

A

Human RNASET2
HvRNASET2

B

Local Quality Estimate

Predicted Local Similarity to Target

Residue Number

HvRNASET2 QMEANDisCo

C

D

E

F

Protein	Sequence	Position
Actbind	1 -MSFLPSVGMALGAMQLS--SGAL----ATIDTCSSDSPLSQOTDNEASCCFNPSGGSLLOTQFQVDY-----PS--DGPSGSSNTIHLVFNQNC	81
Human	1 -MRPAALRG-ALLGCLCLAL--L-----CLGGADKRLRD-----NHGWKLIIMVQHAPETVCEKIQN-----DCRDP--PDYNTIHLVFPKKS	72
T.curvispic	1 ----MRK-YSI-ASCI-VLLYL-LTHGIYFNTREYRKQT-----SNEFDVLI FTQQAPLTACFWKNKSDTRSCSLPR-HDENTIHLVIMPTKY	81
Hydra	1 MFAFQQLTI-FVLI-AMLMRMFEGLPVPVNIHQETSNPKVNI-----AVEVDYFMLVTEWPGSSCYVYVATHQHHTTCYIPDAVIGNTIHLVLPVSE	88
Hirudo	1 -----MLL-SVCFVLLASY-----CTARPLK-----BELVDHFVFTQWPOSIQNELDY-TEEEECMLPEKTIHMLHGLWPSYQ	68
C.gigas	1 -----MLALLLIQL-----CATYSAY-----SDMDIFTYQWNPVAVCIKGG-----EEHTCTIPFGVQGLIHLWVTKT	63
Actbind	82 DGTGYCEYCDSESYNSITSILEAQNRTELLSYMKWVDPVEGA-DEDESPWEHGWKHTGQINTIEPSCTDYIAQEEVGDFQGVVLDKFTLDSYALSDA	182
Human	73 EG-----CNRSWPF-----NLEEIKDILPEMRAWPDVISHFPNRSFVWKHWEKHGTCAAGVDA-----LNSQKYFGRSLELYRELDNSVLLKL	154
T.curvispic	82 NTLGPOFOKSLVF-----NPSAIPISSELKEMALDIHKQ-SKPIFWKHEDKHOTDAVTYKA-----LWNEFPVFEASGLFDKYIMMDVLA	167
Hydra	89 KGQOPFFCEPW-KF-----DEKVKDLEGNLELWPNIFVE-TTPQSPW-HSEYKHGTGASSVKG-----FETEDHYFQKALELREKFDIMRVLS	153
Hirudo	69 NTRGNPFCTKD-KF-----NESLISPLEDOLIIMPNLKPNI-TGKYSPWKHGWKHTGCLSMDE-----LDSELKYFKVLELHKTDFVMKGLKEA	173
C.gigas	64 GTEGPTSCGTG-PF-----HADAITPILPHLIKIMPNMYAD-TSVYSPWEHGWKHTGCLASSLNA-----TSTERYFSKALDLYARFNGQITLANQ	148
Actbind	183 G1TPSEDAITYKLSIDEDALAAIHGVPYVYVCGEDG-----ALSQLYYYFNIVKGSAG1GGTYVASERLEDNSCKDSG1KYPPIKYSKKI1YGGSL	270
Human	155 G1KPSIN-YYQADFQKDALARYGV1PK1I-QCLPPSQDEEVQTIQIIECLCTKQDQOLQNTCEP-----GEQ-----PSPKQE--WLANGAAES	235
T.curvispic	168 N1LPGNK--YMWQMLKG1QK1LNTRGQ1-MCVTDK-THESYVIEMLRCFDKTLQVNCDG1Y--HFPTNCRSKELIYPSHVPH--YYVTQT	252
Hydra	174 K1VPSTSSYQFSDIEALKSOYSKACVF-ECSQIK--HSQQVLSAGYVCLNKOLEQIDCGYCE-----HGCKTDEPIFYHKS--NLYESVVA	258
Hirudo	154 GFGPSDKDSYQEDLDALESV1GVKGM1-MCYNPRN-EPLQYLAQIEFLCKDSFQPMCPCHPS-----YEASLENPDQSLHRS1--DFESTVLESKERN	244
C.gigas	149 G1VPSQTATYDIKTSEALKKELGVNALI-QCTYDHN-TSRQV1YE1E1CLSKNIFPVDCYFDE-----GNTSGKRSHH--HH--KYSS	226
Actbind	236 -----RGLRVCEGDPVYFPPPKTKH-----	256
Human	245 LHKVLMKRIHNKNTNTFTGORSQGEFKMRELRI1ICSDKKEIMYP1IDHWQMIQHSNS	304
Hydra	227 -----HPHSSCPESYGFYPP1IDGVYSNP1-----	251

Figure S1. (A) Three-dimensional alignment of human RNASET2 (in cyan) and *H. verbana* HvRNASET2 (in orange). The secondary structures (β -strands and α -helix) appear extremely conserved. (B) Graphical representation of the HvRNASET2 QMEANDisCo score. The plot shows the precise QMean value of every amino acid. (C-E) Alternative three-dimensional models of HvRNASET2 obtained with the following servers for 3D structures prediction: Phyre2 (C), Robetta-Baker Lab (D) and RaptorX Contact Predict (E). Of note, the antimicrobial peptide (QVLKMRIHNKNNNTNTFT), represented in orange, is specifically localized on the external surface of the enzyme. (F) Multiple sequence alignments. The HvRNASET2 amino acid sequence has been

compared with all the sequences considered in the Figure 1. The complete alignment confirms that the conserved active sites (CAS I and CAS II) are extremely preserved. Different blue shades identify the diverse conservation of each amino acid.