

Supplementary Figure 1

A. Multiple sequence alignment of mammalian OX40R (TNFRSF4) proteins

OX40R_HUMAN	MCVGARRLRGPGCAALLLLGLGLST-VTGLHCVGDTYPSNDRCCHECR-PGNGMVSRCR	58
OX40R_MOUSE	MYVWVQQ-----PTALLLLALTLGVTARRLNCVKHTYPSGHKCCRECQ-PGHGMVSRCDH	54
OX40R_PIG	MRVGAQP-PRALSSALLLLGLVLGA-VARLTCVGDTPSGRRCCKECQ-PGYGMERRCTD	57
OX40R_HORSE	MCVEAQR-PRAPCAALLLLGLVLGA-AAGQNCVGNTYPSGGRCCQECD-PGYGMESRCTQ	57
OX40R_BOVIN	MCVGTQP-PRAPGSALLLLGLVLGA-AAQPHCTGDTYPSGNRCCKECP-PGYGMESRCNH	57
OX40R_GOAT	MCVGTQP-PRAPGSALLLLGLVLSA-AAQPHCTGDTYPSGNRCCKECQ-PGYGMESRCIH	57
OX40R_SHEEP	MCVGTQP-PRAPGSALLLLGLVLSA-AAQPHCTGDTYPSGNRCCKECQPAGYGMESRCIH	58
	* * .: :*****.* *.. * .*****. :*:** * ** *	
OX40R_HUMAN	SQNTVCRPCGPGFYNDVSSKPKPCTWCNLRSGSERKQLCTATQDTVCRCRAGTQPLD-	117
OX40R_MOUSE	TRDTLCHPCETGFYNEAVNYDTCKQCTQCNHRSGSELKQNCPTPTQDTVCRCRPGTQPRQD	114
OX40R_PIG	TQETEC SRCKPGFYNEAVNYEPCPKPTQCNQSRGSEVKQRCTNTTDTVCGCRPGTQPDG	117
OX40R_HORSE	RKDTVCLPCKPGYYNEATNYEACKPCTQCNQSRGSEPKQRCTSTQDTVCRCRPGTQPKH-	116
OX40R_BOVIN	NQDTVCSPPCKPGYYNEAVNYEPCPKPTQCSQSRGSEPKQRCTPTTRDTVCGCRPGSQPDS	117
OX40R_GOAT	NRDTVCSPPCKPGYYNEAVNYEPCPKPTQCSQSRGSEPKQRCTPTTRDTVCGCRPGSQPDS	117
OX40R_SHEEP	NRDTVCSPPCKPGYYNEAVNYEPCPKPTQCSQSRGSEPKQRCTPTTRDTVCGCQAGQASATN	118
	:* * * *:***:.. . ** ** *. ***** ** ** * ***** *: *	
OX40R_HUMAN	-SYKPGVDCAPCPPGHFSPGNDQACKPWTNCTLAG-KHTLQPASNSSDAICEDRDPPATQ	175
OX40R_MOUSE	SGYKLGVD CVPCPPGHFSPGNQACKPWTNCTLSG-KQTRHPASDSLDAVCEDRSLLATL	173
OX40R_PIG	FGYKRGVDCVRCPPGHFSPGNDQACQPTWNTCTLVG-KRTLQAASNSSDAVCEDRSPPATP	176
OX40R_HORSE	-GYKLGVDCA PCPPGHFSPGNQACKPWTNCTSVG-KRTLQLASNSSDAVCEDRSPPATP	174
OX40R_BOVIN	YGYKRGVDCAPCPPGHFSPGNDQACQPTWNTCTLLG-KRTLRAANSSSDAICEDRSPPATP	176
OX40R_GOAT	YGYKRGVDCTPCPPGHFSPGNDQACQPTWNTCTLLG-KRTLRAANSSSDAICEDRSPPATP	176
OX40R_SHEEP	VELVRGPYCAPCPPGHFSPGNDQACQPTWNTPTPLCDGCPHHNSSDAICEDRSPPATP	178
	* * . *****:****:*** * . * *:*****. **	
OX40R_HUMAN	PQETQGPPARPITVQPTAWPRTSQQGPSTRPVEVPGGRAVAAILGLGLVLGLLGLPLAILL	235
OX40R_MOUSE	LWETQRPTFRPTTVQSTTVWPRTSELSPPTLVTPGPAFAVLLGL--GLGLLAPLTVLL	231
OX40R_PIG	PQETQGPPARSPTARPTTAWPRTSQEPSTPHTESPKGP ELAAVLGLGLGLVLLAPVA AVL	236
OX40R_HORSE	PWETQGPPAWAPTQTPTTSWPRVSQGPSTPTTEPPRGPELAAILGLALGLGLLAPVA AVL	234
OX40R_BOVIN	PWETQGPPVQSTTAKPTTSWSKASQGSMPHTEPPKAPELSAVLGLGLGLGLLAPVAAML	236
OX40R_GOAT	PWETQGPPVQSTTAKPTTSWSKASQGSMPHTEPPKAPELSAVLGLGLGLGLLAPVAAML	236
OX40R_SHEEP	PWETQGPPVQSTTAKPTTSWSKASQGSMPHTEPPKAPELSAVLGLGLGLGLLAPVAAML	238
	*** * *: * * :*: * * . .:*** * ***: : *	
OX40R_HUMAN	ALYLLRRDQRLPPDAHKKPPGGGSFRTPIQEEQADAHSTLAKI	277
OX40R_MOUSE	ALYLLRKAWRL-PNTPKPCWGNSFRTPIQEEHTDAHFTLAKI	272
OX40R_PIG	VLLHHRRAWRLLPNAPKPPRENGFRIPQEEHADANSSLAKT	278
OX40R_HORSE	ALFLHHRRAWRLPPNVKPPGGNSFRTPIQEEHADANSTLAKI	276
OX40R_BOVIN	ALLHHRRAWRLLTNTPKPPGGNSFRTPIQEEHTDANSSLAKI	278
OX40R_GOAT	ALLHHRRAWRLLTNTPKPPGGNSFRTPIQEEHTDANSSLAKI	278
OX40R_SHEEP	ALLHHRRAWRLLTNTPKPPGGNSFRTPIQEEHTDANSSLAKI	280
	. * * :: ** :. ** ..** *****:***: :***	

Sequences were retrieved from Uniprot (<https://www.uniprot.org>) with the accession numbers in brackets as follows: OX40R_HUMAN (P43489), OX40R_MOUSE (P47741|TNR4_MOUSE), OX40R_PIG (A0A287A7B3), OX40R_HORSE (A0A5F5PWA8), OX40R_BOVIN (A5PJH6), OX40R_GOAT (A0A452FBG5) and OX40R_SHEEP (W5P810). Multiple sequence alignments were performed using Clustal omega software (<https://www.ebi.ac.uk/Tools/msa/clustalo/>) under default settings. Fully conserved sites are indicated with asterisks. The following elements have been highlighted on the sequence of the human orthologue: transmembrane domain in red letters, full TNFR repeats as identified by SMART (SM000208) by blue lines above the sequence and a TRAF binding motif in blue letters.

CD27_HUMAN	MARPHPWWL CVL GLTLVGLSATPAPKSCPERHYWAQGGKLCQMC	60
CD27_MOUSE	MAWPPPYWLCMLGLTLVGLSATLAPNSCPDKHYWTGGGLCCRMCE	60
CD27_PIG	MARSPICWLWVLGLTLAGLSATPAPQSCPEKHYWARGELCCQMCQ	60
CD27_HORSE	MARPPPCWLWVLGLTLAGLSATPAPKSCPEKHYWARGELCCPMCKP	60
CD27_BOVIN	MARLPPCWLWVLGLTLAGLSATPDKSCPEKHYWAQGGWCCQMC	60
CD27_GOAT	MARLPPCWLWVLGLTLAGLSATPGPKSCPEKHYWAQGGWCCQMC	60
CD27_SHEEP	MAWLPPCWLWVLGLTLAGLSATPGPKSCLEKHYWAQGGWCCQMC	60
:*.******:**::***: * ** **:*** *: **: . :		

CD27_HUMAN	QCDPCIPGVSFSPDHHTRPHCESCRHCNSGLLVRNCTITANAECAC	120
CD27_MOUSE	QCDPCIPGTSFSPDYHTRPHCESCRHCNSGFLIRNCTVTANAECSC	120
CD27_PIG	RCDPCKQGVSFSPDYHSRPHCESCRHCNSGLFVNCTLTANAKCAC	120
CD27_HORSE	QCDSCIPGVSFSPDYHARPHCESCRHCNSGLLIRNCTLTANTECG	120
CD27_BOVIN	QCNPCTPGVSFMPDHHSRPHCESCRHCNSGLLIRNCTLTANSECA	120
CD27_GOAT	QCDPCTPGVSFTPDHHSRPHCESCRHCNSGLLIRNCTLTANSECA	120
CD27_SHEEP	QCDPCTPGVSFTPDHHSRPHCESCRHCNSGLLIRNCTLTANSKCA	120
:*: * *.** **:*:*****:::***:***:*. * . **:*** **		
CD27_HUMAN	DPLPNPSLTARSSQALSPHPQPTHLPYVSEMLEARTAGHMQTLADF	180
CD27_MOUSE	DPPLNPALTRQPSETPSPQPPPTHLPHGTEKPSW-----PLHR	171
CD27_PIG	DGPA-----QTPGPHQPSSHSPYAEAIPEARTSRYTQTLADVGQ	171
CD27_HORSE	DPPANPSLTTPRPSQA--PGPQPTHLPYAKMPEARTVRHVQTLADF	178
CD27_BOVIN	DGPA-----QAPGPHQPShLPYAEIEAESRTDRHTQTLANSRWL	171
CD27_GOAT	DGPA-----QAPGPHQPShLPYAEIEPEARTDRHTQTLANSRWL	171
CD27_SHEEP	DGPA-----QAPGPHQPShLPYAEIEPEARTDRHTQTLANSRWL	171
*:: * * **: * . : * .:		
CD27_HUMAN	QRSLCSSDFIRILVIFSGMFLVFTLAGALFLHQRRKYRSNKGESPV	240
CD27_MOUSE	HRPLCSSDCIRIFVTFSSMFLIFVLGAILFFHQRRNHGPNEDRQA-V	230
CD27_PIG	Q--RCSSECIRILVVLSGVFLAFTTVVGALFLYQQRKYGLNTGEC	229
CD27_HORSE	QRSLCSTDCIRIFVIFSGMFLAFTMVGALFLHQQRKYGLNKGESPA	237
CD27_BOVIN	QRSLCSANCIRIFVLLSGMFLAFTIVGALFLHQQRK--LNAGESPV	229
CD27_GOAT	QRSLCSVNCVIRIFVLLSGMFLAFTIVGALFLHQQRK--LNAGESPV	229
CD27_SHEEP	QRSLCSVNCVIRIFVLLSGMFLAFTIVGALFLHQQRK--LNAGESPV	229
: ** : **: * :*:** *: . **:***: * .. ** *: **		
CD27_HUMAN	EGSTIPIQEDYRKPEPACSP-----	260
CD27_MOUSE	EGSAIPIQEDYRKPEPAFY-----	250
CD27_PIG	EGSAIPIQEDYRKPELASYL-----	249
CD27_HORSE	EGSAFIPIQEDYRKPEPASYP-----	257
CD27_BOVIN	EGSAIPIQEDYRKPEPTSYP-----	249
CD27_GOAT	EGSAIPIQEDYRKPELTSYSEPVLLREGHHCNQVLASTSLH	270
CD27_SHEEP	EGSAIPIQEDYRKPELTSYSEPVLLREGHHCNQVLASTSPH	270
:**:		

[illegible]

C. Multiple sequence alignment of mammalian OX40L (TNFSF4) proteins

OX40L_HUMAN	--MERVQPLEENVGNAARPRFERNK- LLL VASVIQGLG LLLCFTYICLHFSAL QVSHRYP	57
OX40L_MOUSE	MEGEVQPLDENLENGSRPRFKWKKTLRLVVSGIKGAGMLLCFIYVCLQLSS--SPAKDP	58
OX40L_PIG	--MEGVQPLDENVGNAPEGRRLLRNK-LLLVASVIQGLG LLCLTYICLHLYA -QVPSQYP	56
OX40L_HORSE	--MEGVQPLEENVGNTPGRRFQNRK-LLLVTSIIQGLG LLCLTYVCLHFYTSQVPSQYP	57
OX40L_BOVIN	MKMEGVQPLDENVGNPGRRFLRNK-LLLVASIIQGLG LLCLTYICLHFYA -QVPSQYP	58
OX40L_GOAT	--MEGVQPLDENVGNAPEGRRFLRNK-LLLVASIIQGLG LLCLTYICLHFYA -QVPSQYP	56
OX40L_SHEEP	--MEGVQPLDENVGNAPEGRRFLRNK- LLL VAS IIQGLGLLCLTYICLHFYA -QVPSQYP	56
	* ****:***: * *: : * * *. * *: * **: * **: * : : *	
OX40L_HUMAN	RIQSIK VFTEYKKEKGFILTSQKEDEIMKVQNNSVI INCDGFY ISLKGYSQEVNISL	117
OX40L_MOUSE	PIQLRGAVTRCEDGQLFISSYKNEYQTM EVQNNSVVIKCDGLYIIYLKGSFFQEVKIDL	118
OX40L_PIG	PIQSIK VFTEKENDNGFIITPSSKDGTMKVQNN SVIINCDGFY ISLKGYSQELSLML	116
OX40L_HORSE	PIQSIR VQFTSCENEKGFII TSPNQDEIMKVQ DN SVIINCDGFY ISLKGYSQELSLSL	117
OX40L_BOVIN	PIQSIR VQFTK ENENGFIITSPDADG TMKVQNN SVIITCDGFY ISLKGYSQELSLRL	118
OX40L_GOAT	PIQSIRVR FTK ENENGFIITSPDADG TMKVQNN SVIITCDGFY ISLKGYSQKLSLRL	116
OX40L_SHEEP	PIQSIRVRFTK ENENGFIITSPDADG TMKVQNN SVIITCDGFY ISLKGYSQKLSLRL	116
	** :: .* .: : ** : . *: **: **: *: *. **: *: * * * *: *: *	
OX40L_HUMAN	HYQKDEEPLFQ --LKKVRSVNSLMVAS LT YKDKVYLN VTTDNTSLDDFHVNGGELILIHQ	175
OX40L_MOUSE	HFREDHNPISIPMLNDGRRIVFTVVASLAFKDKVYLT VNAPDTLCEHLQINDGELIVVQL	178
OX40L_PIG	QYRKGRKPLFS--LNKVKSVD SVTVADLAFKDKVFLNV TTHSAS CDIQVNGGELILIHQ	174
OX40L_HORSE	HYRKGREPLSS--LSKVRSVNSIMVAYLAFKDKVYLN VTTHTNTSCDDIQVNGGELILIHQ	175
OX40L_BOVIN	LYRKGREPLFS--LNMVKIVDS VTVAYLRFKDKVYLNMT TQNAS CDIQVNGGELILIHQ	176
OX40L_GOAT	LYRKGREPLFS--LNMVKIVDS VTVAYLRFKDKVYLNVT TQNAS CDIQVNGGELILIHQ	174
OX40L_SHEEP	LYRKGREPLFS --LNMVKIVDS VTVAYLRFKDKVYLNVT TQNAS CDIQVNGGELILIHQ	174
	: : : : : *: * . : : * * * : **: *: . : : : : . : : : : : : *. **: *: :	
OX40L_HUMAN	NPGEFCVL -----	183
OX40L_MOUSE	TPG-YCAPEGSYHSTVN QVPL	198
OX40L_PIG	NPGGFCVY-----	182
OX40L_HORSE	NPGGFCAY-----	183
OX40L_BOVIN	NPGGFCVY-----	184
OX40L_GOAT	NPGGFCVY-----	182
OX40L_SHEEP	NPGGFCVY -----	182
	. ** : * .	

Sequences were retrieved from Uniprot (<https://www.uniprot.org>) with the accession numbers in brackets as follows: OX40L_HUMAN (P23510), OX40L_MOUSE (P43488), OX40L_PIG (Q4QTJ8), OX40L_HORSE (F6UJR4), OX40L_BOVIN (E1BGY4), OX40L_GOAT (A0A452FAW5) and OX40L_SHEEP (W5PZ67). Multiple sequence alignments were performed using Clustal omega software (<https://www.ebi.ac.uk/Tools/msa/clustalo/>) under default settings. Fully conserved sites are indicated with asterisks. For human and ovine sequences, transmembrane domains are indicated in red letters and TNF homology domains (SMART TNF domain SM000207) in green letters. The predicted extracellular region of the ovine orthologue that was cloned is indicated by a blue line under the text.

CD70_HUMAN	-----	0
CD70_MOUSE	-----	0
CD70_PIG	-----	0
CD70_HORSE	-----MQR	3
CD70_BOVIN	MVERAWSLPLTDIPREGHWSLAGSDRLRGPRGCEKAEASFPLPACPLRTLPAATQLMKC	60
CD70_GOAT	MVERAWSLPLTDIPREEHGWSLAGSDRPREPCGCEKAEASFPLPACPLRTLPAATQLMKC	60
CD70_SHEEP	-----MKC	3
CD70_HUMAN	-----MPEEGSGCSVRRRPYGC VLRA --- ALVPLVAGLVICLVVCI QRFAQAQQQLPLE	51
CD70_MOUSE	-----MPEEGRPCPWVRWSGTAFQRQWPWLLLVFITVFCWFHCSGLLSKQQ-QRLLE	53
CD70_PIG	-----MEEEGSGCNVPRLPWASILRA---ALLLLLIGMVIYCFLCGQRFTQ-Q---QLD	47
CD70_HORSE	RPR-TAMAEEGSGCLVRRLPWVTILRV---AFLLLIGMVIYCFVCNQRLAQQQ---QLE	56
CD70_BOVIN	SWRTMMAPEEAASCQVPRWPASILRV---TISVLLSTG-TCYLVNCLFSQQQ---QLD	113
CD70_GOAT	SWKTMATEEAASCQVTRRPWASILRV---TIPVLLSIG-TCYLICTLCFRQQQ---QLD	113
CD70_SHEEP	SWRTIMATEEAASYQVNRWPWAS ILRV --- IIPVLLSIG-TCYLVNCLCF RQQQ---QLD	56
	** * . * : :. . * : : * *:	
CD70_HUMAN	SLGWDVAEL QLNHTGPPQDPRLYWQGGPALGRSFLHGPELD-KGQLRIHRDGIYMVHIQV	110
CD70_MOUSE	HPEPHTAELQLNLTVPRKDPTLRWGAGPALGRSFTHGPELE-EGHLRIHQDGLYRLHIQV	112
CD70_PIG	STGWDLAELLNHTESRQDPRLRWQGSPALGRSFVHGPELD-NGQLRIQRTGIYRLHIQV	106
CD70_HORSE	SSGWAVALQLNHTGPRHDARLHWQGNPALGRSFVHGLELD-YGQLRIQHPGIYRLHIQV	115
CD70_BOVIN	STRWDLAELQLNHTGSRQDPRLPWQGSPALGRSFLHGPKLDDNGQLQIQRDGIYRLHIQV	173
CD70_GOAT	STRWDLAELQLNHTGSRQDPRLRWQGSPALGRSFLHGPELDDNGQLRIQRDGIYRLHIQV	173
CD70_SHEEP	STRWDLAEL QLNHTGSRQDPRLRWQGSPALGRSFLHGPELDDNGQLRIQRDGIYRLHIQV	116
	*** ** * ::* * * .***** ** *: *:*:*:*: *:* :****	
CD70_HUMAN	TLAICSSTTA-SRHHP TLAVGICSPASRSISLLRLSFHQ-GCTIASQRLTPLARGDTLC	168
CD70_MOUSE	TLANCSSPGS-TLQHRATLAVGICSPAAGISLLRGRFGQ-DCTVALQRLTYLVHGDVLC	170
CD70_PIG	TLTNCSSTWTVMRQATLTLGICSPTHSISLLRLNFHH-TCRVASQRLTPLAKGDVLC	165
CD70_HORSE	TLTNCS-STWTNAVRRATLAVGICSSATHSISLLRLNFYN-ACTVASQRLTYLAKGDTLC	173
CD70_BOVIN	TLANCSSSTWTAEPQATLTVAICSPAHSISLLRLSFHRGGCWVASQRLTFLARGDILC	233
CD70_GOAT	TLANCSSSTWTAEPQATLTVAICSPAHSISLLRLSFHRGACWVASQRLTFLALGDILC	233
CD70_SHEEP	TLANCSSSTWTAEPQATLTVAICSPAHSISLLRLSFHRGACWVASQRLTFLAHGDILC	176
	*: ** : *:*:*.*** :::*.***** * . * *: **** *. ** **	
CD70_HUMAN	TNLTGTLPLPSRNTDETFFGVQVVRP	193
CD70_MOUSE	TNLTLPPLPSRNADETFFGVQWICP	195
CD70_PIG	TNLTLPPLPSRNADETFFGVQLVRP	190
CD70_HORSE	TNLTLPWLPSRNSDETFFGVQWVHL	198
CD70_BOVIN	TNLTLPPLPSRNADETFFGIQWVHP	258
CD70_GOAT	TNLTLPPLPSRNADETFFGIQWVHP	258
CD70_SHEEP	TNLTLPPLPSRNTDETFFGIQVVRP	201
	**** *****.***** .	

Sequences were retrieved from Uniprot (<https://www.uniprot.org>) with the accession numbers in brackets as follows: CD70_HUMAN (P32970), CD70_MOUSE (O55237), CD70_PIG (Q3ZDR4), CD70_HORSE (F6XHL7), CD70_BOVIN (E1B972), CD70_GOAT (A0A452G8J0) and CD70_SHEEP (W5P639). Multiple sequence alignments were performed using Clustal omega software (<https://www.ebi.ac.uk/Tools/msa/clustalo/>) under default settings. Fully conserved sites are indicated with asterisks. For human and ovine sequences, transmembrane domains are indicated in red letters and TNF homology domains (SMART TNF domain SM000207) in green letters. The predicted extracellular region of the ovine orthologue that was cloned is indicated by a blue line under the text.