```
                         10        20        30        40        50        60        70        80        90       100
                 ....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|
daphnia          ------------------------------------------------------------------------------------------------------
silkworm         ------------------------------------------------------------------------------------------------------
butterfly        ------------------------------------------------------------------------------------------------------
bee              ------------------------------------------------------------------------------------------------------
fly              ------------------------------------------------------------------------------------------------------
mansoni          ------------------------------------------------------------------------------------------------------
viverrini        ------------------------------------------------------------------------------------------------------
sinensis         ------------------------------------------------------------------------------------------------------
anemone          ------------------------------------------------------------------------------------------------------
Trichoplax       ------------------------------------------------------------------------------------------------------
urchin           ------------------------------------------------------------------------------------------------------
Saccoglossus     ------------------------------------------------------------------------------------------------------
ciona            ------------------------------------------------------------------------------------------------------
telata           MIHEWHVRQCKVIEKIIKYTLTEYLESNNRYPQNPFRVMTQFVYYASSWLGKLKNLRNICEIKSRLQITFNIHCTQKQVATNSQNLADDLIADIIVLINR
Medaka           ------------------------------------------------------------------------------------------------------
tilapia          ------------------------------------------------------------------------------------------------------
stickleback      ------------------------------------------------------------------------------------------------------
molly            ------------------------------------------------------------------------------------------------------
platyfish        ------------------------------------------------------------------------------------------------------
mouse            ------------------------------------------------------------------------------------------------------
human            ------------------------------------------------------------------------------------------------------
cat              ------------------------------------------------------------------------------------------------------
cattle           ------------------------------------------------------------------------------------------------------
python           ------------------------------------------------------------------------------------------------------
chick            ------------------------------------------------------------------------------------------------------
xenopus          ------------------------------------------------------------------------------------------------------
shark            ------------------------------------------------------------------------------------------------------
gar              ------------------------------------------------------------------------------------------------------
zebrafish        ------------------------------------------------------------------------------------------------------
tetra            ------------------------------------------------------------------------------------------------------
cavefish         ------------------------------------------------------------------------------------------------------
limpet           ------------------------------------------------------------------------------------------------------
oyster           ------------------------------------------------------------------------------------------------------
aplysia          ------------------------------------------------------------------------------------------------------
Clustal Consensus

                        110       120       130       140       150       160       170       180       190       200
                 ....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|
daphnia          --------------------MQ------NQLYLQ---VLRRSQSEGPHQR--AGGAGPGGAQGG----VAAC----------------------EPGPMA
silkworm         --------------------MERSILA-ESRHLR------WASELHSEYR-------STYRWHE----FKEQ----------------------QQGVVK
butterfly        ----------------MLVISLHQLL-HSEYRS---TYRWHEYKEQQQQ--QGVVKQPAPTPP----TALP----------------------IARGAI
bee              --------------------MPANKGN-LS------------------------TPHKEKSGNG----LTTG----------------------ASKKKK
fly              ------MIGSFWNLCRACPSMPVD-KL-HSEYRS---TYRWH--EFTGNS--RPEVVRRAPAPN-----PSQ----------------------FVGATN
mansoni          ---------MGKITEEPLFQKKRKFEL-TNEFNL---NTQFANPKEDDYFVIGPSDGKFSNSIA----YRNK----------------------MKRNAR
viverrini        --------------------MVQATD-ETLYQQGQGFNKSKEHSLGRYY--SDPNQDDYFIIG-----PTD----------------------KF----
sinensis         --------------------MVQTTE-KTLFQQRPHFNKENEHSLGGHY--SDPTQDDYFIIG-----PTD--------------------------KF
anemone          --------------------MHRKCQY-ESEYHA---NF----------------------------KPF----------------------EVQLNK
```

```
Trichoplax      --------------------MPVRFENQAANFQD--------------------RPTVEKSSTAG----IPSE----------------------ESSTAR
urchin          --------------------MPVRAKS-SSEYVK---KFRWNDSVKSASF--TPTKEQNAPQAGMSSVGHAD----------------------SFAITR
Saccoglossus    ------------------------------------------------------------------------------------------------
ciona           --------------------MPVKFRG-ASEYTS---TYKWSPSYRSAEF--QPTEQQLAVEAG----LRSD----------------------EMGLLM
telata          NSMIVETNLKDCHMLHIFTIAYCHTTG-RTEYNS---QF-----KRKQAS--KNSKNHTSRVAG----VASI----------------------DIGDIN
Medaka          --------------------MTVRFKS-QTEYQR---SF-----TLPRPS--GARALACDPAAH----PSSD----------------------PTRNTF
tilapia         --------------------MTVRFKS-QTEYQK---SF-----GVSRSR--SASPQRCMPLAG----LRSD----------------------QSGVSR
stickleback     --------------------MTARFKC-RSEYQK---SF-----RVPRST--SVCPQRGAPPAG----LRCD----------------------QMGICR
molly           --------------------MTVRFKS-QSEYQK---SY-----GVPRSR--SVSPQRCRPLAG----LRPD----------------------QNRISR
platyfish       --------------------MTVRFKS-QSEYQK---SY-----GVPRSR--SVSPQRCRPLAG----FRPD----------------------QNRISR
mouse           --------------------MPVRFKG-LSEYQR---NFLWKKSYLSESY--NPSVGQKYSWAG----LRSD----------------------QLGITK
human           --------------------MPVRFKG-LSEYQR---NFLWKKSYLSESC--NSSVGRKYPWAG----LRSD----------------------QLGITK
cat             --------------------MPVRFKG-LSEYQR---NFLWKKSYLSESY--NPSVGRRYPWAG----LRSD----------------------QLGITK
cattle          ------------------------LQG-LSEYQR---NFLWKKSYLSESC--NSSMGRRHPWAG----LRSD----------------------QLGITR
python          --------------------MPVRWKG-LSEYKR---NFKWRQSDQSRLC--SSTHEQKCRWAG----LRSD----------------------EFGISR
chick           --------------------MPVRFRG-LSEYKR---NFRW---KTPELC--SPSQEQKSPWAG----LRSD----------------------QLGITR
xenopus         --------------------MPVQFKG-LSEYDR---NYTWKNHEDLEQ------EPTCSRWAG----LRSD----------------------ELGISK
shark           ---------------------PVHFRG-LSEYKR---NFKWNDSKRSRSC--SPSPEQKALWAG----LPSE----------------------QLGNTR
gar             ------------------MKMPVRFKG-VTEYKK---RYGWKDSGSP------VSPDLRAPGAG----LRSD----------------------QLGITK
zebrafish       --------------------MPVRFKG-ISEYRS---KY---KGRTSRSR--SDSPHRRMRLAG----LRSD----------------------QSGITQ
tetra           --------------------M-------LCLYVF-------------------------------------------------------------
cavefish        --------------------MTVRFKG-ITEYQN---KY---KARARRVK--SAPPQRRMRLAG----VRSD----------------------QLGISR
limpet          -------------------MMPVRFKG-KSEYDT---HYKWVESYRGKNF--KPSLEQAAPQAGGTSEYKEQYKPFDNMLVEMNGKTHNTALDIPQQKGM
oyster          --------------------MFIQVQG-KSEYDR---NYKWLDSFKSKSF--TPTIEQIAPAAG----CESI----------------------ELGTVM
aplysia         --------------------MPVHFKG-ASEYKV---HYKWMDSFRSKSF--QPSQEQAARRAG----QISV----------------------NSSLTV
Clustal Consensus
```

```
                        210       220       230       240       250       260       270       280       290       300
                ....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|
daphnia         AWVHGRRRHV---------------------------TEQQRPEHWLVSA-------------------------------------------------
silkworm        QPAPTPPSALPIARGPIE-------------------PAIPRRKKYPGVA-----------------------YKTNELFDPVPADG-------------
butterfly       EPAMPRRKKYPGVA-----------------------YKTNELFDPAPAD-------------------------------------------------
bee             RCTVKHKRHCKQYLQLH--------------------SEYRSTYTWHEYT----------------------GPHQEQVVRRAPQPP-------------
fly             EPPLPRRKKCPEL------------------------AYKSHEFIIGSEY-------------------------------------------------
mansoni         SVSPKKKQENIGNG-----------------------LKQQSSAQINRQI-----------------------RKSSPILKPYRDEA-------------
viverrini       APSIAYRNRLKYRRRSASLRRQDSPGNPPN-------QQIPGNYLKKLKI-----------------------DRGNQKRHHKRENI-------------
sinensis        APSIAYRNRLKYRRRS---------------------ASLGRQDSLGHPS--------------------NQQGPGNNLKKLKIDHG-------------
anemone         EPKFSPAK-----------------------------PKVQET-----------------------------KVAETLHKSSHNTH-------------
Trichoplax      EPPLQRKKRVTIQH-----------------------PDSAGESLKYQEA-------------------------NNKINQARPYTA-------------
urchin          EPPLQRRRKPIQEDNKM--------------------TYTTKQFMAAGDS-----------------------EDSSDIGKPNKIPG-------------
Saccoglossus    ------------------------------------------------------------------------------------------------
ciona           EPTFTRKRRVMHRE-----------------------PEAQNCLQWWEEEQ----------------DLDAGEKKDFSEEVAGKTYVKKKTSVVPQGKE
telata          EPSFPSKKRDSHSPCNHSSAPGIVMEPPLQRKKKPVTPMTTSTTQWHEES-----------------------GRGSDYILLGNQ---------------
Medaka          SAGALRSSAHRKPN-----------------------KPPTGSA--GNPE-----------------------SLSEPEPPAGPRPP-------------
tilapia         EPGLQRLRRPLGPA-----------------------QSSTSLLHPPGDE-----------------------QQHSLAHRAAPSA--------------
stickleback     EPGLQRRKRLGPPG-----------------------PAESCSVLLCPPD-----------------------PRNSSAPPAATQSP-------------
molly           PPGLQRLKRPG--------------------------PPESGNFLPGSPA--------------------------DPVCRATPSTG-------------
platyfish       PLGLQPLKRPG--------------------------PAESGDFLPGSPA--------------------------APVCRTAPSTG-------------
mouse           EPGFISKRRVPYHD-----------------------PQISKYLEWNGTV-----------------------RKKDTLVPPEPQAF-------------
human           EPSFISKRRVPYHD-----------------------PQISKSLEWNGAI-----------------------SESNVVASPEPEAP-------------
cat             EPSFISKRRVPYHD-----------------------PQISKSLEWNGAI-----------------------SENDMVSPKPEAA-------------
```

```
cattle          EPSFISKRRVPHHD-----------------------PQISKSLEWNAAT-----------------------SENDVVLSPETEAP-------------
python          EPNFISKRRVPYYD-----------------------TQISKSFEWNGDN-----------------------GLEKEALSELEVSEP-------------
chick           EPNFISKRRVPYHN-----------------------PQISKSFEWTGDC-----------------------DSDDPVETEALKTA-------------
xenopus         EPRFPSKRRVPYYK-----------------------AQISKSFQWKEPR-----------------------DNGYNISESIMEEP-------------
shark           EPSFISKKRVPYYR-----------------------PQVSKSFQWDWNS-----------------------NSGQDLQEPKPKES-------------
gar             EPSFTSKKRVPFYR-----------------------PLISRSFQWEQGD-----------------------GSERSQPAAAEERP-------------
zebrafish       EPQFISKRRVPFYP-----------------------SQVSSSFRWEGRD-----------------------HSQQQLEKSRSPAV-------------
tetra           ------------------------------PQ-----------------------------------------------------------------
cavefish        EPQFQSKRRVPFYP-----------------------PQVSSSLQWRDSA-----------------------------------------------------
limpet          EPSIQQKKRVEGPTTSMSCDFFQR-------------PPPEEYIVLGGQDKFSTNNVKYVPKKRLVMDNVNRSEANSHFIQPQPDEPIRSMDFHLKK---
oyster          EPPLQRKKRCTGPP-----------------------TTLSTDFNQFPDA-----------------------ASDDFALLGRNDKFMENVRYKAKSHHT
aplysia         EPPLQHKKRLEGPPTSLSTNYFSV-------------PSKEMDYALLGQQ-----------------------EKFAPNVRYQPKPS-------------
Clustal Consensus

                        310       320       330       340       350       360       370       380       390       400
                ....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|
daphnia         ---------------------------------------------SAAAVGSSSG-------------------------------------------
silkworm        ---------------------------------------------IRPQGSAADRARSAQRNDADR-------------------------------
butterfly       -------------------------------------DIRPQ--QASAFERARS-AQRNDSER-----------------------------------
bee             ---------------------------------------------PTSTKQASAK-LQSAKSTEDENN-----------EGPTLEPP-------------
fly             -------------------------------------TDGRR--DASAHRLARS-EERGGT-------------------------------------
mansoni         --------------------IQTDGAHKALEEEIRRIRTEIENRKRILRAREEAKENKKHVKIENEIK-----------QKPHTK---------------
viverrini       --------------------QTEGPRKLLEEEIRRIRAELEQ--RKHRLKNVET-TSQPLPQNSQPH-----------ESGELKLKL-------------
sinensis        -----------NQRHYKRESTQTESPHKVLEEEIRRIRAELEQ--RKHSLKNVET-TSQSLPQNNEPY-----------ESGELKLNL-------------
anemone         ------------------------------------------------------------------------------------------------------
Trichoplax      ------------------------------------------------------------------------------------------------------
urchin          ---------------------SSLSKTFLKKVDMPAKTRPPID--KTLKTEKNKA-LAAQTRVISKPS----------QPPPPPKKVA-------------
Saccoglossus    ------------------------------------------------------------------------------------------------------
ciona           KIMNGVGNKTYAKK-------TKDSSPGRDEIKRSLVERVDAK--LDATKRIKKV-AKQDKQVSENNQTNKKTIREFSKPQPRPEVQHSLTRKHSP----
telata          ---------------------GKFASNVQYNPKRAWKKKEPVK--ESSPRSKPAV-PSAAPDKATPTS-----------PPPAPRLIAPAPKVVVDTGAP
Medaka          ---------------------A----------------D----------PCPPKR-PGLEPSV----------------RPAAVGESD-------------
tilapia         ---------------------------------------------DCQVLGATQ--PTGGCPPQSPIH-------------------------------
stickleback     ---------------------SAHGKKTALEP-------------NPPTPPGPRADPGLGTQGAGPAA-----------DPGSVEPGAAGKSA-------
molly           -------------------------------------RKDSPVSKPPNVSGSEPEPGFRPAADGKSV-------------------------------
platyfish       -------------------------------------RKDSPVSKSPNVSGSEPEPGSRPVADGTSV-------------------------------
mouse           ---------------------GTPKPQEAEQGE-----DANQE--AVLSLEASRV-PKRTRSHSADSR-----------AEGVSDTVE-------------
human           --------------------------ETPKSQEAEQKDVIQE--RVHSLEASRV-PKRTRSHSADSR-----------AEGASDV---------------
cat             --------------------------ETELQEAEQKEDVNQE--RVLALEASRV-PKRTRSHSTDSR-----------AEGASDIVE-------------
cattle          --------------------------RTPESQEAEQTDVNQE--RLLAVEASRG-PKRTRSHSADSR-----------SEGASDIVE-------------
python          ----------------------------IELHRNGSKDVEMNQEPTETPDAPRV-PEKVHLNSSGSR-----------PESTVAL---------------
chick           -----------------------------ESLAEHSNDVNQE--NTETPEGPRL-PPKVRSHSSDSG-----------VETALALAG-------------
xenopus         ---------------------------------VQLRLDLDRESLAEEKLHTPDA-PRLSEKANNYAV-----------SSKMVKDVG-------------
shark           ---------------------QPVKSQTSVLSE-----GMNAE--DCKTPEAPRS-LRFGRSRSMDCR-----------LHSALEPPM-------------
gar             ----------------------------------------LSPE--RTETPPAPRV-PRLPRSPSEDLN-----------PQPFPVANG-------------
zebrafish       ---------------------------------SPVLRATSAE--RQVTPLAPRDPPEG-----------------------------------------
tetra           ------------------------------------------------------------------------------------------------------
cavefish        ------------------------------------------------------------------GSLR-------------------------------
limpet          ---------------------DKEIQVETLKPAKSPPKVNTRQFTDPLTPLAPRE-PKYPTETHATQT-----------LNQEPQLQHKQKSHLNKNGLE
oyster          APAREASPPKQQRLQEKENRRKAPKPTPAPFVDTTKFRQQSKS--EEQQPSTPLT-PRKEKNESSSLY-----------KEIALREKEAALRQKFSKLDR
aplysia         ------------HSGQKIYKNKENFDNAPPPSKQLKMQKRIKPLFKERHPTVSRSPPRQAPTTSTILS-----------PPPAPRVPKESLDIKEALRDK
Clustal Consensus
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```
                          410       420       430       440       450       460       470       480       490       500
                 ....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|
daphnia          -LAAENRAGAPPGSFSQQQ-------------------------------------------------------------QEQQQHNQKRVVVLAGETTANKRT
silkworm         -AGRRSKSEGPRQPRWTDTVE-----------------------------------------------------------PKATTALGEVVVAKEPDMVS----
butterfly        -AGRRSKSEGPRQPRWTDTVE-----------------------------------------------------------PKATTALGEVLAAKEPETVS----
bee              -LPRRKKCPELAYKTHEFITAADGGGIDAVD-------------------------------------------------SNVVADKVREVTTQSGLPPSQLSK
fly              -PSRRSKSEGPPVVPNGRA-------------------------------------------------------------YPIATEIDGTTRKQAGESNGLLKK
mansoni          -TPKPIESDYPMVTRAPDATRQHKSN------------------------------------------------------KMPLQEYSENWKLEPPKAAV-YTC
viverrini        -GDSPVVTGSHKTPQAPRAVRKKGTLE-----------------------------------------------------YIVAPNIENKRRRKSYSPLAQPRL
sinensis         -KDSPVVPGSHKTPQAPRAVRKKGTLE-----------------------------------------------------YIVAPNIENKRRRRSSSPFAQPRL
anemone          ---------------------------------------------------------------------------------NHEDDKENRALEYKAGLAPAMPRT
Trichoplax       -------PDDTPQSLVQEVRQKAAI-------------------------------------------------------KDEDKIGSKALQYKAGLRPTNPPR
urchin           -PPSPIRAAKGPAITKTGKHVPKAGGDASKTK------------------------------------------------GKAEQETDEALQYRAGIKAR-P-G
Saccoglossus     ---------------------------------------------------------------------------------
ciona            -KRKSIQEQSGPVSPTKSIKSPKSSP------------------------------------------------------KKETKSKNIPLRYR---SLN-SRL
telata           KKTRPVKPTSPPAKKTKVVAIETKAPEEAKKLKESVNLSKMEAKKENDARRVYEVQLAKEEDLIRRQVEKEREIEQKKKALKGNYAMKYRSGVAPP-RSR
Medaka           -KPHPFRGHSQPQPSSPVPAAAANELQP----------------------------------------------------PPPAMKADHVTRRRAGSKAP-GHG
tilapia          -QHPPEEIPDPPQSRKLQPDHDLLRNR-----------------------------------------------------QLMENLIDYALRQKAGLRSG-GQR
stickleback      -KPRPSKLDSRPQPSQPLTSAP----------------------------------------------------------DGRANEVQRALRWRVGLK---GQR
molly            -KLRPSEPGGPAEPE-----------------------------------------------------------------QQPGNQVDKAWGQR----------
platyfish        -KLRPFEPGGPAEPE-----------------------------------------------------------------QQPGNQVGKAWGQR----------
mouse            -KHQGVTRSHAPVSADVELRPSSKQPLS----------------------------------------------------QSIDPRLDRHLRKKAGLAVV-PTN
human            -ENNEGVTNHTPVNENVELEHSTKVLS-----------------------------------------------------ENVDNGLDRLLRKKAGLTVV-PSY
cat              -NNEDVIEGHIPVNENEELEHSTKLLS-----------------------------------------------------ENVDNGLNRVLRKKAGLTVV-PSH
cattle           -NKEDIKANDIPANENVELKHSTKPLS-----------------------------------------------------ENVDDRLNRLLQKKAGLTVV-PSH
python           -GRSKKSVSQTPVHENKVLASTKKDL------------------------------------------------------GKTDHGLNRVLQRRAGMNIS-QSR
chick            -NSMKKTPPVAPPNQKEAFVSPKKEA------------------------------------------------------EKVNNGLHRVLQRKGGMNTP-HLS
xenopus          -STVKKTAIEAPEDNRETVAPSKKVNS-----------------------------------------------------QAKANGVHRVLKKKAGLSTA-PLQ
shark            -AGDKPQVAEAQKSKKDNNTPPKKEGAD----------------------------------------------------EGIANGVSVVLQKKSGLKTA-PRK
gar              -KNLPSSDPDKHCPTRTAAAAERS--------------------------------------------------------DAGLDGVHRVMQKKAGLKST-VRR
zebrafish        -TTAPSQPPQAEAAQTSTFAVQKQ--------------------------------------------------------KQALNGINHALRMKAGLRSE-HQR
tetra            ---------------------------------------------------------------------------------LNYALRKKAGLRTA-RQR
cavefish         -QQEIARPGSPPASVHVTRTS-----------------------------------------------------------
limpet           KSSSHHDTHHAHQQNQERQNIPKTHKTKMAARKNPEEIRYKAGLKDKNIQDVLENKKFPNKMNEFTQANIKKGILDSAPEATADYSLQYKAGVA---PLR
oyster           EGGRKTAPSALRQSKEQYSKTIDDNRME-------------------SAVKSWVKDKNVGSMNEFAQTNLDKGIADSAPEAPADYALRYKTGVSVPRPRR
aplysia          -DLKDVLGDQAPPPKEAGVKTRESDAQL--------------------------EKGRGNNMNEFVQTNMKKGVALSGPEAPAEYALKYKAGVAPPRPVK
Clustal Consensus
```

```
                          510       520       530       540       550       560       570       580       590       600
                 ....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|
daphnia          ISTTGSSEYQLQFAW-----------------------------------PPS---GV--KNISNTSSAFSN-----------------------------
silkworm         ------TEYRNQFAWPKD--------------------DT--------TPR-------KSISMGALKKAA-----------------------------
butterfly        ------TEYRNQFAWPKD--------------------EV--------VPR-------KSISMGALKKAA-----------------------------
bee              AISRISTEYRLQFAWPRR------PQLTNGETVAPGVTAAGLPAGTTGPPR-------KSLSMGALKQGI-----------------------------
fly              TINKLSTEYRLQFVWPTV-----RRIKGGGEATSRAAAGD--------YPR-------KSISLGALRSG-----------------------------
mansoni          EKSRL-SEYQSAFKAPQF-----NYKLEPTKSTRPFTCKL--------DKF---QS--CKISYDTEYRHE-----------------------------
viverrini        ------TEYQRAYKAPELTPIPQRPRTAQSE--FPTTFKA--------SSH---HG--QIDIFETEYARE-----------------------------
sinensis         ------TEYQRAYKAPEITSVPQRPKTAQSE--FQTAFKA--------RSY---HG--QIDSFETEYARE-----------------------------
anemone          KKQRYVSEYQKQFYWKKP-VGREAPILSAEKVVFSSQDNL--------PPA---KPVKISMPTKSEYQLQ-----------------------------
Trichoplax       LAYGK-SEYQRQYDWKKL-PERASPIIAADNTIFKSSTDI--------APVKVDMG--PRPNVKSEYQRQ-----------------------------
```

```
urchin            GPRYS-SEYQRQFAWKQP--SKESPLMAAEQMVHTSNANL--------APY---VP--DKIPRHTEYQRQ------------------------------
Saccoglossus      -------------------------------MIYNSN-AI--------QTY---MP--KNVPSKSEYDAQ------------------------------
ciona             MSAHQ-TEYQQMFRQPAR-FVPSSPLISALDVVHQSSAAI--------PPHVINKS--PKMRLTTEYSSK------------------------------
telata            GPKRL-SEYQLQFKWMKG--VANSPLLAADQVVHKSNTQI--------GPY---KT--ETANKKSEYATQ------------------------------
Medaka            SGRQ------------KP-LMAASPLLTAEQVLYAGSRGI--------TPY---RM--KPVSMETEYRRN------------------------------
tilapia           SGGKH-SEYHRQFGWKKPTAAAASPILTAEQVLHSSSRSV--------PPF---KI--NPVSMETEYQRS------------------------------
stickleback       SGIQR-TEYHRQFSWKKP-ATAASPILAAEQLLYSGSRCV--------PPF---KK--HPIPLETEYRRS------------------------------
molly             ------SEYHRQFGWKKP-VSAASPLLTAEQVLHSTSRSI--------PPF---KN--IPVPMETEYRRS------------------------------
platyfish         ------SEYHRQFGWKKP-VTAASPLLTAEQVLHSSSRSI--------PPF---KK--NPVPMETEYRRS------------------------------
mouse             NALRN-SEYQRQFVWKTS--KESAPVFASNQVFRNKSQII--------PQF---QG--NTFTHETEYKRN------------------------------
human             NALRN-SEYQRQFVWKTS--KETAPAFAANQVFHNKSQFV--------PPF---KG--NSVIHETEYKRN------------------------------
cat               DILRN-SEYQRQFVWKTP--KEAAPVFTANQVFHNKSKFV--------PQF---KG--NSIIHETEYRRN------------------------------
cattle            NVLRN-SEYQRQFVWKTP--KQPAPAFAANQVFHNKSKFI--------PQF---KG--NSFIHETEYKRN------------------------------
python            SFPRS-SEYQRQFVWKTP--QKLSPVLAADQFIHSSSQSI--------PPF---KS--PVIIPETEYERN------------------------------
chick             TFPRN-SEYQSQFVWKSP--HEKSPILAAEEALYNVSKPV--------PPL---KS--PAITSETENVRN------------------------------
xenopus           HPLKM-SEYRRQFERKTP--TENSPMLAAEQVIYNKNKSI--------PPF---NV--DALKTETEYKSR------------------------------
shark             NLARS-SEYQRQFSWKTQ--MENSPLLVADQVIHNRNQEI--------PPF---KS--GKVCRETEYSSQ------------------------------
gar               SAAQN-SEYQRQFSWKTA--PVSSPLLAAEQVIYNRNRDV--------PPF---KS--DAVVLESEYKKN------------------------------
zebrafish         NGLN--SEYQRQFMWKTP--VAESPLLAAHQMLYSNNRAI--------PPF---KT--NPVIMESEYKRS------------------------------
tetra             NGRQS-SEYQRQFLWKTP--ANESPLLAAQQMLYTSNRSI--------PPF---KF--NPVEIETEYKRN------------------------------
cavefish          ------------------------------------------------------------SPEKVETPLAPRTSKPQRAKKTSQHVESVSCSQVRSPSADQQ
limpet            KGRKW-SEYQKEFDWKNR--VESSPLIAADQVVHKSNTVL--------VAP---KQ--IPKPRASEYKSQ------------------------------
oyster            HKF---SEYQKSFSWKDG--AKASPVLAAEQVVYNSNPAL--------VP----PQ--KSFVKDSEYAAQ------------------------------
aplysia           KF----SEYQRQFQWKDG--MKASPLLAAEEIVYKSNAEL--------GPY---KT--DAIPKLSEYRQQ------------------------------
Clustal Consensus                                                                          :

                          610       620       630       640       650       660       670       680       690       700
                  ....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|
daphnia           ------------SRRMP--ESLDSLLNH---SQDGEREAAGLLSSRINNGTGTTTRSQEMVY-----------------------HAAEELLLNHQQQQQ
silkworm          ------------AAEGS--VEVEPLMNH----VDGDHDEGHKRYIEDYLWNGQKPGVQRKST---------------------------FRNALSA-LI
butterfly         ------------VAEGL--VEAEPLMNH----VDGDHEDGPKRYIEDYLWNGQKPGVQRKST---------------------------FRSALSA-LI
bee               -------------------APTGPAPVHKKRPGDVDHKRDGMQASE-LEPLVGGTGTDTIDG------------------------VVPEGDEREEDMSD
fly               ---------------GQ--GHCHSHTQN-----QNQSQSQGLTQAQNGHTHHTMMGGGAGLP---------------TVHKKRTTNQKEATLHELEP-LV
mansoni           ------------YKPFK--YVPIDQLKS----------SEVIENKDVHIIPLKRPSSAYGIR-----------------EITMNNINDTEKRRIRALTPP
viverrini         ------------YKPFR--YVPIDKLNA----------TTFIRDPNVNIVPIPRPKSAYTLV----------------RSQQIKDTENGYPRSRQETSSQ
sinensis          ------------YMPFR--YVPIDKLNA----------TTFIRDPNVNIVPIPRPKSAYTLV----------------RAQQPEDKANDYPRIRPET-SH
anemone           ------------FVKYP--LVTTLR--------DDECAGSQGKEKEAGANKKAELQPPAGVA---------------------------SSPDKQQTPL
Trichoplax        ------------YQDWR--QSMQQSTKP-----AAQDQSSRLARPSRSIDERSESSLDTTKSILDGDYYNKKEKSEDIKASGYKDKISDYMERLEQS-EN
urchin            ------------FKQQN---HGGPLVQD-----QLMQNAQQEIKAKYRVKTKSKRGKKLTPD-------------KQQPAGVLSVISHDDPRLVKSS-QN
Saccoglossus      ------------FQAWN--ESRPSQVEM------LKEHAKRDAELEVKQKKKSSKGKRRKSG-------SKKEVVTPDQMPAAGVPTFHLPEQLKNA-QN
ciona             ------------YQNRS--PL-----------------------SKSMTLPTSPASPSLKMK--------------------------------VK-NL
telata            ------------FKQYQ--PVQSAEPAR-----KPAKVKRSRSLEAVVSPDHLPPAGLNRVT------------------------ADFDPRLVQESLN
Medaka            ------------FRGLI--PPTGPRLRN-----YLDHELE----PLFHSYEVNRRTREEEPA------------------------SKLRLKHDSHPEE
tilapia           ------------FQGLA--PPAGPRLRK-----HLEHQRV----PLFQTYKETRRERRDEEE--------------TTRRRKEESQKKPRLQRDALQ-RD
stickleback       ------------FRGQV--PSPGPRLRE-----HLEHHQRA---PLFHVHTTNKKKREESVK--------------------------KTRPRQDN-VT
molly             ------------FQGLV--PPSGPRLRR-----NLGH-------PVFHTYRTHRRKSLDAQS-----------------------NELPVKQETGSQL
platyfish         ------------FQGLA--PPSSLRLRR-----NLGH-------PVFHTYRTHRRKSLDGQN--------------------NKLPVKQETTQGDGGSRL
mouse             ------------FKGLT--PVKEPKSRE-----YLKGNSS----LEMLTPVKKADEPLDLEV-----------------------DMASEDSDQ-SV
human             ------------FKGLS--PVKEPKLRN-----DLRENRN----LETVSPERKSNKIDDRLK-----------------------LEAEMELKDLHQ-PK
cat               ------------FKGLS--PVKEPKLRN-----DLKENGN----FETVSPEKKCNKTDDPLK-----------------------LEAEMESKESNQ-PK
cattle            ------------FKGLS--PVKEPKLRS-----HLKENGN----FETISPEKKCNKTDDPLK-----------------------SEAEMESKDSNQ-PK
```

```
python          ------------FKPSS--PIKELKQTS-----FLEESEC----PRSESVEVSSGEKNEKNK--------------TTKAIEDSSNQIKLETKQKEE-KL
chick           ------------LKGSP--AAKGPQEKC-------SEEKEFLVHEQTKREELIQKPAEDASK---------------------QEKSEQKHPKRKNKQHI
xenopus         ------------FKGSP--PAKGPVLRK-----DWEEKHVPKYEPEDPSIKRKEKRIQINEA-----------ICSPPKNDKSETEAKQRIHARKHKEKV
shark           ------------FQGTP--LPKGPRFRK-----DFEEKEALFFEPENDSPPKQTPSSSKQVG----------------------ARIKEQESEQLLKQQN
gar             ------------FKGLV--LPKGPRLRR-----DVEEREAVLYEPENISPDKTPKSKKNKKG----------GSTKHNNTSSVPHPRRERERQVSRK-QN
zebrafish       ------------FKGSP--LPRPPRLRR-----DVEQYEVPEFLTESKTPEKSKRKKKKKER--------------PHSRKSSPEQEVAYLQQQEVK-SP
tetra           ------------FKGSP--PHRPPRLRR-----DVELNEL----PENISSDKQEREKKREQR--------------LSRKPRSREDSHPEPQPVQQE-VI
cavefish        EQEHPSNGIPFCYESNN--QIKSNQIYLYSAFYNWCWHKAALQKLNKGIESIPEPSCFEKLG---------VRNNYDKMKPRSREDSHPEPQPVQQE-VI
limpet          ------------FKAWK--VKPVPVGRK-----DVNEE------PEIKKAKIKRNKSMGAID--------------------------RKVQVDKENIEA
oyster          ------------FKQYNAMPVSSDDLKA---IPRAEKPRSKVKRSKSTGALRVDKRPAAGSG--------------PLITPDNKRQTIESELQGEPQ-DA
aplysia         ------------FQKWKA-PDFAADVNL-----NVSEKMATAASQQKQEKKRTVAKRSKSAG------------AVLHQEPEEVDDEMGAEGADSEE-QL
Clustal Consensus

                         710       720       730       740       750       760       770       780       790       800
                ....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|
daphnia         QNELCDDQPRRRRYKTEYKKKFRPFSLYQYVD--GKFQKSSSDKIPTSSST-----------------------VDGPARQQQQPGDKMDKDTWYGEVLE
silkworm        SNGEDRSKDNRKRYKSEYKKKFRPFSQYVYEASKGKFTKCRGKGKSNEEASERMLGENQGSGEGGQGGGVEDS-ASTLRAAGLQPLGLAQGDSWYREVLD
butterfly       YNGEDRSKDNRKRYKSEYKKKFRPFSQYVYEASKGTFTKCRGKGKSIEEASERLVGDTEGAGAGAGDGAAVEDTASTLRAAGLQPLGLAQGDSWYREVLD
bee             LKITFRGKKSGRTVRIS------------DDK--G-------------------------------------------LREKPQEKPFPT---------AEVIE
fly             SDTDDRKTHEKQVTIMERKTTSRPFSQAIDQERLNHFITKKENFGFADAAVAAAALKDEVDNRQAGESG-----QVVVMNGSAPPHSKPNLDLWFKEMVE
mansoni         SQIHTKPIQHRKKYTTEYNAKYID-----YSD-----------------------------------------------VLDVPQNQMKSSNKSISHDWYQETVV
viverrini       PDLSKKTRSHESRYTSEYGAKYHN-----YFG-----------------------------------------------LQPNSNGSTE---------WMRVLEG
sinensis        PDLAKKTKSHESRYTSEYGAKYHS-----YFG-----------------------------------------------LQPNSNGSTE---------WMRVLEG
anemone         PLAPEVPYKPM-KFQSEYHTNFQPPSMFDYID--GAWVGADP--------------------------------PHLYPLEKPSDDVHPVTLSWFKQVTE
Trichoplax      PDRPFFPHRRRNYLLTYFYDLYIQDDDNSPVI-----------------------------------------------SPDGTPS---------WYKQILE
urchin          PQRPFFPHATVRKWRSEYKSNFKTPQVFSYEN--GVWKGADPPHVQPRDESSD---------------------RGGKPEQLTRSKSVGDLPNWFSEVLE
Saccoglossus    PQKPFFPHAAIKKWKSEYRSNYHDPRVFSYMD--GVWRGADPPHIEPRDESSKQEKIGVAPDWFGEVRGT----PKQFSNYSDKKKDSVHDAKWFKEVVE
ciona           PFSPVQHHRSPKKVISEYSTQF--PDREFPLE--P-------------------------------------------------------------LSN
telata          PNHFSFPHGKFKSSNSEYHRNFRPPKDYVYQD--GAWGGVVP--------------------------------PRVEPVMEPEAEEGAPTNSWYSEVME
Medaka          EDTPPLLGHRGRRMLTEYQSSFRSPLHRKPEG--N-----------------------------------------TNGAALQ-------------VTE
tilapia         MPPPPRQVRRGYRMLTEYESSFRSPLCRIPEG--GG----------------------------------------AMDSTAQQ-------------VKE
stickleback     PTQVQRGPRI--------------------PEG--GG----------------------------------------ATEGDAQ-------------VRE
molly           PLTTAPPPAQVRRRHRN------------PKG--GG----------------------------------------TTDDLTEQ-------------VKE
platyfish       PLTTALPPAQVRRRHRN------------LKG--GG----------------------------------------ATDDFTEQ-------------VKE
mouse           KKPASWRHQRLGKVNSEYRAKFLSPAQYFYKA--GAW-------------------------------------TRVKENLSNQ-------------VKE
human           RKLTPWKHQRLGKVNSEYRAKFLSPAQYLYKA--GAW-------------------------------------THVKGNMPNQ-------------VKE
cat             KKLTPWRHQRLGKVNSEYRAKFLSPAQYLYKA--GAW-------------------------------------TRVKENIPDQ-------------VKE
cattle          KKLTPWRHQRLGKVNSEYRAKFLSPAQYLYKA--GAW-------------------------------------TRVKENIPNQ-------------VKE
python          KQKPLCSHRSLKKMNTEYRSKFLSPNQYVYKQ--GAW-------------------------------------VHVRKNIPYQGSQNTLNTMWYIEVKE
chick           SQKPLSLHTHRGKMNTEYRSKFLSPAQYFYKD--GAW-------------------------------------SRIRSKVPNQASQNPLNSMWYMEVRE
xenopus         IQQLKHSSKSCRRIKSEYTSNFLSPSEYLYKD--GAW-------------------------------------VRAKKQMHEQ-------------INE
shark           PHKPPFPHKGHGKIKSEYRTNYLSPDQYQYRE--GAW-------------------------------------KAKRSFVAEEGTESKLSFPWYAEIKE
gar             PKRPFFPHRGCGKQKSEYSANFRSPLLYRYKD--GAW-------------------------------------IKSPCVGEEGSQRTLNHMWYNEVKE
zebrafish       HNLKDPSPKVMRKGKTEYRSNFHSPLQYSYKD--GAW-------------------------------------LKIKSAKEE--------------VKE
tetra           SSQKDSSPKVLRKVKTEYTSNFRSPLQYRYKD--GAW-------------------------------------IRSRVSGEEG-------HEWYHEVQD
cavefish        SSQKDSSPKVLRKVKTEYTSNFRSPLQYRYKD--GAW-------------------------------------IRSRVSGEEH---GQMGHEWYHEVQD
limpet          GEVIKSTHGKLRKRESEYDANFKAPQEFQYMN--GAWHGANPPQLYTSIKPVRQVCCSVKLWSKFAVRPKPVKKSKEKKALVEAEDIQPEQTNWYTEVLE
oyster          PSSPPIHQGNLKRPRSEYTSNFRSPTKFQYD---GAWHGADPPHLQPTREPEK---------------------EKPVKKSGPVEDSAPALSNWFAEVIE
aplysia         KTKLLKSHGKIKRLGSEYKANFKSPLRYSYAE--GAWRGAAPPQMMPQTSSAENTDAN----------------NDKENNNNNNASEEAPLSNWFAEVLE
Clustal Consensus
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                         810       820       830       840       850       860       870       880       890       900
                 ....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|
daphnia          LRKKAGEYKYRGL-GGELMSDHMADLYAKQFDVWEQVSRRSSLS---------------ALALAATSPRPGSE---------------------------
silkworm         LRKRAGEYKYRGW-GTELAPEHLTQLYNKQIELWYQVSRRSSLS--ALSLASTNHKVLPRDEKDGKESKNQSP---------------------------
butterfly        LRKRAGEYKYRGW-GTELAPEHITQLYNKQIELWYQVSRRSSLS--ALSLASTNHKALPRDEKDGKESRNLSP---------------------------
bee              LRRLADEYKHRDW-GCGLAAE-------DEASLWKRVSSNHALN------ALSLARSVTKEEKEKENTRKVAPVTAAMTMPPAGRPSSVQARPIHGILQD
fly              LRKKAGEYKCRGW-GIEIDPE----LYKKQKDLWDQVSKRSSLS--ALSLASSVHRPITKEEKEQENNKKSTPLQKAQKPRVPGQAFLIDNKDEISALPA
mansoni          LRKKADAYRKRDR-ESHFSREHLAQLESDYVDHWDPPSDDNYME--------NLEKYREVLQMPRAGKPSTDL---------------------------
viverrini        IRNQADLYRKRDL-ESHFTRDHLAQLASAFVDYWDQPSSDRYAR-----------NREKSLTTLAQPPAGKPS---------------------------
sinensis         IRNQADSYRKRDL-ESHFTRDHLAQLASAFVGYWDQPSSDRYAR-----------NREKFLKILAQPPAGKPS---------------------------
anemone          LRNKAQSYKTRAR-GDSQFLGILKSLEEQQSITLEKANKRTPSA--QHRLRDDEANRVPDMRIECLEERQEKA---------------------------
Trichoplax       LREKVQLFRERSQQGTFFTRKNLLVMEMAQEDLWEPASDTSRSG-----------------------------------------------------
urchin           LRERAKEYQKRSR-GTHFTRQHLGQLLANQAKLWEESSDQLSTS--------------SSISTQTTGSEKKDE---------------------------
Saccoglossus     LRKKAQEYQKRAR-GTHFSREHLAQLLAQQVKMWEMESVSSTST---------LTPSERTVSTARPAAGKTYT---------------------------
ciona            IHQEANQNKQNRD-ANSFDPDHATQLHSPKNKFWEIMSATESNV-------DTVSNSTSSVKKVVESLKSKDV---------------------------
telata           LRKKAAEYRLRAR-GTHFSRSHLAQLYAQNAELWDSYSVVSALS-----------------------------------------------------
Medaka           LRQRALMYRRRAW-GANFSRDHLGQLLSHQNALWEPSSTTDSMA----------DASPLAAGPSPDPGSHSGS---------------------------
tilapia          LRQKALLYRHRAW-GTNFSRDHLSQLVSEHNALWELTDTTVSAN--------DPASPRLPPNPSPDRDSHSTS---------------------------
stickleback      LRLKASSYRRRAW-GANFDRDHLSQLLSEHNALWEPTDTT------------DGPTPRPTFDLHADPDSCGTS---------------------------
molly            RRQQAQAYRRRAW-GTNFSRDHLSQLLSEHNALWEPADSHSDPS-----------TPLPNRDLSPEPDSRRAS---------------------------
platyfish        RRQQAQAYRRRAW-GTNFSRDHLSQLLSEHNALWEPTDSHSDPF-----------TPPPNRDLSPEPDSRSAS---------------------------
mouse            LREKAESYRKRVQ-GTHFSRDHLNQIMSDSNCCWDVSSVTSSEG--------TVSSNIRALDLAGDLTNHRTP---------------------------
human            LREKAEFYRKRVQ-GTHFSRDHLNQILSDSNCCWDVSSTTSSEG--------TVSSNIRALDLAGDPTSHKTL---------------------------
cat              LREKAEFYRKRVQ-GTHFSRDHLNQLLSDNNCCWDVSSTTSSEG--------TISSNIRALDLAGDPTSHKTL---------------------------
cattle           LREKAEFYRKRVQ-GTHFSRDHLNQILSENNRCWDVSSTTSSEG--------TISSNLRALDLAGDPTSHKTL---------------------------
python           LREKAEAYRQRIQ-GTHFSRDHLNQILSDNNRFWDLSSESSVEE--------TMSNNVRALDLARVPENKQSL---------------------------
chick            LRARAKAYRQRIE-GTHFSRYHLNQLLSDNNSLWDVSSNSSSEE--------GISNDIRALDLAGVSEKETAP---------------------------
xenopus          LREKADYYRRREQ-GTHFSRNHLNQILSVNNKFWDVSSNSSSEE--------QVSHNIKALDLAGFQAHSKKE---------------------------
shark            LREKAEVYKRRAL-GTHFSRDHLSQILSPENKLWELSSTSTSEE--------SVCDSVRALDLERARETPKIP---------------------------
gar              LRERAEAYKKRAW-GTHFSREHLSQILSEQNRLWEVNSSSTVTE-------DTVSDTVNALDLARARDVKRSP---------------------------
zebrafish        LRERAEAYKKRAW-GTHFSRQHLNQILSDQNWMWEPSSGTSSSS-IESEACRSTSHIIEALDLARAGSVRESS---------------------------
tetra            LRAKADAYRKRAW-GTHFSRQHLSQVISEQNCLWEASSASSSSTLTEQDSHSHSSPTIEALDLARVDSVRGS----------------------------
cavefish         LRAKADAYRKRAW-GTHFSRQHLSQVISEQNCLWEASSASSSSTLTEQDSHSHSSPTIEALDLARNRVLVYQV----------------------------
limpet           LRQKADEYRKRGQ-GSHFSRAHLAQLLARQTELWDCETCSTTEA-----------STISALSLETGSSPAGLA---------------------------
oyster           LRRKAAEYKKRAQ-GTHFSREHLVQLIAQQNQAWDNLSTARSGS-----------STLSALSLESGASAKLRA---------------------------
aplysia          LRRRAQEYRKRAQ-GTHFSREHLVQLMAKQNECWDLHSDGSSTV--------------RALNLETSGAHLRGK---------------------------
Clustal Consensus  :  .   : .
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                         910       920       930       940       950       960       970       980       990      1000
                 ....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|
daphnia          ----------------------------------------KVDMTSAIN----------SKRGSPAKTAPQPNQSARPGHAQPLV----------PT
silkworm         ----------KKFRS-----------------------FRSAPHQSIHAKLQETK-------ALERSPHKTSPQKQRKKLQGHSFDE-----------GA
butterfly        ----------KKFRS-----------------------FRSAPHQSIHAKLQETK-------ALERSPHKTSPQKQRKKLQGHSFDE-----------GA
bee              DSKADTERAIARARKDFLIRHHLDRTTGVGDGALLPSPTREKLEPVIPRRREETKEHREEIQPKTKSSPKNSPRTGRSQSLGPTVTERRSPKRQPPRAPS
fly              RFSNIRHHLERTTGPDVEEGALLPSPTREKLMPAITKRESESQRGSPKKTALSRHGSPQKGSPQKGSPKKVLKTRSQSAGPGVAENESPKRQIRS---AS
mansoni          ------------------------------------------------------------------------IFNPDEAVLPA----------IQ
viverrini        ------------------------------------------------------------------ELCSEENEECEAHSTI------------SA
sinensis         ------------------------------------------------------------------ELCSEETEEREAHTTT------------SA
anemone          ----------------------------------------QPVSDHMIRKAE-------TGNQEKRNEFSGKNNNNEHGIHLVPTDDRASIDQGSGH
Trichoplax       ------------------------------------------------------------RENRTTNERGSYSTTSKKVSQVQQLP----------PS
urchin           ------------------------------------------------------------------PKEGARPSASAPDLGHE--------------PT
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Saccoglossus    ------------------------------------------KEVAAQQQAKLA-------REEERRKLTPSPSPSPHDSERTPQPA----------SV
ciona           ------------------------------------------DSCSVESIKGSD-------DDDCDVIRDENSVSCSSRQSLKGEL-----------PV
telata          ------------------------------------------------------------------LETGSKSSRGGGDDSDR----------PS
Medaka          ------------------------------------------------------------CVDALDLASVSSLSRSAASELKTR---------TQ
tilapia         ------------------------------------------GVEPLDLASHSS-------KRSSIAGSETQQMSKDTRIKKQAIPGP---------PA
stickleback     ------------------------------------------------------------PAEALSPARSSRRSSVTSSTDRNTPT----------PP
molly           ------------------------------------------CVEALDL------------ASMSSRRSSVSGGKTQRSAGRETPPGP---------GA
platyfish       ------------------------------------------CIEALDL------------ASMSSRRSSVSGGKTQRNAGRETPPGP---------GA
mouse           ------------------------------------------QKHPPTKL-----------EERKVASGEQPLKNSTRRLEMP-EPAA---------LV
human           ------------------------------------------QKCPSTEP-----------EEKGNIVEEQPQKNTTEKLGVS-APTI---------PV
cat             ------------------------------------------QKCPPTTL-----------EEKKPALEEQPQKTTTEKLGVSDAPTL---------PV
cattle          ------------------------------------------QKCPSTQL-----------EEKRTVLEEQPQKTTTEKLGVSNAPI----------PV
python          ------------------------------------------------------------------AQPEQFQPNNSGNLGVSDAATV---------PV
chick           ------------------------------------------RPKMLQ----------------QPGSREQSHQDDTEKKGLSDAPTV---------PV
xenopus         ------------------------------------------------------------NVHKSSIEENEDTGTLGISDVPTV---------PV
shark           ------------------------------------------RPKQQRSHSESA-------VENAAPSQNPPKFDDTGKNGISNVPTF---------PV
gar             ------------------------------------------SPVSPGSL--------------SPVGNAKSRTEETEQAGLHSRPTL---------PV
zebrafish       ------------------------------------------------------------SPGHSASVVVSRRSSSGEVGLPEEPTL---------PV
tetra           ----------------------------------------------CSPG----------------ASVSLSTSRRSSFEGVGLSDGPTL---------PL
cavefish        ------------------------------------------IVCHPQTYCKM--------QVLSSLKQHVNMRSSFEGVGLSDGPTL---------PL
limpet          ------------------------------------------ERPPQ-----------------RPPRLELNEKNLERKSRIQDRKLKKFSDLD---ST
oyster          ------------------------------------------QKIELSEKPLLK-------IENIDTNNETLDNELCKGVRKSNDKMQQLKA-D---PV
aplysia         ------------------------------------------------------------EKNLAQTAPADLVDALSHEATEGDS----------PL
Clustal Consensus

                        1010      1020      1030      1040      1050      1060      1070      1080      1090      1100
                ....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|
daphnia         S-----RNKDN-----------NIRNKGSDSTERARRDMSQHRSISSEGSKSRSKSAKPAKSPAQPTSGTGTGNVTLAIRPSLVSRPPARSASLGPERRM
silkworm        ALDGV-KTGEN-------------------------------------------------SAFKSPRRR-----------------------------------
butterfly       VQDGA-KSEGS----------------FRSPRRRPRS--------------------ADPAPAPPR-----------------------------------
bee             VTKDA-KEKEK-----------------ESKEKE-----------------------KEQREKGGE-----------------------------------
fly             QAPSS-RKKTPTTGSGSERKARPSTLSTTFQSRI-----------------------KSSSLPPPN-----------------------------------
mansoni         RRRAM-LGSHN-------------------------------------------------VAEIMDQDD-----------------------------------
viverrini       RRRAM-MDSHH-------------------------------------------------VAELLHEYQ-----------------------------------
sinensis        RRRAM-MDSHH-------------------------------------------------VAELLDEHQ-----------------------------------
anemone         RKREA-WAEPG--------------PIYPRAAIPPYG--------------------VSESLPTSR-----------------------------------
Trichoplax      QPKEA-WTVEA-------------------------------------------------NENETEESN-----------------------------------
urchin          RRKLA-WHANN-------------------------------------------------NKAEEEPNP-----------------------------------
Saccoglossus    KRKLA-WPVDE-------------------------------------------------KPRQEEVSS-----------------------------------
ciona           ARKLA-WGESD-------------------------------------------------SQSNDVDAV-----------------------------------
telata          VVAEA-WKEKD-------------------------------------------------SKASNSTAR-----------------------------------
Medaka          RRTHAETHTTA-------------------------------------------------EEEQRPDG-----------------------------------
tilapia         ERRTA-WGEEE-------------------------------------------------KEDEEEEEK--------------------REEEETTDE-----
stickleback     GQAA--RGGGG-------------------------------------------------EYERSEE-----------------------------------
molly           ERHSA-WAEEE-------------------------------------------------EETEEEE-----------------------------------
platyfish       ERHAA-WAEEE-------------------------------------------------EETEEEE-----------------------------------
mouse           RRKLA-WDAEE--------------STKEDTQEEPRA--------------------EEDGREERG-----------------------------------
human           RRRLA-WDTEN---------------TSEDVQKQPGE--------------------KEEEDDNEE-----------------------------------
cat             RRRLA-WDAEN---------------TDEGVQKQPRE--------------------EEEEETEKD-----------------------------------
cattle          RRRLA-WDAED--------------TT-EDVQKQPSG------------------E-EEKEEEEKE--------------------EGDK----Q-----
python          KRRLV-WDESG--------------NDEQQENQSPAL--------------------GECKEEEKK-----------------------------------
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chick            KRRLV-WGEQE--------------GTAEKDSQQ--L------------------T-EEEEKENEQ--------------------AAVVTQNLE-----
xenopus          RRRLA-WDENN---------------NSELAQERAALTVED----------------KNVETTDAD----------------------------------
shark            RQRLA-WNDEE--------------GETAPGRDLPES--------------------DQEESDGVE----------------------------------
gar              QRRLA-WEQED------------RGPESKGEEQGEHT--------------------GDLGRQEEE----------------------------------
zebrafish        QRKLA-WDEEE-----------QLGEREEIVQD------------------------RLTDKEGKT----------------------------------
tetra            QRKQA-WDEEERPYVNGVSEIKPLREEPPVQQA------------------------EESDEEEDT----------------------------------
cavefish         QRKQA-WDEEERPYVNGVSEIKPLREEPPVQQA------------------------EESDEEEDT----------------------------------
limpet           KATIA-ETPAP---------------SVNGGNERRTY--------------------KPRYTQDSR----------------------------------
oyster           VMETK-FNNKLRL----------ETKKENTNHRNVKTKSKKVEMANKIEDDVSLMAHEGSDEEQGKPDFVPEKHMDLTTKQRYKKSQSRKKAWQEMDESR
aplysia          MSDVE-EAEPQ---------------RKEGKKKKGR--------------------RGGKSKGGR--------------------KSRKMAWLE-----
Clustal Consensus

                         1110      1120      1130      1140      1150      1160      1170      1180      1190      1200
                 ....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|
daphnia          PKSVSSSTTGGNVGSSATKASPVKARPAHNEDGIKDPVKVTMKNHLGDEGKENVIINEPASSSLPVIQQEPLPALIKALPEPTRVKSPEQLVVRSPDPVN
silkworm         ----------------------------PRSADPAPAHLKHAPNGHDARP-----IKPSDDEIP----SH------------------------------
butterfly        ---------------------------AATDAERPHKPTGLPLSRGSSSRV----RSTSRGGRSP---SAP------------------------------
bee              --------------PERHPRPTGVSVTGPGHVRWSIREPSTVSSTGSSTSVPPLPPPPSGPGPTPFYRRSP------------------------------
fly              -------------GRVASAPP------ATAAAASAAKSALSANQAHANQSQSSHAKSGSISGRIS----KP------------------------------
mansoni          ---------------------------------CSDTDYDQNIEYNN-------------DHLS----TQ------------------------------
viverrini        ---------------------------------VYDPKSYSSEVKPESTH-------SKGEKNN----QR------------------------------
sinensis         -------------------------------------VYDPESYSSEVKL----------GKWF----ST------------------------------
anemone          --------------------------SASSIGSDSMSDVTLTDDLMNERP---RSTPDDKMRKP----TT------------------------------
Trichoplax       ---------------------------------KADEDYDDEETLSERPG---------NGNIE----------------------------------
urchin           -------------NQNIAHLE------RRSSISSVTTPESMPSMSSRSSEI----ESIEENGRLT----TP------------------------------
Saccoglossus     ----------------------------IGTIPTPESLQSSSRDTLTPNDD-------DEEGRIP----TP------------------------------
ciona            --------------AHD-----------------EEDSDVASTVTLTESNT--------NEGRLP----TP------------------------------
telata           -----------------------------------SNTVSVLNSEASESST----FAASEAGRLP----TP------------------------------
Medaka           ------------------------------------------------------------------------------------------------------
tilapia          --------------SLLIKNE------KKTDEEIILKSQIEMSISAEENNQ----SSLAHSQKLK----TP------------------------------
stickleback      ------------------------------------------------------------GRLP----TP------------------------------
molly            ------------------------------------------------------------GRLP----TP------------------------------
platyfish        ------------------------------------------------------------GRLP----TP------------------------------
mouse            --------------QGKQTCA------VELEKPDTQTPKADRLTEGSETSS----VSSGKGGRLP----TP------------------------------
human            --------------EGDRKTGKQAFMGEQEKLDVHEKSKADKMKEGSDSSV-----SSEKGGRLP----TP------------------------------
cat              --------------RQVHNGE-------LEKVEVPEKSKAEKIKEGSDSSS----VSSGKGGRLP----TP------------------------------
cattle           --------------VNVEELE------KLEV---QEKSKADKIKEESESSS----MSSGKGGRLP----TP------------------------------
python           --------------QDIEEVKQVEKNDKDANINNQQKENISSSEDMVDSSE-----SLRTFGRLP----TP------------------------------
chick            --------------KNNEGIN------EDNRIEGENTCLLNSPAAVSESSS----VSSEPGGRLP----TP------------------------------
xenopus          --------------VVEDAEEMHAISEEVKRPDRLHSTTTNPSVDGLECIS----LPSEEGGRLP----TP------------------------------
shark            --------------KELGNAEEVGAVSKRKEDPIDEANLSTANLDSNETSE----LGSEVGGRLP----TP------------------------------
gar              --------------QADGNKKGDDAQAGQQQKEVKATEQRSSSRSSSDVTAGSSETSSDGGGRLP----TP------------------------------
zebrafish        --------------RNENGME------RNERLNSLESESLSSAEEGSEASV--------NGGRLP----TP------------------------------
tetra            ---------------NEHLED------KGEKFRVPVNEHLSPA-AGTRCSV--------EEGRLP----TP------------------------------
cavefish         ---------------NEHLED------KGEKFRVPVNEHLSPA-AGTRCSV--------EEGRLP----TP------------------------------
limpet           --------------GRTRQVKTAWQYDEPEEIYNGDSAEVDEEVETPVDED-YSNNNYRRGGRLP----TP------------------------------
oyster           DYRQDDLSLMVQEGSERRAKS------RGRKKHRSRRARRREQEEASEVTP----DFPSDTGRIP----TP------------------------------
aplysia          --------------EQKESVA------EQRRQLEETRQREDMKDDDDNDSE----GLVGKEGRLP----TP------------------------------
Clustal Consensus

                         1210      1220      1230      1240      1250      1260      1270      1280      1290      1300
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                    ....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|
daphnia             WTVPLDTGKTFTVTQNI-RGGEIITSRPHSELKVSMTVRPPAPAVAAVHSPMIPIVSSSSAAAVTKPSEQQQQESQLNSGPAPDDPVPCNETEEETSKVA
silkworm            --------------RSA------SVAKDHFFD--------DSPVVKS----------------------------------------PPEPTRVKSP---
butterfly           --------------TKT------GTGLVNGAV--------EANGAGR-------------VNVTTPPARR-----------------SRSVSKVGIK---
bee                 -----------QVHRKSFLATTAPPYRPLHHIKPSTTTTSTTTITTTTTTTTITTTTNTTSTSVKPPVKHSIHTS------------VHHPPTSSAAAAA
fly                 -----------SASSAQ-QQ---QQQQQQQQMRKKDKDRSNSSCIGS-------------GSHVGAGSGS-----------------QANSVKHLQN---
mansoni             -----------------------PCRRYKADM---------KCTRDN-------------YVGILPAATK-----------------YNHTDEAYDS---
viverrini           -----------QLVRQN-DA---QALSTHFEN--------QLSST------------------------------------------SPDIEMEKHG---
sinensis            --------------QSTCSK---GGEKNNQSQ--------PVSQNDA-------------RTLSAHFDNQLSST-------------SPNIEMEKHG---
anemone             -----------GL----------GDVAIQHAQ--------GE----G-------------AVGIDPPRVS-----------------TREENSRPRV---
Trichoplax          -----------------------AGQGNGNDQ---------FEKLGS-------------NTIVER----------------------RNPIDNKAYE---
urchin              -----------TL-KES-EQQSHGSKRHHLDR--------TTPAKGG-------------ALLTSPASRRRATHVPKTTVTYPRQGELMKPSSRTYVARS
Saccoglossus        -----------RLTKKP-DA---SKQRHHLAR--------TTPAVGG-------------ALLSSPNIKRSSGVK------------KQSPSSKESGAKL
ciona               -----------QL-K-K-LG---GALRTHHDI--------TTPSRGG-------------ALLSSPPRPR----------------RMISS--------
telata              -----------QG-RKR-SS---PYVRHHLDR--------TTPCAGG-------------ALLSTPPKAKVTEFKAIRGQEEITSDDRPASPERVSCTCG
Medaka              ------------L-K---AK---PVQRSRSDL--------GSPAAGG-------------TVLVGQQGNA-----------------DVSSPKKVQR---
tilapia             -----------EI-K---LK---PVQRTHHDL--------TTPAAGM-------------QTSFLHISVQ-----------------RCGSAVSM-----
stickleback         -----------RL---K-MR---PVQRTHHDL--------TTPATGG-------------AILVGKLSSD-----------------EASPNKPRRE---
molly               -----------RL---R-TR---PVQRTHHDL--------TTPATGG-------------AILVGKPTNR-----------------DDSSPIKQKQ---
platyfish           -----------RL-KTR------PVQRTHHDL--------TTPATGG-------------AILVGKPTNR-----------------DDSSPIKQKP---
mouse               -----------RL-R-E-L----GIQRTHHDL--------TTPAVGG-------------AVLVSPSKVK-----------------PPGLEQRRRA---
human               -----------KL-R-E-LG---GIQRTHHDL--------TTPAVGG-------------AVLVSPSKMK-----------------PPALEQRKRM---
cat                 -----------KL-R-E-LG---GIQRTHHDL--------TTPAVGG-------------AVLVSPSKVK-----------------PPVPEQRKRV---
cattle              -----------KL-R-E-LG---GIQRTHHDL--------TTPAVGG-------------AVLVSPSKVK-----------------PPVIEQRKRI---
python              -----------QL---RALG---GIQRTHHDL--------TTPAAGG-------------AVLVSPQKVK-----------------HSSSLQIKKG---
chick               -----------KL-R-A-LG---RAQRTHHDL--------TTPAVGG-------------AVLVSPPKFK-----------------SSTSQQRMRS---
xenopus             -----------KL---KEFG---LSQRTHHDR--------TTPSTGG-------------ALLVSPMKEH-----------------LHTPEDKKKG---
shark               -----------KL-K-T-MV---APRRTHHDL--------TTPAVGG-------------AVLVSPYKIR-----------------SPSPHRKRNQAP-
gar                 -----------KM---KTSG---VAQRTHHDL--------TTPATGG-------------AILVSPPKQK-----------------PSPQRVPRKSEPP
zebrafish           -----------KL-K-T-MQ---TVQRTHHDR--------TTPSIDF-------------NLHYIAKAAN-------------------------------
tetra               -----------KL-K-T-IR---TVQRTHHDR--------TTPTIGG-------------VVLVSPPKTK-----------------NSSRTARRSEAP-
cavefish            -----------KL-K-T-IR---TVQRTHHDR--------TTPTIGG-------------VVLVSPPKTK-----------------NSSRTARRSEAP-
limpet              -----------HL-QKQ-DR---PVSRHHFDL--------TTPSVGG-------------ALLSSPPSVR-----------------SLPAKTRLSR---
oyster              -----------KM-R-S-KS---AGARHHLDR--------TTPVVGG-------------AMLSSPPRPE-----------------KKSPVKVSRSWCT
aplysia             -----------LL-Q-G-DS---SARRHHLDL--------TTPAVGG-------------AILTCPPSKS-----------------SKLIITSR-----
Clustal Consensus
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                            1310      1320      1330      1340      1350      1360      1370      1380      1390      1400
                    ....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|
daphnia             SQDETTGEQHPVEEDPVDQEKVAVAAEEETNPVEISSGEKEEEEEEEKEEVDCKAEESVEAEIKAQEEEEVEKETVKEKEAEEKSMDEIKEIRPADERQD
silkworm            ------------------------------------------------------------------------------------EQMNMRSPDPV-----
butterfly           -------LDDDIPNHRSASVAKDHFFDD--------------SPIVKSPPEPTRVKSP-------------------------EQMNMRSPDPVNWTV-
bee                 RPDRVKDISRSHQGPNEAQAKTGRDQSAAAAAAAAVADPSKSSSDSRYASNQAATAVQPMTAEPQVNGDVTGGESSVASTPPSQSQAPVSATAAS-----
fly                 -------KQKQQQLQQQQQQKQQQQQQPQQQQQKQQQKQQQQLDVAAAATAAAATSAP--------------------------PQNPTRPATIN-----
mansoni             ------------------------------------------------------ANHSLKS--------------------------ETDSIRLANSN-----
viverrini           ------------------------------------------------------------------------------------TAGQLSNIHRT-----
sinensis            ------------------------------------------------------------------------------------AASQPSHIHRT-----
anemone             -------EDQTLRGKGIGKAKDARVTHL-------RRLPTLHELNEPIDDRTRKLFTG--------------------------RHHVASDDRS-----
Trichoplax          ------------------------------------------------------------------------------------PKNGLNKEYKG-----
urchin              APVKAIIPGGITKGFEYDSDDDDDEDDVDLDRTLTRGQQTPPRNPTQQKQMGRFLHSS--------------------------PSAGRRTSDPH-----
Saccoglossus        QPASENGYRSDDEDSVPQLSRKMVQKSS--PKHSRYQADKVPCSCGADVKSHTKLIKS--------------------------PSAGVHTRDPD-----
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ciona            --------------------------------------------------SSSPTLLS---------------------------KASSVCSVNNK-----
telata           -------VGSSLSPSPDEAPSQEKGVQT---------------------RTSSRLVFN---------------------------RDGSLVDPRKI-----
Medaka           --------------------------------------------------SSSLVSMT---------------------------TEAGIPCGMPV-----
tilapia          ------------------------------------------------------------------------------------AAGS--ETPA-----
stickleback      ------------------------------------------------------------------------------------------SSADQ-----
molly            ------------------------------------------------------------KFAS---------------------------PEFGSEVGVNK-----
platyfish        ------------------------------------------------------------KFAS---------------------------PEFGSEVSVNK-----
mouse            ---------------SSQDGLETLKKDI----------------TKKGKPRPMSLLTS---------------------------PAAGMKTVDPL-----
human            ---------------TSQDCLETSKNDF-----------------TKKESRAVSLLTS---------------------------PAAGIKTVDPL-----
cat              ---------------SSQDGLETAKNDF-----------------RKKESRAIALLTS---------------------------PAAGIKTVDPL-----
cattle           -------SSQD--------GLETLKNDF-------RKK----------ESRTISLLTS---------------------------PAAGIKTVDPL-----
python           -------SSEKQSLANSQVSREQLKRKT-------------------IRGEEKAVSNS---------------------------PAAGLETLDPL-----
chick            -------LGTDPSSVGQGASEASQRRSF-------RPGA---------KLKAVSLLTS---------------------------PPAGLGTVDPL-----
xenopus          -------YFVSSTPPKKAVCKKDIKTKL----------------IKDKELTGTPNTSP---------------------------PVAGIRTVDPL-----
shark            -------LGKSYSPYRCFSSGSPKKKLT-----------------------KTESLQQS---------------------------PAAGIRTPDPI-----
gar              -------LGKPYSPYKHLARDSSPPQNP-------------------SKAEERCSSQSP---------------------------PAAGLKTTDPI-----
zebrafish        ------------------------------------------------------GSLPRSS---------------------------PVAGLTTVDVL-----
tetra            -------LGKVHSPFRHLSHGSPPRAHS-------------------KAENGSLPRSS---------------------------PAAGLATIDPL-----
cavefish         -------LGKVHSPFRHLSHGSPPRAHS-------------------KAENGSLPRSS---------------------------PAAGLATIDPL-----
limpet           --------TQPIPPYDQDLNEDDEEEAR----------------MIGKTYNLIKNTPK---------------------------PTYGLPSRDTH-----
oyster           -------PQDVYDDEVSTVLSSDRFEPV-------VGQK----LAKTYDVKKGPLATT---------------------------PTFGLASKDTH-----
aplysia          -------SGDSYVTASDDLPVRGEQKKY----------------------NMDKLLTL---------------------------PAGGKPSPDTH-----
Clustal Consensus

                         1410      1420      1430      1440      1450      1460      1470      1480      1490      1500
                 ....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|
daphnia          EKCSPVSDPLGAAIVLQGKGPLN-EDVPA----AIAPVESVTSIVPGTTLRRLEDPTPFLFSRPGTLGSLNAGQPMASSTSLS----DTKPKAPRYRVLE
silkworm         --------------------------NWT-------------VPLDTGKTFTVTQNVK---------------NDESIKRPSS----EFKSGSIA-----
butterfly        --------------------PLDTGKTFT----VTQNVKSEIAPIHHQQMSPIRSLKKSESPTSLS-------KRTDKTPTTP----ISLTPIDE-----
bee              --------------------PWI-DDEPV----VKSPPEPTRVKSPEQMIMRSPEPVNWTVPLDTGKTFTVTQNVREEPLTRPHSEAKSWAPSS------
fly              --------------------IKRLTVPGQDRKLAENEGEDGRETAISISSCSPQPPVP---EVPEE-------PLVKSPPEPT----RVKSPEQI-----
mansoni          --------------------EPRTNNSYI-------------------------------------------------------------KQWSNDSK-----
viverrini        --------------------SQQGNSLSP-----------------------------------------------VSTKSIM----SSATPISE-----
sinensis         --------------------SRKGNSLSP-----------------------------------------------VSTKSIM----SSATPISE-----
anemone          --------------------PRN-DSPPT----RQPPEQQRVDSKTRKLFTGRPLETSDSTELELS-------VDTSASNSTT----HSSLPPPR-----
Trichoplax       --------------------NLKNVDTYS---------KAKTTVGFANHKNEATKENR---------------NLTSDSNIRP----PKSSNLRR-----
urchin           --------------------PLN-EELISPGFQRHSERFFETSPGMPTIPNKIEPPKTWAAPWAGL-------KTAPPAGKGP----LERPHSGR-----
Saccoglossus     --------------------PIE-ENYPTSPFQRHSQNRFETGPVRLPEESSPPRPVD---SRPLKTWAGHPVDQPRPKVTPK----KDSRESDQ-----
ciona            --------------------TFL-EDSKS------------------------KRSPS---PGCRM-------VRTDQGLPRR----LQASLRAP-----
telata           --------------------QVNLEEIFA----DRKPVERKLTDDSVEGSDGLPTFGM-----PTRDTHELLDEEASTDRPLA----THYVQTPQ-----
Medaka           --------------------KRK-E-AWP----EKV-------STHQHEPFFSPSPKP---NS-------------QASSSPP----LAPPPLHA-----
tilapia          --------------------KRK-E-AWS----DNIAVSYS--PAHDHKSASSPSFKP---TRMKQ-------TLSPAAAPPP----LVPAPLHG-----
stickleback      --------------------PVKLKEAWS----DNSPAFAHTGPSLDHKPATSPASKP---IRTKQ-------T--SPMAPRP----LAPPPPHC-----
molly            --------------------PVKLKEAWP----ENSPVSLSPPPTNQQTPSPQPQPIR---TKQAP-------P--SPAAPPP----LGSPPQHG-----
platyfish        --------------------PVKLKEAWP----ENTPMSLNPPPTNKQTPSPQPQPIRTKQAPP------------SPVAPPP----LGSPPQHG-----
mouse            --------------------PLR-EDCEA-----NVLRFAEGTLPVSKILDRQPSTPG-----------------QLPPCAP----PYCHPSSR-----
human            --------------------PLR-EDSED-----NIHKFAEATLP----VSKIPKYPT---NPPGQ---------LPSPPHVP----SYWHPSRR-----
cat              --------------------PLR-EDSEI-----SIPRRAEVALP----VSKILEYPA---NTPGQ-------S--PSPPYAP----SYWHPSRR-----
cattle           --------------------PLR-EDSEP-----NIPKFVETTLP----VSKMPEYPP---NTPGK-------S--ASPPCAT----SYWHPSRR-----
python           --------------------PLRKDQCTNQGTNQDTSGTRNYETSVHSEQMPTVSETN------------------LAKGSSL----PYWSPLCR-----
chick            --------------------PLR-QDQWH-----PNGVSGETVAI----NSAYQERSS---TPPVL-------K--STKNRPM----PCWSPSPR-----
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xenopus          --------------------PLR-EDPWP-----------------IAYISNTSSPPRVTVPASKS-------PEPRAYVSMS----PLWNTSCR-----
shark            --------------------PLR-EECWI--------------PNTPGCLKTIPSVLALLKPDCTF-------DEKSASVPAS----PEKGYLHR-----
gar              --------------------PLR-VDSWP----SDSPHKAQTSPT-------AAKPFR---------------KHSASLAPVP----AGRTPACR-----
zebrafish        --------------------PMR-EDVWS--------------------DEEVTDYRSLKPPKPSR-------KQQSSQRHKA----NAAPPANR-----
tetra            --------------------PLR-DDTWA----RDSP---------------EPKPVR---TPQRR-------T--LSATLIA----TSSPRANR-----
cavefish         --------------------PLR-DDTWA----RDSP---------------EPKPVR---TPQRR-------T--LSATLIA----TSSPRANR-----
limpet           --------------------YLL-DEEAS----TDRPMRTQFLQTEVFDDGDTESTVT---EGEIQ-------TTQPKIVDEP----RYKRQSPS-----
oyster           --------------------FLR-DDEVS----VDKPLETVFVDS-------PAKVRM---TGNVS-------S--GDEKPAR----KSK-KPTK-----
aplysia          --------------------ALR-DDVAE----SDQALVTQY----------IVSPPL---PGSEE-------DKENKGQRKK----KSKGQKPG-----
Clustal Consensus

                         1510      1520      1530      1540      1550      1560      1570      1580      1590      1600
                 ....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|
daphnia          APGMMSD--PV---VHEPSYEPHPL---------------------QSSSSTAPMMTSSSPYKGRVLEAPSSPP-------KSSTSSSAAAFTSSPSTDS
silkworm         EEGVIVK--PA-------------------------------------------------------------------------------------GT
butterfly        ----TKA--LD---------LNKVN---------------------GVNGLNSNQLTPETPVQEHLAEKEVIKK-------STEATQVAPGVVDTTVVNE
bee              VPSAPQSAPPELAAQHKSQHSQHSGYKSPESESVSIGSFSGLNGHKDMDSERDSPLP--SNIQTGGTPTHVDDE-------TGGIEEESKEQRSEPSIKS
fly              ---IMRS--PD----------PVNW---------------------TVPLDTGKTFT--VTQNVKDGENYSRPQ-------SEIKASTPV--------EK
mansoni          NHASKRQ--NH---------WFHNE-----------------------------------YERKQRTVDETESLT-------S--CSSLSE--------KS
viverrini        ---------PT-------------------------------------N------------YTNEQRNHAVNDNSH-------QR---------------RC
sinensis         ---------PA-------------------------------------S------------YTNKQRNYAVNDSNN-------QR---------------RI
anemone          VDSRTKH--IH-------------------------------------MGRPAGGRAT--STESESYSSGDELSS-------SLSSDALSF--------EA
Trichoplax       KFGQNATTIVK---------RNENG---------------------NVAGNENSTDRGYYSNSHRNTGDNNPHDGNIAEISDR-ISKLKNRLLDDRESVS
urchin           IGGRPQTAVPQ---------TREAA---------------------SQQVQRLHSFM--SPRSNGLESPDD-------------WNLTPP--------RG
Saccoglossus     PPSYLRK--PAEAWSVPLEPSTRAA---------------------QYSRPDSGFIT--PPPRPEARLDLQDDE-------DR-WSVKST--------GT
ciona            IKGALKS--QE---------FQHCG---------------------KNSRPMTA-------------------V-------DR-LSMVSN--------RS
telata           NARLARQKFPE---------ADIPS---------------------TIDENMAQTFNKNKLLPGEVCLDDIPNW-------RRDEDALSTSV------RS
Medaka           IQGSMRH--PD---------FQHNG---------------------E----------------------HR--Q-------NG-LVMSGP--------PD
tilapia          LQGTLRH--PD---------FQHNG---------------------ELG---LRFRE--RPCPGGGCCSDE--D-------DR-LSVMSW--------RS
stickleback      IRGTLRN--AD---------FQHNG---------------------ELGLRFRE-----LRCPGRGSCSHE--D-------DR-LSVMSW--------RS
molly            IQGTLRH--PD---------FQHNG---------------------EL-------------------------------------------------QT
platyfish        IQGMLRH--PD---------FQHNG---------------------DLGLRFRE-----LPCSRGGCGSDE--D-------DR-LSVMSW--------RS
mouse            IQGRLRD--PE---------FQHNN---------------------A----------------------------------DR-LSEISA--------RS
human            IQGSLRD--PE---------FQHN----------------------VGKARMNNLQ--LPQHEAFNDED---E-------DR-LSEISA--------RS
cat              IQGSLRD--PE---------FQHN----------------------VGKARMNNFQ--LPQHEVFNDED---E-------DR-LSEISA--------RS
cattle           IQGSLRD--PE---------FQH-----------------------NVGKSRMNNFQ--LHQHEA-FNDED--E-------DR-LSEISA--------RS
python           IQGTLRD--PE---------FQHNG---------------------NIASPKRSWLQ--LPLQERNYNDEDD-D-------DR-LSQLSA--------RS
chick            IQGTLKD--PE---------FQHNG---------------------NVGNPKMGSFQ--LPLQER-NYNNE--D-------DR-LSQISA--------RS
xenopus          IQGALRD--PE---------FQHNG---------------------NFGS---------PGLHRTAYSDDCSID-------DDRLSQISE--------RS
shark            IQGTLRN--PE---------FQHNG---------------------NTGGPRSSILR--MQSTDSAAAADE--D-------DR-LSQISA--------RS
gar              IQGALRD--PE---------FQHNG---------------------NLGDLRPGLFA--FSSNDSDISDN---D-------DR-MSQISS--------RS
zebrafish        IQGTMRN--AE---------FQHNG---------------------NLGIFRPELFV--LPQSDSALSDN---D-------DK-MSQISS--------RS
tetra            IQGTLRN--PE---------FQHNG---------------------NLGLHRPDQFV--FLSSDSGVSDN---D-------DR-MSQISS--------RS
cavefish         IQGTLRN--PE---------FQHNG---------------------NLGLHRPDQFV--FLSSDSGVSDN---D-------DR-MSQISS--------RS
limpet           --APAMD--PI---------YENFG---------------------QTYNKAYVPPI--YSYNDVENYYRDDDD-------NESVLSLSV--------RS
oyster           FE--AQR--TI---------KEGYG---------------------QTYNK---PMV--WGIDGGMTIPRIEPD-------DD-ALSLSV--------RS
aplysia          SLTTIKE---------------GYG---------------------KTYQPKPF-----LDLDDIKAGTLDKKD-------DD-VLSVSL--------MS
Clustal Consensus

                         1610      1620      1630      1640      1650      1660      1670      1680      1690      1700
                 ....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|
```

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daphnia          LTSSRSL-------------------------------------------------------------------------------A-SDVLEKA
silkworm         -TNTATA-------------------------------------------------------------------------------------------
butterfly        TPTGGLT-------------------------------------------------------------------------------A-SEVLDRA
bee              VAGTSLRCLEDPSFEYERKKEGSQPVTTAAMTAPSSTTTPQQGYRILEAESPQGGAIDSGGAGSVGGIGSSGGGYHVLEAPTVVPGSAQRSAASEVLEKA
fly              PPPPPQS-------------------------------------------------------------------------------APPQLTEQA
mansoni          MESSARL-------------------------------------------------------------------------------A-HETLERA
viverrini        TLPSGDY-------------------------------------------------------------------------------L-CHPYAEN
sinensis         IHPSGDY-------------------------------------------------------------------------------L-CHPYAES
anemone          MKKRKDL-------------------------------------------------------------------------------A-TKTLQRA
Trichoplax       -SMASSY-------------------------------------------------------------------------------A-SDVLERS
urchin           GGGGGET-------------------------------------------------------------------------------AMSSPYQPC
Saccoglossus     VSSSCSL-------------------------------------------------------------------------------A-SEVLERA
ciona            ----NAS-------------------------------------------------------------------------------A-AKLLERS
telata           VASSCSV-------------------------------------------------------------------------------A-SEIFERA
Medaka           -SAP----------------------------------------------------------------------------------------------
tilapia          -AASCST-------------------------------------------------------------------------------A-SAVLERA
stickleback      -AASCSA-------------------------------------------------------------------------------A-SVVLERA
molly            -PVLCLH-------------------------------------------------------------------------------L-SFH----
platyfish        -AASCSA-------------------------------------------------------------------------------A-SAVLERA
mouse            -AVSSLR-------------------------------------------------------------------------------A-FQTLARA
human            -AASSLR-------------------------------------------------------------------------------A-FQTLARA
cat              -AASSLQ-------------------------------------------------------------------------------A-FQTLARA
cattle           -AASSLQ-------------------------------------------------------------------------------A-FQTLARA
python           -AVSGSF-------------------------------------------------------------------------------A-SQVLERA
chick            -AASSSL-------------------------------------------------------------------------------A-SQILERA
xenopus          -AATGSL-------------------------------------------------------------------------------A-SQVLERA
shark            -AASSTL-------------------------------------------------------------------------------A-SQVLERA
gar              -AASSSL-------------------------------------------------------------------------------A-SEILERA
zebrafish        -AASCSM-------------------------------------------------------------------------------A-SEVLGRA
tetra            -AASCSM-------------------------------------------------------------------------------A-SEVLDRA
cavefish         -AASCSM-------------------------------------------------------------------------------A-SEVLDRA
limpet           IASSCSY-------------------------------------------------------------------------------A-SEILERS
oyster           IASSCSL-------------------------------------------------------------------------------A-SEVYERA
aplysia          VASSGSL-------------------------------------------------------------------------------A-SEVLERA
Clustal Consensus

                         1710      1720      1730
                 ....|....|....|....|....|....|....
daphnia          RTRFDRFWTKKESDK-------------------
silkworm         ---------------------------------
butterfly        RTRFDKFWGKKEDDV-------------------
bee              RNRFDKFWGKGSGSEN------------------
fly              KMDGKPLSTLQ-----------------------
mansoni          QKQHERILREQKQYNENIYSPNAYSECECKRIEI
viverrini        HEYRS--WDYI-----------------------
sinensis         QEYRS--WNYI-----------------------
anemone          RNRGARF---------------------------
Trichoplax       KQRKENFWGRK-----------------------
urchin           PMHPAAV---------------------------
Saccoglossus     RRRRDEFWGKQPSVQTK-----------------
ciona            MQR-QDFWANK-----------------------
```

```
telata             KKRRDLFWAPNGENSDVSHRHRIMLLVGTSTHGS
Medaka             ----------------------------------
tilapia            QKRREDFWGKR-----------------------
stickleback        QKRREHFWGKR-----------------------
molly              ----------------------------------
platyfish          QKRREDFWGKR-----------------------
mouse              QKRKENFWGKP-----------------------
human              KKRKENFWGKT-----------------------
cat                QKRKENFWGKT-----------------------
cattle             QKRKENFWGKT-----------------------
python             QRRKENFWGKM-----------------------
chick              QKRKEDFWGKT-----------------------
xenopus            QRRKEDFWGKK-----------------------
shark              QMRRDSFWGKNPRNEQ------------------
gar                QRRKENFWGKS-----------------------
zebrafish          QRRKQEFWGKS-----------------------
tetra              QRRKEDFWGKT-----------------------
cavefish           QRRKEDFWGKT-----------------------
limpet             KDRRDNFWNNNTRVPTK-----------------
oyster             QKRTQEFWGKDG-IASR-----------------
aplysia            RKR-QEFWNKKDS---------------------
Clustal Consensus
```