAPSFTAPSFLKSFYQNSGRLSPQYENEIRQDTASESSDGEGRKRTSSTCSNESLSVGGTSVTPRRI
SWRQRIFLRVASPMNKSPSAMQQQDGLDRNELLPLSPLSPTMEEEPLVVFLSGEDDPEKIEERKKSKELR
SLWRKAIHQQILLLRMEKENQKLEASRDELQSRKVKLDYEEVGACQKEVLITWDKKLLNCRAKIRCDMED
IHTLLKEGVPKSRRGEIWQFLALQYRLRHRLPNKQQPPDISYKELLKQLTAQQHAILVDLGRTFPTHPYF
SVQLGPGQLSLFNLLKAYSLLDKEVGYCQGISFVAGVLLLHMSEEQAFEMLKFLMYDLGFRKQYRPDMMS
LQIQMYQLSRLLHDYHRDLYNHLEENEISPSLYAAPWFLTLFASQFSLGFVARVFDIIFLQGTEVIFKVA
LSLLSSQETLIMECESFENIVEFLKNTLPDMNTSEMEKIITQVFEMDISKQLHAYEVEYHVLQDELQESS
YSCEDSETLEKLERANSQLKRQNMDLLEKLQVAHTKIQALESNLENLLTRETKMKSLIRTLEQEKMAYQK
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TVEQLRKLLPADALVNCDLLLRDLNCNPNNKAKIGNKP
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Notes

This is a RabGAP implicated in insulin-stimulated regulation of GLUT4 trafficking and uptake of glucose from blood into tissues.

References to 14-3-3 binding to TBC1D4 (AS160)

Geraghty KM, Chen S, Harthill JE, Ibrahim AF, Toth R, Morrice NA, Vandermoere F, Moorhead GB, Hardie DG, MacKintosh C. Regulation of multisite phosphorylation and 14-3-3 binding of AS160 in response to IGF-1, EGF, PMA and AICAR. Biochem J. 2007 Oct 15;407(2):231-41.

Ramm G, Larance M, Guilhaus M, James DE. A role for 14-3-3 in insulin-stimulated GLUT4 translocation through its interaction with the RabGAP AS160. J Biol Chem. 2006 Sep 29;281(39):29174-80.

Human TGM2 tissue transglutaminase (Swissprot = P21980)

```
        1 MAEELVLERC DLELETNGRD HHTADLCREK LVVRRGQPFW LTLHFEGRNY EASVDSLTFS
       61 VVTGPAPSQE AGTKARFPLR DAVEEGDWTA TVVDQQDCTL SLQLTTPANA PIGLYRLSLE
      121 ASTGYQGSSF VLGHFILLFN AWCPADAVYL DSEEERQEYV LTQQGFIYQG SAKFIKNIPW
      181 NFGQFEDGIL DICLILLDVN PKFLKNAGRD CSRRSsPVYV GRVVSGMVNC NDDQGVLLGR
      241 WDNNYGDGVS PMSWIGSVDI LRRWKNHGCQ RVKYGQCWVF AAVACTVLRC LGIPTRVVTN
      301 YNSAHDQNSN LLIEYFRNEF GEIQGDKSEM IWNFHCWVES WMTRPDLQPG YEGWQALDPT
      361 PQEKSEGTYC CGPVPVRAIK EGDLSTKYDA PFVFAEVNAD VVDWIQQDDG SVHKSINRSL
      421 IVGLKISTKS VGRDEREDIT HTYKYPEGSS EEREAFTRAN HLNKLAEKEE TGMAMRIRVG
      481 QSMNMGSDFD VFAHITNNTA EEYVCRLLLC ARTVSYNGIL GPECGTKYLL NLNLEPFSEK
      541 SVPLCILYEK YRDCLTESNL IKVRALLVEP VINSYLLAER DLYLENPEIK IRILGEPKQK
      601 RKLVAEVSLQ NPLPVALEGC TFTVEGAGLT EEQKTVEIPD PVEAGEEVKV RMDLLPLHMG
      661 LHKLVVNFES DKLKAVKGFR NVIIGPA
>gi|20141877|sp|P21980.2|TGM2_HUMAN RecName: Full=Protein-glutamine gamma-
glutamyltransferase 2; AltName: Full=Tissue transglutaminase; AltName:
Full=TGase C; Short=TGC; Short=TG(C); AltName: Full=Transglutaminase-2;
AltName: Full=TGase-H
MAEELVLERCDLELETNGRDHHTADLCREKLVVRRGQPFWLTLHFEGRNYEASVDSLTFSVVTGPAPSQE
AGTKARFPLRDAVEEGDWTATVVDQQDCTLSLQLTTPANAPIGLYRLSLEASTGYQGSSFVLGHFILLFN
AWCPADAVYLDSEEERQEYVLTQQGFIYQGSAKFIKNIPWNFGQFEDGILDICLILLDVNPKFLKNAGRD
CSRRSSPVYVGRVVSGMVNCNDDQGVLLGRWDNNYGDGVSPMSWIGSVDILRRWKNHGCQRVKYGQCWVF
AAVACTVLRCLGIPTRVVTNYNSAHDQNSNLLIEYFRNEFGEIQGDKSEMIWNFHCWVESWMTRPDLQPG
YEGWQALDPTPQEKSEGTYCCGPVPVRAIKEGDLSTKYDAPFVFAEVNADVVDWIQQDDGSVHKSINRSL
IVGLKISTKSVGRDEREDITHTYKYPEGSSEEREAFTRANHLNKLAEKEETGMAMRIRVGQSMNMGSDFD
VFAHITNNTAEEYVCRLLLCARTVSYNGILGPECGTKYLLNLNLEPFSEKSVPLCILYEKYRDCLTESNL
IKVRALLVEPVINSYLLAERDLYLENPEIKIRILGEPKQKRKLVAEVSLQNPLPVALEGCTFTVEGAGLT
EEQKTVEIPDPVEAGEEVKVRMDLLPLHMGLHKLVVNFESDKLKAVKGFRNVIIGPA
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Notes

TGM2 an enzyme of the transglutaminase family that catalyzes the crosslinking of proteins and the conjugation of polyamines to proteins. While the primary structure of transglutaminases is not conserved, they all have the same amino acid sequence at their active sites and their activity is calcium-dependent. The protein encoded by this gene acts as a monomer, is induced by retinoic acid, and appears to be involved in apoptosis. Is the autoantigen in coeliac disease and plays a role in apoptosis, cellular differentiation and matrix stabilisation. Three alternatively spliced isoforms have been described.

14-3-3 co-immunoprecipitated with TG2 antiserum after activation of PKA from mouse embryonic fibroblasts (MEF)(TG2+/+) cells but not from MEF(TG2-/-) cells. In summary, we provide convincing evidence that phosphorylation of TG2 by PKA creates binding site(s) for 14-3-3 both in vitro and in vivo. This is a phosphoSer-Pro site, not conventional for PKA or 14-3-3.

References to 14-3-3 binding to TGM2

Mishra S, Murphy LJ. Phosphorylation of transglutaminase 2 by PKA at Ser216 creates 14-3-3 binding sites. Biochem Biophys Res Commun. 2006 Sep 8;347(4):1166-70.

Human TH Tyrosine 3-hydroxylase is an enzyme involved in the conversion of tyrosine to dopamine. (Swissprot = P07101)

```
        1 MPTPDATTPQ AKGFRRAVSE LDAKQAEAIM VRGQGAPGPS LTGSPWPGTA APAASYTPTP
       61 RSPRFIGRRQ sLIEDARKER EAAVAAAAAA VPSEPGDPLE AVAFEEKEGK AVLNLLFSPR
      121 ATKPSALSRA VKVFETFEAK IHHLETRPAQ RPRAGGPHLE YFVRLEVRRG DLAALLSGVR
      181 QVSEDVRSPA GPKVPWFPRK VSELDKCHHL VTKFDPDLDL DHPGFSDQVY RQRRKLIAEI
      241 AFQYRHGDPI PRVEYTAEEI ATWKEVYTTL KGLYATHACG EHLEAFALLE RFSGYREDNI
      301 PQLEDVSRFL KERTGFQLRP VAGLLSARDF LASLAFRVFQ CTQYIRHASS PMHSPEPDCC
      361 HELLGHVPML ADRTFAQFSQ DIGLASLGAS DEEIEKLSTL SWFTVEFGLC KQNGEVKAYG
      421 AGLLSSYGEL LHCLSEEPEI RAFDPEAAAV QPYQDQTYQS VYFVSESFSD AKDKLRSYAS
      481 RIQRPFSVKF DPYTLAIDVL DSPQAVRRSL EGVQDELDTL AHALSAIG
>gi|239938945|sp|P07101.5|TY3H_HUMAN RecName: Full=Tyrosine 3-monooxygenase;
AltName: Full=Tyrosine 3-hydroxylase; Short=TH
MPTPDATTPQAKGFRRAVSELDAKQAEAIMVRGQGAPGPSLTGSPWPGTAAPAASYTPTPRSPRFIGRRQ
SLIEDARKEREAAVAAAAAAVPSEPGDPLEAVAFEEKEGKAVLNLLFSPRATKPSALSRAVKVFETFEAK
IHHLETRPAQRPRAGGPHLEYFVRLEVRRGDLAALLSGVRQVSEDVRSPAGPKVPWFPRKVSELDKCHHL
VTKFDPDLDLDHPGFSDQVYRQRRKLIAEIAFQYRHGDPIPRVEYTAEEIATWKEVYTTLKGLYATHACG
EHLEAFALLERFSGYREDNIPQLEDVSRFLKERTGFQLRPVAGLLSARDFLASLAFRVFQCTQYIRHASS
PMHSPEPDCCHELLGHVPMLADRTFAQFSQDIGLASLGASDEEIEKLSTLYWFTVEFGLCKQNGEVKAYG
AGLLSSYGELLHCLSEEPEIRAFDPEAAAVQPYQDQTYQSVYFVSESFSDAKDKLRSYASRIQRPFSVKF
DPYTLAIDVLDSPQAVRRSLEGVQDELDTLAHALSAIG
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Notes

Two 14-3-3-binding sites on tyrosine hydroxylase are RRAVpS^{19}ELD and IGRRQpS^{40}LIEDA (= Ser70 in P07101)

References to 14-3-3 binding to tyrosine hydroxylase

Itagaki C, Stimulus-coupled interaction of tyrosine hydroxylase with 14-3-3 proteins. Biochemistry. 1999 Nov

23;38(47):15673-80 Obsilova V, The 14-3-3 protein affects the conformation of the regulatory domain of human tyrosine hydroxylase. Biochemistry. 2008 Feb 12;47(6):1768-77. Epub 2008 Jan 9 Wang J, Lou H, Pedersen CJ, Smith AD, Perez RG.14-3-3zeta contributes to tyrosine hydroxylase activity in MN9D cells: Localization of dopamine regulatory proteins to mitochondria. J Biol Chem. 2009 May 22;284(21):14011-9. Ichimura T, Isobe T, Okuyama T, Yamauchi T, Fujisawa H. Brain 14-3-3 protein is an activator protein that activates tryptophan 5-monooxygenase and tyrosine 3-monooxygenase in the presence of Ca2+,calmodulin-dependent protein kinase II. FEBS Lett. 1987 Jul 13;219(1):79-82. Kleppe R, Toska K, Haavik J. Interaction of phosphorylated tyrosine hydroxylase with 14-3-3 proteins: evidence for a phosphoserine 40-dependent association. J Neurochem. 2001 May;77(4):1097-107. Halskau O Jr, Ying M, Baumann A, Kleppe R, Larrea DR, Almaas B, Haavik J, Martinez A. Three-way interaction between 14-3-3 proteins, the N-terminal region of tyrosine hydroxylase and negatively charged membranes. J Biol Chem. 2009 Sep 28. [Epub ahead of print]	
Human Tiam1 T-cell lymphoma invasion and metastasis 1 (Swissprot = Q13009) 1 MGNAESQHVE HEFYGEKHAS LGRKHTSRSL RLSHKTRRTR HASSGKVIHR NSEVSTRSSs 61 TPSIPQSLAE NGLEPFSQDG TLEDFGSPIW VDRVDMGLRP VSYTDSSVTP SVDSSIVLTA 121 ASVQSMPDTE ESRLYGDDAT YLAEGGRRQH SYTSNGPTFM ETASFKKKRS KsADIWREDS 181 LEFSLSDLSQ EHLTSNEEIL GSAEEKDCEE ARGMETRASP RQLSTCQRAN sLGDLYAQKN 241 SGVTANGGPG SKFAGYCRNL VSDIPNLANH KMPPAAAEET PPYSNYNTLP CRKSHCLSEG 301 ATNPQISHSN SMQGRRAKTT QDVNAGEGSE FADSGIEGAT TDTDLLSRRS NATNSSYSPT 361 TGRAFVGSDS GSSSTGDAAR QGVYENFRRE LEMSTTNSES LEEAGSAHSD EQSSGTLSSP 421 GQSDILLTAA QGTVRKAGAL AVKNFLVHKK NKKVESATRR KWKHYWVSLK GCTLFFYESD 481 GRSGIDHNSI PKHAVWVENS IVQAVPEHPK KDFVFCLSNS LGDAFLFQTT SQTELENWIT 541 AIHSACATAV ARHHHKEDTL RLLKSEIKKL EQKIDMDEKM KKMGEMQLSS VTDSKKKKTI 601 LDQIFVWEQN LEQFQMDLFR FRCYLASLQG GELPNPKRLL AFASRPTKVA MGRLGIFSVS 661 SFHALVAART GETGVRRRTQ AMSRSASKRR SRFSSLWGLD TTSKKKQGRP SINQVFGEGT 721 EAVKKSLEGI FDDIVPDGKR EKEVVLPNVH QHNPDCDIWV HEYFTPSWFC LPNNQPALTV 781 VRPGDTARDT LELICKTHQL DHSAHYLRLK FLIENKMQLY VPQPEEDIYE LLYKEIEICP 841 KVTQSIHIEK SDTAADTYGF SLSSVEEDGI RRLYVNSVKE TGLASKKGLK AGDEILEINN 901 RAADALNSSM LKDFLSQPSL GLLVRTYPEL EEGVELLESP PHRVDGPADL GESPLAFLTS 961 NPGHSLCSEQ GSSAETAPEE TEGPDLESSD ETDHSSKSTE QVAAFCRSLH EMNPSDQSPS 1021 PQDSTGPQLA TMRQLSDADK LRKVICELLE TERTYVKDLN CLMERYLKPL QKETFLTQDE 1081 LDVLFGNLTE MVEFQVEFLK TLEDGVRLVP DLEKLEKVDQ FKKVLFSLGG SFLYYADRFK 1141 LYSAFCASHT KVPKVLVKAK TDTAFKAFLD AQNPKQQHSS TLESYLIKPI QRILKYPLLL 1201 RELFALTDAE SEEHYHLDVA IKTMNKVASH INEMQKIHEE FGAVFDQLIA EQTGEKKEVA 1261 DLSMGDLLLH TTVIWLNPPA SLGKWKKEPE LAAFVFKTAV VLVYKDGSKQ KKKLVGSHRL 1321 SIYEDWDPFR FRHMIPTEAL QVRALASADA EANAVCEIVH VKSESEGRPE RVFHLCCSSP 1381 ESRKDFLKAV HSILRDKHRR QLLKTESLPS SQQYVPFGGK RLCALKGARP AMSRAVSAPS 1441 KSLGRRRRRL ARNRFTIDSD AVSASSPEKE SQQPPGGGDT DRWVEEQFDL AQYEEQDDIK 1501 ETDILSDDDE FCESVKGASV DRDLQERLQA TSISQRERGR KTLDSHASRM AQLKKQAALS 1561 GINGGLESAS EEVIWVRRED FAPSRKLNTE I >gi|152031709|sp|Q13009.2|TIAM1_HUMAN RecName: Full=T-lymphoma invasion and metastasis-inducing protein 1; Short=TIAM-1 MGNAESQHVEHEFYGEKHASLGRKHTSRSLRLSHKTRRTRHASSGKVIHRNSEVSTRSSSTPSIPQSLAE NGLEPFSQDGTLEDFGSPIWVDRVDMGLRPVSYTDSSVTPSVDSSIVLTAASVQSMPDTEESRLYGDDAT YLAEGGRRQHSYTSNGPTFMETASFKKKRSKSADIWREDSLEFSLSDLSQEHLTSNEEILGSAEEKDCEE ARGMETRASPRQLSTCQRANSLGDLYAQKNSGVTANGGPGSKFAGYCRNLVSDIPNLANHKMPPAAAEET PPYSNYNTLPCRKSHCLSEGATNPQISHSNSMQGRRAKTTQDVNAGEGSEFADSGIEGATTDTDLLSRRS NATNSSYSPTTGRAFVGSDSGSSSTGDAARQGVYENFRRELEMSTTNSESLEEAGSAHSDEQSSGTLSSP GQSDILLTAAQGTVRKAGALAVKNFLVHKKNKKVESATRRKWKHYWVSLKGCTLFFYESDGRSGIDHNSI PKHAVWVENSIVQAVPEHPKKDFVFCLSNSLGDAFLFQTTSQTELENWITAIHSACATAVARHHHKEDTL RLLKSEIKKLEQKIDMDEKMKKMGEMQLSSVTDSKKKKTILDQIFVWEQNLEQFQMDLFRFRCYLASLQG GELPNPKRLLAFASRPTKVAMGRLGIFSVSSFHALVAARTGETGVRRRTQAMSRSASKRRSRFSSLWGLD TTSKKKQGRPSINQVFGEGTEAVKKSLEGIFDDIVPDGKREKEVVLPNVHQHNPDCDIWVHEYFTPSWFC LPNNQPALTVVRPGDTARDTLELICKTHQLDHSAHYLRLKFLIENKMQLYVPQPEEDIYELLYKEIEICP KVTQSIHIEKSDTAADTYGFSLSSVEEDGIRRLYVNSVKETGLASKKGLKAGDEILEINNRAADALNSSM LKDFLSQPSLGLLVRTYPELEEGVELLESPPHRVDGPADLGESPLAFLTSNPGHSLCSEQGSSAETAPEE TEGPDLESSDETDHSSKSTEQVAAFCRSLHEMNPSDQSPSPQDSTGPQLATMRQLSDADKLRKVICELLE TERTYVKDLNCLMERYLKPLQKETFLTQDELDVLFGNLTEMVEFQVEFLKTLEDGVRLVPDLEKLEKVDQ FKKVLFSLGGSFLYYADRFKLYSAFCASHTKVPKVLVKAKTDTAFKAFLDAQNPKQQHSSTLESYLIKPI QRILKYPLLLRELFALTDAESEEHYHLDVAIKTMNKVASHINEMQKIHEEFGAVFDQLIAEQTGEKKEVA DLSMGDLLLHTTVIWLNPPASLGKWKKEPELAAFVFKTAVVLVYKDGSKQKKKLVGSHRLSIYEDWDPFR FRHMIPTEALQVRALASADAEANAVCEIVHVKSESEGRPERVFHLCCSSPESRKDFLKAVHSILRDKHRR QLLKTESLPSSQQYVPFGGKRLCALKGARPAMSRAVSAPSKSLGRRRRRLARNRFTIDSDAVSASSPEKE SQQPPGGGDTDRWVEEQFDLAQYEEQDDIKETDILSDDDEFCESVKGASVDRDLQERLQATSISQRERGR KTLDSHASRMAQLKKQAALSGINGGLESASEEVIWVRREDFAPSRKLNTEI **Notes** Human Tiam 1 was reported to bind directly in a phosphorylation-dependent manner by Pozuelo Rubio et al (2004). Woodstock et al studied mouse Tiam1. "There are four putative phospho-serine-containing 14-3-3 binding motifs, and we confirm that two of them (Ser172 and Ser231) are phosphorylated in cells using mass spectrometry. Moreover, we show that phosphorylation at three of these motifs (containing Ser60, Ser172 and Ser231) is required for the binding of 14-3-3 proteins to this region of Tiam1. We show that phosphorylation of these sites does not affect Tiam1 activity; significantly however, we demonstrate that phosphorylation of the Ser60-containing motif is	THREE PHOSPHORYLATED SITES IMPLICATED IN 14-3-3 BINDING. NOT IN WEBLOGO.

required for the degradation of Tiam1. (Woodcock et al 2009)" Tiam1 is a GEF for Rac. Note that phosphorylation at Ser60 was not shown directly, but mutation of this residue had functional effect. Not yet clear how three phosphorylated sites might contribute to 14-3-3 binding of Tiam1.

References to 14-3-3 binding to Tiam1

Pozuelo Rubio M, Geraghty KM, Wong BH, Wood NT, Campbell DG, Morrice N, Mackintosh C. 14-3-3-affinity purification of over 200 human phosphoproteins reveals new links to regulation of cellular metabolism, proliferation and trafficking. Biochem J. 2004 Apr 15;379(Pt 2):395-408.

Woodcock SA, Jones RC, Edmondson RD, Malliri A. A Modified Tandem Affinity Purification Technique Identifies That 14-3-3 Proteins Interact with Tiam1, an Interaction Which Controls Tiam1 Stability. J Proteome Res. 2009 Nov 9. [Epub ahead of print]

Human TP53 p53 (Swissprot = P04637)

```
        1 MEEPQSDPSV EPPLSQETFS DLWKLLPENN VLSPLPSQAM DDLMLSPDDI EQWFTEDPGP
       61 DEAPRMPEAA PRVAPAPAAP TPAAPAPAPS WPLSSSVPSQ KTYQGSYGFR LGFLHSGTAK
      121 SVTCTYSPAL NKMFCQLAKT CPVQLWVDST PPPGTRVRAM AIYKQSQHMT EVVRRCPHHE
      181 RCSDSDGLAP PQHLIRVEGN LRVEYLDDRN TFRHSVVVPY EPPEVGSDCT TIHYNYMCNS
      241 SCMGGMNRRP ILTIITLEDS SGNLLGRNSF EVRVCACPGR DRRTEEENLR KKGEPHHELP
      301 PGSTKRALPN NTSSSPQPKK KPLDGEYFTL QIRGRERFEM FRELNEALEL KDAQAGKEPG
      361 GSRAHsSHLK SKKGQSTSRH KKLMFKtEGP DSD
>gi|205829174|sp|P04637.3|P53_HUMAN RecName: Full=Cellular tumor antigen p53;
AltName: Full=Tumor suppressor p53; AltName: Full=Phosphoprotein p53;
AltName: Full=Antigen NY-CO-13
MEEPQSDPSVEPPLSQETFSDLWKLLPENNVLSPLPSQAMDDLMLSPDDIEQWFTEDPGPDEAPRMPEAA
PRVAPAPAAPTPAAPAPAPSWPLSSSVPSQKTYQGSYGFRLGFLHSGTAKSVTCTYSPALNKMFCQLAKT
CPVQLWVDSTPPPGTRVRAMAIYKQSQHMTEVVRRCPHHERCSDSDGLAPPQHLIRVEGNLRVEYLDDRN
TFRHSVVVPYEPPEVGSDCTTIHYNYMCNSSCMGGMNRRPILTIITLEDSSGNLLGRNSFEVRVCACPGR
DRRTEEENLRKKGEPHHELPPGSTKRALPNNTSSSPQPKKKPLDGEYFTLQIRGRERFEMFRELNEALEL
KDAQAGKEPGGSRAHSSHLKSKKGQSTSRHKKLMFKTEGPDSD
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Notes

References to 14-3-3 binding to TP53 (p53)

Rajagopalan S, Jaulent AM, Wells M, Veprintsev DB, Fersht AR.14-3-3 activation of DNA binding of p53 by enhancing its association into tetramers.Nucleic Acids Res. 2008 Oct;36 (18):5983-91

Waterman MJ, Stavridi ES, Waterman JL, Halazonetis TD. ATM-dependent activation of p53 involves dephosphorylation and association with 14-3-3 proteins. Nat Genet. 1998 Jun;19(2):175-8.

Lee MK, Sabapathy K. Phosphorylation at carboxyl-terminal S373 and S375 residues and 14-3-3 binding are not required for mouse p53 function. Neoplasia. 2007 Sep;9(9):690-8.

Huang WG, Cheng AL, Chen ZC, Peng F, Zhang PF, Li MY, Li F, Li JL, Li C, Yi H, Li XH, Yi B, Xiao ZQ. Targeted proteomic analysis of 14-3-3 sigma in nasopharyngeal carcinoma. Int J Biochem Cell Biol. 2009 Oct 11. [Epub ahead of print]

Rajagopalan S, Sade RS, Townsley FM, Fersht AR. Mechanistic differences in the transcriptional activation of p53 by 14-3-3 isoforms. Nucleic Acids Res. 2009 Nov 20. [Epub ahead of print]

Human TPD52L1 Tumour protein D53 (also known as PrLZ and hD53) (Swissprot = Q16890)

```
        1 MEAQAQGLLE TEPLQGTDED AVASADFSSM LSEEEKEELK AELVQLEDEI TTLRQVLSAK
       61 ERHLVEIKQK LGMNLMNELK QNFSKSWHDM QTTTAYKKTH ETLSHAGQKA TAAFSNVGTA
      121 ISKKFGDMSY SIRHSIsMPA MRNSPTFKSF EERVETTVTS LKTKVGGTNP NGGSFEEVLS
      181 STAHASAQSL AGGSRRTKEE ELQC
>gi|12585368|sp|Q16890.1|TPD53_HUMAN RecName: Full=Tumor protein D53;
Short=hD53; AltName: Full=Tumor protein D52-like 1
MEAQAQGLLETEPLQGTDEDAVASADFSSMLSEEEKEELKAELVQLEDEITTLRQVLSAKERHLVEIKQK
LGMNLMNELKQNFSKSWHDMQTTTAYKKTHETLSHAGQKATAAFSNVGTAISKKFGDMSYSIRHSISMPA
MRNSPTFKSFEERVETTVTSLKTKVGGTNPNGGSFEEVLSSTAHASAQSLAGGSRRTKEEELQC
```

Notes

D52 (TPD52)-like proteins are coiled-coil motif-bearing proteins first identified through their expression in human breast carcinoma, which have been proposed to represent signalling intermediates and regulators of vesicle trafficking. The canonical sequence is P55327-1 (different from that shown). Boutros et al (2003) and Boutros and Byrne (2005) worked on the hD53 (TPD52L1) version, which is shown. There are other splice variants. A sequence alignment the various forms is given in Wang et al (2009). 14-3-3-binding site, encoded by exon 6, defined by mutagenesis in a yeast 2-hybrid assay by Boutros et al (2003). Some other splice variants lack the proposed 14-3-3 binding site. Wang et al (2009) worked with the longest isoform that they refer to as Genbank GQ499328 = Prostate-specific PrLZ-247 (247 is the longest isoform).

References to 14-3-3 binding to TPD52 (also known as PrLZ and hD53)

Boutros R, Bailey AM, Wilson SH and Byrne JA. Alternative splicing as a mechanism for regulating 14-3-3 binding: interactions between hD53 (TPD52L1) and 14-3-3 proteins, *J. Mol. Biol.* 332 (2003), 675–687.

Boutros R and Byrne JA. D53 (TPD52L1) is a cell cycle-regulated protein maximally expressed at the G2-M transition in breast cancer cells, *Exp. Cell Res.* 310 (2005), 152–165.

Wang R, He H, Sun X, Xu J, Marshall FF, Zhau H, Chung LW, Fu H, He D. Transcription variants of the prostate-specific PrLZ gene and their interaction with 14-3-3 proteins. Biochem Biophys Res Commun. 2009 Sep 1. [Epub ahead of print]

Human TPH2 Neuronal tryptophan hydroxylase (TPH2) an enzyme that is rate-limiting in the biosynthesis of seroto (Swissprot = Q8IWU9)

```
        1 MQPAMMMFSS KYWARRGFsL DSAVPEEHQL LGSSTLNKPN SGKNDDKGNK GSSKREAATE
       61 SGKTAVVFSL KNEVGGLVKA LRLFQEKRVN MVHIESRKSR RRSsEVEIFV DCECGKTEFN
      121 ELIQLLKFQT TIVTLNPPEN IWTEEEELED VPWFPRKISE LDKCSHRVLM YGSELDADHP
      181 GFKDNVYRQR RKYFVDVAMG YKYGQPIPRV EYTEEETKTW GVVFRELSKL YPTHACREYL
      241 KNFPLLTKYC GYREDNVPQL EDVSMFLKER SGFTVRPVAG YLSPRDFLAG LAYRVFHCTQ
      301 YIRHGSDPLY TPEPDTCHEL LGHVPLLADP KFAQFSQEIG LASLGASDED VQKLATCYFF
      361 TIEFGLCKQE GQLRAYGAGL LSSIGELKHA LSDKACVKAF DPKTTCLQEC LITTFQEAYF
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```
      421 VSESFEEAKE KMRDFAKSIT RPFSVYFNPY TQSIEILKDT RSIENVVQDL RSDLNTVCDA
      481 LNKMNQYLGI
>gi|30580625|sp|Q8IWU9.1|TPH2_HUMAN RecName: Full=Tryptophan 5-hydroxylase 2;
AltName: Full=Tryptophan 5-monooxygenase 2; AltName: Full=Neuronal tryptophan
hydroxylase
MQPAMMMFSSKYWARRGFSLDSAVPEEHQLLGSSTLNKPNSGKNDDKGNKGSSKREAATESGKTAVVFSL
KNEVGGLVKALRLFQEKRVNMVHIESRKSRRRSSEVEIFVDCECGKTEFNELIQLLKFQTTIVTLNPPEN
IWTEEEELEDVPWFPRKISELDKCSHRVLMYGSELDADHPGFKDNVYRQRRKYFVDVAMGYKYGQPIPRV
EYTEEETKTWGVVFRELSKLYPTHACREYLKNFPLLTKYCGYREDNVPQLEDVSMFLKERSGFTVRPVAG
YLSPRDFLAGLAYRVFHCTQYIRHGSDPLYTPEPDTCHELLGHVPLLADPKFAQFSQEIGLASLGASDED
VQKLATCYFFTIEFGLCKQEGQLRAYGAGLLSSIGELKHALSDKACVKAFDPKTTCLQECLITTFQEAYF
VSESFEEAKEKMRDFAKSITRPFSVYFNPYTQSIEILKDTRSIENVVQDLRSDLNTVCDALNKMNQYLGI
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Notes

Catalyzes the biopterin dependent monooxygenation of tryptophan to 5-hydroxytryptophan (5HT), which is subsequently decarboxylated to form the neurotransmitter serotonin. Its expression is limited to a few specialized tissues: raphe neurons, pinealocytes, mast cells, mononuclear leukocytes, beta-cells of the islets of Langerhans, and intestinal and pancreatic enterochromaffin cells. Two alternatively spliced isoforms have been described. Isoform 2 appears to be expressed exclusively in the brain, and is expressed at significantly higher levels in the raphe nuclei than isoform 1. In contrast with the WT enzyme, neither phosphorylated TPH2 S19E nor TPH2 S19A bound more strongly to 14-3-3 proteins than non-phosphorylated TPH2. However, when analysing the phosphorylated S104E mutants, the binding intensity to the 14-3-3g increased 50-fold relative to the non-phosphorylated S104E mutant enzyme. Thus phosphorylation-dependent binding to 14-3-3s was observed for all forms of TPH2 having an intact Ser^{19} phosphorylation site. Although phosphorylation of Ser^{104} did not appear to be directly involved in 14-3-3 binding to TPH2, this phosphorylation site could contribute indirectly by increasing enzyme stability and stoichiometry of Ser^{19} phosphorylation.

References to 14-3-3 binding to tryptophan hydroxylase

Winge I, McKinney JA, Ying M, D'Santos CS, Kleppe R, Knappskog PM, Haavik J. Activation and stabilization of human tryptophan hydroxylase 2 by phosphorylation and 14-3-3 binding. Biochem J. 2008 Feb 15;410(1):195-204

Furukawa Y, Ikuta N, Omata S, Yamauchi T, Isobe T, Ichimura T.Demonstration of the phosphorylation-dependent interaction of tryptophan hydroxylase with the 14-3-3 protein. Biochem Biophys Res Commun. 1993 Jul 15;194(1):144-9.

Human TSC2 Tuberin (Swissprot = P49815)

```
        1 MAKPTSKDSG LKEKFKILLG LGTPRPNPRS AEGKQTEFII TAEILRELSM ECGLNNRIRM
       61 IGQICEVAKT KKFEEHAVEA LWKAVADLLQ PERTLEARHA VLALLKAIVQ GQGERLGVLR
      121 ALFFKVIKDY PSNEDLHERL EVFKALTDNG RHITYLEEEL ADFVLQWMDV GLSSEFLLVL
      181 VNLVKFNSCY LDEYIARMVQ MICLLCVRTA SSVDIEVSLQ VLDAVVCYNC LPAESLPLFI
      241 VTLCRTINVK ELCEPCWKLM RNLLGTHLGH SAIYNMCHLM EDRAYMEDAP LLRGAVFFVG
      301 MALWGAHRLY SLRNSPTSVF PSFYQAMACP NEVVSYEIVL SITRLIKKYR KELQVVAWDI
      361 LLNIIERLLQ QLQTLDSPEL RTIVHDLLTT VEELCDQNEF HGSQERYFEL VERCADQRPE
      421 SSLLNLISYR AQSIHPAKDG WIQNLQALME RFFRSESRGA VRIKVLDVLS FVLLINRQFY
      481 EEELINSVVI SQLSHIPEDK DHQVRKLATQ LLVDLAEGCH THHFNSLLDI IEKVMARSLS
      541 PPPELEERDV AAYSASLEDV KTAVLGLLVI LQTKLYTLPA SHATRVYEML VSHIQLHYKH
      601 SYTLPIASSI RLQAFDFLFL LRADSLHRLG LPNKDGVVRF SPYCVCDYME PERGSEKKTS
      661 GPLSPPTGPP GPAPAGPAVR LGSVPYSLLF RVLLQCLKQE SDWKVLKLVL GRLPESLRYK
      721 VLIFTSPCSV DQLCSALCSM LSGPKTLERL RGAPEGFSRT DLHLAVVPVL TALISYHNYL
      781 DKTKQREMVY CLEQGLIHRC ARQCVVALSI CSVEMPDIII KALPVLVVKL THISATASMA
      841 VPLLEFLSTL ARLPHLYRNF AAEQYASVFA ISLPYTNPSK FNQYIVCLAH HVIAMWFIRC
      901 RLPFRKDFVP FITKGLRSNV LLSFDDTPEK DSFRARSTsL NERPKSLRIA RPPKQGLNNS
      961 PPVKEFKESS AAEAFRCRSI SVSEHVVRSR IQTSLTSASL GSADENSVAQ ADDSLKNLHL
     1021 ELTETCLDMM ARYVFSNFTA VPKRSPVGEF LLAGGRTKTW LVGNKLVTVT TSVGTGTRSL
     1081 LGLDSGELQS GPESSSSPGV HVRQTKEAPA KLESQAGQQV SRGARDRVRS MSGGHGLRVG
     1141 ALDVPASQFL GSATSPGPRT APAAKPEKAS AGTRVPVQEK TNLAAYVPLL TQGWAEILVR
     1201 RPTGNTSWLM sLENPLSPFS SDINNMPLQE LSNALMAAER FKEHRDTALY KSLsVPAAST
     1261 AKPPPLPRSN TVASFSSLYQ SSCQGQLHRS VSWADSAVVM EEGSPGEVPV LVEPPGLEDV
     1321 EAALGMDRRT DAYSRSSSVS SQEEKSLHAE ELVGRGIPIE RVVSSEGGRP SVDLSFQPSQ
     1381 PLSKSSSSPE LQTLQDILGD PGDKADVGRL SPEVKARSQS GTLDGESAAW SASGEDSRGQ
     1441 PEGPLPSSSP RSPSGLRPRG YTISDSAPSR RGKRVERDAL KSRATASNAE KVPGINPSFV
     1501 FLQLYHSPFF GDESNKPILL PNESQSFERS VQLLDQIPSY DTHKIAVLYV GEGQSNSELA
     1561 ILSNEHGSYR YTEFLTGLGR LIELKDCQPD KVYLGGLDVC GEDGQFTYCW HDDIMQAVFH
     1621 IATLMPTKDV DKHRCDKKRH LGNDFVSIVY NDSGEDFKLG TIKGQFNFVH VIVTPLDYEC
     1681 NLVSLQCRKD MEGLVDTSVA KIVSDRNLPF VARQMALHAN MASQVHHSRS NPTDIYPSKW
     1741 IARLRHIKRL RQRICEEAAY SNPSLPLVHP PSHSKAPAQT PAEPTPGYEV GQRKRLISSV
     1801 EDFTEFV
>gi|1717799|sp|P49815.1|TSC2_HUMAN RecName: Full=Tuberin; AltName:
Full=Tuberous sclerosis 2 protein
MAKPTSKDSGLKEKFKILLGLGTPRPNPRSAEGKQTEFIITAEILRELSMECGLNNRIRMIGQICEVAKT
KKFEEHAVEALWKAVADLLQPERTLEARHAVLALLKAIVQGQGERLGVLRALFFKVIKDYPSNEDLHERL
EVFKALTDNGRHITYLEEELADFVLQWMDVGLSSEFLLVLVNLVKFNSCYLDEYIARMVQMICLLCVRTA
SSVDIEVSLQVLDAVVCYNCLPAESLPLFIVTLCRTINVKELCEPCWKLMRNLLGTHLGHSAIYNMCHLM
EDRAYMEDAPLLRGAVFFVGMALWGAHRLYSLRNSPTSVFPSFYQAMACPNEVVSYEIVLSITRLIKKYR
KELQVVAWDILLNIIERLLQQLQTLDSPELRTIVHDLLTTVEELCDQNEFHGSQERYFELVERCADQRPE
SSLLNLISYRAQSIHPAKDGWIQNLQALMERFFRSESRGAVRIKVLDVLSFVLLINRQFYEEELINSVVI
SQLSHIPEDKDHQVRKLATQLLVDLAEGCHTHHFNSLLDIIEKVMARSLSPPPELEERDVAAYSASLEDV
KTAVLGLLVILQTKLYTLPASHATRVYEMLVSHIQLHYKHSYTLPIASSIRLQAFDFLFLLRADSLHRLG
LPNKDGVVRFSPYCVCDYMEPERGSEKKTSGPLSPPTGPPGPAPAGPAVRLGSVPYSLLFRVLLQCLKQE
SDWKVLKLVLGRLPESLRYKVLIFTSPCSVDQLCSALCSMLSGPKTLERLRGAPEGFSRTDLHLAVVPVL
```

```
TALISYHNYLDKTKQREMVYCLEQGLIHRCARQCVVALSICSVEMPDIIIKALPVLVVKLTHISATASMA
VPLLEFLSTLARLPHLYRNFAAEQYASVFAISLPYTNPSKFNQYIVCLAHHVIAMWFIRCRLPFRKDFVP
FITKGLRSNVLLSFDDTPEKDSFRARSTSLNERPKSLRIARPPKQGLNNSPPVKEFKESSAAEAFRCRSI
SVSEHVVRSRIQTSLTSASLGSADENSVAQADDSLKNLHLELTETCLDMMARYVFSNFTAVPKRSPVGEF
LLAGGRTKTWLVGNKLVTVTTSVGTGTRSLLGLDSGELQSGPESSSSPGVHVRQTKEAPAKLESQAGQQV
SRGARDRVRSMSGGHGLRVGALDVPASQFLGSATSPGPRTAPAAKPEKASAGTRVPVQEKTNLAAYVPLL
TQGWAEILVRRPTGNTSWLMSLENPLSPFSSDINNMPLQELSNALMAAERFKEHRDTALYKSLSVPAAST
AKPPPLPRSNTVASFSSLYQSSCQGQLHRSVSWADSAVVMEEGSPGEVPVLVEPPGLEDVEAALGMDRRT
DAYSRSSSVSSQEEKSLHAEELVGRGIPIERVVSSEGGRPSVDLSFQPSQPLSKSSSSPELQTLQDILGD
PGDKADVGRLSPEVKARSQSGTLDGESAAWSASGEDSRGQPEGPLPSSSPRSPSGLRPRGYTISDSAPSR
RGKRVERDALKSRATASNAEKVPGINPSFVFLQLYHSPFFGDESNKPILLPNESQSFERSVQLLDQIPSY
DTHKIAVLYVGEGQSNSELAILSNEHGSYRYTEFLTGLGRLIELKDCQPDKVYLGGLDVCGEDGQFTYCW
HDDIMQAVFHIATLMPTKDVDKHRCDKKRHLGNDFVSIVYNDSGEDFKLGTIKGQFNFVHVIVTPLDYEC
NLVSLQCRKDMEGLVDTSVAKIVSDRNLPFVARQMALHANMASQVHHSRSNPTDIYPSKWIARLRHIKRL
RQRICEEAAYSNPSLPLVHPPSHSKAPAQTPAEPTPGYEVGQRKRLISSVEDFTEFV
```

Notes

Two 14-3-3 binding sites are RSTpS^{939}LN and KSLpS^{1210}VP (=Ser1254 in P49815) (Liu et al 2002) whereas Ser1210 SWLMpS^{1210}LENPLSPFS (=Ser1211 P49815) and not RSTpS^{939}LN is reported by Li et al (2002).

Tuberin and Hamartin (TSC1) form a tumor suppressor heterodimer that inhibits the mTOR nutrient signaling.

TSC1/TSC2 targets the small G protein Rheb, a novel mediator of the nutrient signaling input to mTOR. Functions as a Rheb GTPase activating protein (GAP). Four alternatively spliced isoforms have been described.

TSC2 mutants that do not bind 14-3-3 are inactive in hypoxia signaling to mTORC1. TSC2, but not TSC1, associates with 14-3-3 in vivo.

Controversy about whether Akt/PKB phosphorylation leads to 14-3-3 binding. Sites marked are based on available information, but not 100% certain.

References to 14-3-3 binding to TSC2

Hengstschläger M, Rosner M, Fountoulakis M, Lubec G.Tuberous sclerosis genes regulate cellular 14-3-3 protein levels. Biochem Biophys Res Commun. 2003 Dec 19;312(3)

Li Y, Regulation of TSC2 by 14-3-3 binding. J Biol Chem. 2002 Nov 22;277(47):44593-6

Nellist M, Goedbloed MA, Halley DJ. Regulation of tuberous sclerosis complex (TSC) function by 14-3-3 proteins.Biochem Soc Trans. 2003 Jun;31(Pt 3):587-91.

Li Y, Inoki K, Vacratsis P, Guan KL. The p38 and MK2 kinase cascade phosphorylates tuberin, the tuberous sclerosis 2 gene product, and enhances its interaction with 14-3-3.J Biol Chem. 2003 Apr 18;278(16):13663-71.

Shumway SD, Li Y, Xiong Y. 14-3-3beta binds to and negatively regulates the tuberous sclerosis complex 2 (TSC2) tumor suppressor gene product, tuberin. J Biol Chem. 2003 Jan 24;278(4):2089-92.

Li Y, Inoki K, Yeung R, Guan KL. Regulation of TSC2 by 14-3-3 binding. J Biol Chem. 2002 Nov 22;277(47):44593-6.

Nellist M, Goedbloed MA, de Winter C, Verhaaf B, Jankie A, Reuser AJ, van den Ouweland AM, van der Sluijs P, Halley DJ.Identification and characterization of the interaction between tuberin and 14-3-3zeta. J Biol Chem. 2002 Oct 18;277(42):39417-24.

Liu MY, Cai S, Espejo A, Bedford MT, Walker CL. 14-3-3 interacts with the tumor suppressor tuberin at Akt phosphorylation site(s). Cancer Res. 2002 Nov 15;62(22):6475-80.

Mancini M, Petta S, Martinelli G, Barbieri E, Santucci MA. RAD 001 (everolimus) prevents mTOR and Akt late re-activation in response to imatinib in chronic myeloid leukemia. J Cell Biochem. [Epub ahead of print]

<u>Human USP8</u> Deubiquitinating enzyme (Swissprot = P40818)

```
   1 MPAVASVPKE LYLSSSLKDL NKKTEVKPEK ISTKSYVHSA LKIFKTAEEC RLDRDEERAY
  61 VLYMKYVTVY NLIKKRPDFK QQQDYFHSIL GPGNIKKAVE EAERLSESLK LRYEEAEVRK
 121 KLEEKDRQEE AQRLQQKRQE TGREDGGTLA KGSLENVLDS KDKTQKSNGE KNEKCETKEK
 181 GAITAKELYT MMTDKNISLI IMDARRMQDY QDSCILHSLS VPEEAISPGV TASWIEAHLP
 241 DDSKDTWKKR GNVEYVVLLD WFSSAKDLQI GTTLRSLKDA LFKWESKTVL RNEPLVLEGG
 301 YENWLLCYPQ YTTNAKVTPP PRRQNEEVSI SLDFTYPSLE ESIPSKPAAQ TPPASIEVDE
 361 NIELISGQNE RMGPLNISTP VEPVAASKSD VSPIIQPVPS IKNVPQIDRT KKPAVKLPEE
 421 HRIKSESTNH EQQSPQSGKV IPDRSTKPVV FSPTLMLTDE EKARIHAETA LLMEKNKQEK
 481 ELRERQQEEQ KEKLRKEEQE QKAKKKQEAE ENEITEKQQK AKEEMEKKES EQAKKEDKET
 541 SAKRGKEITG VKRQSKSEHE TSDAKKSVED RGKRCPTPEI QKKSTGDVPH TSVTGDSGSG
 601 KPFKIKGQPE SGILRTGTFR EDTDDTERNK AQREPLTRAR SEEMGRIVPG LPSGWAKFLD
 661 PITGTFRYYH SPTNTVHMYP PEMAPSSAPP STPPTHKAKP QIPAERDREP SKLKRSYsSP
 721 DITQAIQEEE KRKPTVTPTV NRENKPTCYP KAEISRLSAS QIRNLNPVFG GSGPALTGLR
 781 NLGNTCYMNS ILQCLCNAPH LADYFNRNCY QDDINRSNLL GHKGEVAEEF GIIMKALWTG
 841 QYRYISPKDF KITIGKINDQ FAGYSQQDSQ ELLLFLMDGL HEDLNKADNR KRYKEENNDH
 901 LDDFKAAEHA WQKHKQLNES IIVALFQGQF KSTVQCLTCH KKSRTFEAFM YLSLPLASTS
 961 KCTLQDCLRL FSKEEKLTDN NRFYCSHCRA RRDSLKKIEI WKLPPVLLVH LKRFSYDGRW
1021 KQKLQTSVDF PLENLDLSQY VIGPKNNLKK YNLFSVSNHY GGLDGGHYTA YCKNAARQRW
1081 FKFDDHEVSD ISVSSVKSSA AYILFYTSLG PRVTDVAT
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>gi|731046|sp|P40818.1|UBP8_HUMAN RecName: Full=Ubiquitin carboxyl-terminal
hydrolase 8; AltName: Full=Ubiquitin thioesterase 8; AltName: Full=Ubiquitin-
specific-processing protease 8; AltName: Full=Deubiquitinating enzyme 8;
Short=hUBPy
MPAVASVPKELYLSSSLKDLNKKTEVKPEKISTKSYVHSALKIFKTAEECRLDRDEERAYVLYMKYVTVY
NLIKKRPDFKQQQDYFHSILGPGNIKKAVEEAERLSESLKLRYEEAEVRKKLEEKDRQEEAQRLQQKRQE
TGREDGGTLAKGSLENVLDSKDKTQKSNGEKNEKCETKEKGAITAKELYTMMTDKNISLIIMDARRMQDY
QDSCILHSLSVPEEAISPGVTASWIEAHLPDDSKDTWKKRGNVEYVVLLDWFSSAKDLQIGTTLRSLKDA
LFKWESKTVLRNEPLVLEGGYENWLLCYPQYTTNAKVTPPPRRQNEEVSISLDFTYPSLEESIPSKPAAQ
TPPASIEVDENIELISGQNERMGPLNISTPVEPVAASKSDVSPIIQPVPSIKNVPQIDRTKKPAVKLPEE
HRIKSESTNHEQQSPQSGKVIPDRSTKPVVFSPTLMLTDEEKARIHAETALLMEKNKQEKELRERQQEEQ
KEKLRKEEQEQKAKKKQEAEENEITEKQQKAKEEMEKKESEQAKKEDKETSAKRGKEITGVKRQSKSEHE
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TSDAKKSVEDRGKRCPTPEIQKKSTGDVPHTSVTGDSGSGKPFKIKGQPESGILRTGTFREDTDDTERNK
AQREPLTRARSEEMGRIVPGLPSGWAKFLDPITGTFRYYHSPTNTVHMYPPEMAPSSAPPSTPPTHKAKP
QIPAERDREPSKLKRSYSSPDITQAIQEEEKRKPTVTPTVNRENKPTCYPKAEISRLSASQIRNLNPVFG
GSGPALTGLRNLGNTCYMNSILQCLCNAPHLADYFNRNCYQDDINRSNLLGHKGEVAEEFGIIMKALWTG
QYRYISPKDFKITIGKINDQFAGYSQQDSQELLLFLMDGLHEDLNKADNRKRYKEENNDHLDDFKAAEHA
WQKHKQLNESIIVALFQGQFKSTVQCLTCHKKSRTFEAFMYLSLPLASTSKCTLQDCLRLFSKEEKLTDN
NRFYCSHCRARRDSLKKIEIWKLPPVLLVHLKRFSYDGRWKQKLQTSVDFPLENLDLSQYVIGPKNNLKK
YNLFSVSNHYGGLDGGHYTAYCKNAARQRWFKFDDHEVSDISVSSVKSSAAYILFYTSLGPRVTDVAT
```

Notes

USP8 (=UBPY) The 14-3-3 binding of UBPY was inhibited by mutating the consensus 14-3-3-binding motif RSYS(680)SP, by phosphatase treatment, and by competition with the Ser(680)-phosphorylated RSYS(680)SP peptide. Metabolic labeling with [(32)P]orthophosphate and immunoblotting using antibody against the phosphorylated 14-3-3-binding motif showed that Ser(680) is a major phosphorylation site in UBPY. Ser680 in the form of USP8 studied by Mizuno et al (2007) = Ser718 in P40818.

References to 14-3-3 binding to USP8

Mizuno E, Kitamura N, Komada M.14-3-3-dependent inhibition of the deubiquitinating activity of UBPY and its cancellation in the M phase. Exp Cell Res. 2007 Oct 1;313(16):3624-34.

<u>Human WWTR1 (TAZ)</u> WW domain-containing transcription regulator protein 1functions as a transcriptional coactivator (Q9GZV5)

```
        1 MNPASAPPPL PPPGQQVIHV TQDLDTDLEA LFNSVMNPKP SSWRKKILPE SFFKEPDSGS
       61 HSRQSSTDSS GGHPGPRLAG GAQHVRSHsS PASLQLGTGA GAAGSPAQQH AHLRQQSYDV
      121 TDELPLPPGW EMTFTATGQR YFLNHIEKIT TWQDPRKAMN QPLNHMNLHP AVSSTPVPQR
      181 SMAVSQPNLV MNHQHQQQMA PSTLSQQNHP TQNPPAGLMS MPNALTTQQQ QQQKLRLQRI
      241 QMERERIRMR QEELMRQEAA LCRQLPMEAE TLAPVQAAVN PPTMTPDMRS ITNNSSDPFL
      301 NGGPYHSREQ STDSGLGLGC YSVPTTPEDF LSNVDEMDTG ENAGQTPMNI NPQQTRFPDF
      361 LDCLPGTNVD LGTLESEDLI PLFNDVESAL NKSEPFLTWL
>gi|67462080|sp|Q9GZV5.1|WWTR1_HUMAN RecName: Full=WW domain-containing
transcription regulator protein 1; AltName: Full=Transcriptional coactivator
with PDZ-binding motif
MNPASAPPPLPPPGQQVIHVTQDLDTDLEALFNSVMNPKPSSWRKKILPESFFKEPDSGSHSRQSSTDSS
GGHPGPRLAGGAQHVRSHSSPASLQLGTGAGAAGSPAQQHAHLRQQSYDVTDELPLPPGWEMTFTATGQR
YFLNHIEKITTWQDPRKAMNQPLNHMNLHPAVSSTPVPQRSMAVSQPNLVMNHQHQQQMAPSTLSQQNHP
TQNPPAGLMSMPNALTTQQQQQQKLRLQRIQMERERIRMRQEELMRQEAALCRQLPMEAETLAPVQAAVN
PPTMTPDMRSITNNSSDPFLNGGPYHSREQSTDSGLGLGCYSVPTTPEDFLSNVDEMDTGENAGQTPMNI
NPQQTRFPDFLDCLPGTNVDLGTLESEDLIPLFNDVESALNKSEPFLTWL
```

Notes

This protein is related to YAP1 (YAP65). TAZ plays a role in the migration, invasion, and tumorigenesis of breast cancer cells and thus presents a novel target for the detection and treatment of breast cancer. 14-3-3 binding requires TAZ phosphorylation on a single serine residue (Ser89), resulting in the inhibition of TAZ transcriptional co-activation through 14-3-3-mediated nuclear export. TAZ may link events at the plasma membrane and cytoskeleton to nuclear transcription in a manner that can be regulated by 14-3-3.

References to 14-3-3 binding to WWTR1 (TAZ)

Kanai F, Marignani PA, Sarbassova D, Yagi R, Hall RA, Donowitz M, Hisaminato A, Fujiwara T, Ito Y, Cantley LC, Yaffe MB.TAZ: a novel transcriptional co-activator regulated by interactions with 14-3-3 and PDZ domain proteins. EMBO J. 2000 Dec 15;19(24):6778-91

Chan SW, Lim CJ, Guo K, Ng CP, Lee I, Hunziker W, Zeng Q, Hong W.A role for TAZ in migration, invasion, and tumorigenesis of breast cancer cells. Cancer Res. 2008 Apr 15;68(8):2592-8

Wang K, Degerny C, Xu M, Yang XJ. YAP, TAZ, and Yorkie: a conserved family of signal-responsive transcriptional coregulators in animal development and human disease. Biochem Cell Biol. 2009 Feb;87(1):77-91.

Lei QY, Zhang H, Zhao B, Zha ZY, Bai F, Pei XH, Zhao S, Xiong Y, Guan KL.TAZ promotes cell proliferation and epithelial-mesenchymal transition and is inhibited by the hippo pathway. Mol Cell Biol. 2008 Apr;28(7):2426-36.

Hong JH, Hwang ES, McManus MT, Amsterdam A, Tian Y, Kalmukova R, Mueller E, Benjamin T, Spiegelman BM, Sharp PA, Hopkins N, Yaffe MB. TAZ, a transcriptional modulator of mesenchymal stem cell differentiation. Science. 2005 Aug 12;309(5737):1074-8.

<u>Human YAP1 (YAP65)</u> Co-activator for TEAD/TEF transcription factors (Swissprot = P46937)

```
        1 MDPGQQPPPQ PAPQGQGQPP SQPPQGQGPP SGPGQPAPAA TQAAPQAPPA GHQIVHVRGD
       61 SETDLEALFN AVMNPKTANV PQTVPMRLRK LPDSFFKPPE PKSHSRQAST DAGTAGALTP
      121 QHVRAHsSPA SLQLGAVSPG TLTPTGVVSG PAATPTAQHL RQSSFEIPDD VPLPAGWEMA
      181 KTSSGQRYFL NHIDQTTTWQ DPRKAMLSQM NVTAPTSPPV QQNMMNSASA MNQRISQSAP
      241 VKQPPPLAPQ SPQGGVMGGS NSNQQQQMRL QQLQMEKERL RLKQQELLRQ VRPQELALRS
      301 QLPTLEQDGG TQNPVSSPGM SQELRTMTTN SSDPFLNSGT YHSRDESTDS GLSMSSYSVP
      361 RTPDDFLNSV DEMDTGDTIN QSTLPSQQNR FPDYLEAIPG TNVDLGTLEG DGMNIEGEEL
      421 MPSLQEALSS DILNDMESVL AATKLDKESF LTWL
>gi|1175423|sp|P46937.1|YAP1_HUMAN RecName: Full=65 kDa Yes-associated
protein; AltName: Full=YAP65
MDPGQQPPPQPAPQGQGQPPSQPPQGQGPPSGPGQPAPAATQAAPQAPPAGHQIVHVRGDSETDLEALFN
AVMNPKTANVPQTVPMRLRKLPDSFFKPPEPKSHSRQASTDAGTAGALTPQHVRAHSSPASLQLGAVSPG
TLTPTGVVSGPAATPTAQHLRQSSFEIPDDVPLPAGWEMAKTSSGQRYFLNHIDQTTTWQDPRKAMLSQM
NVTAPTSPPVQQNMMNSASAMNQRISQSAPVKQPPPLAPQSPQGGVMGGSNSNQQQQMRLQQLQMEKERL
RLKQQELLRQVRPQELALRSQLPTLEQDGGTQNPVSSPGMSQELRTMTTNSSDPFLNSGTYHSRDESTDS
GLSMSSYSVPRTPDDFLNSVDEMDTGDTINQSTLPSQQNRFPDYLEAIPGTNVDLGTLEGDGMNIEGEEL
MPSLQEALSSDILNDMESVLAATKLDKESFLTWL
```

Notes

While PKB has been reported to phosphorylate the 14-3-3-binding site at Ser127 (Basu et al 2003), this HxRxx(pS) site does not conform to the PKB consensus, and more recent data indicate that this site is phosphorylated by

LATS kinases (Zhao et al 2007, Hao et al 2008, Lee et al 2008).

References to 14-3-3 binding to human YAP65 and Drosophila Yorkie

Vassilev A, Kaneko KJ, Shu H, Zhao Y, DePamphilis ML. TEAD/TEF transcription factors utilize the activation domain of YAP65, a Src/Yes-associated protein localized in the cytoplasm. Genes Dev. 2001 May 15;15(10):1229-41.

Badouel C, Gardano L, Amin N, Garg A, Rosenfeld R, Le Bihan T, McNeill H. The FERM-domain protein Expanded regulates Hippo pathway activity via direct interactions with the transcriptional activator Yorkie. Dev Cell. 2009 Mar;16(3):411-20.

Wang K, Degerny C, Xu M, Yang XJ. YAP, TAZ, and Yorkie: a conserved family of signal-responsive transcriptional coregulators in animal development and human disease. Biochem Cell Biol. 2009 Feb;87(1):77-91.

Zhao B, Wei X, Li W, Udan RS, Yang Q, Kim J, Xie J, Ikenoue T, Yu J, Li L, Zheng P, Ye K, Chinnaiyan A, Halder G, Lai ZC, Guan KL. Inactivation of YAP oncoprotein by the Hippo pathway is involved in cell contact inhibition and tissue growth control. Genes Dev. 2007 Nov 1;21(21):2747-61.

Basu S, Totty NF, Irwin MS, Sudol M, Downward J. Akt phosphorylates the Yes-associated protein, YAP, to induce interaction with 14-3-3 and attenuation of p73-mediated apoptosis. Mol Cell. 2003 Jan;11(1):11-23.

Vassilev A, Kaneko KJ, Shu H, Zhao Y, DePamphilis ML. TEAD/TEF transcription factors utilize the activation domain of YAP65, a Src/Yes-associated protein localized in the cytoplasm. Genes Dev. 2001 May 15;15(10):1229-41.

Kanai F, Marignani PA, Sarbassova D, Yagi R, Hall RA, Donowitz M, Hisaminato A, Fujiwara T, Ito Y, Cantley LC, Yaffe MB. TAZ: a novel transcriptional co-activator regulated by interactions with 14-3-3 and PDZ domain proteins. EMBO J. 2000 Dec 15;19(24):6778-91.

Zhao B, Li L, Tumaneng K, Wang CY, Guan KL. A coordinated phosphorylation by Lats and CK1 regulates YAP stability through SCF(beta-TRCP). Genes Dev. 2010 Jan 1;24(1):72-85.

Human ZBTB17 (Miz1) Zinc finger & BTB domain-containing protein 17 (Myc-interacting zinc finger protein) (Swissprot = Q13105)

```
      1 MDFPQHSQHV LEQLNQQRQL GLLCDCTFVV DGVHFKAHKA VLAACSEYFK MLFVDQKDVV
     61 HLDISNAAGL GQVLEFMYTA KLSLSPENVD DVLAVATFLQ MQDIITACHA LKSLAEPATS
    121 PGGNAEALAT EGGDKRAKEE KVATSTLSRL EQAGRSTPIG PSRDLKEERG GQAQSAASGA
    181 EQTEKADAPR EPPPVELKPD PTSGMAAAEA EAALSESSEQ EMEVEPARKG EEEQKEQEEQ
    241 EEEGAGPAEV KEEGSQLENG EAPEENENEE SAGTDSGQEL GSEARGLRSG tYGDRTESKA
    301 YGSVIHKCED CGKEFTHTGN FKRHIRIHTG EKPFSCRECS KAFSDPAACK AHEKTHSPLK
    361 PYGCEECGKS YRLISLLNLH KKRHSGEARY RCEDCGKLFT TSGNLKRHQL VHSGEKPYQC
    421 DYCGRSFsDP TSKMRHLETH DTDKEHKCPH CDKKFNQVGN LKAHLKIHIA DGPLKCRECG
    481 KQFTTSGNLK RHLRIHSGEK PYVCIHCQRQ FADPGALQRH VRIHTGEKPC QCVMCGKAFT
    541 QASSLIAHVR QHTGEKPYVC ERCGKRFVQS SQLANHIRHH DNIRPHKCSV CSKAFVNVGD
    601 LSKHIIIHTG EKPYLCDKCG RGFNRVDNLR SHVKTVHQGK AGIKILEPEE GSEVSVVTVD
    661 DMVTLATEAL AATAVTQLTV VPVGAAVTAD ETEVLKAEIS KAVKQVQEED PNTHILYACD
    721 SCGDKFLDAN SLAQHVRIHT AQALVMFQTD ADFYQQYGPG GTWPAGQVLQ AGELVFRPRD
    781 GAEGQPALAE TSPTAPECPP PAE
>gi|62906906|sp|Q13105.3|ZBT17_HUMAN RecName: Full=Zinc finger and BTB
domain-containing protein 17; AltName: Full=Zinc finger protein 60; AltName:
Full=Zinc finger protein 151; AltName: Full=Myc-interacting zinc finger
protein; AltName: Full=Miz-1
MDFPQHSQHVLEQLNQQRQLGLLCDCTFVVDGVHFKAHKAVLAACSEYFKMLFVDQKDVVHLDISNAAGL
GQVLEFMYTAKLSLSPENVDDVLAVATFLQMQDIITACHALKSLAEPATSPGGNAEALATEGGDKRAKEE
KVATSTLSRLEQAGRSTPIGPSRDLKEERGGQAQSAASGAEQTEKADAPREPPPVELKPDPTSGMAAAEA
EAALSESSEQEMEVEPARKGEEEQKEQEEQEEEGAGPAEVKEEGSQLENGEAPEENENEESAGTDSGQEL
GSEARGLRSGTYGDRTESKAYGSVIHKCEDCGKEFTHTGNFKRHIRIHTGEKPFSCRECSKAFSDPAACK
AHEKTHSPLKPYGCEECGKSYRLISLLNLHKKRHSGEARYRCEDCGKLFTTSGNLKRHQLVHSGEKPYQC
DYCGRSFSDPTSKMRHLETHDTDKEHKCPHCDKKFNQVGNLKAHLKIHIADGPLKCRECGKQFTTSGNLK
RHLRIHSGEKPYVCIHCQRQFADPGALQRHVRIHTGEKPCQCVMCGKAFTQASSLIAHVRQHTGEKPYVC
ERCGKRFVQSSQLANHIRHHDNIRPHKCSVCSKAFVNVGDLSKHIIIHTGEKPYLCDKCGRGFNRVDNLR
SHVKTVHQGKAGIKILEPEEGSEVSVVTVDDMVTLATEALAATAVTQLTVVPVGAAVTADETEVLKAEIS
KAVKQVQEEDPNTHILYACDSCGDKFLDANSLAQHVRIHTAQALVMFQTDADFYQQYGPGGTWPAGQVLQ
AGELVFRPRDGAEGQPALAETSPTAPECPPPAE
```

Notes

RSGpT^{291}YG, CGRSFpS^{428}DP

References to 14-3-3 binding to Miz1

Wanzel M, Kleine-Kohlbrecher D, Herold S, Hock A, Berns K, Park J, Hemmings B, Eilers M. Akt and 14-3-3eta regulate Miz1 to control cell-cycle arrest after DNA damage. Nat Cell Biol. 2005 Jan;7(1):30-41.

Human ZFP36L1 BRF1 (butyrate response factor 1; EGF-response factor) (Swissprot = Q07352)

```
      1 MTTTLVSATI FDLSEVLCKG NKMLNYSAPS AGGCLLDRKA VGTPAGGGFP RRHSVTLPSS
     61 KFHQNQLLSS LKGEPAPALS SRDSRFRDRS FsEGGERLLP TQKQPGGGQV NSSRYKTELC
    121 RPFEENGACK YGDKCQFAHG IHELRSLTRH PKYKTELCRT FHTIGFCPYG PRCHFIHNAE
    181 ERRALAGARD LSADRPRLQH SFsFAGFPSA AATAAATGLL DSPTSITPPP ILSADDLLGS
    241 PTLPDGTNNP FAFSSQELAS LFAPSMGLPG GGSPTTFLFR PMSESPHMFD SPPSPQDSLS
    301 DQEGYLSSSS SSHSGSDSPT LDNSRRLPIF SRLSISDD
>gi|1351254|sp|Q07352.1|TISB_HUMAN RecName: Full=Butyrate response factor 1;
AltName: Full=Protein TIS11B; AltName: Full=EGF-response factor 1; Short=ERF-
1
MTTTLVSATIFDLSEVLCKGNKMLNYSAPSAGGCLLDRKAVGTPAGGGFPRRHSVTLPSSKFHQNQLLSS
LKGEPAPALSSRDSRFRDRSFSEGGERLLPTQKQPGGGQVNSSRYKTELCRPFEENGACKYGDKCQFAHG
IHELRSLTRHPKYKTELCRTFHTIGFCPYGPRCHFIHNAEERRALAGARDLSADRPRLQHSFSFAGFPSA
AATAAATGLLDSPTSITPPPILSADDLLGSPTLPDGTNNPFAFSSQELASLFAPSMGLPGGGSPTTFLFR
PMSESPHMFDSPPSPQDSLSDQEGYLSSSSSSHSGSDSPTLDNSRRLPIFSRLSISDD
```

Notes

SRDSRFRDRSF(pS92)EGGERLLP

A zinc finger protein that plays an important role in the assembly of the RNA polymerase III initiation factor TFIIIB. Regulates mRNA levels by targeting transcripts containing AREs (AU-rich elements) into the decay pathway. Phosphorylation by Akt apparently generates 14-3-3 binding sites and inhibits BRF1 from promoting mRNA activity. Contains 2 C3H1-type zinc fingers. Phosphorylation by PKB at both S92 and S203. Mutation leads to complete loss of PKB regulation of BRF1 and constituative mRNA decay. Cell compartment fractionation experiments support a model in which binding to 14-3-3 sequesters BRF1 through relocalization and prevents it from executing its mRNA decay activity, as well as from proteasomal degradation, thereby maintaining high BRF1 protein levels that are required to reinstate decay upon dissipation of the stabilizing signal.

References to 14-3-3 binding to BRF1

Schmidlin M, Lu M, Leuenberger SA, Stoecklin G, Mallaun M, Gross B, Gherzi R, Hess D, Hemmings BA, Moroni C. The ARE-dependent mRNA-destabilizing activity of BRF1 is regulated by protein kinase B.EMBO J. 2004 Dec 8;23(24):4760-9.

Benjamin D, Schmidlin M, Min L, Gross B, Moroni C. BRF1 Protein Turnover and mRNA Decay Activity Are Regulated by Protein Kinase B at the Same Phosphorylation Sites. Mol Cell Biol. 2006 December; 26(24): 9497–9507

Human ZNF395 (Huntington disease gene regulatory region-binding protein 2, HDBP2) (Papillomavirus-binding factor, PBF) (Swissprot = Q9H8N7)

```
       1 MASVLSRRLG KRSLLGARVL GPSASEGPSA APPSEPLLEG AAPQPFTTSD DTPCQEQPKE
      61 VLKAPSTSGL QQVAFQPGQK VYVWYGGQEC TGLVEQHSWM EGQVTVWLLE QKLQVCCRVE
     121 EVWLAELQGP CPQAPPLEPG AQALAYRPVS RNIDVPKRKS DAVEMDEMMA AMVLTSLSCS
     181 PVVQSPPGTE ANFSASRAAC DPWKESGDIS DSGSSTTSGH WSGSSGVSTP SPPHPQASPK
     241 YLGDAFGSPQ TDHGFETDPD PFLLDEPAPR KRKNSVKVMY KCLWPNCGKV LRSIVGIKRH
     301 VKALHLGDTV DSDQFKREED FYYTEVQLKE ESAAAAAAAA AGTPVPGTPT SEPAPTPSMT
     361 GLPLSALPPP LHKAQSSGPE HPGPESSLPS GALSKsAPGS FWHIQADHAY QALPSFQIPV
     421 SPHIYTSVSW AAAPSAACSL SPVRSRSLSF sEPQQPAPAM KSHLIVTSPP RAQSGARKAR
     481 GEAKKCRKVY GIEHRDQWCT ACRWKKACQR FLD
>gi|84028224|sp|Q9H8N7.2|ZN395_HUMAN RecName: Full=Zinc finger protein 395;
AltName: Full=Papillomavirus-binding factor; AltName: Full=Papillomavirus
regulatory factor 1; Short=PRF-1; AltName: Full=Huntington disease gene
regulatory region-binding protein 2; Short=HDBP-2; Short=HD gene regulatory
region-binding protein 2; AltName: Full=HD-regulating factor 2; Short=HDRF-2
MASVLSRRLGKRSLLGARVLGPSASEGPSAAPPSEPLLEGAAPQPFTTSDDTPCQEQPKEVLKAPSTSGL
QQVAFQPGQKVYVWYGGQECTGLVEQHSWMEGQVTVWLLEQKLQVCCRVEEVWLAELQGPCPQAPPLEPG
AQALAYRPVSRNIDVPKRKSDAVEMDEMMAAMVLTSLSCSPVVQSPPGTEANFSASRAACDPWKESGDIS
DSGSSTTSGHWSGSSGVSTPSPPHPQASPKYLGDAFGSPQTDHGFETDPDPFLLDEPAPRKRKNSVKVMY
KCLWPNCGKVLRSIVGIKRHVKALHLGDTVDSDQFKREEDFYYTEVQLKEESAAAAAAAAAGTPVPGTPT
SEPAPTPSMTGLPLSALPPPLHKAQSSGPEHPGPESSLPSGALSKSAPGSFWHIQADHAYQALPSFQIPV
SPHIYTSVSWAAAPSAACSLSPVRSRSLSFSEPQQPAPAMKSHLIVTSPPRAQSGARKARGEAKKCRKVY
GIEHRDQWCTACRWKKACQRFLD
```

Notes

Inspection of the PBF amino acid sequence revealed two motifs from amino acids 444 to 453 (the sequence RSRSLSFSEP), and from amino acids 393 to 398 (the sequence LSKSAP), that resembled “mode I”, although neither motif was perfect. Individual mutation of the potential binding serine at position 396 to alanine (S396A; PBFmt4) or the serine at position −2 to the potential binding serine (S394A; PBFmt5) did not significantly affect the ability of this protein to interact with HA-14-3-3β. However, simultaneous mutation of both residues in PBF-S394/396A (PBFmt4/5) resulted in a clear reduction in the association with over-expressed HA-14-3-3β. Thus, this binding motif relied on the presence of one of the two phosphoserines for its activity. While the site at S394/396 mediates high-affinity binding, the site at S447/449/451 appears to act as a low-affinity motif.

References to 14-3-3-binding to Zinc finger protein 395

Sichtig N, Silling S, Steger G. Papillomavirus binding factor (PBF)-mediated inhibition of cell growth is regulated by 14-3-3beta. Arch Biochem Biophys. 2007 Aug 1;464(1):90-9.

Tanaka K, Shouguchi-Miyata J, Miyamoto N, Ikeda JE. Novel nuclear shuttle proteins, HDBP1 and HDBP2, bind to neuronal cell-specific cis-regulatory element in the promoter for the human Huntington's disease gene. J Biol Chem. 2004 Feb 20;279(8):7275-86.

Human ZNRF2 E3 ubiquitin ligase (Swissprot = Q8NHG8)

```
       1 MGAKQSGPAA ANGRTRAYsG SDLPSSSSGG ANGTAGGGGG ARAAAAGRFP AQVPSAHQPS
      61 ASGGAAAAAA APAAPAAPRS RSLGGAVGSV ASGARAAQSP FSIPNSSSGP YGSQDSVHSS
     121 PEDGGGGRDR PVGGSPGGPR LVIGSLPAHL SPHMFGGFKC PVCSKFVSSD EMDLHLVMCL
     181 TKPRITYNED VLSKDAGECA ICLEELQQGD TIARLPCLCI YHKGCIDEWF EVNRSCPEHP
     241 SD
>gi|74762595|sp|Q8NHG8.1|ZNRF2_HUMAN RecName: Full=E3 ubiquitin-protein
ligase ZNRF2; AltName: Full=Zinc/RING finger protein 2; AltName: Full=RING
finger protein 202; AltName: Full=Protein Ells2
MGAKQSGPAAANGRTRAYSGSDLPSSSSGGANGTAGGGGGARAAAAGRFPAQVPSAHQPSASGGAAAAAA
APAAPAAPRSRSLGGAVGSVASGARAAQSPFSIPNSSSGPYGSQDSVHSSPEDGGGGRDRPVGGSPGGPR
LVIGSLPAHLSPHMFGGFKCPVCSKFVSSDEMDLHLVMCLTKPRITYNEDVLSKDAGECAICLEELQQGD
TIARLPCLCIYHKGCIDEWFEVNRSCPEHPSD
```

Notes

MAGE domain = Ala41 to Ser120
Zn finger = Cys160 to Cys179
RING finger = Cys199 to Pro240
14-3-3 binding site = pSer19 + one other unknown site

References to 14-3-3 binding to ZNRF2

Dubois F, Vandermoere F, Gernez A, Murphy J, Toth R, Chen S, Geraghty KM, Morrice NA and MacKintosh C

(2009) Differential 14-3-3-affinity capture reveals new downstream targets of PI 3-kinase signaling (2009 Aug 1)

Mouse AKR13b CAI52035 (mouse) Ankyrin repeat domain 13b

```
          1 KTGILGWRSE KTEMVNGYEA KVYGASNVEL ITRTRTEHLS EQHKGKVKGC KTPLQSFLGI
         61 AEQHGGPQNG TLITQTLSQA NPPAITAEEY FNPNFELGNR AMGRPMELTT KTQNFPYPLG
        121 SGGPGSRPSC GCVRSTPCPC VSRWLPSLTS WLSATHFLPS SGTSSRCACL LASQSRLKSR
        181 FFTSSTPASP SGTSMAAMSQ CPRCEVAPAA RR
```

Notes

Ankyrin repeat domain 13b CAI52035 (mouse)

References to 14-3-3 binding to AKR13b

Wanna W, Rexroad CE 3rd, Yao J. Identification of a Functional Splice Variant of 14-3-3E1 in Rainbow Trout. Mar Biotechnol (NY). 2009 Jul 10. CAI52035 (mouse)

14-3-3-binding sites not defined, therefore NO WEBLOGO ANALYSIS

Mouse CCT-alpha Phosphorylcholine transferase A (Swissprot = P49586)

```
1 MDAQSSAKVN SRKRRKEAPG PNGATEEDGI PSKVQRCAVG LRQPAPFSDE IEVDFSKPYV
         61 RVTMEEACRG TPCERPVRVY ADGIFDLFHS GHARALMQAK NLFPNTYLIV GVCSDELTHN
        121 FKGFTVMNEN ERYDAVQHCR YVDEVVRNAP WTLTPEFLAE HRIDFVAHDD IPYSSAGSDD
        181 VYKHIKDAGM FAPTQRTEGI STSDIITRIV RDYDVYARRN LQRGYTAKEL NVSFINEKKY
        241 HLQERVDKVK KKVKDVEEKS KEFVQKVEEK SIDLIQKWEE KSREFIGsFL EMFGPEGALK
        301 HMLKEGKGRM LQAISPKQSP SSSPTHERSP SPSFRWPFSG KTSPSSSPAS LSRCRAVTCD
        361 ISEDEED
```

Notes

In addition to Ser288 (in yellow), a second 14-3-3-binding site is proposed to exist within residues 32 to 343. 14-3-3 binding to CCT-alpha in response to Ca2+ signals is associated with nuclear import of the enzyme.

References to 14-3-3 binding to CCT-alpha

Agassandian M, Chen BB, Schuster CC, Houtman JC, Mallampalli RK. 14-3-3{zeta} escorts CCT{alpha} for calcium-activated nuclear import in lung epithelia. FASEB J. [Epub ahead of print]

Mouse Edc3 mRNA Enhancer of mRNA-decapping protein 3 (Swissprot = Q8K2D3)

```
1 MAMDWLGSIV SINCGDSLGV YQGRVSAVDQ VSQTISLTRP FHNGVKCLVP EVTFRAGDIT
         61 ELKILEIPGP GDNQQVGDLH QTELGPSGVG YQMSISQNGT GKVVKKPASS SSAPQSIPKR
        121 TDVKSQDVAI SPQQQQCSKS YVDRHMESLS QSKSFRRRHN sWSSSSRHPN QATPKKSGLK
        181 NGQMKNKDDE CFGDDIEELP DTDFDFEGNL ALFDKAAVFE EIDTYERRSG SRSRGVPNER
        241 PARYRHDENI LESEPIVYRR ITVPHSVSKE FCTDSGLVVP SVSYELHKKL LSVAEKHGLT
        301 LERRLEMTGV CASQMALTLL GGPNRLNPKN VHQRPTVALL CGPHVKGAQG ISCGRHLANH
        361 DVQVILFLPN FVKMLESITN ELSLFSKTQG QQVSSLRDLP ASPVDLVINC LDCPENAFLR
        421 DQPWYKAAVA WANQNRAPVL SIDPPVHEVE QGIDAKWSLA LGLPLPLGEH AGRVYLCDIG
        481 IPQQVFQEVG INYHSPFGCK FVIPLHSA
```

Notes

Ser161 is phosphorylated in response to insulin.

References to 14-3-3 binding to Edc3

Larance M, Rowland AF, Hoehn K, Humphreys DT, Preiss T, Guilhaus M, James DE. Global phosphoproteomics identifies a major role for akt and 14-3-3 in regulating Edc3. Mol Cell Proteomics. 2010 Jan 5. [Epub ahead of print]

Mouse GEM (Swissprot = P55041)

```
          1 MTLNNVTMRQ GTVGMQPQQR WsIPADARHL MVQKDPHPCN LRNRHSTAPE EHCRRSWSSD
         61 STDSVISSES GNTYYRVVLI GEQGVGKSTL ANIFAGVHDS MDSDCEVLGE DTYERTLVVD
        121 GESATIILLD MWENKGENEW LHDHCMQVGD AYLIVYSITD RASFEKASEL RIQLRRARQT
        181 EDIPIILVGN KSDLVRCREV SVSEGRACAV VFDCKFIETS AAVQHNVKEL FEGIVRQVRL
        241 RRDSKEKNER RLAYQKRRES IPRKARRFWG KIVAKNNKNM AFKLKSKsCH DLSVL
>gi|38258884|sp|P55041.2|GEM_MOUSE RecName: Full=GTP-binding protein GEM;
AltName: Full=GTP-binding mitogen-induced T-cell protein; AltName: Full=RAS-
like protein KIR
MTLNNVTMRQGTVGMQPQQRWSIPADARHLMVQKDPHPCNLRNRHSTAPEEHCRRSWSSDSTDSVISSES
GNTYYRVVLIGEQGVGKSTLANIFAGVHDSMDSDCEVLGEDTYERTLVVDGESATIILLDMWENKGENEW
LHDHCMQVGDAYLIVYSITDRASFEKASELRIQLRRARQTEDIPIILVGNKSDLVRCREVSVSEGRACAV
VFDCKFIETSAAVQHNVKELFEGIVRQVRLRRDSKEKNERRLAYQKRRESIPRKARRFWGKIVAKNNKNM
AFKLKSKSCHDLSVL
```

Notes

Member of RGK small GTP-binding protein family, which includes Kir/Gem, Rad, Rem and Rem2.

Mouse - Phosphorylation on S22 and S288 (QQRWpS^{22}IP and KLKSKpS^{289}CH) is required for binding of 14-3-3, which also retains Kir/Gem in the cytosol, whereas phosphorylation on S286 prevents the association and/or favors the dissociation of 14-3-3 via an unknown mechanism (Mahalaskshmi et al 2007).

Human - Phosphorylation of serine 289 in conjunction with serine 23 results in bidentate 14-3-3 binding, leading to increased Gem protein half-life (Ward et al 2004). (Ser23 in human GEM corresponds to Ser22 in mouse GEM)

References to 14-3-3 binding to Kir/Gem

Mahalakshmi RN, Nagashima K, Ng MY, Inagaki N, Hunziker W, Béguin P.Nuclear transport of Kir/Gem requires specific signals and importin alpha5 and is regulated by calmodulin and predicted serine phosphorylations. Traffic. 2007 Sep;8(9):1150-63.

Mahalakshmi RN, Ng MY, Guo K, Qi Z, Hunziker W, Béguin P. Nuclear localization of endogenous RGK proteins and modulation of cell shape remodeling by regulated nuclear transport. Traffic. 2007 Sep;8(9):1164-78.

Béguin P, Mahalakshmi RN, Nagashima K, Cher DH, Takahashi A, Yamada Y, Seino Y, Hunziker W. 14-3-3 and calmodulin control subcellular distribution of Kir/Gem and its regulation of cell shape and calcium channel activity. J Cell Sci. 2005 May 1;118(Pt 9):1923-34.

Ward Y, Spinelli B, Quon MJ, Chen H, Ikeda SR, Kelly K. Phosphorylation of critical serine residues in Gem separates cytoskeletal reorganization from down-regulation of calcium channel activity. Mol Cell Biol. 2004 Jan;24(2):651-61.

Mouse Grb10 Growth factor receptor-bound protein 10 (GRB10 adapter protein) (Swissprot = Q60760)

```
        1 MNNDINSSVE SLNSACNMQS DTDTAPLLED GQHASNQGAA SSSRGQPQAS PRQKMQRSQP
       61 VHILRRLQEE DQQLRTASLP AIPNPFPELT GAAPGSPPSV APSSLPPPPS QPPAKHCGRC
      121 EKWIPGENTR GNGKRKIWRW QFPPGFQLSK LTRPGLWTKT TARFSKKQPK NQCPTDTVNP
      181 VARMPTSQME KLRLRKDVKV FSEDGTSKVV EILTDMTARD LCQLLVYKSH CVDDNSWTLV
      241 EHHPQLGLER CLEDHEIVVQ VESTMPSESK FLFRKNYAKY EFFKNPVNFF PDQMVNWCQQ
      301 SNGGQAQLLQ NFLNTSSCPE IQGFLQVKEV GRKSWKKLYV CLRRSGLYYS TKGTSKEPRH
      361 LQLLADLEES SIFYLIAGKK QYNAPNEHGM CIKPNKAKTE MKELRLLCAE DEQIRTCWMT
      421 AFRLLKYGML LYQNYRIPQR KGLPPPFNAP MRSVsENSLV AMDFSGQIGR VIDNPAEAQS
      481 AALEEGHAWR KRSTRMNILS SQSPLHPSTL NAVIHRTQHW FHGRISREES HRIIKQQGLV
      541 DGLFLLRDSQ SNPKAFVLTL CHHQKIKNFQ ILPCEDDGQT FFTLDDGNTK FSDLIQLVDF
      601 YQLNKGVLPC KLKHHCIRVA L
>gi|57015407|sp|Q60760.2|GRB10_MOUSE RecName: Full=Growth factor receptor-
bound protein 10; AltName: Full=GRB10 adapter protein
MNNDINSSVESLNSACNMQSDTDTAPLLEDGQHASNQGAASSSRGQPQASPRQKMQRSQPVHILRRLQEE
DQQLRTASLPAIPNPFPELTGAAPGSPPSVAPSSLPPPPSQPPAKHCGRCEKWIPGENTRGNGKRKIWRW
QFPPGFQLSKLTRPGLWTKTTARFSKKQPKNQCPTDTVNPVARMPTSQMEKLRLRKDVKVFSEDGTSKVV
EILTDMTARDLCQLLVYKSHCVDDNSWTLVEHHPQLGLERCLEDHEIVVQVESTMPSESKFLFRKNYAKY
EFFKNPVNFFPDQMVNWCQQSNGGQAQLLQNFLNTSSCPEIQGFLQVKEVGRKSWKKLYVCLRRSGLYYS
TKGTSKEPRHLQLLADLEESSIFYLIAGKKQYNAPNEHGMCIKPNKAKTEMKELRLLCAEDEQIRTCWMT
AFRLLKYGMLLYQNYRIPQRKGLPPPFNAPMRSVSENSLVAMDFSGQIGRVIDNPAEAQSAALEEGHAWR
KRSTRMNILSSQSPLHPSTLNAVIHRTQHWFHGRISREESHRIIKQQGLVDGLFLLRDSQSNPKAFVLTL
CHHQKIKNFQILPCEDDGQTFFTLDDGNTKFSDLIQLVDFYQLNKGVLPCKLKHHCIRVAL
```

Notes

"The 14-3-3.Grb10 interaction requires phosphorylation of Grb10, and only the phosphorylated form of Grb10 co-immunoprecipitates with endogenous 14-3-3. We could identify a putative phosphorylation site in Grb10, which is located in a classical 14-3-3 binding motif, RSVSEN. Mutation of this site in Grb10 diminished binding to 14-3-3. Thus, Grb10 exists in two different states of phosphorylation and complexes with 14-3-3 when phosphorylated on serine 428." (Urschel et al 2005) (RSVpS^{428}EN = Ser455 in Swissprot Q60760)

"Mutagenesis of serine 428 to alanine, an Akt phosphorylation site known to promote the interaction of Grb10 to 14-3-3 (21), also prevented the Grb10 anti-apoptotic activity." (Kebache et al 2007) Kebache et al (2007) used the isoform Mouse Grb10(delta).

References to 14-3-3 binding to Grb10

Urschel S, Bassermann F, Bai RY, Münch S, Peschel C, Duyster J. Phosphorylation of grb10 regulates its interaction with 14-3-3. J Biol Chem. 2005 Apr 29;280(17):16987-93.

Kebache S, Ash J, Annis MG, Hagan J, Huber M, Hassard J, Stewart CL, Whiteway M, Nantel A. Grb10 and active Raf-1 kinase promote Bad-dependent cell survival. J Biol Chem. 2007 Jul 27;282(30):21873-83.

Mouse KCNK18 (TRESK) Potassium channel subfamily K member 18 (SwissProt =Q6VV64)

```
        1 MEAEEPPEAR RCCPEALGKA RGCCPEALGK LLPGLCFLCC LVTYALVGAA LFSAVEGRPD
       61 PEAEENPELK KFLDDLCNIL KCNLTVVEGS RKNLCEHLQH LKPQWLKAPQ DWSFLSALFF
      121 CCTVFSTVGY GHMYPVTRLG KFLCMLYALF GIPLMFLVLT DIGDILATIL SRAYSRFQAL
      181 LCLPHDIFKW RSLPLCRKQP DSKPVEEAIP QIVIDAGVDE LLNPQPSKDP PSPSCNVELF
      241 ERLVAREKKN KLQPPTRPVE RSNsCPELVL GRLSCSILSN LDEVGQQVER LDIPLPVIAL
      301 VVFAYISCAA AILPFWETEL GFEDAFYFCF VTLTTIGFGD IVLVHPHFFL FFSIYIIVGM
      361 EILFIAFKLM QNRLLHTYKT LMLFVCQREV SLPW
>gi|81893086|sp|Q6VV64.1|KCNKI_MOUSE RecName: Full=Potassium channel
subfamily K member 18; AltName: Full=Two-pore-domain potassium channel TRESK
MEAEEPPEARRCCPEALGKARGCCPEALGKLLPGLCFLCCLVTYALVGAALFSAVEGRPDPEAEENPELK
KFLDDLCNILKCNLTVVEGSRKNLCEHLQHLKPQWLKAPQDWSFLSALFFCCTVFSTVGYGHMYPVTRLG
KFLCMLYALFGIPLMFLVLTDIGDILATILSRAYSRFQALLCLPHDIFKWRSLPLCRKQPDSKPVEEAIP
QIVIDAGVDELLNPQPSKDPPSPSCNVELFERLVAREKKNKLQPPTRPVERSNSCPELVLGRLSCSILSN
LDEVGQQVERLDIPLPVIALVVFAYISCAAAILPFWETELGFEDAFYFCFVTLTTIGFGDIVLVHPHFFL
FFSIYIIVGMEILFIAFKLMQNRLLHTYKTLMLFVCQREVSLPW
```

Notes

KCNK18 (TRESK) Outward rectifying potassium channel. Produces rapidly activating outward rectifier K(+) currents. May function as background potassium channel that sets the resting membrane potential. Inhibited by arachidonic acid and other naturally occurring unsaturated free fatty acids. Channel activity is enhanced by volatile anesthetics, such as isoflurane. Belongs to the two pore domain potassium channel (TC 1.A.1.8) family. Coexpression of 14-3-3eta with TRESK blocked, whereas the coexpression of a dominant negative form of 14-3-3eta accelerated the return of the K(+) current to the resting state after the activation mediated by calcineurin in Xenopus oocytes. Phosphorylation of serine 264 in mouse TRESK was required for the binding of 14-3-3eta.

References to 14-3-3 binding to KCNK18 (TRESK)

Czirják G, Vuity D, Enyedi P. Phosphorylation-dependent binding of 14-3-3 proteins controls TRESK regulation. J Biol Chem. 2008 Jun 6;283(23):15672-80.

Mouse lipin-1alpha Fatty liver dystrophy protein (Swissprot for lipin-1 = Q91ZP3)

SITE(S) NOT DEFINED. NOT IN WEBLOGO.

```
1 MNYVGQLAGQ VFVTVKELYK GLNPATLSGC IDIIVIRQPN GSLQCSPFHV RFGKMGVLRS
       61 REKVVDIEIN GESVDLHMKL GDNGEAFFVQ ETDNDQEIIP MYLATSPILS EGAARMESQL
      121 KRNSVDRIRC LDPTTAAQGL PPSDTPSTGS LGKKRRKRRR KAQLDNLKRD DNVNSSEDED
      181 MFPIEMSSDE DTAPMDGSRT LPNDVPPFQD DIPKENFPSI STHPQSASYP SSDREWSPSP
      241 SSLVDCQRTP PHLAEGVLSS SCPLQSCHFH ASESPSGSRP STPKSDSELV SKSADRLTPK
      301 NNLEMLWLWG ELPQAAKSSS PHKMKESSPL GSRKTPDKMN FQAIHSESSD TFSDQSPTMA
      361 RGLLIHQSKA QTEMQFVNEE DLESLGAAAP PSPVAEELKA PYPNTAQSSS KTDSPSRKKD
      421 KRSRHLGADG VYLDDLTDMD PEVAALYFPK NGDPGGLPKQ ASDNGARSAN QSPQSVGGSG
      481 IDSGVESTSD SLRDLPSIAI SLCGGLSDHR EITKDAFLEQ AVSYQQFADN PAIIDDPNLV
      541 VKVGNKYYNW TTAAPLLLAM QAFQKPLPKA TVESIMRDKM PKKGGRWWFS WRGRNATIKE
      601 ESKPEQCLTG KGHNTGEQPA QLGLATRIKH ESSSSDEEHA AAKPSGSSHL SLLSNVSYKK
      661 TLRLTSEQLK SLKLKNGPND VVFSVTTQYQ GTCRCEGTIY LWNWDDKVII SDIDGTITRS
```

<table>
<tr><td>721 DTLGHILPTL GKDWTHQGIA KLYHKVSQNG YKFLYCSARA IGMADMTRGY LHWVNERGTV
781 LPQGPLLLSP SSLFSALHRE VIEKKPEKFK VQCLTDIKNL FFPNTEPFYA AFGNRPADVY
841 SYKQVGVSLN RIFTVNPKGE LVQEHAKTNI SSYVRLCEVV DHVFPLLKRS HSCDFPCSDT
901 FSNFTFWREP LPPFENQDMH SASA
Notes
Insulin stimulated 14-3-3 binding to lipin-1alpha in 3T3-L1 adipocytes, and a serine-rich region (residues 218 to 260) was implicated in binding to 14-3-3, but precise site(s) were not defined (Péterfy et al 2009).
References to 14-3-3 binding to lipin-1alpha
Péterfy M, Harris TE, Fujita N, Reue K. Insulin-stimulated interaction with 14-3-3 promotes cytoplasmic localization of lipin-1 in adipocytes. J Biol Chem. 2009 Dec 2. [Epub ahead of print]</td><td></td></tr>
<tr><td>**Mouse Myo1c** (Swissprot = Q9WTI7)
1 MALQVELIPT GEIIRVVHPH RPCKLALGSD GVRVTMESAL TARDRVGVQD FVLLENFTSE
61 AAFIENLRRR FRENLIYTYI GPVLVSVNPY RDLQIYSRQH MERYRGVSFY EVPPHLFAVA
121 DTVYRALRTE RRDQAVMISG ESGAGKTEAT KRLLQFYAET CPAPERGGAV RDRLLQSNPV
181 LEAFGNAKTL RNDNSSRFGK YMDVQFDFKG APVGGHILSY LLEKSRVVHQ NHGERNFHVF
241 YQLLEGGEEE TLRRLGLERN PQSYLYLVKG QCAKVSSIND KSDWKVMRKA LSVIDFTEDE
301 VEDLLSIVAS VLHLGNIHFA ADEDSNAQVT TENQLKYLTR LLGVEGTTLR EALTHRKIIA
361 KGEELLSPLN LEQAAYARDA LAKAVYSRTF TWLVRKINRS LASKDAESPS WRSTTVLGLL
421 DIYGFEVFQH NSFEQFCINY CNEKLQQLFI ELTLKSEQEE YEAEGIAWEP VQYFNNKIIC
481 DLVEEKFKGI ISILDEECLR PGEATDLTFL EKLEDTVKPH PHFLTHKLAD QKTRKSLDRG
541 EFRLLHYAGE VTYSVTGFLD KNNDLLFRNL KETMCSSMNP IMAQCFDKSE LSDKKRPETV
601 ATQFKMSLLQ LVEILRSKEP AYIRCIKPND AKQPGRFDEV LIRHQVKYLG LMENLRVRRA
661 GFAYRRKYEA FLQRYKSLCP ETWPMWAGRP QDGVAVLVRH LGYKPEEYKM GRTKIFIRFP
721 KTLFATEDSL EVRRQsLATK IQAAWRGFHW RQKFLRVKRS AICIQSWWRG TLGRRKAAKR
781 KWAAQTIRRL IRGFILRHSP RCPENAFFLD HVRASFLLNL RRQLPRNVLD TSWPTPPPAL
841 REASELLREL CMKNMVWKYC RSISPEWKQQ LQQKAVASEI FKGKKDNYPQ SVPRLFISTR
901 LGTEEISPRV LQSLGSEPIQ YAVPVVKYDR KGYKPRPRQL LLTPSAVVIV EDAKVKQRID
961 YANLTGISVS SLSDSLFVLH VQREDNKQKG DVVLQSDHVI ETLTKTALSA DRVNNININQ
1021 GSITFAGGPG RDGIIDFTSG SELLITKAKN GHLAVVAPRL NSR
>gi|226693542|sp|Q9WTI7.2|MYO1C_MOUSE RecName: Full=Myosin-Ic; AltName: Full=Myosin I beta; AltName: Full=MMI-beta; Short=MMIb
MALQVELIPTGEIIRVVHPHRPCKLALGSDGVRVTMESALTARDRVGVQDFVLLENFTSEAAFIENLRRR
FRENLIYTYIGPVLVSVNPYRDLQIYSRQHMERYRGVSFYEVPPHLFAVADTVYRALRTERRDQAVMISG
ESGAGKTEATKRLLQFYAETCPAPERGGAVRDRLLQSNPVLEAFGNAKTLRNDNSSRFGKYMDVQFDFKG
APVGGHILSYLLEKSRVVHQNHGERNFHVFYQLLEGGEEETLRRLGLERNPQSYLYLVKGQCAKVSSIND
KSDWKVMRKALSVIDFTEDEVEDLLSIVASVLHLGNIHFAADEDSNAQVTTENQLKYLTRLLGVEGTTLR
EALTHRKIIAKGEELLSPLNLEQAAYARDALAKAVYSRTFTWLVRKINRSLASKDAESPSWRSTTVLGLL
DIYGFEVFQHNSFEQFCINYCNEKLQQLFIELTLKSEQEEYEAEGIAWEPVQYFNNKIICDLVEEKFKGI
ISILDEECLRPGEATDLTFLEKLEDTVKPHPHFLTHKLADQKTRKSLDRGEFRLLHYAGEVTYSVTGFLD
KNNDLLFRNLKETMCSSMNPIMAQCFDKSELSDKKRPETVATQFKMSLLQLVEILRSKEPAYIRCIKPND
AKQPGRFDEVLIRHQVKYLGLMENLRVRRAGFAYRRKYEAFLQRYKSLCPETWPMWAGRPQDGVAVLVRH
LGYKPEEYKMGRTKIFIRFPKTLFATEDSLEVRRQSLATKIQAAWRGFHWRQKFLRVKRSAICIQSWWRG
TLGRRKAAKRKWAAQTIRRLIRGFILRHSPRCPENAFFLDHVRASFLLNLRRQLPRNVLDTSWPTPPPAL
REASELLRELCMKNMVWKYCRSISPEWKQQLQQKAVASEIFKGKKDNYPQSVPRLFISTRLGTEEISPRV
LQSLGSEPIQYAVPVVKYDRKGYKPRPRQLLLTPSAVVIVEDAKVKQRIDYANLTGISVSSLSDSLFVLH
VQREDNKQKGDVVLQSDHVIETLTKTALSADRVNNININQGSITFAGGPGRDGIIDFTSGSELLITKAKN
GHLAVVAPRLNSR
Notes
Myo1c undergoes insulin-dependent phosphorylation at S701 (EVRRQ(pS701)LATKKQAA). Phosphorylation was accompanied by enhanced 14-3-3 binding and reduced calmodulin binding. Ser701= Ser736 in Q9WT17.
References to 14-3-3 binding to Myo1c
Yip MF, Ramm G, Larance M, Hoehn KL, Wagner MC, Guilhaus M, James DE.CaMKII-mediated phosphorylation of the myosin motor Myo1c is required for insulin-stimulated GLUT4 translocation in adipocytes. Cell Metab. 2008 Nov;8(5):384-98.
Dubois F, Vandermoere F, Gernez A, Murphy J, Toth R, Chen S, Geraghty KM, Morrice NA, Mackintosh C. Differential 14-3-3-affinity capture reveals new downstream targets of PI 3-kinase signaling. Mol Cell Proteomics. 2009 Aug 1.</td><td></td></tr>
<tr><td>**Mouse Synpo2** Synaptopodin 2 (myopodin) (Swissprot = Q91YE8
1 MGTGDFICIS MTGGAPWGFR LQGGKEEQQP LQVAKIRSQS KASGSGLREG DEVVSINGNP
61 CADLTYPEVI KLMEGITDSL HLLVKRPSSG TSETLDSESE TTNHQHLTHE GPMESTTLQI
121 QQATETQSED FFLAPVQTKV PLTEDQSNAW GYAECPKEEQ APPMLGSQEG HLVEEVILRQ
181 KAEAGQPGHV VELQLSLSKE RHQCTSGPIV TLQGNDKSTS PDPDWSSQLE RTVHINSIPA
241 PEKADTSLTS STSSGRELRV IQGRDPGGAG LPQVEVILDC SDRLKAEECR LQTGRGCVAS
301 PVEGGRSEAP PSLVSFAVSS EGTEHGEDQR SGKDQSRPHK HRARHARLRR SESLSEKQVK
361 EAKSKCKSIA LLLTDAPNPN SKGVLMFKKR RRRARKYTLV SYGTGELERE EEEEEDQEAG
421 DKDEISEVAF LGTSESEVDE ELLSDVDDNT QVVNFDWDSG LVDIEKRLNR GDKMEMLPDT
481 TGKGALMFAK RRERMEQFTA QNEEEKTGGM AGGGPDALQT DGLRTMTSYQ RKEESVRMQS
541 SVSESSFQMG RSLAsVPQQN GFSGVSETAG AQRMFPMNRT AKPFLGSMNQ PAAPFSPTRS
601 VtSPISDFPA PPPYSAVSPP PEAFSRGVSS PVAGPAQPPP WPQPAPWSQP AFYDSSEQIA
661 SRDERIAVPA KRTGILQEAK RRGTTKPMFT FKETKVSPNP ELLSLLQNAE GKRGTGGDSG
721 PEEDYLSLGA EACNFMQSSA KQKTPPPVAP KPAVKSPSSS QPVAPVSPVW SPGVAPAQRP
781 AFSTSNPPNP PQVTAVSSIK IAQPAAPPAR PASALNLAGP FKGPQAVVVS HNYTPKPSAP
841 TPLVNAAPAG AGGPSNELPG MSGKGAQLFA KRQSRMEKYV VDSDTVQAHT VRAQSPTPSL
901 PASWKYSSNV RAPPPVAYNP IHSPSYPLAA IKSQPPGAQA SKTSKKKGKK PLNTLDVMKH
961 QPYQLNASLF TFQPPDSKDG LPQKSTVKVS SAPAMKQALP PRQANVGSPT NAQASSVYSV
1021 PAYTSQPNFF AAEATSPVSA SPVPVSVPTS PKQESTSTSY FVAPRPKFSA KKSGVTVQEN</td><td>SEQUENCES DIFFER FROM 1078aa</td></tr>
</table>

1081 GRSLSLPGRS APPIISASPW LYQSACNYSS KPTFELEKAN KRPTPWEAAA RSPLGLVDDA 1141 FRPRNIQESI VAHVVSAARR KVSPGSQEDW KERLSFVPQT QKTNMSFSER QEYPAPSPVN 1201 SHVSSHSLYS SQLPYVCYRQ ESRNDLKTMS METRSEYCLP LGGYDYNPHP RGWRQQP >gi|51702128|sp|Q91YE8.2|SYNP2_MOUSE RecName: Full=Synaptopodin-2; AltName: Full=Myopodin MGTGDFICISMTGGAPWGFRLQGGKEEQQPLQVAKIRSQSKASGSGLREGDEVVSINGNPCADLTYPEVI KLMEGITDSLHLLVKRPSSGTSETLDSESETTNHQHLTHEGPMESTTLQIQQATETQSEDFFLAPVQTKV PLTEDQSNAWGYAECPKEEQAPPMLGSQEGHLVEEVILRQKAEAGQPGHVVELQLSLSKERHQCTSGPIV TLQGNDKSTSPDPDWSSQLERTVHINSIPAPEKADTSLTSSTSSGRELRVIQGRDPGGAGLPQVEVILDC SDRLKAEECRLQTGRGCVASPVEGGRSEAPPSLVSFAVSSEGTEHGEDQRSGKDQSRPHKHRARHARLRR SESLSEKQVKEAKSKCKSIALLLTDAPNPNSKGVLMFKKRRRRARKYTLVSYGTGELEREEEEEEDQEAG DKDEISEVAFLGTSESEVDEELLSDVDDNTQVVNFDWDSGLVDIEKRLNRGDKMEMLPDTTGKGALMFAK RRERMEQFTAQNEEEKTGGMAGGGPDALQTDGLRTMTSYQRKEESVRMQSSVSESSFQMGRSLASVPQQN GFSGVSETAGAQRMFPMNRTAKPFLGSMNQPAAPFSPTRSVTSPISDFPAPPPYSAVSPPPEAFSRGVSS PVAGPAQPPPWPQPAPWSQPAFYDSSEQIASRDERIAVPAKRTGILQEAKRRGTTKPMFTFKETKVSPNP ELLSLLQNAEGKRGTGGDSGPEEDYLSLGAEACNFMQSSAKQKTPPPVAPKPAVKSPSSSQPVAPVSPVW SPGVAPAQRPAFSTSNPPNPPQVTAVSSIKIAQPAAPPARPASALNLAGPFKGPQAVVVSHNYTPKPSAP TPLVNAAPAGAGGPSNELPGMSGKGAQLFAKRQSRMEKYVVDSDTVQAHTVRAQSPTPSLPASWKYSSNV RAPPPVAYNPIHSPSYPLAAIKSQPPGAQASKTSKKKGKKPLNTLDVMKHQPYQLNASLFTFQPPDSKDG LPQKSTVKVSSAPAMKQALPPRQANVGSPTNAQASSVYSVPAYTSQPNFFAAEATSPVSASPVPVSVPTS PKQESTSTSYFVAPRPKFSAKKSGVTVQVWKPSVVEE **Notes** S225 and T272 mediate the phosphorylation-dependent binding of myopodin to 14-3-3ß (The authors must have been working on a shorter protein because in the reference sequence the matching sites for RSLA(pS225)VP and RSV(pT272)SP = Ser555 and Th602) **References to 14-3-3 binding to myopodin** Faul C, Dhume A, Schecter AD, Mundel P. Protein kinase A, Ca2+/calmodulin-dependent kinase II, and calcineurin regulate the intracellular trafficking of myopodin between the Z-disc and the nucleus of cardiac myocytes. Mol Cell Biol. 2007 Dec;27(23):8215-27.	
Mouse WEE1 (SwissProt= P30291) 1 MSFLSRQQPP PPRRAGAACT LRQKLIFSPC SDCEEEEEEE EEEGSGHSTG EDSAFQEPDS 61 PLPPARSPTE PGPERRRSPG PAPGSPGELE EDLLLPGACP GADEAGGGAE GDSWEEEGFG 121 SSSPVKSPAA PYFLGSSFSP VRCGGPGDAS PRGCGARRAG EGRRSPRPDH PGTPPHKTFR 181 KLRLFDTPHT PKSLLSKARG IDSSSVKLRG SSLFMDTEKS GKREFDVRQT PQVNINPFTP 241 DSLLLHSSGQ CRRRKRTYWN DSCGEDMEAS DYELEDETRP AKRITITESN MKSRYTTEFH 301 ELEKIGSGEF GSVFKCVKRL DGCIYAIKRS KKPLAGSVDE QNALREVYAH AVLGQHSHVV 361 RYFSAWAEDD HMLIQNEYCN GGSLADAISE NYRIMSYFKE AELKDLLLQV GRGLRYIHSM 421 SLVHMDIKPS NIFISRTSIP NAASEEGDED DWASNKVMFK IGDLGHVTRI SSPQVEEGDS 481 RFLANEVLQE NYTHLPKADI FALALTVVCA AGAEPLPRNG DQWHEIRQGR LPRIPQVLSQ 541 EFTELLKVMI HPDPERRPSA MALVKHSVLL SASRKSAEQL RIELNAEKFK NSLLQKELKK 601 AQMAKAAAEE RALFTDRMAT RSTTQSNRTS RLIGKKMNRS VsLTIY >gi|1351419|sp|P30291.2|WEE1_HUMAN RecName: Full=Wee1-like protein kinase; AltName: Full=Wee1A kinase; AltName: Full=WEE1hu MSFLSRQQPPPPRRAGAACTLRQKLIFSPCSDCEEEEEEEEEEGSGHSTGEDSAFQEPDSPLPPARSPTE PGPERRRSPGPAPGSPGELEEDLLLPGACPGADEAGGGAEGDSWEEEGFGSSSPVKSPAAPYFLGSSFSP VRCGGPGDASPRGCGARRAGEGRRSPRPDHPGTPPHKTFRKLRLFDTPHTPKSLLSKARGIDSSSVKLRG SSLFMDTEKSGKREFDVRQTPQVNINPFTPDSLLLHSSGQCRRRKRTYWNDSCGEDMEASDYELEDETRP AKRITITESNMKSRYTTEFHELEKIGSGEFGSVFKCVKRLDGCIYAIKRSKKPLAGSVDEQNALREVYAH AVLGQHSHVVRYFSAWAEDDHMLIQNEYCNGGSLADAISENYRIMSYFKEAELKDLLLQVGRGLRYIHSM SLVHMDIKPSNIFISRTSIPNAASEEGDEDDWASNKVMFKIGDLGHVTRISSPQVEEGDSRFLANEVLQE NYTHLPKADIFALALTVVCAAGAEPLPRNGDQWHEIRQGRLPRIPQVLSQEFTELLKVMIHPDPERRPSA MALVKHSVLLSASRKSAEQLRIELNAEKFKNSLLQKELKKAQMAKAAAEERALFTDRMATRSTTQSNRTS RLIGKKMNRSVSLTIY **Notes** A sequence in the carboxyl terminus was thought to be necessary for the binding, but precise sites not defined though Ser642 is possible. Wee1 a protein kinase that catalyzes the inhibitory tyrosine phosphorylation of CDC2/cyclin B kinase, and appears to coordinate the transition between DNA replication and mitosis by protecting the nucleus from cytoplasmically activated CDC2 kinase. **References to 14-3-3 binding to mouse wee1** Honda R, Ohba Y, Yasuda H.14-3-3 zeta protein binds to the carboxyl half of mouse wee1 kinase. Biochem Biophys Res Commun. 1997 Jan 13;230(2):262-5.	SITES NOT DEFINED PRECISELY. NOT IN WEBLOGO.
Mouse ZFP36 Tristetraprolin (TTP) (Swissprot = P22893) 1 MDLSAIYESL QSMSHDLSSD HGGTESLGGL WNINSDSIPS GVTSRLTGRS TsLVEGRSCG 61 WVPPPPGFAP LAPRPGPELS PSPTSPTATP TTSSRYKTEL CRTYSESGRC RYGAKCQFAH 121 GLGELRQANR HPKYKTELCH KFYLQGRCPY GSRCHFIHNP TEDLALPGQP HVLRQSIsFS 181 GLPSGRRSSP PPPGFSGPSL SSCSFSPSSS PPPPGDLPLS PSAFSAAPGT PVTRRDPNQA 241 CCPSCRRSTT PSTIWGPLGG LARSPSAHSL GSDPDDYASS GSSLGGSDSP VFEAGVFGPP 301 QTPAPPRRLP IFNRISVSE >gi|135862|sp|P22893.1|TTP_MOUSE RecName: Full=Tristetraproline; Short=TTP; AltName: Full=Zinc finger protein 36; Short=Zfp-36; AltName: Full=Protein TIS11A; Short=TIS11; AltName: Full=Growth factor-inducible nuclear protein NUP475; AltName: Full=TPA-induced sequence 11 MDLSAIYESLQSMSHDLSSDHGGTESLGGLWNINSDSIPSGVTSRLTGRSTSLVEGRSCGWVPPPPGFAP LAPRPGPELSPSPTSPTATPTTSSRYKTELCRTYSESGRCRYGAKCQFAHGLGELRQANRHPKYKTELCH KFYLQGRCPYGSRCHFIHNPTEDLALPGQPHVLRQSISFSGLPSGRRSSPPPPGFSGPSLSSCSFSPSSS PPPPGDLPLSPSAFSAAPGTPVTRRDPNQACCPSCRRSTTPSTIWGPLGGLARSPSAHSLGSDPDDYASS	

GSSLGGSDSPVFEAGVFGPPQTPAPPRRLPIFNRISVSE **Notes** Tristetraprolin (TTP) is a regulatory protein with a zinc finger structure that regulates cellular responses to growth factors. MAPKAP kinase-2 (MK2)-induced phosphorylation at serines 52 (RST(pS52)LV) and 178 (RQSI(pS178)FS), which promotes the assembly of TTP:14-3-3 complexes LRQSI(pS)FSGLPC **References to 14-3-3 binding to tristetraprolin** Johnson BA, Stehn JR, Yaffe MB, Blackwell TK. Cytoplasmic localization of tristetraprolin involves 14-3-3-dependent and -independent mechanisms. J Biol Chem. 2002 May 17;277(20):18029-36. Chrestensen CA, Schroeder MJ, Shabanowitz J, Hunt DF, Pelo JW, Worthington MT, Sturgill TW. MAPKAP kinase 2 phosphorylates tristetraprolin on in vivo sites including Ser178, a site required for 14-3-3 binding. J Biol Chem. 2004 Mar 12;279(11):10176-84. Stoecklin G, Stubbs T, Kedersha N, Wax S, Rigby WF, Blackwell TK, Anderson P. MK2-induced tristetraprolin:14-3-3 complexes prevent stress granule association and ARE-mRNA decay. EMBO J. 2004 Mar 24;23(6):1313-24. Rigby WF, Roy K, Collins J, Rigby S, Connolly JE, Bloch DB, Brooks SA. Structure/function analysis of tristetraprolin (TTP): p38 stress-activated protein kinase and lipopolysaccharide stimulation do not alter TTP function. J Immunol. 2005 Jun 15;174(12):7883-93. Gringhuis SI, García-Vallejo JJ, van Het Hof B, van Dijk W. Convergent actions of I kappa B kinase beta and protein kinase C delta modulate mRNA stability through phosphorylation of 14-3-3 beta complexed with tristetraprolin. Mol Cell Biol. 2005 Aug;25(15):6454-63. Marderosian M, Sharma A, Funk AP, Vartanian R, Masri J, Jo OD, Gera JF. Tristetraprolin regulates Cyclin D1 and c-Myc mRNA stability in response to rapamycin in an Akt-dependent manner via p38 MAPK signaling. Oncogene. 2006 Oct 12;25(47):6277-90. Sun L, Stoecklin G, Van Way S, Hinkovska-Galcheva V, Guo RF, Anderson P, Shanley TP. Tristetraprolin (TTP)-14-3-3 complex formation protects TTP from dephosphorylation by protein phosphatase 2a and stabilizes tumor necrosis factor-alpha mRNA. J Biol Chem. 2007 Feb 9;282(6):3766-77.	
Rabbit CSNK1A1 Casein kinase I isoform alpha (Swissprot = P67828) 1 MASSSGSKAE FIVGGKYKLV RKIGSGSFGD IYLAINITNG EEVAVKLESQ KARHPQLLYE 61 SKLYKILQGG VGIPHIRWYG QEKDYNVLVM DLLGPSLEDL FNFCSRRFTM KTVLMLADQM 121 ISRIEYVHTK NFIHRDIKPD NFLMGIGRHC NKLFLIDFGL AKKYRDNRTR QHIPYREDKN 181 LTGTARYASI NAHLGIEQSR RDDMESLGYV LMYFNRTsLP WQGLKAATKK QKYEKISEKK 241 MsTPVEVLCK GFPAEFAMYL NYCRGLRFEE APDYMYLRQL FRILFRTLNH QYDYTFDWTM 301 LKQKAAQQAA SSSGQGQQAQ TPTGF >gi|54037515|sp|P67828.1|KC1A_RABIT RecName: Full=Casein kinase I isoform alpha; Short=CKI-alpha; AltName: Full=CK1 MASSSGSKAEFIVGGKYKLVRKIGSGSFGDIYLAINITNGEEVAVKLESQKARHPQLLYESKLYKILQGG VGIPHIRWYGQEKDYNVLVMDLLGPSLEDLFNFCSRRFTMKTVLMLADQMISRIEYVHTKNFIHRDIKPD NFLMGIGRHCNKLFLIDFGLAKKYRDNRTRQHIPYREDKNLTGTARYASINAHLGIEQSRRDDMESLGYV LMYFNRTSLPWQGLKAATKKQKYEKISEKKMSTPVEVLCKGFPAEFAMYLNYCRGLRFEEAPDYMYLRQL FRILFRTLNHQYDYTFDWTMLKQKAAQQAASSSGQGQQAQTPTGF **References to 14-3-3 binding to rat casein kinase I alpha** Clokie S, Falconer H, Mackie S, Dubois T, Aitken A. The interaction between casein kinase Ialpha and 14-3-3 is phosphorylation dependent. FEBS J. 2009 Oct 27. [Epub ahead of print]	
Rat Ankrd6 Ankyrin repeat domain 6 (Swissprot = B5DEH9) 1 MSQQDAVAAL SERLLIAAYK GQTENVVQLI NKGAKVAVTK HGRTPLHLAA NKGHLSVVQI 61 LLKAGCDLDV QDDGDQTALH RATVVGNTEI LTALIREGCA LDRQDKDGNT ALHEAAWHGF 121 SQSAKLLVKA GANVLARNKA GNTALHLACQ NSHSQSTRVL LLGGSRADLK NNAGDTCLHV 181 AARYNHLSVV RLLLSAFCSV HEKNQAGDTA LHVAAALNHK KVVKILLEAG ADTTLVNNAG 241 QTPLETARYH DNPEVALLLT KAPQILRFSR GRSLRKRRER LKEERRAQSV PRDEVAQSKG 310 SVSAGDTPSS EQAVPEKEEA RRDCPPASQE PRKDERRRKs RPEVSALSDP TPAADQQPGH 361 QKNLHGHHHQ KKKSRHRCWS PPPPHGFRAY QLYTLYRGED GKVMQAPIKG CRCEPLINKL 421 ENQLEAAVEE LRAELGTVQD KVNTKLGHME SKSQHQMCVL DKLMVERLSA ERTECLNRLQ 481 QHAAAEKQEG EKRQMSLVDE LKSWCMLKIQ NLELRLSGES RTFRAKSTPS PSDSSPAVDQ 541 PVVAAGPGAA SDSSSQVVRP KDKALNATAV PRHQQELLPS DCTGSGLRKV KAPAASRLGD 601 QQTGSCVNRG TQTKKSARGG QTKHRGQQPT ASSPSGQQPS AASSDARDAS QALELTQYFF 661 EAVSAQMEKW YERKIEEARS QASQKAQQDE ATLKEHIRSL EEEVAKLRTK MHK **Notes** In silico analysis. No experimental data, though suggested site is EPRKDERRRKSRPEVSALSDP Ser 340 (mouse) (714 aa) with six ankyrin (Ank) repeats and two coiled-coil regions. **References to 14-3-3 binding to rat Ankrd6** Katoh M, Katoh M. Identification and characterization of rat Ankrd6 gene in silico. Int J Mol Med. 2005 Feb;15(2):359-63.	NOT IN WEBLOGO
Rat ATP1A1 (Na^+, K^+-ATPase α1-subunit) (Swissprot = P05023) 1 MGKGVGRDKY EPAAVSEQGD KKGKKGKKDR DMDELKKEVS MDDHKLSLDE LHRKYGTDLS 61 RGLTSARAAE ILARDGPNAL TPPPTTPEWI KFCRQLFGGF SMLLWIGAIL CFLAYSIQAA 121 TEEEPQNDNL YLGVVLSAVV IITGCFSYYQ EAKSSKIMES FKNMVPQQAL VIRNGEKMSI 181 NAEEVVVGDL VEVKGGDRIP ADLRIISANG CKVDNSSLTG ESEPQTRSPD FTNENPLETR 241 NIAFFSTNCV EGTARGIVVY TGDRTVMGRI ATLASGLEGG QTPIAAEIEH FIHIITGVAV 301 FLGVSFFILS LILEYTWLEA VIFLIGIIVA NVPEGLLATV TVCLTLTAKR MARKNCLVKN 361 LEAVETLGST STICSDKTGT LTQNRMTVAH MWFDNQIHEA DTTENQSGVS FDKTSATWLA 421 LSRIAGLCNR AVFQANQENL PILKRAVAGD ASESALLKCI ELCCGSVKEM RERYAKIVEI 481 PFNSTNKYQL SIHKNPNTSE PQHLLVMKGA PERILDRCSS ILLHGKEQPL DEELKDAFQN 541 AYLELGGLGE RVLGFCHLFL PDEQFPEGFQ FDTDDVNFPI DNLCFVGLIS MIDPPRAAVP 601 DAVGKCRSAG IKVIMVTGDH PITAKAIAKG VGIISEGNET VEDIAARLNI PVSQVNPRDA 661 KACVVHGSDL KDMTSEQLDD ILKYHTEIVF ARTSPQQKLI IVEGCQRQGA IVAVTGDGVN 721 DSPALKKADI GVAMGIAGSD VSKQAADMIL LDDNFASIVT GVEEGRLIFD NLKKSIAYTL	SITES NOT CERTAIN. NOT IN WEBLOGO

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      781 TSNIPEITPF LIFIIANIPL PLGTVTILCI DLGTDMVPAI SLAYEQAESD IMKRQPRNPK
      841 TDKLVNERLI SMAYGQIGMI QALGGFFTYF VILAENGFLP IHLLGLRVDW DDRWINDVED
      901 SYGQQWTYEQ RKIVEFTCHT AFFVSIVVVQ WADLVICKTR RNSVFQQGMK NKILIFGLFE
      961 ETALAAFLSY CPGMGVALRM YPLKPTWWFC AFPYSLLIFV YDEVRKLIIR RRPGGWVEKE
     1021 TYY
>gi|114374|sp|P05023.1|AT1A1_HUMAN RecName: Full=Sodium/potassium-
transporting ATPase subunit alpha-1; Short=Sodium pump subunit alpha-1;
AltName: Full=Na(+)/K(+) ATPase alpha-1 subunit; Flags: Precursor
MGKGVGRDKYEPAAVSEQGDKKGKKGKKDRDMDELKKEVSMDDHKLSLDELHRKYGTDLSRGLTSARAAE
ILARDGPNALTPPPTTPEWIKFCRQLFGGFSMLLWIGAILCFLAYSIQAATEEEPQNDNLYLGVVLSAVV
IITGCFSYYQEAKSSKIMESFKNMVPQQALVIRNGEKMSINAEEVVVGDLVEVKGGDRIPADLRIISANG
CKVDNSSLTGESEPQTRSPDFTNENPLETRNIAFFSTNCVEGTARGIVVYTGDRTVMGRIATLASGLEGG
QTPIAAEIEHFIHIITGVAVFLGVSFFILSLILEYTWLEAVIFLIGIIVANVPEGLLATVTVCLTLTAKR
MARKNCLVKNLEAVETLGSTSTICSDKTGTLTQNRMTVAHMWFDNQIHEADTTENQSGVSFDKTSATWLA
LSRIAGLCNRAVFQANQENLPILKRAVAGDASESALLKCIELCCGSVKEMRERYAKIVEIPFNSTNKYQL
SIHKNPNTSEPQHLLVMKGAPERILDRCSSILLHGKEQPLDEELKDAFQNAYLELGGLGERVLGFCHLFL
PDEQFPEGFQFDTDDVNFPIDNLCFVGLISMIDPPRAAVPDAVGKCRSAGIKVIMVTGDHPITAKAIAKG
VGIISEGNETVEDIAARLNIPVSQVNPRDAKACVVHGSDLKDMTSEQLDDILKYHTEIVFARTSPQQKLI
IVEGCQRQGAIVAVTGDGVNDSPALKKADIGVAMGIAGSDVSKQAADMILLDDNFASIVTGVEEGRLIFD
NLKKSIAYTLTSNIPEITPFLIFIIANIPLPLGTVTILCIDLGTDMVPAISLAYEQAESDIMKRQPRNPK
TDKLVNERLISMAYGQIGMIQALGGFFTYFVILAENGFLPIHLLGLRVDWDDRWINDVEDSYGQQWTYEQ
RKIVEFTCHTAFFVSIVVVQWADLVICKTRRNSVFQQGMKNKILIFGLFEETALAAFLSYCPGMGVALRM
YPLKPTWWFCAFPYSLLIFVYDEVRKLIIRRRPGGWVEKETYY

Human P06685   1 MGKGVGRDKY EPAAVSEQGD KKGKKGKKDR DMDELKKEVS MDDHKLSLDE
LHRKYGTDLS
```

Notes

Cannot find the phosphorylated Ser 18 studied by Efendiev et al (2005) in the rat (P05023) or human protein (P06685), appears to be KKGKK.

KKpS^{18}KK   PP78PTTP Y537LEL

References to 14-3-3 binding to Na$^+$, K$^+$-ATPase α1-subunit

Efendiev R, Chen Z, Krmar RT, Uhles S, Katz AI, Pedemonte CH, Bertorello AM. The 14-3-3 protein translates the NA+,K+-ATPase {alpha}1-subunit phosphorylation signal into binding and activation of phosphoinositide 3-kinase during endocytosis. J Biol Chem. 2005 Apr 22;280(16):16272-7.

Rat BCAR1 (p130cas) (Crk-associated substrate)   (Swissprot = Q63767)

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        1 MKYLVSVGAG PARRAGGLED VSWGPRVSRR PQSYRAARHV NESLPRSAFR VPAAHGASVT
       61 PSAALGSGLP ETQPEAVCRG TEKPRFAEGC KPAASRDKNV LAKALYDNVA ESPDELSFRK
      121 GDIMTVLERD TQGLDGWWLC SLHGRQGIVP GNRLKILVGM YDKKPAAPGP GPPATPPQPQ
      181 PSLPQGVHTP VPPASQYSPM LPTAYQPQPD NVYLVPTPSK TQQGLYQAPG PNPQFQSPPA
      241 KQTSTFSKQT PHHSFPSPAT DLYQVPPGPG SPAQDIYQVP PSAGTGHDIY QVPPSLDTRS
      301 WEGTKPPAKV VVPTRVGQGY VYEASQAEQD EYDTPRHLLA PGSQDIYDVP PVRGLLPNQY
      361 GQEVYDTPPM AVKGPNGRDP LLDVYDVPPS VEKGLPPSNH HSVYDVPPSV SKDVPDGPLL
      421 REETYDVPPA FAKPKPFDPT RHPLILAAPP PDSPPAEDVY DVPPPAPDLY DVPPGLRRPG
      481 PGTLYDVPRE RVLPPEVADG SVIDDGVYAV PPPAEREAPT DGKRLSASST GSTRSSQSAS
      541 SLEVVVPGRE PLELEVAVET LARLQQGVST TVAHLLDLVG SASGPGGWRS TsEPQEPPVQ
      601 DLKAAVAAVH GAVHELLEFA RSAVSSATHT SDRTLHAKLS RQLQKMEDVY QTLVVHGQVL
      661 DSGRGGPGFT LDDLDRLVAC SRAVPEDAKQ LASFLHGNAS LLFRRTKAPG PGPEGSSSLH
      721 LNPTDKASSI QSRPLPSPPK FTSQDSPDGQ YENSEGGWME DYDYVHLQGK EEFEKTQKEL
      781 LEKGNIVRQG KGQLELQQLK QFERLEQEVS RPIDHDLANW TPAQPLVPGR TGGLGPSDRQ
      841 LLLFYLEQCE ANLTTLTDAV DAFFTAVATN QPPKIFVAHS KFVILSAHKL VFIGDTLSRQ
      901 AKAADVRSKV THYSNLLCDL LRGIVATTKA AALQYPSPSA AQDMVDRVKE LGHSTQQFRR
      961 VLGQLAAA
>gi|8134344|sp|Q63767.1|BCAR1_RAT RecName: Full=Breast cancer anti-estrogen
resistance protein 1; AltName: Full=CRK-associated substrate; AltName:
Full=p130cas
MKYLVSVGAGPARRAGGLEDVSWGPRVSRRPQSYRAARHVNESLPRSAFRVPAAHGASVTPSAALGSGLP
ETQPEAVCRGTEKPRFAEGCKPAASRDKNVLAKALYDNVAESPDELSFRKGDIMTVLERDTQGLDGWWLC
SLHGRQGIVPGNRLKILVGMYDKKPAAPGPGPPATPPQPQPSLPQGVHTPVPPASQYSPMLPTAYQPQPD
NVYLVPTPSKTQQGLYQAPGPNPQFQSPPAKQTSTFSKQTPHHSFPSPATDLYQVPPGPGSPAQDIYQVP
PSAGTGHDIYQVPPSLDTRSWEGTKPPAKVVVPTRVGQGYVYEASQAEQDEYDTPRHLLAPGSQDIYDVP
PVRGLLPNQYGQEVYDTPPMAVKGPNGRDPLLDVYDVPPSVEKGLPPSNHHSVYDVPPSVSKDVPDGPLL
REETYDVPPAFAKPKPFDPTRHPLILAAPPPDSPPAEDVYDVPPPAPDLYDVPPGLRRPGPGTLYDVPRE
RVLPPEVADGSVIDDGVYAVPPPAEREAPTDGKRLSASSTGSTRSSQSASSLEVVVPGREPLELEVAVET
LARLQQGVSTTVAHLLDLVGSASGPGGWRSTSEPQEPPVQDLKAAVAAVHGAVHELLEFARSAVSSATHT
SDRTLHAKLSRQLQKMEDVYQTLVVHGQVLDSGRGGPGFTLDDLDRLVACSRAVPEDAKQLASFLHGNAS
LLFRRTKAPGPGPEGSSSLHLNPTDKASSIQSRPLPSPPKFTSQDSPDGQYENSEGGWMEDYDYVHLQGK
EEFEKTQKELLEKGNIVRQGKGQLELQQLKQFERLEQEVSRPIDHDLANWTPAQPLVPGRTGGLGPSDRQ
LLLFYLEQCEANLTTLTDAVDAFFTAVATNQPPKIFVAHSKFVILSAHKLVFIGDTLSRQAKAADVRSKV
THYSNLLCDLLRGIVATTKAAALQYPSPSAAQDMVDRVKELGHSTQQFRRVLGQLAAA
```

Notes

RSTpS^{592}EP

References to 14-3-3 binding to p130cas

Garcia-Guzman M, Dolfi F, Russello M, Vuori K. Cell adhesion regulates the interaction between the docking protein p130(Cas) and the 14-3-3 proteins. J Biol Chem. 1999 Feb 26;274(9):5762-8.

Briknarová K, Nasertorabi F, Havert ML, Eggleston E, Hoyt DW, Li C, Olson AJ, Vuori K, Ely KR. The serine-rich domain from Crk-associated substrate (p130cas) is a four-helix bundle. J Biol Chem. 2005 Jun

10;280(23):21908-14.

Rat CaMKK1 Calcium/calmodulin-dependent protein kinase kinase 1 (CaMKK) (Swissprot = P97756)

```
        1 MERSPAVCCQ DPRAELVERV AAISVAHLEE AEEGPEPASN GVDPPPRARA ASVIPGSASR
       61 PTPVRPSLSA RKFsLQERPA GSCLEAQVGP YSTGPASHMS PRAWRRPTIE SHHVAISDTE
      121 DCVQLNQYKL QSEIGKGAYG VVRLAYNERE DRHYAMKVLS KKKLLKQYGF PRRPPPRGSQ
      181 APQGGPAKQL LPLERVYQEI AILKKLDHVN VVKLIEVLDD PAEDNLYLVF DLLRKGPVME
      241 VPCDKPFPEE QARLYLRDII LGLEYLHCQK IVHRDIKPSN LLLGDDGHVK IADFGVSNQF
      301 EGNDAQLSST AGTPAFMAPE AISDTGQSFS GKALDVWATG VTLYCFVYGK CPFIDEYILA
      361 LHRKIKNEAV VFPEEPEVSE ELKDLILKML DKNPETRIGV SDIKLHPWVT KHGEEPLPSE
      421 EEHCSVVEVT EEEVKNSVKL IPSWTTVILV KSMLRKRSFG NPFEPQARRE ERSMSAPGNL
      481 LLKEGCGEGG KSPELPGVQE DEAAS
>gi|56404324|sp|P97756.1|KKCC1_RAT RecName: Full=Calcium/calmodulin-dependent
protein kinase kinase 1; Short=CaMKK 1; AltName: Full=Calcium/calmodulin-
dependent protein kinase kinase alpha; Short=CaM-kinase kinase alpha;
Short=CaM-KK alpha; Short=CaMKK alpha; AltName: Full=alpha CaMKK; AltName:
Full=CaM-kinase IV kinase
MERSPAVCCQDPRAELVERVAAISVAHLEEAEEGPEPASNGVDPPPRARAASVIPGSASRPTPVRPSLSA
RKFSLQERPAGSCLEAQVGPYSTGPASHMSPRAWRRPTIESHHVAISDTEDCVQLNQYKLQSEIGKGAYG
VVRLAYNEREDRHYAMKVLSKKKLLKQYGFPRRPPPRGSQAPQGGPAKQLLPLERVYQEIAILKKLDHVN
VVKLIEVLDDPAEDNLYLVFDLLRKGPVMEVPCDKPFPEEQARLYLRDIILGLEYLHCQKIVHRDIKPSN
LLLGDDGHVKIADFGVSNQFEGNDAQLSSTAGTPAFMAPEAISDTGQSFSGKALDVWATGVTLYCFVYGK
CPFIDEYILALHRKIKNEAVVFPEEPEVSEELKDLILKMLDKNPETRIGVSDIKLHPWVTKHGEEPLPSE
EEHCSVVEVTEEEVKNSVKLIPSWTTVILVKSMLRKRSFGNPFEPQARREERSMSAPGNLLLKEGCGEGG
KSPELPGVQEDEAAS
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Notes

RKFpS^{74}LQ (CaMKK)

References to 14-3-3 binding to CaMKK1

Davare MA, Saneyoshi T, Guire ES, Nygaard SC, Soderling TR. Inhibition of calcium/calmodulin-dependent protein kinase kinase by protein 14-3-3. J Biol Chem. 2004 Dec 10;279(50):52191-9.

Rat Chrnb4 Nicotinic acetylcholine receptor α 4 subunit (AChRα4) (Swissprot = P09483)

```
        1 MANSGTGAPP PLLLLPLLLL LGTGLLPASS HIETRAHAEE RLLKRLFSGY NKWSRPVANI
       61 SDVVLVRFGL SIAQLIDVDE KNQMMTTNVW VKQEWHDYKL RWDPGDYENV TSIRIPSELI
      121 WRPDIVLYNN ADGDFAVTHL TKAHLFYDGR VQWTPPAIYK SSCSIDVTFF PFDQQNCTMK
      181 FGSWTYDKAK IDLVSMHSRV DQLDFWESGE WVIVDAVGTY NTRKYECCAE IYPDITYAFI
      241 IRRLPLFYTI NLIIPCLLIS CLTVLVFYLP SECGEKVTLC ISVLLSLTVF LLLITEIIPS
      301 PTSLVIPLIG EYLLFTMIFV TLSIVITVFV LNVHHRSPRT HTMPAWVRRV FLDIVPRLLF
      361 MKRPSVVKDN CRRLIESMHK MANAPRFWPE PVGEPGILSD ICNQGLSPAP TFCNPTDTAV
      421 ETQPTCRSPP LEVPDLKTSE VEKASPCPSP GSCPPPKSSS GAPMLIKARS LsVQHVPSSQ
      481 EAAEDGIRCR SRSIQYCVSQ DGAASLADSK PTSSPTSLKA RPSQLPVSDQ ASPCKCTCKE
      541 PSPVSPVTVL KAGGTKAPPQ HLPLSPALTR AVEGVQYIAD HLKAEDTDFS VKEDWKYVAM
      601 VIDRIFLWMF IIVCLLGTVG LFLPPWLAAC
>gi|8469182|sp|P09483.3|ACHA4_RAT RecName: Full=Neuronal acetylcholine
receptor subunit alpha-4; Flags: Precursor
MANSGTGAPPPLLLLPLLLLLGTGLLPASSHIETRAHAEERLLKRLFSGYNKWSRPVANISDVVLVRFGL
SIAQLIDVDEKNQMMTTNVWVKQEWHDYKLRWDPGDYENVTSIRIPSELIWRPDIVLYNNADGDFAVTHL
TKAHLFYDGRVQWTPPAIYKSSCSIDVTFFPFDQQNCTMKFGSWTYDKAKIDLVSMHSRVDQLDFWESGE
WVIVDAVGTYNTRKYECCAEIYPDITYAFIIRRLPLFYTINLIIPCLLISCLTVLVFYLPSECGEKVTLC
ISVLLSLTVFLLLITEIIPSPTSLVIPLIGEYLLFTMIFVTLSIVITVFVLNVHHRSPRTHTMPAWVRRV
FLDIVPRLLFMKRPSVVKDNCRRLIESMHKMANAPRFWPEPVGEPGILSDICNQGLSPAPTFCNPTDTAV
ETQPTCRSPPLEVPDLKTSEVEKASPCPSPGSCPPPKSSSGAPMLIKARSLSVQHVPSSQEAAEDGIRCR
SRSIQYCVSQDGAASLADSKPTSSPTSLKARPSQLPVSDQASPCKCTCKEPSPVSPVTVLKAGGTKAPPQ
HLPLSPALTRAVEGVQYIADHLKAEDTDFSVKEDWKYVAMVIDRIFLWMFIIVCLLGTVGLFLPPWLAAC
```

Notes

RSLpS^{441}VQ (= Ser472 in P09483)

References to 14-3-3 binding to nicotinic acetylcholine receptor α 4 subunit

Jeanclos EM, Lin L, Treuil MW, Rao J, DeCoster MA, Anand R. The chaperone protein 14-3-3eta interacts with the nicotinic acetylcholine receptor alpha 4 subunit. Evidence for a dynamic role in subunit stabilization. J Biol Chem. 2001 Jul 27;276(30):28281-90.

Rat Huntingtin-associated protein 1 (isoform 1A only)

NOT IN WEBLOGO

p-HAP1a, CGHPPASGTSYRSSpTL), in which the Thr-598 residue is phosphorylated ?

References to 14-3-3 binding to HAP1A

Rong J, Li S, Sheng G, Wu M, Coblitz B, Li M, Fu H, Li XJ. (2007) 14-3-3 protein interacts with Huntingtin-associated protein 1 and regulates its trafficking. J Biol Chem. 282, 4748-4756.

Rat MYLK2 (Rat myosin light chain kinase 2 (MLCK)) (Swissprot = P20689)

```
        1 MATENGAVEL GTQSLSTDHP PTDAAGDGSP ASEKEPSLPD TEKDLGPTNT KKDPGAPDPK
       61 KNPDPPSLKK TPEAPGPEKK GDSAPASASN QGPSGEGDGG GGPAEGGTGP PAVLPQPTAT
      121 ADASIQKLDA TQAPSGNQES GEAKAGKKAA ECREAGRRGS PAFLHSPsCP AIISCSEKTL
      181 AMKPLSETTE LIFAGVSETP DPQDPGPAKD EGGTNTLADG KEEAEAGQAE QAKVQGDTSQ
      241 RIGFQAVPSE RAEVGQALCL TAKEEDCFQI LDDCPPPPAP FPHRIVELRT GNVSSEFSMN
      301 SKEALGGGKF GAVCTCTERS TGLKLAAKVI KKQTPKDKEM VLLEIEVMNQ LNHRNLIQLY
      361 SAIETSHEII LFMEYIEGGE LFERIVDEDY QLTEVDTMVF VRQICDGILF MHKMRVLHLD
      421 LKPENILCVN TTGHLVKIID FGLARRYNPN EKLKVNFGTP EFLSPEVVNY DQISDKTDMW
      481 SLGVITYMLL SGLSPFLGDD DTETLNNVLS ANWYFDEETF EAVSDEAKDF VSNLITKDQS
      541 ARMSAEQCLA HPWLNNLAEK AKRCNRRLKS QILLKKYLMK RRWKKNFIAV SAANRFKKIS
      601 SSGALMALGV
>gi|125494|sp|P20689.2|MYLK2_RAT RecName: Full=Myosin light chain kinase 2,
```

```
skeletal/cardiac muscle; Short=MLCK2
MATENGAVELGTQSLSTDHPPTDAAGDGSPASEKEPSLPDTEKDLGPTNTKKDPGAPDPKKNPDPPSLKK
TPEAPGPEKKGDSAPASASNQGPSGEGDGGGGPAEGGTGPPAVLPQPTATADASIQKLDATQAPSGNQES
GEAKAGKKAAECREAGRRGSPAFLHSPSCPAIISCSEKTLAMKPLSETTELIFAGVSETPDPQDPGPAKD
EGGTNTLADGKEEAEAGQAEQAKVQGDTSQRIGFQAVPSERAEVGQALCLTAKEEDCFQILDDCPPPPAP
FPHRIVELRTGNVSSEFSMNSKEALGGGKFGAVCTCTERSTGLKLAAKVIKKQTPKDKEMVLLEIEVMNQ
LNHRNLIQLYSAIETSHEIILFMEYIEGGELFERIVDEDYQLTEVDTMVFVRQICDGILFMHKMRVLHLD
LKPENILCVNTTGHLVKIIDFGLARRYNPNEKLKVNFGTPEFLSPEVVNYDQISDKTDMWSLGVITYMLL
SGLSPFLGDDDTETLNNVLSANWYFDEETFEAVSDEAKDFVSNLITKDQSARMSAEQCLAHPWLNNLAEK
AKRCNRRLKSQILLKKYLMKRRWKKNFIAVSAANRFKKISSSGALMALGV
```

Notes

FLHSP(pS161)CPA in rabbit MLCK phosphorylated by MAPKAP-K2 binds to 14-3-3 (= Ser168 in rat MLCK P206

References to 14-3-3 binding to MLCK

Haydon CE, Watt PW, Morrice N, Knebel A, Gaestel M, Cohen P. Identification of a phosphorylation site on skeletal muscle myosin light chain kinase that becomes phosphorylated during muscle contraction. Arch Biochem Biophys. 2002 Jan 15;397(2):224-31.

<u>Rat Nr4a1(Nur77)</u> Nuclear receptor subfamily 4 group A member 1 (Swissprot = P22829)

```
        1 MPCIQAQYGT PATSPGPRDH LTGDPLALEF SKPTMDLASP ETAPTAPATL PSFSTFMDGG
       61 YTGEFDTFLY QLPGTAQPCS SASSTSSSSS SATSPASASF KFEDFQVYGC YPGTLSGPLD
      121 ETLSSSGSDY YGSPCSAPSP PTPNFQPSQL SPWDGSFGHF SPSQTYEGLR VWTEQLPKAS
      181 GPPPPPTFFS FSPPTGPSPS LAQSSLKLFP APATHQLGEG ESYSVPAAFP GLAPTSPNCD
      241 TSGILDAPVT STKARSGSSG GSEGRCAVCG DNASCQHYGV RTCEGCKGFF KRTVQKSAKY
      301 ICLANKDCPV DKRRRNRCQF CRFQKCLAVG MVKEVVRTDS LKGRRGRLPs KPKQPPDASP
      361 TNLLTSLIRA HLDSGPNTAK LDYSKFQELV LPRFGKEDAG DVQQFYDLLS GSLDVIRKWA
      421 EKIPGFIELS PGDQDLLLES AFLELFILRL AYRSKPGEGK LIFCSGLVLH RLQCARGFGD
      481 WIDNILAFSR SLHSLGVDVP AFACLSALVL ITDRHGLQDP RRVEELQNRI ASCLKEHMAA
      541 VAGDPQPASC LSRLLGKLPE LRTLCTQGLQ RIFCLKLEDL VPPPPIVDKI FMDTLSF
>gi|1709263|sp|P22829.2|NR4A1_RAT RecName: Full=Nuclear receptor subfamily 4
group A member 1; AltName: Full=Orphan nuclear receptor HMR; AltName:
Full=Nerve growth factor-induced protein I-B; Short=NGFI-B; AltName:
Full=NUR77
MPCIQAQYGTPATSPGPRDHLTGDPLALEFSKPTMDLASPETAPTAPATLPSFSTFMDGGYTGEFDTFLY
QLPGTAQPCSSASSTSSSSSSATSPASASFKFEDFQVYGCYPGTLSGPLDETLSSSGSDYYGSPCSAPSP
PTPNFQPSQLSPWDGSFGHFSPSQTYEGLRVWTEQLPKASGPPPPPTFFSFSPPTGPSPSLAQSSLKLFP
APATHQLGEGESYSVPAAFPGLAPTSPNCDTSGILDAPVTSTKARSGSSGGSEGRCAVCGDNASCQHYGV
RTCEGCKGFFKRTVQKSAKYICLANKDCPVDKRRRNRCQFCRFQKCLAVGMVKEVVRTDSLKGRRGRLPS
KPKQPPDASPTNLLTSLIRAHLDSGPNTAKLDYSKFQELVLPRFGKEDAGDVQQFYDLLSGSLDVIRKWA
EKIPGFIELSPGDQDLLLESAFLELFILRLAYRSKPGEGKLIFCSGLVLHRLQCARGFGDWIDNILAFSR
SLHSLGVDVPAFACLSALVLITDRHGLQDPRRVEELQNRIASCLKEHMAAVAGDPQPASCLSRLLGKLPE
LRTLCTQGLQRIFCLKLEDLVPPPPIVDKIFMDTLSF
```

Notes

VRTDSLKGRRGRLP(pS350)KPKQP (conserved in human and mouse sequences)

References to 14-3-3 binding to Nur77

Wingate AD, Campbell DG, Peggie M, Arthur JS. Nur77 is phosphorylated in cells by RSK in response to mitogenic stimulation.
Biochem J. 2006 Feb 1;393(Pt 3):715-24.

Masuyama N, Oishi K, Mori Y, Ueno T, Takahama Y, Gotoh Y. Akt inhibits the orphan nuclear receptor Nur77 and T-cell apoptosis. J Biol Chem. 2001 Aug 31;276(35):32799-805.

<u>Rat NUMB</u> (Swissprot = Q3MUI1)

```
        1 MNKLRQSFRR KKDVYVPEAS RPHQWQTDEE GVRTGKCSFP VKYLGHVEVD ESRGMHICED
       61 AVKRLKATGK KAVKAVLWVS ADGLRVVDEK TKDLIVDQTI EKVSFCAPDR NFDRAFSYIC
      121 RDGTTRRWIC HCFMAVKDTG ERLSHAVGCA FAACLERKQK REKECGVTAT FDASRTTFTR
      181 EGSFRVTTAT EQAEREEIMK QLQDAKKAET DKTVGPSVAP GNSAPSPSSP TSPTLDPTAS
      241 LEMNNPHAIP RRHAPIEQLA RQGsFRGFPA LSQKMSPFKR QLsLRINELP STMQRKTDFP
      301 IKNTVPEVEG EAESISSLCS QITSAFSTPC EDPFSSAPMT KPVTLVAPQS PVLQGTEWGQ
      361 SSGAASPGLF QAGHRRTPSE ADRWLEEVSK SVRAQQPQAS AAPLQPVLQP PPPAAIAPPA
      421 PPFQGHAFLT SQPVPVGVVP PLQPAFVSTQ SYPVANGMPY PASNVPVVGI TPSQMVANVF
      481 GTAGHPQATH PHQSPSLAKQ QTFPQYETSS ATTSPFFKPS AQHLNGSAAF NGVDNSGLVS
      541 GNRPAQVPPG TCPVDPFEAQ WAALESKPKQ RTNPSPTNPF SSDAQKAFEI
>gi|123786330|sp|Q3MUI1|Q3MUI1_RAT Numb
MNKLRQSFRRKKDVYVPEASRPHQWQTDEEGVRTGKCSFPVKYLGHVEVDESRGMHICEDAVKRLKATGK
KAVKAVLWVSADGLRVVDEKTKDLIVDQTIEKVSFCAPDRNFDRAFSYICRDGTTRRWICHCFMAVKDTG
ERLSHAVGCAFAACLERKQKREKECGVTATFDASRTTFTREGSFRVTTATEQAEREEIMKQLQDAKKAET
DKTVGPSVAPGNSAPSPSSPTSPTLDPTASLEMNNPHAIPRRHAPIEQLARQGSFRGFPALSQKMSPFKR
QLSLRINELPSTMQRKTDFPIKNTVPEVEGEAESISSLCSQITSAFSTPCEDPFSSAPMTKPVTLVAPQS
PVLQGTEWGQSSGAASPGLFQAGHRRTPSEADRWLEEVSKSVRAQQPQASAAPLQPVLQPPPPAAIAPPA
PPFQGHAFLTSQPVPVGVVPPLQPAFVSTQSYPVANGMPYPASNVPVVGITPSQMVANVFGTAGHPQATH
PHQSPSLAKQQTFPQYETSSATTSPFFKPSAQHLNGSAAFNGVDNSGLVSGNRPAQVPPGTCPVDPFEAQ
WAALESKPKQRTNPSPTNPFSSDAQKAFEIEL
```

References to 14-3-3 binding (see NUMBL)

<u>Rat NUMBL</u> Numblike (Swissprot = Q3MUI2)

```
        1 MSRSAAASGG PRRPDQHLPP APCGASGPPE TFRTESDGAG TMNKLRQSLR RRKPAYVPEA
       61 SRPHQWQADE DAVRKGTCSF PVRYLGHVEV EESRGMHVCE DAVKKLKAMG RKSVKSVLWV
      121 SADGLRVVDD KTKDLLVDQT IEKVSFCAPD RNLDKAFSYI CRDGTTRRWI CHCFLALKDS
      181 GERLSHAVGC AFAACLERKQ RREKECGVTA AFDASRTSFA REGSFRLSGG GRPAEREAGD
      241 KKKEAAAAPA VAPGPAQPGH VSPTPATTSP GEKGEAGTPV AAGTTAAAIP RRHAPLEQLV
```

```
      301 RQGsFRGFPA LSQKNSPFKR QLsLRLNELP STLQRRTDFQ VKGTVPEMEP PGTGDSDGIS
      361 ALCTQISSSF ASAGAPVPGP PSATTGTSAW GEPSVPAATA FQPGHKRTPS EAERWLEEVS
      421 QVAKAQQQQQ QQQQQQQQQQ QQQQQQQQQQ QQQQATSVPP MPTMAPTLQP FSAPVGPFDT
      481 AAAQVAVFLP PTHMQPPFVP AYPGLGYPPM PRVPVVGITP SQMVANAFCS AAQLQPQPAT
      541 LLGKAGAFPP PTAPSAPGGQ ARPRPNGAPW PPEPAPAPAP ELDPFEAQWA ALEGKPAVEK
      601 PSNPFSGDLQ KTFEIEL
>gi|123789641|sp|Q3MUI2|Q3MUI2_RAT Numb-like
MSRSAAASGGPRRPDQHLPPAPCGASGPPETFRTESDGAGTMNKLRQSLRRRKPAYVPEASRPHQWQADE
DAVRKGTCSFPVRYLGHVEVEESRGMHVCEDAVKKLKAMGRKSVKSVLWVSADGLRVVDDKTKDLLVDQT
IEKVSFCAPDRNLDKAFSYICRDGTTRRWICHCFLALKDSGERLSHAVGCAFAACLERKQRREKECGVTA
AFDASRTSFAREGSFRLSGGGRPAEREAGDKKKEAAAAPAVAPGPAQPGHVSPTPATTSPGEKGEAGTPV
AAGTTAAAIPRRHAPLEQLVRQGSFRGFPALSQKNSPFKRQLSLRLNELPSTLQRRTDFQVKGTVPEMEP
PGTGDSDGISALCTQISSSFASAGAPVPGPPSATTGTSAWGEPSVPAATAFQPGHKRTPSEAERWLEEVS
QVAKAQQQQQQQQQQQQQQQQQQQQQQQQQQQQATSVPPMPTMAPTLQPFSAPVGPFDTAAAQVAVFLP
PTHMQPPFVPAYPGLGYPPMPRVPVVGITPSQMVANAFCSAAQLQPQPATLLGKAGAFPPPTAPSAPGGQ
ARPRPNGAPWPPEPAPAPAPELDPFEAQWAALEGKPAVEKPSNPFSGDLQKTFEIEL
```

Notes

Numb and Numbl were efficiently and stoichiometrically phosphorylated in vitro at equivalent Ser residues (Ser264 in Numb and Ser304 in Numbl) by activated CaM-KI and also by two other CaM-Ks (CaM-KII and CaM-KIV). Recruitment of 14-3-3 proteins was the functional consequence of the phosphorylation of the Numb family proteins. Interaction of 14-3-3 protein with phosphorylated Numbl-blocked dephosphorylation of Ser304.

References to 14-3-3 binding to Numb

Tokumitsu H, Hatano N, Inuzuka H, Sueyoshi Y, Yokokura S, Ichimura T, Nozaki N, Kobayashi R. Phosphorylation of Numb family proteins. Possible involvement of Ca2+/calmodulin-dependent protein kinases. J Biol Chem. 2005 Oct 21;280(42):35108-18.

Tokumitsu H, Hatano N, Yokokura S, Sueyoshi Y, Nozaki N, Kobayashi R. Phosphorylation of Numb regulates its interaction with the clathrin-associated adaptor AP-2. FEBS Lett. 2006 Oct 16;580(24):5797-801

Rat RPS6KA1 Ribosomal S6 kinase 1 (p90RSK1) (Swissprot = Q63531)

```
1 MPLAQLKEPW PLMELVPLDP ENGQASGEEA GLQPSKDEGI LKEISITHHV KAGSEKADPS
       61 HFELLKVLGQ GSFGKVFLVR KVTRPDNGHL YAMKVLKKAT LKVRDRVRTK MERDILADVN
      121 HPFVVKLHYA FQTEGKLYLI LDFLRGGDLF TRLsKEVMFT EEDVKFYLAE LALGLDHLHS
      181 LGIIYRDLKP ENILLDEEGH IKLTDFGLSK EAIDHEKKAY SFCGTVEYMA PEVVNRQGHT
      241 HSADWWSYGV LMFEMLTGSL PFQGKDRKET MTLILKAKLG MPQFLSTEAQ SLLRALFKRN
      301 PANRLGSGPD GAEEIKRHIF YSTIDWNKLY RREIKPPFKP AVAQPDDTFY FDTEFTSRTP
      361 RDSPGIPPSA GAHQLFRGFS FVATGLMEDD SKPRATQAPL HSVVQQLHGK NLVFSDGYIV
      421 KETIGVGSYS VCKRCVHKAT NMEYAVKVID KSKRDPSEEI EILLRYGQHP NIITLKDVYD
      481 DSKHVYLVTE LMRGGELLDK ILRQKFFSER EASFVLYTIS KTVEYLHSQG VVHRDLKPSN
      541 ILYVDESGNP ECLRICDFGF AKQLRAENGL LMTPCYTANF VAPEVLKRQG YDEGCDIWSL
      601 GVLLYTMLAG YTPFANGPSD TPEEILTRIS SGKFTLSGGN WNTVSETAKD LVSKMLHVDP
      661 HQRLTAKQVL QHPWITQKDK LPQSQLSHQD LQLVKGGMAA TYSALSSSKP TPQLKPIESS
      721 ILAQRRVRKL PSTTL
>gi|11132671|sp|Q63531.1|KS6A1_RAT RecName: Full=Ribosomal protein S6 kinase
alpha-1; Short=S6K-alpha 1; AltName: Full=90 kDa ribosomal protein S6 kinase
1; AltName: Full=p90-RSK 1; AltName: Full=Ribosomal S6 kinase 1; Short=RSK-1;
AltName: Full=pp90RSK1; AltName: Full=p90S6K; AltName: Full=MAP kinase-
activated protein kinase 1a; Short=MAPKAPK1A
MPLAQLKEPWPLMELVPLDPENGQASGEEAGLQPSKDEGILKEISITHHVKAGSEKADPSHFELLKVLGQ
GSFGKVFLVRKVTRPDNGHLYAMKVLKKATLKVRDRVRTKMERDILADVNHPFVVKLHYAFQTEGKLYLI
LDFLRGGDLFTRLSKEVMFTEEDVKFYLAELALGLDHLHSLGIIYRDLKPENILLDEEGHIKLTDFGLSK
EAIDHEKKAYSFCGTVEYMAPEVVNRQGHTHSADWWSYGVLMFEMLTGSLPFQGKDRKETMTLILKAKLG
MPQFLSTEAQSLLRALFKRNPANRLGSGPDGAEEIKRHIFYSTIDWNKLYRREIKPPFKPAVAQPDDTFY
FDTEFTSRTPRDSPGIPPSAGAHQLFRGFSFVATGLMEDDSKPRATQAPLHSVVQQLHGKNLVFSDGYIV
KETIGVGSYSVCKRCVHKATNMEYAVKVIDKSKRDPSEEIEILLRYGQHPNIITLKDVYDDSKHVYLVTE
LMRGGELLDKILRQKFFSEREASFVLYTISKTVEYLHSQGVVHRDLKPSNILYVDESGNPECLRICDFGF
AKQLRAENGLLMTPCYTANFVAPEVLKRQGYDEGCDIWSLGVLLYTMLAGYTPFANGPSDTPEEILTRIS
SGKFTLSGGNWNTVSETAKDLVSKMLHVDPHQRLTAKQVLQHPWITQKDKLPQSQLSHQDLQLVKGGMAA
TYSALSSSKPTPQLKPIESSILAQRRVRKLPSTTL
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Notes

p90RSK an AGC kinase of the RSK family. Phosphorylated and activated by Erk1 and -2 in response to many growth factors, polypeptide hormones and neurotransmitters. Several phosphorylation sites are important for its activation. Possesses two kinase domains connected by a regulator linker region. Phosphorylates a wide range of substrates including ribosomal protein S6. Prominently expressed in brain structures essential for cognitive function and learning. RSK1 specifically and directly binds 14-3-3beta. This interaction was dependent on phosphorylation of serine 154 within the motif RLSKEV of RSK1. Binding of RSK1 to 14-3-3beta was maximal under basal conditions and decreased significantly upon mitogen stimulation. 14-3-3beta binding negatively regulates RSK1 activity to maintain signal specificity and that association/dissociation of the 14-3-3beta-RSK1 complex is likely to be important for mitogen-mediated RSK1 activation.

References to 14-3-3 binding to RPS6KA1

Cavet ME, Lehoux S, Berk BC. 14-3-3beta is a p90 ribosomal S6 kinase (RSK) isoform 1-binding protein that negatively regulates RSK kinase activity. J Biol Chem. 2003 May 16;278(20):18376-83

Rat TESK1 human testicular protein kinase 1 (a TKL kinase of the LISK fanily. (Rattus norvegicus D50864.1)

```
        1 MAGERPPLRG PGPGETPVEG PGGAGGGPGR GRPSSYRALR SAVSSLARVD DFDCAEKIGA
       61 GFFSEVYKVR HRQSGQVMVL KMNKLPSNRS NTLREVQLMN RLRHPNILRF MGVCVHQGQL
      121 HALTEYMNGG TLEQLLSSPE PLSWPVRLHL ALDIAQGLRY LHAKGVFHRD LTSKNCLVRR
      181 EDGGFTAVVG DFGLAEKIPV YREGARKEPL AVVGSPYWMA PEVLRGELYD EKADVFAFGI
      241 VLCELIARVP ADPDYLPRTE DFGLDVPAFR TLVGNDCPLP FLLLAIHCCS MEPSARAPFT
```

301 EITQHLEQIL EQLPEPTPLA KMPLAKAPLT YNQGSVPRGG PSATLPRSDP RLSRSRSDLF 361 LPPSPESPPS WGDNLTRVNP FSLREDLRGG KIKLLDTPCK PATPLPLVPP SPLTSTQLPL 421 VASPESLVQP ETPVRRCRsL PSSPELPRRM ETALPGPGPS PVGPSTEERM DCEGSSPEPE 481 PPGPAPQLPL AVATDNFIST CSSASQPWSA RPGPSLNNNP PAVVVNSPQG WAREPWNRAQ 541 HSLPRAAALE RTEPSPPPSA PREQEEGLPC PGCCLSPFSF GFLSMCPRPT PAVARYRNLN 601 CEAGSLLCHR GHHAKPPTPS LQLPGARS **Notes** TESK1 a TKL kinase of the LISK fanily. Its testicular germ cell-specific expression and developmental pattern of expression in the mouse suggests that this kinase plays an important role at and after the meiotic phase of spermatogenesis. 14-3-3beta interacts with TESK1 through the C-terminal region of TESK1 and in a manner dependent on the phosphorylation of Ser439 within an RXXSXP motif. Binding of 14-3-3beta inhibited the kinase activity of TESK1. **References to 14-3-3 binding to TESK1** Toshima JY, Toshima J, Watanabe T, Mizuno K.Binding of 14-3-3beta regulates the kinase activity and subcellular localization of testicular protein kinase 1. J Biol Chem. 2001 Nov 16;276(46):43471-81	

B. Non-mammalian animal proteins reported to interact directly with 14-3-3	
Ancylostoma caninum DAF-16 (Dog hookworm DAF16; a forkhead transcription factor) (Swissprot = B3G3K1) 1 MSNHLSQTQC LPPQLPTFGV VPPLSFQPQC YISTSSSILP PGPPYPSLNT TSPSSDSLFS 61 VSTSLNSLPS ECPPRRSDLD LKMETPDGDD GDDFFDLEKH QKARSAsFGG STQYSSQLAI 121 ARHGLFAPSL DTIGSVASGL YDSAENLNSR LGATSVASSG ALLHSPDGNN TFSPSSCNMS 181 SPVMNDQLAP AGATDAGDGV AGAGAAKKST TRRNAWGNLS YADLITQAIM QSPEKRLTLS 241 QVYEWMVQNV PYFRDKGDSN SSAGWKNSIR HNLSLHSRFM RIQNEGAGKS SWWVINPDAK 301 PGRNPRRVRA StLDTTSKAT LSKKLKGARK RIHDIRAVSG LHSGVSSLAG SQASIMSHDI 361 YGDEEAMQAS FDPMFRPRTQ SNLSVPGSST RVSPSMEHPF DDFEFPSWVN DATAASAAAN 421 AAANAANHTG AAPIPTDILD RTDQMRIDSC RIMMNGVKQE PKPIKTESPV APPPSYLELS 481 SVRNQSQLQN PLLRTQLASV KFPTAGLPLP YQTYSPWPTH TPLLPPSSCA AVAQANSVAA 541 AAALPSDLES LTLPDQPLMD FEVESLLRHE LSQTTDHRLN FDNL **Notes** Ac-FTT-2 was expressed in HEK 293T cells, and was recognized by an antibody against human 14-3-3beta isoform. Reciprocal co-immunoprecipitations using anti-epitope tag antibodies indicated that Ac-FTT-2 (14-3-3) interacts with Ac-DAF-16 when co-expressed in serum-stimulated HEK 293T cells. This interaction requires intact Akt consensus phosphorylation sites at serine107 and threonine312, but not serine381. **References to 14-3-3 binding to dog hookworm DAF16** Kiss JE, Gao X, Krepp JM, Hawdon JM. Interaction of hookworm 14-3-3 with the forkhead transcription factor DAF-16 requires intact Akt phosphorylation sites. Parasit Vectors. 2009 Apr 24;2(1):21.	
Caenorhabditis elegans DAF-16 (Dauer formation protein 16) Forkhead box protein O (AAC47803.1 GI:2623943) 1 MMEMLVDQGT DASSSASTST SSVSRFGADT FMNTPDDVMM NDDMEPIPRD RCNtWPMRRP 61 QLEPPLNSSP IIHEQIPEED ADLYGSNEQC GQLGGASSNG STAMLHTPDG SNSHQTSFPS 121 DFRMSESPDD TVSGKKTTTR RNAWGNMSYA ELITTAIMAS PEKRLTLAQV YEWMVQNVPY 181 FRDKGDSNSS AGWKNSIRHN LSLHSRFMRI QNEGAGKSSW WVINPDAKPG RNPRRTRERs 241 NtIETTTKAQ LEKSRRGAKK RIKERALMGS LHSTLNGNSI AGSIQTISHD LYDDDSMQGA 301 FDNVPSSFRP RTQSNLSIPG SSSRVSPAIG SDIYDDLEFP SWVGESVPAI PSDIVDRTDQ 361 MRIDATTHIG GVQIKQESKP IKTEPIAPPP SYHELNSVRG SCAQNPLLRN PIVPSTNFKP 421 MPLPGAYGNY QNGGITPINW LSTSNSSPLP GIQSCGIVAA QHTVASSSAL PIDLENLTLP 481 DQPLMDTMDV DALIRHELSQ AGGQHIHFDL >gi|2623943|gb|AAC47803.1| DAF-16 [Caenorhabditis elegans] MMEMLVDQGTDASSSASTSTSSVSRFGADTFMNTPDDVMMNDDMEPIPRDRCNTWPMRRPQLEPPLNSSP IIHEQIPEEDADLYGSNEQCGQLGGASSNGSTAMLHTPDGSNSHQTSFPSDFRMSESPDDTVSGKKTTTR RNAWGNMSYAELITTAIMASPEKRLTLAQVYEWMVQNVPYFRDKGDSNSSAGWKNSIRHNLSLHSRFMRI QNEGAGKSSWWVINPDAKPGRNPRRTRERSNTIETTTKAQLEKSRRGAKKRIKERALMGSLHSTLNGNSI AGSIQTISHDLYDDDSMQGAFDNVPSSFRPRTQSNLSIPGSSSRVSPAIGSDIYDDLEFPSWVGESVPAI PSDIVDRTDQMRIDATTHIGGVQIKQESKPIKTEPIAPPPSYHELNSVRGSCAQNPLLRNPIVPSTNFKP MPLPGAYGNYQNGGITPINWLSTSNSSPLPGIQSCGIVAAQHTVASSSALPIDLENLTLPDQPLMDTMDV DALIRHELSQAGGQHIHFDL **References to 14-3-3 binding to Caenorhabditis elegans DAF-16** RdRCN(pT)WP RTRER(S)N(T)IE (not certain whether Ser240 and/or Ser242 is the 14-3-3-binding site) Araiz C, Château MT, Galas S. 14-3-3 regulates life span by both DAF-16-dependent and -independent mechanisms in Caenorhabditis elegans. Exp Gerontol. 2008 Jun;43(6):505-19. Li J, Tewari M, Vidal M, Lee SS. The 14-3-3 protein FTT-2 regulates DAF-16 in Caenorhabditis elegans. Dev Biol. 2007 Jan 1;301(1):82-91. Wang Y, Oh SW, Deplancke B, Luo J, Walhout AJ, Tissenbaum HA. C. elegans 14-3-3 proteins regulate life span and interact with SIR-2.1 and DAF-16/FOXO. Mech Ageing Dev. 2006 Sep;127(9):741-7. Lehtinen MK, Yuan Z, Boag PR, Yang Y, Villén J, Becker EB, DiBacco S, de la Iglesia N, Gygi S, Blackwell TK, Bonni A. A conserved MST-FOXO signaling pathway mediates oxidative-stress responses and extends life span. Cell. 2006 Jun 2;125(5):987-1001. Cahill CM, Tzivion G, Nasrin N, Ogg S, Dore J, Ruvkun G, Alexander-Bridges M.Phosphatidylinositol 3-kinase signaling inhibits DAF-16 DNA binding and function via 14-3-3-dependent and 14-3-3-independent pathways. J Biol Chem. 2001 Apr 20;276(16):13402-10.	ONLY pTHR54 IN WEBLOGO.
Dictyostelium AX4 Ankyrin repeat-containing protein tyrosine kinase A (Swissprot = Q54HC6) 1 MSIKLPLSNI NSGGNSNNSS SSNSTSNNNI NINIGNGIPT NIEKMTFEDS ETQKLNIKQQ 61 SNNNTSTSVC VSSIHSSSPI SSPTSHQVNK SSGSLPPVIK RSPTTTHHHN SSGSNSSSSS 121 SGSNNNNNQI KTSNGMNKPN PTGFLFGSKP RENSQNKIDD NKGVNLAVST SNSSNNFHKS 181 HSESNIININ APPVETVNME EIYNNIPSSI SMENIRENEN NNNSSNNNSN NNNNNNNNNN	

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     241 NSNNINNVNG NKSSLASSTS SISSLSSVST LSTSNAATNT NTNANTTSTT KTTSTVRSTS
     301 PTQFKPRVEF DENNPNAIIL SRQRCKSISS PSDFRLNPPS NVHMPTSSLS TSTSTTNVNG
     361 LLLPNGVGGV SMSFTPSGLP MTPPTNSSQV DTLQMSTESI TIQPSSLDSS SESVSDGLQS
     421 VSGSPVTASP SPTISNNTNA TTTNNNNNTN TNNNNNNNNN QHNHHHHQHS HSQQHDVYQI
     481 KKENFPSSPT SPTLLPSETH DFSSEYSSNP GGKCAICRKP LWSFPISDKS RRCRDCSLVV
     541 HRACVPLATE CPSAKKSPSK LSVPNGNQSN SSSSSSSSSS SSSSSNSSSS NTKGHSRTPs
     601 SPSVSSIPGF QLTSNASQNL HVNSHTLSLL VNGATIDSNH YKRNKKSLEA GARDFHFIFR
     661 GCGIPLDEFP LDSYVCGLYS YFAHGRLYLT ESYVCFYDGF VFDRTKERTK IIKVSNIASI
     721 EKRSSGLNPS AIKIKTFDDQ SFIFTHFMHR EVAFDDLEGL LIHQESLHFA HSIVANNFPG
     781 MNEAIRGQTK RLLSRARLDG HYQIHSKIRC PMPSKEILLM SAIKNNNLDM VVTLLNYYCQ
     841 VNSDEINSVD SKGYTPLHNA VFSECSDQIF MHLLNQKEVR VRERNMDGNT PLHYFCQKFK
     901 SPECQRIVQA MIEKGANINE QNYNGETPLH KAIFNHSVRL LMVYILLKNN ANVNIVNNAG
     961 ESPLHYAVRL GRLDVAKMLL AAGADPTIIS LRDRKTALAL AVDYDVCPEI SDLLRRLDTI
    1021 TTSLEMYELE KFQASLVVEE LQKENVVARL DEKLLDKIGC TDKEERRKFL SLKSNRLLIH
    1081 HPARTQGAKI ILKEMETMDI KNGKLIISET ELEYTEKIGS GASGKVFKGI YRGRVVAIKV
    1141 LKSADDEMTR EDFLKEFGVL ASLESHTIVG LYGVVLEPKI CLVMEYCSNG SIYHSIRKNP
    1201 PSWERFFSFV QQMLAGINAL HQSTPQVLHR DIKTLNFLVN HNNKVKVADF GLSRFNTESN
    1261 QETLNKTRGT SVYCAPEVFE GKEYNERSDM YSMGIVMWEI VYCVVYGCYM IPYQEYNKMF
    1321 NAFQVALLVN SSKRVLRPTI PIGVPQVLKD LIYCLWDHDV SSRPTATEAM TALAVCEKEY
    1381 KQNKAQWELV ITKKEPTPLP RVAPLPAFPG YRQFYEQNLD IKPIPEEEQI YQEAMEKQRR
    1441 NQEASANRNQ KNKELLNNNN
>gi|74852181|sp|Q54HC6.1|ARKA_DICDI RecName: Full=Ankyrin repeat-containing
protein kinase A; AltName: Full=Ankyrin repeat-containing protein kinase 1
MSIKLPLSNINSGGNSNNSSSSNSTSNNNINININIGNGIPTNIEKMTFEDSETQKLNIKQQSNNNTSTSVC
VSSIHSSSPISSPTSHQVNKSSGSLPPVIKRSPTTTHHHNSSGSNSSSSSSGSNNNNNQIKTSNGMNKPN
PTGFLFGSKPRENSQNKIDDNKGVNLAVSTSNSSNNFHKSHSESNIININAPPVETVNMEEIYNNIPSSI
SMENIRENENNNNSSNNNSNNNNNNNNNNNNSNNINNVNGNKSSLASSTSSISSLSSVSTLSTSNAATNT
NTNANTTSTTKTTSTVRSTSPTQFKPRVEFDENNPNAIILSRQRCKSISSPSDFRLNPPSNVHMPTSSLS
TSTSTTNVNGLLLPNGVGGVSMSFTPSGLPMTPPTNSSQVDTLQMSTESITIQPSSLDSSSESVSDGLQS
VSGSPVTASPSPTISNNTNATTTNNNNNTNTNNNNNNNNNQHNHHHHQHSHSQQHDVYQIKKENFPSSPT
SPTLLPSETHDFSSEYSSNPGGKCAICRKPLWSFPISDKSRRCRDCSLVVHRACVPLATECPSAKKSPSK
LSVPNGNQSNSSSSSSSSSSSSSSSNSSSSNTKGHSRTPSSPSVSSIPGFQLTSNASQNLHVNSHTLSLL
VNGATIDSNHYKRNKKSLEAGARDFHFIFRGCGIPLDEFPLDSYVCGLYSYFAHGRLYLTESYVCFYDGF
VFDRTKERTKIIKVSNIASIEKRSSGLNPSAIKIKTFDDQSFIFTHFMHREVAFDDLEGLLIHQESLHFA
HSIVANNFPGMNEAIRGQTKRLLSRARLDGHYQIHSKIRCPMPSKEILLMSAIKNNNLDMVVTLLNYYCQ
VNSDEINSVDSKGYTPLHNAVFSECSDQIFMHLLNQKEVRVRERNMDGNTPLHYFCQKFKSPECQRIVQA
MIEKGANINEQNYNGETPLHKAIFNHSVRLLMVYILLKNNANVNIVNNAGESPLHYAVRLGRLDVAKMLL
AAGADPTIISLRDRKTALALAVDYDVCPEISDLLRRLDTITTSLEMYELEKFQASLVVEELQKENVVARL
DEKLLDKIGCTDKEERRKFLSLKSNRLLIHHPARTQGAKIILKEMETMDIKNGKLIISETELEYTEKIGS
GASGKVFKGIYRGRVVAIKVLKSADDEMTREDFLKEFGVLASLESHTIVGLYGVVLEPKICLVMEYCSNG
SIYHSIRKNPPSWERFFSFVQQMLAGINALHQSTPQVLHRDIKTLNFLVNHNNKVKVADFGLSRFNTESN
QETLNKTRGTSVYCAPEVFEGKEYNERSDMYSMGIVMWEIVYCVVYGCYMIPYQEYNKMFNAFQVALLVN
SSKRVLRPTIPIGVPQVLKDLIYCLWDHDVSSRPTATEAMTALAVCEKEYKQNKAQWELVITKKEPTPLP
RVAPLPAFPGYRQFYEQNLDIKPIPEEEQIYQEAMEKQRRNQEASANRNQKNKELLNNNN
```

Notes

1460 amino acids. Potential 14-3-3 interaction site within the sequence 597RTPSSP. The fragment 467–667 including both motifs (CRD + 14-3-3 site) as well as the larger N-terminal region (Fig. 2B) were able to interact with Dictyostelium 14-3-3 as indicated by yeast growth and β-galactosidase activity on protein-interaction selective media (GAL-UHTLXgal; data not shown). However, deletion of either motif (fragments 467–571 and 562–667) completely abolished interaction.   14-3-3-binding site = Ser600 in Q54HC6.

References to 14-3-3 binding to human ARCK-1

Aubry L, Lee S, Ravanel K, Firtel RA. The novel ankyrin-repeat containing kinase ARCK-1 acts as a suppressor of the Spalten signaling pathway during Dictyostelium development. Dev Biol. 2003 Nov 15;263(2):308-22.

Drosophila FOXO Forkhead box transcription factor (Swissprot = Q95V55)

```
       1 MMDGYAQEWP RLTHTDNGLA MDQLGGDLPL DVGFEPQTRA RSNtWPCPRP ENFVEPTDEL
      61 DSTKASNQQL APGDSQQAIQ NANAAKKNSS RRNAWGNLSY ADLITHAIGS ATDKRLTLSQ
     121 IYEWMVQNVP YFKDKGDSNS SAGWKNSIRH NLSLHNRFMR VQNEGTGKSS WWMLNPEAKP
     181 GKSVRRRAAs METSRYEKRR GRAKKRVEAL RQAGVVGLND ATPSPSSSVS EGLDHFPESP
     241 LHSGGGFQLS PDFRQRASSN ASSCGRLSPI RAQDLEPDWG FPVDYQNTTM TQAHAQALEE
     301 LTGTMADELT LCNQQQQGFS AASGLPSQPP PPPYQPPQHQ QAQQQQQQQS PYALNGPASG
     361 YNTLQPQSQC LLHRSLNCSC MHNARDGLSP NSVTTTMSPA YPNSEPSSDS LNTYSNVVLD
     421 GPADTAALMV QQQQQQQQQQ QLSASLEGQC LEVLNNEAQP IDEFNLENFP VGNLECNVEE
     481 LLQQEMSYGG LLDINIPLAT VNTNLVNSSS GPLSISNISN LSNISSNSGS SLSLNQLQAQ
     541 LQQQQQQQQA QQQQQAQQQQ QQHQQHQQQL LLNNNNNSSS SLELATQTAT TNLNARVQYS
     601 QPSVVTSPPS WVH
>gi|75019834|sp|Q95V55.1|FOXO_DROME RecName: Full=Forkhead box protein O;
Short=dFOXO; AltName: Full=Protein FKHR
MMDGYAQEWPRLTHTDNGLAMDQLGGDLPLDVGFEPQTRARSNTWPCPRPENFVEPTDELDSTKASNQQL
APGDSQQAIQNANAAKKNSSRRNAWGNLSYADLITHAIGSATDKRLTLSQIYEWMVQNVPYFKDKGDSNS
SAGWKNSIRHNLSLHNRFMRVQNEGTGKSSWWMLNPEAKPGKSVRRRAASMETSRYEKRRGRAKKRVEAL
RQAGVVGLNDATPSPSSSVSEGLDHFPESPLHSGGGFQLSPDFRQRASSNASSCGRLSPIRAQDLEPDWG
FPVDYQNTTMTQAHAQALEELTGTMADELTLCNQQQQGFSAASGLPSQPPPPPYQPPQHQQAQQQQQQQS
PYALNGPASGYNTLQPQSQCLLHRSLNCSCMHNARDGLSPNSVTTTMSPAYPNSEPSSDSLNTYSNVVLD
GPADTAALMVQQQQQQQQQQQLSASLEGQCLEVLNNEAQPIDEFNLENFPVGNLECNVEELLQQEMSYGG
LLDINIPLATVNTNLVNSSSGPLSISNISNLSNISSNSGSSLSLNQLQAQLQQQQQQQQAQQQQQAQQQQ
QQHQQHQQQLLLNNNNNSSSSLELATQTATTNLNARVQYSQPSVVTSPPSWVH
```

References to 14-3-3 binding to Drosophila FOXO

Nielsen MD, Luo X, Biteau B, Syverson K, Jasper H. 14-3-3 Epsilon antagonizes FoxO to control growth, apoptosis and longevity in Drosophila. Aging Cell. 2008 Oct;7(5):688-99.

Drosophila Yki (Yorkie) Drosophila transcriptional activator related to Yap (Swissprot = Q0E8X1)

```
     1  MLTTMSASSN TNSLIEKEID DEDMLSPIKS NNLVVRVNQD TDDNLQALFD SVLNPGDAKR
    61  PLQLPLRMRK LPNSFFTPPA PSHSRANSAD STYDAGSQSS INIGNKASIV QQPDGQSPIA
   121  AIPQLQIQPS PQHSRLAIHH SRARsSPASL QQNYNVRARS DAAAANNPNA NPSSQQQPAG
   181  PTFPENSAQE FPSGAPASSA IDLDAMNTCM SQDIPMSMQT VHKKQRSYDV ISPIQLNRQL
   241  GALPPGWEQA KTNDGQIYYL NHTTKSTQWE DPRIQYRQQQ QILMAERIKQ NDVLQTTKQT
   301  TTSTIANNLG PLPDGWEQAV TESGDLYFIN HIDRTTSWND PRMQSGLSVL DCPDNLVSSL
   361  QIEDNLCSNL FNDAQAIVNP PSSHKPDDLE WYKIN
```

Notes

Yorkie phosphorylation at S168, which is critical for 14-3-3 binding. Two other sites are also phosphorylated (SHSRANsADST) and VHKKQRsYDVI) (Badouel et al 2009). Ser145 in Q0E8X1 is equivalent to the reported phosphorylated Ser168 14-3-3-binding site.

References to 14-3-3 binding to Yorkie

Badouel C, Gardano L, Amin N, Garg A, Rosenfeld R, Le Bihan T, McNeill H. The FERM-domain protein Expanded regulates Hippo pathway activity via direct interactions with the transcriptional activator Yorkie. Dev Cell. 2009 Mar;16(3):411-20.

Ren F, Zhang L, Jiang J. Hippo signaling regulates Yorkie nuclear localization and activity through 14-3-3 dependent and independent mechanisms. Dev Biol. 2009 Nov 6. [Epub ahead of print]

Xenopus casp2 Capsase-2 from Xenopus laevis (Swissprot = Q9IB67)

```
        1 MLGGMQQHHR KALQRLRVSL ASEMIIEELL DHLVSSEILT NNMHSNIMAY RSDYAQNVAL
       61 LNLLPKRGPR AFSAFCNALH STNQEHLAQQ VEKEALLQEE FITSKVHHGS FPLPVQESTL
      121 SRPGRQICRE YREEsIDDGD GPVTVQLCSV NFYITHCQQA YKMHSCPRGR ALLISNVKFE
      181 TPDLDYRCGG EVDLASLEKL FSSLGYQVDV RCNLNAQSMM SQLGAFSALP VHSALDSCVV
      241 AILSHGLDGA VYGTDGKLVQ LQEVFTALDN AHCPQLQNKP KMFFIQACRG EETDRGVDQR
      301 DGREQSGSPG CEQSDAGRED IKVRLPTQSD MICAYACLKG TVSLRNTKRG SWFVQDLVSV
      361 FSQHSKDTHV ADMLVKVNAL IKEREGHAPG TEFHRCKEMS EYCSTLCRDL YLFPGSPSNG
      421 LPK
>gi|82221953|sp|Q9IB67|Q9IB67_XENLA Caspase-2 (XCaspase-2 protein)
MLGGMQQHHRKALQRLRVSLASEMIIEELLDHLVSSEILTNNMHSNIMAYRSDYAQNVALLNLLPKRGPR
AFSAFCNALHSTNQEHLAQQVEKEALLQEEFITSKVHHGSFPLPVQESTLSRPGRQICREYREESIDDGD
GPVTVQLCSVNFYITHCQQAYKMHSCPRGRALLISNVKFETPDLDYRCGGEVDLASLEKLFSSLGYQVDV
RCNLNAQSMMSQLGAFSALPVHSALDSCVVAILSHGLDGAVYGTDGKLVQLQEVFTALDNAHCPQLQNKP
KMFFIQACRGEETDRGVDQRDGREQSGSPGCEQSDAGREDIKVRLPTQSDMICAYACLKGTVSLRNTKRG
SWFVQDLVSVFSQHSKDTHVADMLVKVNALIKEREGHAPGTEFHRCKEMSEYCSTLCRDLYLFPGSPSNG
LPK
```

Notes

Ser135 to Ala mutation prevented 14-3-3 binding

References to 14-3-3 binding to Xenopus Caspase-2

Nutt LK, Buchakjian MR, Gan E, Darbandi R, Yoon SY, Wu JQ, Miyamoto YJ, Gibbon JA, Andersen JL, Freel CD, Tang W, He C, Kurokawa M, Wang Y, Margolis SS, Fissore RA, Kornbluth S. Metabolic control of oocyte apoptosis mediated by 14-3-3zeta-regulated dephosphorylation of caspase-2. Dev Cell. 2009 Jun;16(6):856-66.

Xenopus wee1 Xenopus Wee1 (Swissprot = P47817 for Xenopus laevis Wee1)

```
        1 MRTAMSCGGG LVQRLDFSSS DEEDGLSNGI NEGPQKGSPV SSWRTNNCPF PITPQRNERE
       61 LSPTQELSPS SDYSPDPSVG AECPGTPLHY STWKKLKLCD TPYTPKSLLY KTLPSPGSRV
      121 HCRGQRLLRF VAGTGAELDD PSLVNINPFT PESYRQTHFQ PNGKRKERPE DDCRTDRQMK
      181 YAEKEHPAVF QSKRFVLRET NMGSRYKTEF LEIEKIGAGE FGSVFKCVKR LDGCFYAIKR
      241 SKKPLAGSTD EQLALREVYA HAVLGHHPHV VRYYSAWAED DHMIIQNEYC NGGSLQDLIV
      301 DNNKEGQFVL EQELKEILLQ VSMGLKYIHG SGLVHMDIKP SNIFICRKQT ELGQEESDGE
      361 DDLSSGSVLY KIGDLGHVTS ILNPQVEEGD SRFLANEILQ EDYSQLPKAD IFALGLTIAL
      421 AAGAAPLPCN EDSWHHIRKG NLPHVPQLLT PVFLALLKLL VHPDPVMRPP AASLAKNSVL
      481 RRCVGKAAQL QKQLNVEKFK TAMLERELKA AKLAQTSGKD ECSDLPPMSG FSCRGRKRLV
      541 GAKNTRSLsF TCGGY
>gi|1351421|sp|P47817.1|WEE1A_XENLA RecName: Full=Wee1-like protein kinase
MRTAMSCGGGLVQRLDFSSSDEEDGLSNGINEGPQKGSPVSSWRTNNCPFPITPQRNERELSPTQELSPS
SDYSPDPSVGAECPGTPLHYSTWKKLKLCDTPYTPKSLLYKTLPSPGSRVHCRGQRLLRFVAGTGAELDD
PSLVNINPFTPESYRQTHFQPNGKRKERPEDDCRTDRQMKYAEKEHPAVFQSKRFVLRETNMGSRYKTEF
LEIEKIGAGEFGSVFKCVKRLDGCFYAIKRSKKPLAGSTDEQLALREVYAHAVLGHHPHVVRYYSAWAED
DHMIIQNEYCNGGSLQDLIVDNNKEGQFVLEQELKEILLQVSMGLKYIHGSGLVHMDIKPSNIFICRKQT
ELGQEESDGEDDLSSGSVLYKIGDLGHVTSILNPQVEEGDSRFLANEILQEDYSQLPKADIFALGLTIAL
AAGAAPLPCNEDSWHHIRKGNLPHVPQLLTPVFLALLKLLVHPDPVMRPPAASLAKNSVLRRCVGKAAQL
QKQLNVEKFKTAMLERELKAAKLAQTSGKDECSDLPPMSGFSCRGRKRLVGAKNTRSLSFTCGGY
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Notes

Binding of 14-3-3 to Xwee1 occurs during interphase, but not M-phase, and requires phosphorylation of Xwee1 on Ser-549. A mutant of Xwee1 (S549A) that cannot bind 14-3-3 is substantially less active than wild-type Xwee1 in its ability to phosphorylate Cdc2. Two primers (S549A-T, 5'-CACTCGATCGCTAGCCTTCAC; and S549A-B, 5'-GCAGGTGAAGGCTAGCGATCG) were used for mutagenesis of serine-549 to alanine.

References to 14-3-3 binding to Xenopus wee1

Lee J, Kumagai A, Dunphy WG. Positive regulation of Wee1 by Chk1 and 14-3-3 proteins. Mol Biol Cell. 2001 Mar;12(3):551-63.

Fungal proteins reported to interact directly with 14-3-3

Saccharomyces cerevisiae Acm1 (APC/C-CDH1 modulator 1) (yeast) Anaphase-promoting complex (APC) inhibitor (YPL267W)

<table>
<tr><td>1 MISPSKKRTI LSSKNINQKP RAVVKGNELR SPSKRRSQID TDYALRRSPI KTIQISKAAQ
61 FMLYEETAEE RNIAVHRHNE IYNNNNSVSN ENNPSQVKEN LSPAKICPYE RAFLREGGRI
121 ALKDLSVDEF KGYIQDPLTD ETIPLTLPLG DKKISLPSFI tPPRNSKISI FFTSKHQGQN
181 PETKISRSTD DVSEKKVVRK LSFHVYEDE
Notes
T161A (DKKISLPSFItPPRNSKISIF) mutation abolished 14-3-3 binding. However, 5 additional phospho sites were identified (Ser37, Ser48, Ser102, Ser126, Ser155, Ser166, Ser202) and Acm1 showed reduced BMH1/2 binding when all sites except T161 were mutated suggesting T161 is the major site but that another site is required for optimal binding. Relevant kinase = Cdc28 in the CMGC subfamily of protein kinases. (The sequence surrounding Thr-161 (FIpTPP) is both highly conserved in ACM1 orthologs and resembles the mode II 14-3-3 consensus binding sequence (RX(Y/F)XpSXP)).
References to 14-3-3 binding to yeast Acm1
Hall MC, Jeong DE, Henderson JT, Choi E, Bremmer SC, Iliuk AB, Charbonneau H. Cdc28 and Cdc14 control stability of the anaphase-promoting complex inhibitor Acm1. J Biol Chem. 2008 Apr 18;283(16):10396-407.
Dial JM, Petrotchenko EV, Borchers CH. Inhibition of APCCdh1 activity by Cdh1/Acm1/Bmh1 ternary complex formation. J Biol Chem. 2007 Feb 23;282(8):5237-48.
Martinez JS, Jeong DE, Choi E, Billings BM, Hall MC. Acm1 is a negative regulator of the CDH1-dependent anaphase-promoting complex/cyclosome in budding yeast. Mol Cell Biol. 2006 Dec;26(24):9162-76</td><td></td></tr>
<tr><td>**Saccharomyces cerevisiae Fin1** Filament protein FIN1 (Filaments in between nuclei protein 1) (Swissprot = Q03898)
1 MSNKSNRRSL RDIGNTIGRN NIPSDKDNVF VRLSMSPLRT TSQKEFLKPP MRISPNKTDG
61 MKHSIQVTPR RIMSPECLKG YVSKETQSLD RPQFKNSNKN VKIQNSDHIT NIIFPTSPTK
121 LTFSNENKIG GDGSLTRIRA RFKNGLMSPE RIQQQQQQHI LPSDAKSNTD LCSNTELKDA
181 PFENDLPRAK LKGKNLLVEL KKEEEDVGNG IESLTKSNTK LNSMLANEGK IHKASFQKSV
241 KFKLPDNIVT EETVELKEIK DLLLQMLRRQ REIESRLSNI ELQLTEIPKH K
>gi|41017084|sp|Q03898.1|FIN1_YEAST RecName: Full=Filament protein FIN1; AltName: Full=Filaments in between nuclei protein 1
MSNKSNRRSLRDIGNTIGRNNIPSDKDNVFVRLSMSPLRTTSQKEFLKPPMRISPNKTDGMKHSIQVTPR
RIMSPECLKGYVSKETQSLDRPQFKNSNKNVKIQNSDHITNIIFPTSPTKLTFSNENKIGGDGSLTRIRA
RFKNGLMSPERIQQQQQQHILPSDAKSNTDLCSNTELKDAPFENDLPRAKLKGKNLLVELKKEEEDVGNG
IESLTKSNTKLNSMLANEGKIHKASFQKSVKFKLPDNIVTEETVELKEIKDLLLQMLRRQREIESRLSNI
ELQLTEIPKHK
Notes
"Our results suggest that both sequences around residue 58 and the C-terminal part of Fin1p are required for association with Bmh2p (van Hemert et al 2003)." 14-3-3-binding site(s) not defined precisely
References to 14-3-3 binding to Saccharomyces cerevisiae Fin1
van Hemert MJ, Deelder AM, Molenaar C, Steensma HY, van Heusden GP. Self-association of the spindle pole body-related intermediate filament protein Fin1p and its phosphorylation-dependent interaction with 14-3-3 proteins in yeast. J Biol Chem. 2003 Apr 25;278(17):15049-55.
Mayordomo I, Sanz P. The Saccharomyces cerevisiae 14-3-3 protein Bmh2 is required for regulation of the phosphorylation status of Fin1, a novel intermediate filament protein. Biochem J. 2002 Jul 1;365(Pt 1):51-6.</td><td>NO SITES FOR WEBLOGO.</td></tr>
<tr><td>**Saccharomyces cerevisiae Msn2** Zinc finger protein MSN2 (Multicopy suppressor of SNF1 protein 2) (Swissprot = P33748)
1 MTVDHDFNSE DILFPIESMS SIQYVENNNP NNINNDVIPY SLDIKNTVLD SADLNDIQNQ
61 ETSLNLGLPP LSFDSPLPVT ETIPSTTDNS LHLKADSNKN RDARTIENDS EIKSTNNASG
121 SGANQYTTLT SPYPMNDILY NMNNPLQSPS PSSVPQNPTI NPPINTASNE TNLSPQTSNG
181 NETLISPRAQ QHTSIKDNRL SLPNGANSNL FIDTNPNNLN EKLRNQLNSD TNSYSNSISN
241 SNSNSTGNLN SSYFNSLNID SMLDDYVSSD LLLNDDDDDT NLSRRRFSDV ITNQFPSMTN
301 SRNSISHSLD LWNHPKINPS NRNTNLNITT NSTSSSNASP NTTTMNANAD SNIAGNPKNN
361 DATIDNELTQ ILNEYNMNFN DNLGTSTSGK NKSACPSSFD ANAMTKINPS QQLQQQLNRV
421 QHKQLTSSHN NSSTNMKSFN SDLYSRRQRA SLPIIDDSLS YDLVNKQDED PKNDMLPNSN
481 LSSSQQFIKP SMILSDNASV IAKVATTGLS NDMPFLTEEG EQNANSTPNF DLSITQMNMA
541 PLSPASSSST SLATNHFYHH FPQQGHHTMN SKIGSSLRRR KSAVPLMGTV PLTNQQNNIS
601 SSSVNSTGNG AGVTKERRPS YRRKSMTPSR RSSVVIESTK ELEEKPFHCH ICPKSFKRSE
661 HLKRHVRSVH SNERPFACHI CDKKFSRSDN LSQHIKTHKK HGDI
>gi|462625|sp|P33748.1|MSN2_YEAST RecName: Full=Zinc finger protein MSN2; AltName: Full=Multicopy suppressor of SNF1 protein 2
MTVDHDFNSEDILFPIESMSSIQYVENNNPNNINNDVIPYSLDIKNTVLDSADLNDIQNQETSLNLGLPP
LSFDSPLPVTETIPSTTDNSLHLKADSNKNRDARTIENDSEIKSTNNASGSGANQYTTLTSPYPMNDILY
NMNNPLQSPSPSSVPQNPTINPPINTASNETNLSPQTSNGNETLISPRAQQHTSIKDNRLSLPNGANSNL
FIDTNPNNLNEKLRNQLNSDTNSYSNSISNSNSNSTGNLNSSYFNSLNIDSMLDDYVSSDLLLNDDDDDT
NLSRRRFSDVITNQFPSMTNSRNSISHSLDLWNHPKINPSNRNTNLNITTNSTSSSNASPNTTTMNANAD
SNIAGNPKNNDATIDNELTQILNEYNMNFNDNLGTSTSGKNKSACPSSFDANAMTKINPSQQLQQQLNRV
QHKQLTSSHNNSSTNMKSFNSDLYSRRQRASLPIIDDSLSYDLVNKQDEDPKNDMLPNSNLSSSQQFIKP
SMILSDNASVIAKVATTGLSNDMPFLTEEGEQNANSTPNFDLSITQMNMAPLSPASSSSTSLATNHFYHH
FPQQGHHTMNSKIGSSLRRRKSAVPLMGTVPLTNQQNNISSSSVNSTGNGAGVTKERRPSYRRKSMTPSR
RSSVVIESTKELEEKPFHCHICPKSFKRSEHLKRHVRSVHSNERPFACHICDKKFSRSDNLSQHIKTHKK
HGDI
Notes
TOR inhibits expression of carbon-source-regulated genes by stimulating the binding of the transcriptional activators MSN2 and MSN4 to the cytoplasmic 14-3-3 protein BMH2. 14-3-3-binding site(s) not defined.
References to 14-3-3 binding to Saccharomyces cerevisiae Msn2 and Msn4
Beck T, Hall MN. The TOR signalling pathway controls nuclear localization of nutrient-regulated transcription factors. Nature. 1999 Dec 9;402(6762):689-92.
Bruckmann A, Steensma HY, Teixeira De Mattos MJ, Van Heusden GP.
Regulation of transcription by Saccharomyces cerevisiae 14-3-3 proteins. Biochem J. 2004 Sep 15;382(Pt 3):867-75.</td><td>NO SITES FOR WEBLOGO.</td></tr>
</table>

Santhanam A, Hartley A, Düvel K, Broach JR, Garrett S. PP2A phosphatase activity is required for stress and Tor kinase regulation of yeast stress response factor Msn2p. Eukaryot Cell. 2004 Oct;3(5):1261-71.	
Saccharomyces cerevisiae Pik1 Yeast phosphatidylinositol 4-kinase 1 MHKASSSKKS FDDTIELKKN EQLLKLINSS EFTLHNCVEL LCKHSENIGI HYYLCQKLAT 61 FPHSELQFYI PQLVQVLVTM ETESMALEDL LLRLRAENPH FALLTFWQLQ ALLTDLSTDP 121 ASYGFQVARR VLNNLQTNLF NTSSGSDKNV KIHENVAPAL VLSSMIMSAI AFPQLSEVTK 181 PLVESQGRRQ KAFVFKLARS AMKDFTKNMT LKNTLLNKKT SRSKRVSSNR SSTPTSPIDL 241 IDPIKTKEDA SFRKSRHSEV KLDFDIVDDI GNQVFEERIS SSIKLPKRKP KYLDNSYVHR 301 TYDGKNINRD GSISNTAKAL DGNKGDYISP KGRNDENNEI GNNEDETGGE TEEDADALNS 361 DHFTSSMPDL HNIQPRTSSA SSASLEGTPK LNRTNsQPLS RQAFKNSKKA NSSLSQEIDL 421 SQLSTTSKIK MLKANYFRCE TQFAIALETI SQRLARVPTE ARLSALRAEL FLLNRDLPAE 481 VDIPTLLPPN KKGKLHKLVT ITANEAQVLN SAEKVPYLLL IEYLRDEFDF DPTSETNERL 541 LKKISGNQGG LIFDLNYMNR KENNENRNES TLTSNNTRSS VYDSNSFNNG ASRNEGLSST 601 SRSDSASTAH VRTEVNKEED LGDMSMVKVR NRTDDEAYRN ALVIQSAANV PILPDDSQDR 661 SPELNFGSNL DEVLIENGIN SKNIHSQTDA LADQMRVSAV MLAQLDKSPQ QLSESTKQIR 721 AQIISSMKEV QDKFGYHDLE ALHGMAGERK LENDLMTGGI DTSYLGEDWA TKKERIRKTS 781 EYGHFENWDL CSVIAKTGDD LRQEAFAYQM IQAMANIWVK EKVDVWVKRM KILITSANTG 841 LVETITNAMS VHSIKKALTK KMIEDAELDD KGGIASLNDH FLRAFGNPNG FKYRRAQDNF 901 ASSLAAYSVI CYLLQVKDRH NGNIMIDNEG HVSHIDFGFM LSNSPGSVGF EAAPFKLTYE 961 YIELLGGVEG EAFKKFVELT KSSFKALRKY ADQIVSMCEI MQKDNMQPCF DAGEQTSVQL 1021 RQRFQLDLSE KEVDDFVENF LIGKSLGSIY TRIYDQFQLI TQGIYS **Notes** 390-LNRTN(pS)QP-399 **References to 14-3-3 binding to Pik1** Demmel L, Beck M, Klose C, Schlaitz AL, Gloor Y, Hsu PP, Havlis J, Shevchenko A, Krause E, Kalaidzidis Y, Walch-Solimena C. Nucleocytoplasmic shuttling of the Golgi phosphatidylinositol 4-kinase Pik1 is regulated by 14-3-3 proteins and coordinates Golgi function with cell growth. Mol Biol Cell. 2008 Mar;19(3):1046-61.	NO SWISS PROT
Saccharomyces cerevisiae Rtg3 Retrograde regulation protein 3 (Swissprot = P38165) 1 MMNNNESEAE NQRLLDELMN QTKVLQETLD FSLVTPTPHH NDDYKIHGSA YPGGETPAQQ 61 HEKLSYINTH NSNDNNNLMG SQARSNSQTP TASTIYEEAE SQSSYLDDMF RTSQGGRPVT 121 QNSISSIGQG PLRSSYSMAY DSPVDRAMNT PLQQQEGLKA ELPHDFLFQH GTDDTMYNLT 181 DDLSSSLSSS INSDMMTPNT YSSSFSYNPQ SLGPASVSST YSPKVRSPSS SFRAGSFLSS 241 SFRHGSINTP RTRHTSISSN MTENIGPGSV PKILGGLTSD EKLRRKREFH NAVERRRREL 301 IKQKIKELGQ LVPPSLLNYD DLGKQIKPNK GIILDRTVEY LQYLAEILEI QARKKKALLA 361 KIKELEEKKS SVAALSPFTN NHHASSGQNN SENSEERIID IRSVPNALMN EQNSKAELHN 421 WEPPLYDSVG NHNHAGTMES HPHTNIHEEL KEFLSGDLIE AEDNAKLMFG DDNSNPADYL 481 LEFGSG >gi|1710804|sp|P38165.2|RTG3_YEAST RecName: Full=Retrograde regulation protein 3 MMNNNESEAENQRLLDELMNQTKVLQETLDFSLVTPTPHHNDDYKIHGSAYPGGETPAQQHEKLSYINTH NSNDNNNLMGSQARSNSQTPTASTIYEEAESQSSYLDDMFRTSQGGRPVTQNSISSIGQGPLRSSYSMAY DSPVDRAMNTPLQQQEGLKAELPHDFLFQHGTDDTMYNLTDDLSSSLSSSINSDMMTPNTYSSSFSYNPQ SLGPASVSSTYSPKVRSPSSSFRAGSFLSSSFRHGSINTPRTRHTSISSNMTENIGPGSVPKILGGLTSD EKLRRKREFHNAVERRRRELIKQKIKELGQLVPPSLLNYDDLGKQIKPNKGIILDRTVEYLQYLAEILEI QARKKKALLAKIKELEEKKSSVAALSPFTNNHHASSGQNNSENSEERIIDIRSVPNALMNEQNSKAELHN WEPPLYDSVGNHNHAGTMESHPHTNIHEELKEFLSGDLIEAEDNAKLMFGDDNSNPADYLLEFGSG **Notes** bZip/HLH transcription factor. 14-3-3-binding site(s) not defined. **References to 14-3-3 binding to Saccharomyces cerevisiae Rtg3** van Heusden GP, Steensma HY. 14-3-3 Proteins are essential for regulation of RTG3-dependent transcription in Saccharomyces cerevisiae. Yeast. 2001 Dec;18(16):1479-91. Ichimura T, Kubota H, Goma T, Mizushima N, Ohsumi Y, Iwago M, Kakiuchi K, Shekhar HU, Shinkawa T, Taoka M, Ito T, Isobe T. Transcriptomic and proteomic analysis of a 14-3-3 gene-deficient yeast. Biochemistry. 2004 May 25;43(20):6149-58. Bruckmann A, Steensma HY, Teixeira De Mattos MJ, Van Heusden GP. Regulation of transcription by Saccharomyces cerevisiae 14-3-3 proteins. Biochem J. 2004 Sep 15;382(Pt 3):867-75.	NO SITES FOR WEBLOGO.
Schizosaccharomyces pombe Cdc25 (uniprot P06652) (GenBank: CAA90849.1) 1 MDSPLSSLSF TNTLSGKRNV LRPAARELKL MSDRNANQEL DFFFPKSKHI ASTLVDPFGK 61 TCSTASPASS LAADMSMNMH IDESPALPTP RRTLFRSLSC TVETPLANKT IVSPLPESPS 121 NDALTESYFF RQPASKYSIT QDSPRVSSTI AYSFKPKASI ALNTTKSEAT RSSLSSSSFD 181 SYLRPNVSRS RSSGNAPPFL RSRSSSSYSI NKKKGTSGGQ ATRHLTYALS RTCSQSSNTT 241 SLLESCLTDD TDDFELMSDH EDTFTMGKVA DLPESSVELV EDAASIQRPN SDFGACNDNS 301 LDDLFQASPI KPIDMLPKIN KDIAFPSLKV RSPSPMAFAM QEDAEYDEQD TPVLRRTQSM 361 FLNSTRLGLF KSQDLVCVTP KQSTKESERF ISSHVEDLSL PCFAVKEDSL KRITQETLLG 421 LLDGKFKDIF DKCIIIDCRF EYEYLGGHIS TAVNLNTKQA IVDAFLSKPL THRVALVFHC 481 EHSAHRAPHL ALHFRNTDRR MNSHRYPFLY YPEVYILHGG YKSFYENHKN RCDPINYVPM 541 NDASHVMTCT KAMNNFKRNA TFMRTKSYTF GQSVLASPDV NDSPTAMHSL STLRRF >sp|P06652|MPIP_SCHPO M-phase inducer phosphatase OS=Schizosaccharomyces pombe GN=cdc25 PE=1 SV=2 MDSPLSSLSFTNTLSGKRNVLRPAARELKLMSDRNANQELDFFFPKSKHIASTLVDPFGK TCSTASPASSLAADMSMNMHIDESPALPTPRRTLFRSLSCTVETPLANKTIVSPLPESPS NDALTESYFFRQPASKYSITQDSPRVSSTIAYSFKPKASIALNTTKSEATRSSLSSSSFD SYLRPNVSRSRSSGNAPPFLRSRSSSSYSINKKKGTSGGQATRHLTYALSRTCSQSSNTT SLLESCLTDDTDDFELMSDHEDTFTMGKVADLPESSVELVEDAASIQRPNSDFGACNDNS LDDLFQASPIKPIDMLPKINKDIAFPSLKVRSPSPMAFAMQEDAEYDEQDTPVLRRTQSM FLNSTRLGLFKSQDLVCVTPKQSTKESERFISSHVEDLSLPCFAVKEDSLKRITQETLLG	Sites of 14-3-3 binding not defined. NO WEBLOGO.

LLDGKFKDIFDKCIIIDCRFEYEYLGGHISTAVNLNTKQAIVDAFLSKPLTHRVALVFHC EHSAHRAPHLALHFRNTDRRMNSHRYPFLYYPEVYILHGGYKSFYENHKNRCDPINYVPM NDASHVMTCTKAMNNFKRNATFMRTKSYTFGQSVLASPDVNDSPTAMHSLSTLRRF **References to 14-3-3 binding to Cdc25** Sorrell DA, Marchbank AM, Chrimes DA, Dickinson JR, Rogers HJ, Francis D, Grierson CS, Halford NG. The Arabidopsis 14-3-3 protein, GF14omega, binds to the Schizosaccharomyces pombe Cdc25 phosphatase and rescues checkpoint defects in the rad24- mutant. Planta. 2003 Nov;218(1):50-7.	
Schizosaccharomyces pombe Mei2P (Meiosis protein 2) P08965 1 MIMETESPLS ITSPSPSDST FQVDMEKTMH ALPSSLLDSP LLSTNEHYPP KSTLLLSGPS 61 PIRNIQLSAT KSSESNSIDY LTDTQNIFPN FVNNENNYQF STAPLNPIDA CRVGERKVFT 121 TGNVLLSADR QPLSTWQQNI SVLSESPPQN GIQSYISSSE QAAQALTRKP SVTGFRSSSL 181 NSNSDDIDIF SHASRYLFVT NLPRIVPYAT LLELFSKLGD VKGIDTSSLS TDGICIVAFF 241 DIRQAIQAAK SLRSQRFFND RLLYFQFCQR SSIQKMINQG ATIQFLDDNE GQLLLNMQGG 301 SVLSILQLQS ILQTFGPLLI MKPLRSQNVS QIICEFYDTR DASFALDELD GRIIHNCCLQ 361 VAYYDAMADS VSTSSASSLS VPRGFSGMLN NNSEWNNSMT MSSNQETPTA ASCAVSRIGS 421 SYGMSNNFGS VPLGRTEsSP AWGTSGYYDV SSTSPVAPSD RNPSRQYNSI RYGLDVNPIA 481 PPNSSRLKQR NSDLLNGINP QWSPFSSNTG KVFDSPTGSL GMRRSLtVGA NASCSNPTNL 541 SFASLTLHDS KADSTLSASS LNPDLNLQRY TPTVEKHASD RNSVDYAQIA SGIDTRTTVM 601 IKNIPNKFTQ QMLRDYIDVT NKGTYDFLYL RIDFVNKCNV GYAFINFIEP QSIITFGKAR 661 VGTQWNVFHS EKICDISYAN IQGKDRLIEK FRNSCVMDEN PAYRPKIFVS HGPNRGMEEP 721 FPAPNNARRK LRSIASAQQI GLFPPTASKC >gi|126947|sp|P08965.1|MEI2_SCHPO RecName: Full=Meiosis protein mei2 MIMETESPLSITSPSPSDSTFQVDMEKTMHALPSSLLDSPLLSTNEHYPPKSTLLLSGPSPIRNIQLSAT KSSESNSIDYLTDTQNIFPNFVNNENNYQFSTAPLNPIDACRVGERKVFTTGNVLLSADRQPLSTWQQNI SVLSESPPQNGIQSYISSSEQAAQALTRKPSVTGFRSSSLNSNSDDIDIFSHASRYLFVTNLPRIVPYAT LLELFSKLGDVKGIDTSSLSTDGICIVAFFDIRQAIQAAKSLRSQRFFNDRLLYFQFCQRSSIQKMINQG ATIQFLDDNEGQLLLNMQGGSVLSILQLQSILQTFGPLLIMKPLRSQNVSQIICEFYDTRDASFALDELD GRIIHNCCLQVAYYDAMADSVSTSSASSLSVPRGFSGMLNNNSEWNNSMTMSSNQETPTAASCAVSRIGS SYGMSNNFGSVPLGRTESSPAWGTSGYYDVSSTSPVAPSDRNPSRQYNSIRYGLDVNPIAPPNSSRLKQR NSDLLNGINPQWSPFSSNTGKVFDSPTGSLGMRRSLTVGANASCSNPTNLSFASLTLHDSKADSTLSASS LNPDLNLQRYTPTVEKHASDRNSVDYAQIASGIDTRTTVMIKNIPNKFTQQMLRDYIDVTNKGTYDFLYL RIDFVNKCNVGYAFINFIEPQSIITFGKARVGTQWNVFHSEKICDISYANIQGKDRLIEKFRNSCVMDEN PAYRPKIFVSHGPNRGMEEPFPAPNNARRKLRSIASAQQIGLFPPTASKC **Notes** Mei2p Phosphorylated by Pat1 Kinase Has a Higher Affinity for Rad24p (S. pombe 14-3-3), and the two sites implicated by mutagenesis are RTEpS^{438}SP and RSLpT^{527}VG **References to 14-3-3 binding to Mei2P** Sato M, Watanabe Y, Akiyoshi Y, Yamamoto M. 14-3-3 protein interferes with the binding of RNA to the phosphorylated form of fission yeast meiotic regulator Mei2p.Curr Biol. 2002 Jan 22;12(2):141-5.	
Ustilago maydis cdc25s **Fungal cdc25s** Mielnichuk N, Pérez-Martín J. 14-3-3 regulates the G2/M transition in the basidiomycete Ustilago maydis. Fungal Genet Biol. 2008 Aug;45(8):1206-15. Pan S, Sehnke PC, Ferl RJ, Gurley WB. Specific interactions with TBP and TFIIB in vitro suggest that 14-3-3 proteins may participate in the regulation of transcription when part of a DNA binding complex. Plant Cell. 1999 Aug;11(8):1591-602.	Sites of 14-3-3 binding not defined. NO WEBLOGO.

Plant proteins reported to interact directly with 14-3-3	
Arabidopsis AKR2 Ankyrin repeat-containing protein 2 (U70425) 1 MASNSEKNPL LSDEKPKSTE ENKSSKPESA SGSSTSSAMP GLNFNAFDFS NMASILNDPS 61 IREMAEQIAK DPAFNQLAEQ LQRSIPNAGQ EGGFPNFDPQ QYVNTMQQVM HNPEFKTMAE 121 KLGTALVQDP QMSPFLDAFS NPETAEHFTE RMARMKEDPE LKPILDEIDA GGPSAMMKYW 181 NDPEVLKKLG EAMGMPVAGL PDQTVSAEPE VAEEGEEEES IVHQTASLGD VEGLKAALAS 241 GGNKDEEDSE GRTALHFACG YGELKCAQVL IDAGASVNAV DKNKNTPLHY AAGYGRKESV 301 SLLLENGAAV TLQNLDEKTP IDVAKLNSQL EVVKLLEKDA FL **Notes** Yeast 2-hybrid screen. 14-3-3 binding site not identified. **References to 14-3-3 binding to AKR2** Yan J, Wang J, Zhang H (2002) An ankyrin repeat-containing protein plays a role in both disease resistance and antioxidation metabolism. Plant J 29:193–202	Sites of 14-3-3 binding not defined. NO WEBLOGO.
Arabidopsis APX3 (peroxisomal membrane-bound ascorbate peroxidase) (UNIPROT Q42564) 1 MAAPIVDAEY LKEITKARRE LRSLIANKNC APIMLRLAWH DAGTYDAQSK TGGPNGSIRN 61 EEEHTHGANS GLKIALDLCE GVKAKHPKIT YADLYQLAGV VAVEVTGGPD IVFVPGRKDS 121 NVCPKEGRLP DAKQGFQHLR DVFYRMGLSD KDIVALSGGH TLGRAHPERS GFDGPWTQEP 181 LKFDNSYFVE LLKGESEGLL KLPTDKTLLE DPEFRRLVEL YAKDEDAFFR DYAESHKKLS 241 ELGFNPNSSA GKAVADSTIL AQSAFGVAVA AAVVAFGYFY EIRKRMK >sp|Q42564|APX3_ARATH L-ascorbate peroxidase 3, peroxisomal OS=Arabidopsis thaliana GN=APX3 PE=1 SV=1 MAAPIVDAEYLKEITKARRELRSLIANKNCAPIMLRLAWHDAGTYDAQSKTGGPNGSIRN EEEHTHGANSGLKIALDLCEGVKAKHPKITYADLYQLAGVVAVEVTGGPDIVFVPGRKDS NVCPKEGRLPDAKQGFQHLRDVFYRMGLSDKDIVALSGGHTLGRAHPERSGFDGPWTQEP LKFDNSYFVELLKGESEGLLKLPTDKTLLEDPEFRRLVELYAKDEDAFFRDYAESHKKLS ELGFNPNSSAGKAVADSTILAQSAFGVAVAAAVVAFGYFYEIRKRMK **Notes** Arabidopsis ATF1 (14-3-3) was bait in Y2H and APX3 interacted	Sites of 14-3-3 binding not defined. NO WEBLOGO.

117 – 122 is a possible motif for 14-3-3 binding but was not tested In vitro binding of bacterially expressed proteins found no interaction of ATF1 (14-3-3) and APX3 but they admit that the protein may not be phosphorylated in this system **References to 14-3-3 binding to APX3** Zhang H, Wang J, Nickel U, Allen RD, Goodman HM. Cloning and expression of an Arabidopsis gene encoding a putative peroxisomal ascorbate peroxidase. Plant Mol Biol. 1997 Aug;34(6):967-71..	
Arabidopsis BZR1 Brassinosteroid receptor (Brassinazole-resistant 1) (Swissprot = Q8S307) 1 MTSDGATSTS AAAAAAAAAA ARRKPSWRER ENNRRRERRR RAVAAKIYTG LRAQGDYNLP 61 KHCDNNEVLK ALCVEAGWVV EEDGTTYRKG CKPLPGEIAG TSSRVTPYSS QNQSPLSSAF 121 QSPIPSYQVS PSSSSFPSPS RGEPNNNMSS TFFPFLRNGG IPSSLPSLRI SNsCPVTPPV 181 SSPTSKNPKP LPNWESIAKQ SMAIAKQSMA SFNYPFYAVS APASPTHRHQ FHTPATIPEC 241 DESDSSTVDS GHWISFQKFA QQQPFSASMV PTSPTFNLVK PAPQQMSPNT AAFQEIGQSS 301 EFKFENSQVK PWEGERIHDV GMEDLELTLG NGKARG >gi|57012606|sp|Q8S307.1|BZR1_ARATH RecName: Full=Protein BRASSINAZOLE-RESISTANT 1; AltName: Full=Protein BIN2 SUBSTRATE 2 MTSDGATSTSAAAAAAAAAAARRKPSWRERENNRRRERRRRAVAAKIYTGLRAQGDYNLPKHCDNNEVLK ALCVEAGWVVEEDGTTYRKGCKPLPGEIAGTSSRVTPYSSQNQSPLSSAFQSPIPSYQVSPSSSSFPSPS RGEPNNNMSSTFFPFLRNGGIPSSLPSLRISNSCPVTPPVSSPTSKNPKPLPNWESIAKQSMAIAKQSMA SFNYPFYAVSAPASPTHRHQFHTPATIPECDESDSSTVDSGHWISFQKFAQQQPFSASMVPTSPTFNLVK PAPQQMSPNTAAFQEIGQSSEFKFENSQVKPWEGERIHDVGMEDLELTLGNGKARG **Notes** The 14-3-3-binding site reported in Gampala et al (2007) is PSLRISN(pS)CPVTP in the Arabidopsis protein. BIN2-catalyzed phosphorylation of BZR1/BZR2 not only inhibits DNA binding, but also promotes binding to the 14-3-3 proteins. Mutations of a BIN2-phosphorylation site in BZR1 (PSLRISN(pS)CPVTP) abolish 14-3-3 binding and lead to increased nuclear localization of BZR1 protein and enhanced BR responses in transgenic plants (Gampala et al 2007). Mutation of a putative 14-3-3-binding site of OsBZR1 ($_{152}$RVSS(pS)AP$_{158}$) abolished its interaction with the 14-3-3 proteins in yeast and in vivo. (Bai et al 2007). **References to 14-3-3 binding to Arabidopsis and rice BZR1** Gampala SS, Kim TW, He JX, Tang W, Deng Z, Bai MY, Guan S, Lalonde S, Sun Y, Gendron JM, Chen H, Shibagaki N, Ferl RJ, Ehrhardt D, Chong K, Burlingame AL, Wang ZY. An essential role for 14-3-3 proteins in brassinosteroid signal transduction in Arabidopsis. Dev Cell. 2007 Aug;13(2):177-89. Ryu H, Kim K, Cho H, Park J, Choe S, Hwang I. Nucleocytoplasmic shuttling of BZR1 mediated by phosphorylation is essential in Arabidopsis brassinosteroid signaling. Plant Cell. 2007 Sep;19(9):2749-62. Bai MY, Zhang LY, Gampala SS, Zhu SW, Song WY, Chong K, Wang ZY. Functions of OsBZR1 and 14-3-3 proteins in brassinosteroid signaling in rice. Proc Natl Acad Sci U S A. 2007 Aug 21;104(34):13839-44.	
Arabidopsis CaS Calcium-sensing receptor (AY341888) 1 MAMAEMATKS SLSAKLTLPS SSTKKTLSLR QVSVSLPTST SISLLSLFAS PPHEAKAAVS 61 IPKDQIVSSL TEVEKTINQV QETGSSVFDA TQRVFQVVGD ALKPALDTAL PIAKQAGEEA 121 MKLASPAFSE ASKKAQEAMQ SSGFDSEPVF NAAKTVTDVA QQTSKAIEDA KPIASSTMDT 181 ISSADPSVIV VAAGAAFLAY LLLPPVFSAI SFNFRGYKGD LTPAQTLDLL CTKNYLMVDI 241 RSEKDKEKAG IPRLPSNAKN RVISIPLEEL PNKVKGIVRN SKRVEAEIAA LKISYLKKIN 301 KGSNIIILDS YTDSAKIVAK TLKVLGYKNC YIVTDGFSGG RGWLQSRLGT DSYNFSFAQV 361 LSPSRIIPAA SRSFGTRSGT KFLPSSD >tr|Q9FN48|Q9FN48_ARATH Emb|CAB75797.1 OS=Arabidopsis thaliana GN=CaS PE=2 SV=1 MAMAEMATKSSLSAKLTLPSSSTKKTLSLRQVSVSLPTSTSISLLSLFASPPHEAKAAVS IPKDQIVSSLTEVEKTINQVQETGSSVFDATQRVFQVVGDALKPALDTALPIAKQAGEEA MKLASPAFSEASKKAQEAMQSSGFDSEPVFNAAKTVTDVAQQTSKAIEDAKPIASSTMDT ISSADPSVIVVAAGAAFLAYLLLPPVFSAISFNFRGYKGDLTPAQTLDLLCTKNYLMVDI RSEKDKEKAGIPRLPSNAKNRVISIPLEELPNKVKGIVRNSKRVEAEIAALKISYLKKIN KGSNIIILDSYTDSAKIVAKTLKVLGYKNCYIVTDGFSGGRGWLQSRLGTDSYNFSFAQV LSPSRIIPAASRSFGTRSGTKFLPSSD **Notes** 14-3-3 binding site not strictly defined i.e. no direct experimental evidence The phosphorylation level of CaS responded strongly to light intensity. The light-dependent thylakoid protein kinase STN8 is required for CaS phosphorylation (assessed by LC-MS/MS of stn8 knockout plants). The phosphorylation site was mapped to the stroma-exposed Thr380, located in a motif for interaction with 14-3-3 proteins and proteins with forkhead-associated domains, which suggests the involvement of CaS in stress responses and signaling pathways. The knockout Arabidopsis lines revealed a significant role for CaS in plant growth and development. VLSPSRIIPAASRSFGTRSGTKFLPSSD – T380 **References to 14-3-3 binding to Arabidopsis CaS** Vainonen JP, Sakuragi Y, Stael S, Tikkanen M, Allahverdiyeva Y, Paakkarinen V, Aro E, Suorsa M, Scheller HV, Vener AV, Aro EM. Light regulation of CaS, a novel phosphoprotein in the thylakoid membrane of Arabidopsis thaliana. FEBS J. 2008 Apr;275(8):1767-77.	Sites of 14-3-3 binding not defined. NO WEBLOGO.
Arabidopsis CDPK (calcium-dependent protein kinase) – NP_196107.1 1 MGNTCVGPSR NGFLQSVSAA MWRPRDGDDS ASMSNGDIAS EAVSGELRSR LSDEVQNKPP 61 EQVTMPKPGT DVETKDREIR TEsKPETLEE ISLESKPETK QETKSETKPE SKPDPPAKPK 121 KPKHMKRVSS AGLRTESVLQ RKTENFKEFY SLGRKLGQGQ FGTTFLCVEK TTGKEFACKS 181 IAKRKLLTDE DVEDVRREIQ IMHHLAGHPN VISIKGAYED VVAVHLVMEC CAGGELFDRI 241 IQRGHYTERK AAELTRTIVG VVEACHSLGV MHRDLKPENF LFVSKHEDSL LKTIDFGLSM 301 FFKPDDVFTD VVGSPYYVAP EVLRKRYGPE ADVWSAGVIV YILLSGVPPF WAETEQGIFE 361 QVLHGDLDFS SDPWPSISES AKDLVRKMLV RDPKKRLTAH QVLCHPWVQV DGVAPDKPLD 421 SAVLSRMKQF SAMNKFKKMA LRVIAESLSE EEIAGLKEMF NMIDADKSGQ ITFEELKAGL 481 KRVGANLKES EILDLMQAAD VDNSGTIDYK EFIAATLHLN KIEREDHLFA AFTYFDKDGS 541 GYITPDELQQ ACEEFGVEDV RIEELMRDVD QDNDGRIDYN EFVAMMQKGS ITGGPVKMGL	Sites of 14-3-3 binding not defined. NO WEBLOGO.

<table>
<tr><td>601 EKSFSIALKL
>gi|15238353|ref|NP_196107.1| CPK1 (CALCIUM DEPENDENT PROTEIN KINASE 1); calmodulin-dependent protein kinase/ kinase [Arabidopsis thaliana]
MGNTCVGPSRNGFLQSVSAAMWRPRDGDDSASMSNGDIASEAVSGELRSRLSDEVQNKPPEQVTMPKPGT
DVETKDREIRTESKPETLEEISLESKPETKQETKSETKPESKPDPPAKPKKPKHMKRVSSAGLRTESVLQ
RKTENFKEFYSLGRKLGQGQFGTTFLCVEKTTGKEFACKSIAKRKLLTDEDVEDVRREIQIMHHLAGHPN
VISIKGAYEDVVAVHLVMECCAGGELFDRIIQRGHYTERKAAELTRTIVGVVEACHSLGVMHRDLKPENF
LFVSKHEDSLLKTIDFGLSMFFKPDDVFTDVVGSPYYVAPEVLRKRYGPEADVWSAGVIVYILLSGVPPF
WAETEQGIFEQVLHGDLDFSSDPWPSISESAKDLVRKMLVRDPKKRLTAHQVLCHPWVQVDGVAPDKPLD
SAVLSRMKQFSAMNKFKKMALRVIAESLSEEEIAGLKEMFNMIDADKSGQITFEELKAGLKRVGANLKES
EILDLMQAADVDNSGTIDYKEFIAATLHLNKIEREDHLFAAFTYFDKDGSGYITPDELQQACEEFGVEDV
RIEELMRDVDQDNDGRIDYNEFVAMMQKGSITGGPVKMGLEKSFSIALKL
Notes
Used a solution of radiolabelled Arabidopsis CPK-1 for an overlay to probe three separate GF-14 (14-3-3) isoforms that had been separated by SDS-PAGE to show that CPK-1 bound 14-3-3s
GST-CPK1 was immobilised on agarose beads and purified GF-14 bound but this was greatly reduced when the Raf259 phosphopeptide was included in the assay.
14-3-3 isoforms stimulated the kinase activity of CPK-1 by up to 2-fold in the presence of calcium in in vitro phosphoprylations of MBP.
Site(s) of 14-3-3 binding not defined but the authors note a 14-3-3 motif at S83
References to 14-3-3 binding to CDPK
Camoni L, Harper JF, Palmgren MG.14-3-3 proteins activate a plant calcium-dependent protein kinase (CDPK). FEBS Lett. 1998 Jul 3;430(3):381-4.</td><td></td></tr>
<tr><td>Arabidopsis CONSTANS
Notes
Paper doesn’t specify isoform. Sites of 14-3-3 binding not defined
Constans is a central regulator of the photoperiod pathway
References to 14-3-3 binding to Arabidopsis CONSTANS
Mayfield JD, Folta KM, Paul AL, Ferl RJ. The 14-3-3 Proteins mu and upsilon influence transition to flowering and early phytochrome response. Plant Physiol. 2007 Dec;145(4):1692-702.</td><td>Sites of 14-3-3 binding not defined.
NO WEBLOGO.</td></tr>
<tr><td>Arabidopsis F2KP Arabidopsis 6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase (Swissprot = Q9SP17)
1 MGSGASKNTE EDDDGSNGGG GQLYVSLKME NSKVEGELTP HVYGSLPLIG SWDPSKALPM
61 QRESALMSEL SFVVPPDHET LDFKFLLKPK NRNTPCIVEE GENRLLTGGS LQGDARLALF
121 RLEGDVIVEF RVFINADRVS PIDLATSWRA YRENLQPSTV RGIPDVSINP DPKSAECPLE
181 SLELDLAHYE VPAPAPSANS YLVYAADNAE NPRSLSASGs FRNDSTPKAA QRNSEDSGVT
241 VDGSPSAKEM TIVVPDSSNI YSAFGEAESK SVETLSPFQQ KDGQKGLFVD RGVGSPRLVK
301 SLsASSFLID TKQIKNSMPA AAGAVAAAAV ADQMLGPKED RHLAIVLVGL PARGKTFTAA
361 KLTRYLRWLG HDTKHFNVGK YRRLKHGVNM SADFFRADNP EGVEARTEVA ALAMEDMIAW
421 MQEGGQVGIF DATNSTRVRR NMLMKMAEGK CKIIFLETLC NDERIIERNI RLKIQQSPDY
481 SEEMDFEAGV RDFRDRLANY EKVYEPVEEG SYIKMIDMVS GNGGQIQVNN ISGYLPGRIV
541 FFLVNTHLTP RPILLTRHGE SMDNVRGRIG GDSVISDSGK LYAKKLASFV EKRLKSEKAA
601 SIWTSTLQRT NLTASSIVGF PKVQWRALAE INAGVCDGMT YEEVKKNMPE EYESRKKDKL
661 RYRYPRGESY LDVIQRLEPV IIELERQRAP VVVISHQAVL RALYAYFADR PLKEIPQIEM
721 PLHTIIEIQM GVSGVQEKRY KLMD
>gi|75206988|sp|Q9SP17|Q9SP17_ARATH Fructose-6-phosphate 2-kinase/fructose-2,6-bisphosphatase
MGSGASKNTEEDDDGSNGGGGQLYVSLKMENSKVEGELTPHVYGSLPLIGSWDPSKALPMQRESALMSEL
SFVVPPDHETLDFKFLLKPKNRNTPCIVEEGENRLLTGGSLQGDARLALFRLEGDVIVEFRVFINADRVS
PIDLATSWRAYRENLQPSTVRGIPDVSINPDPKSAECPLESLELDLAHYEVPAPAPSANSYLVYAADNAE
NPRSLSASGSFRNDSTPKAAQRNSEDSGVTVDGSPSAKEMTIVVPDSSNIYSAFGEAESKSVETLSPFQQ
KDGQKGLFVDRGVGSPRLVKSLSASSFLIDTKQIKNSMPAAAGAVAAAAVADQMLGPKEDRHLAIVLVGL
PARGKTFTAAKLTRYLRWLGHDTKHFNVGKYRRLKHGVNMSADFFRADNPEGVEARTEVAALAMEDMIAW
MQEGGQVGIFDATNSTRVRRNMLMKMAEGKCKIIFLETLCNDERIIERNIRLKIQQSPDYSEEMDFEAGV
RDFRDRLANYEKVYEPVEEGSYIKMIDMVSGNGGQIQVNNISGYLPGRIVFFLVNTHLTPRPILLTRHGE
SMDNVRGRIGGDSVISDSGKLYAKKLASFVEKRLKSEKAASIWTSTLQRTNLTASSIVGFPKVQWRALAE
INAGVCDGMTYEEVKKNMPEEYESRKKDKLRYRYPRGESYLDVIQRLEPVIIELERQRAPVVVISHQAVL
RALYAYFADRPLKEIPQIEMPLHTIIEIQMGVSGVQEKRYKLMD
Notes
SLSASGpS^{220}FR, RLVKSLpS^{303}ASSF
References to 14-3-3 binding to F2KP
Kulma A, Villadsen D, Campbell DG, Meek SE, Harthill JE, Nielsen TH, MacKintosh C.Phosphorylation and 14-3-3 binding of Arabidopsis 6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase. Plant J. 2004 Mar;37(5):654-67.</td><td></td></tr>
<tr><td>Arabidopsis KAT1
Notes
14-3-3 has been implicated in the regulation of two specific K+ channels, AtTPK1 (KCO1), a vacuolar membrane localized K+ channel [45] and KAT1, a PM inward rectifying K+ channel [46].
References to 14-3-3 binding to Arabidopsis KAT1
Sottocornola B, Gazzarrini S, Olivari C, Romani G, Valbuzzi P, Thiel G, Moroni A. 14-3-3 proteins regulate the potassium channel KAT1 by dual modes. Plant Biol (Stuttg). 2008 Mar;10(2):231-6.
Sottocornola B, Visconti S, Orsi S, Gazzarrini S, Giacometti S, Olivari C, Camoni L, Aducci P, Marra M, Abenavoli A, Thiel G, Moroni A. The potassium channel KAT1 is activated by plant and animal 14-3-3 proteins. J Biol Chem. 2006 Nov 24;281(47):35735-41.</td><td>Sites of 14-3-3 binding not defined.
NO WEBLOGO.</td></tr>
<tr><td>Arabidopsis KCO1
1 MSSDAARTPL LPTEKIDTMA QDFNLNSRTS SSRKRRLRRS RsAPRGDCMY NDDVKIDEPP
61 PHPSKIPMFS DLNPNLRRVI MFLALYLTIG TLCFYLVRDQ ISGHKTSGVV DALYFCIVTM
121 TTVGYGDLVP NSSASRLLAC AFVFSGMVLV GHLLSRAADY LVEKQEALLV RAFHLRQSFG</td><td></td></tr>
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<table>
<tr><td>181 PTDILKELHT NKLRYKCYAT CLVLVVLFIV GTIFLVMVEK MPVISAFYCV CSTVTTLGYG
241 DKSFNSEAGR LFAVFWILTS SICLAQFFLY VAELNTENKQ RALVKWVLTR RITNNDLEAA
301 DLDEDGVVGA AEFIVYKLKE MGKIDEKDIS GIMDEFEQLD YDESGTLTTS DIVLAQTTSQ
361 IQR
>gi|30696631|ref|NP_851196.1| ATKCO1; calcium-activated potassium channel/ ion channel/ outward rectifier potassium channel [Arabidopsis thaliana]
MSSDAARTPLLPTEKIDTMAQDFNLNSRTSSSRKRRLRRSRSAPRGDCMYNDDVKIDEPPPHPSKIPMFS
DLNPNLRRVIMFLALYLTIGTLCFYLVRDQISGHKTSGVVDALYFCIVTMTTVGYGDLVPNSSASRLLAC
AFVFSGMVLVGHLLSRAADYLVEKQEALLVRAFHLRQSFGPTDILKELHTNKLRYKCYATCLVLVVLFIV
GTIFLVMVEKMPVISAFYCVCSTVTTLGYGDKSFNSEAGRLFAVFWILTSSICLAQFFLYVAELNTENKQ
RALVKWVLTRRITNNDLEAADLDEDGVVGAAEFIVYKLKEMGKIDEKDISGIMDEFEQLDYDESGTLTTS
DIVLAQTTSQIQR
Notes
KCO1 is a calcium-binding, calcium-activated channel
S42A mutant no longer co-localises with 14-3-3 in the vacuole.
More 14-3-3 co-purifies with GST-KCO1 N-terminus that has been phosphorylated in vitro with PKB than the S42A or non-phos. Interacts preferentially with GRF6, (14-3-3). 14-3-3 binding has no effect on localisation
Channel is activated by 14-3-3 binding in patch clamp measurements.
14-3-3 has been implicated in the regulation of two specific K+ channels, AtTPK1 (KCO1), a vacuolar membrane localized K+ channel [45] and KAT1, a PM inward rectifying K+ channel [46].
DFNLNSRTSSSRKRRLRRSRSAPRGDCMYNDDVKIDEPPPH
References to 14-3-3 binding to Arabidopsis KCO1
Latz A, Becker D, Hekman M, Müller T, Beyhl D, Marten I, Eing C, Fischer A, Dunkel M, Bertl A, Rapp UR, Hedrich R. TPK1, a Ca(2+)-regulated Arabidopsis vacuole two-pore K(+) channel is activated by 14-3-3 proteins. Plant J. 2007 Nov;52(3):449-59.</td><td></td></tr>
<tr><td>**Arabidopsis KCO1** AtTPK1 Ca(2+)-regulated Arabidopsis vacuole two-pore K(+) channel (Swissport = Q8LBL1)
1 MSSDAARTPL LPTEKIDTMA QDFNLNSRTS SSRKRRLRRS RsAPRGDCMY NDDVKIDEPP
61 PHPSKIPMFS DLNPNLRRVI MFLALYLTIG TLCFYLVRDQ ISGHKTSGVV DALYFCIVTM
121 TTVGYGDLVP NSSASRLLAC AFVFSGMVLV GHLLSRAADY LVEKQEALLV RAFHLRQSFG
181 PTDILKELHT NKLRYKCYAT CLVLVVLFIV GTIFLVMVEK MPVISAFYCV CSTVTTLGYG
241 DKSFNSEAGR LFAVFWILTS SICLAQFFLY VAELNTENKQ RALVKWVLTR RITNNDLEAA
301 DLDEDGVVGA AEFIVYKLKE MGKIDEKDIS GIMDEFEQLD YDESGTLTTS DIVLAQTTSQ
361 IQR
>gi|38604893|sp|Q8LBL1.2|KCO1_ARATH RecName: Full=Calcium-activated outward-rectifying potassium channel 1; Short=AtKCO1
MSSDAARTPLLPTEKIDTMAQDFNLNSRTSSSRKRRLRRSRSAPRGDCMYNDDVKIDEPPPHPSKIPMFS
DLNPNLRRVIMFLALYLTIGTLCFYLVRDQISGHKTSGVVDALYFCIVTMTTVGYGDLVPNSSASRLLAC
AFVFSGMVLVGHLLSRAADYLVEKQEALLVRAFHLRQSFGPTDILKELHTNKLRYKCYATCLVLVVLFIV
GTIFLVMVEKMPVISAFYCVCSTVTTLGYGDKSFNSEAGRLFAVFWILTSSICLAQFFLYVAELNTENKQ
RALVKWVLTRRITNNDLEAADLDEDGVVGAAEFIVYKLKEMGKIDEKDISGIMDEFEQLDYDESGTLTTS
DIVLAQTTSQIQR
Notes
Co-localization of wild-type TPK1, but not the TPK1-S42A mutant, indicates that phosphorylation of the 14-3-3 binding motif of TPK1 represents a prerequisite for interaction.
References to 14-3-3 binding to AtKCO1
Latz A, Becker D, Hekman M, Müller T, Beyhl D, Marten I, Eing C, Fischer A, Dunkel M, Bertl A, Rapp UR, Hedrich R.
TPK1, a Ca(2+)-regulated Arabidopsis vacuole two-pore K(+) channel is activated by 14-3-3 proteins. Plant J. 2007 Nov;52(3):449-59.
Dunkel M, Latz A, Schumacher K, Müller T, Becker D, Hedrich R. Targeting of Vacuolar Membrane Localized Members of the TPK Channel Family. Mol Plant. 2008 Nov;1(6):938-49.</td><td></td></tr>
<tr><td>**Arabidopsis NIA1** (NR1, Arabidopsis nitrate reductase 1) (Swissprot = P11832)
1 MATSVDNRHY PTMNGVAHAF KPPLVPSPRS FDRHRHQNQT LDVILTETKI VKETEVITTV
61 VDSYDDSSSD DEDESHNRNV PYYKELVKKS NSDLEPSILD PRDESTADSW IQRNSSMLRL
121 TGKHPFNAEA PLPRLMHHGF ITPVPLHYVR NHGAVPKANW SDWSIEITGL VKRPAKFTME
181 ELISEFPSRE FPVTLVCAGN RRKEQNMVKQ TIGFNWGSAG VSTSLWKGIP LSEILRRCGI
241 YSRRGGALNV CFEGAEDLPG GGGSKYGTSI KKEMAMDPAR DIILAYMQNG ELLTPDHGFP
301 VRVIVPGFIG GRMVKWLKRI IVTPQESDSY YHYKDNRVLP SLVDAELANS EAWWYKPEYI
361 INELNINSVI TTPGHAEILP INAFTTQKPY TLKGYAYSGG GKKVTRVEVT LDGGDTWSVC
421 ELDHQEKPNK YGKFWCWCFW SLDVEVLDLL SAKDVAVRAW DESFNTQPDK LIWNLMGMMN
481 NCWFRIRTNV CKPHRGEIGI VFEHPTRPGN QSGGWMAKER QLEISSESNN TLKKSVsSPF
541 MNTASKMYSI SEVRKHNTAD SAWIIVHGHI YDCTRFLKDH PGGTDSILIN AGTDCTEEFE
601 AIHSDKAKKL LEDYRIGELI TTGYDSSPNV SVHGASNFGP LLAPIKELTP QKNIALVNPR
661 EKIPVRLIEK TSISHDVRKF RFALPSEDQQ LGLPVGKHVF VCANINDKLC LRAYTPTSAI
721 DAVGHIDLVV KVYFKDVHPR FPNGGLMSQH LDSLPIGSMI DIKGPLGHIE YKGKGNFLVS
781 GKPKFAKKLA MLAGGTGITP IYQIIQSILS DPEDETEMYV VYANRTEDDI LVREELEGWA
841 SKHKERLKIW YVVEIAKEGW SYSTGFITEA VLREHIPEGL EGESLALACG PPPMIQFALQ
901 PNLEKMGYNV KEDLLIF
>gi|21431787|sp|P11832.3|NIA1_ARATH RecName: Full=Nitrate reductase [NADH] 1; Short=NR1
MATSVDNRHYPTMNGVAHAFKPPLVPSPRSFDRHRHQNQTLDVILTETKIVKETEVITTVVDSYDDSSSD
DEDESHNRNVPYYKELVKKSNSDLEPSILDPRDESTADSWIQRNSSMLRLTGKHPFNAEAPLPRLMHHGF
ITPVPLHYVRNHGAVPKANWSDWSIEITGLVKRPAKFTMEELISEFPSREFPVTLVCAGNRRKEQNMVKQ
TIGFNWGSAGVSTSLWKGIPLSEILRRCGIYSRRGGALNVCFEGAEDLPGGGGSKYGTSIKKEMAMDPAR
DIILAYMQNGELLTPDHGFPVRVIVPGFIGGRMVKWLKRIIVTPQESDSYYHYKDNRVLPSLVDAELANS
EAWWYKPEYIINELNINSVITTPGHAEILPINAFTTQKPYTLKGYAYSGGGKKVTRVEVTLDGGDTWSVC</td><td></td></tr>
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ELDHQEKPNKYGKFWCWCFWSLDVEVLDLLSAKDVAVRAWDESFNTQPDKLIWNLMGMMNNCWFRIRTNV
CKPHRGEIGIVFEHPTRPGNQSGGWMAKERQLEISSESNNTLKKSVSSPFMNTASKMYSISEVRKHNTAD
SAWIIVHGHIYDCTRFLKDHPGGTDSILINAGTDCTEEFEAIHSDKAKKLLEDYRIGELITTGYDSSPNV
SVHGASNFGPLLAPIKELTPQKNIALVNPREKIPVRLIEKTSISHDVRKFRFALPSEDQQLGLPVGKHVF
VCANINDKLCLRAYTPTSAIDAVGHIDLVVKVYFKDVHPRFPNGGLMSQHLDSLPIGSMIDIKGPLGHIE
YKGKGNFLVSGKPKFAKKLAMLAGGTGITPIYQIIQSILSDPEDETEMYVVYANRTEDDILVREELEGWA
SKHKERLKIWYVVEIAKEGWSYSTGFITEAVLREHIPEGLEGESLALACGPPPMIQFALQPNLEKMGYNV
KEDLLIF
```

Arabidopsis NIA2 (NR2, Arabidopsis nitrate reductase 2) (Swissprot = P11035)

```
      1 MAASVDNRQY ARLEPGLNGV VRSYKPPVPG RSDSPKAHQN QTTNQTVFLK PAKVHDDDED
     61 VSSEDENETH NSNAVYYKEM IRKSNAELEP SVLDPRDEYT ADSWIERNPS MVRLTGKHPF
    121 NSEAPLNRLM HHGFITPVPL HYVRNHGHVP KAQWAEWTVE VTGFVKRPMK FTMDQLVSEF
    181 AYREFAATLV CAGNRRKEQN MVKKSKGFNW GSAGVSTSVW RGVPLCDVLR RCGIFSRKGG
    241 ALNVCFEGSE DLPGGAGTAG SKYGTSIKKE YAMDPSRDII LAYMQNGEYL TPDHGFPVRI
    301 IIPGFIGGRM VKWLKRIIVT TKESDNFYHF KDNRVLPSLV DAELADEEGW WYKPEYIINE
    361 LNINSVITTP CHEEILPINA FTTQRPYTLK GYAYSGGGKK VTRVEVTVDG GETWNVCALD
    421 HQEKPNKYGK FWCWCFWSLE VEVLDLLSAK EIAVRAWDET LNTQPEKMIW NLMGMMNNCW
    481 FRVKTNVCKP HKGEIGIVFE HPTLPGNESG GWMAKERHLE KSADAPPSLK KSVsTPFMNT
    541 TAKMYSMSEV KKHNSADSCW IIVHGHIYDC TRFLMDHPGG SDSILINAGT DCTEEFEAIH
    601 SDKAKKMLED YRIGELITTG YSSDSSSPNN SVHGSSAVFS LLAPIGEATP VRNLALVNPR
    661 AKVPVQLVEK TSISHDVRKF RFALPVEDMV LGLPVGKHIF LCATINDKLC LRAYTPSSTV
    721 DVVGYFELVV KIYFGGVHPR FPNGGLMSQY LDSLPIGSTL EIKGPLGHVE YLGKGSFTVH
    781 GKPKFADKLA MLAGGTGITP VYQIIQAILK DPEDETEMYV IYANRTEEDI LLREELDGWA
    841 EQYPDRLKVW YVVESAKEGW AYSTGFISEA IMREHIPDGL DGSALAMACG PPPMIQFAVQ
    901 PNLEKMQYNI KEDFLIF
>gi|128188|sp|P11035.1|NIA2_ARATH RecName: Full=Nitrate reductase [NADH] 2;
Short=NR2
MAASVDNRQYARLEPGLNGVVRSYKPPVPGRSDSPKAHQNQTTNQTVFLKPAKVHDDDEDVSSEDENETH
NSNAVYYKEMIRKSNAELEPSVLDPRDEYTADSWIERNPSMVRLTGKHPFNSEAPLNRLMHHGFITPVPL
HYVRNHGHVPKAQWAEWTVEVTGFVKRPMKFTMDQLVSEFAYREFAATLVCAGNRRKEQNMVKKSKGFNW
GSAGVSTSVWRGVPLCDVLRRCGIFSRKGGALNVCFEGSEDLPGGAGTAGSKYGTSIKKEYAMDPSRDII
LAYMQNGEYLTPDHGFPVRIIIPGFIGGRMVKWLKRIIVTTKESDNFYHFKDNRVLPSLVDAELADEEGW
WYKPEYIINELNINSVITTPCHEEILPINAFTTQRPYTLKGYAYSGGGKKVTRVEVTVDGGETWNVCALD
HQEKPNKYGKFWCWCFWSLEVEVLDLLSAKEIAVRAWDETLNTQPEKMIWNLMGMMNNCWFRVKTNVCKP
HKGEIGIVFEHPTLPGNESGGWMAKERHLEKSADAPPSLKKSVSTPFMNTTAKMYSMSEVKKHNSADSCW
IIVHGHIYDCTRFLMDHPGGSDSILINAGTDCTEEFEAIHSDKAKKMLEDYRIGELITTGYSSDSSSPNN
SVHGSSAVFSLLAPIGEATPVRNLALVNPRAKVPVQLVEKTSISHDVRKFRFALPVEDMVLGLPVGKHIF
LCATINDKLCLRAYTPSSTVDVVGYFELVVKIYFGGVHPRFPNGGLMSQYLDSLPIGSTLEIKGPLGHVE
YLGKGSFTVHGKPKFADKLAMLAGGTGITPVYQIIQAILKDPEDETEMYVIYANRTEEDILLREELDGWA
EQYPDRLKVWYVVESAKEGWAYSTGFISEAIMREHIPDGLDGSALAMACGPPPMIQFAVQPNLEKMQYNI
KEDFLIF
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Notes

RTApS^{543} TP (Spinach) Arabidopsis NR1 and NR2 isoforms expressed from two genes, taken as representative of all NRs studied. A transgenic Nicotiana plumbaginifolia line (S521) has been constructed where the regulatory, conserved Ser 521 of tobacco NR (corresponding to Ser 534 in Arabidopsis) was mutated into Asp.

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Arabidopsis NUDT7 – (in paper = At4g12720)
`1 MGTRAQQIPL LEGETDNYDG VTVTMVEPMD SEVFTESLRA SLSHWREEGK KGIWIKLPLG`
`61 LANLVEAAVS EGFRYHHAEP EYLMLVSWIS ETPDTIPANA SHVVGAGALV INKNTKEVLV`
`121 VQERSGFFKD KNVWKLPTGV INEGEDIWTG VAREVEEETG IIADFVEVLA FRQSHKAILK`
`181 KKTDMFFLCV LSPRSYDITE QKSEILQAKW MPIQEYVDQP WNKKNEMFKF MANICQKKCE`
`241 EEYLGFAIVP TTTSSGKESF IYCNADHAKR LKVSRDQASA SL`
`>gi|30682219|ref|NP_849368.1| NUDT7; ADP-ribose diphosphatase/ NAD or NADH binding / hydrolase/ nucleoside-diphosphatase/ protein homodimerization [Arabidopsis thaliana]`
`MGTRAQQIPLLEGETDNYDGVTVTMVEPMDSEVFTESLRASLSHWREEGKKGIWIKLPLGLANLVEAAVS`
`EGFRYHHAEPEYLMLVSWISETPDTIPANASHVVGAGALVINKNTKEVLVVQERSGFFKDKNVWKLPTGV`
`INEGEDIWTGVAREVEEETGIIADFVEVLAFRQSHKAILKKKTDMFFLCVLSPRSYDITEQKSEILQAKW`
`MPIQEYVDQPWNKKNEMFKFMANICQKKCEEEYLGFAIVPTTTSSGKESFIYCNADHAKRLKVSRDQASA`
`SL`
Notes – 14-3-3 binding sites not well defined see below
“Mutant plants deprived of AtNUDT7, exhibit growth retardation, spontaneous cell death and increased resistance to pathogen infection”.
Wildtype and **V26A** mutations had no effect on 14-3-3 binding
V69A, F73A and **V168A** all had no interaction with 14-3-3 in Y2H assay
14-3-3 beads pulled out NUDT7 from Arabidopsis cell extracts
F73A and V168A have problems dimerizing and instead aggregate NUDT7
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	`Sites of 14-3-3 binding not defined.`
	`NO WEBLOGO.`

Arabidopsis OMT1 caffeic acid/5-hydroxyferulic acid O-methyltransferase **Notes** Sequence not defined. **References to 14-3-3 binding to** OMT1 Zhang H, Wang J, Goodman HM. An Arabidopsis gene encoding a putative 14-3-3-interacting protein, caffeic acid/5-hydroxyferulic acid O-methyltransferase. Biochim Biophys Acta. 1997 Sep 12;1353(3):199-202	`Sites of 14-3-3 binding not defined.` `NO WEBLOGO.`

Arabidopsis PHOT1 (Phototropin receptor kinase from Arabidopsis) (Swissprot = O48963)
`1 MEPTEKPSTK PSSRTLPRDT RGSLEVFNPS TQLTRPDNPV FRPEPPAWQN LSDPRGTSPQ`
`61 PRPQQEPAPS NPVRSDQEIA VTTSWMALKD PSPETISKKT ITAEKPQKSA VAAEQRAAEW`
`121 GLVLKTDTKT GKPQGVGVRN SGGTENDPNG KKTTSQRNSQ NSCRSSGEMS DGDVPGGRSG`
`181 IPRVSEDLKD ALSTFQQTFV VSDATKPDYP IMYASAGFFN MTGYTSKEVV GRNCRFLQGS`
	`Three sites implicated in 14-3-3 binding, but not`

241 GTDADELAKI RETLAAGNNY CGRILNYKKD GTSFWNLLTI APIKDESGKV LKFIGMQVEV 301 SKHTEGAKEK ALRPNGLPES LIRYDARQKD MATNSVTELV EAVKRPRALs ESTNLHPFMT 361 KSESDELPKK PARRMsENVV PSGRRNSGGG RRNSMQRINE IPEKKSRKSs LSFMGIKKKS 421 ESLDESIDDG FIEYGEEDDE ISDRDERPES VDDKVRQKEM RKGIDLATTL ERIEKNFVIT 481 DPRLPDNPII FASDSFLELT EYSREEILGR NCRFLQGPET DLTTVKKIRN AIDNQTEVTV 541 QLINYTKSGK KFWNIFHLQP MRDQKGEVQY FIGVQLDGSK HVEPVRNVIE ETAVKEGEDL 601 VKKTAVNIDE AVRELPDANM TPEDLWANHS KVVHCKPHRK DSPPWIAIQK VLESGEPIGL 661 KHFKPVKPLG SGDTGSVHLV ELVGTDQLFA MKAMDKAVML NRNKVHRARA EREILDLLDH 721 PFLPALYASF QTKTHICLIT DYYPGGELFM LLDRQPRKVL KEDAVRFYAA QVVVALEYLH 781 CQGIIYRDLK PENVLIQGNG DISLSDFDLS CLTSCKPQLL IPSIDEKKKK KQQKSQQTPI 841 FMAEPMRASN SFVGTEEYIA PEIISGAGHT SAVDWWALGI LMYEMLYGYT PFRGKTRQKT 901 FTNVLQKDLK FPASIPASLQ VKQLIFRLLQ RDPKKRLGCF EGANEVKQHS FFKGINWALI 961 RCTNPPELET PIFSGEAENG EKVVDPELED LQTNVF >gi|25090817|sp|O48963.1|PHOT1_ARATH RecName: Full=Phototropin-1; AltName: Full=Non-phototropic hypocotyl protein 1; AltName: Full=Root phototropism protein 1 MEPTEKPSTKPSSRTLPRDTRGSLEVFNPSTQLTRPDNPVFRPEPPAWQNLSDPRGTSPQPRPQQEPAPS NPVRSDQEIAVTTSWMALKDPSPETISKKTITAEKPQKSAVAAEQRAAEWGLVLKTDTKTGKPQGVGVRN SGGTENDPNGKKTTSQRNSQNSCRSSGEMSDGDVPGGRSGIPRVSEDLKDALSTFQQTFVVSDATKPDYP IMYASAGFFNMTGYTSKEVVGRNCRFLQGSGTDADELAKIRETLAAGNNYCGRILNYKKDGTSFWNLLTI APIKDESGKVLKFIGMQVEVSKHTEGAKEKALRPNGLPESLIRYDARQKDMATNSVTELVEAVKRPRALS ESTNLHPFMTKSESDELPKKPARRMSENVVPSGRRNSGGGRRNSMQRINEIPEKKSRKSSLSFMGIKKKS ESLDESIDDGFIEYGEEDDEISDRDERPESVDDKVRQKEMRKGIDLATTLERIEKNFVITDPRLPDNPII FASDSFLELTEYSREEILGRNCRFLQGPETDLTTVKKIRNAIDNQTEVTVQLINYTKSGKKFWNIFHLQP MRDQKGEVQYFIGVQLDGSKHVEPVRNVIEETAVKEGEDLVKKTAVNIDEAVRELPDANMTPEDLWANHS KVVHCKPHRKDSPPWIAIQKVLESGEPIGLKHFKPVKPLGSGDTGSVHLVELVGTDQLFAMKAMDKAVML NRNKVHRARAEREILDLLDHPFLPALYASFQTKTHICLITDYYPGGELFMLLDRQPRKVLKEDAVRFYAA QVVVALEYLHCQGIIYRDLKPENVLIQGNGDISLSDFDLSCLTSCKPQLLIPSIDEKKKKKQQKSQQTPI FMAEPMRASNSFVGTEEYIAPEIISGAGHTSAVDWWALGILMYEMLYGYTPFRGKTRQKTFTNVLQKDLK FPASIPASLQVKQLIFRLLQRDPKKRLGCFEGANEVKQHSFFKGINWALIRCTNPPELETPIFSGEAENG EKVVDPELEDLQTNVF **Notes** Phospho-serine residues required for 14-3-3 binding to Arabidopsis phot1 have been mapped to the intervening linker region between LOV1 and LOV2. Although mutation of Ser350 and Ser376 to alanine substantially reduced the interaction, residual 14-3-3 λ binding to phot1 in response to PKA treatment could still be detected. Mutation of Ser410 to alanine (408KS(pS)LSFMGIK417) abolished this interaction demonstrating an accessory role for this residue in mediating 14-3-3 λ binding to phot1 (Sullivan et al 2009). The form of the protein studied by the authors must be different from the reference sequence because the residue numbers are different. **References to 14-3-3 binding to Phototropin** Sullivan S, Thomson CE, Kaiserli E, Christie JM. Interaction specificity of Arabidopsis 14-3-3 proteins with phototropin receptor kinases. FEBS Lett. 2009 Jul 7;583(13):2187-93. Inoue S, Kinoshita T, Matsumoto M, Nakayama KI, Doi M, Shimazaki K. Blue light-induced autophosphorylation of phototropin is a primary step for signaling. Proc. Natl. Acad. Sci. USA. 2008;105:5626–5631. Kinoshita T, Emi T, Tominaga M, Sakamoto K, Shigenaga A, Doi M, et al. Blue-light- and phosphorylation-dependent binding of a 14-3-3 protein to phototropins in stomatal guard cells of broad bean. Plant Physiol. 2003;133:1453–1463.	clear which interact directly. NO WEBLOGO.
Arabidopsis photosystem I N-subunit (At pPSI-N, full length precursor) **Notes** **References to 14-3-3 binding to Arabidopsis photosystem I N-subunit** Sehnke PC, Henry R, Cline K, Ferl RJ. Interaction of a plant 14-3-3 protein with the signal peptide of a thylakoid-targeted chloroplast precursor protein and the presence of 14-3-3 isoforms in the chloroplast stroma. Plant Physiol. 2000 Jan;122(1):235-42.	Sites of 14-3-3 binding not defined. NO WEBLOGO.
Arabidopsis PMA1 Plasma membrane H+-ATPase (Swissprot = P20649) 1 MSGLEDIKNE TVDLEKIPIE EVFQQLKCTR EGLTTQEGED RIVIFGPNKL EEKKESKILK 61 FLGFMWNPLS WVMEAAALMA IALANGDNRP PDWQDFVGII CLLVINSTIS FIEENNAGNA 121 AAALMAGLAP KTKVLRDGKW SEQEAAILVP GDIVSIKLGD IIPADARLLE GDPLKVDQSA 181 LTGESLPVTK HPGQEVFSGS TCKQGEIEAV VIATGVHTFF GKAAHLVDST NQVGHFQKVL 241 TSIGNFCICS IAIGIAIEIV VMYPIQHRKY RDGIDNLLVL LIGGIPIAMP TVLSVTMAIG 301 SHRLSQQGAI TKRMTAIEEM AGMDVLCSDK TGTLTLNKLS VDKNLVEVFC KGVEKDQVLL 361 FAAMASRVEN QDAIDAAMVG MLADPKEARA GIREVHFLPF NPVDKRTALT YIDSDGNWHR 421 VSKGAPEQIL DLANARPDLR KKVLSCIDKY AERGLRSLAV ARQVVPEKTK ESPGGPWEFV 481 GLLPLFDPPR HDSAETIRRA LNLGVNVKMI TGDQLAIGKE TGRRLGMGTN MYPSAALLGT 541 DKDSNIASIP VEELIEKADG FAGVFPEHKY EIVKKLQERK HIVGMTGDGV NDAPALKKAD 601 IGIAVADATD AARGASDIVL TEPGLSVIIS AVLTSRAIFQ RMKNYTIYAV SITIRIVFGF 661 MLIALIWEFD FSAFMVLIIA ILNDGTIMTI SKDRVKPSPT PDSWKLKEIF ATGIVLGGYQ 721 AIMSVIFFWA AHKTDFFSDK FGVRSIRDNN DELMGAVYLQ VSIISQALIF VTRSRSWSFV 781 ERPGALLMIA FVIAQLVATL IAVYADWTFA KVKGIGWGWA GVIWIYSIVT YFPQDILKFA 841 IRYILSGKAW ASLFDNRTAF TTKKDYGIGE REAQWAQAQR TLHGLQPKED VNIFPEKGSY 901 RELSEIAEQA KRRAEIARLR ELHTLKGHVE SVAKLKGLDI DTAGHHYtV >gi|12644156|sp|P20649.3|PMA1_ARATH RecName: Full=ATPase 1, plasma membrane-type; AltName: Full=Proton pump 1 MSGLEDIKNETVDLEKIPIEEVFQQLKCTREGLTTQEGEDRIVIFGPNKLEEKKESKILKFLGFMWNPLS WVMEAAALMAIALANGDNRPPDWQDFVGIICLLVINSTISFIEENNAGNAAAALMAGLAPKTKVLRDGKW SEQEAAILVPGDIVSIKLGDIIPADARLLEGDPLKVDQSALTGESLPVTKHPGQEVFSGSTCKQGEIEAV VIATGVHTFFGKAAHLVDSTNQVGHFQKVLTSIGNFCICSIAIGIAIEIVVMYPIQHRKYRDGIDNLLVL LIGGIPIAMPTVLSVTMAIGSHRLSQQGAITKRMTAIEEMAGMDVLCSDKTGTLTLNKLSVDKNLVEVFC	

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KGVEKDQVLLFAAMASRVENQDAIDAAMVGMLADPKEARAGIREVHFLPFNPVDKRTALTYIDSDGNWHR
VSKGAPEQILDLANARPDLRKKVLSCIDKYAERGLRSLAVARQVVPEKTKESPGGPWEFVGLLPLFDPPR
HDSAETIRRALNLGVNVKMITGDQLAIGKETGRRLGMGTNMYPSAALLGTDKDSNIASIPVEELIEKADG
FAGVFPEHKYEIVKKLQERKHIVGMTGDGVNDAPALKKADIGIAVADATDAARGASDIVLTEPGLSVIIS
AVLTSRAIFQRMKNYTIYAVSITIRIVFGFMLIALIWEFDFSAFMVLIIAILNDGTIMTISKDRVKPSPT
PDSWKLKEIFATGIVLGGYQAIMSVIFFWAAHKTDFFSDKFGVRSIRDNNDELMGAVYLQVSIISQALIF
VTRSRSWSFVERPGALLMIAFVIAQLVATLIAVYADWTFAKVKGIGWGWAGVIWIYSIVTYFPQDILKFA
IRYILSGKAWASLFDNRTAFTTKKDYGIGEREAQWAQAQRTLHGLQPKEDVNIFPEKGSYRELSEIAEQA
KRRAEIARLRELHTLKGHVESVAKLKGLDIDTAGHHYTV
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Notes

The mode III 14-3-3-binding site (Y(pT)V-COOH) is found in members of the large family of V-type plasma membrane proton pumps (see sequence alignment in Duby and Boutry 2008). The sequence of PMA1 is given here. Structural studies indicate that a hexameric complex resulting from the assembly of three H+-ATPase dimers linked by three 14–3–3 dimers. The complex is stabilised by fusicoccin, which binds to the 14-3-3 and H+-ATPase within the central groove of the 14-3-3 dimer.

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Arabidopsis RPW8.2 (Swissprot = Q9C5Z6)
`1 MIAEVAAGGA LGLALSVLHE AVKRAKDRSV TTRFILHRLE ATIDSITPLV VQIDKFSEEM`
`61 EDSTSRKVNK RLKLLLENAV SLVEENAELR RRNVRKKFRY MRDIKEFEAK LRWVVDVDVQ`
`121 VNQLADIKEL KAKMSEISTK LDKIMPQPKF EIHIGWCSGK TNRAIRFTFC SDDS`
`>gi|75169011|sp|Q9C5Z6|Q9C5Z6_ARATH RPW8.2`
`MIAEVAAGGALGLALSVLHEAVKRAKDRSVTTRFILHRLEATIDSITPLVVQIDKFSEEMEDSTSRKVNK`
	`Sites of 14-3-3 binding not defined.`
	`NO WEBLOGO.`

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RLKLLLENAVSLVEENAELRRRNVRKKFRYMRDIKEFEAKLRWVVDVDVQVNQLADIKELKAKMSEISTK
LDKIMPQPKFEIHIGWCSGKTNRAIRFTFCSDDS
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Notes

The RPW8 locus from Arabidopsis thaliana Ms-0 includes two functional paralogous genes (RPW8.1 and RPW8.2) and confers broad-spectrum resistance via the salicylic acid-dependent signaling pathway to the biotrophic fungal pathogens Golovinomyces spp. that cause powdery mildew diseases on multiple plant species. The C-terminal domain of RPW8.2 is required for the interaction of this protein with 14-3-3 (Yang et al 2009). **References to 14-3-3 binding to Arabidopsis RPW8.2**

Yang X, Wang W, Coleman M, Orgil U, Feng J, Ma X, Ferl R, Turner JG, Xiao S. Arabidopsis 14-3-3 lambda is a positive regulator of RPW8-mediated disease resistance. Plant J. 2009 Jul 16. [Epub ahead of print]

Arabidopsis SERK1 (uniprot Q94AG2)

```
     1  MESSYVVFIL LSLILLPNHS LWLASANLEG DALHTLRVTL VDPNNVLQSW DPTLVNPCTW
    61  FHVTCNNENS VIRVDLGNAE LSGHLVPELG VLKNLQYLEL YSNNITGPIP SNLGNLTNLV
   121  SLDLYLNSFS GPIPESLGKL SKLRFLRLNN NSLTGSIPMS LTNITTLQVL DLSNNRLSGS
   181  VPDNGSFSLF TPISFANNLD LCGPVTSHPC PGSPPFSPPP PFIQPPPVST PSGYGITGAI
   241  AGGVAAGAAL LFAAPAIAFA WWRRRKPLDI FFDVPAEEDP EVHLGQLKRF SLRELQVASD
   301  GFSNKNILGR GGFGKVYKGR LADGTLVAVK RLKEERTPGG ELQFQTEVEM ISMAVHRNLL
   361  RLRGFCMTPT ERLLVYPYMA NGSVASCLRE RPPsQPPLDW PTRKRIALGS ARGLSYLHDH
   421  CDPKIIHRDV KAANILLDEE FEAVVGDFGL AKLMDYKDTH VTTAVRGTIG HIAPEYLSTG
   481  KSSEKTDVFG YGIMLLELIT GQRAFDLARL ANDDDVMLLD WVKGLLKEKK LEMLVDPDLQ
   541  TNYEERELEQ VIQVALLCTQ GSPMERPKMS EVVRMLEGDG LAEKWDEWQK VEILREEIDL
   601  SPNPNSDWIL DSTYNLHAVE LSGPR
>sp|Q94AG2|SERK1_ARATH Somatic embryogenesis receptor kinase 1 OS=Arabidopsis
thaliana GN=SERK1 PE=1 SV=2
MESSYVVFILLSLILLPNHSLWLASANLEGDALHTLRVTLVDPNNVLQSWDPTLVNPCTW
FHVTCNNENSVIRVDLGNAELSGHLVPELGVLKNLQYLELYSNNITGPIPSNLGNLTNLV
SLDLYLNSFSGPIPESLGKLSKLRFLRLNNNSLTGSIPMSLTNITTLQVLDLSNNRLSGS
VPDNGSFSLFTPISFANNLDLCGPVTSHPCPGSPPFSPPPPFIQPPPVSTPSGYGITGAI
AGGVAAGAALLFAAPAIAFAWWRRRKPLDIFFDVPAEEDPEVHLGQLKRFSLRELQVASD
GFSNKNILGRGGFGKVYKGRLADGTLVAVKRLKEERTPGGELQFQTEVEMISMAVHRNLL
RLRGFCMTPTERLLVYPYMANGSVASCLRERPPSQPPLDWPTRKRIALGSARGLSYLHDH
CDPKIIHRDVKAANILLDEEFEAVVGDFGLAKLMDYKDTHVTTAVRGTIGHIAPEYLSTG
KSSEKTDVFGYGIMLLELITGQRAFDLARLANDDDVMLLDWVKGLLKEKKLEMLVDPDLQ
TNYEERELEQVIQVALLCTQGSPMERPKMSEVVRMLEGDGLAEKWDEWQKVEILREEIDL
SPNPNSDWILDSTYNLHAVELSGPR
```

Notes

14-3-3 binding site has not been confirmed, but there is a putative binding site at S394.

Just used 266 – 625 of AtSERK1, (kinase domain) as bait in Y2H of silique tissue.

Found GF14λ (14-3-3) and more experiments in yeast showed that GF14 interacted with the kinase domain but not the LRR

Expressed GST-AtSERK1 kinase domain in E. coli and phosphorylated it by adding ATP (autophosphorylation). Although GF14 showed basal binding to non-phosphorylated SERK, in pulldowns of bacterially expressed proteins this was enhanced when phosphorylated SERK was used but seemed to require the first 38 aa of GF14.

GF14 can be phosphorylated in vitro with AtSERK

GF14 binding to SERK has no effect on the kinase acitivity of SERK

References to 14-3-3 binding to SERK1

Rienties IM, Vink J, Borst JW, Russinova E, de Vries SC. The Arabidopsis SERK1 protein interacts with the AAA-ATPase AtCDC48, the 14-3-3 protein GF14lambda and the PP2C phosphatase KAPP. Planta. 2005 Jun;221(3):394-405.

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Sites of
14-3-3
binding not
confirmed.
NO WEBLOGO.
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Arabidopsis SPS ATSPS1F (sucrose phosphate synthase 1F) (NM_122035.2)

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        1 MAGNDWVNSY LEAILDVGQG LDDARSSPSL LLRERGRFTP SRYFVEEVIT GYDETDLHRS
       61 WVKAVATRSP QERNTRLENM CWRIWNLARQ KKQHEEKEAQ RLAKRRLERE KGRREATADM
      121 SEEFSEGEKG DIISDISTHG ESTKPRLPRI NSAESMELWA SQQKGNKLYL VLISLHGLIR
      181 GENMELGRDS DTGGQVKYVV ELARALGSMP GVYRVDLLTR QVsSPDVDYS YGEPTEMLTP
      241 RDSEDFSDEM GESSGAYIVR IPFGPKDKYI PKELLWPHIP EFVDGAMSHI MQMSNVLGEQ
      301 VGVGKPIWPS AIHGHYADAG DATALLSGAL NVPMLLTGHS LGRDKLEQLL RQGRLSKEEI
      361 NSTYKIMRRI EGEELSLDVS EMVITSTRQE IDEQWRLYDG FDPILERKLR ARIKRNVSCY
      421 GRFMPRMVKI PPGMEFNHIV PHGGDMEDTD GNEEHPTSPD PPIWAEIMRF FSNSRKPMIL
      481 ALARPDPKKN ITTLVKAFGE CRPLRELANL ALIMGNRDGI DEMSSTSSSV LLSVLKLIDK
      541 YDLYGQVAYP KHHKQSDVPD IYRLAAKSKG VFINPAIIEP FGLTLIEAAA HGLPMVATKN
      601 GGPVDIHRVL DNGLLVDPHD QQSISEALLK LVADKHLWAK CRQNGLKNIH QFSWPEHCKT
      661 YLSRITSFKP RHPQWQSDDG GDNSEPESPS DSLRDIQDIS LNLKFSFDGS GNDNYMNQEG
      721 SSMDRKSKIE AAVQNWSKGK DSRKMGSLER SEVNSGKFPA VRRRKFIVVI ALDFDGEEDT
      781 LEATKRILDA VEKERAEGSV GFILSTSLTI SEVQSFLVSG GLNPNDFDAF ICNSGSDLHY
      841 TSLNNEDGPF VVDFYYHSHI EYRWGGEGLR KTLIRWASSL NEKKADNDEQ IVTLAEHLST
      901 DYCYTFTVKK PAAVPPVREL RKLLRIQALR CHVVYSQNGT RINVIPVLAS RIQALRYLFV
      961 RWGIDMAKMA VFVGESGDTD YEGLLGGLHK SVVLKGVSCS ACLHANRSYP LTDVISFESN
     1021 NVVHASPDSD VRDALKKLEL LKD
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Notes

In dicotyledonous plants there are three SPS gene families: A, B, and C, and five families (A, B, C, and two D subfamilies) of SPS genes in wheat (Triticum aestivum) and other monocotyledonous plants from the family Poaceae (grasses) (Castleden et al 2004). The 14-3-3-binding site Ser229 is found within the A type SPS sequences (LTRQVSSP in Nicotiana sequence). The sequence of the Arabidopsis version of SPSA (SPS1F) is given.

References to 14-3-3 binding to SPS

Börnke F. The variable C-terminus of 14-3-3 proteins mediates isoform-specific interaction with sucrose-phosphate synthase in the yeast two-hybrid system. J Plant Physiol. 2005 Feb;162(2):161-8.

Castleden CK, Aoki N, Gillespie VJ, MacRae EA, Quick WP, Buchner P, Foyer CH, Furbank RT, Lunn JE. Evolution and function of the sucrose-phosphate synthase gene families in wheat and other grasses. Plant Physiol. 2004 Jul;135(3):1753-64. Toroser D, Athwal GS, Huber SC. Site-specific regulatory interaction between spinach leaf sucrose-phosphate synthase and 14-3-3 proteins. FEBS Lett. 1998 Sep 11;435(1):110-4. Moorhead G, Douglas P, Cotelle V, Harthill J, Morrice N, Meek S, Deiting U, Stitt M, Scarabel M, Aitken A, MacKintosh C. Phosphorylation-dependent interactions between enzymes of plant metabolism and 14-3-3 proteins. Plant J. 1999 Apr;18(1):1-12. Langenkämper G, Fung RW, Newcomb RD, Atkinson RG, Gardner RC, MacRae EA. Sucrose phosphate synthase genes in plants belong to three different families. J Mol Evol. 2002 Mar;54(3):322-32. Chen S, Hajirezaei M, Börnke F.Differential expression of sucrose-phosphate synthase isoenzymes in tobacco reflects their functional specialization during dark-governed starch mobilization in source leaves. Plant Physiol. 2005 Nov;139(3):1163-74.	
Arabidopsis thaliana PDK1 3-phosphoinositide-dependent protein kinase-1 **Notes: Sites not identified** **References to 14-3-3 binding to PDK1** Otterhag L, Gustavsson N, Alsterfjord M, Pical C, Lehrach H, Gobom J, Sommarin M. Arabidopsis PDK1: identification of sites important for activity and downstream phosphorylation of S6 kinase. Biochimie. 2006 Jan;88(1):11-21.	Sites of 14-3-3 binding not defined. NO WEBLOGO.
Arabidopsis TPS5 Arabidopsis trehalose-phosphate synthase 5 (Swissprot = O23617) 1 MVSRsYSNLL DLASGNFHSF SREKKRFPRV AtVTGVLSEL DDDNNSNSVC SDAPSSVTQD 61 RIIIVGNQLP IKSHRNSAGK LSFSWDNDSL LLQLKDGMRE DMEVVYIGCL KEQIDTVEQD 121 DVSQRLLENF KCVPAYIPPE LFTKYYHGFC KQHLWPLFHY MLPLTPDLGG RFDRSLWQAY 181 LSVNKIFADK VMEVISPDDD FVWVHDYHLM VLPTFLRKRF NRVKLGFFLH SPFPSSEIYR 241 TLPVRNELLR ALLNADLIGF HTFDYARHFL SCCSRMLGLS YQSKRGTIGL EYYGRTVSIK 301 ILPVGIHISQ LQSILNLPET QTKVAELRDQ FLDQKVLLGV DDMDIFKGIS LKLLAMEQLL 361 TQHPEKRGRV VLVQIANPAR GRGKDVQEVQ SETEATVKRI NEMFGRPGYQ PVVLIDTPLQ 421 FFERIAYYVI AECCLVTAVR DGMNLIPYEY IICRQGNPKL NETIGLDPSA AKKSMLVVSE 481 FIGCSPSLSG AIRVNPWNID AVTEAMDYAL IVSEAEKQMR HEKHHKYVST HDVAYWARSF 541 IQDLERACGD HVRKRCWGIG FGLGFRVVAL DPSFKKLSIE HIVSAYKRTK NRAILLDYDG 601 TMVQPGSIRT TPTRETIEIL NNLSSDPKNI VYLVSGKDRR TLTEWFSSCD DLGLGAEHGY 661 FIRPNDGTDW ETSSLVSGFE WKQIAEPVMR LYTETTDGST IETKETALVW NYQFADPDFG 721 SCQAKELMEH LESVLTNDPV SVKTGQQLVE VKPQGVNKGL VAERLLTTMQ EKGKLLDFIL 781 CVGDDRSDED MFEVIMSAKD GPALSPVAEI FACTVGQKPS KAKYYLDDTA EIIRMLDGLA 841 ATNTTISDQT DSTATVPTKD LF >gi|172044488|sp|O23617.2|TPS5_ARATH RecName: Full=Alpha,alpha-trehalose-phosphate synthase [UDP-forming] 5; AltName: Full=Trehalose-6-phosphate synthase 5; Short=AtTPS5 MVSRSYSNLLDLASGNFHSFSREKKRFPRVATVTGVLSELDDDNNSNSVCSDAPSSVTQDRIIIVGNQLP IKSHRNSAGKLSFSWDNDSLLLQLKDGMREDMEVVYIGCLKEQIDTVEQDDVSQRLLENFKCVPAYIPPE LFTKYYHGFCKQHLWPLFHYMLPLTPDLGGRFDRSLWQAYLSVNKIFADKVMEVISPDDDFVWVHDYHLM VLPTFLRKRFNRVKLGFFLHSPFPSSEIYRTLPVRNELLRALLNADLIGFHTFDYARHFLSCCSRMLGLS YQSKRGTIGLEYYGRTVSIKILPVGIHISQLQSILNLPETQTKVAELRDQFLDQKVLLGVDDMDIFKGIS LKLLAMEQLLTQHPEKRGRVVLVQIANPARGRGKDVQEVQSETEATVKRINEMFGRPGYQPVVLIDTPLQ FFERIAYYVIAECCLVTAVRDGMNLIPYEYIICRQGNPKLNETIGLDPSAAKKSMLVVSEFIGCSPSLSG AIRVNPWNIDAVTEAMDYALIVSEAEKQMRHEKHHKYVSTHDVAYWARSFIQDLERACGDHVRKRCWGIG FGLGFRVVALDPSFKKLSIEHIVSAYKRTKNRAILLDYDGTMVQPGSIRTTPTRETIEILNNLSSDPKNI VYLVSGKDRRTLTEWFSSCDDLGLGAEHGYFIRPNDGTDWETSSLVSGFEWKQIAEPVMRLYTETTDGST IETKETALVWNYQFADPDFGSCQAKELMEHLESVLTNDPVSVKTGQQLVEVKPQGVNKGLVAERLLTTMQ EKGKLLDFILCVGDDRSDEDMFEVIMSAKDGPALSPVAEIFACTVGQKPSKAKYYLDDTAEIIRMLDGLA ATNTTISDQTDSTATVPTKDLF **Notes** ((pS22)YSNLLDLASGNFHSFSR) and (VA(pT49)VTGVLSELDDDNNSNSVCSDAPSSVTQDR) in Harthill et al (2006) = Ser5 and Thr32 in O23617. Both sites are conserved in TPS5, 7, 9 and 10. **References to 14-3-3 binding to TPS5** Harthill JE, Meek SE, Morrice N, Peggie MW, Borch J, Wong BH, Mackintosh C. Phosphorylation and 14-3-3 binding Arabidopsis trehalose-phosphate synthase 5 in response to 2-deoxyglucose. Plant J. 2006 Jul;47(2):211-23. Moorhead G, Douglas P, Cotelle V, Harthill J, Morrice N, Meek S, Deiting U, Stitt M, Scarabel M, Aitken A, MacKintosh C. Phosphorylation-dependent interactions between enzymes of plant metabolism and 14-3-3 proteins. Plant J. 1999 Apr;18(1):1-12.	
Hordeum vulgare ABF1, 2 and 3 ABF transcription factors **Notes** **References to 14-3-3 binding to ABF1, 2 and 3** Schoonheim PJ, Costa Pereira DD, De Boer AH. Dual role for 14-3-3 proteins and ABF transcription factors in gibberellic acid and abscisic acid signalling in barley (Hordeum vulgare) aleurone cells. Plant Cell Environ. 2009 May;32(5):439-47. Takahashi Y, Kinoshita T, Shimazaki K. Protein phosphorylation and binding of a 14-3-3 protein in Vicia guard cells in response to ABA. Plant Cell Physiol. 2007 Aug;48(8):1182-91. Schoonheim PJ, Sinnige MP, Casaretto JA, Veiga H, Bunney TD, Quatrano RS, de Boer AH. 14-3-3 adaptor proteins are intermediates in ABA signal transduction during barley seed germination. Plant J. 2007 Jan;49(2):289-301.	Sites of 14-3-3 binding not defined. NO WEBLOGO.
Hordeum vulgare lipoxygenase 2 (LoxC) (13-LOX) 13-lipoxygenase (L37358) (GI:2429087) 1 MLGVGGIVSD LTGGIRGAHL KGSVVLMRKN ALDFNDFGAH VMDGVTELLG RGVTCQLISS 61 TNVDHNNGGR GKVGAEANLE QWLLPTNLPF ITTGENKFAV TFDWSVDKLG VPGAIIVKNN 121 HASEFFLKTI TLDNVPGRGT IVFVANSWVY PQAKYRYNRV FFANDTYLPH QMPAALKPYR 181 DDELRNLRGD DQQGPYLDHD RVYRYDVYND LGDSRDVLGG SKDLPYPRRC RTGRKPSDSK	Sites of 14-3-3 binding not defined. NO WEBLOGO.

241 PDHESRLLLL VQNVYVLRDE LFGHLKQSDL LGYTLKGWLD GIILAIRTYV DLSPGEFDSF 301 ADILKLYEGG IKLPNIPALE EVRKRFPLQL VKDLIPKGGD FLLKLPKPEI IKVDQKAWMT 361 DEEFAREMLA GVNPMMIKRL TEFPPKSTLD PSKYGDHTST MTEEHVAKSL EGLTVQQALA 421 GNRLYIVDQH DNLMPFLIDI NNLDASFVYA TRTLLFLRGD GTLAPVAIEL SSPLIQGELT 481 TAKSAVYTPQ HAGVEGWIWQ LAKAYASVND YGWHQLISHW LNTHAVMEPF VIATNRQLSV 541 THPVYKLLHP HYRDTMNINA RARGLLINAG GVIEMTVFPH KHAMPMSSMV YKHWNFTEQA 601 LPADLIKRGM AVEDASSPHK VRLLIKDYPY ATDGLAVWDA IEQWVSDYLT IYYPNDGVLQ 661 GDVELQAWWK EVREVGHGDL KDAAWWPKMQ TVAELIKACA TIIWTGSALH AAVNFGQYPY 721 SGYHPNKPSA SRRPMPVQGS EEYAELERDP EKAFIRTITS QFHALVGISL MEILSKHSSD 781 EVYLGQHDTP AWTSDAKALE AFKRFGAKLE GIEKQVVAMN SDPQLKNRTG PAKFPYMLLY 841 PNTSDHTGQA EGLTARGIPN SISI >gi|2429087|gb|AAB70865.1| lipoxygenase 2 [Hordeum vulgare subsp. vulgare] MLGVGGIVSDLTGGIRGAHLKGSVVLMRKNALDFNDFGAHVMDGVTELLGRGVTCQLISSTNVDHNNGGR GKVGAEANLEQWLLPTNLPFITTGENKFAVTFDWSVDKLGVPGAIIVKNNHASEFFLKTITLDNVPGRGT IVFVANSWVYPQAKYRYNRVFFANDTYLPHQMPAALKPYRDDELRNLRGDDQQGPYLDHDRVYRYDVYND LGDSRDVLGGSKDLPYPRRCRTGRKPSDSKPDHESRLLLLVQNVYVLRDELFGHLKQSDLLGYTLKGWLD GIILAIRTYVDLSPGEFDSFADILKLYEGGIKLPNIPALEEVRKRFPLQLVKDLIPKGGDFLLKLPKPEI IKVDQKAWMTDEEFAREMLAGVNPMMIKRLTEFPPKSTLDPSKYGDHTSTMTEEHVAKSLEGLTVQQALA GNRLYIVDQHDNLMPFLIDINNLDASFVYATRTLLFLRGDGTLAPVAIELSSPLIQGELTTAKSAVYTPQ HAGVEGWIWQLAKAYASVNDYGWHQLISHWLNTHAVMEPFVIATNRQLSVTHPVYKLLHPHYRDTMNINA RARGLLINAGGVIEMTVFPHKHAMPMSSMVYKHWNFTEQALPADLIKRGMAVEDASSPHKVRLLIKDYPY ATDGLAVWDAIEQWVSDYLTIYYPNDGVLQGDVELQAWWKEVREVGHGDLKDAAWWPKMQTVAELIKACA TIIWTGSALHAAVNFGQYPYSGYHPNKPSASRRPMPVQGSEEYAELERDPEKAFIRTITSQFHALVGISL MEILSKHSSDEVYLGQHDTPAWTSDAKALEAFKRFGAKLEGIEKQVVAMNSDPQLKNRTGPAKFPYMLLY PNTSDHTGQAEGLTARGIPNSISI **Notes** RKPSDSKP at position 234 is suggested as a potential 14-3-3-binding site, but no experimental data on site. **References to 14-3-3 binding to 13-LOX** Holtman WL, Roberts MR, Oppedijk BJ, Testerink C, van Zeijl MJ, Wang M.14-3-3 proteins interact with a 13-lipoxygenase, but not with a 9-lipoxygenase.FEBS Lett. 2000 May 26;474 (1):48-52. Holtman WL, Roberts MR, Wang M. 14-3-3 proteins and a 13-lipoxygenase form associations in a phosphorylation-dependent manner. Biochem Soc Trans. 2000 Dec;28(6):834-6.	
Hordeum vulgare vacuolar H(+)-ATPase (V-ATPase) (Genbank Q40002) 1 ELVRVGHDSL IGEIIRLEGD SATIQVYEET AGLTVNDPVL RTKKPLSCEL GPGILGNIFD 61 GIQRPLKTIA IKSRDVYIPR GVSVPALDKD QLWEFQPNKL GVGDNITNGD LYATVFENTL 121 MKHHIALPPG AMGKISYIAP AGQYSLQDTV LELEFQGIKK EFTMLHTWPV RTPRPVASKL 181 AADTPLLTGQ RVLDALFPSV LGGTCAIPGA FGCGKTVISQ ALSKYSNSDT VVYVGCGERG 241 NEMAEVLMDF PQLTMTLPDG REESVMKRTT LVANTSNMPV AAREASIYTG ITIAEYFRDM 301 GYNVSMMADS TSRWAEALRE ISGRLAEMPA DSGYPAYLAS RLASFYERAG KVQCLGSPDR 361 TGSVTIVGAV SPPGGDFSDP VTSATLSIVQ VFWGLDKKLA QRKHFPSVNW LISYSKYSTA 421 LEGYYEKFDP GFIDMRTKAR EVLQREDDLN EIVQLVGKDA LGESDKITLE TAKLLREDYL 481 AQNAFTPYDK YCPFYKSVWM MRNIIHFNQL ANQAVERAAN ADGHKITYAV VKSRMGDLFY 541 RLVSQKFEDP AEGEDVLVAK FQKLYDDLTA GFRNLEDEAR >gi|2493123|sp|Q40002.1|VATA_HORVU RecName: Full=V-type proton ATPase catalytic subunit A; Short=V-ATPase subunit A; AltName: Full=Vacuolar proton pump subunit alpha; AltName: Full=V-ATPase 69 kDa subunit ELVRVGHDSLIGEIIRLEGDSATIQVYEETAGLTVNDPVLRTKKPLSCELGPGILGNIFDGIQRPLKTIA IKSRDVYIPRGVSVPALDKDQLWEFQPNKLGVGDNITNGDLYATVFENTLMKHHIALPPGAMGKISYIAP AGQYSLQDTVLELEFQGIKKEFTMLHTWPVRTPRPVASKLAADTPLLTGQRVLDALFPSVLGGTCAIPGA FGCGKTVISQALSKYSNSDTVVYVGCGERGNEMAEVLMDFPQLTMTLPDGREESVMKRTTLVANTSNMPV AAREASIYTGITIAEYFRDMGYNVSMMADSTSRWAEALREISGRLAEMPADSGYPAYLASRLASFYERAG KVQCLGSPDRTGSVTIVGAVSPPGGDFSDPVTSATLSIVQVFWGLDKKLAQRKHFPSVNWLISYSKYSTA LEGYYEKFDPGFIDMRTKAREVLQREDDLNEIVQLVGKDALGESDKITLETAKLLREDYLAQNAFTPYDK YCPFYKSVWMMRNIIHFNQLANQAVERAANADGHKITYAVVKSRMGDLFYRLVSQKFEDPAEGEDVLVAK FQKLYDDLTAGFRNLEDEAR **Notes** **14-3-3 binding sites not defined** Klychnikov et al (2007) used endogenous protein from barley tonoplast membranes but suggested the sequence above and mentioned RGVS^{83}VP and RLVS^{544}QK as being putative 14-3-3 binding sites that are conserved in other species with the 544 site being phosphorylated in the Maize equivalent. The catalytic A subunit of the V-ATPase binds directly to 14-3-3s in an overlay and can be phosphorylated in vitro with endogenous kinases in the tonoplast membrane purification (where the kinase properties are affected by blue light) but sites of phosphorylation were not identified. Conclusions, "the data show that besides the P- and F-type H+-ATPases, the V-type H+-ATPase also interacts with 14-3-3 proteins" **References to 14-3-3 binding to V-ATPase** Klychnikov OI, Li KW, Lill H, de Boer AH. The V-ATPase from etiolated barley (Hordeum vulgare L.) shoots is activated by blue light and interacts with 14-3-3 proteins. J Exp Bot. 2007;58(5):1013-23.	Sites of 14-3-3 binding not defined. NO WEBLOGO.
Medicago truncatula GS2 (plastid glutamine synthetase) (Genbank AY225150) 1 MAQILAPSTQ CQARITKISP VATPISSKMW SSLVMKQNKK VARSAKFRVM AVNSGTINRV 61 EDLLNLDITP FTDSIIAEYI WIGGTGIDVR SKSRTIsKPV EHPSELPKWN YDGSSTGQAP 121 GEDSEVILYP QAIFKDPFRG GNNILVICDA YTPQGEPIPT NKRHKAAEIF SNPKVEAEIP 181 WYGIEQEYTL LQTDVKWPLG WPVGGYPGPQ GPYYCAAGAD KSFGRDISDA HYKACLYAGI 241 NISGTNGEVM PGQWEYQVGP SVGIEAGDHI WASRYILERI TEQAGVVLTL DPKPIEGDWN 301 GAGCHTNYST KSMREDGGFE VIKKAILNLS LRHKIHIEAY GEGNERRLTG KHETASINTF 361 SWGVANRGCS IRVGRDTEKN GKGYLEDRRP ASNMDPYVVT ALLAESTLLW EPTLEAEALA 421 AQKIALKV	

>gi|28629470|gb|AAO37651.1| glutamine synthetase [Medicago truncatula] MAQILAPSTQCQARITKISPVATPISSKMWSSLVMKQNKKVARSAKFRVMAVNSGTINRVEDLLNLDITP FTDSIIAEYIWIGGTGIDVRSKSRTISKPVEHPSELPKWNYDGSSTGQAPGEDSEVILYPQAIFKDPFRG GNNILVICDAYTPQGEPIPTNKRHKAAEIFSNPKVEAEIPWYGIEQEYTLLQTDVKWPLGWPVGGYPGPQ GPYYCAAGADKSFGRDISDAHYKACLYAGINISGTNGEVMPGQWEYQVGPSVGIEAGDHIWASRYILERI TEQAGVVLTLDPKPIEGDWNGAGCHTNYSTKSMREDGGFEVIKKAILNLSLRHKIHIEAYGEGNERRLTG KHETASINTFSWGVANRGCSIRVGRDTEKNGKGYLEDRRPASNMDPYVVTALLAESTLLWEPTLEAEALA AQKIALKV **Notes** (Ser97) crucial for the interaction with 14-3-3s. Different plant expracts were used as kinase in in vitro phosphorylations. CDPK (calcium dependent protein kinase) phosphorylates GS2 Leaf extract passed over a 14-3-3 column – GS2 degradation product appeared to be specifically eluted (shown by anti-GS antibody) and this product showed no GS activity suggesting GS2 degradation is induced by 14-3-3 binding. 14-3-3 only bound a phosphorylated GS column and the GS (only in this sample) had the degradation product S97A mutant shows 2 fold reduction in incorporation of 32P-ATP so is phosphorylated in leaf extracts Site is well conserved among other plant chloroplastic GS GS2 WT and S97A were bound to a column and in vitro phosphorylated with leaf extract. 14-3-3 was added. **Result**: 14-3-3 only bound the WT column and GS was only degraded in this sample. **S97D phosphomimetic bound** to the 14-3-3 column but no degradation S97D phosphomimetic phosphorylated with leaf extract bound the column and there was degradation so the protease comes from the leaf extract Conclusions: S97 phosphorylation induces 14-3-3 binding and GS2 is proteolytically cleaved. Proteolytic cleavage decreases the GS activity not 14-3-3 binding. AEYIWIGGTGIDVRSKSRTISKPVEHPSELPKWNYDGSSTG – SER 97 **References to 14-3-3 binding to GS2** Lima L, Seabra A, Melo P, Cullimore J, Carvalho H. Phosphorylation and subsequent interaction with 14-3-3 proteins regulate plastid glutamine synthetase in Medicago truncatula. Planta. 2006 Feb;223(3):558-67. Finnemann J, Schjoerring JK. Post-translational regulation of cytosolic glutamine synthetase by reversible phosphorylation and 14-3-3 protein interaction. Plant J. 2000 Oct;24(2):171-81. Riedel J, Tischner R, Mäck G. The chloroplastic glutamine synthetase (GS-2) of tobacco is phosphorylated and associated with 14-3-3 proteins inside the chloroplast. Planta. 2001 Jul;213(3):396-401.	
Nicotiana tabacum DBP1 (DNA-binding protein phosphatase-1) (GenBank AF520810) 1 MCVQESEEVS EEMENLDISK SDENIKIGSL QVEDELGNTQ KENCEKNTSS SFSVIRNSFP 61 MESISEDTTI ADRKQILSNK FLPTLRSGEW SDIGGRLDME DTHICIADLA KNFGQSILGE 121 EEAVSFYGVF DGHGGKGAAL FVRDFLPRII VEDADFPLKL EKVVSKSFLE TDAAFAKSCS 181 ADSDLSSGTT ALTAMIFGRS LLVANAGDCR AVLSRGGLAI EMSKDHRPCC VSERTRVESL 241 GGFVDDGYLN GQLGVTRALG DWHIKGLKEV EKGGPLSAEP ELKLLTLTKE DEFLIIGSDG 301 IWDVFRSQNA VDFARRRLQE HNNAKLCCKE VVDEAKKRGA IDNLTVVMVC FHSEPPPTIV 361 FQRSRIRKCI SAEGLQNLRS LLDG >gi|21693562|gb|AAM75346.1|AF520810_1 DNA-binding protein phosphatase 2C [Nicotiana tabacum] MCVQESEEVSEEMENLDISKSDENIKIGSLQVEDELGNTQKENCEKNTSSSFSVIRNSFPMESISEDTTI ADRKQILSNKFLPTLRSGEWSDIGGRLDMEDTHICIADLAKNFGQSILGEEEAVSFYGVFDGHGGKGAAL FVRDFLPRIIVEDADFPLKLEKVVSKSFLETDAAFAKSCSADSDLSSGTTALTAMIFGRSLLVANAGDCR AVLSRGGLAIEMSKDHRPCCVSERTRVESLGGFVDDGYLNGQLGVTRALGDWHIKGLKEVEKGGPLSAEP ELKLLTLTKEDEFLIIGSDGIWDVFRSQNAVDFARRRLQEHNNAKLCCKEVVDEAKKRGAIDNLTVVMVC FHSEPPPTIVFQRSRIRKCISAEGLQNLRSLLDG **Notes** **14-3-3 binding sites not defined** “Tobacco DBP1 is the founding member of a novel class of plant transcription factors featuring sequence-specific DNA binding and protein phosphatase activity”. Underlined region is necessary for 14-3-3 G isoform binding using Y2H and is contained in the sequence-specific DNA binding domain (1-87). Same result with the Arabidopsis homologue (DBP1 - NM_128120 and GRF6 - NM_121083) DBP1 has an NLS in the c-term and binds the CEVI1 gene promoter in healthy leaves to repress CEVI1 translation. In excised leaves, 14-3-3 G accumulates in the nucleus and binds DBP1, which is then exported to the cytoplasm, allowing CEVI1 expression. **References to 14-3-3 binding to Tobacco DBP1** Carrasco JL, Castelló MJ, Vera P. 14-3-3 mediates transcriptional regulation by modulating nucleocytoplasmic shuttling of tobacco DNA-binding protein phosphatase-1. J Biol Chem. 2006 Aug 11;281(32):22875-81.	Sites of 14-3-3 binding not defined. NO WEBLOGO.
Nicotiana tabacum RhoGTPase activating protein 1 (Genbank DQ813657) 1 MTEVLHSSSP SSSSPSISTP TRNGHTLFVE EEIERGSEVA VCDSEEEIEE KKRDKERRDH 61 LSLLALLVTL FRKSFWMACK TDREGGGDLC GGSRGMEIGW PTNVRHVAHV TFDRFNGFLG 121 LPVEFEPEVS RRAPSASTTV FGVSTESMQL SFDSRGNsVP TILLLMQRRL YAQGGLQAEG 181 IFRINAENSE EELVREQLNR GIVPDGIDVH CLAGLIKAWF RELPSGVLDT LSPEQVMQCQ 241 SEDDSIALVR LLPPTEAALL DWAINLMADV VQEEHLNKMN TRNIAMVFAP NMTQMADPLT 301 ALMYAVQVMN FLRTLIERTL KEREDSLIEP ASVSNLGRPD ENGRQSPPQL SLGNSNESNE 361 LTEQVYTVEE PDSARVSESN RVDNITDDEY LSYTTSSEES DDSVSCETPI HVSTMAREAC 421 VTKGPNFEED AQRIGQSSDS SPMKDVLKID LEPTAVQSLG NDSKSKGISN LSRINSMTER 481 TEAWR >gi|110676572|gb|ABG85154.1| RhoGAP1 [Nicotiana tabacum] MTEVLHSSSPSSSSPSISTPTRNGHTLFVEEEIERGSEVAVCDSEEEIEEKKRDKERRDHLSLLALLVTL FRKSFWMACKTDREGGGDLCGGSRGMEIGWPTNVRHVAHVTFDRFNGFLGLPVEFEPEVSRRAPSASTTV FGVSTESMQLSFDSRGNSVPTILLLMQRRLYAQGGLQAEGIFRINAENSEEELVREQLNRGIVPDGIDVH CLAGLIKAWFRELPSGVLDTLSPEQVMQCQSEDDSIALVRLLPPTEAALLDWAINLMADVVQEEHLNKMN TRNIAMVFAPNMTQMADPLTALMYAVQVMNFLRTLIERTLKEREDSLIEPASVSNLGRPDENGRQSPPQL	Sites of 14-3-3 binding not certain. NO WEBLOGO.

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SLGNSNESNELTEQVYTVEEPDSARVSESNRVDNITDDEYLSYTTSSEESDDSVSCETPIHVSTMAREAC
VTKGPNFEEDAQRIGQSSDSSPMKDVLKIDLEPTAVQSLGNDSKSKGISNLSRINSMTERTEAWR
```

Notes – 14-3-3 binding sites not clearly defined but S158 may be involved

Good sequence conservation of the RhoGap and CRIB (Cdc42/Rac-interactive binding = domain is thought to specifically bind activated GTPases but function of RhoGAPs Crib domain is unknown) domains between other plant species.

N-terminus of RhoGAP1 necessary for subapical localization i.e. did Y2H with N-term.

N. tabacum 14-3-3 b-1 (GenBank accession number BAD12169) came out.

In vitro, 14-3-3 b-1 had no effect on the GAP activity of RhoGAP1 for RAC5

S158A mutant in a 14-3-3 consensus localised more strongly to the membrane however, yeast two-hybrid interaction assays and attempts to demonstrate in vitro interaction differences could not confirm these data

References to 14-3-3 binding to Tobacco RhoGTPase activating protein 1

Klahre U, Kost B. Tobacco RhoGTPase ACTIVATING PROTEIN1 spatially restricts signaling of RAC/Rop to the apex of pollen tubes. Plant Cell. 2006 Nov;18(11):3033-46.

<u>Nicotiana tabacum RSG</u> (Tobacco Repression of shoot growth; bzip transcription factor) (Swissprot = Q9LRC7)

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        1 MDPKFSGKPI PIPFLAGRTD LDQMPDTPTR IARHRRAQSE TFFRFPDFDD DILLDDVVAD
       61 FNLDISAPSL SPSADTHMQP ANSADSSSTG GPGLMSGPGA NNNPRPLNHF RSLsVDADFF
      121 DGLEFGATTP GAAAEEEKKV FGSSSVSGSG TRHRHSNSMD GSFSTASFEA ECSSSVKKAM
      181 APDRLAELAL IDPKRAKRIL ANRQSAARSK ERKIRYTSEL ERKVQTLQTE ATTLSAQITV
      241 LQRDNSGLTN ENKELKLRLQ ALEQGAHLRD ALNEALREEL QRLKIAAGQI LGANGNRGPR
      301 PHFPPQPQSF VQCGSHHAQQ QQQHMPHSTT STQNIGGQTQ PSFMNFNNRG
>gi|75311483|sp|Q9LRC7|Q9LRC7_TOBAC BZIP transcriptional activator RSG
MDPKFSGKPIPIPFLAGRTDLDQMPDTPTRIARHRRAQSETFFRFPDFDDDILLDDVVADFNLDISAPSL
SPSADTHMQPANSADSSSTGGPGLMSGPGANNNPRPLNHFRSLSVDADFFDGLEFGATTPGAAAEEEKKV
FGSSSVSGSGTRHRHSNSMDGSFSTASFEAECSSSVKKAMAPDRLAELALIDPKRAKRILANRQSAARSK
ERKIRYTSELERKVQTLQTEATTLSAQITVLQRDNSGLTNENKELKLRLQALEQGAHLRDALNEALREEL
QRLKIAAGQILGANGNRGPRPHFPPQPQSFVQCGSHHAQQQQQHMPHSTTSTQNIGGQTQPSFMNFNNRG
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Notes

RSG is a bzip transcription factor . NHFRSLpS^{114}VDAD

References to 14-3-3 binding to RSG

Ishida S, Yuasa T, Nakata M, Takahashi Y. A tobacco calcium-dependent protein kinase, CDPK1, regulates the transcription factor REPRESSION OF SHOOT GROWTH in response to gibberellins. Plant Cell. 2008 Dec;20(12):3273-88.

Schoonheim PJ, Veiga H, Pereira Dda C, Friso G, van Wijk KJ, de Boer AH. A comprehensive analysis of the 14-3-3 interactome in barley leaves using a complementary proteomics and two-hybrid approach. Plant Physiol. 2007 Feb;143(2):670-83.

Ishida S, Fukazawa J, Yuasa T, Takahashi Y. Involvement of 14-3-3 signaling protein binding in the functional regulation of the transcriptional activator REPRESSION OF SHOOT GROWTH by gibberellins. Plant Cell. 2004 Oct;16(10):2641-51.

Igarashi D, Ishida S, Fukazawa J, Takahashi Y.14-3-3 proteins regulate intracellular localization of the bZIP transcriptional activator RSG. Plant Cell. 2001 Nov;13(11):2483-97.

Nakata M, Yuasa T, Takahashi Y, Ishida S.CDPK1, a calcium-dependent protein kinase, regulates transcriptional activator RSG in response to gibberellins. Plant Signal Behav. 2009 May;4(5):372-4.

<u>Poplar NIMA-related kinase 1 (PNek1) (Uniprot Q8SA64)</u>

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        1 MEQYEVLEQI GKGSFGSALL VKHKHEKKKY VLKKIRLARQ TDRSRRSAHQ EKELISRIRN
       61 PFIVEYKDSW VEKGCYVCII IGYCEGGDMA EAIKKANGVH FPEEKLCKWL VQLLMALDYL
      121 HMNHILHRDV KCSNIFLTKG QDIRLGDFGL AKILTSDDLA SSVVGTPSYM CPELLADIPY
      181 GSKSDIWSLG CCIYEMTSLK PAFKAFDMQA LINKINKSIV APLPTKYSGA FRGLVKSMLR
      241 KNPELRPSAA ELLRHPHLQP YVLKIHIKMN SPRQNTLPFQ WPEPHYMKKT KFLVPEDNPL
      301 KAHREKRYSL SNDRALNPSI SAAEQDSVCS TEGIHDTPSY LNQSLSDSSI ESSHEGTVIC
      361 RSIASKPSNF AKTTKPAPTK ASVTTRRRTE PVKKRESLPV TRTPTKKSNP TTRRTsLPLP
      421 SRTAIQNSAH GTNNSILLQI KSPDVSVNAP RIDRIAEFPL ASYDKPYLPF RRTSSTSAQG
      481 SSNSLHHGDR SITKDKCTVQ ISDRTSAKPN FTEAWQGIEH GMFQVDEENG SNSSNQNATA
      541 GASSRTSSDI RRRRFDTSSF QQRAEALEGL LEFSARLLQD ARYDELGVLL KPFGPGKVSP
      601 RETAIWLTKS FKENTAKTED C
>tr|Q8SA64|Q8SA64_9ROSI NIMA-related protein kinase OS=Populus tremula x
Populus alba PE=2 SV=1
MEQYEVLEQIGKGSFGSALLVKHKHEKKKYVLKKIRLARQTDRSRRSAHQEKELISRIRN
PFIVEYKDSWVEKGCYVCIIIGYCEGGDMAEAIKKANGVHFPEEKLCKWLVQLLMALDYL
HMNHILHRDVKCSNIFLTKGQDIRLGDFGLAKILTSDDLASSVVGTPSYMCPELLADIPY
GSKSDIWSLGCCIYEMTSLKPAFKAFDMQALINKINKSIVAPLPTKYSGAFRGLVKSMLR
KNPELRPSAAELLRHPHLQPYVLKIHIKMNSPRQNTLPFQWPEPHYMKKTKFLVPEDNPL
KAHREKRYSLSNDRALNPSISAAEQDSVCSTEGIHDTPSYLNQSLSDSSIESSHEGTVIC
RSIASKPSNFAKTTKPAPTKASVTTRRRTEPVKKRESLPVTRTPTKKSNPTTRRTSLPLP
SRTAIQNSAHGTNNSILLQIKSPDVSVNAPRIDRIAEFPLASYDKPYLPFRRTSSTSAQG
SSNSLHHGDRSITKDKCTVQISDRTSAKPNFTEAWQGIEHGMFQVDEENGSNSSNQNATA
GASSRTSSDIRRRRFDTSSFQQRAEALEGLLEFSARLLQDARYDELGVLLKPFGPGKVSP
RETAIWLTKSFKENTAKTEDC
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Notes

Within 463 – 606 is a homodimerisation domain

T276, T389 and S416 are putative 14-3-3 binding motifs

In Y2H only S416A reduced interaction with 14-3-3

Four Arabidopsis Neks show good sequence conservation of the 14-3-3 motif at S416 with only differences in the -1, +1 or +2 position

K33R mutation in the ATP binding loop abolishes kinase activity and decreased 14-3-3 binding.

T389A weakened homodimerisation

383 – 457 was not enough to bind 14-3-3 in the Y2H domain suggesting that homodimerisation domain was necessary too. In silico analyses predict that mammalian Nek1, Nek3, Nek4, Nek9, Nek10 and Neurospora Nim1 have potential 14-3-3 interaction motifs, all located in their C-terminal region (data not shown). Expression of the mRNA is cell cylce regulated but no mention of what kinase phosphorylates it and protein shows a nucleolar localisation. No mention of how 14-3-3 fits into this. **References to 14-3-3 binding to Pnek1** Cloutier M, Vigneault F, Lachance D, Séguin A. Characterization of a poplar NIMA-related kinase PNek1 and its potential role in meristematic activity. FEBS Lett. 2005 Aug 29;579(21):4659-65.	
Rice ACC synthase 1 (Genbank AC135965 but this gives a human chromosome 3 complete clone) **Notes** **References to 14-3-3 binding to rice ACC synthase 1** Yao Y, Du Y, Jiang L, Liu JY. Interaction between ACC synthase 1 and 14-3-3 proteins in rice: a new insight. Biochemistry (Mosc). 2007 Sep;72(9):1003-7.	Sites of 14-3-3 binding not defined. NO WEBLOGO.
Rice VP1 (VIVIPAROUS1) **Notes** **References to 14-3-3 binding to VP1** Schultz TF, Medina J, Hill A, Quatrano RS. 14-3-3 proteins are part of an abscisic acid-VIVIPAROUS1 (VP1) response complex in the Em promoter and interact with VP1 and EmBP1. Plant Cell. 1998 May;10(5):837-47.	Sites of 14-3-3 binding not defined. NO WEBLOGO.
Tomato SPAK (Genbank acc. = AF079103) 1 MEQYEILEQI GKGAFGSAVL VKHKLEKKKY VLKKIRLARQ TDRTRRNAHQ EMALISSMQN 61 PFIVEYKDSW VEKGCYVCIV IGYCEGGDMA EAIKKAKGVH FLEEKLCKWL VQLLMALDYL 121 HTNHILHRDV KCSNIFLTRE QDIRLGDFGL AKMLTSDDLA SSIVGTPSYM CPELLADIPY 181 GSKSDIWSLG CCIYEMAAFK PAFKAFDMQA LINKINKSIV APLPTKYSGP FRGLVKSMLR 241 KNPELRPSAA ELLRNPLLQP YVINTHLKLN GPRRNsLPAC LPDNDVKKTR FAISESTPVK 301 KNREKRMSCG NDRTLNPSVS DHDYTFSNRR YPKTPSRVSE LSVGSPDRGS TVTKKITSKA 361 LLVNKNPQVI VPKLTTTPAR QVDLRNSDMA SRTLVKRSVS TTRRAsLPLT NKAAVQELPR 421 RPSLSFLDCI KSPDVSVNAP RIDKMLEFPL ASYEDPFHPI RRTSSNSAQG SSGSPQAEYS 481 VMKDKCTIQI PDSKFDRMSS NDAWQGYEGP MVHVDREDIT DSSDQNATAG ASSRTSSDTR 541 RRRFNMSSYK QRAEALEGLL EFSARLLQED RFDELGVLLK PFGPEKVSPR ETAIWLTKSI 601 KENAPKQED >gi|15637110|gb|AAL04423.1| LSTK-1-like kinase [Lycopersicon esculentum] MEQYEILEQIGKGAFGSAVLVKHKLEKKKYVLKKIRLARQTDRTRRNAHQEMALISSMQNPFIVEYKDSW VEKGCYVCIVIGYCEGGDMAEAIKKAKGVHFLEEKLCKWLVQLLMALDYLHTNHILHRDVKCSNIFLTRE QDIRLGDFGLAKMLTSDDLASSIVGTPSYMCPELLADIPYGSKSDIWSLGCCIYEMAAFKPAFKAFDMQA LINKINKSIVAPLPTKYSGPFRGLVKSMLRKNPELRPSAAELLRNPLLQPYVINTHLKLNGPRRNSLPAC LPDNDVKKTRFAISESTPVKKNREKRMSCGNDRTLNPSVSDHDYTFSNRRYPKTPSRVSELSVGSPDRGS TVTKKITSKALLVNKNPQVIVPKLTTTPARQVDLRNSDMASRTLVKRSVSTTRRASLPLTNKAAVQELPR RPSLSFLDCIKSPDVSVNAPRIDKMLEFPLASYEDPFHPIRRTSSNSAQGSSGSPQAEYSVMKDKCTIQI PDSKFDRMSSNDAWQGYEGPMVHVDREDITDSSDQNATAGASSRTSSDTRRRRFNMSSYKQRAEALEGLL EFSARLLQEDRFDELGVLLKPFGPEKVSPRETAIWLTKSIKENAPKQED **Notes** A recessive mutation in the SELF-PRUNING (SP) gene confers accelerated termination of stem units until the shoot is eventually terminated by two consecutive inflorescences Y2H screen with SP as bait, identified 5 SIPs (SP interacting proteins) SIP2 and SIP74 were ID'd as 14-3-3 proteins, the SIP74 is epsilon and SIP2 is a novel one SIP3 was SP-assocoated kinase (SPAK) SPAK is 60-65% similar in catalytic kinase domain with NIMA (never in mitosis A) group of kinases. Orthologues of SP bound to the SIPs ID'd above by Y2H SPAK forms homodimrs in yeast By Y2H, 14-3-3 isoforms can interact with SPAK and SP and SIP4 In vitro binding results consistant with Y2H results SPAK autophosphorylates a truncated SPAK lacking the kinase domain (SPAK exprd in bacteria) SPAK also phosphorylates the SIP4 protein and only phosphorylated SIP4 binds 14-3-3 In Red is the region required for homodimerisation of SPAK (deduced in Y2H asssay) 389 – 417 is required for SP and 14-3-3 to bind but this only when the c-terminal dimerization domain is present S406A resulted in no interaction with SP or 14-3-3 using Y2H In paper this is S274 = S276 in AF079103. A second putative 14-3-3 site but not rigourously tested PLLQPYVINTHLKLNGPRRN**S**LPACLPDNDVKKTRFAISES – S274/6 = POSSIBLE SITE NSDMASRTLVKRSVSTTRRA**S**LPLTNKAAVQELPRRPSLSF – S406 = 14-3-3 SITE BY Y2H **References to 14-3-3 binding to SPAK** Pnueli L, Gutfinger T, Hareven D, Ben-Naim O, Ron N, Adir N, Lifschitz E. Tomato SP-interacting proteins define a conserved signaling system that regulates shoot architecture and flowering. Plant Cell. 2001 Dec;13(12):2687-702.	
Triticum aestivum GAPN (non-phosphorylating glyceraldehyde-3-phosphate dehydrogenase (Swissprot = Q8LK61) 1 MAGTGVFADV LDGEVYKYYA DGEWRASASG KTVAIVNPTT RQTQYRVQAC TQEEVNKVMD 61 AAKVAQKSWA RTPLWKRAEL LHKAAAILKE HKTPIAESLV KEIAKPAKDA VSEVVRSGDL 121 VSYTAEEGVR ILGEGKLLVS DSFPGNERNK YCLSSKVPLG VVLAIPPFNY PVNLAVSKIG 181 PALIAGNSLV LKPPTQGAVA ALHMVHCFHL AGFPKGLISC VTGKGSEIGD FLTMHPGVNC 241 ISFTGGDTGI AISKKAGMVP LQMELGGKDA CIVLEDADLD LVAANIVKGG FSYSGQRCTA 301 VKVVLIMEAV ADTVVEKVNA KLAKLKVGPP EDDSDITPVV TESSANFIEG LVMDAKEKGA 361 TFCQEYRREG NLIWPLLLDH VRPDMRIAWE EPFGPVLPVI RINsVEEGIH HCNASNFGLQ 421 GCVFTRDINK AIMISDAMES GTVQINSAPA RGPDHFPFQG LKDSGIGSQG ITNSINMMTK 481 VKSTVINLPS PSYTMG >sp|Q8LK61|GAPN_WHEAT NADP-dependent glyceraldehyde-3-phosphate dehydrogenase OS=Triticum aestivum GN=GAPN PE=1 SV=2	SITE NOT CLEAR – NOT IN WEBLOGO

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MAGTGVFADVLDGEVYKYYADGEWRASASGKTVAIVNPTTRQTQYRVQACTQEEVNKVMD
AAKVAQKSWARTPLWKRAELLHKAAAILKEHKTPIAESLVKEIAKPAKDAVSEVVRSGDL
VSYTAEEGVRILGEGKLLVSDSFPGNERNKYCLSSKVPLGVVLAIPPFNYPVNLAVSKIG
PALIAGNSLVLKPPTQGAVAALHMVHCFHLAGFPKGLISCVTGKGSEIGDFLTMHPGVNC
ISFTGGDTGIAISKKAGMVPLQMELGGKDACIVLEDADLDLVAANIVKGGFSYSGQRCTA
VKVVLIMEAVADTVVEKVNAKLAKLKVGPPEDDSDITPVVTESSANFIEGLVMDAKEKGA
TFCQEYRREGNLIWPLLLDHVRPDMRIAWEEPFGPVLPVIRINSVEEGIHHCNASNFGLQ
GCVFTRDINKAIMISDAMESGTVQINSAPARGPDHFPFQGLKDSGIGSQGITNSINMMTK
VKSTVINLPSPSYTMG
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Notes

The ARAApSAPA phosphopeptide that competes for 14-3-3 binding increased the activity of specifically the phosphorylated GAPN enzyme almost 3-fold. Suggested to be 1 mol tetrameric GAPN to 2 mol dimeric 14-3-3.
Mg2+ disrupts the GAPN-14-3-3 interaction which is unusual, divalent cations normally stabilize it.
A computer model putting S404 in one of the pockets implicates S447 as being in the other pocket although there is no experimental evidence for this.

Plant non-phosphorylating glyceraldehyde-3-phosphate dehydrogenase (NP-Ga3PDHase) – sites not well defined

References to 14-3-3 binding to NP-Ga3PDHase

Bustos DM, Bustamante CA, Iglesias AA. Involvement of non-phosphorylating glyceraldehyde-3-phosphate dehydrogenase in response to oxidative stress. J Plant Physiol. 2008 Mar 13;165(4):456-61.
Bustos DM, Iglesias AA. A model for the interaction between plant GAPN and 14-3-3zeta using protein-protein docking calculations, electrostatic potentials and kinetics. J Mol Graph Model. 2005 Jun;23(6):490-502.
Bustos DM, Iglesias AA. Phosphorylated non-phosphorylating glyceraldehyde-3-phosphate dehydrogenase from heterotrophic cells of wheat interacts with 14-3-3 proteins. Plant Physiol. 2003 Dec;133(4):2081-8.

Triticum aestivum WPK4 (Wheat protein kinase) (Swissprot = Q41592)

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         1 MSAIKPPPPD RPPQAARLPS PSSSSSAAAA AKQGGTGSRG LLMGRYELGR VLGKGTFAKV
        61 YHARHVQTGE SVAIKVLDRE KAVRSGLVSH IKREIAVLRR VRHPNIVHLF EVMATKTKIY
       121 FVMELLVRGG ELFSRVSKGR LKEDIARRYF QHLISAVGFC HTRGVFHRDL KPENLLVDEA
       181 GNLKVSDFGL SAVAEPFQPE GLLHTFCGTP AYVAPEVLAR RGYEGAKADI WSCGVILFVL
       241 MAGYLPFHDQ NLMAMYRKVY KGEFRCPRWF SKDLTSLIMR FLDTNPSTRI TLPEVMESRW
       301 FKKGFRPVKF YIEDDQLYNV IDAENDMLDL GLPDPLPQPL PPPPPSPSPQ QVDGDDSGSE
       361 SDASVVSCPA TSSFEERHRL RGPLPRPASL NAFDIISFSR GFNLSGLFEE KGDEVRFISG
       421 EPMPDIITKL EEIANVKSFA VRKKDWRVSL EGTREGVKGP LTICAEIFEL TPSLVVVEVK
       481 KKAGDKEEYD DFCNKELKPG MQHLVHQMVP VPNTPTISEL AERPSR
>tr|Q41592|Q41592_WHEAT Wpk4 protein kinase OS=Triticum aestivum GN=wpk4 PE=2
SV=3
MSAIKPPPPDRPPQAARLPSPSSSSSAAAAAKQGGTGSRGLLMGRYELGRVLGKGTFAKV
YHARHVQTGESVAIKVLDREKAVRSGLVSHIKREIAVLRRVRHPNIVHLFEVMATKTKIY
FVMELLVRGGELFSRVSKGRLKEDIARRYFQHLISAVGFCHTRGVFHRDLKPENLLVDEA
GNLKVSDFGLSAVAEPFQPEGLLHTFCGTPAYVAPEVLARRGYEGAKADIWSCGVILFVL
MAGYLPFHDQNLMAMYRKVYKGEFRCPRWFSKDLTSLIMRFLDTNPSTRITLPEVMESRW
FKKGFRPVKFYIEDDQLYNVIDAENDMLDLGLPDPLPQPLPPPPPSPSPQQVDGDDSGSE
SDASVVSCPATSSFEERHRLRGPLPRPASLNAFDIISFSRGFNLSGLFEEKGDEVRFISG
EPMPDIITKLEEIANVKSFAVRKKDWRVSLEGTREGVKGPLTICAEIFELTPSLVVVEVK
KKAGDKEEYDDFCNKELKPGMQHLVHQMVPVPNTPTISELAERPSR
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Notes

Interacted with 14-3-3 by Y2H
T204 in paper but T205 in this sequence? Is an autophosphorylation site in the activation loop
T204A reduced binding to 14-3-3 by 25% indicating that binding was dependent on the kinase activity
K75D mutant shows no kinase activity and this mutant had an 80% reduction in 14-3-3 binding by Y2H reporter assay
Kinase dead can't pull down 14-3-3 (in vitro bacterially expressed proteins)
S388A and S418A single mutants show mild reduction in 14-3-3 binding by quantitative Y2H
S388A/S418A double shows only ~25% binding of WT and in WT, these sites are probably autophosphorylation sites.
1 to 314 fragment lacking putative residues showed only 10% binding
Overlay assay was done on C-terminal fragment containing the putative binding sites and it was found that the double mutant showed only a modest reduction suggesting additional 14-3-3 binding site in C-terminus

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S388 – PATSSFEERHRLRGPLPRPASLNAFDIISFSRGFNLSGLFE
S418 – SRGFNLSGLFEEKGDEVRFISGEPMPDIITKLEEIANVKSF
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References to 14-3-3 binding to WPK4

Nozawa A, Sawada Y, Akiyama T, Koizumi N, Sano H. Variable interactions between sucrose non-fermented 1-related protein kinases and regulatory proteins in higher plants. Biosci Biotechnol Biochem. 2003 Dec;67(12):2533-40.
Ikeda Y, Koizumi N, Kusano T, Sano H. Specific binding of a 14-3-3 protein to autophosphorylated WPK4, an SNF1-related wheat protein kinase, and to WPK4-phosphorylated nitrate reductase. J Biol Chem. 2000 Oct 13;275(41):31695-700.

SITE NOT CLEAR – NOT IN WEBLOGO

Zea mays HOX1a Maize homeodomain protein with PHD and leucine zipper (Arabidopsis relative HAT3.1) (Swissprot = P46605)

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         1 MEKNIAHCPV EGNGEIENGA SSSQNPESLE HSVLLSTSQT MPNNLGIRKN YKRAANRGKK
        61 GSQGLTGQAY TLMSSNSDVR VLRSTSSSKT TSTEHVQAPV QPAAKRRKMS RASNKSSTDE
       121 FSQIRKRVRY ILNRMNYEQS LIEAYASEGW KNQSLDKIRP EKELERAKSE ILRCKLRIRE
       181 VFRNIDSLLS KGKIDETLFD SEGEISCEDI FCSTCGSNDA TLGNDIILCD GACDRGFHQN
       241 CLNPPLRTED IPMGDEGWLC PACDCKIDCI DLINELHGSN ISIEDSWEKV FPDAAAMAND
       301 SKQDDAFDLP SDDSDDNDFD PNMPEEHVVG KDEESSEEDE DGGSDSDDSD FLTCSDDSEP
       361 LIDKKVDDLR LPSEDSEDDD YDPAGPDSDK DVEKKSSSDE SDFTSDSDDF CKEISKSGHD
```

Sites of
14-3-3
binding not
defined.
NO WEBLOGO.

421 EVSSPLLPDA KVGDMEKITA QAKTTSSADD PMETEIDQGV VLPDSRRRQA ERLDYKKLYD 481 EAYGEASSDS SDDEEWSGKN TPIIKSNEEG EANSPAGKGS RVVHHNDELT TQSTKKSLHS 541 IHGSVDEKPG DLTSNGSNST ARKGHFGPVI NQKLHEHFKT QPYPSRSVKE SLAEELGLTF 601 RQVNKWFETR RHSARVASSR KGISLDKHSP QNTNSQVTAS MEPKEPEGTV VEESNVCLNG 661 GTTISKEAVS SKVGSRTPGS DVGGSKVDSA EDQNPGPDLA EKARQKAIQQ ELRKKKMGR >gi|1170434|sp|P46605.1|HOX1A_MAIZE RecName: Full=Homeobox protein HOX1A MEKNIAHCPVEGNGEIENGASSSQNPESLEHSVLLSTSQTMPNNLGIRKNYKRAANRGKKGSQGLTGQAY TLMSSNSDVRVLRSTSSSKTTSTEHVQAPVQPAAKRRKMSRASNKSSTDEFSQIRKRVRYILNRMNYEQS LIEAYASEGWKNQSLDKIRPEKELERAKSEILRCKLRIREVFRNIDSLLSKGKIDETLFDSEGEISCEDI FCSTCGSNDATLGNDIILCDGACDRGFHQNCLNPPLRTEDIPMGDEGWLCPACDCKIDCIDLINELHGSN ISIEDSWEKVFPDAAAMANDSKQDDAFDLPSDDSDDNDFDPNMPEEHVVGKDEESSEEDEDGGSDSDDSD FLTCSDDSEPLIDKKVDDLRLPSEDSEDDDYDPAGPDSDKDVEKKSSSDESDFTSDSDDFCKEISKSGHD EVSSPLLPDAKVGDMEKITAQAKTTSSADDPMETEIDQGVVLPDSRRRQAERLDYKKLYDEAYGEASSDS SDDEEWSGKNTPIIKSNEEGEANSPAGKGSRVVHHNDELTTQSTKKSLHSIHGSVDEKPGDLTSNGSNST ARKGHFGPVINQKLHEHFKTQPYPSRSVKESLAEELGLTFRQVNKWFETRRHSARVASSRKGISLDKHSP QNTNSQVTASMEPKEPEGTVVEESNVCLNGGTTISKEAVSSKVGSRTPGSDVGGSKVDSAEDQNPGPDLA EKARQKAIQQELRKKKMGR **Notes** Several plant homeodomain proteins have a conserved architecture, with a leucine zipper followed by a PHD domain. The leucine zipper region of was found to bind to 14-3-3 in a yeast two-hybrid assay, but the precise site is not defined. It is suggested that a leucine zipper-like segment in helix alpha 4 of 14-3-3 interacts with the leucine zipper of the homeodomain proteins. **References to 14-3-3 binding to Plant homeodomain proteins with PHD and leucine zipper** Halbach T, Scheer N, Werr W. Transcriptional activation by the PHD finger is inhibited through an adjacent leucine zipper that binds 14-3-3 proteins. Nucleic Acids Res. 2000 Sep 15;28(18):3542-50.	
Zea mays MPK6 A MAP kinase **(Uniprot Q6TAR9)** 1 MQHDQKKKAP SEMDFFTEYG EGSRYKIEEV IGKGSYGVVC SAVDTHTGEK VAIKKINDIF 61 EHVSDATRIL REIKLLRLLR HPDIVEIKHI LLPPSRREFR DIYVVFELME SDLHQVIKAN 121 DDLTPEHYQF FLYQLLRGLK YIHTANVFHR DLKPKNILAN ADCKLKICDF GLARVAFNDT 181 PTAIFWTDYV ATRWYRAPEL CGSFFSKYTP AIDIWSIGCI FAELLTGKPL FPGKNVVHQL 241 DIITDLLGTP SPEAISRIRN EKARRYLSSM RRKKPIPFTQ KFPNADPLAL CLLERMLAFE 301 PKDRPSAEEA LADPYFKNIA SVDREPSAQA VTKLEFEFER RRVTKEDIRE LIYREILEYH 361 PKMLREFLEG TESSGFMYPS AVDHFKKQFA YLEEHYAKGS TGTPPERQHN SLPRPSVVYS 421 DNRSQTTANI TEDLSKCMLR ENTQKTHPYS ASVASKFPPH VPQGDVARPG KAVGSVMQYS 481 PCPAPAAERY EQRRIARHPA VAPNNIPSGS SYPRRSQTCK SETGDAESHM DANQARQPKP 541 YAANKLPATV DSRGGHW >tr|Q6TAR9|Q6TAR9_MAIZE Putative uncharacterized protein OS=Zea mays PE=2 SV=1 MQHDQKKKAPSEMDFFTEYGEGSRYKIEEVIGKGSYGVVCSAVDTHTGEKVAIKKINDIF EHVSDATRILREIKLLRLLRHPDIVEIKHILLPPSRREFRDIYVVFELMESDLHQVIKAN DDLTPEHYQFFLYQLLRGLKYIHTANVFHRDLKPKNILANADCKLKICDFGLARVAFNDT PTAIFWTDYVATRWYRAPELCGSFFSKYTPAIDIWSIGCIFAELLTGKPLFPGKNVVHQL DIITDLLGTPSPEAISRIRNEKARRYLSSMRRKKPIPFTQKFPNADPLALCLLERMLAFE PKDRPSAEEALADPYFKNIASVDREPSAQAVTKLEFEFERRRVTKEDIRELIYREILEYH PKMLREFLEGTESSGFMYPSAVDHFKKQFAYLEEHYAKGSTGTPPERQHNSLPRPSVVYS DNRSQTTANITEDLSKCMLRENTQKTHPYSASVASKFPPHVPQGDVARPGKAVGSVMQYS PCPAPAAERYEQRRIARHPAVAPNNIPSGSSYPRRSQTCKSETGDAESHMDANQARQPKP YAANKLPATVDSRGGHW **Notes; Binding sites not identified but region identified** In vitro data: Bacterially expressed full length protein bound plant 14-3-3 GF14-6 in vitro in the overlay assay (radiolablelled 14-3-3s) but not the K56E mutant and is phosphorylation dependent. 14-3-3 beads bound ZmMPK6 from a bacterial lysate 14-3-3 binding does not affect the catalytic activity of ZmMPK6 in a kinase assay using MBP as substrate S411A mutation of a mode II 14-3-3 binding site was still able to bind 14-3-3. Deletion constructs were expressed and 14-3-3 binding was found to be in 337 - 467 **References to 14-3-3 binding to ZmMPK6** Lalle M, Visconti S, Marra M, Camoni L, Velasco R, Aducci P. ZmMPK6, a novel maize MAP kinase that interacts with 14-3-3 proteins. Plant Mol Biol. 2005 Nov;59(5):713-22.	Sites of 14-3-3 binding not defined, though binding region identified. NO WEBLOGO.

Proteins from bacteria and viruses that interact with 14-3-3 inside eukaryotic host cells	
Agrobacterium rhizogenes RolB (Swissprot= P49408) 1 MAEFDLCALF SSLKVGDVSS SDELKKHIQS ASKERTPLTE PGEGQSMDID EEGGRQDPGI 61 LYLYVDCPTM MRCFYGGSLP YNSRHGALIT NLPPYQKDVS LGEVCRGLRQ ASGFFGYEDV 121 IRSAYFAALS VPGYFVKLDG QMELTSTKGK SLTFDLYASN QLRLEPGALV RHGECKFGME >gi|1350824|sp|P49408.1|ROC2_AGRRH RecName: Full=Cytokinin-beta-glucosidase; AltName: Full=ROL C protein MAEFDLCALFSSLKVGDVSSSDELKKHIQSASKERTPLTEPGEGQSMDIDEEGGRQDPGILYLYVDCPTM MRCFYGGSLPYNSRHGALITNLPPYQKDVSLGEVCRGLRQASGFFGYEDVIRSAYFAALSVPGYFVKLDG QMELTSTKGKSLTFDLYASNQLRLEPGALVRHGECKFGME **Notes** Soil-borne Gram-negative bacterium and causal agent of hairy root disase in many dicotyledonous plants. rolB gene derived from pRi1724 in A. rhizogenes MAFF301724, named 1724rolB. Hydrolyzes cytokinin glucosides thus liberating free cytokinins. Contributes to the root inducing activity. Interacts directly with 14-3-3 omega inside Arabidopsis cells. **References to 14-3-3 binding to RolB** Moriuchi H, Okamoto C, Nishihama R, Yamashita I, Machida Y, Tanaka N. Nuclear localization and	INTERACTION MIGHT BE PHOSPHORYLATION-INDEPENDENT – NOT IN WEBLOGO

interaction of RolB with plant 14-3-3 proteins correlates with induction of adventitious roots by the oncogene rolB. Plant J. 2004 Apr;38(2):260-75.	
<u>Pseudomonas aeruginosa ExoS</u> exoenzyme S of Pseudomonas aeruginosa (NC_002516.2) 1 MHIQSLQQSP SFAVELHQAA SGRLGQIEAR QVATPSEAQQ LAQRQDAPKG EGLLARLGAA 61 LVRPFVAIMD WLGKLLGSHA RTGPQPSQDA QPAVMSSAVV FKQMVLQQAL PMTLKGLDKA 121 SELATLTPEG LAREHSRLAS GDGALRSLST ALAGIRAGSQ VEESRIQAGR LLERSIGGIA 181 LQQWGTTGGA ASQLVLDASP ELRREITDQL HQVMSEVALL RQAVESEVSR VSADKALADG 241 LVKRFGADAE KYLGRQPGGI HSDAEVMALG LYTGIHYADL NRALRQGQEL DAGQKLIDQG 301 MSAAFEKSGQ AEQVVKTFRG TRGGDAFNAV EEGKVGHDDG YLSTSLNPGV ARSFGQGTIS 361 TVFGRSGIDV SGISNYKNEK EILYNKETDM RVLLSASDEQ GVTRRVLEEA ALGEQSGHSQ 421 GllDAlDlAS KPERSGEVQE QDVRLRMRGL DLA >gi|450297|gb|AAA66491.1| exoenzyme S [Pseudomonas aeruginosa] MHIQSLQQSPSFAVELHQAASGRLGQIEARQVATPSEAQQLAQRQDAPKGEGLLARLGAALVRPFVAIMD WLGKLLGSHARTGPQPSQDAQPAVMSSAVVFKQMVLQQALPMTLKGLDKASELATLTPEGLAREHSRLAS GDGALRSLSTALAGIRAGSQVEESRIQAGRLLERSIGGIALQQWGTTGGAASQLVLDASPELRREITDQL HQVMSEVALLRQAVESEVSRVSADKALADGLVKRFGADAEKYLGRQPGGIHSDAEVMALGLYTGIHYADL NRALRQGQELDAGQKLIDQGMSAAFEKSGQAEQVVKTFRGTRGGDAFNAVEEGKVGHDDGYLSTSLNPGV ARSFGQGTISTVFGRSGIDVSGISNYKNEKEILYNKETDMRVLLSASDEQGVTRRVLEEAALGEQSGHSQ GLLDALDLASKPERSGEVQEQDVRLRMRGLDLA **Notes** The <u>phosphorylation-independent</u> interaction between ExoS and 14-3-3 occurs in a completely novel reversed fashion and is dependent on hydrophobic interactions (residues Lue422, Leu423, Leu426 and Leu428) rather than being electrostatically driven, as occurs with mode I–III consensus peptides.Exoenzyme-S, ADP-ribosylation. **References to 14-3-3 binding to ExoS** Fu H, Coburn J, Collier RJ.The eukaryotic host factor that activates exoenzyme S of Pseudomonas aeruginosa is a member of the 14-3-3 protein family. Proc Natl Acad Sci U S A. 1993 Mar 15;90(6):2320-4. Ottmann C, Yasmin L, Weyand M, Veesenmeyer JL, Diaz MH, Palmer RH, Francis MS, Hauser AR, Wittinghofer A, Hallberg B. Phosphorylation-independent interaction between 14-3-3 and exoenzyme S: from structure to pathogenesis. EMBO J. 2007 Feb 7;26(3):902-13. Yasmin L, Jansson AL, Panahandeh T, Palmer RH, Francis MS, Hallberg B. Delineation of exoenzyme S residues that mediate the interaction with 14-3-3 and its biological activity. FEBS J. 2006 Feb;273(3):638-46. Henriksson ML, Francis MS, Peden A, Aili M, Stefansson K, Palmer R, Aitken A, Hallberg B. A nonphosphorylated 14-3-3 binding motif on exoenzyme S that is functional in vivo. Eur J Biochem. 2002 Oct;269(20):4921-9. Zhang L, Wang H, Masters SC, Wang B, Barbieri JT, Fu H. Residues of 14-3-3 zeta required for activation of exoenzyme S of Pseudomonas aeruginosa. Biochemistry. 1999 Sep 14;38(37):12159-64. Masters SC, Pederson KJ, Zhang L, Barbieri JT, Fu H. Interaction of 14-3-3 with a nonphosphorylated protein ligand, exoenzyme S of Pseudomonas aeruginosa. Biochemistry. 1999 Apr 20;38(16):5216-21.	NOT IN WEBLOGO AS THIS IS A PHOSPHORYLATION-INDEPENDENT INTERACTION THAT CANNOT BE ‘CENTRED’
<u>Polyomavirus Middle T antigen</u> (Swissprot = P03076) 1 MDRVLSRADK ERLLELLKLP RQLWGDFGRM QQAYKQQSLL LHPDKGGSHA LMQELNSLWG 61 TFKTEVYNLR MNLGGTGFQV RRLHADGWNL STKDTFGDRY YQRFCRMPLT CLVNVKYSSC 121 SCILCLLRKQ HRELKDKCDA RCLVLGECFC LECYMQWFGT PTRDVLNLYA DFIASMPIDW 181 LDLDVHSVYN PKRRSEELRR AATVHYTMTT GHSAMEASTS QGNGMISSES GTPATSRRLR 241 LPSLLSNPTY SVMRSHsYPP TRVLQQIHPH ILLEEDEILV LLSPMTAYPR TPPELLYPES 301 DQDQLEPLEE EEEEYMPMED LYLDILPEEQ VPQLIPPPII PRAGLSPWEG LILRDLQRAH 361 FDPILDASQR MRATHRAALR AHSMQRHLRR LGRTLLLVTF LAALLGICLM LFILIKRSRH 421 F **Notes** RSH(pS)YPPT – phosphorylation identified by solid phase Edman sequencing fater protein extracted from NIH 3T3 cells. **References to 14-3-3 binding to polyomavirus middle T antigen** Culleré X, Rose P, Thathamangalam U, Chatterjee A, Mullane KP, Pallas DC, Benjamin TL, Roberts TM, Schaffhausen BS. Serine 257 phosphorylation regulates association of polyomavirus middle T antigen with 14-3-3 proteins. J Virol. 1998 Jan;72(1):558-63.	

Supplementary Table 2. Reported 14-3-3-binding sites flanked by 20 amino acids on either side, based on the data collated in Supplementary Table 1. A. Mammalian proteins; B. Non-mammalian animal proteins; C. Fungal proteins; D. Plant proteins; E. Bacterial and viral proteins that interact with 14-3-3s inside eukaryotic host cells.

Where two sites have been identified for a given protein, the sequence around the second site is in pink type. Where sites are near the N-terminus or C-terminus of a protein, gaps (-) were introduced because the Weblogo programme requires all aligned sequences to be the same length. **Caveat emptor:** The data collected here is likely to include assignments that are incorrect, due to inaccuracies in the original assignments, or our interpretation of authors' intentions for which we apologise. To aid future improvements in the dataset, we ask authors to report any corrections to c.mackintosh@dundee.ac.uk.

Mammalian proteins reported to interact directly with 14-3-3	Sequences for WEBLOGO analysis
Human AANAT Serotonin N-acetyltransferase; arylalkylamine *N*-acetyltransferase. (Swissprot = Q16613)	PEAPRLPPGIPESPSCQRRHtLPASEFRCLTPEDAVSAFEI
	SLTFMELHCSLRGHPFLRRNsGC--------------------
Human Abl1 Abelson murine leukemia viral oncogene homolog 1 (Tyrosine kinase) (Swissprot = P00519)	RSCSASCVPHGAKDTEWRSVtLPRDLQSTGRQFDSSTFGGH
Human ADAM22 Disintegrin and metalloproteinase domain-containing protein 22 (Swissprot = Q9P0K1)	RIPDTKHISDICENGRPRSNsWQGNLGGNKKKIRGKRFRPR
	GNLGGNKKKIRGKRFRPRSNsTETLSPAKSPSSSTGSIASS
Human AKAP13 AKAP-Lbc, guanine nucleotide exchange factor (GEF) for RhoA (Swissprot = Q12802)	PANCSVLRSSMRSLSPFRRHsWGPGKNAASDAEMNHRSSMR
Human AKT1S1 (PRAS40) (Swissprot = Q96B36)	GPPTCSVPPASALPTQQYAKsLPVSVPVWGFKEKRTEARSS
	VLREAEDTQVFGDLPRPRLNtSDFQKLKRKY----------
Human ARaf1 (ARAF) (Swissprot = P10398)	PEHFPFPAPANAPLQRIRSTsTPNVHMVSTTAPMDSNLIQL
	QILATIELLQRSLPKIERSAsEPSLHRTQADELPACLLSAA
Human ARHGEF2 GEF-H1 microtubule-localized Rho exchange factor (Swissprot = Q92974)	TEPLPAEAPWARRPVDPRRRsLPAGDALYLSFNPPQPSRGT
Human ATXN-1 Ataxin-1. PolyQ mutant in spinocerebellar ataxia 1. (Swissprot = P54253)	APFLTKIEPSKPAATRKRRWsAPESRKLEKSEDEPPLTLPK
Human BAD (Swissprot = Q92934)	PTSSSHHGGAGAVEIRSRHSsYPAGTEDDEGMGEEPSPFRG
	GTEDDEGMGEEPSPFRGRSRsAPPNLWAAQRYGRELRRMSD
Human BAIP2 (also known as IRSp53) Brain-specific angiogenesis inhibitor 1-associated protein 2 (Swissprot = Q9UQB8)	QPKSLSPPQSQSKLSDSYSNtLPVRKSVTPKNSYATTENKt
	tLPVRKSVTPKNSYATTENKtLPRSSSMAAGLERNGRMRVK
Human BCL2L11 = Bcl-2-like protein 11 = BimEL =EL isoform of Bim (Swissprot = O43521)	PASPGPFATRSPLFIFMRRSsLLSRSSSGYFSFDTDRSPAP
Human BRaf1 (BRAF) (Swissprot = P15056)	PFRPADEDHRNQFGQRDRSSsAPNVHINTIEPVNIDDLIRD
	QILASIELLARSLPKIHRSAsEPSLNRAGFQTEDFSLYACA
Human Cabin1 (Calcineurin-binding protein cabin-1) (Q9Y6J0)	SGSAQPPEGHPGKPEPSRAKsRPLPNMPKLVIPSAATKFPP
Human CBY1 Chibby = antagonist of β –catenin (ARPP-binding protein) (Swissprot = Q9Y3M2)	-MPFFGNTFSPKKTPPRKSAsLSNLHSLDRSTREVELGLEY
Human CD74 Major histocompatibility complex, class II invariant chain (Swissprot = P04233-1 for canonical long isoform)	-------------MHRRRSRsCREDQKPVMDDQRDLISNNE
Human Cdc25A M-phase inducer phosphatase 1 (Swissprot = P30304)	GCLHSHGLQEGKDLFTQRQNsAPARMLSSNERDSSEPGNFI
Human Cdc25B M-phase inducer phosphatase 2 (Swissprot = P30305)	KEEEKDLVMYSKCQRLFRSPsMPCSVIRPILKRLERPQDRD
Human Cdc25C M-phase inducer phosphatase 3 (Swissprot = P30307)	EFSLKDQEAKVSRSGLYRSPsMPENLNRPRLKQVEKFKDNT
Human CDC2L2=CDK11p110 (Cyclin-dependant Kinase 11) (Swissprot = P21127)	RKEKVHHRKDEKRKEKRRHRsHSAEGGKHARVKEKEREHER
Human CDKN1B (p27Kip1) Cyclin-dependent kinase inhibitor 1B (Swissprot = P46527)	PSDSQTGLAEQCAGIRKRPAtDDSSTQNKRANRTEENVSDG
	SPNAGSVEQTPKKPGLRRQt--------------------
Human CENPJ (Centromere protein J) CPAP (Centrosomal Protein 4.1-Associated Protein) (Swissprot = Q9HC77)	VEKYKKNYLPMQGNPPRRSKsAPPRDLGNLDKGQAASPREP
Human CFL1 Cofilin 1 (Swissprot = P23528)	-------------------MAsGVAVSDGVIKVFNDMKVRKS

	GVAVSDGVIKVFNDMKVRKSsTPEEVKKRKKAVLFCLSEDK
Human CRTC2 (TORC2) (Swissprot = Q53ET0)	NFPAEKGQLFRLPSALNRTSsDSALHTSVMNPSPQDTYPGP
Human CSF2RB (GM-CSF/IL-3/IL-5 cytokine receptor common beta subunit) (Swissprot = P32927)	EKQASSFDFNGPYLGPPHSRsLPDILGQPEPPQEGGSQKSP
Human CTNNB1 Catenin beta-1 (Beta-catenin) **(**Swissprot = P35222**)**	AIPRLVQLLVRAHQDTQRRTsMGGTQQQFVEGVRMEEIVEG
Human Cx43 Connexin43 (Swissprot = P17302)	LQPLAIVDQRPSSRASSRASsRPRPDDLEI-----------
Human DAB2IP Disabled homolog 2-interacting protein; AIP1 ASK1-interacting protein 1 Ras-GAP (Swissprot = Q5VWQ8)	KDLFFVTRSSGVQPSPARSSsYSEANEPDLQMANGGKSLSM
Human DDIT4 DNA-damage-inducible transcript 4 protein (Redd1) (Swissprot = Q9NX09)	LLMPSQLVSQVGKELLRLAYsEPCGLRGALLDVCVEQGKSC
Human DDIT4L DNA-damage-inducible transcript 4-like protein (Redd2) (Swissprot = Q96D03)	VLVPEKLTQRIAQDVLRLSStEPCGLRGCVMHVNLEIENVC
Human FAM82A2 (PTPIP51) (Tyr Pase-interacting protein 51) **(**Swissprot = Q96TC7)	FLCLLYSQRWKRTQRHGRSQsLPNSLDYTQTSDPGRHVMLL
Human FGFR2 Fibroblast growth factor receptor 2 (Swissprot = P21802)	TLTTNEEYLDLSQPLEQYSPsYPDTRSSCSSGDDSVFSPDP
Human FOXO1 Forkhead box protein O1 transcription factor (FKHR) (FOXO1A) (Swissprot = Q12778)	APQVVEIDPDFEPLPRPRSCtWPLPRPEFSQSNSATSSPAP
	WWMLNPEGGKSGKSPRRRAAsMDNNSKFAKSRSRAAKKKAS
Human FOXO3 Forkhead box protein O3 (FKHRL1) (FOXO3A) (Swissprot = O43524)	SPLEVELDPEFEPQSRPRSCtWPLQRPELQASPAKPSGETA
	WWIINPDGGKSGKAPRRRAVsMDNSNKYTKSRGRAAKKKAA
Human FOXO4 Forkhead box protein O4 (AFX, AFX1, MLLT7)) (Swissprot = P98177)	AAAIIDLDPDFEPQSRPRSCtWPLPRPEIANQPSEPPEVEP
	WWMLNPEGGKSGKAPRRRAAsMDSSSKLLRGRSKAPKKKPS
Human GAB2 GRB2-associated binding protein 2 (Swissprot = Q9UQC2)	QEYLYLHQCISRRAENARSAsFSQGTRASFLMRSDTAVQKL
	QRPPISENSRSVAATIPRRNtLPAMDNSRLHRASSCETYEY
Human GEM Kir/Gem, with Rad, Rem and Rem2,member of the RGK small GTP-binding protein family (Swissprot = P55040)	LNNVTMRQGTVGMQPQQQRWsIPADGRHLMVQKEPHQYSHR
	FWGKIVAKNNKNMAFKLKSKsCHDLSVL-------------
Human GFAP Glial fibrillary acidic protein (Swissprot = P14136)	-------------MERRRITsAARRSYVSSGEMMVGGLAPG
Human Gli1 GLI family zinc finger 1 (Glioma-associated oncogene) transcription factor (Swissprot = P08151)	WRSRAEYPGYNPNAGVTRRAsDPAQAADRPAPARVQRFKSL
Human Gli2 GLI family zinc finger 2 (Tax helper protein) transcription factor (Swissprot = P10070)	HAGAAPAFPHEAPGGGARRAsDPVRRPDALSLPRVQRFHST
Human Gli3 GLI family zinc finger 3 transcription factor (Swissprot = P10071)	GYGRRHLQPHDAPGHGVRRAsDPVRTGSEGLALPRVPRFSS
Human GP1BA Glycocalicin Platelet glycoprotein Ib alpha chain (GPIb alpha) (Swissprot = P07359)	ELQRGRQVTVPRAWLLFLRGsLPTFRSSLFLWVRPNGRVGP
	WVRPNGRVGPLVAGRRPSALsQGRGQDLLSTVSIRYSGHS-
Human GRIN2C (NMDAR2C) NMDA receptor subunit 2C (Swissprot = Q14957)	ARREALLHAAWARGSRPRHAsLPSSVAEAFARPSSLPAGCT
Human HDAC4 Histone deacetylase 4 (Swissprot = P56524)	NHPVLGMYDAKDDFPLRKTAsEPNLKLRSRLKQKAERRSSP
	DRVSPSIHKLRQHRPLGRTQsAPLPQNAQALQHLVIQQQHQ
Human HDAC5 Histone deacetylase 5 (Swissprot = Q9UQL6)	KLPLPGPYDSRDDFPLRKTAsEPNLKVRSRLKQKVAERRSS
	ATSMRTVGKLPRHRPLSRTQsSPLPQSPQALQQLVMQQQHQ
Human HDAC7 Histone deacetylase 7 (Swissprot = Q8WUI4)	PPVPSLPSDPPEHFPLRKTVsEPNLKLRYKPKKSLERRKNP
	LMTTERLSGSGLHWPLSRTRsEPLPPSATAPPPPGPMQPRL
Human HDAC9 Histone deacetylase 9 (Swissprot = Q9UKV0)	KYTLPGAQDAKDDFPLRKTAsEPNLKVRSRLKQKVAERRSS
	SPGIRGTHKLPRHRPLNRTQsAPLPQSTLAQLVIQQQHQQF
Human HIST1H3A Histone H3 (Swissprot = P68431)	----------MARTKQTARKsTGGKAPRKQLATKAARKsAP
	RKsTGGKAPRKQLATKAARKsAPATGGVKKPHRYRPGTVAL
Human HJURP Holliday junction recognition protein (Swissprot = Q8NCD3)	MYRGGPASPGGLQGLETRRLsLPSSKAKAKSLSEAFENLGK
Human HspB6 (HSP20) (Swissprot = O14558)	-----MEIPVPVQPSWLRRAsAPLPGLSAPGRLFDQRFGEG
Human IGF1R Insulin-like growth factor I receptor (Swissprot = P08069)	LDLEPENMESVPLDPSASSSsLPLPDRHSGHKAENGPGPGV
Human ING1 (p33ING1b) Inhibitor of growth protein 1 (Swissprot = Q9UK53)	KKAKTSKKKKRSKAKAEREAsPADLPIDPNEPTYCLCNQVS
Human IRS1 Insulin receptor substrate 1 (Swissprot = P35568)	HETILEAMRAMSDEFRPRSKsQSSSNCSNPISVPLRRHHLN
	THAHRHRGSARLHPPLNHSRsIPMPASRCSPSATSPVSLSS
Human ITGA4 (CD49D) Integrin alpha4 (Swissprot = P13612)	VLLLISYVMWKAGFFKRQYKsILQEENRRDSWSYINSKSND
Human ITGB1 Integrin beta 1 subunit (fibronectin receptor) (Swissprot = P05556)	KEKMNAKWDTGENPIYKSAVtTVVNPKYEGK----------
Human ITGB2 Integrin beta 2 subunit. (Swissprot = P05107)	FEKEKLKSQWNNDNPLFKSAtTTVMNPKFAES---------
Human KANK1 kidney ankyrin repeat–containing protein 1 (aka ANKRD15) (Swissprot = Q14678)	LKNQRAASQINVCGVRKRSYsAGNASQLEQLSRARRSGGEL

Human KCNK3 Two-pore-domain potassium channel TASK-1 (Swissprot = O14649)	SVSTGLHSLSTFRGLMKRRSsV-------------------
Human KCNK9 Two-pore-domain potassium channel TASK-3 (Swissprot = Q9NPC2)	SISPGLHSFTDHQRLMKRRKsV-------------------
Human KIF1C (Kinesin-like protein KIF1C) (Swissprot = O43896)	RPPGPRYPPYTTPPRMRRQRsAPDLKESGAAV---------
Human KLC2 (Swissprot = Q9H0B6)	KKLQGGTPQEPPNPRMKRASsLNFLNKSVEEPTQPGGTGLS
Human KRT18 Keratin 18 (Swissprot = P05783	RSLGSVQAPSYGARPVSSAAsVYAGAGGSGSRISVSRSTSF
Human KSR1 (kinase suppressor of Ras) (Swissprot = Q8IVT5)	PSRKKVFQLLPSFPTLTRSKsHESQLGNRIDDVSSMRFDLS
	KEAPACRISFLPLTRLRRTEsVPSDINNPVDRAAEPHFGTL
Human LCP2 (SLP-76) (Lymphocyte cytosolic protein 2, aka SLP-76) (Swissprot = Q13094)	PSSHMPGAFSESNSSFPQSAsLPPYFSQGPSNRPPIRAEGR
Human LSR Isoform 2 of lipolysis-stimulated lipoprotein receptor (Swissprot = Q86X29)	QEPAREQAGGGWRARRPRARsVDALDDLTPPSTAESGSRSP
Human MAP3K3 (MEKK3) Protein kinase of the STE11 family (Swissprot = Q99759)	TYPRRYHVSVHHKDYSDGRRtFPRIRRHQGNLFTLVPSSRS
Human MAP3K5 (ASK1, MEKK5) Apoptosis signal-regulating kinase 1 (Swissprot = Q99683)	KTQPKLSALSAGSNEYLRSIsLPVPVLVEDTSSSSEYGSVS
Human MAP3K6 (ASK2, MAPKKK6, MEKK6) Apoptosis signal-regulating kinase 2 (Swissprot = O95382)	TFPCPQAPSQHPPSPPKRCLsYGGTSQLRVPEEPAAEEPAS
Human MAPK7 (ERK5, BMK1) (Swissprot = Q13164)	KKDGAISDNTKAALKAALLKsLRSRLRDGPSAPLEAPEPRK
Human MAPT Microtubule-associated protein tau) (Swissprot =P10636)	RSGYSSPGSPGTPGSRSRTPsLPTPPTREPKKVAVVRTPPK
	GSVQIVYKPVDLSKVTSKCGsLGNIHHKPGGGQVEVKSEKL
	QVEVKSEKLDFKDRVQSKIGsLDNITHVPGGGNKKIETHKL
Human MARK2 (aka Par-1b/EMK) Swissprot = Q7KZ17 **Not FOUND**	SADLTNSSAPSPSHKVQRSVsANPKQRRFSDQAAGPAIPTS
	SSSGGAPDRTNFPRGVSSRStFHAGQLRQVRDQQNLPYGVT
Human Mdm2 (Swissprot = Q00987)	KPSSSHLVSRPSTSSRRRAIsETEENSDELSGERQRKRHKs
	sETEENSDELSGERQRKRHKsDSISLSFDESLALCVIREIC
Human Mdm4 (MdmX) (Swissprot = O15151)	TAIPEKENEGNDVPDCRRTIsAPVVRPKDAYIKKENSKLFD
Human MEFV Pyrin (Swissprot = O15553)	PGPCRALEGGQAEVRLRRNAssAGRLQGLAGGAPGQKECRP
	GQKECRPFEVYLPSGKMRPRsLEVTISTGEKAPANPEILLT
Human MITF Microphthalmia-associated transcription factor (Accession = NP_937820, isoform 2) **NOT FOUND**	NLIDLYGNQGLPPPGLTISNsCPANLPNIKRELTESEARAL
Human Mlf1 Myeloid leukemia factor 1 isoform 1 (Swissprot = P58340)	FFSESILAHRENMRQMIRSFsEPFGRDLLSISDGRGRAHNR
Human MST1R (Ron) Tyrosine kinase receptor for MSP (macrophage-stimulating protein receptor) (Swissprot = Q04912)	RPEQPQFSPMPGNVRRPRPLsEPPRPT--------------
Human NCOR1 Transcriptional corepressor (Swissprot = O75376) , related to SMRT, which also binds 14-3-3	SPHSGGVCKPKLISKSNSRKsKSPIPGQGYLGTERPSSVSS
Human NEDD4L E3 ubiquitin ligase Nedd4.2 (Swissprot = Q7Z5N3)	NGEQFSSLIQREPSSRLRSCsVTDAVAEQGHLPPPSAPAGR
	SATNSNNHLIEPQIRRPRSLsSPTVTLSAPLEGAKDSPVRR
Human NFATC4 (NFAT3) Nuclear factor of activated T-cells (Swissprot = Q14934)	APGPTPASPRPASPCGKRRYsSSGTPSSASPALSRRGsLGE
	RRYsSSGTPSSASPALSRRGsLGEEGSEPPPPPPLPLARDP
Human NOXA1 activator of NOX1, a superoxide- producing NADPH oxidase (Swissprot = Q86UR1)	WPEGSLNGLDSALDQVQRRGsLPPRQVPRGEVFRPHRWHLK
	RDGRIGIFPKCFVVPAGPRMsGAPGRLPRSQQGDQP-----
Human NRIP1 (RIP140) Receptor interacting protein of 140 kDa (Swissprot = P48552)	KKARLLQSSEDWNAAKRKRLsDSIMNLNVKKEALLAGMVDS
	LNGLMYSSTQPSSCMDNRTFsYPGVVKTPVSPTFPEHLGCA
Human PACS2 phosphofurin acidic cluster sorting protein 2 (Swissprot = Q86VP3)	LVIPSTRSEGKQAGRRGRSTsLKERQAARPQNERANSLDNE
Human PCTK1 PCTAIRE protein kinase 1 [Homo sapiens] (Swissprot = Q00536)	VRMRNHPPRKISTEDINKRLsLPADIRLPEGYLEKLTLNSP
Human PDC Phosducin (Swissprot = P20941)	LESQDSDSIPPSKKEILRQMsSPQSRNGKDSKERVSRKMsI
	MsSPQSRNGKDSKERVSRKMsIQEYELIHKEKEDENCLRKY
Human PDE3A Phosphodiesterase 3A (Swissprot = Q14432)	SDSEESSEKDKLAIPKRLRRsLPPGLLRRVSSTWTTTTSAT
Human PFKFB2 cardiac PFK-2 6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 2 (Swissprot = O60825)	RDKPTNNFPKNQTPVRMRRNsFTPLSSSNTIRRPRNYsVGS
	RRNsFTPLSSSNTIRRPRNYsVGSRPLKPLSPLRAQDMQEG
Human PI4KB (PI4KIIIbeta) phosphatidylinositol 4-kinase III beta (Swissprot = Q9UBF8)	RSKSDATASISLSSNLKRTAsNPKVENEDEELSSSTESIDN
Human PKP2 Plakophilin 2 (Swissprot = Q99959)	QTLARKGRSSVGNGNLHRTSsVPEYVYNLHLVENDFVGGRS
Human PPP1R12A (Swissprot = O14974)	ITASKEGQKEKDTAGVTRSAsSPRLSSSLDNKEKEKDSKGT
Human PRKCE (PKCE) Protein kinase Cepsilon (Swissprot = Q02156)	GAESPQPASGSSPSEEDRSKsAPTSPCDQEIKELENNIRKA
	PTSPCDQEIKELENNIRKALsFNRGEEHRAASSPDGQLMSP

Human PRLR prolactin receptor 1 (PrlR) (Swissprot = P16471)	QCISMEGKIPYFHAGGSKCStWPLPQPSQHNPRSSYHNITD
Human PTPN3 Tyrosine-protein phosphatase non-receptor type 3 (aka Protein-tyrosine phosphatase H1) (Swissprot = P26045)	QYCKKVIGGMVWNPAMRRSLsVEHLETKSLPSRSPPITPNW
	PDDSSDFLEFVNYVRSLRVDsEPVLVHCSAGIGRTGVLVTM
Human Raf1 (CRAF) (Swissprot = P04049)	TFNTSSPSSEGSLSQRQRSTsTPNVHMVSTTLPVDSRMIED
	QILSSIELLQHSLPKINRSAsEPSLHRAAHTEDINACTLTT
Human Raptor Regulatory-associated protein of mTOR (Swissprot = Q8N122)	GGSLTPVRDSPCTPRLRSVSsYGNIRAVATARSLNKSLQNL
	PENEEHILSFETIDKMRRASsYSSLNSLIGVSFNSVYTQIW
Human Rem2 RAS (RAD and GEM)-like GTP binding 2 (Swissprot = Q8IYK8-1)	LAELDRSGLPSAPGAPRRRGsMPVPYKHQLRRAQAVDELDW
	KRFLANLVPRNAKFFKQRSRsCHDLSVL-------------
Human RGS3 (Swissprot = P49796)	QGAEGGLSLRVQNSLRRRTHsEGSLLQEPRGPCFASDTTLH
Human rictor (AAS79796)	PKGGKLSSESKTSNRRIRTLtEPSVDFNHSDDFTPISTVQK
Human RIMS1 Rim1 alpha (Swissprot = Q86UR5)	AEPSQQALGPEQKQASSRSRsEPPRERKKTPGLSEQNGKGA
	GKAADEEKQRKEEDYQTRYRsDPNLARYPVKPPPEEQQMRM
Human RIMS2 Regulating synaptic membrane exocytosis protein 2 (Rab3-interacting molecule 2) (Swissprot = Q9UQ26)	ESRDEYERQRREEEYQSRYRsDPNLARYPVKPQPYEEQMRI
Human Rin1 Ras and Rab interactor 1 (RAS effector/interference protein 1) (Swissprot = Q13671)	RGSPATSPHLGRRRPLLRSMsAAFCSLLAPERQVGRAAAAL
Human RNF11 RING finger protein 11 (Swissprot = Q9Y3C5)	LPCMHIYHLDCIDDWLMRSFtCPSCMEPVDAALLSSYETN-
Human RPH3A Rabphilin3 (Swissprot = Q9Y2J0)	DHSGGAGDSSRSPAGLRRANsVQASRPAPGSVQSPAPPQPG
Human SASH1 Sterile alpha motif and SH3 domain containing 1 (Swissprot = O94885)	YNTCFSDVCERMEELRKRRVsQDLEVEKPDASPTSLQLRSQ
Human SH3BP2 SH3-domain binding protein 2 (Swissprot = P78314)	PPPPVPTPRKPAFSDMPRAHsFTSKGPGPLLPPPPPKHGLP
	PLCPRRAEPCPRVPATPRRMsDPPLSTMPTAPGLRKPPCFR
Human Skp2 S-phase kinase associated protein-2 (Swissprot = Q13309)	PQELLSNLGHPESPPRKRLKsKGSDKDFVIVRRPKLNRENF
Human SLC9A1 (NHE1) NHE1 sodium/hydrogen exchanger 1 (Swissprot = P19634)	YLTVPAHKLDSPTMSRARIGsDPLAYEPKEDLPVITIDPAS
Human SLITRK1_ SLIT- and TRK-like family, member 1 (Swiss-Prot=Q96PX8)	NGPYNADGAHRVYDCGSHSLsD-------------------
Human Snn (Stannin) (Swissprot = O75324)	ALGALILGCWCYLRLQRISQsEDEESIVGDGETKEPFLLVQ
Human SRPK2 Serine/arginine-rich protein-specific kinase 2 (Swiss-Prot = P78362)	SEGSPLTEQEESSPSHDRSRtVSASSTGDLPKAKTRAADLL
Human SSH1L The phosphatase Slingshot 1-like, which dephosphorylates cofilin. (isoform 1, Swissprot = Q8WYL5)	KTICYTPTSSSMSSNLTRSSsSDIHSVRGKPGLVKQRTQEI
	IETRLRLAGLTVSSPLKRSHsLAKLGSLTFSTEDLSSEADP
Human TBC1D1 (SwissProt=Q86TI0)	PHAAPTGSQEPVRRPMRKSFsQPGLRSLAFRKELQDGGLRS
	HLPEEPAPLSPQQAFRRRANtLSHFPIECQEPPQPARGSPG
Human TBC1D4 (AS160) RabGAP TBC1D4 = AS160 (Swissprot = O60343 (longer variant))	GVQRRVHEGSQKSQPRRRHAsAPSHVQPSDSEKNRTMLFQV
	AWQTFPEEDSDSPQFRRRAHtFSHPPSSTKRKLNLQDGRAQ
Human TGM2 tissue transglutamase (Swissprot = P21980)	LLDVNPKFLKNAGRDCSRRSsPVYVGRVVSGMVNCNDDQGV
Human TH Tyrosine 3-hydroxylase is an enzyme involved in the conversion of tyrosine to dopamine. (Swissprot = P07101)	--MPTPDATTPQAKGFRRAVsELDAKQAEAIMVRGQGAPGP
	APAASYTPTPRSPRFIGRRQsLIEDARKEREAAVAAAAAAV
Human TP53 p53 (Swissprot = P04637)	EALELKDAQAGKEPGGSRAHsSHLKSKKGQSTSRHKKLMFK
	SHLKSKKGQSTSRHKKLMFKtEGPDSD--------------
Human TPD52L1 Tumour protein D53 (also known as PrLZ and hD53) (Swissprot = Q16890)	VGTAISKKFGDMSYSIRHSIsMPAMRNSPTFKSFEERVETT
Human TPH2 Neuronal tryptophan hydroxylase (TPH2) (Swissprot = Q8IWU9)	--MQPAMMMFSSKYWARRGFsLDSAVPEEHQLLGSSTLNKP
	FQEKRVNMVHIESRKSRRRSsEVEIFVDCECGKTEFNELIQ
Human TSC2 Tuberin (Swissprot = P49815)	TQGWAEILVRRPTGNTSWLMsLENPLSPFSSDINNMPLQEL
	ALMAAERFKEHRDTALYKSLsVPAASTAKPPPLPRSNTVAS
Human USP8 Deubiquitinating enzyme (Swissprot = P40818)	AKPQIPAERDREPSKLKRSYsSPDITQAIQEEEKRKPTVTP
Human WWTR1 (TAZ) WW domain-containing transcription regulator protein 1, a transcriptional coactivator (Q9GZV5)	SSGGHPGPRLAGGAQHVRSHsSPASLQLGTGAGAAGSPAQQ
Human YAP1 (YAP65) Co-activator for TEAD/TEF transcription factors (Swissprot = P46937)	QASTDAGTAGALTPQHVRAHsSPASLQLGAVSPGTLTPTGV
Human ZBTB17 (Miz1) Zn finger BTB domain-containing protein 17 (Myc-interacting Zn finger protein) (Swissprot = Q13105)	SAGTDSGQELGSEARGLRSGtYGDRTESKAYGSVIHKCEDC
	HQLVHSGEKPYQCDYCGRSFsDPTSKMRHLETHDTDKEHKC
Human ZFP36L1 BRF1 (butyrate response factor 1; EGF-response factor) (Swissprot = Q07352)	KGEPAPALSSRDSRFRDRSFsEGGERLLPTQKQPGGGQVNS

	RALAGARDLSADRPRLQHSFsFAGFPSAAATAAATGLLDSP
Human ZNF395 (HDBP2) (Papillomavirus-binding factor PBF) (Swissprot = Q9H8N7)	SSGPEHPGPESSLPSGALSKsAPGSFWHIQADHAYQALPSF
	AAAPSAACSLSPVRSRSLSFsEPQQPAPAMKSHLIVTSPPR
Human ZNRF2 E3 ubiquitin ligase (Swissprot = Q8NHG8)	--MGAKQSGPAAANGRTRAYsGSDLPSSSSGGANGTAGGGG
Mouse Arhgef2 (also known as Lfc and GEF-H1) Guanine nucleotide exchange factor (GEF) for Rho (Swissprot = Q60875)	QKAALLRNNTALQSVSLRSKtTTRERPTSAIYPSDSFRQSL
	NEPLPAEAPWARRPLDPRRRsLPAGDALYLSFNPPQPSRGH
Mouse CCT-alpha Phosphorylcholine transferase A (Swissprot = P49586)	EEKSIDLIQKWEEKSREFIGsFLEMFGPEGALKHMLKEGKG
Mouse Edc3 mRNA Enhancer of mRNA-decapping protein 3 (Swissprot = Q8K2D3)	YVDRHMESLSQSKSFRRRHNsWSSSSRHPNQATPKKSGLKN
Mouse GEM (Swissprot = P55041)	TLNNVTMRQGTVGMQPQQRWsIPADARHLMVQKDPHPCNLR
	FWGKIVAKNNKNMAFKLKSKsCHDLSVL-------------
Mouse Grb10 Growth factor receptor-bound protein 10 (GRB10 adapter protein) (Swissprot = Q60760)	YRIPQRKGLPPPFNAPMRSVsENSLVAMDFSGQIGRVIDNP
Mouse KCNK18 (TRESK) Potassium channel subfamily K member 18 (SwissProt =Q6VV64)	VAREKKNKLQPPTRPVERSNsCPELVLGRLSCSILSNLDEV
Mouse Myo1c (Swissprot = Q9WTI7)	FIRFPKTLFATEDSLEVRRQsLATKIQAAWRGFHWRQKFLR
Mouse Synpo2 Synaptopodin 2 (myopodin) (Swissprot = Q91YE8)	SVRMQSSVSESSFQMGRSLAsVPQQNGFSGVSETAGAQRMF
	KPFLGSMNQPAAPFSPTRSVtSPISDFPAPPPYSAVSPPPE
Mouse ZFP36 Tristetraprolin (TTP) (Swissprot = P22893)	NINSDSIPSGVTSRLTGRSTsLVEGRSCGWVPPPPGFAPLA
	HNPTEDLALPGQPHVLRQSIsFSGLPSGRRSSPPPPGFSGP
Rabbit CSNK1A1 Casein kinase I isoform alpha (Swissprot = P67828)	QSRRDDMESLGYVLMYFNRTsLPWQGLKAATKKQKYEKISE
	QGLKAATKKQKYEKISEKKMsTPVEVLCKGFPAEFAMYLNY
Rat BCAR1 (p130cas) (Crk-associated substrate) (Swissprot = Q63767)	VAHLLDLVGSASGPGGWRSTsEPQEPPVQDLKAAVAAVHGA
Rat CaMKK1 Calcium/calmodulin-dependent protein kinase kinase 1 (CaMKK) (Swissprot = P97756)	IPGSASRPTPVRPSLSARKFsLQERPAGSCLEAQVGPYSTG
Rat Chrnb4 Nicotinic acetylcholine receptor α 4 subunit (AChRα4) (Swissprot = P09483)	SCPPPKSSSGAPMLIKARSLsVQHVPSSQEAAEDGIRCRSR
Rat MYLK2 (Rat myosin light chain kinase 2 (MLCK)) (Swissprot = P20689)	KAAECREAGRRGSPAFLHSPsCPAIISCSEKTLAMKPLSET
Rat Nr4a1 (Nur77) Nuclear receptor subfamily 4 group A member 1 (Swissprot = P22829)	GMVKEVVRTDSLKGRRGRLPsKPKQPPDASPTNLLTSLIRA
Rat NUMB (Swissprot = Q3MUI1)	NNPHAIPRRHAPIEQLARQGsFRGFPALSQKMSPFKRQLsL
	GsFRGFPALSQKMSPFKRQLsLRINELPSTMQRKTDFPIKN
Rat NUMBL Numblike (Swissprot = Q3MUI2)	TTAAAIPRRHAPLEQLVRQGsFRGFPALSQKNSPFKRQLsL
	GsFRGFPALSQKNSPFKRQLsLRLNELPSTLQRRTDFQVKG
Rat RPS6KA1 Ribosomal S6 kinase 1 (p90RSK1) (Swissprot = Q63531)	EGKLYLILDFLRGGDLFTRLsKEVMFTEEDVKFYLAELALG
Rat TESK1 human testicular protein kinase 1 (a TKL kinase of the LISK fanily. (Rattus norvegicus D50864.1)	PLVASPESLVQPETPVRRCRsLPSSPELPRRMETALPGPGP

Non-mammalian animal proteins reported to interact directly with 14-3-3

Ancylosoma caninum DAF-16 (Dog hookworm DAF16; a forkhead transcription factor (Swissprot = B3G3K1)	DGDDGDDFFDLEKHQKARSAsFGGSTQYSSQLAIARHGLFA
	WWVINPDAKPGRNPRRVRAStLDTTSKATLSKKLKGARKRI
Caenorhabditis elegans DAF-16 (Dauer formation protein 16) Forkhead box protein O (AAC47803.1 GI:2623943)	TPDDVMMNDDMEPIPRDRCNtWPMRRPQLEPPLNSSPIIHE
Dictyostelium AX4 Ankyrin repeat-containing protein tyrosine kinase A (Swissprot = Q54HC6)	SSSSSSNSSSSNTKGHSRTPsSPSVSSIPGFQLTSNASQNL
Drosophila FOXO Forkhead box transcription factor (Swissprot = Q95V55)	LGGDLPLDVGFEPQTRARSNtWPCPRPENFVEPTDELDSTK
	SWWMLNPEAKPGKSVRRRAAsMETSRYEKRRGRAKKRVEAL
Drosophila Yki (Yorkie) Drosophila transcriptional activator related to Yap (Swissprot = Q0E8X1) **NOT FOUND**	LQIQPSPQHSRLAIHHSRARsSPASLQQNYNVRARSDAAAA
Xenopus casp2 Capsase-2 from Xenopus laevis (Swissprot = Q9IB67)	VQESTLSRPGRQICREYREEsIDDGDGPVTVQLCSVNFYIT
Xenopus wee1 Xenopus Wee1 (Swissprot = P47817 for Xenopus laevis Wee1)	SGFSCRGRKRLVGAKNTRSLsFTCGGY--------------

Fungal proteins reported to interact directly with 14-3-3

Saccharomyces cerevisiae Acm1 (APC/C-CDH1 modulator 1) Anaphase-promoting complex (APC) inhibitor (YPL267W)	ETIPLTLPLGDKKISLPSFItPPRNSKISIFFTSKHQGQNP
Saccharomyces cerevisiae Pik1 Yeast phosphatidylinositol 4-kinase **NO SWISS PROT**	RTSSASSASLEGTPKLNRTNsQPLSRQAFKNSKKANSSLSQ

Schizosaccharomyces pombe Mei2P (Meiosis protein 2) (Swissprot = P08965)	IGSSYGMSNNFGSVPLGRTEsSPAWGTSGYYDVSSTSPVAP SNTGKVFDSPTGSLGMRRSLtVGANASCSNPTNLSFASLTL

Plant proteins reported to interact directly with 14-3-3

Arabidopsis BZR1 Brassinosteroid receptor (Brassinazole-resistant 1) (Swissprot = Q8S307)	FPFLRNGGIPSSLPSLRISNsCPVTPPVSSPTSKNPKPLPN
Arabidopsis F2KP Arabidopsis 6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase (Swissprot = Q9SP17)	SYLVYAADNAENPRSLSASGsFRNDSTPKAAQRNSEDSGVT GQKGLFVDRGVGSPRLVKSLsASSFLIDTKQIKNSMPAAAG
Arabidopsis KCO1 AtTPK1 Ca(2+)-regulated Arabidopsis vacuole two-pore K(+) channel (Swissport = Q8LBL1)	DFNLNSRTSSSRKRRLRRSRsAPRGDCMYNDDVKIDEPPPH
Arabidopsis NIA1 (NR1, Arabidopsis nitrate reductase 1) (Swissprot = P11832)	AKERQLEISSESNNTLKKSVsSPFMNTASKMYSISEVRKHN
Arabidopsis NIA2 (NR2, Arabidopsis nitrate reductase 2) (Swissprot = P11035)	AKERHLEKSADAPPSLKKSVsTPFMNTTAKMYSMSEVKKHN
Arabidopsis PMA1 Plasma membrane H+-ATPase (Swissprot = P20649)	HVESVAKLKGLDIDTAGHHYtV-------------------
Arabidopsis SPS ATSPS1F (sucrose phosphate synthase 1F) (NM_122035.2)	ARALGSMPGVYRVDLLTRQVsSPDVDYSYGEPTEMLTPRDS
Arabidopsis TPS5 Arabidopsis trehalose-phosphate synthase 5 (Swissprot = O23617)	----------------MVSRsYSNLLDLASGNFHSFSREKK LASGNFHSFSREKKRFPRVAtVTGVLSELDDDNNSNSVCSD
Medicago truncatula GS2 (plastid glutamine synthetase) (Genbank AY225150)	AEYIWIGGTGIDVRSKSRTIsKPVEHPSELPKWNYDGSSTG
Nicotiana tabacum RSG (Tobacco Repression of shoot growth; bzip transcription factor) (Swissprot = Q9LRC7)	LMSGPGANNNPRPLNHFRSLsVDADFFDGLEFGATTPGAAA
Poplar NIMA-related kinase 1 (PNek1) (Uniprot Q8SA64)	ESLPVTRTPTKKSNPTTRRTsLPLPSRTAIQNSAHGTNNSI
Tomato SPAK (Genbank acc. = AF079103)	NSDMASRTLVKRSVSTTRRAsLPLTNKAAVQELPRRPSLSF

Proteins from bacterial and viruses that interact with 14-3-3 inside eukaryotic host cells

Polyomavirus middle T antigen	RRLRLPSLLSNPTYSVMRSHsYPPTRVLQQIHPHILLEEDE