Figure S1. Alignment of sequences orthologous to Dementin. A minimal consensus sequence for this protein family was derived using seaview software50, followed by manual refinement and is shown in bold. Dashes indicate poor conservation of sequence and distance, X’s indicate conservation of distance but not sequence. The locations of predicted coiled-coil domains are indicated by a row of c’s, and transmembrane domains by a row of t’s, both placed over the aligned sequences. The epitope against which antibody 385 against Dementin was raised is shown underlined and in bold.

Hs.477547 --------------------------------MEPSGSEQLFEDPDPGGKSQDAEARKQTESEQKLSKMTHNALENINVIGQGLKHLFQHQRRRSSV

Mm.425352 --------------------------------MEPSGSEQLYEDPDPGGKSQDAEARRQTESEQKLSKMTHNALENINVIGQGLKHLFQHQRRRSSV

Mm.273785 (TMCC2) MKRCKSDELQQQQGEEDGAGMEDAACLLPGADLRHGEASSANSAGGPTSDAGAAVAPNPGPRSKPPDLKKIQQLSEGSMFGHGLKHLFHSRRRSRER

Hs.6360 (TMCC2) MKRCRSDELQQQQGEEDGAGLEDAASHLPGADLRPGETTGANSAGGPTSDAGAAAAPNPGPRSKPPDLKKIQQLSEGSMFGHGLKHLFHSRRRSRER

Mm.23047 -------------------------------------------------------------------------------------------------

Hs.370410 -------------------------------------------------------------------------------------------------

Cin.32211 ---------------------------------------MEQVDVDDIEEHDGEVIVDAAEPINREHKSSFLPKSVLQLTKFNRAKVADTSSTTSTS

Dm.4403 (Dementin)---------------------------------------MRHNSPVSRERASEAAAATQTAAATAGGATAHSAGGTAGGSAAATTTAGGATSGSGTA

Hs.672606 (Tex28) -------------------------------------------------------------------------------------------------

Mm.475616 (Tex28) -------------------------------------------------------------------------------------------------

Cel.23608 -------------------------------------------------------------------------------------------------

**Consensus -------------------------------------------------------------------------------------------------**

Hs.477547 SPHDVQQIQADP--------------EPEMDLESQNACAEIDGVPTHPTALNRVLQQIRVPPKMKRGTSLH--------------SRRGKPEAPKGS

Mm.425352 SPHDVQQIQTDP--------------EPEVDLDSQNACAEIDGVSTHPTALNRVLQQIRVPPKMKRGTSLH--------------SRRGKSEAPKGS

Mm.273785 (TMCC2) EHQASQEAQQQQQQQGLSDQDSPDEKERSPEMHRVSYAVSLHDLPARPTAFNRVLQQIRSRPSIKRGASLHSS--GGSGG---RRAKSSSLEPQRGS

Hs.6360 (TMCC2) EHQTSQDSQQHQQQQGMSDHDSPDEKERSPEMHRVSYAMSLHDLPARPTAFNRVLQQIRSRPSIKRGASLHSSSGGGSSGSSSRRTKSSSLEPQRGS

Mm.23047 -------------------------------------------MPGSDTALT---------------------------------------------

Hs.370410 -------------------------------------------MPGSDTALT---------------------------------------------

Cin.32211APQTPTDGDVTN--------------PMDDSHATLGVEKEINSVVRSRSLENYYREQLDRNDHKKSFKARLFG--------------STTALPTISA

Dm.4403 (Dementin)SANTNSNSSASS---------------STVAAAQAAVYSGGNTVTGSLGSAGVVARGFRSHSPTHRRRSRERQ--------------RRTHGSDQGG

Hs.672606 (Tex28) -------------------------------------------------------------------------------------------------

Mm.475616 (Tex28) -------------------------------------------------------------------------------------------------

Cel.23608 -------------------------------------------------------------------------------------------------

**Consensus -------------------------------------------------------------------------------------------------**

Hs.477547 PQINRKSGQEMTAVMQSGRPRSSSTTDAPTSSAMMEIACAAAAAAAACLPGEEGTAERIERLEVSSLAQTS---SAVASSTDGSIHTDSVDGTPDPQ

Mm.425352 PQINRKSGQEVAAVIQSGRPRSSSTTDAPTSSSVMEIACAAG----VCVPGEEATAERIERLEVSSLAQTS---SAVASSTDGSIHTESVDGIPDPQ

Mm.273785 (TMCC2) PHLLRKAPQDSSLAAILHQHQGRP----RSSSTTDTALLLADGSSAYLLAEEAESIG--DKGDKGDLVALSLPSGPGHGDSDGPISLDVPDGAPDPQ

Hs.6360 (TMCC2) PHLLRKAPQDSSLAAILHQHQCRP----RSSSTTDTALLLADGSNVYLLAEEAEGIG--DKVDKGDLVALSL--PAGHGDTDGPISLDVPDGAPDPQ

Mm.23047 --VDRTYSD-------PGR--------------------HHRCKSRVDRH---------------------------GSDTN--LNFDVPDGILDFH

Hs.370410 --VDRTYSD-------PGR--------------------HHRCKSRVERH--------------------------GGSDTNL--NFDVPDGILDFH

Cin.32211PSFLRRRNVHDECDEGGGLKLNKRKQRMKGDVTADVEFMWQPSTTREPVHQARSSMDS--TNEIQPIVAPL--LMTTASDVSY-DAVDGSPGVSEAQ

Dm.4403 (Dementin)LLAYSGLVGVNDMTDFLGPQQGGG-----GGGGGGGGGGGGGGSAGTGS----------GLEDSRLSGNEDYYSSFVSDEFDSSK--KVHRRCHERS

Hs.672606 (Tex28) --------------------------------------MVLKAEHT---------------------------------LSSSEDGPSGPSSLADGG

Mm.475616 (Tex28) --------------------------------------MVLKVEST--------------------------------LSSFCEDCPSSHTSFSDGE

Cel.23608 ---------------------------------------------------------------------------------------KSSEGTCSSI

**Consensus -------------------------------------------------------------------------------------------------**

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Hs.477547 QQKILKLTEQIKIAQTARDDNVAEYLKLANSA--------DKQQAARIKQRTKAAIAHLVFEKKNQKSAQTILQLQKKLEHYHRKLREVEQNG-IPR

Mm.425352 QQKILKLTEQIKIAQTARDDNVAEYLKLANSA--------DKQQAARIKQRTKAAIAHLVFEKKNQKSAQTILQLQKKLEHYHRKLREVEQNG-IPR

Mm.273785 (TMCC2) HQKILKITEQIKIEQEARDDNVAEYLKLANNA--------DKQQVSRIKQRTKAAIEHLVFEKKNQKSAQTIAQLHKKLEHYRRRLKEIEQNG-PSR

Hs.6360 (TMCC2) HQKILKITEQIKIEQEARDDNVAEYLKLANNA--------DKQQVSRIKQRTKAAIDHLVFEKKNQKSAQTIAQLHKKLEHYRRRLKEIEQNG-PSR

Mm.23047 RQKILKVTEQIKIEQTSRDGNVAEYLKLVSSA--------DKQQAGRIKQKVKLNADSLVFEKKNQKSAHSIAQLQKKLEQYHRKLREIEQNG-VTR

Hs.370410 KQKILKVTEQIKIEQTSRDGNVAEYLKLVNNA--------DKQQAGRIKQKVKLTADSLVFEKKNQKSAHSIAQLQKKLEQYHRKLREIEQNG-ASR

Cin.32211QQKILKISEAIKLEQSTRDENVGDYLKLAGNA--------DKQQVARIKSRNRQLVEHIVFEKKNQKSNAAIAQLKKKFDTYHRRLREIESSGAVGR

Dm.4403 (Dementin)NTKIQCTKESIRQEQTARDDNVNEYLKLAASA--------DKQQLQRIKASSVQAIDRLVFEKKNQKSAHNISQLQKKLDNYTKRAKDLQNHQFQTK

Hs.672606 (Tex28) RHRILYLSEQLRVEKASRDGNTVSYLKLVSKA--------DRHQVPHIQQLAHNLQDSVAFEKVNQRASATIAQIEHRLHQCHQQLQELEEG-----

Mm.475616 (Tex28) KHRIFYLSEQLRVEKASRDENTMSYLKLVSKA--------DRHQAPHIRKLARNVREGVAFERVNQRTSATIAHIERKLYQCHQQLKELEEG-----

Cel.23608 VQKLIEIKDKLRALNEKREADVEKFLSITRQSEISRGVGADNPQRARIRNGDEREKAKNFERQNRKHAHETEMLQKKLIDYEERLKLVD-------I

**Consensus XQKILKLTEQIKIEQAXRDDNVAEYLKLANNA**--------**DKQQXXRIKQRXKXXXXXLVFEKKNQKSAQXIIQLQKKLEXYHRKLEEXEQNG**----

ccc

Hs.477547 QPKDVF----RDMHQGLKDVGAK-VTG----FSEGVVDSVKGGFSSFSQATHSAAGAVVSKPREIASLIRNKFG-SADNIPNLKDSLEEGQVDDAG-

Mm.425352 QPKDVFR----DMHQGLKDVGA-KVTG----FSEGVVDSVKGGFSSFSQATHSAAGAVVSKPREIASLIRNKFG-SADNIPNLKDSLEEGQVDDG-G

Mm.273785 (TMCC2) QPKDVLR----DMQQGLKDVGAN-MRAGISGFGGGVVEGVKGSLSGLSQATHT---AVVSKPREFASLIRNKFG-SADNIAHLKDPMEDGPPEEA-A

Hs.6360 (TMCC2) QPKDVL----RDMQQGLKDVGAN-VRAGISGFGGGVVEGVKGSLSGLSQATHT---AVVSKPREFASLIRNKFG-SADNIAHLKDPLEDGPPEEAA-

Mm.23047 SSKDISKDSLKEIHHSLKDAHV-KSRTAPHC-----LESSKSSMPGVSLTPPVFV---FNKSREFANLIRNKFG-SADNIAHLKNSLEEFRPEASP-

Hs.370410 SSKDISKDHLKDIHRSLKDAHV-KSRTAPHC-----MESSKSGMPGVSLTPPVFV---FNKSREFANLIRNKFG-SADNIAHLKNSLEEFRPEASA-

Cin.32211QSKSL------------RDVGAN-LRD----FSGGVVDSVKGGLSGLQQATQNAAGAIASKPKDLASKLKNKFG-SADNLSSLK--YEEGGLED---

Dm.4403 (Dementin)SQHRQPREVLRDVGQGLRNVGGN----------------IRDGITGFSG-------SVMSKPREFAHLIKNKFG-SADNINQMSEAELQGM**QSANAD**

Hs.672606 (Tex28) -------------------------------------------------------------------------------------------------

Mm.475616 (Tex28) -------------------------------------------------------------------------------------------------

Cel.23608 -------------------------------SGEYEPSPTKSRVFPTGIRKAKGM-TETMVNAPIEFAQRVKSAFSADNVNSTQNGTTGAPKTGQST

**Consensus -PKDVRR-----DMQGLKDVGAN**----------------**VKGGSTGXXXXXXXXXXXAVSKPREFAXLIRNKFG-SADNIXXLKSGLEEXXXEX**---

Hs.477547 -----------------------------------------------------------------------------KALGVISNFQSSPKYGSEED

Mm.425352 -----------------------------------------------------------------------------KALGVISNFQSSPKYGSEED

Mm.273785 (TMCC2) -----------------------------------------------------------------------------RALSGSATLVSSPKYGSDDE

Hs.6360 (TMCC2) -----------------------------------------------------------------------------RALSGSATLVSSPKYGSDDE

Mm.23047 -----------------------------------------------------------------------------RAYGGSATIVNKPKYGSDDE

Hs.370410 -----------------------------------------------------------------------------RAYGGSATIVNKPKYGSDDE

Cin.32211----------------------------------------------------------------------------------TSLDY---RYTSADD

Dm.4403 (Dementin)**VLGSERLQ**QVPGAGTSTGSGGGGQN--NNTGGAGSGTG--------------------------------------------------KFNSDNGSE

Hs.672606 (Tex28) -CRPEGLLLMAESDPANCEPPSEKALLSEPPEPGGEDG-PVNLPHASRPFILESRFQSLQQGTCLETEDVAQQQNL---------------------

Mm.475616 (Tex28) -CSPTSSVLKVGSGLDSHKQPSGKVSYSKLSKPGGEDSLPINVARSS---TLESHLSEMQQRKFSDKKYVAQQQKLL--------------------

Cel.23608 FFTTRKSADTDEVESNAVHKNRGAKRNSSTLPPNLSLTSPDPLSDSSDPESRPGSAADETSNVPYHTADNSLYLPPNHPYHSAHAAPS---------

**Consensus -----------------------------------------------------------------------------KALXXXXXXXXXPKYGSDDE**

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Hs.477547 CSSATSGSVGANSTTGGIAVGASSSKTNTLDMQSS----GFDALLHEIQEIRETQARLEESFETLKEHYQRDYSLIMQTLQEERYRCERLEEQLNDL

Mm.425352 CSSATSGSVGANSTTGGIAVGASSSKTNTLDMQSSG----FDALLHEVQEIRETQARLEDSFETLKEHYQRDYSLIMQTLQEERYRCERLEEQLNDL

Mm.273785 (TMCC2) CSSASASSAGAGSNSGAGPGGALGSPRSNTLYGAPG---NLDTLLEELREIKEGQSHLEDSMEDLKTQLQRDYTYMTQCLQEERYRYERLEEQLNDL

Hs.6360 (TMCC2) CSSASASSAGAGSNSGAGPGGALGSPKSNALYGAPG---NLDALLEELREIKEGQSHLEDSMEDLKTQLQRDYTYMTQCLQEERYRYERLEEQLNDL

Mm.23047 CSSGTSGSADSNGNQSFGAGGTSTLDSQG----------KIAKIMEELREIKVTQTQLAEDIEALKVQFKREYGFISQTLQEERYRYERLEDQLHDL

Hs.370410 CSSGTSGSADSNGNQSFGAGGASTLDSQG----------KLAVILEELREIKDTQAQLAEDIEALKVQFKREYGFISQTLQEERYRYERLEDQLHDL

Cin.32211VSS-TSSIDIGLSISGPDSPHSGLRRVDPQYMQAIIN--QVAGVKSDLVSTQVAHQQFEVEWEDWKRLEQNTIDLLTRSLQEERFRCERLEVQLNDL

Dm.4403 (Dementin)CSSVTSESIPGGSGKSQSGASQYHI--------------VLKTLLTELAERKAENEKLKERIERLET-GQKEFNNLTATLESERYRAEGLEEQINDL

Hs.672606 (Tex28) ---------------------------------------LLQKVKAELEEAKRFHISLQESYHSLKERSLTDLQLLLESLQEEKCRQALMEEQVNGR

Mm.475616 (Tex28) ----------------------------------------LQKMKEELTEAKKVHASFQVSHQSLKESHMIDVQRILESLQEKKTKQSLMEKQVNDH

Cel.23608 -------------------------------------EEGFNAIHEHLNSILQHLMLIDRKYDRLEDDIKKEIKFYAEALEEERFKTTKLEEILNEA

**Consensus CSSXTSGSA**-------------------------------**LXXLLEEIXEIKXXXXXLEEIQLELKQRYQRDYXLIXXTLQEERYRXERLEEQLNDL**

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Hs.477547 TELHQNEILNLKQELASMEEKIAYQSYERARDIQEALEACQTRISK-MELQQQQQQVVQLEGLENATARNLLGKLINILLAVMAVLLVFVSTVANCV

Mm.425352 TELHQNEILNLKQELASMEEKIAYQSYERARDIQEALEACQTRISK-MELQQQQQQVVQLEGLENATARNLLGKLINILLAVMAVLLVFVSTVANCV

Mm.273785 (TMCC2) TELHQNEMTNLKQELASMEEKVAYQSYERARDIQEAVESCLTRVTK-LELQQQQQQVVQLEGVENANARALLGKFINVILALMAVLLVFVSTIANFI

Hs.6360 (TMCC2) TELHQNEMTNLKQELASMEEKVAYQSYERARDIQEAVESCLTRVTK-LELQQQQQQVVQLEGVENANARALLGKFINVILALMAVLLVFVSTIANFI

Mm.23047 TELHQHETANLKQELASAEEKVAYQAYERSRDIQEALESCQTRISK-LELHQQEQQTLQTDAVN---AKVLLGKCINVVLAFMTVILVCVSTLAKFV

Hs.370410 TDLHQHETANLKQELASIEEKVAYQAYERSRDIQEALESCQTRISK-LELHQQEQQALQTDTVN---AKVLLGRCINVILAFMTVILVCVSTIAKFV

Cin.32211TELHQREVTNLKQELFSMEEKVEYHASERARDMQEAIESCQTRLAK-MELQQQQ--LVSVDGLENATARALLGKLINLLLSVMAVLLVLVSTVSGLL

Dm.4403 (Dementin)TELHQNEIENLKQTIADMEEKVQYQSDERLRDVNEVLENCQTRISK-MEHMSQQQ-YVTVEGIDNSNARALVVKLINVVLTILQVVLLLVATAAGII

Hs.672606 (Tex28) LQGQLNEIYNLKHNLACSEERMAYLSYERAKEIWEITETFKSRISKLEMLQQVTQ--LEAAEHLQSRPPQMLFKFLSPRLSLATVLLVFVSTLCACP

Mm.475616 (Tex28) LQRYLDEICHLKQHLACTEEKMAYLSYERAKEIWDVMEIFKSRITKLETLQQATQ--LEMMASLRTRPKDFLFRFISLLLTLTTILLVVVSTLCSCP

Cel.23608 VELQQAEIATLKEQ-NLMATRVDYQHNDRFRNVEENMESLQNHLVR---IENALMDVRQVKLTSNVWQRVALNAG-NIVVELLKIALFVVASILDLV

**Consensus TELHQNEXXNLKQELASMEEKVAYQSYERARDIQEALEXCQTRXSKXXELQQQQQQQVQLEGXXXNAARXLLGKIXNXXXXXLAMVLVVSTXXXXXX**

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Hs.477547 VPLMKTRNRTFSTLFLVVFIAFLWKHWDALFSYVERFFSSPR---------------

Mm.425352 VPLMKTRNRTFSTLFLVAFIAFLWKHWDALFSYVDRLFSPPR---------------

Mm.273785 (TMCC2) TPLMKTRLRITSTALLLLVLFLLWKHWAS-LTYLLEHVLLPS---------------

Hs.6360 (TMCC2) TPLMKTRLRITSTTLLVLVLFLLWKHWDS-LTYLLEHVLLPS---------------

Mm.23047 SPMMKSRSHILGTFFAVTLLAIFCKNWDHILCAIERII-IPR---------------

Hs.370410 SPMMKSRCHILGTFFAVTLLAIFCKNWDHILCAIERMI-IPR---------------

Cin.32211KPLTKSPVRVISTVVVIISIIIAYKTWDTIP-MMSSMM-SSR---------------

Dm.4403 (Dementin)MPFLKTRVRVLTTFLSICFVIFVIRQWPDVQDIGSGLVRHLKQSLVVK---------

Hs.672606 (Tex28) SSLISSRLCTCTMLMLIGLGVLAWQRWRAIPATDWQEWVPSRCRLYSKDSGPPADGP

Mm.475616 (Tex28) LPLLSSRLRIFIVFMIIGLGTLAWQKRHVISIIDWQAWVPFKWRQDLKDAKPPSDGH

Cel.23608 RPLTGSRNR-SAMAFGLVFL-----AIFFGHHLQKVTYLFGGS--------------

**Consensus XPLMKTRXRXXXXXXXXXXXTVLWKXWDXXXXXXXXXXXXPK**---------------