Table S1. Identification of 65 distinct *T. vaginalis* Rab genes. DNA encoding *T. vaginalis* Rab proteins with significant BLAST scores to Rab sequences were identified from cDNA (EST or RACE clones) and from the TIGR genome sequencing database.

Protein name[1]	Data source[2]	BLAST E-score[3]	% Identity to RabF motif[4]	C-terminus[5]	Accession number[6]
Orthologues of taxonomically broadly distributed subfamilies (14)					
1) TvRab1a	EG	3e-68	70	**..CC**	AY896289
2) TvRab1b	RG	4e-60	81	**.C.C**	AY896243
3) TvRab1c	EG	6e-46	67	**..CC**	AY896244
4) TvRab5a	G	9e-41	59	**..CC**	DQ019033
5) TvRab5b	G	7e-41	59	**..CC**	DQ019034
6) TvRab5c	G	8e-34	55	**..CC**	DQ019035
7) TvRab5d	G	5e-32	48	**.C.C**	DQ019036
8) TvRab6a	G	1e-39	63	**.C.C**	AY896245
9) TvRab6b	G	3e-40	63	**.C.C**	AY896246
10) TvRab7a	EG	7e-52	70	**..CC**	AY896247
11) TvRab7b	EG	3e-38	63	**..CC**	AY896248
12) TvRab7c	G	3e-51	67	**..CC**	AY896249
13) TvRab11a	EG	1e-67	81	**..CC**	AY896250
14) TvRab11b	G	3e-65	81	**..CC**	DQ019037
Orthologues of *Trichomonas* specific subfamilies (32)					
15) TvRabA1	EG	3e-42	78	**..CC**	AY896251
16) TvRabA2	EG	3e-42	74	**..CC**	AY896252
17) TvRabA3	EG	5e-43	56	**..CC**	AY896253
18) TvRabA4	EG	3e-44	79	**.C.C**	AY896254
19) TvRabA5	EG	2e-42	57	**..CC**	AY896255
20) TvRabA6	RG	3e-39	74	**..CC**	AY896256
21) TvRabB1	EG	8e-22	41	**..CC**	AY896257
22) TvRabB2	EG	2e-18	29	**..CC**	AY896258

23) TvRabB3	EG	1e-20	37	**..CC**	AY896259
24) TvRabB4	EG	2e-20	37	**.CC.**	AY896260
25) TvRabC1	EG	1e-36	59	**.C.C**	AY896261
26) TvRabC2	EG	6e-36	63	**..CC**	AY896262
27) TvRabC3	EG	2e-29	56	**..CC**	AY896263
28) TvRabC4	RG	1e-33	59	**..CC**	AY896264
29) TvRabC5	G	8e-36	63	**.C.C**	DQ019038
30) TvRabC6	G	4e-36	55	**.C.C**	DQ019039
31) TvRabC7	G	4e-35	55	**..CC**	DQ019040
32) TvRabC8	G	4e-31	55	SQKM	DQ019041
33) TvRabC9	G	3e-34	55	**..CC**	DQ019042
34) TvRabD1	EG	1e-36	56	**..CC**	AY896265
35) TvRabD2	EG	3e-35	56	**.C.C**	AY896266
36) TvRabD3	EG	8e-35	52	**..CC**	AY896267
37) TvRabD4	EG	6e-27	56	**..CC**	AY896290
38) TvRabD5	G	1e-39	59	**..CC**	DQ019043
39) TvRabD6	G	4e-34	52	**.C.C**	DQ019044
40) TvRabD7	G	8e-34	44	**..CC**	DQ019045
41) TvRabD8	G	5e-33	48	**..CC**	DQ019046
42) TvRabE1	EG	2e-34	41	**.C.C**	AY896268
43) TvRabE2	G	3e-39	44	**..CC**	AY896269
44) TvRabF1	RG	4e-35	37	**.C.C**	AY896270
45) TvRabF2	G	4e-38	61	**..CC**	AY896271
46) TvRabF3	G	2e-37	41	**..CC**	AY896272

***Trichomonas* orphans (19)**

47) TvRabX1	EG	2e-20	33	**..CC**	AY896273
48) TvRabX2	EG	4e-30	52	**..CC**	AY896274
49) TvRabX3	EG	7e-22	37	**..C.**	AY896275
50) TvRabX4	EG	4e-30	63	**.C.C**	AY896276
51) TvRabX5	EG	6e-47	79	**.CC.**	AY896277
52) TvRabX6	EG	3e-14	30	**..CC**	AY896278
53) TvRabX7	EG	4e-37	56	**..CC**	AY896291
54) TvRabX8	EG	1e-40	70	**.CC.**	AY896279

55) TvRabX9	EG	4e-22	30	**..CC**	AY896280
56) TvRabX10	EG	6e-36	74	**..CC**	AY896281
57) TvRabX11	EG	1e-42	67	**..CC**	AY896282
58) TvRabX12	EG	5e-34	52	**..CC**	DQ019047
59) TvRabX13	EG	9e-31	56	**..CC**	AY896283
60) TvRabX14	EG	1e-26	41	**..CC**	AY896292
61) TvRabX15	EG	1e-31	52	**..CC**	AY896284
62) TvRabX16	RG	4e-25	33	**..CC**	AY896285
63) TvRabX17	RG	1e-29	56	**.C.C**	AY896286
64) TvRabX18	RG	1e-29	37	**.C.C**	AY896287
65) TvRabX19	RG	3e-23	52	**..CC**	AY896288

[1]TvRabn are named according to subfamily membership whereas TvRabXn could not be assigned to specific subfamilies (see phylogenies in Figures 1, 2 and S1). This nomenclature is in accordance with the systematic and consistent naming proposed by Pereira-Leal and Seabra (2001) [3].

[2]Three sources of DNA sequences provided Rab genes: EST (E), 5'RACE cloning (R) and genome data at TIGR (G).

[3]Top BLATP hits e-score obtained using the NCBI Blast server, in all cases the top hit was a Rab homologue. RPS-BLAST (Reverse Position-Specific BLAST) [33] also recovered Rab PSSM (Position-Specific Score Matrix) as top hits (namely cd00154 or smart00175) among the different Ras-like small GTPases PSSM (Ras, Sar, Rho, Ran, ARF).

[4]The Rab specific family motifs (RabF) are generally conserved in *Trichomonas* proteins. RabF motifs - total of 27 residues, according to Pereira-Leal and Seabra 2001 [3]; RabF1: IGVDF, RabF2: KLQIW, RabF3: RFRSIT, RabF4: YYRGA and RabF5: LVYDIT, at positions shown in Figure 3.

[5]All but two of the *Trichomonas* putative proteins have predicted characteristic Rab C-terminal double cysteine motifs, key for Rab prenylation (including ..CC, .CC. or .C.C,; dot representing any amino acid). TvRabX3 has only one cysteine towards the C-terminus whereas TvRabC8 has RASQKM as the last six residues.

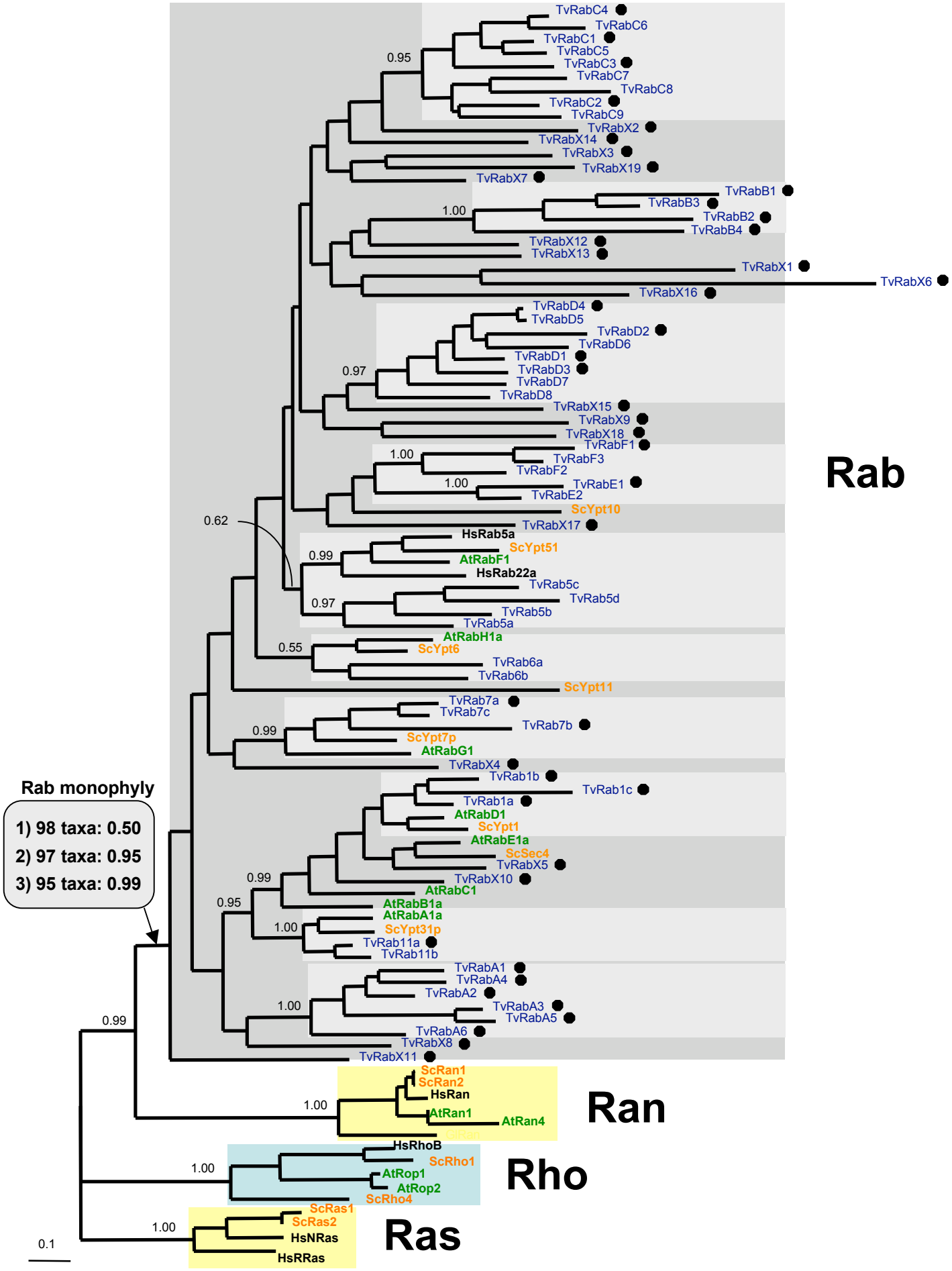
[6]GenBank accession numbers.

Table S2. Comparison of the 11 residues demonstrated to be involved in HsRab5a-rabaptin5 binding with homologous sites from selected Rab sequences.

Sequence name*	Binding residues (11)	Total no. of differences to HsRab5a	No. of non conservative changes to HsRab5a**
HsRab5a	GAFLTWRYLMY	-	-
HsRab5b	GAFLTWRYLMY	0	0
HsRab5c	GAFLTWRYLMY	0	0
HsRab22a	GAFMTWRFLMY	2	1
HsRab22b	GAFMTWRFLMY	2	1
ScYpt51	GAFLTWRFLMY	1	1
ScYpt52	GAFLSWRYLMY	1	0
ScYpt53	GAFLTWRFLMY	1	1
TvRab5a	GAFLSWRYMMY	2	0
TvRab5b	GAFVTWKYLMY	2	0
TvRab5c	GAFTSWKYLMY	3	1
TvRab5d	GAFNSWKYLMY	3	1
TvRabC1	GAFLTWKFLMY	2	1
TvRabC5	GAFLTWKFLMY	2	1
TvRabC3	GAFLTWKFLMY	2	1
TvRabC4	GAFLTWKYLMY	1	0
TvRabC6	GAFHTWKYLMY	2	1
TvRabC2	GAFQNWQSLMY	4	3
TvRabC7	GAFQNWKFLMY	4	2
TvRabC8	GAFQNWKFLMY	4	2
TvRabC9	GALQEWKFLMY	5	3
TvRabD1	GAFVTWVYLMY	2	1
TvRabD2	GAFVTWVYLMY	2	1
TvRabD6	GAFVTWVYLMY	2	1
TvRabD3	GSFFTWVYLMY	2	1
TvRabD4	GAFVTWVYLMY	2	1
TvRabD5	GAFVTWVYLMY	2	1
TvRabD7	GAFVTWLYLMY	2	1
TvRabD8	GAFITWEYLMY	2	1
TvRabA1	GVFDSWRFIAY	6	2
TvRabA2	GVFIAWRFIAY	6	2
TvRabA3	GIYFTWRFIAY	6	2
TvRabA4	GVFDSWRFIAY	6	2
TvRabA5	GIYFTWRFIAY	6	2
TvRabA6	GVFKSWRFVAY	6	2
TvRabB1	APSCNWRFIMF	8	6
TvRabB2	APYSCWRYILF	8	6
TvRabB3	APSCSWRFIMF	8	6
TvRabB4	TPLSPWRYIVF	7	5
TvRabE1	AAFFQWEYLIY	5	3
TvRabE2	SAFFQWEYLIY	5	3
TvRabF1	QPLAQWRYLLF	7	4
TvRabF2	QAFFQWRFLMY	4	3
TvRabF3	QPFCQWRYLLF	6	5

*Hs: *Homo sapiens*, Sc: *Saccharomyces cerevisiae*, Tv: *Trichomonas vaginalis*

**Residue colouring indicates changes in relation to the HsRab5a positions (G54, A55, F57, L58, T59, W74, R81, Y82, L85, M88, and Y89 - see [31]): yellow for identical residues, grey for conservative changes and purple for non-conservative changes, according to the categories implemented in SEAVIEW [29].


TvRabC4
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TvRabC5
TvRabC3
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TvRabC9
TvRabX2
TvRabX14
TvRabX3
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TvRabB4
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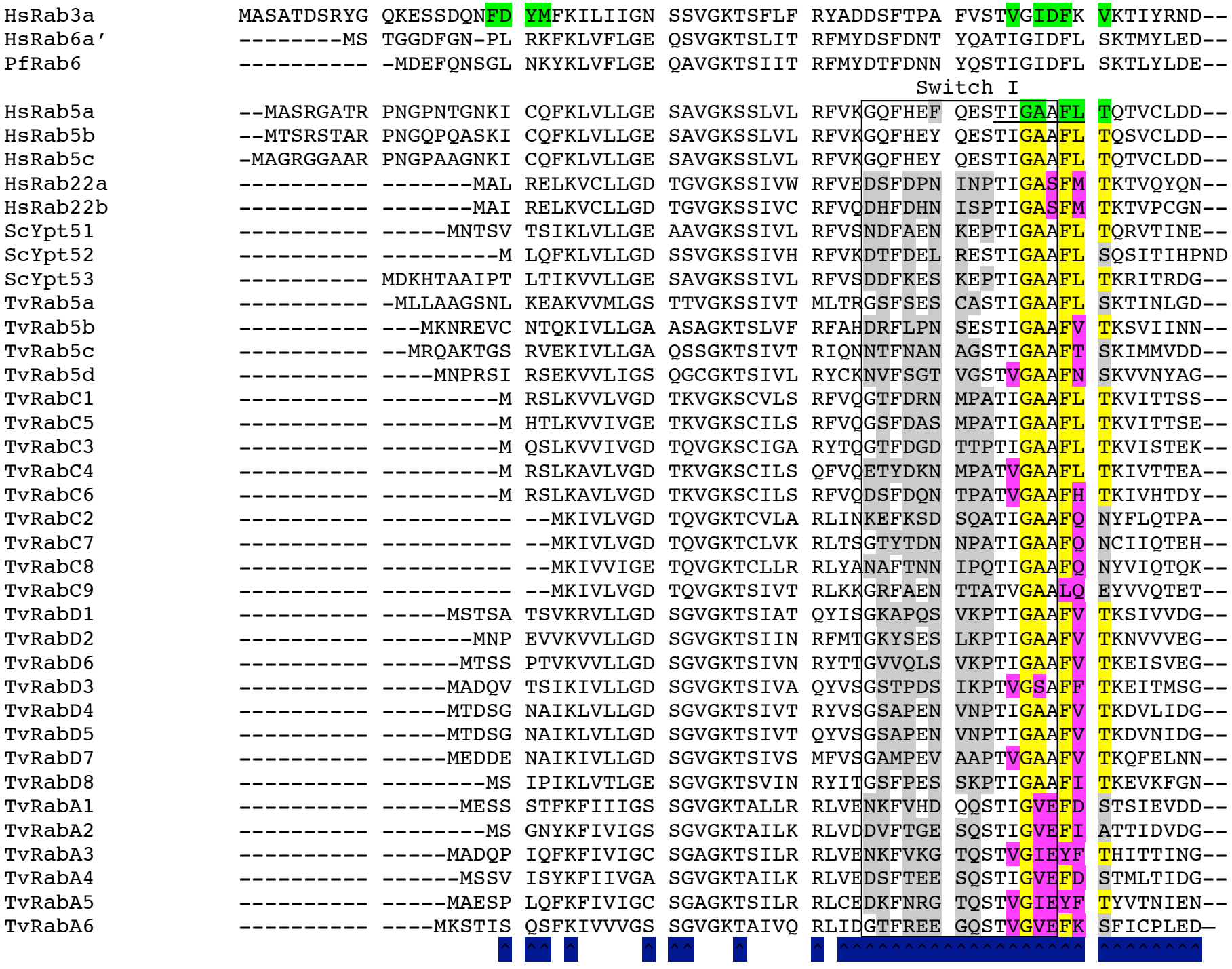
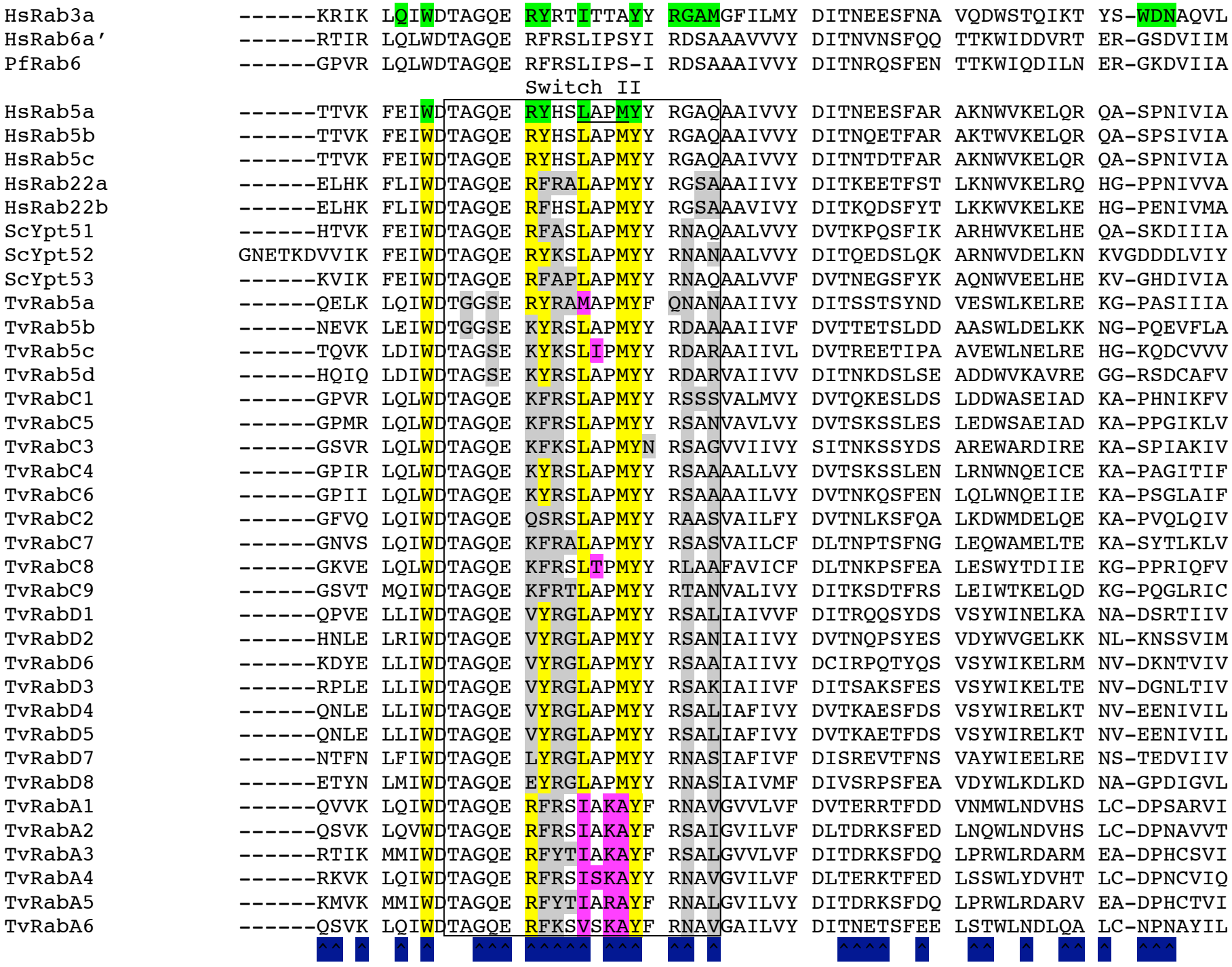
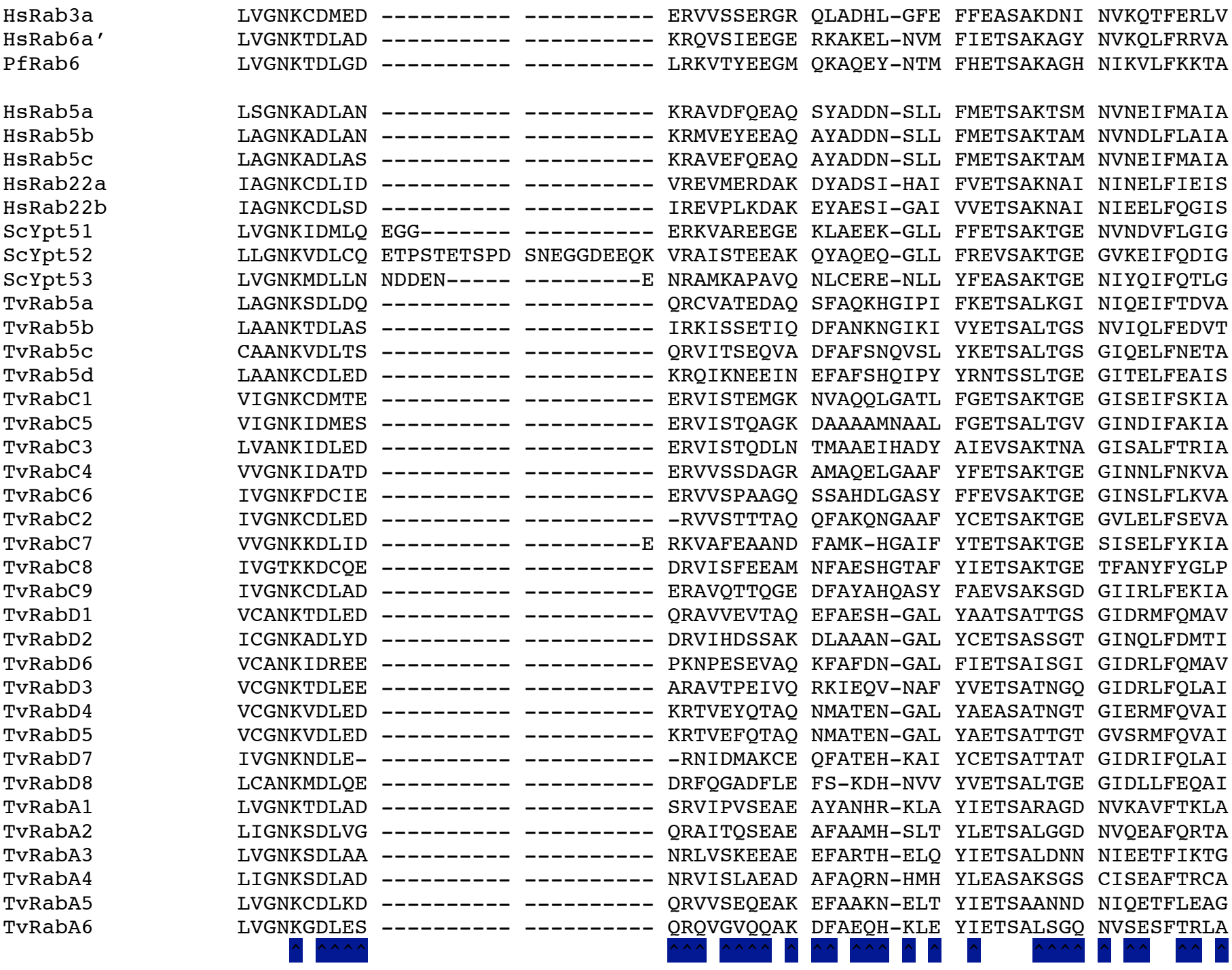
TvRabX16
TvRabD4
TvRabD5
TvRabD2
TvRabD6
TvRabD1
TvRabD3
TvRabD7
TvRabD8
TvRabX15
TvRabX9
TvRabX18
TvRabF1
TvRabF3
TvRabF2
TvRabE1
TvRabE2
ScYpt10
TvRabX17
HsRab5a
ScYpt51
AtRabF1
HsRab22a
TvRab5c
TvRab5d
TvRab5b
TvRab5a
AtRabH1a
ScYpt6
TvRab6a
TvRab6b
ScYpt11
TvRab7a
TvRab7c
TvRab7b
ScYpt7p
AtRabG1
TvRabX4
TvRab1b
TvRab1c
TvRab1a
AtRabD1
ScYpt1
AtRabE1a
ScSec4
TvRabX5
TvRabX10
AtRabC1
AtRabB1a
AtRabA1a
ScYpt31p
TvRab11a
TvRab11b
TvRabA1
TvRabA4
TvRabA2
TvRabA3
TvRabA5
TvRabA6
TvRabX8
TvRabX11
ScRan1
ScRan2
HsRan
AtRan1
AtRan4
GlRan
HsRhoB
ScRho1
AtRop1
AtRop2
ScRho4
ScRas1
ScRas2
HsNRas
HsRRas
0.95
1.00
0.97
1.00
1.00
0.62
0.99
0.97
0.55
0.99
0.99
0.95
1.00
1.00
0.99
1.00
1.00
1.00
0.1
Rab
Ran
Rho
Ras
Rab monophyly
1) 98 taxa: 0.50
2) 97 taxa: 0.95
3) 95 taxa: 0.99

Figure S1. *Trichomonas* Rab proteins cluster with Rab homologues and segregate from other small GTPases. The phylogenetic relationship of putative *Trichomonas vaginalis* (blue) Rabs relative to Ras, Rho, Ran and Rab GTPase representatives from *Homo sapiens* (black), *Saccharomyces cerevisiae* (orange) and *Arabidopsis thaliana* (green) is shown. The shown tree is the consensus Bayesian tree recovered from an alignment including 98 taxa and 161 amino acids with posterior probabilities (PP) shown above the nodes. All putative Rab proteins from *Trichomonas* are part of a monophyletic group (the Rab clade, which is indicated in grey shading) with representative Rab sequences from human and yeast. When TvRabX11 is removed the PP for Rab monophyly increases to 0.95 and when two additional Rab sequences are removed, the highly divergent TvRabX6 and Ypt11, Rab monophyly is supported by PP of 0.99. The scale bar represents 10% sequence divergence. The 45 TvRab that were also recovered as cDNA (EST or RACE clones, see Table S1) are indicated with black dots.


HsRab3a MASATDSRYG QKESSDQNFD YMFKILIIGN SSVGKTSFLF RYADDSFTPA FVSTVGIDFK VKTIYRND--
HsRab6a' --------MS TGGDFGN-PL RKFKLVFLGE QSVGKTSLIT RFMYDSFDNT YQATIGIDFL SKTMYLED--
PfRab6 ---------- -MDEFQNSGL NKYKLVFLGE QAVGKTSIIT RFMYDTFDNN YQSTIGIDFL SKTLYLDE--
Switch I
HsRab5a --MASRGATR PNGPNTGNKI CQFKLVLLGE SAVGKSSLVL RFVKGQFHEF QESTIGAAFL TQTVCLDD--
HsRab5b --MTSRSTAR PNGQPQASKI CQFKLVLLGE SAVGKSSLVL RFVKGQFHEY QESTIGAAFL TQSVCLDD--
HsRab5c -MAGRGGAAR PNGPAAGNKI CQFKLVLLGE SAVGKSSLVL RFVKGQFHEY QESTIGAAFL TQTVCLDD--
HsRab22a ---------- -------MAL RELKVCLLGD TGVGKSSIVW RFVEDSFDPN INPTIGASFM TKTVQYQN--
HsRab22b ---------- -------MAI RELKVCLLGD TGVGKSSIVC RFVQDHFDHN ISPTIGASFM TKTVPCGN--
ScYpt51 ---------- -----MNTSV TSIKLVLLGE AAVGKSSIVL RFVSNDFAEN KEPTIGAAFL TQRVTINE--
ScYpt52 ---------- ---------M LQFKLVLLGD SSVGKSSIVH RFVKDTFDEL RESTIGAAFL SQSITIHPND
ScYpt53 ---------- MDKHTAAIPT LTIKVVLLGE SAVGKSSIVL RFVSDDFKES KEPTIGAAFL TKRITRDG--
TvRab5a ---------- -MLLAAGSNL KEAKVVMLGS TTVGKSSIVT MLTRGSFSES CASTIGAAFL SKTINLGD--
TvRab5b ---------- ---MKNREVC NTQKIVLLGA ASAGKTSLVF RFAHDRFLPN SESTIGAAFV TKSVIINN--
TvRab5c ---------- --MRQAKTGS RVEKIVLLGA QSSGKTSIVT RIQNNTFNAN AGSTIGAAFT SKIMMVDD--
TvRab5d ---------- ----MNPRSI RSEKVVLIGS QGCGKTSIVL RYCKNVFSGT VGSTVGAAFN SKVVNYAG--
TvRabC1 ---------- ---------M RSLKVVLVGD TKVGKSCVLS RFVQGTFDRN MPATIGAAFL TKVITTSS--
TvRabC5 ---------- ---------M HTLKVVIVGE TKVGKSCILS RFVQGSFDAS MPATIGAAFL TKVITTSE--
TvRabC3 ---------- ---------M QSLKVVIVGD TQVGKSCIGA RYTQGTFDGD TTPTIGAAFL TKVISTEK--
TvRabC4 ---------- ---------M RSLKAVLVGD TKVGKSCILS QFVQETYDKN MPATVGAAFL TKIVTTEA--
TvRabC6 ---------- ---------M RSLKAVLVGD TKVGKSCILS RFVQDSFDQN TPATVGAAFH TKIVHTDY--
TvRabC2 ---------- ---------- --MKIVLVGD TQVGKTCVLA RLINKEFKSD SQATIGAAFQ NYFLQTPA--
TvRabC7 ---------- ---------- --MKIVLVGD TQVGKTCLVK RLTSGTYTDN NPATIGAAFQ NCIIQTEH--
TvRabC8 ---------- ---------- --MKIVVIGE TQVGKTCLLR RLYANAFTNN IPQTIGAAFQ NYVIQTQK--
TvRabC9 ---------- ---------- --MKIVLVGD TQVGKTSIVT RLKKGRFAEN TTATVGAALQ EYVVQTET--
TvRabD1 ---------- -----MSTSA TSVKRVLLGD SGVGKTSIAT QYISGKAPQS VKPTIGAAFV TKSIVVDG--
TvRabD2 ---------- -------MNP EVVKVVLLGD SGVGKTSIIN RFMTGKYSES LKPTIGAAFV TKNVVVEG--
TvRabD6 ---------- ------MTSS PTVKVVLLGD SGVGKTSIVN RYTTGVVQLS VKPTIGAAFV TKEISVEG--
TvRabD3 ---------- -----MADQV TSIKIVLLGD SGVGKTSIVA QYVSGSTPDS IKPTVGSAFF TKEITMSG--
TvRabD4 ---------- -----MTDSG NAIKLVLLGD SGVGKTSIVT RYVSGSAPEN VNPTIGAAFV TKDVLIDG--
TvRabD5 ---------- -----MTDSG NAIKLVLLGD SGVGKTSIVT QYVSGSAPEN VNPTIGAAFV TKDVNIDG--
TvRabD7 ---------- -----MEDDE NAIKIVLLGD SGVGKTSIVS MFVSGAMPEV AAPTVGAAFV TKQFELNN--
TvRabD8 ---------- --------MS IPIKLVTLGE SGVGKTSVIN RYITGSFPES SKPTIGAAFI TKEVKFGN--
TvRabA1 ---------- ------MESS STFKFIIIGS SGVGKTALLR RLVENKFVHD QQSTIGVEFD STSIEVDD--
TvRabA2 ---------- --------MS GNYKFIVIGS SGVGKTAILK RLVDDVFTGE SQSTIGVEFI ATTIDVDG--
TvRabA3 ---------- -----MADQP IQFKFIVIGC SGAGKTSILR RLVENKFVKG TQSTVGIEYF THITTING--
TvRabA4 ---------- ------MSSV ISYKFIIVGA SGVGKTAILK RLVEDSFTEE SQSTIGVEFD STMLTIDG--
TvRabA5 ---------- -----MAESP LQFKFIVIGC SGAGKTSILR RLCEDKFNRG TQSTVGIEYF TYVTNIEN--
TvRabA6 ---------- ----MKSTIS QSFKIVVVGS SGVGKTAIVQ RLIDGTFREE GQSTVGVEFK SFICPLED—


HsRab3a ------KRIK LQIWDTAGQE RYRTITTAYY RGAMGFILMY DITNEESFNA VQDWSTQIKT YS-WDNAQVL
HsRab6a' ------RTIR LQLWDTAGQE RFRSLIPSYI RDSAAAVVVY DITNVNSFQQ TTKWIDDVRT ER-GSDVIIM
PfRab6 ------GPVR LQLWDTAGQE RFRSLIPS-I RDSAAAIVVY DITNRQSFEN TTKWIQDILN ER-GKDVIIA
Switch II
HsRab5a ------TTVK FEIWDTAGQE RYHSLAPMYY RGAQAAIVVY DITNEESFAR AKNWVKELQR QA-SPNIVIA
HsRab5b ------TTVK FEIWDTAGQE RYHSLAPMYY RGAQAAIVVY DITNQETFAR AKTWVKELQR QA-SPSIVIA
HsRab5c ------TTVK FEIWDTAGQE RYHSLAPMYY RGAQAAIVVY DITNTDTFAR AKNWVKELQR QA-SPNIVIA
HsRab22a ------ELHK FLIWDTAGQE RFRALAPMYY RGSAAAIIVY DITKEETFST LKNWVKELRQ HG-PPNIVVA
HsRab22b ------ELHK FLIWDTAGQE RFHSLAPMYY RGSAAAVIVY DITKQDSFYT LKKWVKELKE HG-PENIVMA
ScYpt51 ------HTVK FEIWDTAGQE RFASLAPMYY RNAQAALVVY DVTKPQSFIK ARHWVKELHE QA-SKDIIIA
ScYpt52 GNETKDVVIK FEIWDTAGQE RYKSLAPMYY RNANAALVVY DITQEDSLQK ARNWVDELKN KVGDDDLVIY
ScYpt53 ------KVIK FEIWDTAGQE RFAPLAPMYY RNAQAALVVF DVTNEGSFYK AQNWVEELHE KV-GHDIVIA
TvRab5a ------QELK LQIWDTGGSE RYRAMAPMYF QNANAAIIVY DITSSTSYND VESWLKELRE KG-PASIIIA
TvRab5b ------NEVK LEIWDTGGSE KYRSLAPMYY RDAAAAIIVF DVTTETSLDD AASWLDELKK NG-PQEVFLA
TvRab5c ------TQVK LDIWDTAGSE KYKSLIPMYY RDARAAIIVL DVTREETIPA AVEWLNELRE HG-KQDCVVV
TvRab5d ------HQIQ LDIWDTAGSE KYRSLAPMYY RDARVAIIVV DITNKDSLSE ADDWVKAVRE GG-RSDCAFV
TvRabC1 ------GPVR LQLWDTAGQE KFRSLAPMYY RSSSVALMVY DVTQKESLDS LDDWASEIAD KA-PHNIKFV
TvRabC5 ------GPMR LQLWDTAGQE KFRSLAPMYY RSANVAVLVY DVTSKSSLES LEDWSAEIAD KA-PPGIKLV
TvRabC3 ------GSVR LQLWDTAGQE KFKSLAPMYN RSAGVVIIVY SITNKSSYDS AREWARDIRE KA-SPIAKIV
TvRabC4 ------GPIR LQLWDTAGQE KYRSLAPMYY RSAAAALLVY DVTSKSSLEN LRNWNQEICE KA-PAGITIF
TvRabC6 ------GPII LQLWDTAGQE KYRSLAPMYY RSAAAAILVY DVTNKQSFEN LQLWNQEIIE KA-PSGLAIF
TvRabC2 ------GFVQ LQIWDTAGQE QSRSLAPMYY RAASVAILFY DVTNLKSFQA LKDWMDELQE KA-PVQLQIV
TvRabC7 ------GNVS LQIWDTAGQE KFRALAPMYY RSASVAILCF DLTNPTSFNG LEQWAMELTE KA-SYTLKLV
TvRabC8 ------GKVE LQLWDTAGQE KFRSLTPMYY RLAAFAVICF DLTNKPSFEA LESWYTDIIE KG-PPRIQFV
TvRabC9 ------GSVT MQIWDTAGQE KFRTLAPMYY RTANVALIVY DITKSDTFRS LEIWTKELQD KG-PQGLRIC
TvRabD1 ------QPVE LLIWDTAGQE VYRGLAPMYY RSALIAIVVF DITRQQSYDS VSYWINELKA NA-DSRTIIV
TvRabD2 ------HNLE LRIWDTAGQE VYRGLAPMYY RSANIAIIVY DVTNQPSYES VDYWVGELKK NL-KNSSVIM
TvRabD6 ------KDYE LLIWDTAGQE VYRGLAPMYY RSAAIAIIVY DCIRPQTYQS VSYWIKELRM NV-DKNTVIV
TvRabD3 ------RPLE LLIWDTAGQE VYRGLAPMYY RSAKIAIIVF DITSAKSFES VSYWIKELTE NV-DGNLTIV
TvRabD4 ------QNLE LLIWDTAGQE VYRGLAPMYY RSALIAFIVY DVTKAESFDS VSYWIRELKT NV-EENIVIL
TvRabD5 ------QNLE LLIWDTAGQE VYRGLAPMYY RSALIAFIVY DVTKAETFDS VSYWIRELKT NV-EENIVIL
TvRabD7 ------NTFN LFIWDTAGQE LYRGLAPMYY RNASIAFIVF DISREVTFNS VAYWIEELRE NS-TEDVIIV
TvRabD8 ------ETYN LMIWDTAGQE EYRGLAPMYY RNASIAIVMF DIVSRPSFEA VDYWLKDLKD NA-GPDIGVL
TvRabA1 ------QVVK LQIWDTAGQE RFRSIAKAYF RNAVGVVLVF DVTERRTFDD VNMWLNDVHS LC-DPSARVI
TvRabA2 ------QSVK LQVWDTAGQE RFRSIAKAYF RSAIGVILVF DLTDRKSFED LNQWLNDVHS LC-DPNAVVT
TvRabA3 ------RTIK MMIWDTAGQE RFYTIAKAYF RSALGVVLVF DITDRKSFDQ LPRWLRDARM EA-DPHCSVI
TvRabA4 ------RKVK LQIWDTAGQE RFRSISKAYY RNAVGVILVF DLTERKTFED LSSWLYDVHT LC-DPNCVIQ
TvRabA5 ------KMVK MMIWDTAGQE RFYTIARAYF RNALGVILVY DITDRKSFDQ LPRWLRDARV EA-DPHCTVI
TvRabA6 ------QSVK LQIWDTAGQE RFKSVSKAYF RNAVGAILVY DITNETSFEE LSTWLNDLQA LC-NPNAYIL


HsRab3a LVGNKCDMED ---------- ---------- ERVVSSERGR QLADHL-GFE FFEASAKDNI NVKQTFERLV
HsRab6a' LVGNKTDLAD ---------- ---------- KRQVSIEEGE RKAKEL-NVM FIETSAKAGY NVKQLFRRVA
PfRab6 LVGNKTDLGD ---------- ---------- LRKVTYEEGM QKAQEY-NTM FHETSAKAGH NIKVLFKKTA
HsRab5a LSGNKADLAN ---------- ---------- KRAVDFQEAQ SYADDN-SLL FMETSAKTSM NVNEIFMAIA
HsRab5b LAGNKADLAN ---------- ---------- KRMVEYEEAQ AYADDN-SLL FMETSAKTAM NVNDLFLAIA
HsRab5c LAGNKADLAS ---------- ---------- KRAVEFQEAQ AYADDN-SLL FMETSAKTAM NVNEIFMAIA
HsRab22a IAGNKCDLID ---------- ---------- VREVMERDAK DYADSI-HAI FVETSAKNAI NINELFIEIS
HsRab22b IAGNKCDLSD ---------- ---------- IREVPLKDAK EYAESI-GAI VVETSAKNAI NIEELFQGIS
ScYpt51 LVGNKIDMLQ EGG------- ---------- ERKVAREEGE KLAEEK-GLL FFETSAKTGE NVNDVFLGIG
ScYpt52 LLGNKVDLCQ ETPSTETSPD SNEGGDEEQK VRAISTEEAK QYAQEQ-GLL FREVSAKTGE GVKEIFQDIG
ScYpt53 LVGNKMDLLN NDDEN----- ---------E NRAMKAPAVQ NLCERE-NLL YFEASAKTGE NIYQIFQTLG
TvRab5a LAGNKSDLDQ ---------- ---------- QRCVATEDAQ SFAQKHGIPI FKETSALKGI NIQEIFTDVA
TvRab5b LAANKTDLAS ---------- ---------- IRKISSETIQ DFANKNGIKI VYETSALTGS NVIQLFEDVT
TvRab5c CAANKVDLTS ---------- ---------- QRVITSEQVA DFAFSNQVSL YKETSALTGS GIQELFNETA
TvRab5d LAANKCDLED ---------- ---------- KRQIKNEEIN EFAFSHQIPY YRNTSSLTGE GITELFEAIS
TvRabC1 VIGNKCDMTE ---------- ---------- ERVISTEMGK NVAQQLGATL FGETSAKTGE GISEIFSKIA
TvRabC5 VIGNKIDMES ---------- ---------- ERVISTQAGK DAAAAMNAAL FGETSALTGV GINDIFAKIA
TvRabC3 LVANKIDLED ---------- ---------- ERVISTQDLN TMAAEIHADY AIEVSAKTNA GISALFTRIA
TvRabC4 VVGNKIDATD ---------- ---------- ERVVSSDAGR AMAQELGAAF YFETSAKTGE GINNLFNKVA
TvRabC6 IVGNKFDCIE ---------- ---------- ERVVSPAAGQ SSAHDLGASY FFEVSAKTGE GINSLFLKVA
TvRabC2 IVGNKCDLED ---------- ---------- -RVVSTTTAQ QFAKQNGAAF YCETSAKTGE GVLELFSEVA
TvRabC7 VVGNKKDLID ---------- ---------E RKVAFEAAND FAMK-HGAIF YTETSAKTGE SISELFYKIA
TvRabC8 IVGTKKDCQE ---------- ---------- DRVISFEEAM NFAESHGTAF YIETSAKTGE TFANYFYGLP
TvRabC9 IVGNKCDLAD ---------- ---------- ERAVQTTQGE DFAYAHQASY FAEVSAKSGD GIIRLFEKIA
TvRabD1 VCANKTDLED ---------- ---------- QRAVVEVTAQ EFAESH-GAL YAATSATTGS GIDRMFQMAV
TvRabD2 ICGNKADLYD ---------- ---------- DRVIHDSSAK DLAAAN-GAL YCETSASSGT GINQLFDMTI
TvRabD6 VCANKIDREE ---------- ---------- PKNPESEVAQ KFAFDN-GAL FIETSAISGI GIDRLFQMAV
TvRabD3 VCGNKTDLEE ---------- ---------- ARAVTPEIVQ RKIEQV-NAF YVETSATNGQ GIDRLFQLAI
TvRabD4 VCGNKVDLED ---------- ---------- KRTVEYQTAQ NMATEN-GAL YAEASATNGT GIERMFQVAI
TvRabD5 VCGNKVDLED ---------- ---------- KRTVEFQTAQ NMATEN-GAL YAETSATTGT GVSRMFQVAI
TvRabD7 IVGNKNDLE- ---------- ---------- -RNIDMAKCE QFATEH-KAI YCETSATTAT GIDRIFQLAI
TvRabD8 LCANKMDLQE ---------- ---------- DRFQGADFLE FS-KDH-NVV YVETSALTGE GIDLLFEQAI
TvRabA1 LVGNKTDLAD ---------- ---------- SRVIPVSEAE AYANHR-KLA YIETSARAGD NVKAVFTKLA
TvRabA2 LIGNKSDLVG ---------- ---------- QRAITQSEAE AFAAMH-SLT YLETSALGGD NVQEAFQRTA
TvRabA3 LVGNKSDLAA ---------- ---------- NRLVSKEEAE EFARTH-ELQ YIETSALDNN NIEETFIKTG
TvRabA4 LIGNKSDLAD ---------- ---------- NRVISLAEAD AFAQRN-HMH YLEASAKSGS CISEAFTRCA
TvRabA5 LVGNKCDLKD ---------- ---------- QRVVSEQEAK EFAAKN-ELT YIETSAANND NIQETFLEAG
TvRabA6 LVGNKGDLES ---------- ---------- QRQVGVQQAK DFAEQH-KLE YIETSALSGQ NVSESFTRLA

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HsRab3a          DVICEKMSES LDTADPAV-- ---------- -----TGAKQ GPQLSDQQVP PHQDCAC-
HsRab6a'         AALPGMESTQ DRSREDMIDI KLEKP----- ---------- -----QEQPV SEGGCSC-
PfRab6           SKLPNLDNTN NNEANVVDIQ LTNN------ ---------- ---SNKNDKN MLSKCLC-

HsRab5a          KKLPKNEPQN PGANSARGRG VDLTEPT--- ---------- --------QP TRNQCCSN
HsRab5b          KKLPKSEPQN LGGAAGRSRG VDLHEQS--- ---------- --------QQ NKSQCCSN
HsRab5c          KKLPKNEPQN ATGAPGRNRG VDLQENNP-- ---------- ---------A SRSQCCSN
HsRab22a         RRIPSTDANL PSGGKGFKLR RQP------- ---------- --------SE PKRSCC--
HsRab22b         RQIPPLDPHE NGNNGTIKVE KPT------- ---------- --------MQ ASRRCC--
ScYpt51          EKIPLKTAEE QNSASNERES NNQ-RVDLNA AN-------- ------DGTS ANSACSC-
ScYpt52          EKLYDLKKDE ILSKQNRQIG GGNNGQVDIN LQRPS----- --------TN DPTSCCS-
ScYpt53          EKVPCPEQNT RQSSTHDRTI TDNQRIDLES TTV------- ------ESTR ETGGCNC-
TvRab5a          VAIARGAVST APAEQVTL-- ---------- ---------- ---TESNPKD KKKKCC--
TvRab5b          KQVDKFMAEN PTLKRPSK-- ---------- -------EVL DLLQGDDTPT KKSSCC--
TvRab5c          RLLIKLPAVE SQEDTELK-- ---------- -------GLV GNLDTTNQPP PKSGCC--
TvRab5d          DTLSKMTPLQ SANSEIDN-- ---------- ---------L LVGTNSNPPP SSGCNC--
TvRabC1          ELDINQEEII ETTTRVQN-- ---------- ---------- -----RNSNG EQGGCNC-
TvRabC5          EFDTMQDAVY EKPSDWKP-- ---------- ---------- -------TDN ESGGCSC-
TvRabC3          VLCEDGNNYM DKIGDQVI-- ---------- ---------- ------IPEQ SKGGCC--
TvRabC4          ETDIAHDTQI DKPVTKPV-- ---------- ---------- -----KPEGQ EGGGCC--
TvRabC6          ESDIQSDSPV ENERSNQL-- ---------- ---------- -----KDTSE NKGGCSC-
TvRabC2          QLNDATDTVS KKKESMQIPT ---------- ---------- ------ANDN NKKGCC--
TvRabC7          SHGQIESVYS PPPLEPAK-- ---------- ---------- --------PK ESGGCC--
TvRabC8          NYMRA----- ---------- ---------- ---------- ---------- --SQKM--
TvRabC9          TLNEVDNRVT TSEPIEI--- ---------- ---------- ----MALNQN NKSSCC--
TvRabD1          GKLMKDQAGE PVNQNGKQGG GVALRE---- ---------- -------EQN TKKGCC--
TvRabD2          SKMLKDNAVS ENGQEGGIDI KE-------- ---------- -------DKK KDKGCAC-
TvRabD6          LEYSRSAPEP VEPKAPNNNV NLE------- ---------- -----QSKED KGGCSC--
TvRabD3          QRQFSQKQEN QNQDEEKVDL NNTQD----- ---------- -------SNT KKKGCC--
TvRabD4          STLLKQRTPG PSPQPSVNL- ---------- ---------- ---QDGKSKK EKGGCC--
TvRabD5          STLLKQRVPG PPTQDGRVNL E--------- ---------- ---DGKKKDK EGKGCC--
TvRabD7          GEYERTQMNT STS-EIKADT V--------- ---------- --NISEKKKK EKTGCC--
TvRabD8          KLFIKNKNQP IPPNPGNQI- ---------- ---------- -----NNQQS QKSTCC--
TvRabA1          TEVYRSSAKD PSVNPKSITA T--------- ---------- ------GSTT EKSGCC--
TvRabA2          AEVYRRSLMK GDNKSAQPDV KKLD------ ---------- ------NKQG GEKKCC--
TvRabA3          ADLLRKVGTG EIAAAVTPPG SVQGSVTVTD ---------- -----SKDKG KKKNCC--
TvRabA4          TEIISKGLKA SNGNVDKTPL MPD------- ---------- -------SKK EDVCNC--
TvRabA5          RDLLKKVAAG TISGQKSATD GGHSVIIPD- ---------- ----PKTKNK KRNTCC--
TvRabA6          YGVATRVNNG QIQITSGAQK ASPFKVDE-- ---------- ----PPKQQQ SSGGCC—
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Figure S2. Mapping of several functionally investigated Rab residues and structural domains on selected TvRab Rab5-like and TvRabA sequences.

Experimentally established contact sites (highlighted in green) between human Rab5a and its effector rabaptin-5 [31] were mapped (in yellow) on selected TvRab5-like and TvRabA sequences from *Trichomona*s, yeast (ypt51-52-53) and humans (Rab5b-c and Rab22a-b) – differences to the HsRab5a are highlighted in grey. Three Rab sequences, not members of the Rab5 clade, are shown above the alignment for comparison, including the human Rab3a, with contact sites to its effector raphilin-3A [40] highlighted in green. Also shown are the positions of conformational switch regions I and II (boxed) [39]. The underlined motifs in HsRab5a (TIGAAFL, end of switch I and LAPM, within switch II) are well conserved between Rab5-like sequences, with the latter being considered as a signature motif for Rab5 sequences [37]. Differences to these two motifs are highlighted in purple in the other Rab5-like and TvRabA sequences. Also highlighted among the Rab5-like and TvRabA sequences are the differences to HsRab5a-b-c within the conformational switch I and II regions - in grey, when not part of the TIGAAFL or LAPM motifs. Surface accessible residues in the crystal of HsRab5 (PDB: 1tu3) are highlighted with blue arrowheads. The majority of the residues in the switch I and II regions, and those located between these two regions, are exposed on the surface and correspond to residues shown in Fig. 4.