Supplementary Information

Reference gene analysis and its use for kinase expression profiling in *Fasciola hepatica*

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Supplementary Table S1: Accession numbers of reference genes and kinase genes used for the multiple alignments in Supplementary Figures S8 and S9.

Gene	***F. hepatica***	***H. sapiens***	***M. musculus***	***D. melanogaster***	***C. elegans***	***S. mansoni***
tbcd	maker-scaffold10x_815_pilon-snap-gene-1.87	NP_005984.3	NP_084154.1	NP_608648.1	NP_492270.1	Smp_153590
eprs	maker-scaffold10x_14_pilon-snap-gene-0.109	NP_004437.2	NP_084011.1	NP_524471.2	NP_492711.1	Smp_138930
letm1	maker-scaffold10x_721_pilon-snap-gene-0.10	NP_036450.1	NP_062668.1	NP_611922.1	NP_506382.1	Smp_310830.1
actb	augustus_masked-scaffold10x_269_pilon-processed-gene-0.18	NP_001092.1	NP_780706.1	NP_001014725.1	NP_505818.1	Smp_183710
snrpa1	maker-scaffold10x_234_pilon-snap-gene-0.20	NP_003081.2	NP_067311.4	NP_610315.1	NP_494763.1	Smp_141330
ppp1cb	maker-scaffold10x_238_pilon-snap-gene-0.95	NP_002700.1	NP_001357876.1	NP_001262919.1	NP_001022616.1	Smp_028990
psmb7	maker-scaffold10x_1452_pilon-augustus-gene-0.11	NP_002790.1	NP_035317.1	NP_524076.2	NP_493271.1	Smp_073410
gapdh	maker-scaffold10x_2706_pilon-snap-gene-0.15	NP_001276674.1	NP_032110.1	NP_001259584.1	NP_508534.3	Smp_056970.2
abl1	maker-scaffold10x_1995_pilon-snap-gene-0.46	NP_005148.2	NP_001269975.1	NP_001261964.1	NP_509777.2	Smp_246700.1
abl2	maker-scaffold10x_873_pilon-snap-gene-0.69	NP_001129473.1	NP_001129576.1	NP_476849.1	NP_493502.1	Smp_128790.1
akt1	maker-scaffold10x_205_pilon-augustus-gene-0.40	NP_001014431.1	NP_001318036.1	NP_001287353.1	NP_001023646.1	Smp_243630
pkc	maker-scaffold10x_608_pilon-snap-gene-0.5	NP_002731.4	NP_032883.2	NP_001036542.1	NP_495011.1	Smp_096310
plk1	maker-scaffold10x_784_pilon-snap-gene-0.36	NP_005021.2	NP_035251.3	NP_001014592.1	NP_491036.1	Smp_009600

Supplementary Table S2: Primer sequences and product sizes in qRT-PCR

Gene	**Annotation**	**Forward primer (5‘-3‘)**	**Reverse primer (5‘-3‘)**	**PCR product size (bp)**
tbcd	Tubulin-specific chaperone D	CAGCAGCCGCATTTCAGGA	AGCCAAATGGTCAATCATCGC	176
eprs	Glutamyl-prolyl-tRNA synthetase	TACACCACAACCATCGAGGC	GTGGTCAATCCCCACGAGTT	167
letm1	Leucine zipper and EF-hand containing transmembrane protein 1	AGATGGATAAGTTAGCCGAGG	ACCTTTTGGAGACGCCGTAG	184
actb	Actin, cytoplasmic 1	CATGTTTGAGACCTTCAACGCT	AGATCACGCCCAGCAAGGT	189
snrpa1	U2 small nuclear ribonucleoprotein A’	GAGAACATGGGTAGTACATTGG	CCAGATCCTCTGCTATGCG	148
ppp1cb	Protein phosphatase 1 catalytic subunit beta	GCAGTTGGTTACTTTGTTTTCGG	CAGGCCATACCGCATTGAG	161
psmb7	Proteasome subunit beta type 7	TCACCAAGGATTCCACGGAG	GATCTGGCAGATCCCGAATC	171
gapdh	Glyceraldehyde-3-phosphate dehydrogenase	GCCAATGTTCGTGTTCGGAG	TCAACGACCTTCTGAGTGGC	183
abl1	ABL proto-oncogene 1,non-receptor tyrosine kinase	CTGCCTGTACATACTGTGCC	GTGCGGTGAGTTCATGGTTC	154
abl2	ABL proto-oncogene 2,non-receptor tyrosine kinase	CGTTAGCGAATCCCAATCTAG	GGTTCTCTGTGTAGTGACCG	179
akt1	Rac-alpha serine/threonine-protein kinase	TCTCGGTGGTGGTCCTAGT	TATGTACTTCGTGTCCGTAGG	142
pkc	Protein kinase C	TAAAGAGGGCATCACAGCGG	GCCAACATTTTCCCACGGAG	172
plk1	Polo-like kinase 1	ATGGCTAGTAAGGACGCTGC	TGCTTTCGGAACCACTTTTCC	177

Supplementary Table S3: **Expression stability of candidate reference genes based on three different life stages of *F. hepatica*: newly excysted juveniles (NEJs), immature worms, and adults.**

Ranking was based on four different algorithms: NormFinder, BestKeeper, geNorm, and comparative ΔCT method. Candidate reference genes selected for further analyses are written in bold.

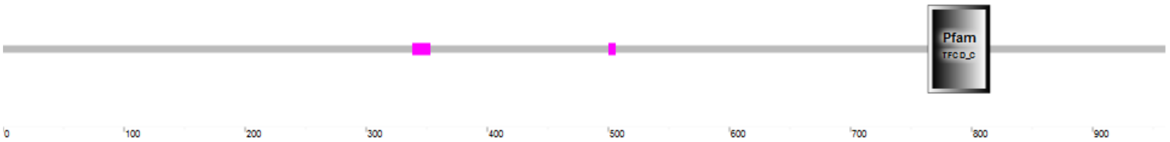
Rank	**NormFinder**		**BestKeeper**		**geNorm**		**ΔCT method**	
	Ref. gene	**Stability value M**	**Ref. gene**	**Coeff. of correlation r**	**Ref. gene**	**Stability value M**	**Ref. gene**	
1	**Fh*eprs***	0.118	Fh*actb*	0.972	**Fh*tbcd*, *Fheprs***	0.298	**Fh*eprs***	0.562
2	Fh*psmb7*	0.194	**Fh*tbcd***	0.971			**Fh*tbcd***	0.600
3	**Fh*tbcd***	0.209	**Fh*eprs***	0.970	Fh*psmb7*	0.360	Fh*psmb7*	0.618
4	Fh*snrpa1*	0.306	Fh*psmb7*	0.936	Fh*snrpa1*	0.415	Fh*snrpa1*	0.661
5	Fh*actb*	0.361	Fh*gapdh*	0.922	Fh*letm1*	0.513	Fh*actb*	0.800
6	Fh*letm1*	0.366	Fh*snrpa1*	0.810	Fh*ppp1cb*	0.597	Fh*letm1*	0.819
7	Fh*ppp1cb*	0.540	Fh*letm1*	0.610	Fh*actb*	0.672	Fh*ppp1cb*	0.966
8	Fh*gapdh*	0.592	Fh*ppp1cb*	0.305	Fh*gapdh*	0.751	Fh*gapdh*	0.989

Supplementary Table S4: **Expression stability of candidate reference genes during *in vitro* growth of *F. hepatica* from newly excysted juveniles (NEJs) to 4 week old juvenile worms.**

Ranking was based on analysis using NormFinder, BestKeeper, geNorm and comparative ΔCT method. Candidate reference genes selected for further analyses are written in bold.

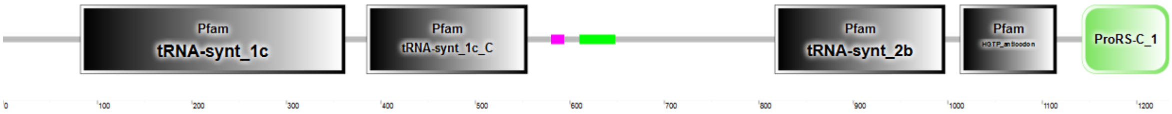
	NormFinder		**BestKeeper**		**geNorm**		**ΔCT method**	
Rank	**Ref. gene**	**Stability value M**	**Ref. gene**	**Coeff. of correlation r**	**Ref. gene**	**Stability value M**	**Ref. gene**	
1	**Fh*psmb7***	0.177	**Fh*psmb7***	0.971	**Fh*tbcd,*** *Fheprs*	0.170	**Fh*tbcd***	0.564
2	**Fh*tbcd***	0.196	**Fh*tbcd***	0.945			**Fh*psmb7***	0.577
3	Fh*eprs*	0.242	Fh*snrpa1*	0.935	**Fh*psmb7***	0.269	Fh*eprs*	0.600
4	Fh*snrpa1*	0.263	Fh*eprs*	0.883	Fh*actb*	0.317	Fh*snrpa1*	0.661
5	Fh*actb*	0.340	Fh*ppp1cb*	0.817	Fh*snrpa1*	0.424	Fh*actb*	0.686
6	Fh*letm1*	0.469	Fh*actb*	0.730	Fh*gapdh*	0.532	Fh*letm1*	0.902
7	Fh*ppp1cb*	0.596	Fh*letm1*	0.670	Fh*letm1*	0.651	Fh*gapdh*	0.988
8	Fh*gapdh*	0.620	Fh*gapdh*	0.201	Fh*ppp1cb*	0.756	Fh*ppp1cb*	1.072

Tubulin-specific chaperone D (FhTbcd*):*



Glutamyl-prolyl-tRNA synthetase (FhEprs):

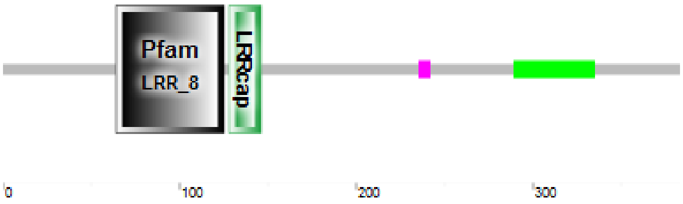
ProRS-C_1, Prolyl-tRNA synthetase, C-terminal



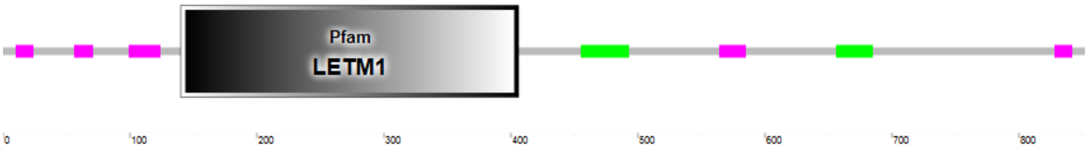
Actin, cytoplasmic 1 (FhActb):

U2 small nuclear ribonucleoprotein A (FhSnrpa1*)*:

LRR, Leucine-rich repeat

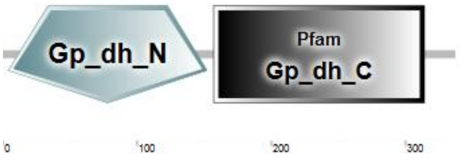


Leucine zipper and EF-hand containing transmembrane protein 1 (FhLetm1):



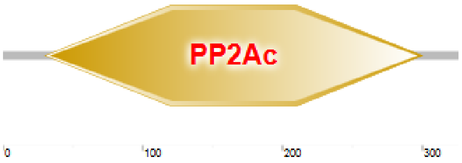
Glyceraldehyde-3-phosphate dehydrogenase (FhGapdh):

Gp_dh_N, Glyceraldehyde 3-phosphate dehydrogenase, NAD binding domain

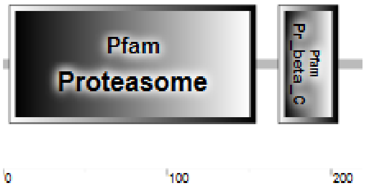


Protein phosphatase 1 catalytic subunit beta (FhPpp1cb):

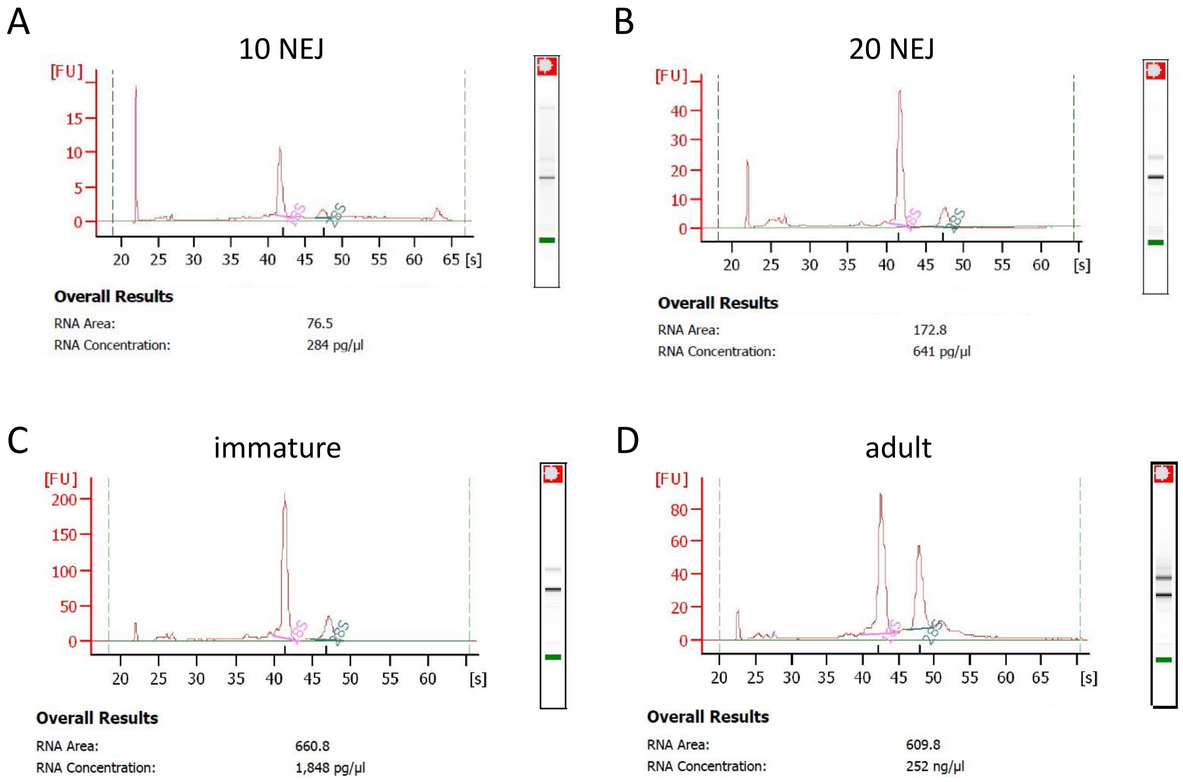
PP2Ac, Protein phosphatase 2A homologues, catalytic domain



Proteasome subunit beta type 7 (FhPsmb7):



Supplementary Figure S1: **Results from SMART analysis of amino acid sequences from eight reference gene candidates of *F. hepatica*.**



A

Overall Results

RNA Area: 76.5
RNA Concentration: 284 pg/µl

B

Overall Results

RNA Area: 172.8
RNA Concentration: 641 pg/µl

C

Overall Results

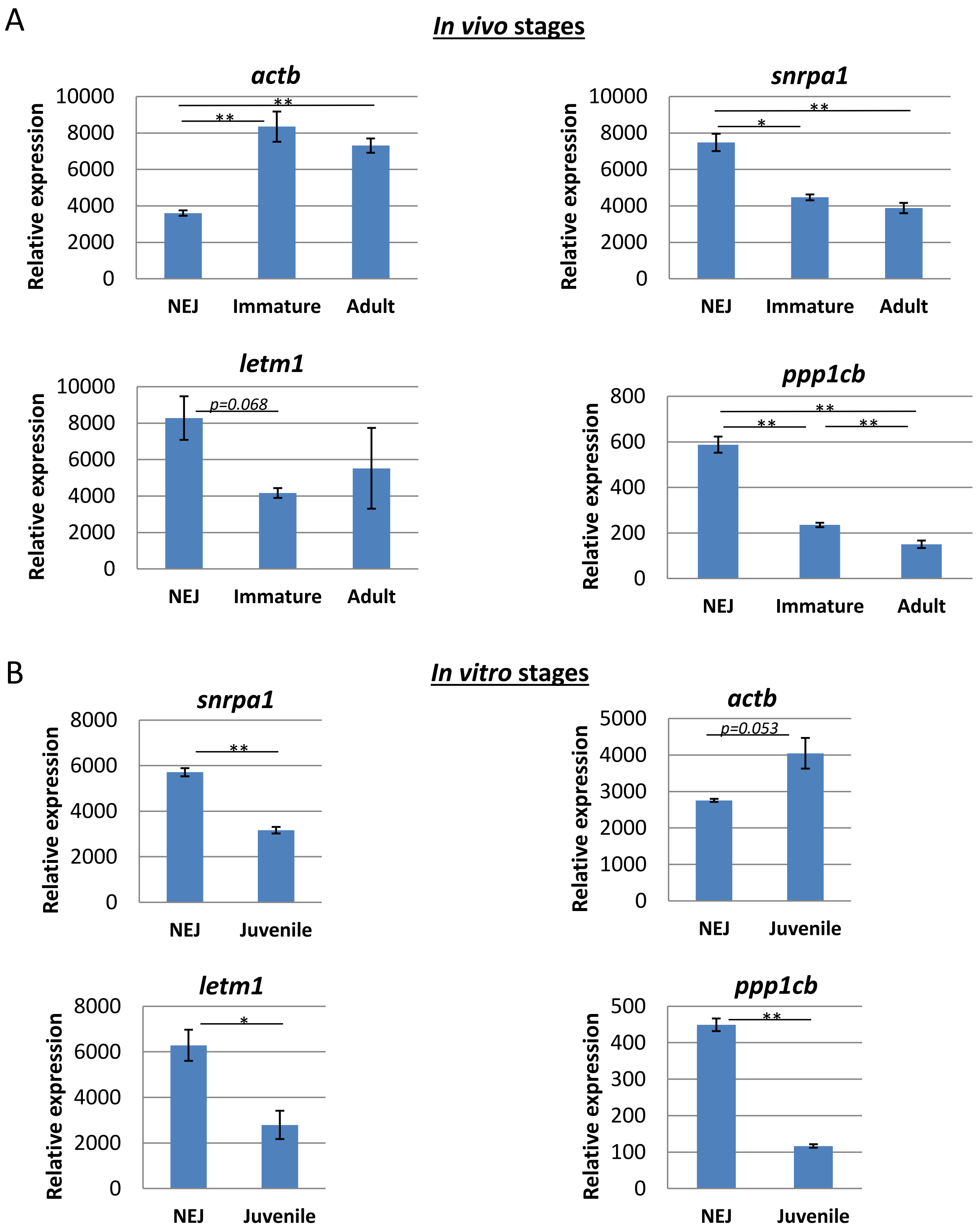
RNA Area: 660.8
RNA Concentration: 1,848 pg/µl

D

Overall Results

RNA Area: 609.8
RNA Concentration: 252 ng/µl

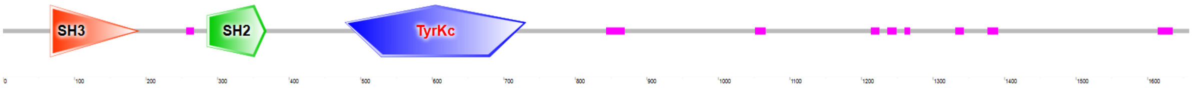
Supplementary Figure S2: **RNA quantity and quality of liver fluke samples from BioAnalyzer analysis.** Electropherograms of RNA extracted from 10 or 20 NEJs (A, B), 4-week old immature (C) or 12-week old adult flukes (D). Agilent RNA 6000 Nano Chips (adult) or Pico Chips (others) were used.



Supplementary Figure S3: **Relative expression levels of reference gene candidates in different intra-mammalian stages of *F. hepatica*.** Data were normalised against the geometric mean of the two most stably expressed genes previously identified (*tbcd* and *eprs* for A, *tbcd* and *psmb7* for B). Average values of 3-4 biological replicates with SEM are shown. Significant differences are indicated with * p<0.05, ** p<0.01 (t-test).

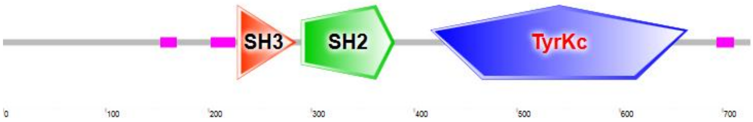
ABL proto-oncogene 1, non-receptor tyrosine kinase *(*FhAbl1*)***:**

SH2, Src homology 2 domain; SH3, Src homology 3 domain; TyrKc, Tyrosine kinase, catalytic domain



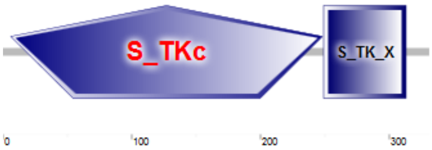
ABL proto-oncogene 2, non-receptor tyrosine kinase (FhAbl2)**:**

SH2, Src homology 2 domain; SH3, Src homology 3 domain; TyrKc, Tyrosine kinase, catalytic domain



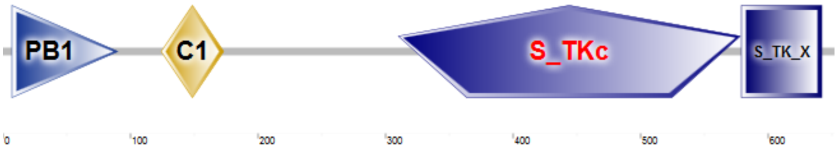
Rac-alpha serine/threonine-protein kinase (FhAkt1)**:**

S_Tkc, Serine/Threonine protein kinases, catalytic domain; S_TK_X, Extension to Ser/Thr-type protein kinases



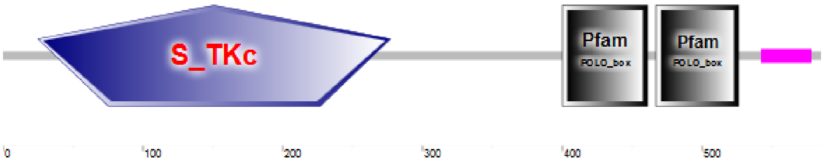
Protein kinase C (FhPkc)**:**

PB1, Phox and Bem1p domain; C1, Protein kinase C conserved region 1 (C1) domain; S_Tkc, Serine/Threonine protein kinases, catalytic domain; S_TK_X, Extension to Ser/Thr-type protein kinases

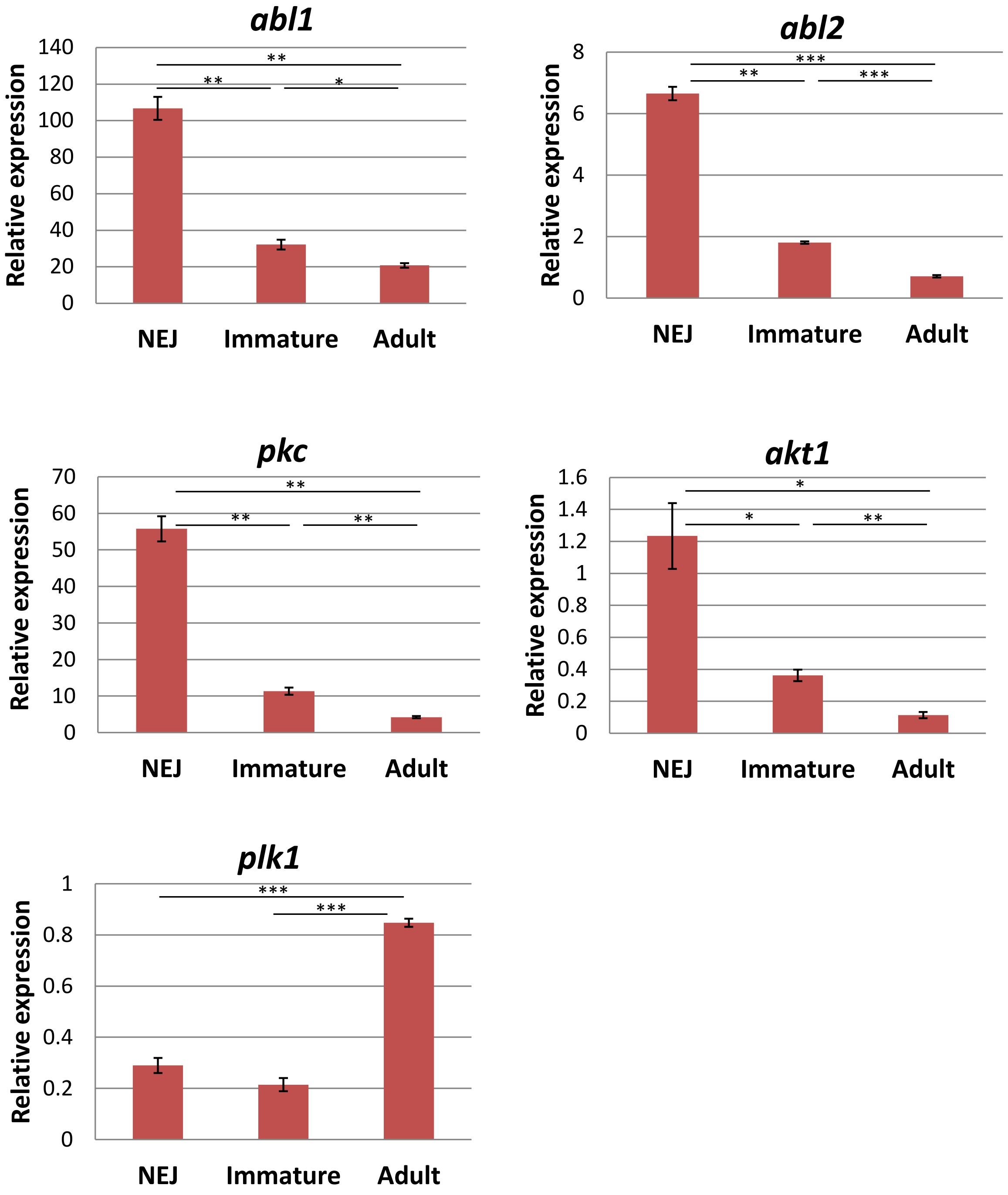


Polo-like kinase 1 (FhPlk1)**:**

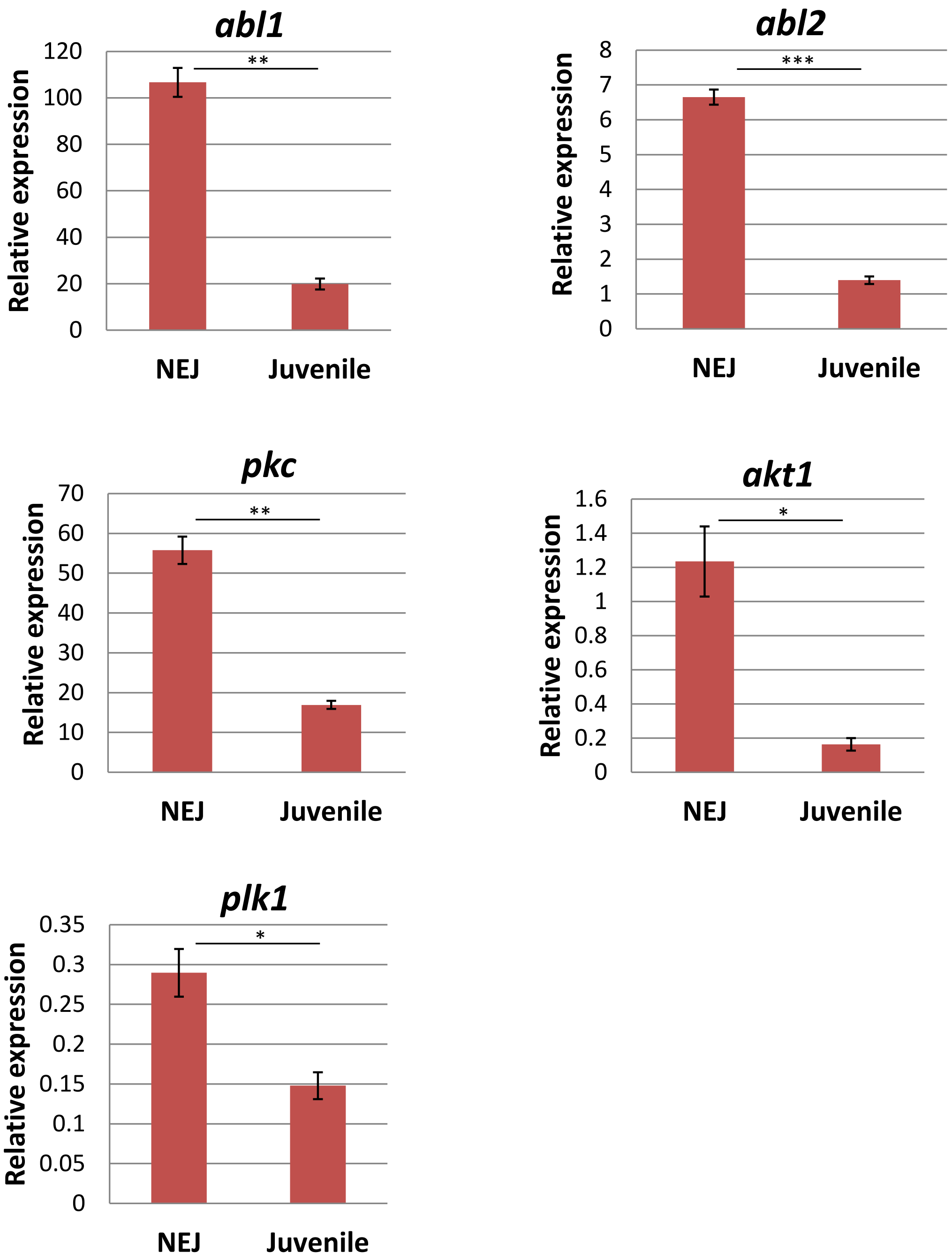
S_Tkc, Serine/Threonine protein kinases, catalytic domain;



Supplementary Figure S4: **Results from SMART analysis of amino acid sequences from five kinases of *F. hepatica*.**

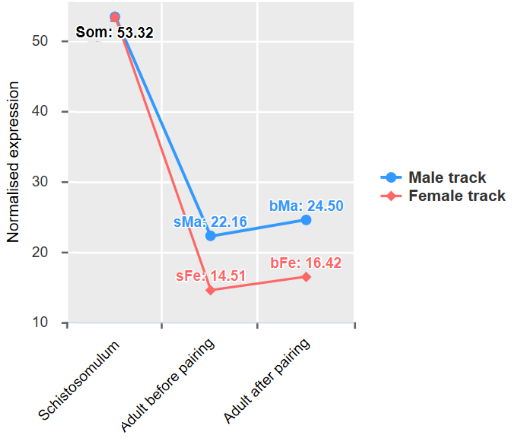


Supplementary Figure S5: **Relative expression levels of kinases in three different intra-mammalian life stages of *F. hepatica* normalised against *gapdh*.** Expression data from NEJs, 4 week-old immature, and 12 week-old adult worms were normalised against the geometric mean of the least stably expressed reference gene candidate, *gapdh*. Average values of 3-4 biological replicates with SEM are shown. Significant differences are indicated with * *p*<0.05, ** *p*<0.01, *** *p*<0.001 (t-test).

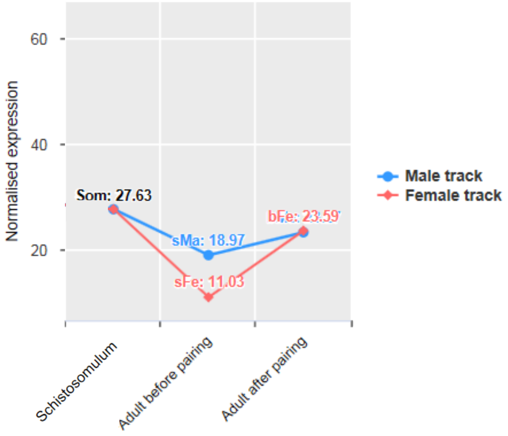


Supplementary Figure S6: **Relative expression levels of kinases during *in vitro* culture of juvenile *F. hepatica* normalised against *gapdh*.** Expression data from NEJs and juvenile worms grown for 4 weeks in serum-rich medium were normalised against the geometric mean of the least stably expressed reference gene candidate, *gapdh*. Average values of 3-4 biological replicates with SEM are shown. Significant differences are indicated with * p<0.05, ** p<0.01, *** p<0.001 (t-test).

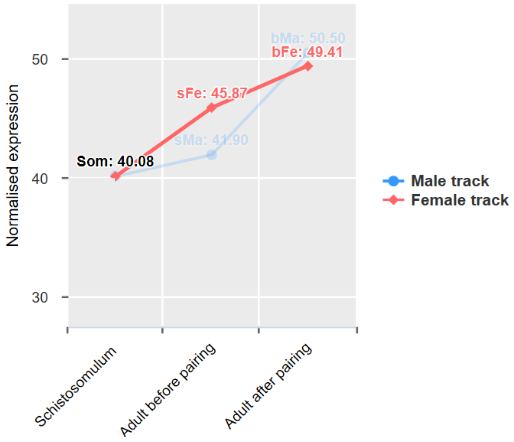
Abl kinase 1 (Smp_246700):



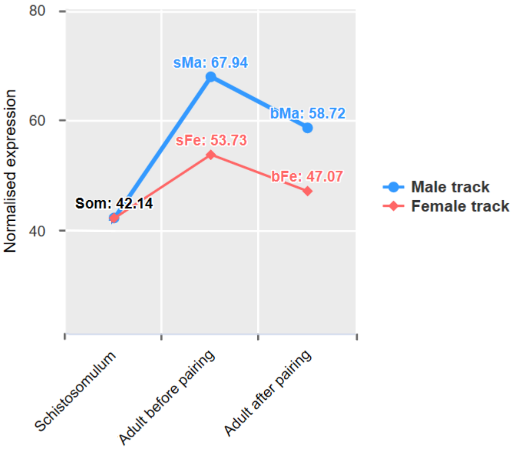
Abl kinase 2 (Smp_128790):



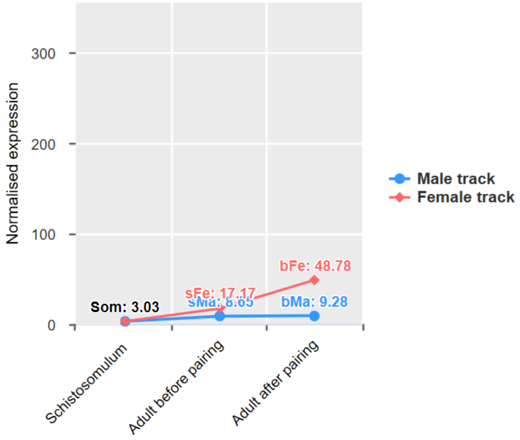
Protein kinase C (Smp_096310):



Akt1 kinase (Smp_243630):



Polo-like kinase 1 (Smp_009600):



Supplementary Figure S7: Relative expression of kinase orthologs in *Schistosoma mansoni* schistosomula and adult stages. Data were extracted from the meta-analysis by Lu et al. 2017 available at https://meta.schisto.xyz/.

Supplementary Figure S8: Multiple alignment of amino acid sequences of orthologs for reference gene candidates. Accession numbers of gene orthologs for *C. elegans* (Ce), *F. hepatica* (Fh), *S. mansoni* (Sm), *D. melanogaster* (Dm), *H. sapiens* (Hs) and *M. musculus* (Mm) are listed in Supplementary Table S1. Conserved protein domains are highlighted. * indicates identical amino acids.

Tubulin-specific chaperone D (Tbcd):

```
Ce      MKKTKYPTLVRISRFLFTDLVSMKIRFQRAWLRNVFADKTTRLTRKCSSSMLHLREFLQF 60
Fh      ------------------------------------------------------------ 0
Sm      ------------------------------------------------------------ 0
Dm      ------------------------------------------------------------ 0
Hs      ------------------------------------------------------------ 0
Mm      ------------------------------------------------------------ 0


Ce      LGFLLKYLSMDEDAPVDESNEGIIGCLPSAVNIHHIEEIKELVDQLPIIFKLENECDETA 120
Fh      ---------MD-SNRDLLPEEEQFLIFN---NFKHYDEVIKLISTITDATK-----LQTT 42
Sm      ------------------------------------------------------------ 0
Dm      ----------M-SNSVEECKDEDL-PANTLEHFTELQQVLEMIDNIKSIAA-----NTF- 42
Hs      --MALSDEPAA-GGPEEEAEDETLAFGAALEAFGESAETRALLGRLREVHG-----GGAE 52
Mm      --MVLSNEPAA-SAAEEEVEDDALVRASALEAFGESAETRALLRSLPAVHR-----ERAS 52


Ce      AEVNYLRYSRLLHLYQEQPRLLDKWIPEIVANLVDLVTLIGIDVSKPRAMTPLSRESLKY 180
Fh      EEHLEEEFIKIFGFYQEQPHLLDPYLPKMISDTLEVVK-------TTKTGSRAFHFAFRV 95
Sm      ------------------------------------------------------------ 0
Dm      -EREFEQYAQVLSRYQEQPHLLDPHLEELLGKLLHKIR-------KPDLDTGELHAAFKY 94
Hs      REVALERFRVIMDKYQEQPHLLDPHLEWMMNLLLDIVQ-------DQTSPASLVHLAFKF 105
Mm      REVAEERFRVIMDKYQEQPHLLDPHLEWMMNSLLDLVQ-------DETSLPDLVHLAFKF 105


Ce      LSDLCIVRGSKTIVRLLPHQVHLLDPLLQTLEYYETSQLSDHNQRNVLLMWLWIVVKNPF 240
Fh      LYLMVKTRGYKSIIRLMPHTVDDIEPTL------------TWETRYVLLLWLSILIMVPF 143
Sm      ---MTKTRGYKAIIRLMPHTVDDIEPTLSLLMEQDINDSKNWETRYVLILWLSILVMVPF 57
Dm      LYIICKVRTYKVLVKFMPHELSDLEFVLDLLGQQNPKEFEQWETRYILLLWMSILVLNPF 154
Hs      LYIITKVRGYKTFLRLFPHEVADVEPVLDLVTIQNPKDHEAWETRYMLLLWLSVTCLIPF 165
Mm      LYIITKVRGYKVFLRLFPHEVANVQPVLDMFTGQNPKDHETWETRYMLLLWLSVTCLIPF 165
           :  .*  * :::::** :  ::  *              : * :*::*: :    **

Ce      DLRRFDPTG-----------------DPDNVITRIMNVALHYMKWDWNSSQASAALVIAH 283
Fh      GLNCLDSE------------------DRAPIVNRILDQSKRYLSLDGRTQ-EAASFLLAR 184
Sm      NLESLDSF------------------GKKPIIERVIDLAKLYLLQDERTQ-EAAAFLLAH 98
Dm      HMSRLDAYDTSTSAPTTNCSPVNHVQSKNTKMDRIFELIQLYVSSNDTCS-SMAAFLAAK 213
Hs      DFSRLDGNLLTQP-----------GQARMSIMDRILQIAESYLIVSDKAR-DAAAVLVSR 213
Mm      DFSRLDGNLSTQT-----------GETRVPTMDRILQIAESYLVVSDKAR-DAAAVLVSK 213
         :  :*                         : *:::    *:  .       *:.: ::

Ce      CLSRTDGIPKV-LSFLSRLLDSIKT----HHENKKLLLADLILLLAILKHVDRRVLTGHI 338
Fh      LVTRPDVVQAHLTPVLDWCLEQIKNADCTTGKGQKLLCGVLRSLANICKVGRRQELLAHA 244
Sm      TVTRPDALHAQLPSIISSAIKNLSFADVINVQDQKQVCGTLRSIANICKLGSRTELLPYA 158
Dm      YFIRSDIKDLYLERFLDWIMEQHQADTLN------VKFGQLAAVAAILKHGKREDLLPYA 267
Hs      FITRPDVKQSKMAEFLDWSLCNLARSSFQTMQGVITMDGTLQALAQIFKHGKREDCLPYA 273
Mm      FITRPDVKQRKMASFLDWSLCTLAHSSFQTIEGVITMDGMLQALAQIFKHGKREDCLPYA 273
         . * *        .:.  :                  . *  :  * *   *     :

Ce      GTIHEQLSFLYPIDEKKGGLICKCLVKVVQRIGLIALKPRTCSWSYNRGKRLLEGMLDDN 398
Fh      PRLLES-ILHMSIAAAKGNWIYRFETKLLQRIGLLFCPPRSFSWQYQRGLRSLADNLAPR 303
Sm      SDLLSA-VLQLPGDSSKGILLCRLETKVLQRIGLLFCPPINTTWQYQRGSRSLQENLESL 217
Dm      DKLLQW-ITSCQYKDDNDFLKYKNYVKIIQRIGLVHLKPRIASWRYKRGTRSLATNLNQT 326
Hs      ATVLRC-LDGCRLPESNQTLLRKLGVKLVQRLGLTFLKPKVAAWRYQRGCRSLAANLQLL 332
Mm      NTVLQC-LDGCRLPESSHTSLRKLGVKLVQRLGLTFLKPKVATWRYQRGCRSLAANLKLC 332
          :             .    :  .*::**:**    *   :* *:** * *   *
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Ce      EEYSDEPSFSNKVNS----NQS----CNNEIDKENQWNDGDELENSEIVEFALMHVLEAL 450
Fh      LRELQNTTDGNTNQA-SNFSTSLERTVTHGLTESTDDDDELDLEHADEVAEVIDRLINSL 362
Sm      LMNHDKNSSVSAKVTDHSSYTSFQNNISSDISGDCSLTMKHEFPNTDEVAEVIDKLISAL 277
Dm      TAAGGEPV-----------------V----LEQSL--EEGEEIVVPDAIEEVIEELLQAL 363
Hs      TQGQSEQK-----------------P----L--ILTEDDDEDDDVPEGVERVIEQLLVGL 369
Mm      APGKSDQK-----------------L----LSDSLTSDGDEDYDVPEGVETVIEQLLVGL 371
             .                        :          :    : :  .: .:: .*

Ce      SHSDTAVRWSAAKGVGRITVRLPNFDLATQVVGSIISSHFGEVAEYSSWHSHGACLALAE 510
Fh      RNQYTVVRWSAAKGLGRMCGRLSR-SMVNDVLSAILL-LCTRLEPFTAW--HGACLALAE 418
Sm      RSQFTGVRWSAAKGIGRICSRLSS-SMVNDVLSAVLS-LCTKLEPYTAW--HGACLALAE 333
Dm      RSGGNDIRWSAAKGLGRVTNRLPK-ELADEVIGSVID-ILNPLEPHEAW--HGACLALAE 419
Hs      KDKDTVVRWSAAKGIGRMAGRLPR-ALADDVVGSVLD-CFSFQETDKAW--HGGCLALAE 425
Mm      KDKDTVVRWSAAKGIGRMAGRLPR-ELADDVVGSVLD-CFSFQETDKAW--HGGCLALAE 427
            . :*******:**:  **    :. :*:.:::           :*  **.******

Ce      LAHRGVLLPSLLEDIVPALELSLVFEDVMGRHQNGNQVRDAACYAVWALSRTYEPSMMAP 570
Fh      LGRRSLLLPSKLPEVMPVILRALFYDERSGDHSYGSNVRDAACYVCWAFARAYQAADLAP 478
Sm      LGRRNLLLPSKLPEVIPVVLRALFYDERSGDHNYGSNVRDAGCYVCWAFARAYHPKDFLD 393
Dm      LAKRGLLLPHRLEELVPLLMQALFYDEMKGYMSVGQHIRDSACYMCWAFARAYNPDDVKP 479
Hs      LGRRGLLLPSRLVDVVAVILKALTYDEKRGACSVGTNVRDAACYVCWAFARAYEPQELKP 485
Mm      LGRRGLLLPSRLSEVVTVILKALTYDEKRGACSVGANVRDAACYVCWAFARAYEPQELTP 487
        *.:*.:***  * :::  :  :* :::  *  . * ::**:.**  **::*:*.   .

Ce      YLQRLASALLCGALFDRQVNLRRAASAALQEMVGRQKNVSHGIPLIQSVDYFAVTNRQKC 630
Fh      YVTQVAQSLVLVSLFDREVNVRRAAAAAFQENVGRQGQFPHGIEILTACDYFAVRNLKNC 538
Sm      YIVPIASSLVLVSLFDREVSVRRAASAAFQENVGR--QFPHGIEILTTCDYFTVGNRAHC 451
Dm      FVHKISSGLLTVAVFDREVNCRRAASAAFQESVGRLGNFPFGIEISTTTDFYSVGIRQNS 539
Hs      FVTAISSALVIAAVFDRDINCRRAASAAFQENVGRQGTFPHGIDILTTADYFAVGNRSNC 545
Mm      FVTAISSALVIAAVFDRNVNCRRAASAAFQENVGRQGTFPHGIDILTTADYFAVGNISNC 547
        ::  ::..*:  ::***::. ****:**:** ***   . .** :  : *:::*    :.

Ce      YEHLCVPVAEYSTYSAIILRHLITKKVVHWDEKIREQAAISLEKISEIRLENVSDDYYME 690
Fh      YLELSAFVAQFPEYTQAMIDHLATKLLGHWDVVIRFLSARALNVLCRFSPE--------- 589
Sm      YLQLSIFVAKFKEYAKPMIDHLVNVRLGHWDDSIRYLAACALGKLYIADPDYMMEIVLPQ 511
Dm      YLNISDYIAQFEVYREPLINHLVQHKVSHWDSAIRELTAKALHKLSLWEPEYMAAVVLPQ 599
Hs      FLVISVFIAGFPEYTQPMIDHLVTMKISHWDGVIRELAARALHNLAQQAPEFSATQVFPR 605
Mm      FLIISVFIAGFQEYTKPMIDHLVSMKINHWDGAIRELSAKALHNLTPQVPEYIAMHVFPA 607
        :  :.  :* :  *   :: **    : ***  **  :* :*  :     :

Ce      ILDDFLKASCETRISPFLRHGYLLASGHLIKGLTSRGMDF------SSKQTEIAWIPHIL 744
Fh      ---------------------------------------------DAIGPELLVQIKEIV 604
Sm      IINGS------INSTLHNQQGCIYGTGELVCSS----------SSCVINEENLLKIKEIV 555
Dm      LLAKT------DTIDINCRHGCVLAMGEITLTLRKLEEKSD-PQVVYLSNQRVAELNELI 652
Hs      LLSMT------LSPDLHMRHGSILACAEVAYALYKLAAQENRPVTDHLDEQAVQGLKQIH 659
Mm      LLLMT------QSPDLHTRHGAILACAEVTYALYKLATQSNRLVTDYLDEKAVQSLKQIH 661
                                                            :  : .:

Ce      WPFCD---MTTQPGALIRRTLCKFIQLVSASKKVLLLEKDKSEWLDVLLQLIT------- 794
Fh      PTLSERNQFRGLSGELLRKASCHLIEKSSRTRLPLHGDPVIETWRLLLDDCVA------- 657
Sm      PALKSANKFRGLSGELIRKATAHFIQKCAMAKLPFHDDPIIEVWREFLDDCVG------- 608
Dm      ITFLDKNFYRGMSGDLMKSCTSSYIKNCSLAKLQATPE-CLVSWQKVIDSCLI------- 704
Hs      QQLYDRQLYRGLGGQLMRQAVCVLIEKLSLSKMPFRGDTVIDGWQWLINDTLRHLHLISS 719
Mm      QQLCDRHLYRGLGGELMRQAVCILIEKLSLSRMPFKGDATVEGWQWLINDTLRSLHLVSS 721
          : .        * *::   .  *:  : ::     :     *  .: . :
```

```
Ce          DPREIIRSLAKTAVGEFVMTYLMNDEELIQKV-K----TRVIAAMTKCSDESERIGMGMI 849
Fh          HKEVEIQKTAVSAYTQLLAAYLYDKDKHLQIAYRDKMFGHLTQQLE-ANSETKQSGFLQV 716
Sm          HKNPEVQKATVNAYPHFLSAYLYDRNGELQLGYKDLLYRNFLLQLN-TNSESKLSGYLQI 667
Dm          TKSNAIRDGAVEAFGELCTTYYCSDSRHGE---NEAIINTYLTGADNDLEEHIRMGYIAA 761
Hs          HSRQQMKDAAVSALAALCSEYYMKEPGEADPAIQEELITQYLAEL-RNPEEMTRCGFSLA 778
Mm          HSRQQIKEVAVSALTALCSEYYVKEPGEAGSSIAKELIPQYLAEL-QSPEEMARCGFSSA 780
                 ::. :  *   :   *  .                         .*    *

Ce          CESLNSEAVDY---EMFESLCNTILTP-------------TSSDAKWALARQQTVFALNR 893
Fh          LADAPADLFTGHVQKTLELVTAACRISTK--------------TRSWGDARASALKSVLG 762
Sm          IGAAPNSLYCGHVADLLDTVTSACRSTSK--------------TKFWVDSRGSALKALVE 713
Dm          LGVLPSFMIRCHLQAILDSLVKHSLTPLQAVLVGEMGDRENIQAYRWSEARTQSVLALTK 821
Hs          LGALPGFLLKGRLQQVLTGLRAVTHTSPE--------------DVSFAESRRDGLKAIAR 824
Mm          LGALPGFLLRGHLQQVLSGLRRVTCISPN--------------DVSFAEARRDGLKAISR 826
                            :  :                          :  :* . : ::

Ce          ISVNSSTET--------FNRIGQKCFETLYKAMTDYTTSANGDIGRFVREASMRAMSTIL 945
Fh          ------------------------------------------------------------ 762
Sm          IIKNLGAHHSE-----LNATILKSTCYILLQSLSDYTMDSRGDVGSLVREVGMKCLDSYI 768
Dm          LVKTVGYG--GGIDSFAEPKNFNKVIECLLRALQEYTLDNRGDIGAWVREAAMSSLYEIV 879
Hs          ICQTVGVKA-GAPDEAVCGENVSQIYCALLGCMDDYTTDSRGDVGTWVRKAAMTSLMDLT 883
Mm          ICQTVGVNTRGPPDEVICKENISEVYAALLGCMSDYTTDSRGDVGAWVREAAMTSLMDLM 886

                                               TFCD_C
                             ___________________________________________
Ce          --VDAKTEPPFLDEHVIKS-AKYMVQQSAERISRTRECACACLKSLVKC-EITGRCLPHI 1001
Fh          ----------------VEEIVVSIVQQSVEKIDRTRAAAGQAFSGILYH-EPPIRYIPHV 805
Sm          EFLVNNQYSELITSDMIEEVMTSIAQQAVEKIDRTRGVAGQVFAHLLHH-DPPIEHISHF 827
Dm          ----TTCPPDLLAPEQVHEIVVGFMQQAVEKIDRTRGLGGRLCCQLIHH-QPRIPYIREH 934
Hs          L-LLARSQPELIEAHTCERIMCCVAQQASEKIDRFRAHAASVFLTLLHFDSPPIPHVPHR 942
Mm          L-LLARTEPVLIEAHICERVMCCVAQQASEKIDRFRAHAARVFLTLLHFDSPPIPHVPHR 945
                             .     . **: *:*.* *  .      ::   .     : .
                                         TFCD_C
            ___________________________________________________________
Ce          DLLMNIYSE----PMDFISDRTVFQLKPLLDLGSEYYEQLILGIVVSAGGLAEGTQKTAK 1057
Fh          KKVKEIFS---------------------------------------------------- 813
Sm          EELKQIFPKSDCDDMIWNSANSTFHRFTKLLDFPEYRYRLILGLIVSVGGLTELTIRCST 887
Dm          SKLLEIFPA-DADSVLWLFADHTFPLFCELLSLPDYSKRVLLGLSASIGQLTESLIKYAS 993
Hs          GELEKLFPRSDVASVNWSAPSQAFPRITQLLGLPTYRYHVLLGLVVSLGGLTESTIRHST 1002
Mm          QELESLFPRSDVATVNWNAPSQAFPLITQLLGLPTYRYHVLLGLAVSVGGLTESTVRHST 1005
              : .::
                                        TFCD_C
            ___________________________________________________________
Ce          QLLLDHQREICENKPRFDHFLSTCADLFQRARKVNRIGNSFMQILPQIFGNLGIYEQCPE 1117
Fh          -----------------------------------NVIVPLFRFVDFLLNDPVIAGAVN- 837
Sm          SALSAYFLDHESDQLFIVEVLKIVGQILQSFRQEERIVVPLFKFLDFLLNDPIVNSTID- 946
Dm          SALFHFLRS---NPETVPRLCSEVVQIFEEHLLNERVTYPLLSFLDILIGSGTVESVLHD 1050
Hs          QSLFEYMKGIQSDPQALGSFSGTLLQIFEDNLLNERVSVPLLKTLDHVLTHGCFDIFTTE 1062
Mm          QSLFEYMKGIQKDAQVLQSFSETLLKVFEDNLLNDRVSVSLLKMLDQLLANGCFDIFTAE 1065
                                               .:   ::  :  ::    .
                    TFCD_C
            _________________________
Ce          TSESII-EMVDTMKTIAVRSSMMSRQRLSIDSLGELLNCGKKSTVYRSALTMILDTLNSQ 1176
Fh          -----------------------------GESFGGMLQFEG--SARKRSASLMMILMAHK 866
Sm          PNSSILLQLTESVWNETKLTKDVQRIKAAIDVFGGMLQFTG--SVRKRSLSLMMIILGSR 1004
Dm          EANPFAEDIFRLLNLEVKGYKKLYKTATSISAFCQLLQVPR--L-SKRILSKLSVFLGLQ 1107
Hs          EDHPFAVKLLALCKKEIKNSKDIQKLLSGIAVFCEMVQFPG--DVRRQALLQLCLLLCHR 1120
Mm          ENHPFCVKLLTLCKEEIKKSKDIQKLRSSIAVLCGMVQFNG--DVRKKILLQLFLLLGHP 1123
                                            :  :::        :     :   :

Ce          QPVLRKSAAERLYEHLC-------CAEESDDEVLEVLATTNWQDENDNVLKQAVA----- 1224
Fh          YPVIRKSAATKLYECLVMFDL---VEPEVMDQVTTLLTETIWESELDEIRPIRNTICEML 923
Sm          YPIIRKATATELYEGLLVYEL---CPSELLDQVSSILTETIWEGDIEAVRPIRNQLCELF 1061
Dm          HVHVRKTAATKLYEALALHGDVTEVPEENMDEILTLLSETDWTQPLVEVRPLRNQLCQLM 1167
Hs          FPLIRKTTASQVYETLLTYSDV--VGADVLDEVVTVLSDTAWDAELAVVREQRNRLCDLL 1178
Mm          FPVIRKSTASQVYEMVLTYSDL--VDAEVLDEVMSVLSDTAWDAELPVVREQRNRLCDLL 1181
               :**::* .:** :           :  *::  :*: * *      :
```

```
Ce      GISEKLIF----------------------------- 1232
Fh      GVPVPRIINPKVTPDSNTPTDQTRSVISVNGDAGDRG 960
Sm      QVPVPRATSKTQNHTSPA------------------- 1079
Dm      DIKPPVSGAAAAAALQQASADK--------------- 1189
Hs      GVPRPQLVPQPGAC----------------------- 1192
Mm      GVPRPQLVPKPIPGS---------------------- 1196
         :
```

Glutamyl-prolyl-tRNA synthetase (Eprs):

```
Ce      MMITRELVLKANREQPPYASILALAASGFSLEKSVQFSEKQQLALNLDG-EL--LSNDVE 57
Fh      -----------------------------MMESAIEWIYNN-LKKNSVDI---------- 20
Sm      ------------------------------MCVCLEAFKES-LKYHLPGL---------- 19
Dm      ----MSIKLKANLNNPPISGLATAHLINGTVPVEIVWSKEE-TSLQFPDNRLLVCHSNND 55
Hs      ---MATLSLTVNSGDPPLGALLAVEHVKDDVSISVEEGKEN--ILHV--SENVIFTDVNS 53
Mm      ---MAALCLTVNAGNPPLEALLAVEHVKGDVSISVEEGKEN--LLRV--SETVAFTDVNS 53
                                      :   :    :.    .

Ce      IARIIAQSTDAADSLLGSSIIDFAVVDDLTNFIADAVTKND-YS-----LLLGKDFPTKI 111
Fh      -----PS-EVLLSIIPKTNGTPSIHVLNWVRFVPAYLMNSKKRSWAMEQLEKSLAHATFL 74
Sm      -----NE-DSLKLALKGIAGEDDLQTYNWVRFATTYLQPQCDFVWAGKEIDKALVNSTYI 73
Dm      VLRALAR-AAPDYKLYGETAIERTQIDHWLSFSLTCE---DDISWALSFLDKSIAPVTYL 111
Hs      ILRYLAR-VATTAGLYGSNLMEHTEIDHWLEFSATKLSSCDSFTSTINELNHCLSLRTYL 112
Mm      ILRYLAR-IATTSGLYGTNLMEHTEIDHWLEFSATKLSSCDRLTSAINELNHCLSLRTYL 112
                      :            .   *                 :       * :

Ce      LDNSLTVADFAIFSVAHNNPQLKAKFSGI-----I----------DKVLKEPTLAAAHNF 156
Fh      VG---------------------------------------------------------- 76
Sm      NGSEFSLSDLAIWTFLEINPDWHKLNESYKTDGSVKSFVNLKQYYDRLITLPSVRKL--K 131
Dm      VANKLTIADFALFNEMHSRY---EFLAAKGIP------QHVQRWYDLITAQPLIQKV--L 160
Hs      VGNSLSLADLCVWATLKGNAAWQEQLKQKKAP------VHVKRWFGFLEAQQAFQSV--G 164
Mm      VGNSLTLADLCVWATLKGSAAWQEHLKQNKTL------VHVKRWFGFLEAQQAFRSV--G 164


Ce      VGLYKS-------------AAAPTATASTGKEKKKDEGKFVELPGAEKGKVVVRFPPEAS 203
Fh      ------------------------------------------------------------ 76
Sm      TEIYESRLQPRGVSVNSEPPSNTIGKTHASDMLFEKGGKFGELPGARVGEVVVRFPPEAS 191
Dm      QSLPEDAKVKR------S-PQSSKEQTPAKTGERKQEGKFVDLPGAEMGKVVVRFPPEAS 213
Hs      TKWDVS-----------------TTKARVAPEKKQDVGKFVELPGAEMGKVTVRFPPEAS 207
Mm      TKWDVS-----------------GNRATVAPDKKQDVGKFVELPGAEMGKVTVRFPPEAS 207

                                          tRNA-synt_1c

Ce      GYLHIGHAKAALLNQYYQQAFEGQLIMRFDDTNPAKENAHFEHVIKEDLSMLNIVPDRWT 263
Fh      ---------DDFSVADLADTFKGRLILRFDDTNPSKEKANFEESILCDLPRIGVKWDVRS 127
Sm      GYLHIGHAKAALLNQHYRDIFKGRLILRFDDTNPDKEKECFEKSILSDLPRIGVTWDAIS 251
Dm      GYLHIGHAKAALLNQYYALAFQGTLIMRFDDTNPAKETVEFENVILGDLEQLQIKPDVFT 273
Hs      GYLHIGHAKAALLNQHYQVNFKGKLIMRFDDTNPEKEKEDFEKVILEDVAMLHIKPDQFT 267
Mm      GYLHIGHAKAALLNQHYQVNFKGKLIMRFDDTNPEKEKEDFEKVILEDVAMLHIKPDQFT 267
                   :        *:* **:******* **.  **. *  *:  : :  *  :
                                     tRNA-synt_1c

Ce      HSSDHFEMLLTMCEKLLKEGKAFVDDTDTETMRNEREQRQDSRNRSNTPEKNLQLWEEMK 323
Fh      HTSDHFDLLINLCEQMLREGKAYVDNTDTETMRTERENRKPSACRENTTQQNLAWWEEMK 187
Sm      STSDHFDEMLKLCEQLIKEGKAYVDNTDTETIRVQREARQMSACRDNSIEQNLSWWGEMK 311
Dm      HTSNYFDLMLDYCVRLIKESKAYVDDTPPEQMKLEREQRVESANRSNSVEKNLSLWEEMV 333
Hs      YTSDHFETIMKYAEKLIQEGKAYVDDTPAEQMKAEREQRIDSKHRKNPIEKNLQMWEEMK 327
Mm      YTSDHFETIMKYAEKLIQEGKAYVDDTPAEQMKAEREQRTESKHRKNSVEKNLQMWEEMK 327
         :*::*: ::  . ::::*.**:**:*  * :: :** *  *  *.*  ::**  * **
                                    tRNA-synt_1c
```

```
Ce          KGSPKGLTCCVRMKIDMKSNNGAMRDPTIYRCKPEEHVRTGLKYKVYPTYDFTCPIVDSV 383
Fh          KGTEFGLKCCVRAKIDMNSNNGAMRDPTIYRCKPESHVRTGTKYNVYPIYDFACPVVDSV 247
Sm          KGTEQGLKCCVRAKIDMSSNNGALRDPTIYRCKIEPHVRTGSKYKVYPLYDFACPVVDSI 371
Dm          KGSEKGQKYCVRAKIDMSSPNGCMRDPTIYRCKNEPHPRTGTKYKVYPTYDFACPIVDAI 393
Hs          KGSQFGQSCCLRAKIDMSSNNGCMRDPTLYRCKIQPHPRTGNKYNVYPTYDFACPIVDSI 387
Mm          KGSQFGQSCCLRAKIDMSSNNGCMRDPTLYRCKIQPHPRTGNKYNVYPTYDFACPIVDSI 387
            **:  * . *:* ****.* **.:****:**** : * *** **:*** ***:**:**::
                                      tRNA-synt_1c
Ce          EGVTHALRTTEYHDRDDQYYFICDALGLRRPHIWEYARLNMTNTVMSKRKLTWFVDEGHV 443
Fh          EGVTHALRTSEYNDRNDQYAWFCQVLGLRCPMVIDYSRLALQNTILSKRKLTWFVEEGLV 307
Sm          EGVTHALRTSEYNDRNEQYAWICKSLGIRCPIVIDYSRLALQNTVLSKRKLAWFVEEGIV 431
Dm          ENVTHTLRTTEYHDRDDQFYWFIDALKLRKPYIWSYSRLNMTNTVLSKRKLTWFVDSGLV 453
Hs          EGVTHALRTTEYHDRDEQFYWIIEALGIRKPYIWEYSRLNLNNTVLSKRKLTWFVNEGLV 447
Mm          EGVTHALRTTEYHDRDEQFYWIIEALGIRKPYIWEYSRLNLNNTVLSKRKLTWFVNEGLV 447
            *.***:***:**:**::*: :: . * :* * : .*:** : **::*****:***:.* *
                                 tRNA-synt_1c
Ce          EGWDDPRLPTVRGVMRRGLTVEGLKQFIVAQGGSRSVVMMEWDKIWAFNKKVIDPVAPRY 503
Fh          DGWDDPRMPTVSGILRRGMTAEGLRQFILAQGSSRSSAQMEWDKIWAFNKKVIDPIAPRF 367
Sm          DGWDDPRMPTVSGILRHGMTAEGLRQFILAQGSSRSSALMEWDKIWSFNKKIIEPVAPRT 491
Dm          DGWDDPRFPTVRGIIRRGMTVEGLKEFIIAQGSSKSVVFMNWDKIWAFNKKVIDPIAPRY 513
Hs          DGWDDPRFPTVRGVLRRGMTVEGLKQFIAAQGSSRSVVNMEWDKIWAFNKKVIDPVAPRY 507
Mm          DGWDDPRFPTVRGVLRRGMTVEGLKQFIAAQGSSRSVVNMEWDKIWAFNKKVIDPVAPRY 507
            :******:*** *::*:*:*.***::** ***.*:* . *:*****:****:*:*:***
                                            tRNA-synt_1c_C
Ce          TALDSTSPL-----------VSIELTDSISDDTSNVSLHPKNAEIGSKDVHKGKKLLLEQ 552
Fh          TGLLLDPSVPQPSPSTPIGLVPVRIHGQSEIQEKSVAVHPKNESLGHREIMVSPLVYVEH 427
Sm          TALLLDSSYMG-HNGTPPGLVRVHIHGQTGYTEKKVQIHPKNESLGYRSILLGPEVFVEQ 550
Dm          TALEKEKRVIVNVAG-------------AKVERIQVSVHPKDESLGKKTVLLGPRIYIDY 560
Hs          VALLKKEVIPVNVPE-------------AQEEMKEVAKHPKNPEVGLKPVWYSPKVFIEG 554
Mm          VALLKKEVVPVNVLD-------------AQEEMKEVARHPKNPDVGLKPVWYSPKVFIEG 554
            ..*                               .*  ***: .:* : :  .  : ::
                                       tRNA-synt_1c_C
Ce          VDAAALKEGEIVTFVNWGNIKIGKIEKKG-AVITKISATLQLDNTDYKKTTKVTWLGDVK 611
Fh          ADATCFKEGENVTFINWGNCRIVKIHRSE-AYITAVDGELNLQDTDYKKTLKITWLPELE 486
Sm          ADALCFKKGENVTFINWGNLRIMDIHRKG-QLIVSIDACLNLEDTDYKKTLKITWLTDPK 609
Dm          VDAEALKEGENATFINWGNILIRKVNKDASGNITSVDAALNLENKDFKKTLKLTWLAVED 620
Hs          ADAETFSEGEMVTFINWGNLNITKIHKNADGKIISLDAKLNLENKDYKKTTKVTWLAETT 614
Mm          ADAETFSEGEMVTFINWGNINITKIHKNADGKITSLDAKLNLENKDYKKTTKITWLAEST 614
            .**  :.:** .**:****  * .:.:.    *  :..  *:*::.*:*** *:***
                                         tRNA-synt_1c_C
Ce          AEAGKTIPVVTADYDHIISKAIIGKDEDWKQFINFDSVHYTKMVGEPAIKNVKKGDIIQI 671
Fh          GKSPALCPVTCLIYDHLLTKGILGKDEDFKPYVNRNSKVEQCLLGDPDLRNLKKGEIIQL 546
Sm          DSHLPLIPVSCLTYDNLLNKAILGKDDDFKLYVNKCSKKEQCLLGDPDLRHVKKGDIIQI 669
Dm          D-PSAYPPTFCVYFDNIISKAVLGKDEDFKQFIGHKTRDEVPMLGDPELKKCKKGDIIQL 679
Hs          H-AL-PIPVICVTYEHLITKPVLGKDEDFKQYVNKNSKHEELMLGDPCLKDLKKGDIIQL 672
Mm          H-AL-SIPAVCVTYEHLITKPVLGKDEDFKQYINKDSKHEELMLGDPCLKDLKKGDIIQL 672
                   *.    :::::.* ::***:*:* ::.  :     ::*:* ::. ***:***:
            tRNA-synt_1c_C
Ce          QRKGFYIVDQPYNPKSELSGVETPLLLIAIPDGHTGKEAEKPPKGA-PVS------AAAS 724
Fh          QRRGYYIVDVPYEAKCKATGFESPCVLIQIPEGTMSKTTTDTAGST-TSQAKK---GGSV 602
Sm          QRRGFFICDAPYESACLATGHESPCVLINIPDGSSKDDNAAI--NS-KVESSK---SGSV 723
Dm          QRRGFFKVDVAYAPPSGYTNVPSPIVLFSIPDGHTKDVPTSGLKVNAPDAKATKKASSPV 739
Hs          QRRGFFICDQPYEPVSPYSCKEAPCVLIYIPDGHTKEMPTSGSKEKTKVEATKNETSAPF 732
Mm          QRRGFFICDQPYEPVSPYSCREAPCILIYIPDGHTKEMPTSGSKEKTKVEISKKETSSAP 732
            **:*::  *  *   .  :   :* :*: **:*   .                   ..

Ce          SGGSDALQLYNSIEQQGGIVRDLKTKDAKSQATKDAIAKLLDLKKKYKELTGSDHKPGAP 784
Fh          KTS--------------------------------------------------------- 605
Sm          KTN--------------------------------------------------------- 726
Dm          SSSGQASELDSQISQQGDLVRDLKSKKAAKDQIDVAVKKLLALKADYKSATGKDWKPGQT 799
Hs          KER--------------------------------------------------------- 735
Mm          KER--------------------------------------------------------- 735
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        .

Ce      PSAPAPTTPS-SSESNSALNIYNLIEAQGLLVRELKGKDAKSQATKDAIAKLLELKKQYK 843
Fh      -----------------------AKQPKAEMTEEEAAK--------ALERQ------RKK 628
Sm      -----------------------KTVKIENLTPEEAAK--------AAEQQ------RRK 749
Dm      SASSAPVPAASSSSANDAVSVNASIVKQGDLVRDLKGKKASKPEIDAAVKTLLELKAQYK 859
Hs      ---PTPSLNNNCTTSEDSLVLYNRVAVQGDVVRELKAKKAPKEDVDAAVKQLLSLKAEYK 792
Mm      ---PAPAVSSTCATAEDSSVLYSRVAVQGDVVRELKAKKAPKEDIDAAVKQLLTLKAEYK 792
                                      :. :  .*                   . *


Ce      EVSGSDHKPGVPPAASVASAPAPAPAAGSTNALDIYHQIESQGALVRELKGKDAKSQATK 903
Fh      EEKKEARKEGRAKAKQAK------------------------------------------ 646
Sm      EEKKEARKEGKLKAKQQQ------------------------------------------ 767
Dm      TLTGQDWKPGTVPTTAAPSASAAPSVGVNDSVAQILSQITAQGDKVRELKSAKADKATVD 919
Hs      EKTGQEYKPGNPPAEIGQNISSNSSASILE-SKSLYDEVAAQGEVVRKLKAEKSPKAKIN 851
Mm      EKTGQEYKPGNPSAAAVQTVSTKSSSNTVE-STSLYNKVAAQGEVVRKLKAEKAPKAKVT 851
          . .  * *   :

Ce      DAIAKLLALKKQYKEVTGSDHKPGVVPVSAPA------------PTPLAGGADIAGQIEA 951
Fh      ETTECSEM------QSTS--------------------MKTQPEPASS----NEQPQNKK 676
Sm      SSENKLRT------TVVG--------------------HETINKPTSD----KLMYKQSN 797
Dm      AAVKTLLSLKADYKAATGSDWKPGTTAPAPAAAPVKVKQEKNPDPASVLTVNTLLNKIAQ 979
Hs      EAVECLLSLKAQYKEKTGKEYIPGQPPLSQSSDSSPT-RNSEPAGLETPEAKVLFDKVAS 910
Mm      EAVECLLSLKAEYKEKTGKDYVPGQPPASQNSHSNPV-SNAQPAGAEKPEAKVLFDRVAC 910
         :              ..                                      :

Ce      QGVLVRDLKNKDSKSQETKDAIAKLLELKKNYKEVTGSDYKPGPAPAAAPAKVTVPAPSV 1011
Fh      QEQ--------------------------------------------------------- 679
Sm      QSD--------------------------------------------------------- 800
Dm      QGDKIRQLKSAKSEKSLVEAEVKLLLALKTDYKSLTGQEWKPGTVAPAP---TTVNVIDL 1036
Hs      QGEVVR------------------------------------------------------ 916
Mm      QGEVVR------------------------------------------------------ 916
        *

Ce      SGGDTL------SKQIDDQALLVRELKMKDAKSQETKDAIAKLLQLKKQYKDATGSDYKP 1065
Fh      ----------------------------------CVKPTVEA-------------VSRPP 692
Sm      ----------------------------------SVKCE-----------------QLK- 808
Dm      TGGDSGSDVGSVLSKIQAQGDKIRKLKSEKAAKNVIDPEVKTLLALKGEYKTLSGKDWTP 1096
Hs      ------------------------KLKTEKAPKDQVDIAVQELLQLKAQYKSLIGVEYKP 952
Mm      ------------------------KLKAEKASKDQVDSAVQELLQLKAQYKSLTGIEYKP 952
                                            .                   .

Ce      APAQLAASAAA--APAPAPAFDEAALLKEIEEQGAVVRDAKSKDPKSQDSADAINKLLAL 1123
Fh      IVA-------ESCSAKSI----------------------K------------------- 704
Sm      -----------PVSPKVI----------------------V------------------- 816
Dm      DAKSEPAVVKKEASPVSMASPAKDELTQEINAQGEKVRAAKGNKAAKEVIDAEVAKLLAL 1156
Hs      VSATGAEDKDKKK--------------KEKENKSE-----KQNKPQKQ------------ 981
Mm      VSATGAEDKDKKK--------------KEKENKSE-----KQNKPQKQ------------ 981


Ce      KANFKKATGKDFPAPSNAQSKKGKKK---------------------------------- 1149
Fh      --------------------------------------IPKSDQVELSKKEGAKKQTRLA 726
Sm      --------------------------------------KNEKQKESLLKMSGTKKQSKLA 838
Dm      KAKYKEVTGTDFPVAGRGGGGGGGSAKKAPKEAQPKPAKPVKKEPAADASGAVKKQTRLG 1216
Hs      ----NDGQRKD-PSKNQGGGLSS---------------------SGAGEGQGPKKQTRLG 1015
Mm      ----NDGQGKD-SSKSQGSGLSS---------------------GGAGEGQGPKKQTRLG 1015


Ce      ------------------------------------------------------------ 1149
Fh      LEATKESEFSEWYSQLITKAELLEYYDISGCYIIRPWAYSLWQTIQRFLDERLHAMGVEN 786
Sm      IEASKETDFSDWYSELIIKSELLDYYDISGCYILRPWAYHMWQSIQCFMDEKLKVMGIEN 898
Dm      LEATKEDNLPDWYSQVITKGEMIEYYDVSGCYILRQWSFAIWKAIKTWFDAEITRMGVKE 1276
```

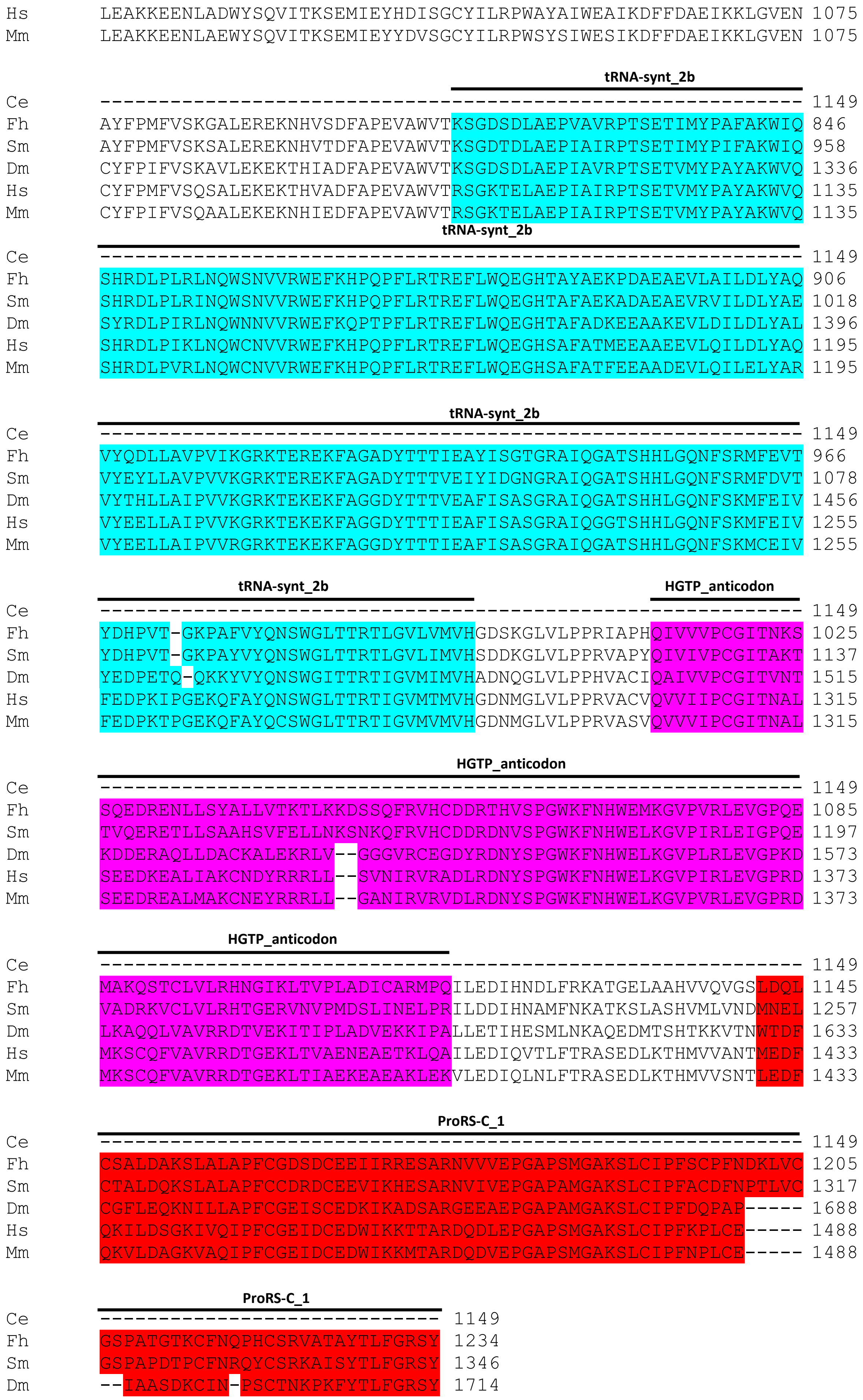

```
Hs          LEAKKEENLADWYSQVITKSEMIEYHDISGCYILRPWAYAIWEAIKDFFDAEIKKLGVEN 1075
Mm          LEAKKEENLAEWYSQVITKSEMIEYYDVSGCYILRPWSYSIWESIKDFFDAEIKKLGVEN 1075

                                                         tRNA-synt_2b
Ce          ------------------------------------------------------------ 1149
Fh          AYFPMFVSKGALEREKNHVSDFAPEVAWVTKSGDSDLAEPVAVRPTSETIMYPAFAKWIQ 846
Sm          AYFPMFVSKSALEREKNHVTDFAPEVAWVTKSGDTDLAEPIAIRPTSETIMYPIFAKWIQ 958
Dm          CYFPIFVSKAVLEKEKTHIADFAPEVAWVTKSGDSDLAEPIAVRPTSETVMYPAYAKWVQ 1336
Hs          CYFPMFVSQSALEKEKTHVADFAPEVAWVTRSGKTELAEPIAIRPTSETVMYPAYAKWVQ 1135
Mm          CYFPIFVSQAALEKEKNHIEDFAPEVAWVTRSGKTELAEPIAIRPTSETVMYPAYAKWVQ 1135
                                       tRNA-synt_2b
Ce          ------------------------------------------------------------ 1149
Fh          SHRDLPLRLNQWSNVVRWEFKHPQPFLRTREFLWQEGHTAYAEKPDAEAEVLAILDLYAQ 906
Sm          SHRDLPLRINQWSNVVRWEFKHPQPFLRTREFLWQEGHTAFAEKADAEAEVRVILDLYAE 1018
Dm          SYRDLPIRLNQWNNVVRWEFKQPTPFLRTREFLWQEGHTAFADKEEAAKEVLDILDLYAL 1396
Hs          SHRDLPIKLNQWCNVVRWEFKHPQPFLRTREFLWQEGHSAFATMEEAAEEVLQILDLYAQ 1195
Mm          SHRDLPVRLNQWCNVVRWEFKHPQPFLRTREFLWQEGHSAFATFEEAADEVLQILELYAR 1195

                                       tRNA-synt_2b
Ce          ------------------------------------------------------------ 1149
Fh          VYQDLLAVPVIKGRKTEREKFAGADYTTTIEAYISGTGRAIQGATSHHLGQNFSRMFEVT 966
Sm          VYEYLLAVPVVKGRKTEREKFAGADYTTTVEIYIDGNGRAIQGATSHHLGQNFSRMFDVT 1078
Dm          VYTHLLAIPVVKGRKTEKEKFAGGDYTTTVEAFISASGRAIQGATSHHLGQNFSKMFEIV 1456
Hs          VYEELLAIPVVKGRKTEKEKFAGGDYTTTIEAFISASGRAIQGGTSHHLGQNFSKMFEIV 1255
Mm          VYEELLAIPVVRGRKTEKEKFAGGDYTTTIEAFISASGRAIQGATSHHLGQNFSKMCEIV 1255

                  tRNA-synt_2b                              HGTP_anticodon
Ce          ------------------------------------------------------------ 1149
Fh          YDHPVT-GKPAFVYQNSWGLTTRTLGVLVMVHGDSKGLVLPPRIAPHQIVVVPCGITNKS 1025
Sm          YDHPVT-GKPAYVYQNSWGLTTRTLGVLIMVHSDDKGLVLPPRVAPYQIVIVPCGITAKT 1137
Dm          YEDPETQ-QKKYVYQNSWGITTRTIGVMIMVHADNQGLVLPPHVACIQAIVVPCGITVNT 1515
Hs          FEDPKIPGEKQFAYQNSWGLTTRTIGVMTMVHGDNMGLVLPPRVACVQVVIIPCGITNAL 1315
Mm          FEDPKTPGEKQFAYQCSWGLTTRTIGVMVMVHGDNMGLVLPPRVASVQVVVIPCGITNAL 1315

                                      HGTP_anticodon
Ce          ------------------------------------------------------------ 1149
Fh          SQEDRENLLSYALLVTKTLKKDSSQFRVHCDDRTHVSPGWKFNHWEMKGVPVRLEVGPQE 1085
Sm          TVQERETLLSAAHSVFELLNKSNKQFRVHCDDRDNVSPGWKFNHWELKGVPIRLEIGPQE 1197
Dm          KDDERAQLLDACKALEKRLV--GGGVRCEGDYRDNYSPGWKFNHWELKGVPLRLEVGPKD 1573
Hs          SEEDKEALIAKCNDYRRRLL--SVNIRVRADLRDNYSPGWKFNHWELKGVPIRLEVGPRD 1373
Mm          SEEDREALMAKCNEYRRRLL--GANIRVRVDLRDNYSPGWKFNHWELKGVPVRLEVGPRD 1373

                 HGTP_anticodon
Ce          ------------------------------------------------------------ 1149
Fh          MAKQSTCLVLRHNGIKLTVPLADICARMPQILEDIHNDLFRKATGELAAHVVQVGSLDQL 1145
Sm          VADRKVCLVLRHTGERVNVPMDSLINELPRILDDIHNAMFNKATKSLASHVMLVNDMNEL 1257
Dm          LKAQQLVAVRRDTVEKITIPLADVEKKIPALLETIHESMLNKAQEDMTSHTKKVTNWTDF 1633
Hs          MKSCQFVAVRRDTGEKLTVAENEAETKLQAILEDIQVTLFTRASEDLKTHMVVANTMEDF 1433
Mm          MKSCQFVAVRRDTGEKLTIAEKEAEAKLEKVLEDIQLNLFTRASEDLKTHMVVSNTLEDF 1433

                                    ProRS-C_1
Ce          ------------------------------------------------------------ 1149
Fh          CSALDAKSLALAPFCGDSDCEEIIRRESARNVVVEPGAPSMGAKSLCIPFSCPFNDKLVC 1205
Sm          CTALDQKSLALAPFCCDRDCEEVIKHESARNVIVEPGAPAMGAKSLCIPFACDFNPTLVC 1317
Dm          CGFLEQKNILLAPFCGEISCEDKIKADSARGEEAEPGAPAMGAKSLCIPFDQPAP----- 1688
Hs          QKILDSGKIVQIPFCGEIDCEDWIKKTTARDQDLEPGAPSMGAKSLCIPFKPLCE----- 1488
Mm          QKVLDAGKVAQIPFCGEIDCEDWIKKMTARDQDVEPGAPSMGAKSLCIPFNPLCE----- 1488

                  ProRS-C_1
Ce          ----------------------------- 1149
Fh          GSPATGTKCFNQPHCSRVATAYTLFGRSY 1234
Sm          GSPAPDTPCFNRQYCSRKAISYTLFGRSY 1346
Dm          --IAASDKCIN-PSCTNKPKFYTLFGRSY 1714
```

```
Hs        --LQPGAKCVC-G--KNPAKYYTLFGRSY 1512
Mm        --LQPGAMCVC-G--KNPAKFYTLFGRSY 1512
```

Actin, cytoplasmic 1 (Actb):

```
                                                    ACTIN
Mm        MVDDELTALVVDNGSGMCKAGFGGDDAPRAVFPSMVGRPRHQGVMVGMGQKDCYVGDEAQ 60
Hs        -MDDDIAALVVDNGSGMCKAGFAGDDAPRAVFPSIVGRPRHQGVMVGMGQKDSYVGDEAQ 59
Dm        MCDEEVAALVVDNGSGMCKAGFAGDDAPRAVFPSIVGRPRHQGVMVGMGQKDSYVGDEAQ 60
Ce        MCDDDVAALVVDNGSGMCKAGFAGDDAPRAVFPSIVGRPRHQGVMVGMGQKDSYVGDEAQ 60
Fh        MGDEDVAALVIDNGSGMCKAGFAGDDAPRAVFPSIVGRPRHQGVMVGMGQKDSYVGDEAQ 60
Sm        MGDEDVAALVIDNGSGMCKAGFAGDDAPRAVFPSIVGRPRHQGVMVGMGQKDSYVGDEAQ 60
            *::::***:***********.***********:*****************.*******
                                                ACTIN
Mm        SKRGILTLKYPIEHGVVTNWDDMEKIWYHTFYNELRVAPDEHPILLTEAPLNPKINREKM 120
Hs        SKRGILTLKYPIEHGIVTNWDDMEKIWHHTFYNELRVAPEEHPVLLTEAPLNPKANREKM 119
Dm        SKRGILTLKYPIEHGIVTNWDDMEKIWHHTFYNELRVAPEEHPVLLTEAPLNPKANREKM 120
Ce        SKRGILTLKYPIEHGIVTNWDDMEKIWHHTFYNELRVAPEEHPVLLTEAPLNPKANREKM 120
Fh        SKRGILTLKYPIEHGIVTNWDDMEKIWHHTFYNELRVAPEEHPVLLTEAPLNPKANREKM 120
Sm        SKRGILTLKYPIEHGIVTNWDDMEKIWHHTFYNELRVAPEEHPVLLTEAPLNPKANREKM 120
          ***************:***********:***********:***:********** *****
                                                ACTIN
Mm        TQIMFEAFNTPAMYVAIQAVLSLYASGRTTGIVMDSGDGVTHTVPIYEGYALPHAILRLD 180
Hs        TQIMFETFNTPAMYVAIQAVLSLYASGRTTGIVMDSGDGVTHTVPIYEGYALPHAILRLD 179
Dm        TQIMFETFNTPAMYVAIQAVLSLYASGRTTGIVLDSGDGVSHTVPIYEGYALPHAILRLD 180
Ce        TQIMFETFNTPAMYVAIQAVLSLYASGRTTGIVLDSGDGVTHTVPIYEGYALPHAILRLD 180
Fh        TQIMFETFNAPAMYVAIQAVLSLYASGRTTGIVLDSGDGVTHTVPIYEGYALPHAILRLD 180
Sm        TQIMFETFNVPAMYVAIQAVLSLYASGRTTGIVLDSGDGVTHTVPIYEGYALPHAILRLD 180
          ******:**.***********************:******:*******************
                                               ACTIN
Mm        LAGRDLTDYLMKILTERGYNFTTTAEREIVRDVKEKLCYVALDFEQEMVTAAASSSLERS 240
Hs        LAGRDLTDYLMKILTERGYSFTTTAEREIVRDIKEKLCYVALDFEQEMATAASSSSLEKS 239
Dm        LAGRDLTDYLMKILTERGYSFTTTAEREIVRDIKEKLCYVALDFEQEMATAASSSSLEKS 240
Ce        LAGRDLTDYLMKILTERGYSFTTTAEREIVRDIKEKLCYVALDFEQEMATAASSSSLEKS 240
Fh        LAGRDLTDHLMKILTERGYSFTTTAEREIVRDIKEKLCYVALDFEQEMGTASASSSLEKS 240
Sm        LAGRDLTDYMMKILTERGYSFTTTAEREIVRDIKEKLCYVALDFEQEMGTAASSSALEKS 240
          ********::*********.************:*************** **::**:**:*
                                               ACTIN
Mm        YELPDGQVITIGNERFRCPEAIFQPSFLGIESRGIHETTFNSIMKCDVDIRKDLFANTVL 300
Hs        YELPDGQVITIGNERFRCPEALFQPSFLGMESCGIHETTFNSIMKCDVDIRKDLYANTVL 299
Dm        YELPDGQVITIGNERFRCPEALFQPSFLGMEACGIHETTYNSIMKCDVDIRKDLYANTVL 300
Ce        YELPDGQVITVGNERFRCPEALFQPSFLGMESAGIHETSYNSIMKCDIDIRKDLYANTVL 300
Fh        YELPDGQVITIGNERFRCPEALFQPSFLGMESAGIHETTYNSIMKCDVDIRKDLYANTVL 300
Sm        YELPDGQVITIGNERFRCPEALFQPSFLGMEASGIHETTYNSIMKCDVDIRKDLYSNTVL 300
          **********:**********:*******:*: *****::*******:******::****
                                              ACTIN
Mm        SGGSTMYPGIADRMQKEIVTLAPSTMKIKIIAPPERKYSVWIGGSILASLSTFQQMWISK 360
Hs        SGGTTMYPGIADRMQKEITALAPSTMKIKIIAPPERKYSVWIGGSILASLSTFQQMWISK 359
Dm        SGGTTMYPGIADRMQKEITALAPSTMKIKIIAPPERKYSVWIGGSILASLSTFQQMWISK 360
Ce        SGGTTMYPGIADRMQKEITALAPSTMKIKIIAPPERKYSVWIGGSILASLSTFQQMWISK 360
Fh        SGGSTMYPGIADRMQKEITALAPSTMKIKIVAPPERKYSVWIGGSILASLSTFQQMWISK 360
Sm        SGGSTMYPGIADRMQKEISALAPSTMKIKIVAPPERKYSVWIGGSILASLSTFQQMWISK 360
          ***:************** :**********:*****************************
                ACTIN
Mm        QEYDEAGPPIVHRKCF       376
Hs        QEYDESGPSIVHRKCF       375
Dm        QEYDESGPSIVHRKCF       376
Ce        QEYDESGPSIVHRKCF       376
Fh        QEYDESGPGIVHRKCF       376
Sm        QEYDESGPSIVHRKCF       376
          *****:** *******
```

U2 small nuclear ribonucleoprotein A (Snrpa1*)*:

```
Ce      MVRLTTELFAERPQFVNSVNMREINLRGQKIPVIENMGVTRDQFDVIDLTDNDIRKLDNF 60
Fh      MVRLTAELIENAPQFTNAIQDRELDLHGYKFPAIENMGSTLDQFDTIDLSGNEIRKLDGF 60
Sm      MVRITSEIVENAPQFTNAIKDRELSLRSYKFPAIENMGCTLDQFDTIDLSDNEIRKLDGF 60
Hs      MVKLTAELIEQAAQYTNAVRDRELDLRGYKIPVIENLGATLDQFDAIDFSDNEIRKLDGF 60
Mm      MVKLTAELIEQAAQYTNAVRDRELDLRGYKIPVIENLGATLDQFDAIDFSDNEIRKLDGF 60
Dm      MVKLTPELINQSMQYINPCRERELDLRGYKIPQIENLGATLDQFDTIDLSDNDLRKLDNL 60
        **::* *:. :  *: *  . **:.*:. *:* ***:* * ****.**::.*::****.:
                                         LRR_8

Ce      PTFSRLNTLYLHNNRINYIAPDIATKLPNLKTLALTNNNICELGDIEPLAECKKLEYVTF 120
Fh      PLLKRLKALILNNNKIVRIAEDLGQQLPYLNTLILTSNSFTELRELDPLATCDKLTFLTL 120
Sm      PMLKRLKSLILTNNKIARIAEDLGQHLPNLLTLILTSNYLSDLKDLDPLSSCDKLNFLSL 120
Hs      PLLRRLKTLLVNNNRICRIGEGLDQALPCLTELILTNNSLVELGDLDPLASLKSLTYLSI 120
Mm      PLLRRLKTLLVNNNRICRIGEGLDQALPCLTELILTNNSLVELGDLDPLASLKSLTYLSI 120
Dm      PHLPRLKCLLLNNNRILRISEGLEEAVPNLGSIILTGNNLQELSDLEPLVGFTKLETICL 120
        * : **: * : **:*  *. .:   :* *  : **.* : :* :::**    .*  : :
         LRR_8       LRRcap

Ce      IGNPITHKDNYRMYMIYKLPTVRVIDFNRVRLTEREAAKKMFKGKSGKKARDAIQK---- 176
Fh      THCPVTMRANYRLYVISLLPSLRFLDYKRVTNSERKLANSMFKRIPAMASSASGVKGAPG 180
Sm      LHCPVTMRANYRLYVISRVASLRFLDYRRVTQAERKLARSMFKRLPALSNSVNNLKAPYQ 180
Hs      LRNPVTNKKHYRLYVIYKVPQVRVLDFQKVKLKERQEAEKMFKGKRGAQLAK-------- 172
Mm      LRNPVTNKKHYRLYVIYKVPQVRVLDFQKVKLKERQEAEKMFKGKRGAQLAK-------- 172
Dm      LINPVSTKPNYREYMAYKFPQLRLLDFRKIKQKDRQAAQEFFRTKQGKDVLK-------- 172
           *:: : :** *:   .  :*.:*:.::   :*: *..:*:   .

Ce      ---------------SVHTEDPSEIEPN-------------------------------- 189
Fh      LRNGIRSQNPAGGTTTVKTFIPGAPLYTNAGVDKEN------------------TA-SID 221
Sm      KANSNRIENSIPAAGVVKTFIPGAPINSNNLLPPGTEPTRSSNEQIHHGEGKENNAAALN 240
Hs      -D----------IARRSKTFNPGAGLPT-------------------------------- 189
Mm      -D----------IARRSKTFNPGAGLPT-------------------------------- 189
Dm      -E----------ISRKSKMSAAAAIAAEA-------------------GNG--------- 193
                         :    .

Ce      -------------------------------ENSSGGGARLTDEDREKIKEAIKNAKSLS 218
Fh      ----------ARGSTETKDISSMPPPPPAAAVQMGNKRPGGSAQDLYAIQEAIKRARTMD 271
Sm      TSVETDQTESTKSDTLVVSSADTPMPPPSTPVTTGNKRPVASSQDLFAIQEAIKRARTMD 300
Hs      ---------------------------------DK-KKGGPSPGDVEAIKNAIANASTLA 215
Mm      ---------------------------------DK-KKGGPSAGDVEAIKNAIANASTLA 215
Dm      ------------------------------KGRGSEGGRLANPQDMQRIREAIKRASSLA 223
                                                 .  *   *::** .* ::

Ce      EVNYLQSILASGKVPEK--GWNRQMDQNGADGEAMES----------------------- 253
Fh      EVDRLHQLLSSGQFAGFAIQWQQQLRLQQQQNQQQRQQQQEQQEQEQQRKAEQEQETSAM 331
Sm      EVERLHQLLSSGQFAGFAAQWQKQLRQQQQQKSSQ------------------------- 335
Hs      EVERLKGLLQSGQIPGRERRSGPT------------D-----------------DGEEEM 246
Mm      EVERLKGLLQSGQIPGRERRSGPS------------D-----------------EGEEEI 246
Dm      EVERLSQILQSGQLPDKFQHEMEAVAQNGAGH---NG-----------------SGAVAM 263
        **: *  :* **:.

Ce      ---------------------------------------------------- 253
Fh      DEEQTEQVQQPETMVQQNELLQHEESTNLEMATQDNIVDQQIHSMEVTQPVE 383
Sm      ---------------------------------------------------- 335
Hs      EEDTVTNGS------------------------------------------- 255
Mm      EDDTVTNGS------------------------------------------- 255
Dm      EY-------------------------------------------------- 265
```

Leucine zipper and EF-hand containing transmembrane protein 1 (Letm1):

```
Fh        ML----------------------VILRNVARPHRV--------RVLCPRRRER--AAGS 28
Sm        ------------------------------------------------------------ 0
Ce        ------------------------------------------------------------ 0
Dm        MNALLRHKGRNLRTSHLAQNVYKRFLKSNCCACSSVNVTDEPAKEDELPRRSAS-TSVLE 59
Hs        MA---------------------SILLRSCRGRAPARLPPP--PRYTVPRGSPGDPAHLS 37
Mm        MA---------------------SILLRSCRGRGPARLAP---PRAASPRGSLRDRACLS 36

Fh        SFQNAGHYIHNRAVFG---PS-----VFRTQSTSQWNLSLRSLH-LNSSLWSG----TET 75
Sm        ------------------------------------------------------------ 0
Ce        ---------------------MSLRYASNAYHIGRYAQRLFATGQRNRVFHQYIASTSLQ 39
Dm        LSRSLGTYRRF-------QPH-ANY----GYDYSGYGFRHLH---TSRTLL--------E 96
Hs        CASTLGLRNCLNVPFGCCTPIHPVYTSSRGDHLGCWALRPECLRIVSRAPW--------T 89
Mm        CTRTLGLTSRESVLSRCCTPAHPVYLCFKGEPLSCWTQRPECQGTAARTTW--------T 88

Fh        TNSLRVGDSR-----P-----EKYHPSLFLVDNPPPETSS-KKPPAKS---------ESS 115
Sm        ------------------------------------------------------------ 0
Ce        TTSLRYAST----------------------------DRSKVEYTLKMLREDVQKQDEE- 70
Dm        TSSSKIDATVKKLKNQQKEKVEEIMKEVANGQAAAVRASSAATATASSEKGQNASATAGS 156
Hs        STSVGFVAV-----GPQCLPVRGWH------SSRPVRDDSVVEKSLKSLKDKNKKLEEGG 138
Mm        PASARLVVT-----GPQYLPVRGWH------SSSPLGEDSVIEKSLKSLKDKNKKLEEGG 137

                                                   Letm1
Fh        SSALSETPEDPEKNESNTEQKKLSMWQKVKKEVAHYYHGFRLLGLEVKIASGICIRLLCG 175
Sm        ------------------------------------------------------------ 0
Ce        ----AQKVLSLMKSDKDVATVKPPLKDRIIHELKHYYHGFRLLALETRVSAKYLWTVLRG 126
Dm        TSATASTTSLAKTADKSVAKPKKPLRTRIWDELVHYYHGFRLLFIDVAICSKLLWRVLNG 216
Hs        PV----------YSPPAEVVVKKSLGQRVLDELKHYYHGFRLLWIDTKIAARMLWRILNG 188
Mm        PV----------YSPPAQVVVRKSLGQKVLDELRHYYHGFRLLWIDTKIAARMLWRILNG 187

                                        Letm1
Fh        NSLTRRERKQLVRTVADIIRLVPFAVFIIVPFMEFLLPFYLKFFPFMLPSTFKYKSTEAE 235
Sm        ----------------------------------------------MLPSTFKDKSTEAN 14
Ce        ATLSRRERQQLVRTVSDLFRLVPFSFFIIVPFMELALPIFIKLFPGMLPSTFQESSKEEE 186
Dm        KTLTRRENKQLQRTTSDLFRLIPFSVFIIVPFMELLLPLFIKFFPGMLPSTFQTSTDRQE 276
Hs        HSLTRRERRQFLRICADLFRLVPFLVFVVVPFMEFLLPVAVKLFPNMLPSTFETQSLKEE 248
Mm        HTLTRRERRQFLRICADLFRLVPFLVFVVVPFMEFLLPVVVKLFPNMLPSTFETQSIKEE 247
                                                        ******: .: . :
                                       Letm1
Fh        KIRQRVKAKLEMTRFLQETLHHTTGAVSEGEK-SPSFEQFQGFLKKVQESGQFLSDEEIT 294
Sm        AIQQRLKAKLELTRFLQETLMQTAGALKSSSD-APTVAEFQEFIKKVQKSGEQAHAKDIT 73
Ce        KWRKQVKLRVEMAKFLQDTIEEIGLERKTRNKESTRSLEFALFIKKVRNEGGYVSNEELL 246
Dm        KLRQSLSVRLEVAKFLQQTLDQMPVQHKEHSSE--EAKQFEAFFTKIRNPTEPVSNDEII 334
Hs        RLKKELRVKLELAKFLQDTIEEMALKNKAAKGS--ATKDFSVFFQKIRETGERPSNEEIM 306
Mm        RLKKELRVKLELAKFLQDTIEEMALKNKAAKGN--ATKDFSAFFQKIRETGERPSNEEIM 305
            :: :  ::*:::***:*: .     .  .       :*  *: *:::       .::
                                         Letm1
Fh        RFSKLFEDQITLDSLELNQLKMLCRLLSLPTMGPSNLLRFQLQMRVRQLKAEDRLLA-KE 353
Sm        RFSKLFEDQVTLDSLDNKQLRMLCRLLSLPTIGPSHLLRFQIWIRVRQLKAEDKLIA-NE 132
Ce        KFSKLFEDEITLDNLSMGQLRSLCRLMSINSLGSPEILRFQLNMKIRELKADDKQIAAEG 306
Dm        KFAKRFDDEITLDSLSREQLAALCRVLELNTIGTTTLLRFQLRLKLRSLATDDRVIA-RE 393
Hs        RFSKLFEDELTLDNLTRPQLVALCKLLELQSIGTNNFLRFQLTMRLRSIKADDKLIA-EE 365
Mm        RFSKLFEDELTLDNLTRPQLVALCKLLELQSIGTNNFLRFQLTMRLRSIKADDKLIS-EE 364
          :*:* *:*::***.*   **  **:::.: ::*   :****: :::*.: ::*: :: .
                                 Letm1
Fh        GVNTIPAWELQTLCQDRGMRSVGLTEERLRNQLAQWLNLHLEKNVPVTLLLFSRALHVSK 413
Sm        GVDQIPPWELQSLCQERGMRSVGLPKEKLQSQLSEWLDLHLEKNVPITLLLFSRALHVTQ 192
Ce        GVDALSSIDLQSACRARGMRAIGVSEERLKEQLVQWLELSLNDKVPPALLLLSRTLYLPE 366
Dm        GVDSLDLLELQQACKARGMRAYGLTEERLRFQLKEWIDLSLNEQVPPTLLLLSRTMLISD 453
Hs        GVDSLNVKELQAACRARGMRALGVTEDRLRGQLKQWLDLHLHQEIPTSLLILSRAMYLPD 425
Mm        GVDSLTVKELQAACRARGMRALGVTEDRLKGQLKQWLDLHLHHEIPTSLLILSRAMYLPD 424
          **: :   :**  *: ****: *: :::*: ** :*::* *..::* :**::**:: : .
```

```
Fh      ASTAELPLKEAIAQLPTAASEEATARVLESALPTELDPRTKIELLRKEQANIKAARIQRK 473
Sm      ALVDQNPLQQAIAQLPPSASSEAVARVLETTPHDELDPVTKIKVLREEQDSIKAERVQRK 252
Ce      EVSFPDRLKAIVQNLPDGLAETTKQKLTEM-EGGQIDHKARIELIRSIESAIANEKKDEE 425
Dm      DSITTDKLKETIRVLPDAVGAHTRHAIGES-EG-KVDNKTKIEIIKEEERKIREEREEER 511
Hs      TLSPADQLKSTLQTLPEIVAKEAQVKVAEV-EGEQVDNKAKLEATLQEEAAIQQEHREK- 483
Mm      TLSPADQLKSTLQTLPEIVAKEAQVKVAEV-EGEKVDNKAKLEATLQEEAAIQQEHLEE- 482
               *:  :  **   .  :   : *     ::*  ::::   . :  *   : :.

Fh      QELAEQKKAAASELDAKSAREQKLAPAAEDLVDKAPVLKGLPKEELENVKEAPSVSVVST 533
Sm      QELIEKQKSEKGKTGL-------------LEGDQAPLLKGLKNEELDKVTPVLTDSAAFM 299
Ce      KKKKAAEEALKSKEEAEKAKVQE------------K---EK----------LVDVAAQAI 460
Dm      EETIAKRSAIKEEIP------------------------------------AP-----YV 530
Hs      --ELQKRSEVAKDFEPERV-VAA------------P---QRP-----GTEPQPEMPDTVL 520
Mm      ---LKRASEAVKDIQPEVAEATL------------P---GRP-----GPEPQPPVDDVIL 519
               .    .

Fh      TEEP-LALTIEGKK-SQTAVAAQATPTESTSSKELQLKE-ALKKVLAAKVTKEEEPEITV 590
Sm      SENTEIQPEIRKHVQNIPPIHAVQTAFDGKSKDDSHIDSLSMKPEKPKTSDTEEVTEISA 359
Ce      VH--------ELKKDIYDAVASTSSTTEA--------KEPAAKPSEAKEEKK-EDITVDK 503
Dm      FA--------EKLSG-------SQDLLDH--------KEQSSVSETDKGISS-TDVQLLS 566
Hs      QS--------ETLKD-------TAPVLEG---------------LKEEEITK-EEIDILS 549
Mm      PS--------EVLTD-------TAPVLEG---------------LKGEEITK-EEIDILS 548
                  .                :                       .     :

Fh      VDLAQIESAIAESSGALHEEAMEGLKEEVAETAT---KHTASLVSADRTVDKRTTKAAQR 647
Sm      GDLAEIHSAIAESTPHLDSETIDGLKEQVAKTAKLQQKRQAELLASEEVTDKRKSKAALH 419
Ce      KDLSHIEEIIVGGPIKEAKHDILGLREKVLEHKEDLMEINS------LDGAFAETKIAKR 557
Dm      EALKTLS---SDKQLVVEKETIKELKEELADYKEDVEELREVRQV--VKEPVRESRAAKL 621
Hs      DACSKLQE--QKKSLTKEKEELELLKEDVQDYSEDLQEIKKELSKTGEEKYVEESKASKR 607
Mm      DACSKLQE--QKKSLTKEKEELELLKEDVQDYSEDLQEIKKELSKTGEEKYIEESAASKR 606
             :            .. :  *:*.: .      :                :  :

Fh      LASRVGRMIGEMDTMMDKLAEEKQQLLKNIELHEVHVKHSTEPTEKSEILDAIKADHERV 707
Sm      LESRVENLIKEMDTMVDKLNDKRTQLLKDIEVCESHINKSTESKERSKIMDQIKADHDRM 479
Ce      LRHKLNSMIEDVDSMVDKLEDEKRNIREMLI--------------DPTVENSVDLKKERE 603
Dm      LYNRVNKMISQLDNVLNDLEARQHQIKQAES--------------SDYAASSPTVEPQQM 667
Hs      LTKRVQQMIGQIDGLISQLEMDQQAGKLAPA--------------NGMP------TGENV 647
Mm      LSKRVQQMIGQIDGLITQLETTQQDGKLGPS--------------QSTP------TGESV 646
        *  ::  :* ::* :: .*   :                                  :

Fh      VDINDLLLALRRLQKVP-----DDTR---WQKILDVLDEDHDGKIEMQHVLSVIELLGAE 759
Sm      VDINDLLVSLKRIRNIP-----DDTR---WEKILKVLDEDRDGKIELNHVLSVIELLGSE 531
Ce      VRIQDVIDSLAKLKESKGEQADDGEQRERIEALLKTIDEDSDGIVDKQLVLEVIELLEKH 663
Dm      VHIDELVATIRRMKEAS-----DEERFKVVGDLLVKLDADKDGVISVNEITKAVQSIDRE 722
Hs      ISVAELINAMKQVKHIP-----ESK----LTSLAAALDENKDGKVNIDDLVKVIELVDKE 698
Mm      ISITELISAMKQIKHIP-----EHK----LISLTSALDDNKDGNINIDDLVKVIDLVNKE 697
        : : ::: :: :::.       :         :   :* : ** :. : : ..:: :  .

Fh      -NVKLSSKEIKRVLEMVDNE----HLAEIVQSQEIEDEARKT-AAVDNTTTE-------- 805
Sm      -NVKLSSKEIARVLEMIDNE----HLAEEIPTEDLKADKNRLKSSVDHS----------- 575
Ce      TDVHVSAAQMASMIGTLKK------EDEVAGLTE---EIRKVQSGNYQMPILPTGPSSAD 714
Dm      -ATNIDKKQLEEFTELLSKLASRRRHEEIVHIDDLMNNIKVLKETSDEAR-LKHIEAVLE 780
Hs      -DVHISTSQVAEI----------------------------------------------- 710
Mm      -DVQISTTQVAEI----------------------------------------------- 709
          .::.  ::  .


Fh      ---------------------------------------------------QVQS----- 809
Sm      ---------------------------------------------------QVTS----- 579
Ce      AFNQ-PQGVYTASK---------------------QVPARSEQEGVEQKQQVTSTL--- 748
Dm      KFDADKDGVVTVNDIRKVLESIGRDNIKLSDKAIEELISLLDKEQVLQAEQKIEKAIAKS 840
Hs      -------------------------------------VATLEKEEKVEEKEKAKEKA--- 730
```

```
Mm      -------------------------------------VATLEKEEKIEEKEKAKEKA--- 729
                                                           :  .

Fh      ------------------------------------------------------------ 809
Sm      ------------------------------------------------------------ 579
Ce      ------------------------------------------------------------ 748
Dm      MKEAEKLKSEVDKADKDLSKLVNDIHDSAKEIQDIANEMRDKEETVPDKAKELKAEPAFK 900
Hs      EKEVAEVKS--------------------------------------------------- 739
Mm      EKEAAEVKN--------------------------------------------------- 738


Fh      ------------------ESLSSPGSSTVITDATTTGGISASSGAPKSSDSTISNQTDRK 851
Sm      ------------------K----------------------------------------- 580
Ce      ------QQNSSK---------TSSSSTTKSTSD--SKSA--------------------- 770
Dm      DTAKTLKDNAKDLDDLAKDPKSDPKSPTKASTG--SGPAGLSGGGPSSGSSGIATGSTTE 958
Hs      ------------------------------------------------------------ 739
Mm      ------------------------------------------------------------ 738


Fh      R------------------------------------------------------      852
Sm      -------------------------------------------------------      580
Ce      -------------------------------------------------------      770
Dm      SALREAAERQMEKILPSTDIGLPPTIQTPSQPPTSKKATATASTLSTTITAKKLL      1013
Hs      -------------------------------------------------------      739
Mm      -------------------------------------------------------      738
```

Glyceraldehyde-3-phosphate dehydrogenase (Gapdh):

```
                                      Gp_dh_N
Fh      MGKARVGINGFGRIGRLVLRAAVEKGIVDVVAVNDPFIDLDYMRYMLKYDSTHGRFPYDI 60
Sm      MSRAKVGINGFGRIGRLVLRAAFLKNTVDVVSVNDPFIDLEYMVYMIKRDSTHGTFPGEV 60
Ce      MTKPSVGINGFGRIGRLVLRAAVEKDSVNVVAVNDPFISIDYMVYLFQYDSTHGRFKGTV 60
Dm      --MSKIGINGFGRIGRLVLRAAIDKGA-NVVAVNDPFIDVNYMVYLFKFDSTHGRFKGTV 57
Hs      MGKVKVGVNGFGRIGRLVTRAAFNSGKVDIVAINDPFIDLNYMVYMFQYDSTHGKFHGTV 60
Mm      --MVKVGVNGFGRIGRLVTRAAICSGKVEIVAINDPFIDLNYMVYMFQYDSTHGKFNGTV 58
             :*:********** ***. ..  ::*::*****.::** *::: ***** *   :
                                    Gp_dh_N

Fh      TIDQNKLIVRN-----NPISVHNERDPTQIPWGASQAEYVVESTGVFTTIDKAKAHLAG- 114
Sm      STENGKLKVNG-----KLISVHCERDPANIPWDKDGAEYVVESTGVFTTIDKAQAHIKNN 115
Ce      AHEGDYLLVAKEGKSQHKIKVYNSRDPAEIQWGASGADYVVESTGVFTTIEKANAHLKG- 119
Dm      AAEGGFLVVNG-----QKITVFSERDPANINWASAGAEYIVESTGVFTTIDKASTHLKG- 111
Hs      KAENGKLVING-----NPITIFQERDPSKIKWGDAGAEYVVESTGVFTTMEKAGAHLQG- 114
Mm      KAENGKLVING-----KPITIFQERDPTNIKWGEAGAEYVVESTGVFTTMEKAGAHLKG- 112
          : . * :       : *.:. .***::* *    *:*:*********::** :*: .
                       Gp_dh_N                          Gp_dh_C

Fh      GAKKVIISAPSADAPMFVFGVNHEKYSKD-MSVVSNASCTTNCLAPLAKVINDKFGIVEG 173
Sm      RAKKVIISAPSADAPMFVVGVNENSYEKS-MSVVSNASCTTNCLAPLAKVIHDKFEIVEG 174
Ce      GAKKVIISAPSADAPMFVVGVNHEKYDHANDHIISNASCTTNCLAPLAKVINDNFGIIEG 179
Dm      GAKKVIISAPSADAPMFVCGVNLDAYKPD-MKVVSNASCTTNCLAPLAKVINDNFEIVEG 170
Hs      GAKRVIISAPSADAPMFVMGVNHEKYDNS-LKIISNASCTTNCLAPLAKVIHDNFGIVEG 173
Mm      GAKRVIISAPSADAPMFVMGVNHEKYDNS-LKIVSNASCTTNCLAPLAKVIHDNFGIVEG 171
         **:************** *** : *.     ::*****************:*:* *:**
                                     Gp_dh_C

Fh      LMTTVHSYTATQKVVDGPSSKAWRDGRGAGQNIIPASTGAAKAVGKVIPELNGKLTGMAF 233
Sm      LMTTVHSFTATQKVVDGPSSKLWRDGRGAMQNIIPASTGAAKAVGKVIPALNGKLTGMAF 234
Ce      LMTTVHAVTATQKTVDGPSGKLWRDGRGAGQNIIPASTGAAKAVGKVIPELNGKLTGMAF 239
Dm      LMTTVHATTATQKTVDGPSGKLWRDGRGAAQNIIPASTGAAKAVGKVIPALNGKLTGMAF 230
Hs      LMTTVHAITATQKTVDGPSGKLWRDGRGALQNIIPASTGAAKAVGKVIPELNGKLTGMAF 233
Mm      LMTTVHAITATQKTVDGPSGKLWRDGRGAAQNIIPASTGAAKAVGKVIPELNGKLTGMAF 231
        ******: *****.*****.* ******* ******************* **********
                                    Gp_dh_C
```

```
Fh        RVPTADVSVVDLTCRLNKAAKYDEIKAAVKAAADGPMKGILDYTEELLVSSDMLGTHCSS 293
Sm        RVPTPDVSVVDLTCRLGKGASYEEIKAAVKAAASGPLKGILEYTEDEVVSSDFVGSTSSS 294
Ce        RVPTPDVSVVDLTARLEKPASLDDIKKVIKAAADGPMKGILAYTEDQVVSTDFVSDTNSS 299
Dm        RVPTPNVSVVDLTVRLGKGASYDEIKAKVQEAANGPLKGILGYTDEEVVSTDFLSDTHSS 290
Hs        RVPTANVSVVDLTCRLEKPAKYDDIKKVVKQASEGPLKGILGYTEHQVVSSDFNSDTHSS 293
Mm        RVPTPNVSVVDLTCRLEKPAKYDDIKKVVKQASEGPLKGILGYTEDQVVSCDFNSNSHSS 291
          **** :******* ** * *. ::**  :: *:.**:**** **:. :** *: .   **
                  Gp_dh_C
Fh        VFDAQAGISLNDNFVKLISWYDNEFGYSCRVVDLINHMFRVDHS  337
Sm        IFDAKAGISLNNNFVKLVSWYDNEFGYSCRVVDLITHMHKVDHA  338
Ce        IFDAGASISLNPHFVKLVSWYDNEFGYSNRVVDLISYIATKA--  341
Dm        VFDAKAGISLNDKFVKLISWYDNEFGYSNRVIDLIKYMQSKD--  332
Hs        TFDAGAGIALNDHFVKLISWYDNEFGYSNRVVDLMAHMASKE--  335
Mm        TFDAGAGIALNDNFVKLISWYDNEYGYSNRVVDLMAYMASKE--  333
           *** *.*:** :****:******:*** **:**: ::
```

Protein phosphatase 1 catalytic subunit beta (Ppp1cb):

```
                                                       PP2Ac
Sm        --MTSEVDVDELISRLLEVRSSRPGTTVNMKEEEVRYLCVTSRQIFLSQPILLELQAPLK 58
Hs        -MADGELNVDSLITRLLEVRGCRPGKIVQMTEAEVRGLCIKSREIFLSQPILLELEAPLK 59
Ce        -MDVEKLNLDNIISRLLEVRGSKPGKNVQLTESEIKGLCQKSREIFLSQPILLELEAPLK 59
Dm        --MSDIMNIDSIISRLLEVRGARPGKNVQLSESEIRSLCLKSREIFLSQPILLELEAPLK 58
Fh        MSDIDKLNVDSVIARLLEVRGSRPGKNVQLTEAEIRALALKSREIFLRQPILLELEAPLK 60
Mm        MADIDKLNIDSIIQRLLEVRGSKPGKNVQLQENEIRGLCLKSREIFLSQPILLELEAPLK 60
                :::*.:* ******..:**. *:: * *:: *. .**:*** *******:****
                                        PP2Ac
Sm        ICGDIHGQYTDLLRLFEYGGFPPESNYLFLGDYVDRGKQSLETICLLLAYKIKHPENFFL 118
Hs        ICGDIHGQYTDLLRLFEYGGFPPEANYLFLGDYVDRGKQSLETICLLLAYKIKYPENFFL 119
Ce        ICGDVHGQYYDLLRLFEYGGFPPESNYLFLGDYVDRGKQSLETICLLLAYKIKYPENFFL 119
Dm        ICGDIHGQYYDLLRLFEYGGFPPESNYLFLGDYVDRGKQSLETICLLLAYKIKYAENFFL 118
Fh        ICGDIHGQYYDLLRLFEYGSFPPEANYLFLGDYVDRGKQSLETICLLLAYKIKYPENFFL 120
Mm        ICGDIHGQYYDLLRLFEYGGFPPESNYLFLGDYVDRGKQSLETICLLLAYKIKYPENFFL 120
          ****:**** *********.****:****************************: *****
                                        PP2Ac
Sm        LRGNHECAAINRIYGFYDECKRRFSVRLWKTFTDCFNCLPIAAIVDSKIFCCHGGLSPDL 178
Hs        LRGNHECASINRIYGFYDECKRRFNIKLWKTFTDCFNCLPIAAIVDEKIFCCHGGLSPDL 179
Ce        LRGNHECASINRIYGFYDECKRRYNIKLWKTFTDCFNCLPVAAIIDEKIFCCHGGLSPDL 179
Dm        LRGNHECASINRIYGFYDECKRRYTIKLWKTFTDCFNCLPVAAIVDEKIFCCHGGLSPDL 178
Fh        LRGNHECASINRIYGFYDECKRRYNIKLWKTFTDCFNCLPIVAIVDEKIFCCHGGLSPDL 180
Mm        LRGNHECASINRIYGFYDECKRRYNIKLWKTFTDCFNCLPIAAIVDEKIFCCHGGLSPDL 180
          ********:**************:.::*************:.**:*.*************
                                       PP2Ac
Sm        QNMDQIRRIMRPSDIPDTGLLCDILWSDPDKDVNGWAENDRGVSFTFGPDVVTKFLNRHD 238
Hs        QSMEQIRRIMRPTDVPDTGLLCDLLWSDPDKDVQGWGENDRGVSFTFGADVVSKFLNRHD 239
Ce        QSMEQIRRIMRPTDVPDQGLLCDLLWSDPDKDVTGWGENDRGVSFTFGPEVVAKFLHKHD 239
Dm        SSMEQIRRIMRPTDVPDQGLLCDLLWSDPDKDTMGWGENDRGVSFTFGAEVVGKFLQKHE 238
Fh        HSMEQIRRIMRPTDVPEQGLLCDLLWSDPDKDITGWGENDRGVSFTFGADVVTKFLHNHD 240
Mm        QSMEQIRRIMRPTDVPDQGLLCDLLWSDPDKDVLGWGENDRGVSFTFGAEVVAKFLHKHD 240
           .*:********:*:*:*: *****:********  **.*********** :** ***:.*:
                                      PP2Ac
Sm        MDLICRAHQVVEDGFEFFCRRQLVTLFSAPNYCGEFDNAGGMMSVDENLTCSFQILKPSE 298
Hs        LDLICRAHQVVEDGYEFFAKRQLVTLFSAPNYCGEFDNAGGMMSVDETLMCSFQILKPSE 299
Ce        LDLICRAHQVVEDGYEFFAKRQLVTLFSAPNYCGEFDNAGSMMTVDETLMCSFQILKPAD 299
Dm        FDLICRAHQVVEDGYEFFAKRQLVTLFSAPNYCGEFDNAGAMMSVDDTLMCSFQILKPAD 298
Fh        LDLICRAHQVVEDGYEFFAKRQLVTLFSAPNYCGEFDNAGAMMSVDESLTCSFQILKPAD 300
Mm        LDLICRAHQVVEDGYEFFAKRQLVTLFSAPNYCGEFDNAGAMMSVDETLMCSFQILKPAE 300
          :*************:***.:********************.**:**:.* ********::

Sm        KKA-KYQYQGVNTTGNQARLPARIP---------------------        322
Hs        KK-AKYQYGGLNSG--RPVTPPRTANPPKKR---------------        327
Ce        KKKYPYGAGGVGSN--RPVTPPRNAPAAQPKKGAKK----------        333
Dm        KRRFVYPNFGS-SG--RPLTPPRGANNKNKKK--------------        327
```

```
Fh          KKKFNLGSLN--AV--WPVTPPRNTKLKDK----------------        326
Mm          KKKPN-------AT--RPVTPPRVGSGLNPSIQKASNYRNNTVLYE        337
            *:          :       * *
```

Proteasome subunit beta type 7 (Psmb7):

```
Ce          MATADVKSTVPHMDMDRGGAFDFSNCIRNQAM----CKMGGKAPKLTSTGTTIVAVAFKG 56
Fh          ------------------------------------------------------------ 0
Sm          --------MSSLVVDRRSGGFSFENCYRNKLI----EQKGFELPKAVKTGTTICGVVFKN 48
Dm          -------MDLDNARDLPRAGFNFDNCKRNATL----LNRGFKPPTTTKTGTTIVGIIYKD 49
Hs          -------MAAVSVYAPPVGGFSFDNCRRNAVLEADFAKRGYKLPKVRKTGTTIAGVVYKD 53
Mm          -------MAAVSVFQPPVGGFSFDNCRRNAVLEADFAKKGFKLPKARKTGTTIAGVVYKD 53

                                                      Proteasome

Ce          GLVMGADSRATAGNIIADKHCEKVHKLTESIYACGAGTAADLDQVTKMLSGNLRLLELNT 116
Fh          -------------------------MTLSFCSCCGAGTAADTEMTTKMISSKVELHRLNT 35
Sm          GVVLGADTRATEGTVVAEKNCSKIHRISENIYCCGAGTAADTQMVTLMISSQVELHSLNT 108
Dm          GVILGADTRATEGPIVSDKNCAKIHYLAKNIYCCGAGTAADTEMTTDLISSQLELHRLQT 109
Hs          GIVLGADTRATEGMVVADKNCSKIHFISPNIYCCGAGTAADTDMTTQLISSNLELHSLST 113
Mm          GIVLGADTRATEGMVVADKNCSKIHFISPNIYCCGAGTAADTDMTTQLISSNLELHSLTT 113
                                            .******** : .* ::*.::.*  * *
                                          Proteasome

Ce          GRKARVITALRQAKQHLFN-----------YQGYIGAYLLIGGVDPTGPHLYMCSANGTT 165
Fh          GRQPRVILPLRLLKDYLFGYRVSLFRVLEIFQGYVGAALILGGVDYQGPHLYSVSPHGCS 95
Sm          GRTPRVIAPLRLLKRYLYQ-----------YQGYVGAALVLGGVDSTGPHLYSIAPHGST 157
Dm          DREVRVVAANTMLKQMLFR-----------YQGHISAALVLGGVDKTGPHIYSIHPHGSS 158
Hs          GRLPRVVTANRMLKQMLFR-----------YQGYIGAALVLGGVDVTGPHLYSIYPHGST 162
Mm          GRLPRVVTANRMLKQMLFR-----------YQGYIGAALVLGGVDVTGPHLYSIYPHGST 162
            .*  **:      *  *:            :**::.* *::****  ***:*    :* :
                                     Proteasome

Ce          MAFPFTAQGSGSYAAITILERDFKVDMTKDEAEKLVQRALEAGMHGDNASGNSLNLVIIE 225
Fh          DKLPYITMGSGCLAALSVLESRFRFDLSRTEAMQLVRDAIAAGILNDLGSGSNVDLCVIT 155
Sm          DKLPYITMGSGSLACMSVLESRFKFDMEQDEAVKLVRDGIAAGIFNDMGSGSNVDICIIT 217
Dm          DKLPYATMGSGSLAAMTVFESRWKPDLSEEEGKKLVRDAIASGVFNDLGSGSNIDLCVIR 218
Hs          DKLPYVTMGSGSLAAMAVFEDKFRPDMEEEEAKNLVSEAIAAGIFNDLGSGSNIDLCVIS 222
Mm          DKLPYVTMGSGSLAAMAVFEDKFRPDMEEEEAKKLVSEAIAAGIFNDLGSGSNIDLCVIS 222
              :*: : ***. *.::::*  :: *: . *. :**  .: :*: .* .**..::: :*
                                       Pr_beta_C

Ce          PSETVFKGPIVPEFCKRPEPNDLVYKFQAGATKVLKHKTYK--YDVVES----------- 272
Fh          KDSTEYIRPHDVAN--KKGQRASKYNLPPGSTAVLSQKIQPVEYDVVTTRVIRDLPDPKT 213
Sm          KDGTTYIRSYDEAN--VKGKRAEKYNPPEGTTSVLHKSVHHVEFDVVTTRVVRDIPAHSV 275
Dm          KGSVEYLRNYELAN--KKGKRQLDYRFKTGTSTVLHTNIKDLLVTERVQAV--------- 267
Hs          KNKLDFLRPYTVPN--KKGTRLGRYRCEKGTTAVLTEKITPLEIEVLEETV--------- 271
Mm          KSKLDFLRPFSVPN--KKGTRLGRYRCEKGTTAVLTEKVTPLEIEVLEETV--------- 271
             .   :              .   *.   *:: **  .

Ce          --MDITH 277
Fh          EAMDTS- 219
Sm          ETMDLS- 281
Dm          -PMEIS- 272
Hs          QTMDTS- 277
Mm          QTMDTS- 277
              *: :
```

Supplementary Figure S9: Multiple alignment of amino acid sequences of orthologs for kinase genes. Accession numbers of gene orthologs for *C. elegans* (Ce), *F. hepatica* (Fh), *S. mansoni* (Sm), *D. melanogaster* (Dm), *H. sapiens* (Hs) and *M. musculus* (Mm) are listed in Supplementary Table S1. Conserved protein domains are highlighted. * indicates identical amino acids.

ABL proto-oncogene 1, non-receptor tyrosine kinase *(*Abl1*)*:

```
Fh          ------------------------------------------------------------ 0
Sm          ------------------------------------------------------------ 0
Ce          ------------------------------------------------------------ 0
Dm          MGAQQGKDRGAHSGGGGSGAPVSCIGLSSSPVASVSPHCISSSSGVSSAPLGGGSTLRGS 60
Hs          ------------------------------------------------------------ 0
Mm          ------------------------------------------------------------ 0


Fh          --------------MG---GNSG---------------------KLATSK---------- 12
Sm          ------------------------------------------------------------ 0
Ce          -----------------------MGHSHSTGKEIN-------DNELFTCEDPVFDQPVAS 30
Dm          RIKSSSSGVASGSGSGGGGGGSGSGLSQRSGGHKDARCNPTVGLNIFTEHNEALLQS--R 118
Hs          --------------------------------------MLEICLK--------LVGC--K 12
Mm          ----------------------------------------MISFD--------LLS---- 8


Fh          -----------------------NGHLQSPRLSSN-----SQNVEGTRTGN-SSYQ--ER 41
Sm          -----------------------MSRVDTSDLSKN-----PKPADLN------KVD--DK 24
Ce          PKSEISSKLAEEIERSKSPLILEMFRPTFDTFRPPNSDSST--FR-----GSQSRE--DL 81
Dm          PLPHIPAGS------TAASLL-----ADAAELQQHQQDSGGLGLQGSSLGGGHSSTTSVF 167
Hs          SKK----GL------SSSSSC-----YLEEALQRP---------------VASDFEPQGL 42
Mm          --D----EL------HLKLLV-----LDVEALQRP---------------VASDFEPQGL 36
                                           :                     .
                                                       SH3
Fh          GSNSSYPLDINCQ--SASETAVHTDKELMVVLYDFTESMRSQISIKRGELVRLLGYSPAG 99
Sm          LSDIRSYTKMDVQ--SSSDSLVLGRGGIMVVLYDFSESMSSQISIKRGELVRLLSYSPAG 82
Ce          VACSSMNSVNNVHDMNTVSSSSSSSAPLFVALYDFHGVGEEQLSLRKGDQVRILGYNKNN 141
Dm          ESAHRWTSKEN----LLAPGPEEDDPQLFVALYDFQAGGENQLSLKKGEQVRILSYNKSG 223
Hs          SEAARWNSKEN----LLA-GPSENDPNLFVALYDFVASGDNTLSITKGEKLRVLGYNHNG 97
Mm          SEAARWNSKEN----LLA-GPSENDPNLFVALYDFVASGDNTLSITKGEKLRVLGYNHNG 91
                      :                ::*.****     . :*: :*: :*:*.*.  .
                                            SH3
Fh          DWSEVETSGLAHPATHPMMETELTNTSTQPSQTQIKSDLTTQRDSVGPGGVGGGSTMSTG 159
Sm          DWSEVEASLVLPPLPKPGPGSSTSGSESHPSQCKGGAT---VKH-------SHGPTMETG 132
Ce          EWCEARLYSTRK------------------------------------------------ 153
Dm          EWCEAHS----------------------------------------------------- 230
Hs          EWCEAQT----------------------------------------------------- 104
Mm          EWCEAQT----------------------------------------------------- 98
            :*.*..
                           SH3
Fh          SGHSINNSAFGNAPVRYRRGWVPTSYLAPANVLSDPNQRLTGHFLPHEVIFPSVGSTSSM 219
Sm          N--SV-NTSCNYLFNNYRRGWVPTSYLATANVFQSSAPSKQ--SYPQQLI-GCEGS--EK 184
Ce          -------NDASNQRRLGEIGWVPSNFIAPYNS---------------------------- 178
Dm          --------------DSGNVGWVPSNYVTPLNS---------------------------- 248
Hs          --------------KNG-QGWVPSNYITPVNS---------------------------- 121
Mm          --------------KNG-QGWVPSNYITPVNS---------------------------- 115
                               ****:.:::  *

Fh          ERCNVTGMDSKVNLVSGPSPMLVMRPGQMGSRSHSSAQATQQQFQPQTNMVDSSPLGLQG 279
Sm          PNCSVNAP-----CLSNS--QSIIANDNMQSR----VQNVSNKGPVHHVMMDSSPLSLLE 233
Ce          ------------------------------------------------------------ 178
Dm          ------------------------------------------------------------ 248
```

```
Hs      ------------------------------------------------------------ 121
Mm      ------------------------------------------------------------ 115

                                       SH2
Fh      PSLVLYPWYHGAVSRHAGEQLLRSGITGSFLVRASESAPGQLSVTVRHLGRVYHYRISQD 339
Sm      PSLLPYSWYHGAVSRQAGEHLLRSGITGSFLVRASESAPGQLSVTVRHLGRVYHYRISQD 293
Ce      --LDKYTWYHGKISRSDSEAILGSGITGSFLVRESETSIGQYTISVRHDGRVFHYRINVD 236
Dm      --LEKHSWYHGPISRNAAEYLLSSGINGSFLVRESESSPGQRSISLRYEGRVYHYRISED 306
Hs      --LEKHSWYHGPVSRNAAEYLLSSGINGSFLVRESESSPGQRSISLRYEGRVYHYRINTA 179
Mm      --LEKHSWYHGPVSRNAAEYLLSSGINGSFLVRESESSPGQRSISLRYEGRVYHYRINTA 173
          *  : **** :**  .* :* ***.****** **:: ** ::::*: ***:****.
                       SH2
Fh      VRGLFYITNVHRFPTVVQLIDHHSRS--ADGLVCPLLYPVPKLQYPTSHMTSVAYSSVPT 397
Sm      SRGLFYITEAHRFPTVVQLIEHHSRS--ADGLVCPLLYSVPKPQFLNQPMQQSCYSSVPQ 351
Ce      NTEKMFITQEVKFRTLGELVHHHSVH--ADGLICLLMYPASKKDKGRGL----------- 283
Dm      PDGKVFVTQEAKFNTLAELVHHHSVPHEGHGLITPLLYPAPKQNKP-TV----------- 354
Hs      SDGKLYVSSESRFNTLAELVHHHSTV--ADGLITTLHYPAPKRNKP-TV----------- 225
Mm      SDGKLYVSSESRFNTLAELVHHHSTV--ADGLITTLHYPAPKRNKP-TI----------- 219
            .:::.  :* *: :*:.***    ..**:  * * . * :

Fh      HAIPSHPHTHLIGGAAQTILPPVPTHPSADSST---TGPDQASFHPRPHNTAQQGMEPFL 454
Sm      TLPSSR-----IPGPNQFEVNPIVHQSNAEISNFPLTHINPVSHVPRPFHPSH--INNSE 404
Ce      ------------------------------------------------------------ 283
Dm      ------------------------------------------------------------ 354
Hs      ------------------------------------------------------------ 225
Mm      ------------------------------------------------------------ 219

                                                  TyrKc
Fh      GLSRTDEPFRKQSWDGWEIDRNEILMRQKLGCGQYGDVYEAIWKRLNTVVAVKTLKQDVN 514
Sm      RLSACSDSIGSMEFDGWEIDRSEIIMRQKLGCGQYGDVYEAVWKRFNSVVAVKTLKQDVN 464
Ce      ------FSLSPNAPDEWELDRSEIIMHNKLGGGQYGDVYEGYWKRHDCTIAVKALKEDA- 336
Dm      ------FPLSPE-PDEWEICRTDIMMKHKLGGGQYGEVYEAVWKRYGNTVAVKTLKEDT- 406
Hs      ------YGVSPN-YDKWEMERTDITMKHKLGGGQYGEVYEGVWKKYSLTVAVKTLKEDT- 277
Mm      ------YGVSPN-YDKWEMERTDITMKHKLGGGQYGEVYEGVWKKYSLTVAVKTLKEDT- 271
                .     * **: *.:* *::*** ****:***. **: . .:***:**:*.
                                        TyrKc
Fh      LNVNDFLKEASIMKKLRHRNLVQLLGVCTREPPLYLITEYMSNGNLLNYLRTRSPGELTP 574
Sm      LNVNDFLKEAAIMKKLRNRNLVQLLGVCTREPPLYLITEYMPNGNLLNYLRTRSPGELTP 524
Ce      MPLHEFLAEAAIMKDLHHKNLVRLLGVCTHEAPFYIITEFMCNGNLLEYLRRTDKSLLPP 396
Dm      MALKDFLEEAAIMKEMKHPNLVQLIGVCTREPPFYIITEFMSHGNLLDFLRSAGRETLDA 466
Hs      MEVEEFLKEAAVMKEIKHPNLVQLLGVCTREPPFYIITEFMTYGNLLDYLRECNRQEVNA 337
Mm      MEVEEFLKEAAVMKEIKHPNLVQLLGVCTREPPFYIITEFMTYGNLLDYLRECNRQEVSA 331
        : :.:** **::**.::: ***:*:****:* *:*:***:*  ****::**  .   :
                                       TyrKc
Fh      PVLLYMAVQIASGMSYLEANNFIHRDLAARNCLVGERHLIKVADFGLARYMQRQDTYTAR 634
Sm      LTLLYMAVQIASGMAYLEANNFIHRDLAARNCLVGDQHLIKVADFGLARYMQRQDTYTAR 584
Ce      IILVQMASQIASGMSYLEARHFIHRDLAARNCLVSEHNIVKIADFGLARFM-KEDTYTAH 455
Dm      VALLYMATQIASGMSYLESRNYIHRDLAARNCLVGDNKLVKVADFGLARLM-RDDTYTAH 525
Hs      VVLLYMATQISSAMEYLEKKNFIHRDLAARNCLVGENHLVKVADFGLSRLM-TGDTYTAH 396
Mm      VVLLYMATQISSAMEYLEKKNFIHRDLAARNCLVGENHLVKVADFGLSRLM-TGDTYTAH 390
          *: ** **:*.* *** .::************.:.:::*:*****:* *   *****:
                                       TyrKc
Fh      NGAKFPIKWTAPEGLAYYVFSSKSDVWAFGVVLWELATYGLSPYPGVELHDVYHILEKGY 694
Sm      NGAKFPIKWTAPEGLSYYLFSSKSDVWAFGVVLWELATYGLSPYPGVELHDVYHLLEKGY 644
Ce      AGAKFPIKWTAPEGLAFNTFSSKSDVWAFGVLLWEIATYGMAPYPGVELSNVYGLLENGF 515
Dm      AGAKFPIKWTAPEGLAYNKFSTKSDVWAFGVLLWEIATYGMSPYPAIDLTDVYHKLDKGY 585
Hs      AGAKFPIKWTAPESLAYNKFSIKSDVWAFGVLLWEIATYGMSPYPGIDLSQVYELLEKDY 456
Mm      AGAKFPIKWTAPESLAYNKFSIKSDVWAFGVLLWEIATYGMSPYPGIDLSQVYELLEKDY 450
         ************.*::  ** *********:***:****::***.::* :**  *::.:
                          TyrKc
Fh      RMERPHGCPEAVYSIMLRCWAWEASLRPSFTEVHAELEQMYTTMNIEAEVARELEKRHAA 754
Sm      RMERPHGCPEAVYSIMLRCWSWDPNLRPSFSEIHAELEQMYTTMNIEAEVALELGKQPAN 704
Ce      RMDGPQGCPPSVYRLMLQCWNWSPSDRPRFRDIHFNLENLISSNSLNDEVQKQLKKNNDK 575
```

```
Dm      RMERPPGCPPEVYDLMRQCWQWDATDRPTFKSIHHALEHMFQESSITEAVEKQLNANATS 645
Hs      RMERPEGCPEKVYELMRACWQWNPSDRPSFAEIHQAFETMFQESSISDEVEKELGKQGVR 516
Mm      RMERPEGCPEKVYELMRACWQWNPSDRPSFAEIHQAFETMFQESSISDEVEKELGKRGTR 510
        **: * ***  ** :*  ** *. . ** * .:*  :* :    .:   *  :*  .

Fh      FTAASSNNQPTGEPSEPVRDLGTGDL---------------------------------- 780
Sm      FIPQQQQQPLVSS--NRFTEIQPHDLQGN------SVNQFNMVFKESLPSSVIPTEIVNS 756
Ce      KLESDKRRSNVRERSD-------SKSRHSSHHD--RDRDRESLHSRN------------- 613
Dm      ASSSAPSTSGVATGGGATTTTAASGCASSSSATASLSLTPQMV-KKGLPGG--------- 695
Hs      GAVSTLLQAPE-------LPTKTRTSRRAAEHR-DTTDVPEMPHSKGQGES--------- 559
Mm      GGAGSMLQAPE-------LPTKTRTCRRAAEQK-DAPDTPELLHTKGLGES--------- 553


Fh      ---------------FVDVRCSGSMSAHGVIEPLNPNTISNSIWLR--ATDSVHHSSQAA 823
Sm      DHIISRHNNAIHSTSNIDFTCNAT-------ESSRPNPVSSYVIMNSVANHSIHHHVENN 809
Ce      --------------------------------------------------------SNPE 617
Dm      -------------------------------QALTPN-----------AHHNDPHQQQAS 713
Hs      -------------------------------DPLDHE----------------PA-VSPL 571
Mm      -------------------------------DALDSE----------------PA-VSPL 565
                                                                 .

Fh      HP---SGL------------------------PNRDVHEGPVRPDVDGG-----DEIQAD 851
Sm      IASLNNNIHNCMKKEKTIFIDQN--------RLSKDKHSVLPYPSSSGGGVGGSDRFDLI 861
Ce      IPNRSFIRTDDSVS---FFNPST---TSKVTSFRAQGPPFPPPPQQNTKP----KLLKSV 667
Dm      TPMSETGSTSTKLS---TFSSQGKGNVQMRRTTNKQGKQAPAPPKRTS-------LLSSS 763
Hs      LPRKERGPPEGGLNEDERLLPKDKKTNLFSALIKKKKKTAPTPPKRSS-------SFREM 624
Mm      LPRKERGPPDGSLNEDERLLPRDRKTNLFSALIKKKKKMAPTPPKRSS-------SFREM 618
                                           .       *.           :

Fh      -D-----GDEDDEEGEF-DESDEEDAQQQWH-EHSNAIQQ------PSDHMARSPEPASS 897
Sm      -TDNLAAVSLDNNNDDI-DNSDDDDENKRPASSNNHAVQYESNSETNPDHMLL---PTSS 916
Ce      LNSNARHASEEFERNE-QDDVVPLAEKN-VR-KAVTRLGG---------T---MP----K 708
Dm      RDSTYRE---EDPANARCNFIDDLSTNG-LA-RDINSLTQRYDSETDPAA---DPDTDAT 815
Hs      DGQPERRGAGEEEGRDISNGALAF--------------TP--LDTADPAK---SPKPSN- 664
Mm      DGQPDRRGASEDDSRELCNGPPAL--------------T---SDAAEPTK---SPKASN- 657
                  :       :

Fh      SNVVGALSRYHVSDPTVVPNALEGVSPAHIMDRLCGQIRAMSLAPR---DGSHLCRTSKS 954
Sm      ---LGQ--------IKFLPNSV--------ISSCSPQMTSIHESSQNGFSNLIQCRTPFS 957
Ce      GQRIDAYL--------------------------------------DSMRRVD------- 723
Dm      GDSLEQSLSQV--IAAPVTNKMQH---------------SLHSGGGGGGIGPR------- 851
Hs      GAGV--------------PN---G---------------ALRESGGSGFRSPH------- 685
Mm      GAGV--------------PN---G---------------AFREPGNSGFRSPH------- 678
           :

Fh      GRWDDNTS-QVAMFASQSPVPITQGQRYYTPPPNVGGLPSAQPHRDLVI----------- 1002
Sm      SNYLTQTQYSPASLSDNGFLPFGEKLCYFIPMSN---NPSYQPNSHITSSNITQN---CG 1011
Ce      ---------------------------------------SWKESTDA--------DNEGA 736
Dm      ---------------------------------------SSQQH---------------- 856
Hs      ---------------------------------------LWKKSSTLTSSRLATGEEEGG 706
Mm      ---------------------------------------MWKKSSTLTGSRLAAAEEESG 699
                                                 :

Fh      ----------------GDVPNSSASNSKHRPMAATSSQSMNSAGYARE-KSDRSTSARPG 1045
Sm      ISNLSQFSNNNPASIVSKIPNLNVANST---------KVVNDRSAIRTNRSIHRNVTSGC 1062
Ce      GS--SSLSRTVSNDSLD---------------TLPLPDSMNSSTYVKMH------PASGE 773
Dm      ----SSFKRPTGTPVMG-----NRGLETRQSKRSQLHSQAPGPGPPSTQ------PHHGN 901
Hs      GSSSKRFLRSCSASCVP---HGAKDTEWR---SVTLPRDLQSTGRQFDS------STFGG 754
Mm      MSSSKRFLRSCSASCMP---HGARDTEWR---SVTLPRDLPSAGKQFDS------STFGG 747
                                                 .

Fh      RSRVCRTRDGTTRSRDTDTPDESGVGESIISNDSPADS---GGGVIGSA-PVNIMSTDRV 1101
Sm      NTQTSSQQNGTTRSQDTDTPDESGVGESIISNESPAESRACGGGIMSNAAGVGVIATMNS 1122
```

```
Ce      NVFLRQIRS--KLKKRSETPELDHIDSDTADETTKSEKSPF--GSLNKSSIKYPIK---- 825
Dm      NGVVTSAHP---I-T---------VGALDVM-NVKQVVNRY--GTLPKGARIGAYL---- 941
Hs      HKSEKPALP---R-KRAGENRSDQVTRGTVT-PPPRLVKKN------EEAADEVFK---- 799
Mm      HKSEKPALP---R-KRTSESRSEQVAKSTAM-PPPRLVKKN------EEAAEEGFK---- 792
        .                       :                      .



Fh      LSLSASCKTA---DTPSVLNTF--AQAKTSHPANL-----VSQSSVP--AGLPSHEVFQP 1149
Sm      ILSSAPSQVDWHFNVPFEVSMPIDDHSQHFHHAQI-----ITPTSNS--V-IHHPHSYPY 1174
Ce      -------------NAPE----FSENHSR-VSP---------------------------- 839
Dm      ----------------D----SLEDSSE-AAPA-LP----ATAPSLPPANGHA------- 968
Hs      ----------------D----IMESSPG-SSPPNLTPKPLRRQVTVAPASGLPHKEE--- 835
Mm      ----------------D----T-ESSPG-SSPPSLTPKLLRRQVTASPSSGLSHKEE--- 827

Fh      LCTAVGTAASSMSTV-LTQGTTRTVSQP-ALRLDAEAMDQFATLPPQDRIGRYLESLN-- 1205
Sm      LFQTTNTSTTRITTTTINTTTTHISSASSTQFNVNPLMEQFSTIPPHDRIGSYLKSLG-- 1232
Ce      -----------------------------------------VPVPPSRNAS------VSV 852
Dm      --------------------T------P----PAARLNPKASPIPPQQMIRSNSSGGVTM 998
Hs      ----------------AGKGS------A------LGTPAAAEPVTPTSKAGSGAPGGTSK 867
Mm      ----------------ATKGS------A----SGMGTPATAEPAPPSNKVG------LSK 855
                                                     *

Fh      ------E-------IGSE-LPSTTSTTTSAQAQTRFYLNHGAVEQQQ---LLLQQRQQQP 1248
Sm      ------E-------LDTG-CGRHHRCNE----PPTFTYHQSQPNELHLPTDILDVN-DKT 1273
Ce      RPDSKAEDSSDETTKDVGMWGPKHAVTRKIEIVKND--------S------YPNV--EGE 896
Dm      QNNAAASLNK--------L--QRHRTTTEGTMMTFSSFRAGGSSSSP-KRSASGV--ASG 1045
Hs      GPA---EESR--------V--RRHKH----------------SSESP-GRDK-------G 890
Mm      ASS---EEMR--------V--RRHKH----------------SSESP-GRDK-------G 878
              .                                     .

Fh      LSTNSLFFLQYPPPPPPPL---PVHTVPISLSPPYVPQDNEA----LFTA-N--PMTASY 1298
Sm      -FNHPSNVLHYPPPPPPVPP-PPHSSIMECCNPPSLPPTSTTNNASIQLSSD--VTSTGE 1329
Ce      -LKAKIRNLRHVPKE--------ESNT------------------SSQED----LPL--- 922
Dm      -VQPALANLEFPPPPLDLPPPPEEFE----GGPPPPPPAPESAVQAIQQHLHAQLPNNGN 1100
Hs      ----KLSRLKPA------PPPPPAASAGKAGGKPSQSPSQEAAGEAV------------- 927
Mm      ----RLAKLKPA------PPPPPACTG--KAGKPAQSPSQEAGEAGG------------- 913
                *.

Fh      LSE----------TQSASNL----RP-QNHE-----------------------LTARLE 1320
Sm      ISK----------SNISQPISPVLRS-KQYF-----------------------HSKAIT 1355
Ce      ---DATDNTN-----DSIIVIPRDEKAKVRQLVTQKVSPLQHHRPFSLQCPNNSTSSAIS 974
Dm      ISNGNGTNNNDSSHNDVSNIAPSVEEASSRFG-----VSLRKREPSTDCSSL------- 1148
Hs      ----LGAKTKATSLVDAVNSDA---------------------------AKP------- 948
Mm      ----PTKTKCTSLAMDAVNTDP---------------------------TKA------- 934

Fh      DSSH------G-------YL---------------------------------------- 1327
Sm      DSET------G---TNMDQP---------------------------------------- 1366
Ce      HSEHADSSETSSLSGVYEERMKPELPRKRSN------------------GDTKVVPVTWI 1016
Dm      ----------GSPPEDLKEKLITEI-------KAAGKDTAPASHLANGSGIAVVDPVSLL 1191
Hs      ----------SQPGEGLKKPVLPATPKPQS-AKPSGTPISPAPVP--------------- 982
Mm      ----------GPPGEGLRKPVPPSVPKPQSTAKPPGTPTSPVSTP--------------- 969
                  .

Fh      ----------------------------------------------------TRCN---- 1331
Sm      ----------------------------------------------------TNCFSSNN 1374
Ce      INGE------------------KEPNGMAR-----------------------------T 1029
Dm      VTELAESMNLPKPPPQQQQKLTNGNSTGSGFKAQLKKVEPKKMSAPMPKAEPANTIIDFK 1251
```

```
Hs      -------STLPSASS----ALAGDQPSSTAF----------------------IPLISTR 1009
Mm      -------STAPAPSP----LAGDQQPSSAAF----------------------IPLISTR 996


Fh      ------------NGINVGNTG------TGNCSSAKE-----SGSKYFRCSSNQPRQRRPL 1368
Sm      QNLSQLKASSEQNNIAVDESSLNHNNSNSNNSDIKDLH---SNTSYS--KISQPRRRIKV 1429
Ce      KSLRDITSKFEQLGTASTIESKI---EEAVPYREHAL-EKKGTSKRFSMLEGSNELKHVV 1085
Dm      AHLRRVDKEKEPATPAPAP-ATVAVANNANCNTTGTLNRKEDGSKKFSQAMQKTEIKIDV 1310
Hs      VSLRKTRQPPERIASGAITKGVVLDSTEALCLAIS---RNSE------------------ 1048
Mm      VSLRKTRQPPERIASGTITKGVVLDSTEALCLAIS---RNSE------------------ 1035
                            .       .

Fh      KN---------GQDSDGEGRRRESL-ERSGEESNTEEVTRSGE---EETLSLASESPSPN 1415
Sm      DTERAVSGNAGHLDYPGVGRRHLPLDDRSEEESNTEEVPRSLE---DETLSIASDSPNNS 1486
Ce      ----------------------------------------------------PPRKNRN- 1092
Dm      T-NSNVEADAGAAGEGDLGKRRSTDD---EEQSHTEGLGSGGQGSADMTQSLYEQKPQIQ 1366
Hs      -----------------------------QMASHSAVLEA-G------------------ 1060
Mm      -----------------------------QMASHSAVLEA-G------------------ 1047


Fh      GDDPVSTNRAIELNGTDLASEEHDTEADDVYQAPEACYSMIAASCGAGNTSAASIVHDGD 1475
Sm      QDNSMSIKPDADLSG--------GGEGDDVYQAPDSYYLPNINNSNSQNLQPN------S 1532
Ce      -------------------------------------------------QDESGSIDEEP 1103
Dm      QKPAVP----------------HKPTKLTIYATPIAKL-----------TEPASSASSTQ 1399
Hs      ------------------------------------------------------------ 1060
Mm      ------------------------------------------------------------ 1047


Fh      SLPKSLPSLITRLERLIDELVRLTQSV-SDNTVCDNNPELALLQVTDTLDAFRAEVEAYV 1534
Sm      TSQESITNL---LERTIE-LVNWTKDLCSYCEMEYEIPNASFIELSNCLDSFRIELEAYI 1588
Ce      VSKDMIVSLLKVIQKEFVNLFNLASSEI------TDEKLQQFVIMADNVQKLHSTCSVYA 1157
Dm      ISRESILELVGLLEGSLK-------HPV------NAIAGSQWLQLSDKLNILHNSCVIFA 1446
Hs      -------------------------------------------------KNLYTFCVSYV 1071
Mm      -------------------------------------------------KNLYTFCVSYV 1058
                                                         . :      :

Fh      VCRETNLDGLPTTVLHACDMLGRQTSLLAFEIGSADTSMTVDTGDSTTQRSRNPWSSLCT 1594
Sm      VEHISINPDLTKTILILCDNLGKQTTNLSLHLKTMEV-------------DKPAFSVHCN 1635
Ce      EQ---IS---PHSKFRFKELLS------QLEIYNRQIKFSHNP------RAKPVDDKLKM 1199
Dm      ENGA-MP---PHSKFQFRELVT------RVEAQSQHLRS-------AGSKNVQDNERLVA 1489
Hs      DS-I-QQ---MRNKFAFREAIN------KLENNLRELQICPAT-AGSGPAATQDFSKLLS 1119
Mm      DS-I-QQ---MRNKFAFREAIN------KLESNLRELQICPAT-ASSGPAATQDFSKLLS 1106
                    . :   : :        ..    .                   .

Fh      SILPALEDLLKNLVRLRGVESISSS---SEVSSNEKP----ESSNSNERPTAIAGPASDR 1647
Sm      SCHSCLKEIHEHIVQLLNKSKVTNAVSTITLTTGSTTSVTNQTHLHNDRSFSTTD-NTTT 1694
Ce      AFQDCFDQIMRLVDR--------------------------------------------- 1214
Dm      EVGQSLRQISNALNR--------------------------------------------- 1504
Hs      ----SVKEISDIVQR--------------------------------------------- 1130
Mm      ----SVKEISDIVRR--------------------------------------------- 1117
            .. ::   : :

Fh      RVCGSVVLGKV    1658
Sm      TTTTTHVFGKV    1705
Ce      -----------    1214
Dm      -----------    1504
Hs      -----------    1130
Mm      -----------    1117
```

ABL proto-oncogene 2, non-receptor tyrosine kinase (Abl2):

```
Fh      MPTKMVGIKHTLDSSINTIGKLKKEVTNQMTKRPGYCHVKHKTWFRKVCSRHLLSEGQRG 60
Dm      ------------------------------------------------------------ 0
Ce      ------------------------------------------------------------ 0
Sm      ------------------------------------------------------------ 0
Hs      ------------------------------------------------------------ 0
Mm      ------------------------------------------------------------ 0


Fh      SADPDPLGKTNYNFLVLECNQGDPTPTVLDQSSRAGSDRRPQIPYKMTMSDFVSGSINES 120
Dm      ------------------------------------------------------------ 0
Ce      ------------------------------------------------------------ 0
Sm      ------------------------------------------------------------ 0
Hs      ---------------------------MGQQVGRVGEAPGLQQPQPRGI----RG---SS 26
Mm      ---------------------------MGQQVGRVGEAPGLQQPQPRGI----RG---SS 26


Fh      NLPSNGRLRSATH-NACPIKGSIKRSPESGTEINSTNPGNNNASNQSQAAFIPPGA--QI 177
Dm      ----------------------------MGNCLTTQKGEPDKPA-----DRIKLDDPPTI 27
Ce      ----------------------------MGSCIGKEDPPPGATS--------PVHTSSTL 24
Sm      -------------------------------------MGAQHTK---E----RPR----R 12
Hs      AARPSGRRRDPAGRTTETGFNIFTQHE-------------------------ALH----R 57
Mm      AARPSGRRRDPAGRTADAGFNVFTQHDHFASCVEDGFEGDKTGGSSPE----VLH----R 78

                                                                SH3
Fh      LVDCGLA----TALPTSASFGHMSEVNLGTTSTGTTVTSTITATTSSANSSGSENLYVAL 233
Dm      GVGVGVP---QIPMPSHAGQ---PPEQI-----RPVPQIP-----ESETAGANAKIFVAL 71
Ce      ----G-----RESLPSHPRI---PS--I-----GPIAASSSGNTIDKNQNISQSANFVAL 65
Sm      TYHPKVDHELQINTSTSWIQNHNPPTNF----KGS-------VAHTSQINQPSDQLLIAL 61
Hs      PYGCDVE-PQALNEAIRWSSKEN----L----L--------------GATESDPNLFVAL 94
Mm      PFGCDAE-SQALNEAIRWSSKEN----L----L--------------GATESDPNLFVAL 115
                                   :                        .    :**
                                  SH3
Fh      HDYVKR----VDDDLNMTKGQTFRILDRS-HCDWWYAECTTTGQRGYVPKNHLARV---- 284
Dm      YDYDAR----TDEDLSFRKGEHLEILNDT-QGDWWLARSKKTRSEGYIPSNYVAKL---- 122
Ce      FQYDAR----TDDDLSFKKDDILEILNDT-QGDWWFARHKATGRTGYIPSNYVARE---- 116
Sm      FDFTPPNTLENQSQVRVEKGDRLQLFGYSADGDWSDVECIRTNERGWIPTNYTGRIPVPP 121
Hs      YDFVAS----GDNTLSITKGEKLRVLGYNQNGEWSEVRS--KNGQGWVPSNYITPV---- 144
Mm      YDFVAS----GDNTLSITKGEKLRVLGYNQNGEWSEVRS--KNGQGWVPSNYITPV---- 165
        .::        :. : . *.: :.::. . . :*  ..   .   *::*.*:
                                                          SH2
Fh      --------------------------------------TSLESNEWYFGELRRIEAEHYL 306
Dm      --------------------------------------KSIEAEPWYFRKIKRIEAEKKL 144
Ce      --------------------------------------KSIESQPWYFGKMRRIDAEKCL 138
Sm      NDHSTTLNTGSASGSSLTFQHTSSHDVSCNGSQGSLARVGLESEKWYHGAIQRSYAEYL- 180
Hs      --------------------------------------NSLEKHSWYHGPVSRSAAEYL- 165
Mm      --------------------------------------NSLEKHSWYHGPVSRSAAEYL- 186
                                               .:* . **.  : *  **
                                       SH2
Fh      QLPGNDHGSFLVRVSESQSSEYSLSVREEDTIKHYRIRSRSSRTNPDLKRFYISRQLPFV 366
Dm      LLPENEHGAFLIRDSESRHNDYSLSVRDGDTVKHYRIRQL------DEGGFFIARRTTFR 198
Ce      LHTLNEHGAFLVRDSESRQHDLSLSVRENDSVKHYRIRQL------DHGGYFIARRRPFA 192
Sm      -LNSGITGSFLIRESESHPGQLTISLRYEGQIWHYRIHRD------DSNMYYVIESNKFT 233
Hs      -LSSLINGSFLVRESESSPGQLSISLRYEGRVYHYRINTT------ADGKVYVTAESRFS 218
Mm      -LSSLINGSFLVRESESSPGQLSISLRYEGRVYHYRINTT------TDSKVYVTAESRFS 239
               *:**:* ***   : ::*:*  . : ****.             ::     *
              SH2                                           TyrKc
Fh      TIQQLVGHYTENQSGLCCRLSRPCIKPTHPEPVGLSHKLIDKWEISKSSIVLKERIGQGQ 426
Dm      TLQELVEHYSKDSDGLCVNLCKPCVQIEKPVTEGLSHRTRDQWEIDRTSLKFVRKLGSGQ 258
Ce      TLHDLIAHYQREADGLCVNLGAPCAKSEAPQTTTF--TYDDQWEVDRRSVRLIRQIGAGQ 250
Sm      SVSDLVHHHEKHSDGLACTLLYPAPKRDRTSSELRMDPSFDIREIDRTEIVMKHKLGSGQ 293
Hs      TLAELVHHHSTVADGLVTTLHYPAPKCNKPT-VYGVSPIHDKWEMERTDITMKHKLGGGQ 277
```

```
Mm              TLAELVHHHSTVADGLVTTLHYPAPKCNKPT-VYGVSPIHDKWEMERTDITMKHKLGGGQ 298
                :: :*: *:    .**   *  *. :              *  *:.: .: : .::* **
                                             TyrKc
Fh              FGEVYKAVWNK-TAIVAVKTLKPSSCDAADFLREAQIMKRLHHPNLIQLYAVCTQSEPFY 485
Dm              FGDVWEGLWNN-TTPVAIKTLKSGTMDPKDFLAEAQIMKKLRHTKLIQLYAVCTVEEPIY 317
Ce              FGEVWEGRWNV-NVPVAVKKLKAGTADPTDFLAEAQIMKKLRHPKLLSLYAVCTRDEPIL 309
Sm              YGVVYEAVWKPYNVLVAVKTLKENVTVRDEFLEEARLMKSLRHPNLVTLLGACTREPPYY 353
Hs              YGEVYVGVWKKYSLTVAVKTLKEDTMEVEEFLKEAAVMKEIKHPNLVQLLGVCTLEPPFY 337
Mm              YGEVYVGVWKKYSLTVAVKTLKEDTMEVEEFLKEAAVMKEIKHPNLVQLLGVCTLEPPFY 358
                :* *: . *:  .  **:*.** .     :** ** :** ::* :*: * ..** . *
                                             TyrKc
Fh              LVTEYMSKGSLLAYLQSPEGRG--LSIQCLVMMAAKIASGMAYLESRRHIHRDLAARNVL 543
Dm              IITELMKHGSLLEYLQAIAGKGRSLKMQTLIDMAAQIAAGMAYLESQNYIHRDLAARNVL 377
Ce              IVTELMQENLL----TFLQRRGRQCQMPQLVEISAQVAAGMAYLEEMNFIHRDLAARNIL 365
Sm              IVTEFMCNGNLLDYLRTHPRTE--LTPSVLLHMATQVARGMAYLEQHNFIHRDLAARNCL 411
Hs              IVTEYMPYGNLLDYLRECNREE--VTAVVLLYMATQISSAMEYLEKKNFIHRDLAARNCL 395
Mm              IVTEYMPYGNLLDYLRECSREE--VTAVVLLYMATQISSAMEYLEKKNFIHRDLAARNCL 416
                ::** *  . *                  *: :::::: .* ***. ..********* *
                                             TyrKc
Fh              VGEQHVVKIADFGLARM-IHNREYVAHAGARFPIKWTAPEAANYSRFTIKSDVWSFGILL 602
Dm              VGDGNIVKIADFGLARL-IKEDEYEARVGARFPIKWTAPEAANYSKFSIKSDVWSFGILL 436
Ce              INNSLSVKIADFGLARILMKENEYEARTGARFPIKWTAPEAANYNRFTTKSDVWSFGILL 425
Sm              VGTQHTIKVADFGLARCIERDLTYRAHEGAKFPIKWTAPEGLVYNLFSTKSDVWAFGILL 471
Hs              VGENHVVKVADFGLSRLMTG-DTYTAHAGAKFPIKWTAPESLAYNTFSIKSDVWAFGVLL 454
Mm              VGENHVVKVADFGLSRLMTG-DTYTAHAGAKFPIKWTAPESLAYNTFSIKSDVWAFGVLL 475
                :.    :*:*****:*       * *: **:*********.  *. *: *****:**:**
                                             TyrKc
Fh              TEIVTYGRSPYPGMHNAEVLRQVEAGYRMSKPSGCPPELYDLMLECWAADENRRPSFAEI 662
Dm              TELVTYGRIPYPGMTNAEVLTQVEHGYRMPQPPNCEPRLYEIMLECWHKDPMRRPTFETL 496
Ce              TEIVTFGRLPYPGMTNAEVLQQVDAGYRMPCPAGCPVTLYDIMQQCWRSDPDKRPTFETL 485
Sm              WEIATYGKTPYPGVELQDVYVLLERGTRMLCPEGCPEPVYELMLQCWQWLPEQRPPFSDI 531
Hs              WEIATYGMSPYPGIDLSQVYDLLEKGYRMEQPEGCPPKVYELMRACWKWSPADRPSFAET 514
Mm              WEIATYGMSPYPGIDLSQVYDLLEKGYRMEQPEGCPPKVYELMRACWKWSPADRPSFAET 535
                 *:.*:*  ****:   :*   :: * **  * .*   :*::*  **      ** *
                TyrKc
Fh              HTRLEEYCEDERPTYRNMGGTNLFAVTRGLRSPTT------------------------- 697
Dm              QWKLEDFYTSDQSDYKEAQAY--------------------------------------- 517
Ce              QWKLEDLFNLDSSEYKEASINF-------------------------------------- 507
Sm              LNQLESMPTNSTMEEEEEQIDFDITSTTSSSLLLNNNEIKVINSSESNRSIKHPPNIAY 591
Hs              HQAFETMFHDSSISEVLLHCAN---QTCITL----------------------------- 542
Mm              HQAFETMFHDSSISEEVAEELG---RTASSSSVV-----------------------PYL 569
                   :*     .

Fh              ---SVNPVPSSSGGSSNARYFQNMENLQISVSP--------------------------- 727
Dm              ------------------------------------------------------------ 517
Ce              ------------------------------------------------------------ 507
Sm              PRPPLPPRPPPPRRSTSCDYL-IDENDDNQFDMIKEDSKSDLGSDIPVNAMNNNKNNVSH 650
Hs              ------------------------------------------------------------ 542
Mm              PRLPLLPSKTRTLRKQG---E-NKENLDGGLDAAES----LASSSAPAGFIRSTQASS-- 619


Fh              ------------------------------------------------------------ 727
Dm              ------------------------------------------------------------ 517
Ce              ------------------------------------------------------------ 507
Sm              KSHRGIFTRSFKNPLSKQLHIGDLSTDEFGTAEKDLPFTNSGSLGRKRTAPRPPRRTTPV 710
Hs              ------------------------------------------------------------ 542
Mm              --GSPALPRKQRDKS-PSSLLEDAKETCFTRDRKG---GFFSSFMKKRNAPTPPKRSSSF 673


Fh              ------------------------------------------------------------ 727
Dm              ------------------------------------------------------------ 517
Ce              ------------------------------------------------------------ 507
Sm              KPLNFLTDFNLLEDNNCVCPNPYRDDFDHAPLPPPPVHLDSSHHQIHQTRSQ-QHPRPAP 769
```

```
Hs        ------------------------------------------------------------ 542
Mm        REMENQPHKKY-----ELTGLPEQDRMA-MTLP---RNCQRSKLQLERTVSTSSQPEENV 724

Fh        ------------------------------------------------------------ 727
Dm        ------------------------------------------------------------ 517
Ce        ------------------------------------------------------------ 507
Sm        QSNNGSLSNNSNSTPFSVPSVMSSSAIFPSSRQFSYVDPIPLDNSLTRSICPDRLISPLA 829
Hs        ------------------------------------------------------------ 542
Mm        DRANDMLPKKSEE------------GAAPA-RE------RPKAKLLPRG----ATALPLR 761

Fh        ------------------------------------------------------------ 727
Dm        ------------------------------------------------------------ 517
Ce        ------------------------------------------------------------ 507
Sm        PPTPSKHVQLSSKSPALSKSTVNSDLSNKTN-PVVDDCHNKRSMDSNFLNESYSGNNVSS 888
Hs        ------------------------------------------------------------ 542
Mm        APDPAIT---ESDSPGVGVAGVAAAPKGKERNGGTRLGVAGVPEDGEQLGWSSPAKAVAV 818

Fh        ------------------------------------------------------------ 727
Dm        ------------------------------------------------------------ 517
Ce        ------------------------------------------------------------ 507
Sm        KPNVHPTN----ISSSV---------FQE-ELRDRLKQHSQ-QLK-SSS--QQKPITPKT 930
Hs        ------------------------------------------------------------ 542
Mm        LPTTHNHKVPVLISPTLKHTPADVQLIGTDSQGNKFKLLSEHQVTSSGDKDRPRRVKPKC 878

Fh        ------------------------------------------------------------ 727
Dm        ------------------------------------------------------------ 517
Ce        ------------------------------------------------------------ 507
Sm        VPNNSPCN--VTNSVMCNQEKSDSKSSVSNSSPYFTIPRLRPPPRSANPPLISSNNTSGS 988
Hs        ------------------------------------------------------------ 542
Mm        APPPPPVMRLLQHPSTCSDPEEEPT----------------APPAGQHTPETQEGG-KKA 921

Fh        ------------------------------------------------------------ 727
Dm        ------------------------------------------------------------ 517
Ce        ------------------------------------------------------------ 507
Sm        SNNQMSTRGKV-----EPPHCSSELIRSLASTQIKNDNASNSTV-TTTSKLPTNINSNNN 1042
Hs        ------------------------------------------------------------ 542
Mm        APGPMPSSGKPGRPVMPPPQVP-LPTSSISPAKMANGTAGTKVALRKTKQAAEKISAD-- 978

Fh        ------------------------------------------------------------ 727
Dm        ------------------------------------------------------------ 517
Ce        ------------------------------------------------------------ 507
Sm        NSPKPHFKRSENEISDKLSDIIQKRLSWTGPTDDNSAGNQKRSQRLYLPTILSTSSTALD 1102
Hs        ------------------------------------------------------------ 542
Mm        ----KISKEALLECADLLSSAITEPV----P----------------------------- 1001

Fh        ------------------------------------------------------------ 727
Dm        ------------------------------------------------------------ 517
Ce        ------------------------------------------------------------ 507
Sm        ETNGNNHCVPPTKYHLKKHLSNILKELERLIRMNDKKIPGNITSSPSSAAISSSSSTSNL 1162
Hs        ------------------------------------------------------------ 542
Mm        -----------------------------------------------------------N 1002

Fh        ------------------------------------------------------------ 727
Dm        ------------------------------------------------------------ 517
Ce        ------------------------------------------------------------ 507
```

```
Sm        EQLIELADQMEACRLSCSAYIDQATCSARAKFNFRDRFSCLQTFSSLLRSKRLDSICNNN 1222
Hs        ------------------------------------------------------------ 542
Mm        SQLV---DTGHQLLDYCSGYVDSIP-QTRNKFAFREAVSKLELSLQELQVS---STA--- 1052


Fh        ------------------------------------------------------------ 727
Dm        ------------------------------------------------------------ 517
Ce        ------------------------------------------------------------ 507
Sm        TSNLSKYNKNNTNLLKDAENAIKEIINDLDKLTDNVNTTLTLETTLNNSNFPEHKPNSNL 1282
Hs        ------------------------------------------------------------ 542
Mm        -AGVPGTNP----VLNNLLSCVQEI-------SDVVQR---------------------- 1078


Fh        --------------------------    727
Dm        --------------------------    517
Ce        --------------------------    507
Sm        ATSNQSNLTCTENLSITDNRSATVFT    1308
Hs        --------------------------    542
Mm        --------------------------    1078
```

Rac-alpha serine/threonine-protein kinase (Akt1):

```
Ce        ------------------------------------------------------------ 0
Fh        ------------------------------------------------------------ 0
Sm        MEILCNYSQNPVVGSSKSSHTEHEPVSVSAKVQDTTASQRRNINCTSSNIFSSLQNAHLP 60
Hs        ------------------------------------------------------------ 0
Mm        ------------------------------------------------------------ 0
Dm        ------------------------------------------------------------ 0


Ce        -----------------------------MSMT-SLSTKSRRQEDVVIEGWLHKKGEHIR 30
Fh        ------------------------------------------------------------ 0
Sm        VVPNPNVLFKNELTENYSDNLTPRISPYLLGMLQCRPVSLPLTRNVVKEGWLMKRGEHIK 120
Hs        ----------------------------------------MSDVAIVKEGWLHKRGEYIK 20
Mm        ----------------------------------------MNDVAIVKEGWLHKRGEYIK 20
Dm        ----------------MSINTTFDL----SSPSVTSGHALTEQTQVVKEGWLMKRGEHIK 40


Ce        NWRPRYFMIFNDGALLGFRAKPKEGQP--FPEPLNDFMIKDAATMLFEKPRPNMFMVRCL 88
Fh        ------------------------------------------------------------ 0
Sm        NWRRRYFKLREDGTFYGYKIQPKDDMA----QPLNNFTVRDCQIICLNKPKPYTFLIRGL 176
Hs        TWRPRYFLLKNDGTFIGYKERPQDVDQ--REAPLNNFSVAQCQLMKTERPRPNTFIIRCL 78
Mm        TWRPRYFLLKNDGTFIGYKERPQDVDQ--RESPLNNFSVAQCQLMKTERPRPNTFIIRCL 78
Dm        NWRQRYFVLHSDGRLMGYRSKPADSASTPSDFLLNNFTVRGCQIMTVDRPKPFTFIIRGL 100


Ce        QWTTVIERTFYAESAEVRQRWIHAIESISKKYKGTNANPQEELMETNQQPKIDEDSEFAG 148
Fh        ------------------------------------------------------------ 0
Sm        QWTNVVERLFFVETEAERNYWLSAIQSVANRLKSSFEQPVSV---HN------------- 220
Hs        QWTTVIERTFHVETPEEREEWTTAIQTVADGLKKQEEEEMDF---RSGSP---------- 125
Mm        QWTTVIERTFHVETPEEREEWATAIQTVADGLKRQEEETMDF---RSGSP---------- 125
Dm        QWTTVIERTFAVESELERQQWTEAIRNVSSRLIDVGEVAMTP---SEQTDMTDVDM--AT 155

                                                                 S_TKc
Ce        AAHAIMGQPSSGHGDNCSIDFRASMISIADTSEAAKRDKITMEDFDFLKVLGKGTFGKVI 208
Fh        -----------------------------------------------MDTLPN-EIQVSI 12
Sm        ------------------LNLAENMI---VDIPQRPVKRYSVNDFRLLKVLGKGTFGKVI 259
Hs        ----------------SDNSGAEEM----EVSLAKPKHRVTMNEFEYLKLLGKGTFGKVI 165
Mm        ----------------SDNSGAEEM----EVSLAKPKHRVTMNEFEYLKLLGKGTFGKVI 165
Dm        ---------------IAEDELSEQFSVQGTTCNSSGVKKVTLENFEFLKVLGKGTFGKVI 200
                                                         :. * :  :   *
                                         S_TKc
```

```
Ce        LCKEKRTQKLYAIKILKKDVIIAREEVAHTLTENRVLQRCKHPFLTELKYSFQTNDRLCF 268
Fh        NILHKRKGTFFGIP------IVSKEEVEHTLTENRVLQQCRHPFMTQLRYSFTTPDRLCF 66
Sm        LCQENETGHFYAMKILKKSVLIEKEEVVHTMTENRVLQQCKHPFMTELRYSFTTPNYLCF 319
Hs        LVKEKATGRYYAMKILKKEVIVAKDEVAHTLTENRVLQNSRHPFLTALKYSFQTHDRLCF 225
Mm        LVKEKATGRYYAMKILKKEVIVAKDEVAHTLTENRVLQNSRHPFLTALKYSFQTHDRLCF 225
Dm        LCREKATAKLYAIKILKKEVIIQKDEVAHTLTESRVLKSTNHPFLISLKYSFQTNDRLCF 260
             .: .   :.:       :: ::** **:**.***:  .***:  *:*** * : ***
                                        S_TKc
```

```
Ce        VMEFAIGGDLYYHLNREVQMNKEGFSEPRARFYGSEIVLALGYLHAN-SIVYRDLKLENL 327
Fh        VMEYVNGGELYFHLSRER-----FFPEERTRFYAAEITLALGYLHSQ-NVVYRDLKLENL 120
Sm        VMEYVNGGELFFHLQRDR-----VFSEERAKFYGAEITLALGYLHHQ-NVVYRDLKLENL 373
Hs        VMEYANGGELFFHLSRER-----VFSEDRARFYGAEIVSALDYLHSEKNVVYRDLKLENL 280
Mm        VMEYANGGELFFHLSRER-----VFSEDRARFYGAEIVSALDYLHSEKNVVYRDLKLENL 280
Dm        VMQYVNGGELFWHLSHER-----IFTEDRTRFYGAEIISALGYLHSQ-GIIYRDLKLENL 314
          **::. **:*::**.::       * * *::**.:**  **.*** : .::*********
                                       S_TKc
```

```
Ce        LLDKDGHIKIADFGLCKEEISFGDKTSTFCGTPEYLAPEVLDDHDYGRCVDWWGVGVVMY 387
Fh        LLDKDGHIKIADFGLCKEEMYYGAFTKTFCGTPEYLAPEVLLDNDYGRAVDWWGLGVVMY 180
Sm        LLDKDGHIKIADFGLCKEDMYYGASTKTFCGTPEYLAPEVLLDNDYGRSVDWWGLGVVMY 433
Hs        MLDKDGHIKITDFGLCKEGIKDGATMKTFCGTPEYLAPEVLEDNDYGRAVDWWGLGVVMY 340
Mm        MLDKDGHIKITDFGLCKEGIKDGATMKTFCGTPEYLAPEVLEDNDYGRAVDWWGLGVVMY 340
Dm        LLDKDGHIKVADFGLCKEDITYGRTTKTFCGTPEYLAPEVLDDNDYGQAVDWWGTGVVMY 374
          :********::******* :  *   .************** *:***:.***** *****
                                          S_TKc
```

```
Ce        EMMCGRLPFYSKDHNKLFELIMAGDLRFPSKLSQEARTLLTGLLVKDPTQRLGGGPEDAL 447
Fh        EMMCGRLPFYSTEHEILFELILQENIEFPSRLSLEAQDILSELLIKDPAKRLGGGPSDAL 240
Sm        EMMCGRLPFYSSDHEVLFELILQENVSFPARLSHPAQDILSRLLIKDPTSRLGGGIQDVL 493
Hs        EMMCGRLPFYNQDHEKLFELILMEEIRFPRTLGPEAKSLLSGLLKKDPKQRLGGGSEDAK 400
Mm        EMMCGRLPFYNQDHEKLFELILMEEIRFPRTLGPEAKSLLSGLLKKDPTQRLGGGSEDAK 400
Dm        EMICGRLPFYNRDHDVLFTLILVEEVKFPRNITDEAKNLLAGLLAKDPKKRLGGGKDDVK 434
          **:*******. :*: ** **:  :: **  :   *: :*: ** *** .***** .*.
            S_TKc                          S_TK_X
```

```
Ce        EICRADFFRTVDWEATYRKEIEPPYKPNVQSETDTSYFDNEFTSQPVQLTPPSRSGALA- 506
Fh        EVMKHHFFFLLDWDRLVRKDILPPWKPDVTSPTDTKYIPEEFQCESIALTPPEKP--VTD 298
Sm        EVMAHLFFASVDWDRLIRKDIQPPWKPDVVDEKDTKYVPDEFKDTSVDLTPPNDNEDNMN 553
Hs        EIMQHRFFAGIVWQHVYEKKLSPPFKPQVTSETDTRYFDEEFTAQMITITPPDQDDS-ME 459
Mm        EIMQHRFFANIVWQDVYEKKLSPPFKPQVTSETDTRYFDEEFTAQMITITPPDQDDS-ME 459
Dm        EIQAHPFFASINWTDLVLKKIPPPFKPQVTSDTDTRYFDKEFTGESVELTPPDPTGP-LG 493
          *:    **  : *     *.: **:**:* . .** *. .**    : :***.
                S_TK_X
```

```
Ce        TVDEQEEMQSNFTQFSFHNVMGSINRIHEASEDNEDYDMG-     546
Fh        HI----LNGPYFEQFSFHGSRQSLSSHMSGFSFTDQF----     331
Sm        RI----VDGPYFEQFSFHGSRQSLNSRVSGYSFGDTF----     586
Hs        CVDS--ERRPHFPQFSYSASGTA------------------     480
Mm        CVDS--ERRPHFPQFSYSASGTA------------------     480
Dm        SIA----EEPLFPQFSYQGDMASTLGTSSHISTSTSLASMQ     530
           :         * ***:      :
```

Protein kinase C (Pkc):

```
                                                    PB1
Fh        ------------------MTVGNEEIPVKYIHNSIAMVTNLPSQADLKAMQSQVMELCQF 42
Sm        ------------------------------------MVTSCPLSANLQVIDQQVRELCSF 24
Ce        -------------MSSPTSLEEDGDIKLKTRFQGQVVVLYARPPLILDDFFALLKDACKQ 47
Dm        ------------------------------------------------------------ 0
Hs        MPTQRDSSTMSHTVAGGGSGDHSHQVRVKAYYRGDIMITHFEPSISFEGLCNEVRDMCSF 60
Mm        MPTQRDSSTMSHTVACGGGGDHSHQVRVKAYYRGDIMITHFEPSISFEGLCSEVRDMCSF 60
```

```
                                 PB1
Fh        SPDCRFTLKWIDEEQDPCVLSSDLELEEAVRLLHLNKECQLTVLVFDGIPLEPGKPCPGE 102
Sm        TKDQPFTIKWIDEEHDPIVISSEMELKEAFRLHEVNKEWQLTVHVFNGVPSEPGKPCPGE 84
Ce        HKKQDITVKWIDEDGDPISIDSQMELDEAVRCLNSSQEAELNIHVFVGKPELPGLPCQGE 107
```

```
Dm            --------------------------------------MGKLACLFPNVPQAPGLSCDGE 22
Hs            DNEQLFTMKWIDEEGDPCTVSSQLELEEAFRLYELNKDSELLIHVFPCVPERPGMPCPGE 120
Mm            DNEQPFTMKWIDEEGDPCTVSSQLELEEAFRLYELNKDSELLIHVFPCVPERPGMPCPGE 120
                                                          :*   *  **  * **

                                                       C1
Fh            DLSMYRRGAKRWKKKYYLLHGHKFAARRFNKNAECAYCHGRIWGLGQQGFKCITCRLLLH 162
Sm            DINMYRRGAKRWKKKFYLLHGHQFAARRFNRNAVCAYCKERIWGLGQQGFKCINCRLLLH 144
Ce            DKTVYRRGARRWKK-IYLYNGHRFQAKRLNRRIQCFICHDYIWGIGRQGFRCVDCRLCVH 166
Dm            DRSIYRRGARRWRK-LYRVNGHIFQAKRFNRRAFCAYCQDRIWGLGRQGFKCIQCKLLVH 81
Hs            DKSIYRRGARRWRK-LYCANGHTFQAKRFNRRAHCAICTDRIWGLGRQGYKCINCKLLVH 179
Mm            DKSIYRRGARRWRK-LYCANGHTFQAKRFNRRAHCAICTDRIWGLGRQGYKCINCKLLVH 179
              * .:*****:**:*  *  :** * *:*:*:.  *  *   ***:*:**::*: *:* :*

                  C1
Fh            RRCRGCVQHKCGEPLTIPGPLNPVTVGRVTPLSPETPNEFAYLNN-------N---ASAN 212
Sm            RRCQGGVRHKCGEAFIRPTYQNMRSISTFSTGS--TPTVWDNNGNRPTTIATNLSSETSN 202
Ce            KKCHRHVRTHCGQALQGPN-IIPMAPASGSLKGAR----------------SN------- 202
Dm            KKCHKLVQKHCTDQPEPLVKERAEE------SSD--PIP----------VPLP------- 116
Hs            KKCHKLVTIECGRHSLPQEPVMPMDQ--SSMHSDHAQTV----------IPYN------- 220
Mm            KKCHKLVTIECGRHSLPPEPMMPMDQ---TMHPDHTQTV----------IPYN------- 219
              ::*:  *  .*

Fh            SRPTSYQLSHAGV-ETPNHNSGASRLEIAYAQQSTFEEERNRPRTGIQNP-------AFV 264
Sm            TLPPRLPVTIQSYKDEPRPPKQEKIIALSERESNQTSDKHITPTSDIKNNLKPGSDNLII 262
Ce            ------TSSSTTR------------SGGG-IDNGAFHEHE------IE------------ 225
Dm            ------PLPYEAM------------SGGA-EACETHDHAH------IV------------ 139
Hs            ------PSSHESL------------DQVG-EEKEA------------------------- 236
Mm            ------PSSHESL------------DQVG-EEKEA------------------------- 235
                                          .

                                                                    S_TKc
Fh            DRR------KPRCTEISVPRPDVVIPILEERIAEMSVITTTSSSGQVGLQDFKLLKVIGR 318
Sm            ERSGVHPSSVPVPVSIIDKVDDKSIPIIEQRIIDIPDI--PITSGRVGLHDFNLLKVIGR 320
Ce            ---------SPGST---------------SHDASRAMNGNGSSKWAVSLNDFRLLTVIGR 261
Dm            ---------APPP---------------------PEDPLEPGTQRQYSLNDFELIRVIGR 169
Hs            ----------------------------------MNTRESGKASSSLGLQDFDLLRVIGR 262
Mm            ----------------------------------MNTRESGKASSSLGLQDFDLLRVIGR 261
                                                        :.   .*:** *: ****
                                             S_TKc
Fh            GSYAKVFQVEHIPTQRIYAMKVIKKETILDEEDIEWVQTEKHVFECATNHPFLVGLHSCF 378
Sm            GSYAKVFQVEHKPTNRIYAMKVIKKETILDEEDIDWVQTEKHVFECATNHPFLVGLHSCF 380
Ce            GSYAKVVQAEHVSTRQIYAIKIIKKEMFNEDEDIDWVQTEKSVFEAASNYPFLVGLHSCF 321
Dm            GSYAKVLMVELRRTRRIYAMKVIKKALVTDDEDIDWVQTEKHVFETASNHPFLVGLHSCF 229
Hs            GSYAKVLLVRLKKTDRIYAMKVVKKELVNDDEDIDWVQTEKHVFEQASNHPFLVGLHSCF 322
Mm            GSYAKVLLVRLKKTDRIYAMKVVKKELVNDDEDIDWVQTEKHVFEQASNHPFLVGLHSCF 321
              ******. ..   * :***:*::**  . ::***:****** *** *:*:**********
                                             S_TKc
Fh            QTDSRLFFVIEFVNGGDLMFYMQRNLRLAEDYARFYSAEICLALNFLHERGIIYRDLKLD 438
Sm            QTRSRLFFVIEFVNGGDLMFYMQRNLRLAEDYARFYAAEICIALNFLHERGIIYRDLKLD 440
Ce            QTESRLFFVIEFVPGGDLMFHMQQQRKLPEEHARFYSGEIILALHFLHSRGIIYRDLKLD 381
Dm            QTPSRLFFVIEFVRGGDLMYHMQRQRRLPEEHARFYAAEISLALNFLHEKGIIYRDLKLD 289
Hs            QTESRLFFVIEYVNGGDLMFHMQRQRKLPEEHARFYSAEISLALNYLHERGIIYRDLKLD 382
Mm            QTESRLFFVIEYVNGGDLMFHMQRQRKLPEEHARFYSAEISLALNYLHERGIIYRDLKLD 381
              ** ********:* *****::**:: :* *::****:.** :**::**.:**********
                                            S_TKc
Fh            NVLMDSEGHIKLTDYGMCKEGITADVMTSTFCGTPNYIAPEILRGENYNFSVDWWALGVL 498
Sm            NVLMDSEGHIKLTDYGMCKEGIIGDMTTTTFCGTPNYIAPEILKGESYSFSVDWWALGVL 500
Ce            NVLIDAEGHIKLTDYGMCKENIKDGDLTSTFCGTPNYIAPEILRGDEYGFSVDWWALGVL 441
Dm            NVLLDHEGHIKLTDYGMCKEGIRPGDTTSTFCGTPNYIAPEILRGEDYGFSVDWWALGVL 349
Hs            NVLLDSEGHIKLTDYGMCKEGLRPGDTTSTFCGTPNYIAPEILRGEDYGFSVDWWALGVL 442
Mm            NVLLDSEGHIKLTDYGMCKEGLRPGDTTSTFCGTPNYIAPEILRGEDYGFSVDWWALGVL 441
              ***:* **************.:  .  *:**************:*:.*.***********
                                            S_TKc
Fh            MFEMLAGRSPWENVGQSVNQDQNSEDYLFQVILTRPIRFPRSISVRATNILRAFLTKNPA 558
Sm            MFEMLAGRSPWEGVGQSANPDQNTEDYLFQIILSRPIRFPRSISVRATSILNAFLQKVPT 560
```

```
Ce      MFEMMAGRSPFDIVGMQ-NSEENTEDYLFQIILERQIRIPRSLSVRASGILKGFLNKDPT 500
Dm      LYEMLAGRSPFDLAGASENPDQNTEDYLFQVILEKTIRIPRSLSVRAASVLKGFLNKNPA 409
Hs      MFEMMAGRSPFDIVGSSDNPDQNTEDYLFQVILEKQIRIPRSLSVKAASVLKSFLNKDPK 502
Mm      MFEMMAGRSPFDIVGSSDNPDQNTEDYLFQVILEKQIRIPRSLSVKAASVLKSFLNKDPK 501
        ::**:*****:: .* . * ::*:******:** : **:***:**:*:.:*..** * * 
                 S_TKc                            S_TK_X

Fh      ERLGCLPD--SNFADIMNHSFFRP-VDWVALEQKQIAPPYRPTYANDYDLTHFDPTFTDE 615
Sm      ERLGCAPN--SSFGDIMEHGFFKP-IDWVALERKEVHPPYRPTCGGDRDLIHFDPAFTDE 617
Ce      ERLGCKLDINEGLRDMKEHQFFRGFIDWEALEQKAVAPPYHPAVESDRDLTHFDHQFTDE 560
Dm      DRLGCHRE--SAFMDIVSHPFFKN-MDWELLERKQVTPPFKPRLDSDRDLANFPPEFTGE 466
Hs      ERLGCHPQ--TGFADIQGHPFFRN-VDWDMMEQKQVVPPFKPNISGEFGLDNFDSQFTNE 559
Mm      ERLGCHPQ--TGFADIQGHPFFRN-VDWDMMEQKQVVPPFKPNISGEFGLDNFDSQFTNE 558
        :****  :    : *:  * **:  :**  :*:* : **::*   .: .* :*   **.*
                  S_TK_X

Fh      PVVFTPDNEEVVSKIDQTEFEGFEYVNPLLMTLEEPV 652
Sm      PVVLTPDNEAVMSRMDQTEFDGFEYVNPLLMSLDEQV 654
Ce      LPQLSPDNPDVIARIDQSEFDGFEYVNPLQMSREDSV 597
Dm      AVQLTPDDDHVIDNIDQSEFEGFEYVNPLLMSLEDCV 503
Hs      PVQLTPDDDDIVRKIDQSEFEGFEYINPLLMSAEECV 596
Mm      PVQLTPDDDDIVRKIDQSEFEGFEYINPLLMSAEECV 595
           ::**:  :: .:**:**:****:*** *: :: *
```

Polo-like kinase 1 (Plk1):

```
                                                              S_TKc
Ce      -----------------MQRVQPSAARVKSQKKEKAPPDVPDVILDGERKTRYEKGKFLG 43
Fh      ----------------------------MASKDAAKNKDPPEIIIDAKNKRKYTRGRFLG 32
Sm      ----------------------------MAANDSAKPKDPPEVIVDVTRKREFLRGRFLG 32
Dm      ----------------------------MAAKPEDKSTDIPDRLVDINQRKTYKRMRFFG 32
Hs      MSAAVTAGKLARAPADPGKAGVPGVAAPGAPAAAPPAKEIPEVLVDPRSRRRYVRGRFLG 60
Mm      MNAAAKAGKLARAPADLGKGGVPGDAVPGAPVAAPLAKEIPEVLVDPRSRRQYVRGRFLG 60
                                     :        : *: ::*   :  : : :*:*
                                      S_TKc
Ce      KGGFAHCYELRNKSTGELFAGKVVPKALLIKQYQRDKMAQEVQIHRNLQHRNVVKLYHFF 103
Fh      KGGFAKCYELVDQETNETFAGKVVPKAALTKASQKEKMQQEINIHRTLRHDNVVGFHGYF 92
Sm      KGGFAKCYELVDKKTGEKYAGKVINKSALVKESQKEKMRQEISIHRSLKHENVVRFYGNF 92
Dm      KGGFAKCYEIIDVETDDVFAGKIVSKKLMIKHNQKEKTAQEITIHRSLNHPNIVKFHNYF 92
Hs      KGGFAKCFEISDADTKEVFAGKIVPKSLLLKPHQREKMSMEISIHRSLAHQHVVGFHGFF 120
Mm      KGGFAKCFEISDADTKEVFAGKIVPKSLLLKPHQKEKMSMEISIHRSLAHQHVVGFHDFF 120
        *****:*:*: : .* : :***:: *  : *  *::*   *: ***.* * ::* ::  *
                                      S_TKc
Ce      EDKSNVYITLELCPRRSLMELHKRRKAVTEPEARYFTYQIVEGVLYLHNLKIVHRDLKLG 163
Fh      EDRDFIYIVLELCKRRSLLELHKRRRFISEPEARYFLRQIVHGCQYLHKNKIMHRDLKLA 152
Sm      EDSEFIYILLELCNRRSLLELHKRRKYVTEPEARYFMKQIVHGCQYLHQNKVMHRDLKLA 152
Dm      EDSQNIYIVLELCKKRSMMELHKRRKSITEFECRYYIYQIIQGVKYLHDNRIIHRDLKLG 152
Hs      EDNDFVFVVLELCRRRSLLELHKRRKALTEPEARYYLRQIVLGCQYLHRNRVIHRDLKLG 180
Mm      EDSDFVFVVLELCRRRSLLELHKRRKALTEPEARYYLRQIVLGCQYLHRNQVIHRDLKLG 180
        ** . ::: **** :**::******: ::* *.**:  **: *  ***  :::******.
                                     S_TKc
Ce      NLFLNDELQVKIGDFGLATTCD-NDERKKTLCGTPNYIAPEVLNKIGHSFEVDLWAIGCI 222
Fh      NLFLSDELIIKIGDFGLASRIVHEGEKKKTLCGTPNYIAPEVLTKGGHSFEVDCWSLGCI 212
Sm      NLFLDDNLKIKIGDFGLASRISHEGEKKKTLCGTPNYIAPEILSKGGHSFEVDSWSLGCI 212
Dm      NLFLNDLLHVKIGDFGLATRIEYEGERKKTLCGTPNYIAPEILTKKGHSFEVDIWSIGCV 212
Hs      NLFLNEDLEVKIGDFGLATKVEYDGERKKTLCGTPNYIAPEVLSKKGHSFEVDVWSIGCI 240
Mm      NLFLNEDLEVKIGDFGLATKVEYEGERKKTLCGTPNYIAPEVLSKKGHSFEVDVWSIGCI 240
        ****.: * :********:    :.*:**************:*.* ******* *::**:
                                    S_TKc
Ce      LYILLFGHPPFESKSLEETYSRIKNNNYVIPTSASAAASQLIRVLLDPVPSRRPNARAVC 282
Fh      LYTLLVGKPPFETSELEKTYTKIRHNEYQIPTRVSTSASKLIRALLHADPSKRPSMFTIL 272
Sm      LYTLLVGSPPFETTKLEETYARIKQNEYRIPIRVSTNASMLIRSLLHADPERRPNMFNVL 272
Dm      MYTLLVGQPPFETKTLKDTYSKIKKCEYRVPSYLRKPAADMVIAMLQPNPESRPAIGQLL 272
Hs      MYTLLVGKPPFETSCLKETYLRIKKNEYSIPKHINPVAASLIQKMLQTDPTARPTINELL 300
Mm      MYTLLVGKPPFETSCLKETYLRIKKNEYSIPKHINPVAASLIQKMLQTDPTARPTIHELL 300
```

```
        :* **.* ****:. *:.** :*:: :* :*      *: ::  :*.  *  **    :
         S_TKc
Ce      RDHFFKSGFMPARLPVSCLTMVPHLNDDEYAEENVS--PSGTIDQRGPHQA-GRSGLSAI 339
Fh      DDEFFK-DYTPNCLPVTALTTCPRFDVT--I--QSGRRPLSDINPLEDLPITSGGGTVQK 327
Sm      DHDFFK-DFTPNGLPVSCLSTCPRFDTMHRP--QTGRRPLSDINPVEDVPITSGGGALGN 329
Dm      NFEFLKGSKVPMFLPSSCLTMAPRIGSNDTIEDSMHRKPLMEMNGIRPD----DTRLEST 328
Hs      NDEFFTSGYIPARLPITCLTIPPRFSIAPSSLDPSNRKPLTVLNKGLENPLPERPREKEE 360
Mm      NDEFFTSGYIPARLPITCLTIPPRFSIAPSSLDPSSRKPLKVLNKGVENPLPDRPREKEE 360
          .*:. .  *  ** :.*:  *::.            *   ::

Ce      PAHLVSRNSERQQTHRMEAYRQPTDCYLSNLLAQVN------------DLLATPTADIDD 387
Fh      PS-----------AAPVD--AEPDDCWLLTLKEEVCLSLCLSNSVQIQTLLKEAEVLESN 374
Sm      VG-----------GAAVDKAVQPDDCWLGLLKHKLG------------RVLEEPKEFDDS 366
Dm      FLKA-NLHDAITASAQVCRHSEDYRSDIESLYQQLT------------NLI-N-GKPRIL 373
Hs      --------------PVVRETGEVVDCHLSDMLQQLH------------SVN-A-SKPSER 392
Mm      --------------PVVRETNEAIECHLSDLLQQLT------------SVN-A-SKPSER 392
                        :    :   . :  :  ::              :
                                                 POLO_box
Ce      AEAALDSYQSPEALPVFWISKWVDYSDKYGIGYQLCDNSVGVLFNDNSRIMLDTAGTQLT 447
Fh      TLLAMEESEHPASCPVYWVSKWVDYSDKYGLGYQLCDNSSGVVFNDVTRLLLAANLQNMQ 434
Sm      SPKAMEESEVPAACPIYWVSKWVDYSDKYGLGYQLCDNSYGVVFNDVTRLLLTTNEQNLQ 426
Dm      QGNLGDENTDPAAQPLFWISKWVDYSDKYGFGYQLCDEGIGVMFNDTTKLILLPNQINVH 433
Hs      GLVRQEEAEDPACIPIFWVSKWVDYSDKYGLGYQLCDNSVGVLFNDSTRLILYNDGDSLQ 452
Mm      GLVRQEEAEDPACIPIFWVSKWVDYSDKYGLGYQLCDNSVGVLFNDSTRLILYNDGDSLQ 452
             :.   * . *::*:***********:******:. **:*** ::::*     .:
                  POLO_box               POLO_box
Ce      YIEKTEKEHYFDMESAIPSGLQKKMTLLKYFRSYMNDHLLQAGQQVTRKVGDDLARLPTL 507
Fh      YIEANGKEHFYTKS-DHPESLMKKITLLNYFKQYMQENLL-------------------- 473
Sm      YIDEHGTERLFTLS-KHPEYLSKKVTLLTCFKAYMHQNLLKAGENIARPDTDAMTRLPFL 485
Dm      FIDKDGKETYMTTT-DYCKSLDKKMKLLSYFKRYMIEHLVKAGANNVNIESDQISRMPHL 492
Hs      YIERDGTESYLTVS-SHPNSLMKKITLLKYFRNYMSEHLLKAGANITPREGDELARLPYL 511
Mm      YIERDGTESYLTVS-SHPNSLMKKITLLNYFRNYMSEHLLKAGANITPREGDELARLPYL 511
        :*:   .*          . **:.**. *: ** ::*:
                                             POLO_box
Ce      RVWFRTKSAIVLHLSNGTVQINFFNDHIKMVLCPLMQAVTFIDENKRMFTYKFSHLAENG 567
Fh      -------------------KINFFEDHAKIILCPLMRAVTYIDSNREFKTYQFKLLSKGG 514
Sm      RRWFRTRSAIVLHLSNGTLQINFFDDHAKIILCPLMRAVTYIDANREFRTYRFKHLREFG 545
Dm      HSWFRTTCAVVMHLTNGSVQLNF-SDHMKLILCPRMSAITYMDQEKNFRTYRFSTIVENG 551
Hs      RTWFRTRSAIILHLSNGSVQINFFQDHTKLILCPLMAAVTYIDEKRDFRTYRLSLLEEYG 571
Mm      RTWFRTRSAIILHLSNGTVQINFFQDHTKLILCPLMAAVTYINEKRDFQTYRLSLLEEYG 571
                           ::** .** *::*** * *:*::: :: : **::. : : *
          POLO_box
Ce      CPEKFLHRIQYAKCMIQRLVEEHTKEETKHNAPAANAV-----RLPSTSSNVRLESAADI 622
Fh      ITQELVNRLNYAIVMIDTLLSPSQNSCPSK----KSAPPDSKSAVAPVSSAVRQATAAGS 570
Sm      LSKDLANRLRYAQEMIERLIPKCGTTSSNVNDPNTKMTVDNGKSNKPVSADVQKTNATGT 605
Dm      VSKDLYQKIRYAQEKLRKMLEKMFT----------------------------------- 576
Hs      CCKELASRLRYARTMVDKLLSSRSASNRLKAS---------------------------- 603
Mm      CCKELASRLRYARTMVDKLLSSRSASNRLKAS---------------------------- 603
          :.:  ::.**   :  ::

Ce      QPAYPSSSRR-----        632
Fh      AAAAKAIARLTKPEN        585
Sm      GAATKKITRPTNQ--        618
Dm      ---------------        576
Hs      ---------------        603
Mm      ---------------        603
```