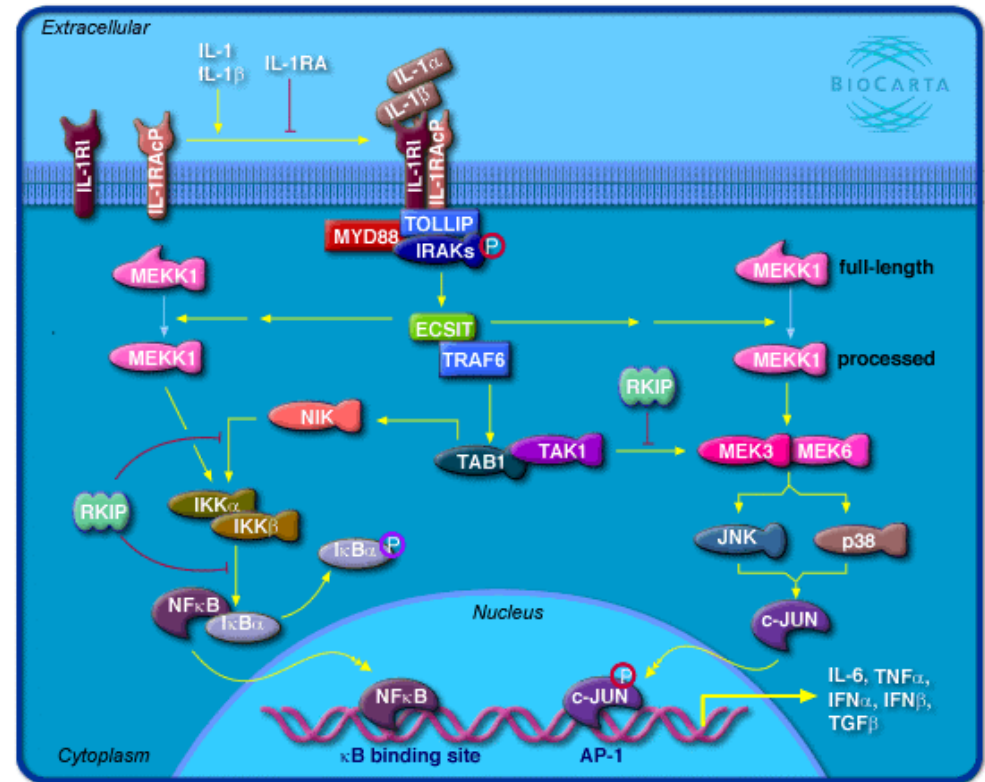
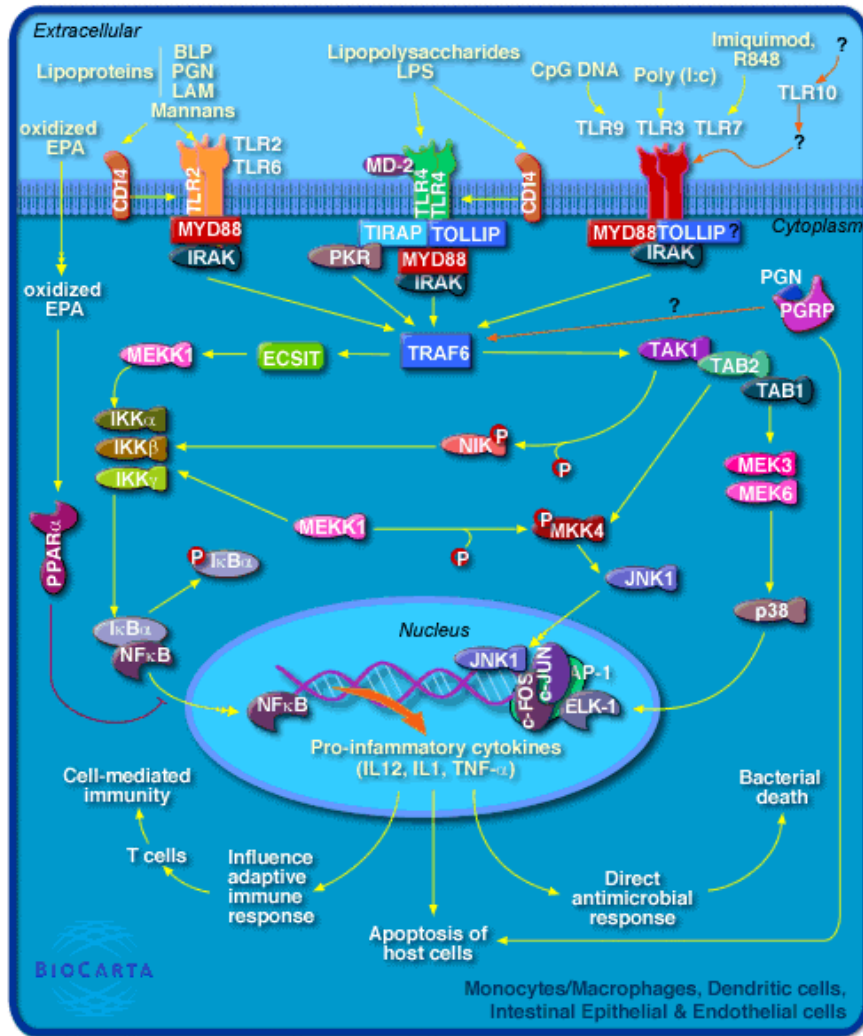
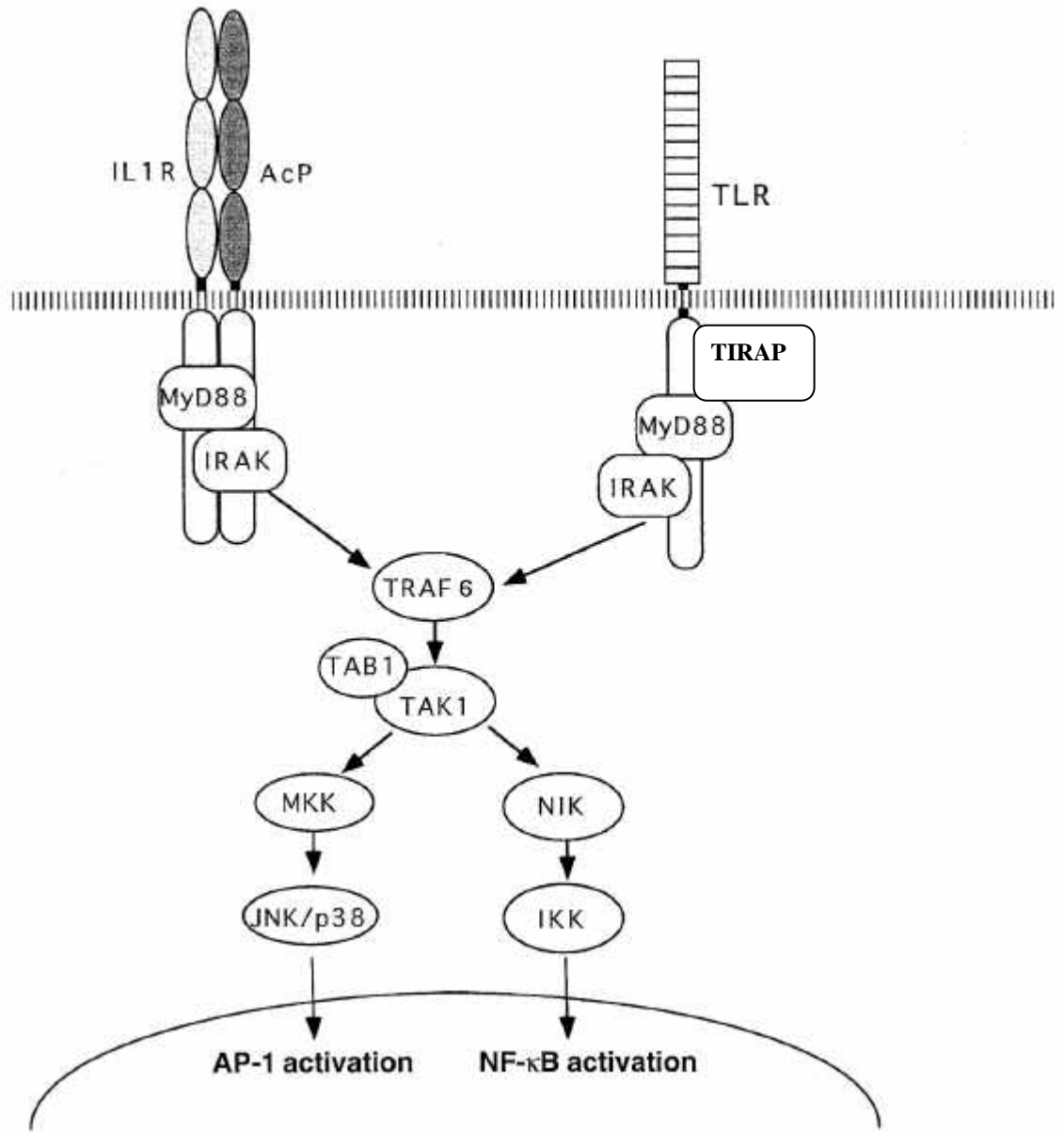


*Differences and similarities
in interleukin signalling
pathways*

IL-1 and TLR pathways



<i>Similarities</i>	<i>Differences</i>
IRAK4	IL-1R ACP
TRAF 6	TIRAP



AcP/CD14

IL-1R Accessory protein (AcP)

Found in IL-1 pathway associated with receptor

Not found in TLR pathway – there are other accessory proteins used e.g CD14

AcP found in mouse and man, no drosophila homologue

Both IL-1R and IL-1RAcP required for signal transduction

Lack of co-receptor results in non-responsiveness to IL-1

AcP has two isoforms – membrane bound and secretory

IL-1R domains

Extracellular – 3 Immunoglobulin domains

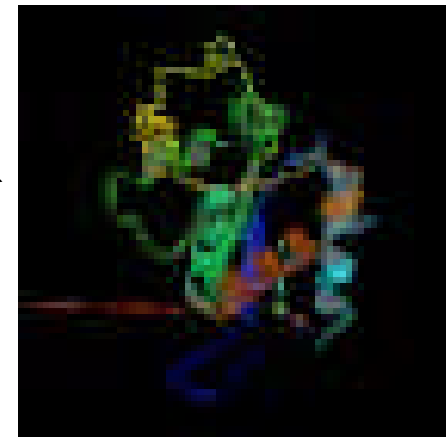
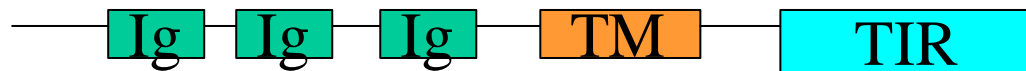
Single span transmembrane domain

Intracellular – Toll/Interleukin-1 Receptor (TIR) domain

Soluble form



Membrane form

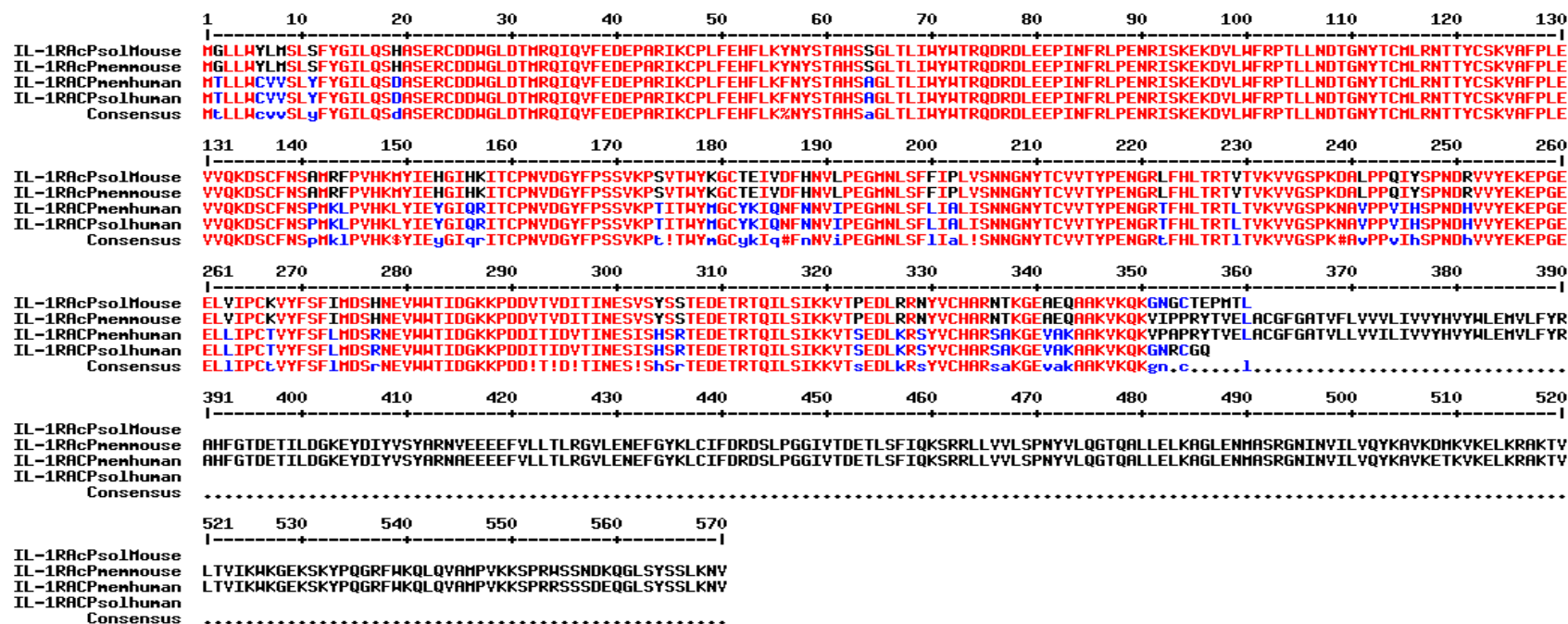


Crystal structure TIR domain from TLR2

Protein sequence alignment of AcP

Mouse and human

Membrane and soluble



Tirap

Tirap functions as an adapter protein
used by TLR4 but not by TLR9 and IL-1R.

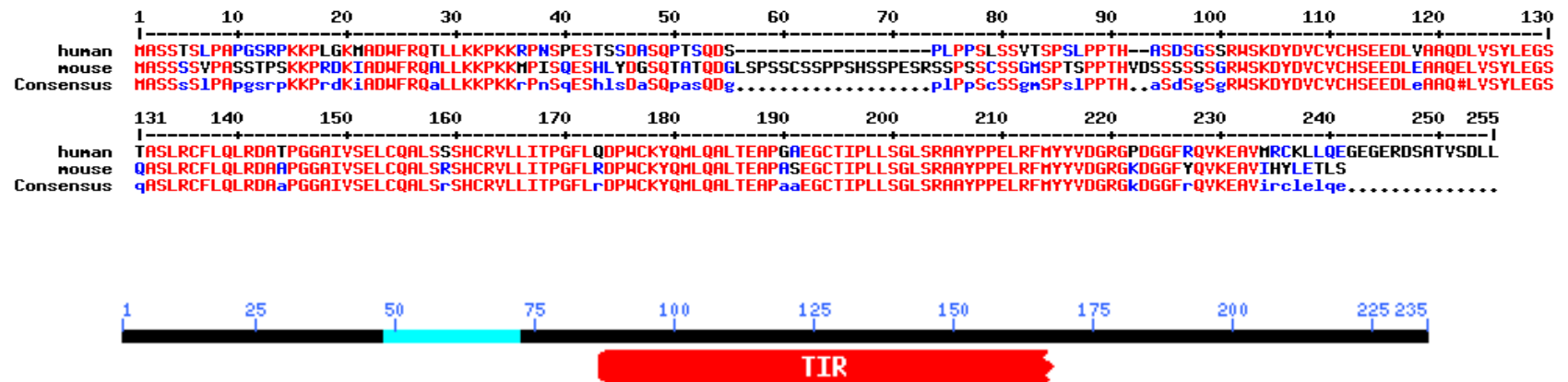
Found in mouse and human.

Tirap Cds alignment

	1	10	20	30	40	50	60	70	80	90	100	110	120	130
mouse	CAGCGTGGAG--CCGCGTAGACTTTAA--GAARCAATATCAACAGCATA--CCGAARACAGAT--CCCGAGTCC--TACCAAGCCA-CTTTTCACAGGC--TTTCTTGTATACCTGCATCCAG													
human	GGGCGCGCAGTCCCGCGCAGCCCTCATCGCAACTGGGCCCGCGCGCAGATCCACCARRAGAGAAAGCAGCCCTGTGCCAGTGTCTTGCCAGCCTTTACAGGAGAAAGTGTCACTGAAATACTACAGCCCC													
Consensus	caGCGcGcAG.CCGCGGaaaCccTAA..GaARCAagacCaaCcaGCAgA..CCaaaAaAcAGAA.....CCCGaggCC...TaCcaagCCA.CcTTTCACAGGa....TgTCacgaGaAaCTaCagCCac													
mouse	131	140	150	160	170	180	190	200	210	220	230	240	250	260
human	AACAGTAACT--CTATATGGAGACACCAAGACCTAGGAAAGACTGTGAGGGCCATGGTCAGCAGGAGGTGCARACCCATGCCAATCTACC TGGA--ATCGGCTGTCTTACCCATTTTATGACT--TTGTT													
Consensus	aACAGgaac.T.CTAcAcAGAAACacaAaG..CT.GaAAAGTGTccaalicacCAgGGaCAgCagcaGgcaCaRaaccagGaAAaAcAcATGga.....ATaGGaaGTCcTcaAaAgagaTgaCT..ccagc													
mouse	261	270	280	290	300	310	320	330	340	350	360	370	380	390
human	TGCCTAGCTGACGGATCTCAAAATGCCCTCCCTGGCCAGGTGAAAGCGGAAACAAATCGCTC--TACCAAGTTCATACCTTGATGGCTGATCCATGAAATTCAGACTGGATCTCTTCTCTCCCGCC													
Consensus	TGCCCTTCC--CCAGATCCGAATATCTCTCGCCAGGTGGAGCAGAAACAGTTCCTCAGCTGGTCATGCTGAGCTCATACCTTGATGGCTGCTCCATGAGTCAAGACTGGGCTCTCTCCCTCTCC													
mouse	391	400	410	420	430	440	450	460	470	480	490	500	510	520
human	GTTCGCCAATGCCCTGCTCTTTCAATGGTTAGTTTGGAGGCCCTGCACTATGGCTCATCTCTCCGCTCCAGCCTCCCTCCACTCCGCTCCAGAAAGCCTCAGACCAAGATAGCTGACTGGTTCAATGGTTCC													
Consensus	ccTTCACCAATGCCCTGCTCTTcaCagGGcTAGTTTgGAGccCcaCaCTATGGCaTcATCCCTCCcTCCAGCccCcgcaCTCcGcCaRAGAAAGCCTcAGaCAAGATaGCTGGTTCaAgcagC													
mouse	521	530	540	550	560	570	580	590	600	610	620	630	640	650
human	ACAGA--CAGCCACACAGGATG--GTCTCTACCCCTCGACTCGAGCTC--ACCCCGAGTACAGATTACCC--CGAGAGCCCGTAGCTC--ACCCTCGAGCTGCAAGTTCAGGAATGTCACCTACCTGCCCACCA													
Consensus	aCaGa..aAGaaaCaCAAGaG.GGcCcAaaacCCcCaaaaaGCAcTc..CcCaagGagTcACAGcccACC..CaaaaGaCagacCaC..ACCcCaAGCcgCAGcTCAGgaAcGTCaCCcAcCccGCCACCa													
mouse	651	660	670	680	690	700	710	720	730	740	750	760	770	780
human	ACACACGTGGACAGCAGCAGCAGCAGCAGTGGCCGCTGGAGCAAAAGACTCGATGCTGCGTGTGCCACAGTGAAGAGGAACTTGGAGGCGCCCAAGAGCTGGTCTCTTACTTGGAGGGCAGCACTGCCA													
Consensus	ACACAcGcGgACAGcAGcAGcAGcAGTgGcCcGcTGGAGcAAAGAcTcGATgCTGcGtGTGCCAcAGTgAAGAGgAAcTtGGAGgCGCCaAGAGcTGGtCTcTtAcTtGGAGggcCAGcAcTgCCa													
mouse	781	790	800	810	820	830	840	850	860	870	880	890	900	910
human	GTCTACGCTGCTTCTCGCACTTCGGATGCAAGCCCGG--TCATCACTCCAGGCTTCTCTGGGACCCCTG													
Consensus	GcCTaCGCTGCTTCTCGCAcCTcCGGATGCAaCCcCaGcGGCGCTATAGTGTCCGAGCTGTGCCAGGCAC TGAGCAGTACTGCTCCGGGTGCTGCTCATCAGcCGGGCTTCTCTcAGGACCCCTG													
mouse	911	920	930	940	950	960	970	980	990	1000	1010	1020	1030	1040
human	GTGCAGTACCCAGATGCTGCAGGCCCTGACGGAGGCCCGGGCTCGAGGGGTTGCACCATACCCCTGCTGTCCGGCCCTGCAGAGCCGCCTACCCGCCGAATCCCGATTCTATGTGTGGATGGC													
Consensus	GTGCAGTACCCAGATGCTGCAGGCCCTGACcGAGGcTCCAGGGcCGAGGGcTGcACcATcCCcCTGcTGTcGGCCcTcAGcAGAGcTGCcTAcCCcCTGAGcTCCGATtCATGTACTACTcGTcGATGGc													
mouse	1041	1050	1060	1070	1080	1090	1100	1110	1120	1130	1140	1150	1160	1170
human	AGAGGCARGGACGGAGGCTTTTACCAAGTCAAGGAGGCTGTATACACTATCTGGAGACACTAAGCTGACACTTGGGCTTTCATTAAGAAAGCTGGGAATAGCTCACAGCAGTCAATTAATCCAGTATATA													
Consensus	AGAGGcAagGAcGGaGGcTTTcAcCAAGTCAAGaAGcGTGTcATAcAcTaTa..AGAcACTA..CAgGAGGG..AGAGGGGAAcGGGATTCAGCTA..CAGTATCTGATCTACTTTG-A													
mouse	1171	1180	1190	1200	1210	1220	1230	1240	1250	1260	1270	1280	1290	1300
human	CAGCAGGCCAGAGCCAGCTGCAACCTGTATTATGACACAGATCAGATTCGCACAGCTTCCATTATCTGGGCCCAAGATGGCCAGGCTGAGATGGGAACCCCCCGCAGGGAGACCAGGARGAA													
Consensus	CagcaaaGacAcAGCC..CTGAcCCTagTa.....GaTCAaAGcG..CAGCTTCgagaAaaGccgGc..CCACAGATGGCCAGGCTGAGATGGGAACCCcCGcAGGGAGAcCCAGGARGAA													
mouse	1301	1310	1320	1330	1340	1350	1360	1370	1380	1390	1400	1410	1420	1430
human	GATGGGGACTCCCCAGAGGGGCGAGGAGGAGCCAGGGACTCCCCAGGAGAGCACAGGAGAGTCAAGAAATTCAGATTGTTCAGGGGACTGTGCTATCGGGAGGCTCAGCAGTGTCCCTCTCGCTGAA													
Consensus													
mouse	1431	1440	1450	1460	1470	1479								
human	CTGGATAGGAAGCTGATACATGGCTGTCTTCTCTCTGGCATCAGGCA													
Consensus													

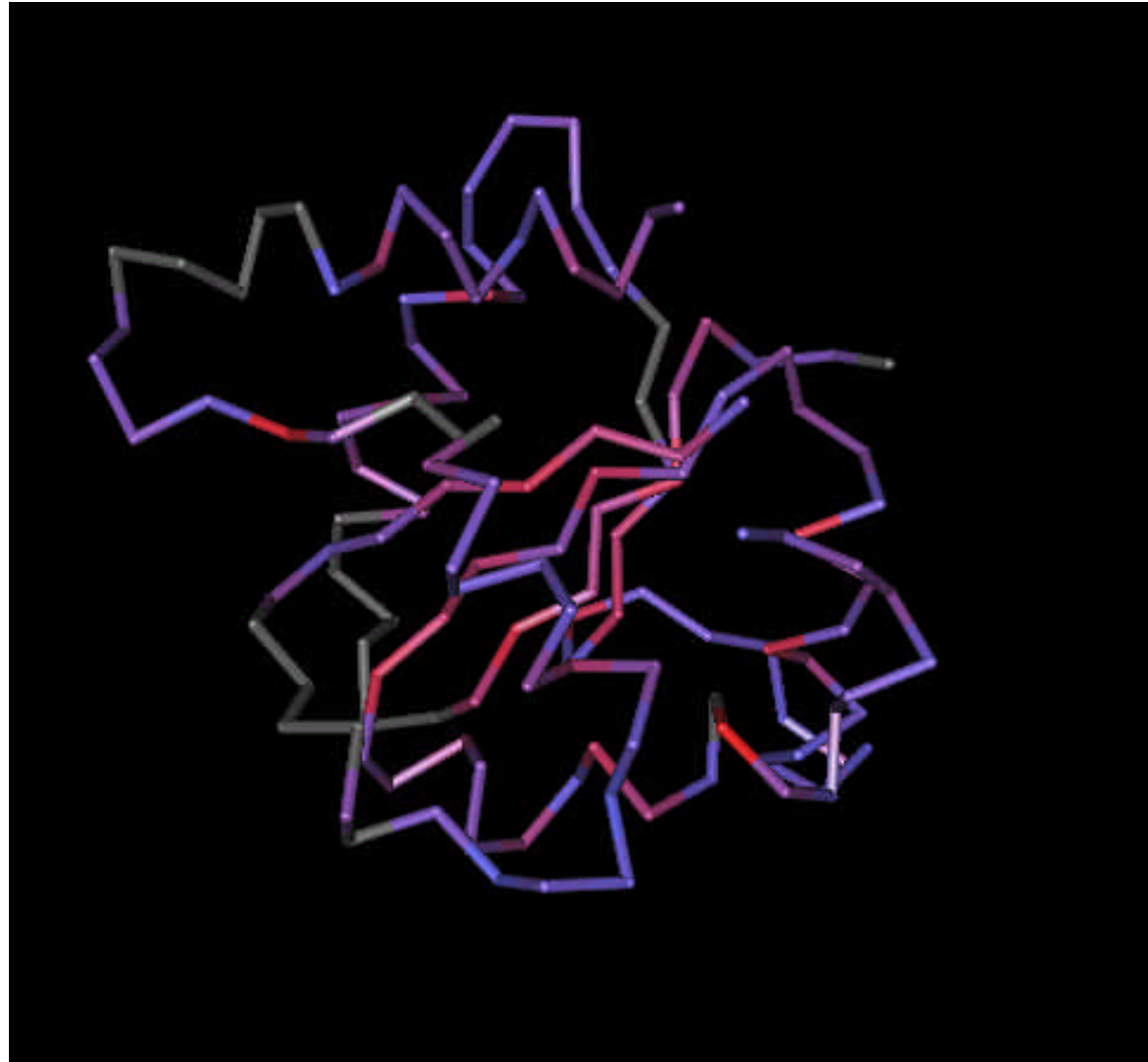
Percentage of homology : 86% for tir domain

Protein alignment



Tir (Toll-IL-1R) is a conserved domain in human and mouse tirap

3D structure of tir domain



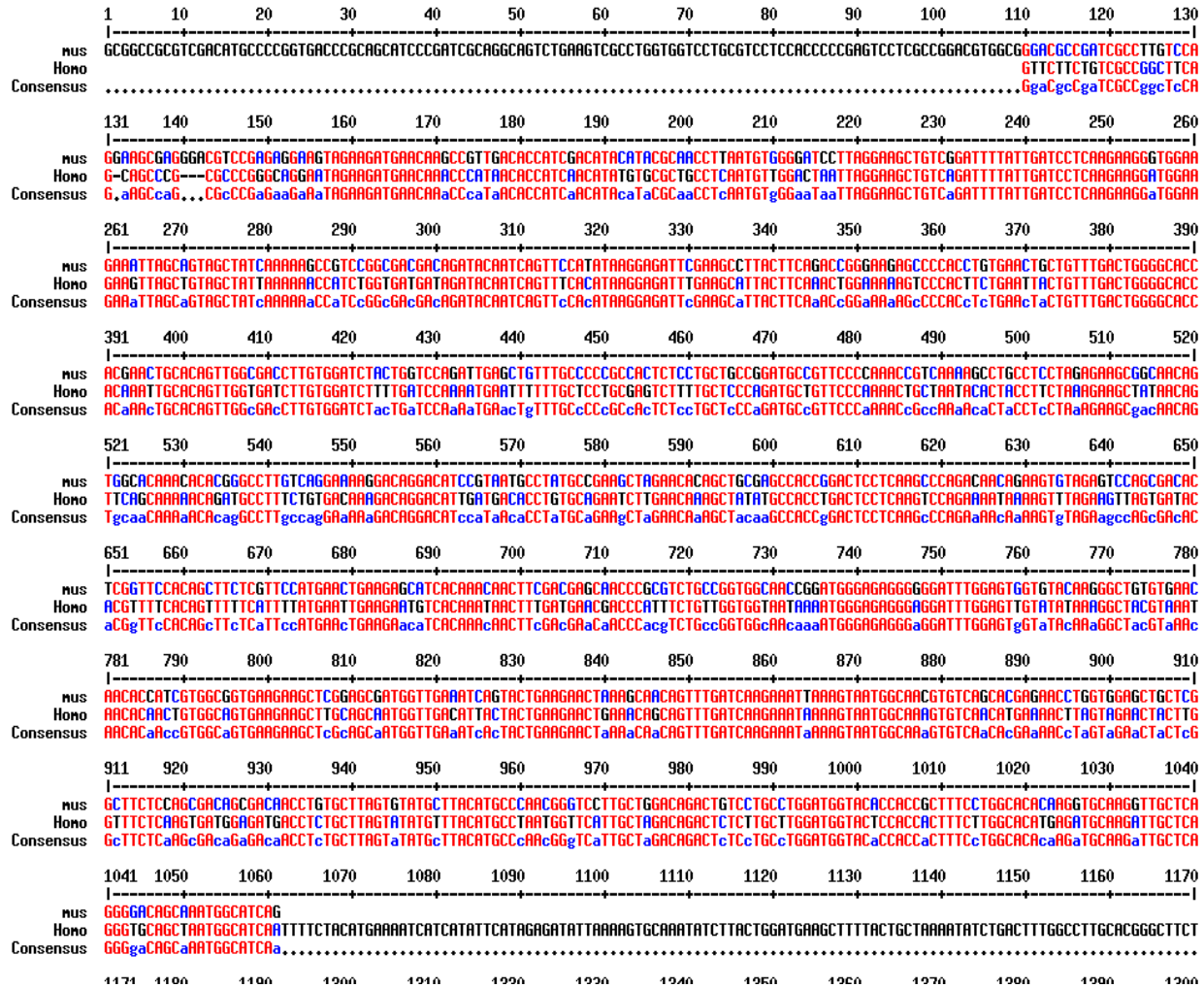
IRAK 4

Interleukin-1 (IL-1) receptor-associated kinases (**IRAKs: IRAK-1, IRAK-4, IRAK-2, IRAK-M**) are central components of Toll/IL-1 receptor (TIR) signaling pathways.

IRAKs mediate activation of nuclear factor-kappaB (NF-kappaB) and mitogen-activated protein kinase (MAPK) pathways.

Found in mouse and human.

IRAK 4 mRNA *Mus musculus/Homo sapiens*



90% homology

IRAK 4 protein *Mus musculus/Homo sapiens*

1 10 20 30 40 50 60 70 80 90 100 110 120 130

|-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+-----|

6 LFDWGTNCTVGDLYDLLIQNEFFAPASLLLPOAVPKTANTLPSKEAITVQQKMPFCOKORTLHTPYQNLQSYMPDSSSPENKSLVSDTRFHSFSFYELKNVTNMFDERPISVGGNKMGEGGFVY

2 LFDWGTNCTVGDLYDLLYQIELFAPATLLLPOAVPQTVKSLPPREARTVAQTHGPCQEKORTSYMPKLEHSCEPPDSSSPDNRVSSDTRFHSFSFHELKSTITNMFDEQPSAGGNRMGEGGFVY

Consensus LFDWGTNCTVGDLYDLL!QnEIFAPASLLLPOAVPqTansLPprEAaTYaQkqgPcc#KORTLnmPnqnLEqScePPDSSSP#NrSIEsSDTRFHSFSFhELKn!TNMFDErPaSaGGNRMGEGGFVY

131 140 150 160 170 180 190 200 210 220 230 240 250 260

|-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+-----|

6 YKGYVNTTIVAVKKLAAAMYDITTEELKQQFDQEIKVMKCOHENLVELLGFSSDGDCLVYYMPNGSLDRLSCLDGTPLSWNRCKIAQGAANGINFLHENHHIHRDIKSANILLDEAFTAKISDF

2 YKGCYVNTTIVAVKKLGAAYEISTEELKQQFDQEIKVMATCOHENLVELLGFSSDSDNCLVYYMPNGSLDRLSCLDGTPLSWNRCKVAQGTANGIRFLHENHHIHRDIKSANILLDKDFTAKISDF

Consensus YKGCvNNTiVAVKLaAMV#IsTEELKQQFDQEIKVMkCOHENLVELLGFSSDgD#LCLVYaYMPNGSLDRLSCLDGTPLSWnrCK!AQGaANGIrFLHENHHIHRDIKSANILLDeaF TAKISDF

261 270 280 290 300 310 320 330 340 350 360 370 380 390

|-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+-----|

6 GLARASEKFAQTYMTRIVGTTAYMAPEALRGEITPKSDIYSFGVYVLELITGLPAYDENREPQLLDIKEEIEDEEKTIEDYIDKKNNDADSTVSEAMYSVASQCLHEKKNRPPDIKKYQQLQEMTAS

2 GLARASARLAQTYMTRIVGTTAYMAPEALRGEITPKSDIYSFGVYVLELITGLRAYDENREPQLLDIKEEIEDEEKTIEDYIDEKMSDADPASVEAMYSASQCLHEKKNRPPDIKKYQQLQEMSA

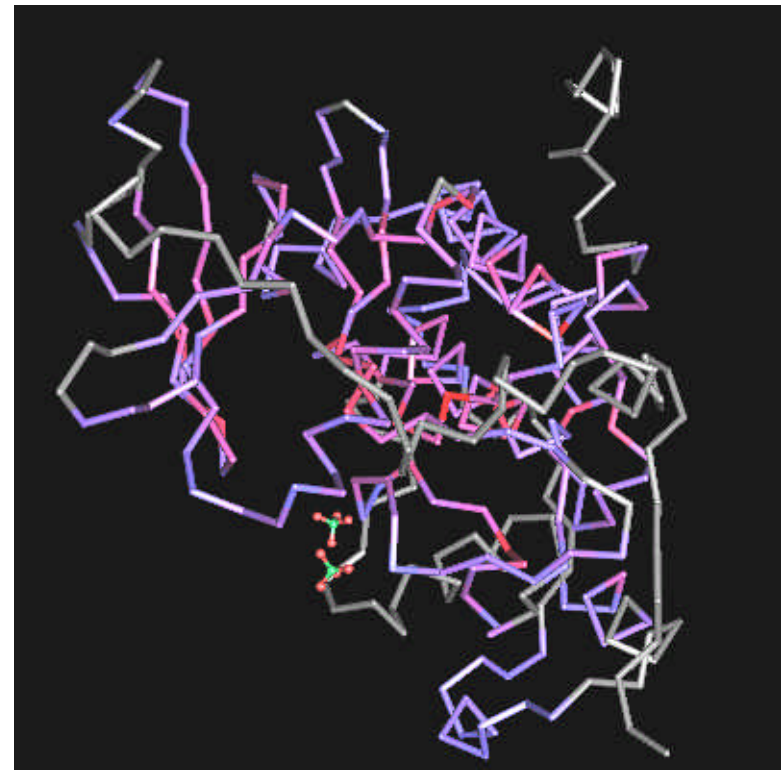
Consensus GLARASarLAQTYMTRIVGTTAYMAPEALRGEITPKSDIYSFGVYVLEiITGLaAYDENREPQLLDIKEEIEDEEKTIEDYideKknDADpaSVEAMYSaASQCLHEKKNrPPDIaKYQQLQEMsa,



p kinase domain



	1	10	20	30	40	50	60	70	80	90	100	110	120	130
pk	----- ----- ----- ----- ----- ----- ----- ----- ----- ----- ----- ----- ----- ----- -----													
kinase	M N K P L T P S T Y I R N L N Y G I L R K L S D F I D P Q E G W K L L A V A I K K P S G D D R Y N Q F H I R R F E A L L Q T G K S P T C E L L F D W G T T N C T Y G D L V D L L V Q I E L F A P A T L L L P D A V P Q T Y K S L P P R E A R T Y A Q T H G P C Q E K													
mus	M N K P L T P S T Y I R N L N Y G I L R K L S D F I D P Q E G W K L L A V A I K K P S G D D R Y N Q F H I R R F E A L L Q T G K S P T C E L L F D W G T T N C T Y G D L V D L L V Q I E L F A P A T L L L P D A V P Q T Y K S L P P R E A R T Y A Q T H G P C Q E K													
Consensus													
	131	140	150	160	170	180	190	200	210	220	230	240	250	260
pk	----- ----- ----- ----- ----- ----- ----- ----- ----- ----- ----- ----- ----- -----													
kinase	D R T S V N P M P K L E H S C P P D S S P D N R S V E S S D T R F H S F S F H E L K S I T N N F D E Q P A S A G G N R M G E G G F G V Y Y K G C Y N N T I V A Y K K L G A N V E I S T E E L K Q F D Q E I K Y M A T C Q H E N L Y E L L G F S S D S D N L C L													
mus	D R T S V N P M P K L E H S C P P D S S P D N R S V E S S D T R F H S F S F H E L K S I T N N F D E Q P A S A G G N R M G E G G F G V Y Y K G C Y N N T I V A Y K K L G A N V E I S T E E L K Q F D Q E I K Y M A T C Q H E N L Y E L L G F S S D S D N L C L													
Consensus													
	261	270	280	290	300	310	320	330	340	350	360	370	380	390
pk	----- ----- ----- ----- ----- ----- ----- ----- ----- ----- ----- ----- ----- -----													
kinase	Y Y A Y M P N G S L L D R L S C L D G T P P L S W A T R C K Y A Q G T A N G I R F L H E N A H I H R D I K S A N I L L K D F T A K I S D F G L A R A S A R L A Q T V M T S R I V G T T A Y M A P E A L R G E I T P K S D I Y S F G V Y L L E L I T G L A A Y D E N													
mus	Y Y A Y M P N G S L L D R L S C L D G T P P L S W A T R C K Y A Q G T A N G I R F L H E N A H I H R D I K S A N I L L K D F T A K I S D F G L A R A S A R L A Q T V M T S R I V G T T A Y M A P E A L R G E I T P K S D I Y S F G V Y L L E L I T G L A A Y D E N													
Consensus	Y Y A Y M P N G S L L D R L S C L D G T P P L S W A T R C K Y A Q G T A N G I R F L H E N A H I H R D I K S A N I L L K D F T A K I S D F G L A R A S A R L A Q T V M T S R I V G T T A Y M A P E A L R G E I T P K S D I Y S F G V Y L L E L I T G L A A Y D E N													
	391	400	410	420	430	440	450	459						
pk	----- ----- ----- ----- ----- ----- ----- ----- -----													
kinase	R E P Q L L L D I K E E T E D E E K T I E D Y T D E K M S D A D P A S V E A M Y S A R S Q C L H E K K N R R P D I A K Y Q L L Q													
mus	R E P Q L L L D I K E E T E D E E K T I E D Y T D E K M S D A D P A S V E A M Y S A R S Q C L H E K K N R R P D I A K Y Q L L Q E M S A													
Consensus	R E P Q L L L D I K E E T E D E E K T I E D Y T D E K M S D A D P A S V E A M Y S A R S Q C L H E K K N R R P D I A K Y Q L L Q , . . .													



TRAF 6 DNA ANALYSIS

- Found in both pathways.
- Comparison of human, mouse, and *Drosophila*.
- Began with cDNA clones then found ORFs.
- Used both Multalin and NCBI pairwise blast.

Summary Of Results Search

- 86% homology between human and mouse.
- No homology between human and drosophila.
- No homology between mouse and drosophila.

Other searches

- Human Genome search to find promoter sequence using ENSEMBL (better than NCBI apparently!).
- Restriction Enzyme map using webcutter.
- Transcription factor search using TESS.

Results

- Both maps give several possible RE or TF sites – too much data!
- To use successfully you need an idea of what you are looking for!

Protein Comparison of mouse, human and drosophila sequence



Conserved sequences of TRAF6

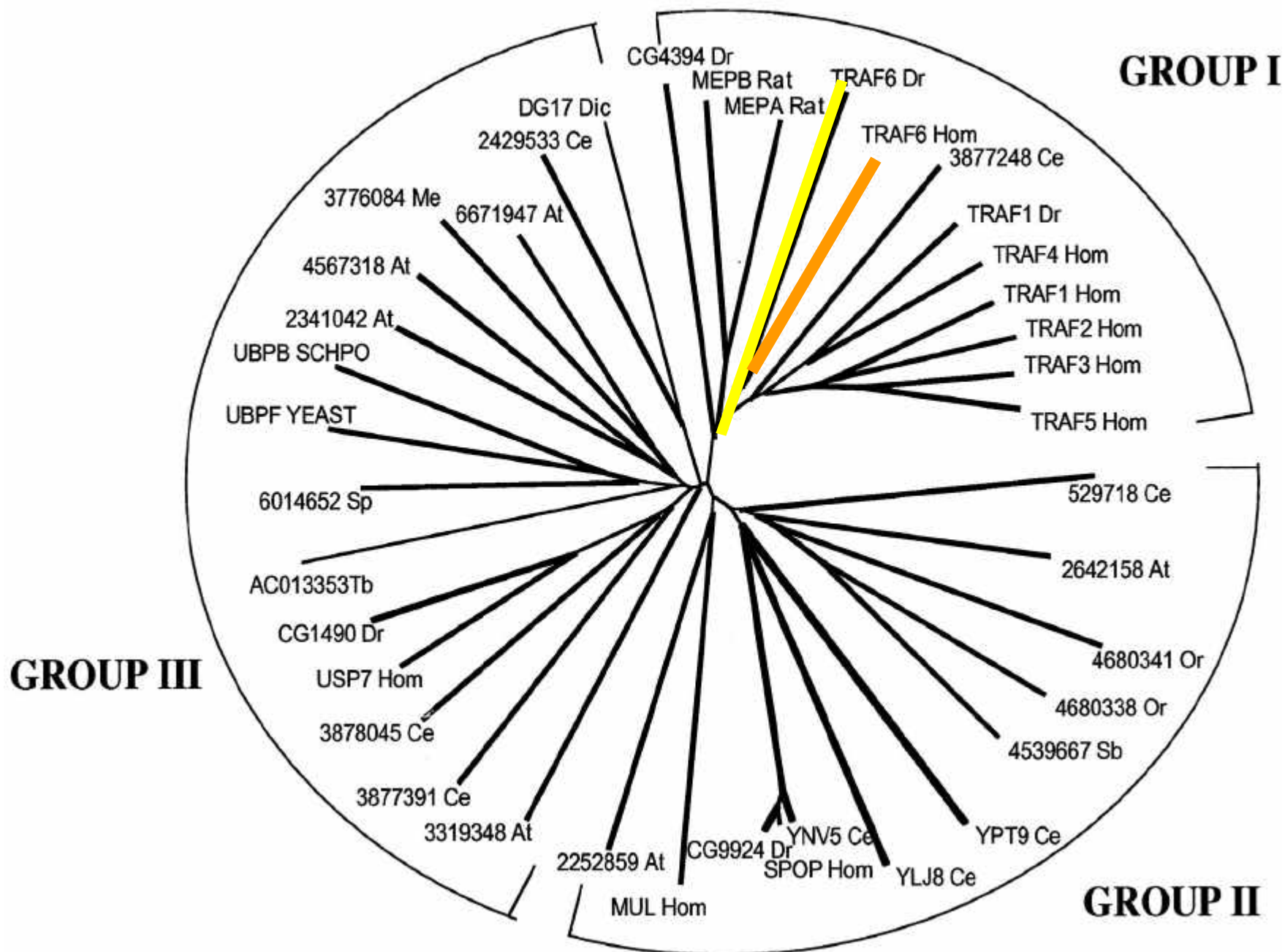
	1	10	20	30	40	50	60	70	80	90	100	110	120																																																																																																														
TRAF_HUMAN					M	S	L	L	N	C	E	N	S	C	G	S	S	S	S	S	D	C	C	V	A	M	A	S	S	C	S	A	Y	T	K	D	D	S	V	G	G	T	A	S	T	G	-----	N	L	S	S	S	F	M	E	E	I	Q	G	Y	D	V	E	F	D	P	P	L	E	S	K	Y	E	C	P	I	C	L	M	A	L	R	E	A	V	Q	T	P	C	G	H	R	F	C	K																												
TRAF_MOUSE					M	S	L	L	N	C	E	N	S	C	G	S	S	S	S	S	D	C	C	A	M	A	S	S	C	S	A	Y	T	K	D	D	S	V	S	G	S	A	S	T	G	-----	N	L	S	S	S	F	M	E	E	I	Q	G	Y	D	V	E	F	D	P	P	L	E	S	K	Y	E	C	P	I	C	L	M	A	L	R	E	A	V	Q	T	P	C	G	H	R	F	C	K																													
Drosophila	M	Q	R	V	Q	A	D	Q	K	P	A	R	M	H	Q	A	H	T	H	S	A	H	S	L	Q	H	A	E	E	K	H	N	S	E	M	T	T	N	L	S	S	T	G	R	I	A	A	G	S	S	A	T	P	S	A	Q	R	E	G	G	A	S	G	D	P	T	P	P	K	S	L	A	N	Q	N	H	Y	A	P	G	S	D	T	S	G	E	Q	E	E	L	L	D	S	R	Y	E	C	A	I	C	I	D	L	N	E	P	V	L	T	S	C	G	H	R	F	C	R						
Consensus	m	s	l	l	n	c	e	n	s	c	g	s	s	s	s	s	d	c	c	a	m	a	s	s	c	s	a	y	t	k	d	d	s	v	s	g	s	a	s	t	g	-----	n	l	s	s	s	f	m	e	e	i	q	g	y	d	v	e	f	d	p	p	l	e	s	k	y	e	c	p	i	c	l	m	a	l	r	e	a	v	q	t	p	c	g	h	r	f	c	k																													
	131	140	150	160	170	180	190	200	210	220	230	240	250																																																																																																														
TRAF_HUMAN	S	I	R	D	A	G	H	K	C	P	V	D	N	E	I	L	-	L	E	N	Q	L	F	P	D	N	F	A	K	R	E	I	L	S	L	M	V	K	C	P	N	K	G	C	L	K	H	M	E	L	R	H	L	E	D	H	Q	A	H	C	F	A	L	M	D	C	P	Q	C	R	P	F	Q	K	F	H	I	N	T	H	I	L	K	D	C	P	R	R	Q	V	S	C	D	N	C	A	S	H	A	F	E	D	K	E	I	H	D	Q	N	C	P	L	A	N	V	I	C	E	Y	C	N	T	
TRAF_MOUSE	S	I	R	D	A	G	H	K	C	P	V	D	N	E	I	L	-	L	E	N	Q	L	F	P	D	N	F	A	K	R	E	I	L	S	L	T	V	K	C	P	N	K	G	C	L	K	H	M	E	L	R	H	L	E	D	H	Q	V	H	C	F	A	L	V	N	C	P	Q	C	R	P	F	Q	K	C	Q	V	N	T	H	I	E	D	C	P	R	R	Q	V	S	C	V	N	C	A	V	S	H	A	F	E	E	K	E	I	H	D	Q	N	C	P	L	A	N	V	I	C	E	Y	C	G	T	
Drosophila	M	Q	R	V	Q	A	D	Q	K	P	A	R	M	H	Q	A	H	T	H	S	A	H	S	L	S	A	E	H	D	I	F	P	D	N	Y	T	R	R	E	I	E	Q	L	K	R	D	C	P	N	S	-----	L	G	C	S	V	V	A	S	P	I	E	-----	L	H	R	H	-	L	P	S	C	P	Y	R	-----	Q	Q	E	P	Q	E	E	K	C	P	F	A	K	I	K	C	D	F	V	G	R																										
Consensus	s	i	r	d	a	g	h	k	c	p	v	d	n	e	i	l	-	l	e	n	q	l	f	p	d	n	f	a	k	r	e	i	l	s	l	m	v	k	c	p	n	k	g	c	l	k	h	m	e	l	r	h	l	e	d	h	q	v	h	c	f	a	l	..	c	p	q	c	r	p	f	q	k	..	n	h	i	l	d	c	p	r	q	v	s	c	n	a	s	h	a	f	e	d	k	e	i	h	d	q	n	c	p	l	a	n	v	i	c	e	y	c	n	t									
	261	270	280	290	300	310	320	330	340	350	360	370	380																																																																																																														
TRAF_HUMAN	Q	M	P	N	H	Y	D	L	D	C	P	T	A	P	I	P	C	T	F	S	T	F	G	C	H	E	K	M	Q	R	N	H	L	A	R	H	L	Q	E	N	T	Q	S	H	R	M	L	A	Q	A	V	H	S	L	S	V	I	-----	P	D	S	G	Y	I	S	E	V	R	N	F	Q	E	T	I	H	Q	L	E	G	R	L	Y	R	Q	D	H	Q	I	R	E	L	T	A	K	M	E	T	Q	S	M	Y	S	E	L	K	R	T	I	R	T	L	E	D	K	V	A							
TRAF_MOUSE	Q	M	P	N	H	Y	D	L	D	C	P	T	A	P	I	P	C	T	F	S	T	F	G	C	H	Q	M	Q	R	N	H	L	A	R	H	L	Q	E	N	T	Q	L	H	M	R	L	L	A	Q	A	V	H	N	V	N	L	A	R	P	C	D	A	A	S	S	R	G	R	C	P	E	D	P	N	Y	E	T	I	K	Q	L	E	S	R	L	Y	R	Q	D	H	Q	I	R	E	L	T	A	K	M	E	T	Q	S	M	Y	S	E	L	K	R	T	I	R	T	L	E	D	K	V	A			
Drosophila	Q	L	E	E	H	L	K	A	D	M	P	H	-----	H	M	Q	L	Q	A	F	Q	T	A	I	A	T	M	Q	P	H	K	P	S	T	S	G	A	V	E	N	G	-----	H	G	Q	Q	L	P	P	P	P	P	Y	A	N	G	V	D	E	Q	I	V	Q	T	M	Y	-----	R	I	V	V	L	E	Q	R	T	R	E	Q	E	T	R	L	E	N	H	Q	Q	L	R	-	L	A	R	Q	A																											
Consensus	q	#	p	#	h	y	d	l	d	c	p	t	a	p	i	p	c	t	f	s	t	f	g	c	h	.k	#	q	r	#	h	l	a	r	h	l	q	e	n	t	q	s	h	r	m	l	a	q	a	v	h	s	l	s	v	i	-----	p	..	g	..	p	e	.pn	%	.#	t	!.	#	l	e	.r	l	v	r	q	d	h	q	i	r	e	l	t	a	k	m	e	t	q	s	m	y	s	e	l	k	r	t	i	r	t	l	e	d	k	v	a															
	391	400	410	420	430	440	450	460	470	480	490	500	510																																																																																																														
TRAF_HUMAN	Q	C	N	G	I	Y	I	N	K	I	G	N	F	G	M	H	L	K	Q	E	E	E	K	P	V	V	I	H	S	P	G	F	Y	T	G	K	P	G	Y	K	L	C	M	R	L	H	L	Q	L	P	T	A	Q	R	C	A	N	Y	I	S	L	F	V	H	T	M	Q	E	Y	D	S	H	L	P	H	P	F	Q	T	I	R	L	T	I	L	D	Q	S	E	A	P	Y	R	Q	N	H	E	E	I	M	D	A	K	P	E	L	L	A	F	Q	R	P	T	I	P	R	N	P	K	G	F	G	
TRAF_MOUSE	Q	C	N	G	I	Y	I	N	K	I	G	N	F	G	M	H	L	K	S	Q	E	E	E	R	P	V	V	I	H	S	P	G	F	Y	T	G	R	P	G	Y	K	L	C	M	R	L	H	L	Q	L	P	T	A	Q	R	C	A	N	Y	I	S	L	F	V	H	T	M	Q	E	Y	D	S	H	L	P	H	P	F	Q	T	I	R	L	T	I	L	D	Q	S	E	A	P	Y	R	Q	N	H	E	E	I	M	D	A	K	P	E	L	L	A	F	Q	R	P	T	I	P	R	N	P	K	G	F	G
Drosophila	Y	S	N	G	T	I	V	W	R	I	E	Q	L	G	A	L	V	A	R	L	R	A	N	N	Q	V	S	H	E	C	Y	T	S	P	H	G	Y	K	F	C	A	R	L	N	I	Q	-----	P	R	K	P	H	V	L	M	Q	S	E	N	D	Y	H	L	D	M	P	F	G	R	I	K	L	C	M	V	H	P	A	D	A	T	L	S	Q	-	H	D	T	I	M	-	T	K	P	E	L	A	F	H	K	P	R	E	A	I	S	T	R	G	F	G												
Consensus	q	c	n	g	i	y	i	n	k	i	g	n	f	g	m	h	l	k	.q	e	e	e	.k	p	v	v	i	h	s	p	g	f	y	t	g	k	p	g	y	k	l	c	m	r	l	h	l	q	l	p	t	a	q	r	c	a	n	y	i	s	l	f	v	h	t	m	q	e	y	d	s	h	l	p	h	p	f	q	t	i	r	l	t	i	l	d	q	s	e	a	p	y	r	q	n	h	e	e	i	m	d	a	k	p	e	l	a	f	q	r	p	t	i	p	r	n	p	k	g	f	g		
	521	530	540	550	560	565																																																																																																																					
TRAF_HUMAN	H	L	E	A	L	R	Q	R	T	F	I	K	D	D	T	L	L	Y	R	C	E	V	S	T	R	F	D	M	G	L	R	R	E	G	F	Q	R	S	T	D	A	G	V																																																																																
TRAF_MOUSE	H	L</																																																																																																																									

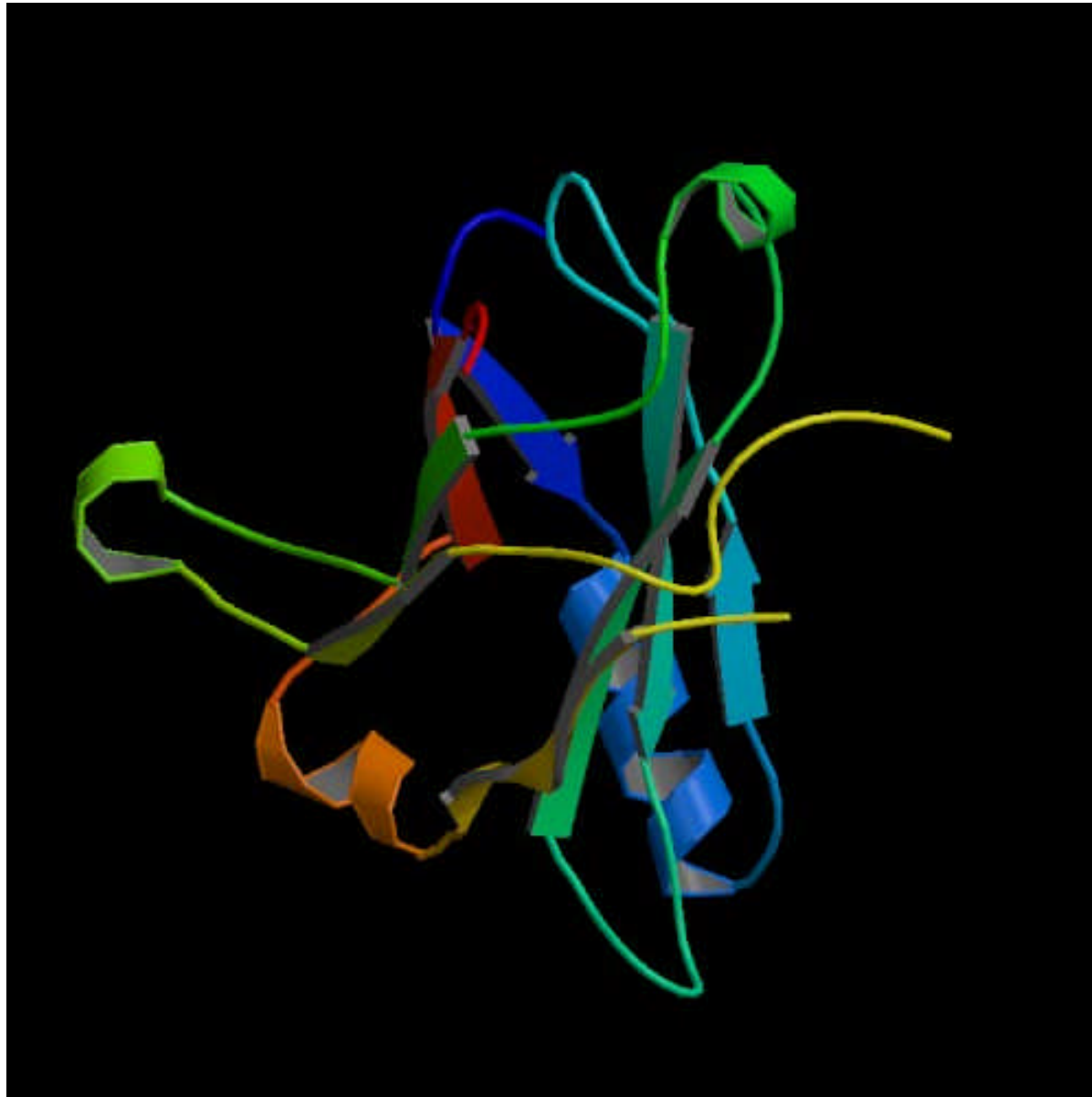
Mouse and human comparison

	1	10	20	30	40	50	60	70	80	90	100	110	120	130
	-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+-----													
TRAGHUMAN	MSLLNCENSCGSSQSESDCCVAMASSCSAVTKDDSVGGTASTGNLSSSFMEIQGYDVEFDPPLESKYECPICLMALREAVQTPCGHRFCACIKSIRDAGHKCPVDMEILLENQLFPDNFAKREILSL													
TRAGMOUSE	MSLLNCENSCGSSQSSDCCAAHAASCSAAVTKDDSVSGSASTGNLSSSFMEIQGYDVEFDPPLESKYECPICLMALREAVQTPCGHRFCACIKSIRDAGHKCPVDMEILLENQLFPDNFAKREILSL													
Consensus	MSLLNCENSCGSSQSeSDCCaAMAaSCSAatKDDSVgGsASTGNLSSSFMEIQGYDVEFDPPLESKYECPICLMALREAVQTPCGHRFCACIKSIRDAGHKCPVDMEILLENQLFPDNFAKREILSL													
	131	140	150	160	170	180	190	200	210	220	230	240	250	260
	-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+-----													
TRAGHUMAN	MYKCPNEGCLHKMELRHLEDHQAHCEFALMDCPQCQRPFQKFHINTIHLKDCPRRQVSCDNCAASMAFEDKEIHDQNCPLANVICEYCNILIREQMPNHYDLDCPTAPIPCTFSTFGCHEKMQRNHLAR													
TRAGMOUSE	TYKCPNKGCLQKMELRHLEDHQVHCEFALVNCPCQRPFQKCVNTHIIEDCPRRQVSCVNCAYSMAYEEKEIHDQSCPLANIICEYCGTILIREQMPNHYDLDCPTAPIPCTFSVFGCHQKMQRNHLAR													
Consensus	MYKCPNeGCLqKMELRHLEDHQaHCEFALn#CPQCQRPFQKcqlNiHiieDCPRRQVSCdNCAaSMa%E#KEIHDQnCPLAN!ICEYcnTILIREQMPNHYDLDCPTAPIPCTFSFGCH#KMQRNHLAR													
	261	270	280	290	300	310	320	330	340	350	360	370	380	390
	-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+-----													
TRAGHUMAN	HLQENTQSHMRMLAQAVHSLSVI-----PDSGYISEVRNFQETIHQLEGRQVLDQHQIRELTAKMETQSMYVSELKRTIRTLEDKVAEIEAQQCNGIYIMKIGNFGMHLKQEEEEKPVYIHSPPGFYT													
TRAGMOUSE	HLQENTQLHMRLLAQAVHNYNLALRPCDAASPDRGCRPEDPNEYEETIKQLESRLVQDQHQIRELTAKMETQSMYVSELKRTIRTLEDKVAEMEAAQQCNGIYIMKIGKFGMHLKSQEEERPVYIHSPPGFYT													
Consensus	HLQENTQLHMR#LAQAVHnlnla.....PdrGcrpEdrN%#ETIHqLEgRLVQDQHQIRELTAKMETQSMYVgELKRTIRTLEDKVAEIEAQQCNGIYIMKIGnFGMHLKcQEEERPVYIHSPPGFYT													
	391	400	410	420	430	440	450	460	470	480	490	500	510	520
	-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+-----													
TRAGHUMAN	GKPGYKLCMRLHLQLPTAQRCAANYISLQVHTMQGEYDHLPPFQGTIRLTILDQSEAPVQRNHEEINDAKPELLAFQRPTIPRNPKGFGYVTFMHLEALRQRFTFIKDDTLVRCVSTRFDMGSLRREG													
TRAGMOUSE	GRPGYKLCMRLHLQLPTAQRCAANYISLQVHTMQGEYDHLPPFQGTIRLTILDQSEALIRQNHEEVMDAKPELLAFQRPTIPRNPKGFGYVTFMHLEALRQGTFTFIKDDTLVRCVSTRFDMGGLRKEG													
Consensus	GrPGYKLCMRLHLQLPTAQRCAANYISLQVHTMQGEYDHLPPFQGTIRLTILDQSEAI!RQNHEE!MDAKPELLAFQRPTIPRNPKGFGYVTFMHLEALRqrFTFIKDDTLVRCVSTRFDMGGLRrEG													
	521	530												

TRAGHUMAN	FQPRSTDAGV													
TRAGMOUSE	FQPRSTDAGV													
Consensus	FQPRSTDAGV													

TEF family dendrogram





TRAF6 structure: residues 348 to 504 (=TRAF domain) (X-ray diffraction)

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