Table S1: Analysis for positive selection in HERC5

Nested models	Log-likelihood	$2(Ln_1-Ln_0)$	Degrees of Freedom	X^2
M8a, M8	-14212, -14193	38	1	<0.001
M7, M8	-14224, -14193	62	2	<0.001

Non-nested model	Log-likelihood	AIC_c Score$^{\Delta}$: $-2*\log L+2p*(N/N-p-1)$	Parameters
M8a, MEC	-14212, -14003	28432, 28016	M8a: 4 free parameters MEC: 5 free parameters

$^{\Delta}$ *L* represents the likelihood of the model given the data, *p* represents the number of free parameters and *N* represents the sequence length. The lower the AIC_C score, the better the fit of the model to the data, and hence the model is considered more justified.

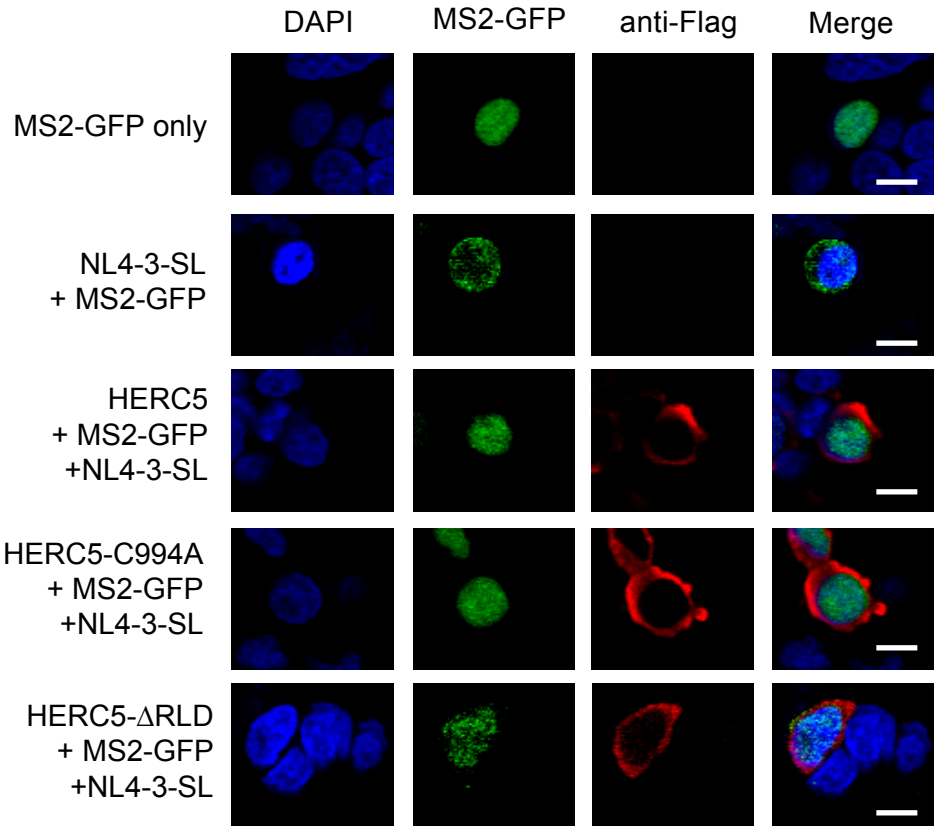
SUPPLEMENTAL FIGURE LEGENDS

Supplemental Figure 1: HERC5 inhibits nuclear export of HIV-1 genomic RNA. A, HeLa cells were co-transfected with plasmids encoding MS2-GFP alone, MS2-GFP and NL4-3-SL, or MS2-GFP, NL4-3-SL and either flag-tagged HERC5, HERC5-C994A or HERC5-ΔRLD. Forty-eight hours post-transfection, cells were fixed, stained with anti-flag and DAPI and imaged using fluorescence confocal microscopy. **B**, Over-exposure of cells exhibiting nuclear localization of MS2-GFP. HeLa cells were co-transfected with plasmids encoding MS2-GFP and NL4-3-SL and either flag-tagged HERC5, or HERC5-C994A. Forty-eight hours post-transfection, cells were fixed, stained with anti-flag and DAPI and imaged using fluorescence confocal microscopy. Cells exhibiting nuclear localization were imaged after increased laser intensity (also see **Figure 3**).

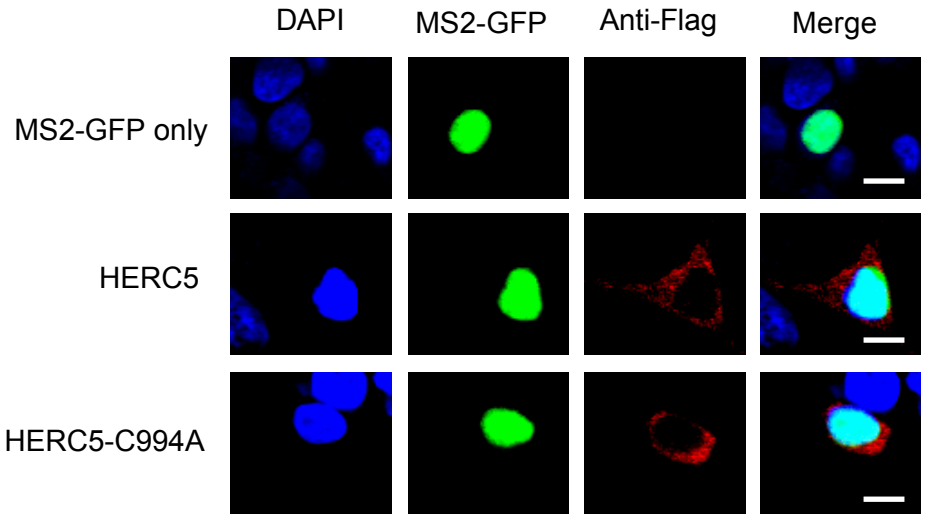
Supplemental Figure 2: Alignment of protein sequence for HERC5 mammalian species. The constraint-based multiple alignment tool (COBALT) was used to perform a progressive multiple alignment of HERC5 amino acid sequences from human, chimpanzee, gorilla, marmoset, baboon, squirrel monkey, gibbon, horse, giant panda, sheep, cow, dog and cat. Pubmed accession numbers are as follows: *Homo sapiens* (”Human”) (NP_057407.2), *Pan troglodytes* (”Chimpanzee”)(XP_003310459.1), *Gorilla gorilla gorilla* (”Gorilla”) (XP_004039179.1), *Callithrix jacchus* (”Marmoset”) (XP_002745648.1), *Papio anubis* (”Baboon”) (XP_003898997.1), *Saimiri boliviensis boliviensis* (”Squirrel monkey”) (XP_003924055.1), *Nomascus leucogenys* (”Gibbon”) (XP_003265940.1), *Equus caballus* (”Horse”) (XP_001915115.2), *Ailuropoda melanoleuca* (Giant Panda”) (XP_002913645.1), *Ovis aries* (”Sheep”) (XP_004009762.1), *Bos taurus* (”Cow”) (NP_001095465.1), *Canis lupus familiaris* (”Dog”) (XP_535652.3), *Felis catus* (”Cat”) (XP_003985249.1) (see also **Figure 6**).

Supplemental Figure 3: Selecton results for HERC5 run on 13 HERC5 sequences with the MEC model. Positive selection is colored in shades of yellow, neutral selection in white, and purifying selection in shades of magenta. Shades of yellow (colors 1 and 2) indicate a Ka/Ks ratio > 1, white indicates a Ka/Ks ratio = 1, and shades of magenta (colors 3 through 7) indicate a Ka/Ks ratio < *1* (see also **Figure 6**).

A



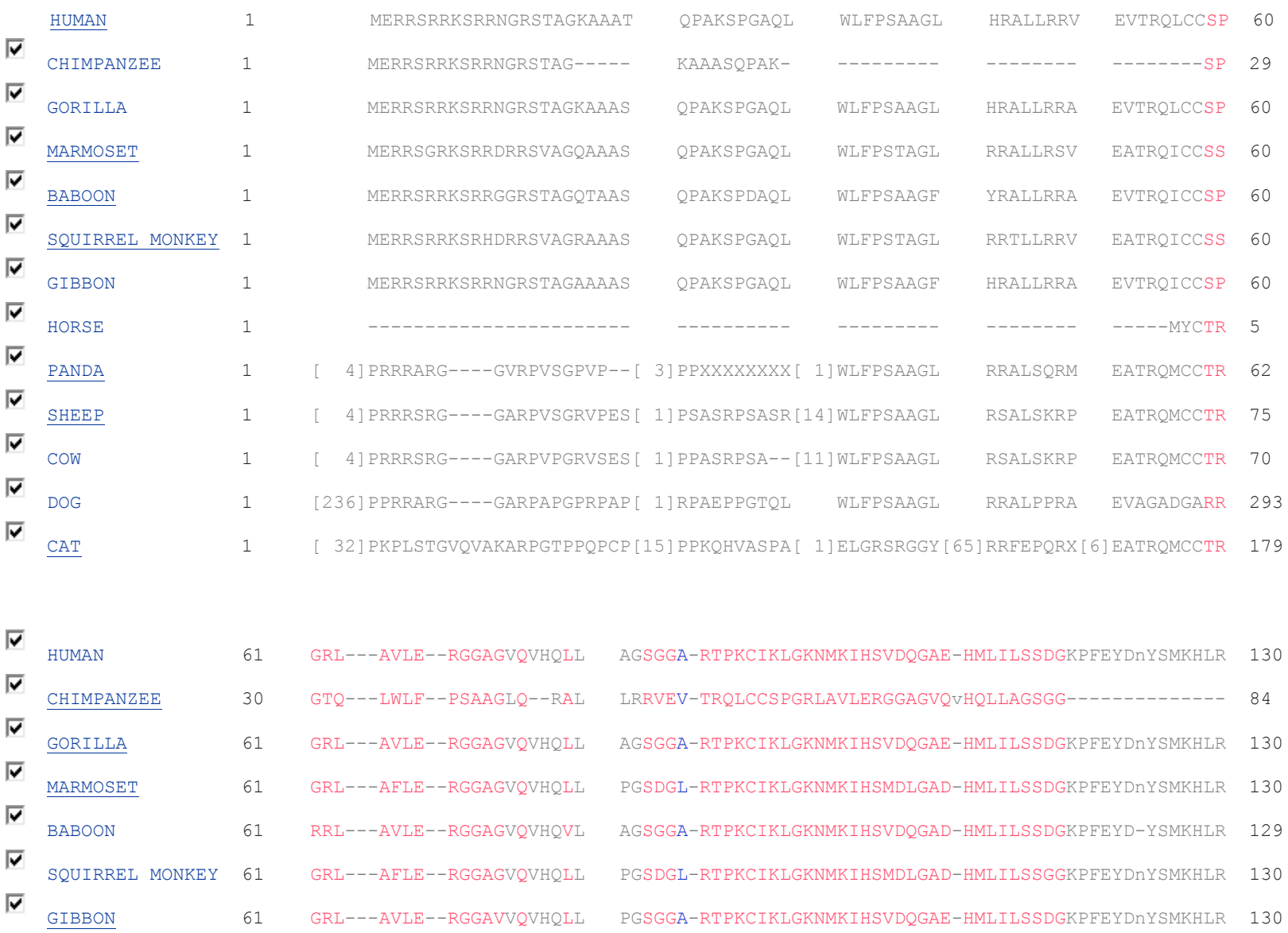
B



Supplementary Figure 1

Supplemental Data

Figure S2: Alignment of protein sequences for HERC5 mammalian species.



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PANDA          63   GRL---VVLE--RGGAGVEVHQLX[9]AGGDPTlQRPACVKLGKKMKIHSVDQGAE-HMLILSSDGKPFEYN-YSIEHAR  141
SHEEP          76   RRL---AVLE--RGGAGVEVHQL-[1]AGSDGA-RKPKCIKLGKKMKIHSMDQGEE-HMLVLSSDGKPFEYK-YSIEHAR  144
COW            71   RRL---AVLE--RGGAGVEVHQL-[1]AGSDGA-RKPKCIKLGKKMKIHSMDQGEE-HMLVLSSDGKPFEYK-YSIEHAR  139
DOG            294  SRQpwpVGLEglEGLEGLEPWRLR[3]--SYSFcDSRECIKLGKKMKIHSVDQGAE-HMLILSSDGKPFEYN-YSIEHAR  369
CAT            180  GRL---VVLE--RGGAGVEVHQL-[1]AGSDGT-RKPKCIKLGKKAKIHSVDQGAE-YMLILSSDGKPFEYN-YSIEHAR  248

HUMAN          131  FESILQEKKIIQITCGDYHSLALSKGGELFAWGQNLHGQLGVGRKFPSTTTPQIVEHLAGVPLAQISAGEAHSMALSMSG  210
CHIMPANZEE     85   ----------------------ARTPSGELFAWGQNLHGQLGVGRKFPSTTTPQIVEHLAGVPLAQISAGEAHSMALSMSG  143
GORILLA        131  FENVLQEKKIIQITCGDYHSLALSKGGELFAWGQNLHGQLGVGRKFPSTTTPQIVEHLAGVPLAQISAGEAHSMALSMSG  210
MARMOSET       131  FESILQEKKIIQITCGDYHSLALSKGGELFAWGQNLHGQLGVGRKFPSTTAPQIVEHLAGIPLAQISAGEAHSMALSMSG  210
BABOON         130  SESILQEKKIIQITCGDYHSLALSKGGELFAWGQNLHGQLGVGRKFPSTTTPQIVEHLAGVPLAQISAGEAHSMALSMSG  209
SQUIRREL MONKEY 131 FESILQEKKIIQITCGDYHSLALSKGGELFAWGQNLHGQLGVGRKFPSTTTPQIVEHLSGIPLAQISAGEAHSMALSMSG  210
GIBBON         131  FESILQEKKIIQITCGDYHSLALSKGGELFAWGQNLHGQLGVGRKFPSTTTPQIVEHLAGVPLAQISAGEAHSMALSMSG  210
HORSE          75   FQCVLQEKNIIQITCGDYHSLALSKGGELFAWGQNTYGQLGVGRTFASTPTPQIVEHLSGVPLVQISAGEAHSMALSMSR  154
PANDA          142  FQCILQEKSIIQIACGDYHSLALSKGGELFAWGQNLHGQLGVGRLFASIPTPQAVEHLSGVPLVQISAGKAHSMALSMSG  221
SHEEP          145  FQCILQEKNIIQITCGDYHSLALSKGGELFAWGQNLDGQLGVGRIFASTSTPEIVENLSGVPLVQISAGEAHSMALSMSG  224
COW            140  FQCILQEKNIIQITCGDYHSLALSKGGELFAWGQNLDGQLGVGRIFASTSTPEIVENLSGVPLVQISAGEAHSMALSMSG  219
DOG            370  FQCILQEKSIIQITCGDYHSLALSKGGELFAWGQNLHGQLGVGRLFTSIPTPQLVEHLSGVPLVQISAGKAHSMALSMSG  449
CAT            249  FQCILQEKXIIQITCGDYHSLALSKGGELFAWGQNLHGQLGIGSQFASIAIPQIVENLSGIPLVQISAGKAHSMALSMSG  328

HUMAN          211  NIYSWGKNECGQLGLGHTESKDDPSLIEGLDNQKVEFVACGGSHSALLTQDGLLFTFGAGKHGQLGHNSTQNELRPCLVA  290
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CHIMPANZEE	144	NIYSWGKNEFGQLGLGHTESKDYPSLIEGLDNQKVEFVACGGSHSALLTQDGLLFTFGAGKHGQLGHNSTQNELRPCLVA	223
GORILLA	211	NIYSWGKNEFGQLGLGHTESKDYPSLIEGLDNQKVEFVACGGSHSALLTQDGLLFTFGAGKHGQLGHNSTQNELRPCLVA	290
MARMOSET	211	NIYSWGKNEFGQLGLDHTESKDSPSLIEALDNQKVEFLACGGSHTALLTQDGLLFTFGAGKHGQLGHNSTQNELRPCLVA	290
BABOON	210	NVYSWGKNEFGQLGLGHTESKDSPSLIEALDNQKVEFLACGGSHSALLTQDGLLFTFGAGKHGQLGHNSTQNELRPCLVA	289
SQUIRREL MONKEY	211	NIYSWGKNEFGQLGLDHTESKDSPSLIEALDNQKVEFLACGGSHTALLTQDGLLFTFGAGKHGQLGHNSTQNELRPCLVA	290
GIBBON	211	NIYSWGKNEFGQLGLGHTESKDYPSLIEALDNQEVEFLACGGSHSALLTQDGLLFTFGAGKHGQLGHNSTQNELRPCLVA	290
HORSE	155	NVYSWGRNDCGQLGLGHTNNKDSPSLIEALDNQEVEFLACGGSHTALLTKDGLVFTFGAGKCGQLGHNSTQNELTPCLVT	234
PANDA	222	NVYSWGRNDLGQLGLGHTDGEDFPSLIETLDNQQVEFLACGGSHTALLTTDGLVFTFGAGKYGQLGHNSTQNELRPRLVT	301
SHEEP	225	NVYSWGRNDCGQLGLGHTYNKDSPSCIEALDDQKVEFLACGGSHTALLTKSGLVFTFGDGKYGQLGHNSTQNELRPCLVA	304
COW	220	NVYSWGRNDCGQLGLGHTYNKESPSCIEALDDQKVEFLACGGCHTALLTKSGLVFTFGDGKYGQLGHNSTQNELRPRLVT	299
DOG	450	NIYSWGRNDLGQLGLGHTNGEDFPSLIEALDNQKVEFLACGGSHTALLTKDGLVFTFGAGKYGQLGHNSTQNELRPRLVT	529
CAT	329	NIYSWGRNDFGQLGLGHTDGKDFPSLIEALDNQKVEFLACGGSHTALLTKDGLVFTFGAGKHGQLGHNSTQNELRPRLVT	408

HUMAN	291	ELVGYRVTQIACGRWHTLAYVSDLGKVFSFGSGKDGQLGNGGTRDQLMPLPVKVSSSEELKLESHTSEKELIMIAGGNQS	370
CHIMPANZEE	224	ELVEYRVTQIACGRWHTLAYVSDLGKVFSFGSGKDGQLGNGGTRDQLMPLPVKVSSSEELKLESHTSEKELIMIAGGNQS	303
GORILLA	291	ELVGYRVTQIACGRWHTLAYVSDLGKVFSFGSGKDGQLGNGGTRDQLMPLPVKVSSSEELKLESHTSEKELIMIAGGNQS	370
MARMOSET	291	ELAGNRVTQIACGRWHTLAYVSDLGKVFSFGSGKEGQLGNGGTRDQLIPLPMKVSSNEDLKFESHTSEKELIMIAGENQS	370
BABOON	290	ELVGNRVTQIACGRWHTLAYVSDLGKVFSFGSGKDGQLGNGGTLDQLIPLPVKVSSSEELKLESHTSEKELIMIAGGNQS	369
SQUIRREL MONKEY	291	ELAGNRVTQIACGRWHTLAYVSDLGKVFSFGSGKEGQLGNGGTRDQLIPLPMKVSSNEDLKFESHTSEKELIMIAGENQS	370
GIBBON	291	ELVGNRVTQIACGRWHTLAYVSDLGKVFSFGSGKDGQLGNGGTRDQLIPLPVKVSSSEELKLETHTSEKELIMIAGGNQS	370
HORSE	235	ELVGKRVTQIACGRRHTLAYVSDLGKVFSFGSGEGGQLGNGATHHQLIPLPMKLPSNEELKFESHTSEKELIMIAGGNQS	314
PANDA	302	ELAGNRVTQIACGRRHTLAYVSDLGKVFSFGSGKEGQLGNGGTHNQLIPLPMKLPSNEELKFESRTSDKELVMIAGGNQS	381
SHEEP	305	GLVGNRVTQIACGRQHTLAYVSDMGKVFSFGSGKEGQLGNGGTCNQLMPRPMKLPSSEELKSESSTSVKELIMVAGGNQS	384

COW	300	GLVGNRVTQIACGRQHTLAYVSDTGKVFSFGSGKEGQLGNGGTRNQLIPRPMKLLSSEELKSESSTSVKELIMVAGGNQS	379
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CAT	409	ELAGNRVTQIACGRQHTLAYVSDLGKVFSFGSGKEGQLGNGGTHNQLIPLPMKLPSNEELTFESRASEKELIMIAGGNQS	488

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CHIMPANZEE	304	ILLWIKKENSYVNLKRTIPTLNEGTVKRWIADVETKRWQSTKREIQEIFSSPACLTGSFLRKRRTTEMMPVYLDLNKARN	383
GORILLA	371	ILLWIKKENSYVNLKRTIPTLNEGTVKRWIADVETKRWQSTKREIQEIFSSPACLTGGFLRKRKDEK----FSSLNFGRT	446
MARMOSET	371	ILLWIKKENSYVNLRRTILTLNEGTIKRWIADVETKRWQSTKREIQEIFSSPACLSGSFLRKRRTTEMLPVYLDLSKARN	450
BABOON	370	ILLWIKKENSYVNLKRTIPTLNEGTVKRWIADVETKRWHSTKREIQEIFSSPACLTGSFLRKRRTAEMMPVYLDLNKARN	449
SQUIRREL MONKEY	371	ILLWIKKENSYVNLRRTILTLNEGTVKRWIADVETKRWQSTKREIQEIFSSPACLSGSFLRKRRTTEMMPVYLDLSKART	450
GIBBON	371	ILLWIKKENSYVNLKRTIPTLNEGTVRRWIADVETKRWQSTKREIQEIFSSPACLTGSFLRKRRTTEMMPVYLDLNKARN	450
HORSE	315	ILLWMEKENPYVNLRRKIPTLNEGTVKRWIADVGTKKWQNTKREIKEIFSSPACLTGSFLRERITAETMSVHLNINKARD	394
PANDA	382	VLLWMEKKNPYVNLRRKIPTLNEGTVKRWIADVGTKQWQNTKREIREIFSSSACLTGSFLREREAAETMLIHLDLNKARN	461
SHEEP	385	ILMWMEKENSYVNLRRKIPTLNEGTVKRWIADVGTKQWQNTKREIREIFSSPACLTGSFLRERIDGEMISIHLDLNAARN	464
COW	380	ILIWMEKENSYVNLRRKIPTLNEGTVKRWIADVGTKRWQNTKREIREIFSSPACLTGSFLRERIDGKMISIHLDLNTARN	459
DOG	610	ILLWMGKKNPYVNLRRRIPTLNEGTVKRWIADVGTKQWQNTKREIREIFSSPACLIGSFLKERIAAETMLIHLDLNKARN	689
CAT	489	ILLWMGKKNSYVNLRRKIPTLNEGTVKRWIADVGTKQWQNTKKEIREIFSSPACLTGSFSRERRAAETMPVHLDLNKARN	568

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CHIMPANZEE	384	IFKELTQKDWITNMITTCLKDNLLKRLPFHSPPQ	EALEIFFLLPECPVMHIS	NNWESLV-VPFAKVVCKMSDQ	455
GORILLA	447	TAPLGVRGE----MITTCLKDNLLKRLPFHSPPQ	EALEIFFLLPECPVMHIS	NNWESLV-VPFAKVVCKMSDQ	514
MARMOSET	451	IFKELIQKDWITNTITTCLKDNLLKRLPFHSPYQ	EALEVFFLLPECPVMHNS	NNWESIV-VAFAKAVCKMSDQ	522
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SQUIRREL MONKEY  451  IFKELTQKDWITNTITTCLKDNLLKRLPFHSPYQ    EALEVFFLLPECPVMHNS   NNWESIV-VAFAKAVCKMSDQ  522
GIBBON           451  IFKELTQKDWITNMITTCLKDNLLKRLPFRSPPQ    EALEVFFLLPECPVMHIS   NNWESLV-VPFAKVVCKMSDQ  522
HORSE            395  TFKELTQKDWITNMITTCLRDNLIKNLPFHSPHR    EALEVFFLLPECPVMHDY   NNWESLV-VPFAEAICKMSNQ  466
PANDA            462  AFKELTQKDWIANTITTCLKDNLLKNLPFHSPHQ[21]ESLVVPFAEVVCAMSDQS[5]EYWASLQdAAFIRLVQMFKRA  560
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COW              460  TFKELTQKDWITNTITSCLKDNLLKNLPFNSPHQ    EALEVFFLLPECPVMHDS   NNWESLV-VPFAEAVCKMNDQ  531
DOG              690  DFKELTQKDWIANMITTSLKDNLLKNLPFHSPHQ[21]ESLVVPFAEAICAMSDQS[5]EYWASLQeAAFIRLVQMFKRA  788
CAT              569  AFKELTQKDWIANTITTCLKDNLLKNLPFHSPHQ[21]ESLVVPFAEAVCAMSNQS[5]EYWASLQePAFSRLVQMFKGA  667

HUMAN            523  SSLVLEEYWATLQESTFSKLVQMFKTAVICQLD-YWDESAEENGNVQ--ALLEMLKKLHRVNQVKCQLPESIFQVDEL-L  598
CHIMPANZEE       456  SSLVLEEYWATLQESTFSKLVQMFKTAVICQLD-YWDESAEENGNVQ--ALLEMLKKLHRVNQVKCQLPESIFQVDEL-L  531
GORILLA          515  SSLVLEEYWATLQESTFSKLVQMFKTAVICQLD-YWDESAEENGNVQ--ALLEMLKKLHRVNQVKCQLPESIFQVDEL-L  590
MARMOSET         523  SSLVLEEYWATLQESTFSKLVQMFKTAVICQLD-YWNENAEENGNVQ--ALLEMLKKLHRVNQMKCLLPESIFQVDEL-L  598
BABOON           522  SSLVLEEYWATLQESTFSKLVQMFKTAVVCQLD-YWDESAEENGNVQ--ALLEMLKKLHRVNQMKCQLPESIFQVDEL-L  597
SQUIRREL MONKEY  523  SSLVLEEYWATLQESTFSKLVQMFKTAIICQLD-YWNENAEENGNVQ--ALLEMLKKLHRVNQMKCLLPESIFQVDEL-L  598
GIBBON           523  SSLVLEEHWATLQESTFSKLVQMFKTAVICQLD-YWDESAEENGNVQ--ALLEMLKKLHRVNQMKYQLPESIFQVDEL-L  598
HORSE            467  SLGVLEEYWASLQESAFSKLVQMFKRAMGAQLH-YWSESVDSNCHVR--ALLEVLKRLHRVNQSNCQVPENIFEVSEL-T  542
PANDA            561  IT--------------------------AQLH-YWTESSENN--YHvkALLEILKKLHRVNQAVCQLPENIFKINELtH  610
SHEEP            537  MS--------------------------RVLEeYWASLKESP--FI--NLVQMFKRA----------------IVAQlH  569
COW              532  MS--------------------------GVLEeYWASLKESI--FI--NLVQMFKRA----------------VIAQlH  564
DOG              789  VT--------------------------AQLH-YWTESSENN--YHvkALLEILKKLHRVNQAKCQLPENIFKVNELtH  838
CAT              668  IT--------------------------AQLH-YWTESSEDN--CHvkALLEMLRKLYRVNQAKCQLPENIFKINELtQ  717
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CHIMPANZEE	532	HRLNFFVEVCRRYLWKMTVDTS-ENV---QCCVIFSHFPFIFNNLSKIKLLHTDTLLKIEGKKHKAYLRSAAIEEEGESE	607
GORILLA	591	HRLNFFVEVCRRYLWKMTVDTS-ENV---ECCVIFSHFPFIFNNLSKIKLLHTDTLLKIEGKKHKAYLRSAAIEEERESE	666
MARMOSET	599	YRLDFFVEVCRRYLWKMTVDTL-ENV---GCCVIFSHFPFIFNNLSKIKLLRTDTLVKIQGKKHKAYFRWAAVEEERESE	674
BABOON	598	YRLNFFVEVCRRCLWKMTVDTS-ENA---GCWVIFSHFPFIFNHLSKIKLLHTDTLLKIEGKKHKAYLMSAAIEEERESE	673
SQUIRREL MONKEY	599	YRLDFFVEVCRRYLWKMTVDTL-ENV---GCCVIFSHFPFIFNNLSKIKLLRTDTLVKIQGKKHKAYFRWAAVEEERESE	674
GIBBON	599	HRLNFFVEVCRRYLWKMTVDTS-ENV---ECCVIFSHFPFIFNNLSKIKLLHTDTLLKIEGKKHKAYLRSAAIEEERESE	674
HORSE	543	HWLDFYGDVYKRSAWKMNSDTS-RDS-----PVVFSHFPFIFNILSKIKLLYADSLLKIWEKEQRRFMTLDGNVDPGEPE	616
PANDA	611	W-LDFYGDAYRRSAWK---INS-DASfdtQYPVIFSHFPFIFNILSKIKLLYADSLLKIQEKKFRACMQLAGLVEQGGSE	685
SHEEP	570	Y----------WT---ESS-ENN---------NHIKALLEVLKKL----------YREKKFQACMRLAGIVDQEGSA	613
COW	565	Y----------WT---ESS-ENN---------SHIKALLEVLKKL----------YREKKFRACMRLAGIVDQERSA	608
DOG	839	W-LDFYGDAYRRSSWK---VNS-DTSvgtQYPVIFSHFPFIFNILSKIKLLYADSLLKIQEKKFRACMRLAGIMEQGGSQ	913
CAT	718	W-LDFYGDAYRRSSWR---VNNlDTSvdtPYPVIFSHFPFIFNILSKIKLLYADSLLKIQEKKFRACMRLAGVVEHGRSE	793

HUMAN	675	FALRPTFDLTVRRNHLIEDVLNQLSQFENEDLRKELWVSFSGEIGYDLGGVKKEFFYCLFAEMIQPEYGMFMYPEGASCM	754
CHIMPANZEE	608	FALRPTFDLTVRRNHLIEDVLNQLSQFENEDLRKELWVSFSGEIGYDLGGVKKEFFYCLFAEMIQPEYGMFMYPEGASCM	687
GORILLA	667	FALRPTFDLTVRRNHLIEDVLNQLSQFENEDLRKELWVSFSGEIGYDLGGVKKEFFYCLFAEMIQPEYGMFMYPEGGSCM	746
MARMOSET	675	FALLPTFDLTVRRNHLIEDVLNQLSQFENEDLRKELWVSFSGEIGYDLGGVKTEFFYCLFEEMTQPEYGLFMYPEGASCM	754
BABOON	674	FALMPTFDLTVRRNHLIEDVLNQLSQFENEDLRKELWVSFSGEIGYDLVGVKREFFYCLFEEMIQPEYGMFMYPEGASCM	753
SQUIRREL MONKEY	675	FALLPTFDLTVRRNHLIEDVLNQLSQFENEDLRKELWVSFSGEIGYDLGGVKTEFFYCLFEEMTQPEYGLFMYPEGASCM	754
GIBBON	675	FALRPTFDLTVRRNHLIEDVLNQLSQFENEDLRKELWVSFSGEIGYDLGGVKKEFFYCLFEEMIQPEYGMFMYPEGASCM	754
HORSE	617	LALSSSFSLTVRRSHLIEDVLNHLNRFENEDLRRELLVSFSGEIPLDYGGVRAEFFHCLFEELTQPEYGLFTYPEEASYM	696
PANDA	686	LALLPTFNLTVRRTHLIEDVLSHLSQFENEDLRRELMVSFSGEIGHDSGGVKVEFFHCLFEEMTRPEYGMFTYPEEASYM	765

SHEEP	614	LSLLPTFNLIVRRSHLIEDVFNQLNQFENEDLRRELMVSFSGEIGYDFGGVRAEFFYCLFQEMTRPEYGMFTYPEEASYM	693
COW	609	LSSLPTFNLIVRRSHLIEDVFSQLNQFENEDLRRELMVSFSGEIGYNFGGVRAEFFYCLFQEMTRPEYGMFTYPEEASYM	688
DOG	914	LALLPTFNLTVRRSHLIEDVLNHLNQFENEDLRRELMVSFSGEIGHDSGGVKVEFFHCLFEEMTRPEYGMFTYPEDASYM	993
CAT	794	LSLLPTFNLTVRRNHLIEDVLSHLNQFENEDLRRELMVSFSGEIGHDSGGVKVEFFHCLFEEMTRPEYGMFTYPEEASYM	873

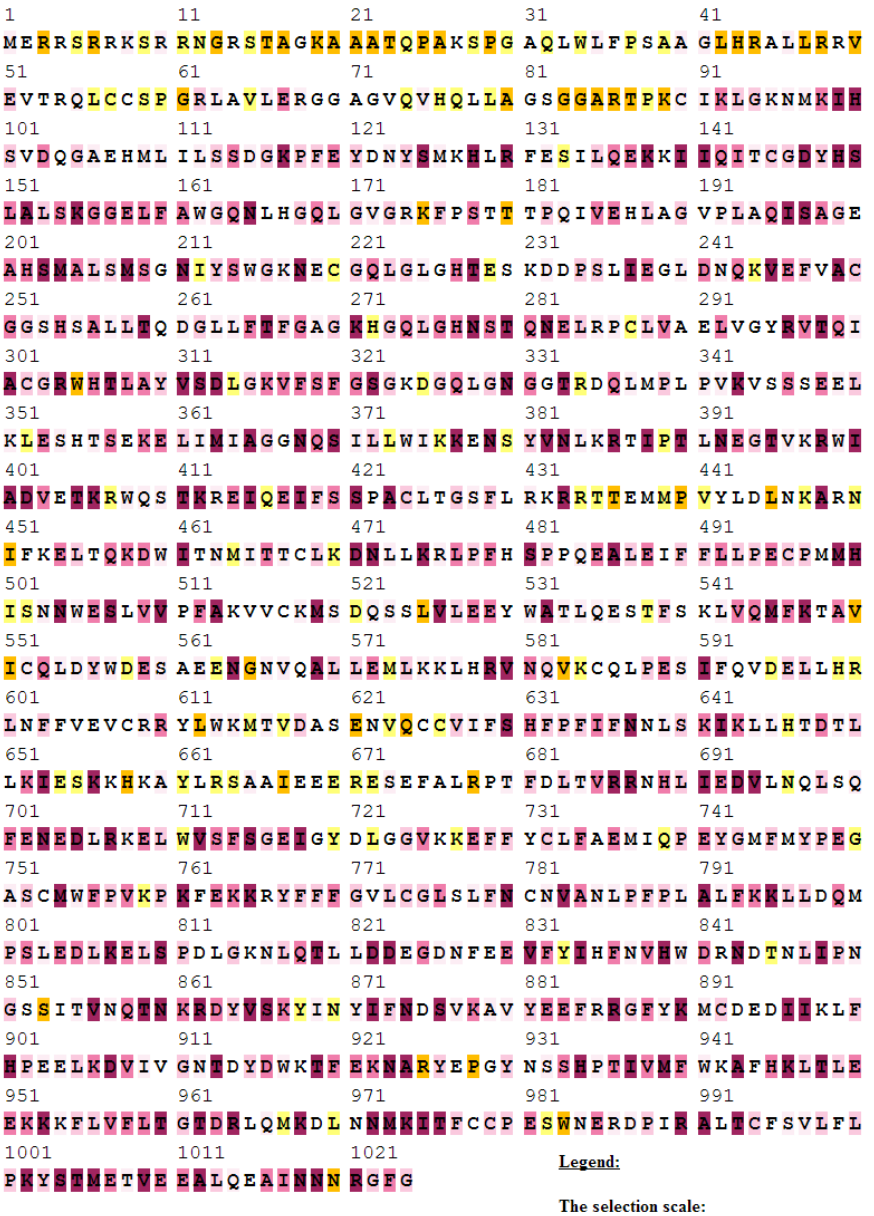
HUMAN	755	WFPVKPKFEKKRYFFFGVLCGLSLFNCNVANLPFPLALFKKLLDQMPSLEDLKELSPDLGKNLQTLLDDEGDNFEEVFYI	834
CHIMPANZEE	688	WFPVKPKFEKKRYFFFGVLCGLSLFNCNVANLPFPLALFKKLLDQMPSLEDLKELSPDLGKNLQTLLDDEGDNFEEVFYI	767
GORILLA	747	WFPVKPKFEKKRYFFFGVLCGLSLFNCNVANLPFPLALFKKLLDQMPSLEDLKELSPVLGKNLQTLLDDEGDNFEEVFYI	826
MARMOSET	755	WFPVKPKFEKKRYFFFGVLCGLSLFNCSVANLPFPLALFKKLLDQMPSLEDLKELSPDLGKNLQTILDDEGDNFEEVFYI	834
BABOON	754	WFPVRPXIEKKRYFFFGLLCGLSLFNCNVANLPFPLALFKKLLDQMPSLEDLKELSPDLGKNLQTLLDDEGDNFEEVFYI	833
SQUIRREL MONKEY	755	WFPVKPKFEKKRYFFFGVLCGLSLFNCSVANLPFPLALFKKLLDQMPSLEDLKELSPDLGKNLQTILDDEGDNFEEVFYI	834
GIBBON	755	WFPVKPKFEKKRYFFFGVLCGLSLFNCNVANLPFPLALFKKLLDQMPSLEDLKELSPDLGKNLQTLLDDEGDNFEEVFYI	834
HORSE	697	WFPVRPKFEKKSYFFFGVLCGLCLFNCNVANIPFPLALFKKLLDQTPSLEDLKELSPVFGRSLQTLLDDEGEDFGEVFYI	776
PANDA	766	WFPVRPKFEKKRYFFFGVLCGLSLFNFNVANIPFPLALFKKLLNQTPSLEDLKELSPVLGKSLQTLLDDEGDDFGEVFYI	845
SHEEP	694	WFPVRPKFEKKSYFFFGLLCGLSLFNCNVADIPFPLALFKKLLDQTPSLEDLKELSPVLGESLQTLLDDDGDDLEEVFHI	773
COW	689	WFPVRPKFEKKSYFFFGLLCGLSLFNCNVADIPFPLALFKKLLDQTPSLEDLKELSPVLGESLQTLLDDDGDDLEEVFHI	768
DOG	994	WFPVTPKFEKKRYFFFGVLCGLSLFNFNVANIPFPLALFKKLLDQTPSLEDLKELSPVLGKSLQTLLDDEGDDFGEVFLI	1073
CAT	874	WFPVRPKFEKKRYFFFGVLCGLSLFNFNVANIPFPLALFKKLLNQAPSLEDLKELSPVLGKSLQTLLDDEGDDFGEVFYI	953

HUMAN	835	HFNVHWDRNDTNLIPNGSSITVNQTNKRDYVSKYINYIFNDSVKAVYEEFRRGFYKMCDEDIIKLFHPEELKDVIVGNTD	914
CHIMPANZEE	768	HFNVHWDRNDTNLIPNGSSITVNQTNKRDYVSKYINYIFNDSVKAVYEEFRRGFYKMCDEDIIKLFHPEELKDVIVGNTD	847
GORILLA	827	HFNVHWDRNDTNLIPNGSSITVNQTNKRDYVSKYINYIFNDSVKAVYEEFRRGFYKMCDEDIIKLFHPEELKDVIVGNTD	906
MARMOSET	835	YFNVHWDRNDTDLIPNGRNIIVNQTNKRDYVSKYIDYIFNDSVKVVYEEFRRGFYKMCEEDIIKLFHPEELKDVIVGNTY	914

BABOON	834	HFNVHWDRNDTNLIPNGSSIIVNQTNKRDYVSKYIDYIFNDSVKAVYEEFRRGFYKMCDEDIIKLFHPEELKDVIVGHTD	913
SQUIRREL MONKEY	835	HFNVHWDRNDTDLIPNGSNIIVNQTNKRDYVSKYIDYIFNDSVKVVYEEFRRGFYKMCEEDIIKLFHPEELKDVIVGNTD	914
GIBBON	835	HFNVHWDRNDTNLIPNGSSIIVNQTNKRDYVSKYIDYIFNDSVKAVYEEFRRGFYKMCDEDIIKLFHPEELKDVIVGNTD	914
HORSE	777	HFTVHWDRNAEELIPNGSDIIVDQTNKRDYVSKCVNYIFNISIKAVYEEFQRGFYKVCDKEIIGFFHPAELKDVIIGNTD	856
PANDA	846	YFNVHWDKNDIDLIPNGSCVIVDQTNKRDYVSKCVSYIFNISVKALYEEFQRGFYKVCDKDIIEFFHPEELKDVIIGNTD	925
SHEEP	774	HFNVHWDKNDVDLIPDGSHIIVDQTNKRDYVSKYVNYIFNISVKAVYEEFQRGFYKVCDKEIIEFFHPEQLKDVIIGNTD	853
COW	769	HFNVHWDKNDVDLIPDGSHVIVDQTNKRDYVSKYVNYIFNISVKAVYEEFQRGFYKVCDKEIIEFFHPEQLKDVIIGNTD	848
DOG	1074	YFNVHWDKNDVDLIPNGSGIIVDQTNKRDYVSKYVNYIFNISVKAVYEEFQRGFYKVCDKDIIEFFHPEELKDVVIGNTD	1153
CAT	954	YFNVHWDKNDVDLIPNGRCIIVDQTNKRDYVSKCVNYIFNISVKAVYEEFQRGFYKVCEKDIIEFFHPEELKDVIVGNTD	1033

HUMAN	915	YDWKTFEKNARYEPGYNSSHPTIVMFWKAFHKLTLEEKKKFLVFLTGTDRLQMKDLNNMKITFCCPESWNERDPIRALTC	994
CHIMPANZEE	848	YDWKTFEKNAHYEPGYNSSHPTIVMFWKAFHKLTLEEKKKFLVFLTGTDRLEMKDLNNMKITFCCPESWNERDPIRALTC	927
GORILLA	907	YDWKTFEKNACYEPGYNSSHPTIVMFWKAFHKLTLEEKKKFLVFLTGTDRLQMKDLNNMKITFCCPESWNERDPIRALTC	986
MARMOSET	915	YDWKTFEKNAHYKPEYDSSHPTIVMFWEAFHKLTLEEKKKFLVFLTGTDRIQIKDLKNMKITFCCPENWNEREPMRALTC	994
BABOON	914	YDWKTFEKNARYEPGYNSSHPTIVMFWKAFHKLTLEEKKKFLVFLTGTDRLQTKDLKNMKITFCCPESWNERDPMRALTC	993
SQUIRREL MONKEY	915	YDWKTFEKNAHYKPEYDSSHPTIVMFWEAFHKLTLEEKKKFLVFLTGTDRIQMKDLKNMKITFCCPENWNERDPMRALTC	994
GIBBON	915	YDWKTFEKNARYEPGYNSSHPTIVMFWKAFHKLTLEEKKQFLVFLTGTDRLQMKDLNNMKITFCCPESWNERDPMRALTC	994
HORSE	857	YDWETFEKNARYAGGYDSSHPTIVMFWEALHKLTLEEKKKFLVFLTGTDRLQVKGVKNMKITFCCPEHLDEKDPIRAQTC	936
PANDA	926	YDWETFEKNAHYEEGYDNSHPTIVMFWKALHKLTLEEKKKFLVFLTGTDRIQVKGLKNMKITFCCPENVNEKDPIRAQTC	1005
SHEEP	854	YDWETFEKNAHYEHGYDSSHPTIVMFWKALHKLTLEEKKKFLVFLTGTDRIQVKGVKNMKITFCCPETLNEKDPIRAQTC	933
COW	849	YDWETFEKNAHYEHGYDSSHPTIVMFWKALHKLTLEEKKKFLVFLTGTDRIQVKGLKNMKITFHCPENLNEKDPIRAQTC	928
DOG	1154	YDWETFEKNAHYEEGYDNSHPTIVMFWKALHKLTLEEKKKFLVFLTGTDRIQVKGLKNMKITFCCPENVNEKDPIRAQTC	1233
CAT	1034	YDWETFEKNAHYEEGYDNSHPTIVMFWKALHKLTLEEKKKFLVFLTGTDRIQVKGLKNMKITFCCPENMNEKDPIRAQTC	1113

HUMAN	995	FSVLFLPKYSTMETVEEALQEAINNNRGFG	1024
CHIMPANZEE	928	FSILFLPKYSTMETVEEALQEAINNSRGFG	957
GORILLA	987	FSVLFLPKYSTMETVEEALQEAINNNRGFG	1016
MARMOSET	995	FSVLFLPKYSTMERVEEALQVAINNNRGFG	1024
BABOON	994	FSVLFLPKYSTMETVEEALQVAINNNRGFG	1023
SQUIRREL MONKEY	995	FSVLFLPKYSTMERVEEALEVAINNNRGFG	1024
GIBBON	995	FNVLFLPKYSTMETVEEALQEAINNSRGFG	1024
HORSE	937	FSVLYLPKYSTMERVEEALQVAINNNRGFG	966
PANDA	1006	ISVLYLPKYSTMERVEEALQVAINNSRGFG	1035
SHEEP	934	FSVLYLPKYSTMERVEEALQVAINNSRGFG	963
COW	929	FSVLYLPKYSTMERVEEALQAAINNKRGFG	958
DOG	1234	ISVLYLPKYSTMERVEEALQVAINNSRGFG	1263
CAT	1114	ISVLYLPKYSTMERVEEALQVAINNSRGFG	1143



Box 1

Sequences queried

NP_057407.2 = Human
XP_003310459.1 = Chimpanzee
XP_004039179.1 = Gorilla
XP_002745648.1 = Marmoset
XP_003898997.1 = Baboon
XP_003924055.1 = Squirrel monkey
XP_003265940.1 = Gibbon
XP_001915115.2 = Horse
XP_002913645.1 = Panda
XP_004009762.1 = Sheep
NP_001095465.1 = Cow
XP_535652.3 = Dog
XP_003985249.1 = Cat

Supplementary Figure 3