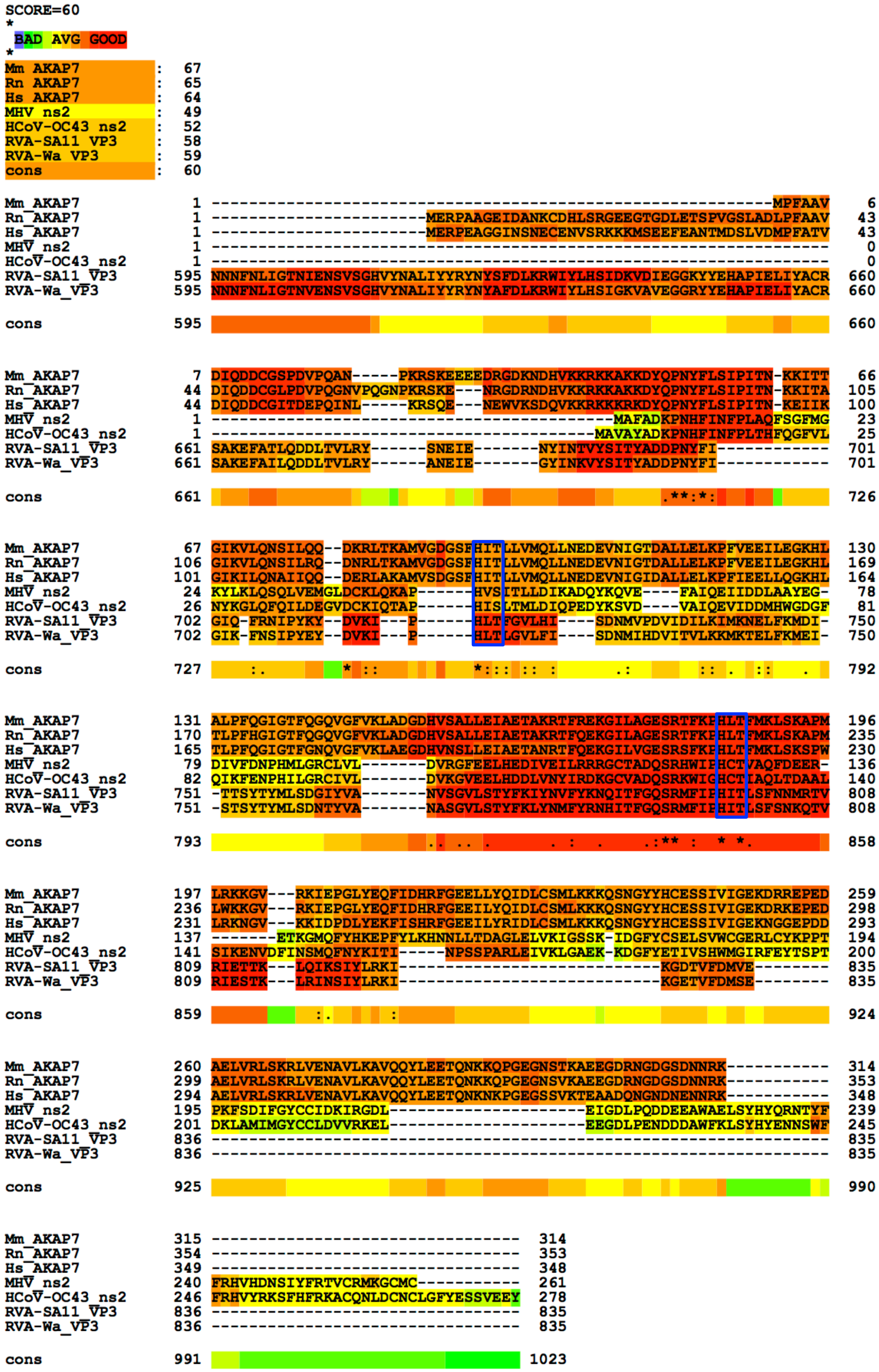
Figure S1.



```
SCORE=60
 *
 BAD AVG GOOD
 *
Mm AKAP7         :  67
Rn AKAP7         :  65
Hs AKAP7         :  64
MHV ns2          :  49
HCoV-OC43 ns2    :  52
RVA-SA11 VP3     :  58
RVA-Wa VP3       :  59
cons             :  60

Mm_AKAP7          1 ------------------------------------------------------------MPFAAV    6
Rn_AKAP7          1 -----------------------MERPAAGEIDANKCDHLSRGEEGTGDLETSPVGSLADLPFAAV   43
Hs_AKAP7          1 -----------------------MERPEAGGINSNECENVSRKKKMSEEFEANTMDSLVDMPFATV   43
MHV_ns2           1 ------------------------------------------------------------------    0
HCoV-OC43_ns2     1 ------------------------------------------------------------------    0
RVA-SA11_VP3    595 NNNFNLIGTNIENSVSGHVYNALIYYRYNYSFDLKRWIYLHSIDKVDIEGGKYYEHAPIELIYACR  660
RVA-Wa_VP3      595 NNNFNLIGTNVENSVSGHVYNALIYYRYNYAFDLKRWIYLHSIGKVAVEGGRYYEHAPIELIYACR  660

cons            595                                                                     660


Mm_AKAP7          7 DIQDDCGSPDVPQAN-----PKRSKEEEEDRGDKNDHVKKRKKAKKDYQPNYFLSIPITN-KKITT   66
Rn_AKAP7         44 DIQDDCGLPDVPQGNVPQGNPKRSKE---NRGDRNDHVKKRKKAKKDYQPNYFLSIPITN-KKITA  105
Hs_AKAP7         44 DIQDDCGITDEPQINL-----KRSQE---NEWVKSDQVKKRKKKRKDYQPNYFLSIPITN-KEIIK  100
MHV_ns2           1 -------------------------------------------MAFADKPNHFINFPLAQFSGFMG   23
HCoV-OC43_ns2     1 -----------------------------------------MAVAYADKPNHFINFPLTHFQGFVL   25
RVA-SA11_VP3    661 SAKEFATLQDDLTVLRY------SNEIE-------NYINTVYSITYADDPNYFI------------  701
RVA-Wa_VP3      661 SAKEFAILQDDLTVLRY------ANEIE-------GYINKVYSITYADDPNYFI------------  701

cons            661                                                 .**:*:              726


Mm_AKAP7         67 GIKVLQNSILQQ--DKRLTKAMVGDGSFHITLLVMQLLNEDEVNIGTDALLELKPFVEEILEGKHL  130
Rn_AKAP7        106 GIKVLQNSILRQ--DNRLTKAMVGDGSFHITLLVMQLLNEDEVNIGTDALLELKPFVEEILEGKHL  169
Hs_AKAP7        101 GIKILQNAIIQQ--DERLAKAMVSDGSFHITLLVMQLLNEDEVNIGIDALLELKPFIEELLQGKHL  164
MHV_ns2          24 KYLKLQSQLVEMGLDCKLQKAP------HVSITLLDIKADQYKQVE----FAIQEIIDDLAAYEG-   78
HCoV-OC43_ns2    26 NYKGLQFQILDEGVDCKIQTAP------HISLTMLDIQPEDYKSVD----VAIQEVIDDMHWGDGF   81
RVA-SA11_VP3    702 GIQ-FRNIPYKY--DVKI---P------HLTFGVLHI----SDNMVPDVIDILKIMKNELFKMDI-  750
RVA-Wa_VP3      702 GIK-FNSIPYEY--DVKI---P------HLTLGVLFI----SDNMIHDVITVLKKMKTELFKMEI-  750

cons            727     :.        * ::          *::: :: :      .:       :: .  ::   .    792


Mm_AKAP7        131 ALPFQGIGTFQGQVGFVKLADGDHVSALLEIAETAKRTFREKGILAGESRTFKPHLTFMKLSKAPM  196
Rn_AKAP7        170 TLPFHGIGTFQGQVGFVKLADGDHVSALLEIAETAKRTFQEKGILAGESRTFKPHLTFMKLSKAPM  235
Hs_AKAP7        165 TLPFQGIGTFGNQVGFVKLAEGDHVNSLLEIAETANRTFQEKGILVGESRSFKPHLTFMKLSKSPW  230
MHV_ns2          79 DIVFDNPHMLGRCLVL-------DVRGFEELHEDIVEILRRRGCTADQSRHWIPHCTVAQFDEER-  136
HCoV-OC43_ns2    82 QIKFENPHILGRCIVL-------DVKGVEELHDDLVNYIRDKGCVADQSRKWIGHCTIAQLTDAAL  140
RVA-SA11_VP3    751 -TTSYTYMLSDGIYVA-------NVSGVLSTYFKIYNVFYKNQITFGQSRMFIPHITLSFNNMRTV  808
RVA-Wa_VP3      751 -STSYTYMLSDNTYVA-------NASGVLSTYFKLYNMFYRNHITFGQSRMFIPHITLSFSNKQTV  808

cons            793                        .. .. .      . :  .    .:** :  * *.         858


Mm_AKAP7        197 LRKKGV---RKIEPGLYEQFIDHRFGEELLYQIDLCSMLKKKQSNGYYHCESSIVIGEKDRREPED  259
Rn_AKAP7        236 LWKKGV---RKIEPGLYEQFIDHRFGEEILYQIDLCSMLKKKQSNGYYHCESSIVIGEKDRKEPED  298
Hs_AKAP7        231 LRKNGV---KKIDPDLYEKFISHRFGEEILYRIDLCSMLKKKQSNGYYHCESSIVIGEKNGGEPDD  293
MHV_ns2         137 -------ETKGMQFYHKEPFYLKHNNLLTDAGLELVKIGSSK-IDGFYCSELSVWCGERLCYKPPT  194
HCoV-OC43_ns2   141 SIKENVDFINSMQFNYKITI-----NPSSPARLEIVKLGAEK-KDGFYETIVSHWMGIRFEYTSPT  200
RVA-SA11_VP3    809 RIETTK---LQIKSIYLRKI----------------------------KGDTVFDMVE--------  835
RVA-Wa_VP3      809 RIESTK---LRINSIYLRKI----------------------------KGETVFDMSE--------  835

cons            859            :.      :                                              924


Mm_AKAP7        260 AELVRLSKRLVENAVLKAVQQYLEETQNKKQPGEGNSTKAEEGDRNGDGSDNNRK-----------  314
Rn_AKAP7        299 AELVRLSKRLVENAVLKAVQQYLEETQNKKQPGEGNSVKAEEGDRNGDGSDNNRK-----------  353
Hs_AKAP7        294 AELVRLSKRLVENAVLKAVQQYLEETQNKNKPGEGSSVKTEAADQNGNDNENNRK-----------  348
MHV_ns2         195 PKFSDIFGYCCIDKIRGDL---------------------EIGDLPQDDEEAWAELSYHYQRNTYF  239
HCoV-OC43_ns2   201 DKLAMIMGYCCLDVVRKEL---------------------EEGDLPENDDDAWFKLSYHYENNSWF  245
RVA-SA11_VP3    836 ------------------------------------------------------------------  835
RVA-Wa_VP3      836 ------------------------------------------------------------------  835

cons            925                                                                     990


Mm_AKAP7        315 ---------------------------------  314
Rn_AKAP7        354 ---------------------------------  353
Hs_AKAP7        349 ---------------------------------  348
MHV_ns2         240 FRHVHDNSIYFRTVCRMKGCMC-----------  261
HCoV-OC43_ns2   246 FRHVYRKSFHFRKACQNLDCNCLGFYESSVEEY  278
RVA-SA11_VP3    836 ---------------------------------  835
RVA-Wa_VP3      836 ---------------------------------  835

cons            991                                    1023
```

Figure S1. Conservation of 2',5'-phosphodiesterases among distantly related taxa. Selected mammalian AKAP7 (mouse NP_061217.3, rat NP_001001801.1, human NP_057461.2), coronavirus ns2 (mouse MHV P19738.1, human HCoV-OC43 AAT84352.1) and group A rotavirus VP3 C-terminal domain (simian RVA-SA11 AFK09591.1, human RVA-Wa AFR77808.1) proteins. Alignment was performed with the Constraint-based Multiple Alignment Tool (COBALT) (1) set on default parameters and subsequently evaluated with T-Coffee Core to assess local reliability of the alignment by pairwise methods utilizing multiple algorithms (Mfast_pair, Mmafft_msa and Mmuscle_msa) (2, 3). To convey confidence in the alignment, scores indicate the percent agreement between all MSA algorithms utilized in the analysis for each protein and for the consensus sequence. Additionally, color-coding indicates positional confidence of each aligned residue based on agreement between MSA algorithms with blue indicating the least and red indicating the greatest confidence in the alignment. Conservation of sequence is indicated by Clustal MSA symbols in the consensus line (cons) with "*****" indicating fully conserved, "**:**" strong conservation of properties and "**.**" weak conservation of properties. Catalytic HxT motifs highlighted (blue boxes).

1. **Papadopoulos JS, Agarwala R.** 2007. COBALT: constraint-based alignment tool for multiple protein sequences. Bioinformatics **23:**1073-1079.
2. **Notredame C, Higgins DG, Heringa J.** 2000. T-Coffee: A novel method for fast and accurate multiple sequence alignment. J Mol Biol **302:**205-217.
3. **Di Tommaso P, Moretti S, Xenarios I, Orobitg M, Montanyola A, Chang JM, Taly JF, Notredame C.** 2011. T-Coffee: a web server for the multiple sequence alignment of protein and RNA sequences using structural information and homology extension. Nucleic Acids Res **39:**W13-17.