FIGURE S1 (related to Figure 1)

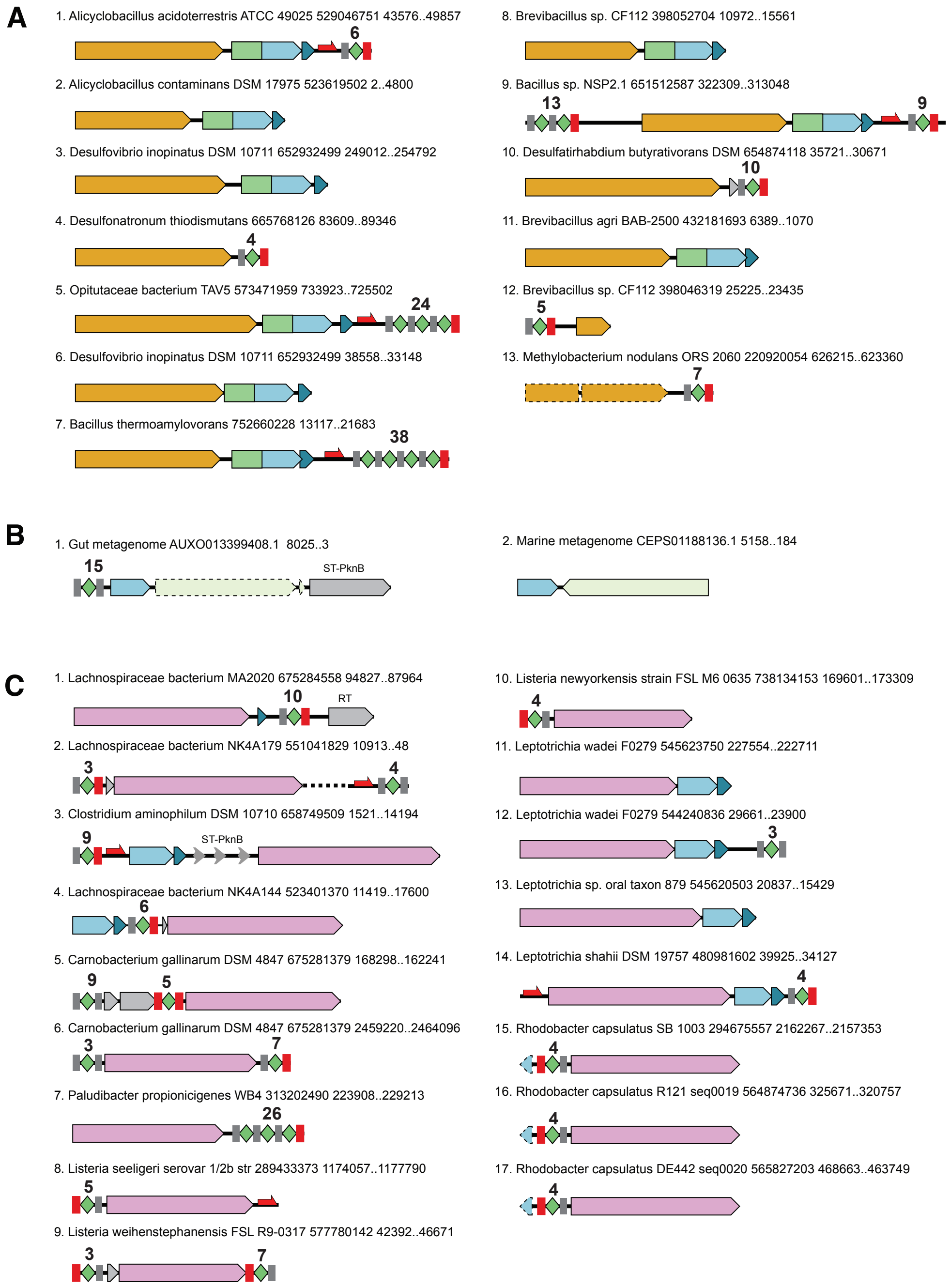

Figure S1 | Genomic architectures of all identified candidate novel CRISPR-Cas loci.

(**A**) The C2c1 loci (subtype V-B). (**B**) The C2c3 loci (subtype V-C). (**C**) The C2c2 loci (type VI). Genes are colored according to the schematic in Figure 2. The number of repeats in CRISPR arrays is indicated. For each genomic contig, Genbank numeric ID and the coordinates of the locus are indicated. Additional designations: ST-PknB, serine/threonine protein kinase; RT, reverse transcriptase.

FIGURE S2 (related to Figure 1)

```
Listeria_weihenstephanensis TGGCTGCTGAGCTGTCTCTTAATTTATGAAAAAATAATTATGTTTTGCTAATCTGTCAAGCTGCAGATTCATTAATAATCTGGTATAGTTATGTTGTTGCAAGCGAATAGGCGGATATATTACCTCAAAACAGAAGAGGA
Listeria_newyorkensis       TGTATTCTGAGTTGTCTCTTAATTTATGAAAAAATAATTATGTTTTGGTAATCTGTCAAGATGCAGATCCATTAATAATCTGGTATAGTTATGTTGTTGCAAG--------TGAATATATTACCTCAAAATAAAAGAGGA

Listeria_weihenstephanensis CTAAAACCCAAACGATTGGTGTTACATTATTTTCATAGATTTAGAGTACCTCAAAACAGAAGAGGACTAAAACGCACTCTCCGACAATAATCTCGTCCATTTTGATTTAGAGTACCTCAAAACAAAAGAGGACTAAAACA
Listeria_newyorkensis       CTAAAACTAATTGGTGGCGTGATACGCCGTAATGCTTGATTTAGAGTACCTCAAAACAAAAGAGGACTAAAAC-TACTTGTCGATATGGTATAGCTTTTTTCAGATTTAGAGTACCTCAAAACAAAAGAGGACTAAAACT

Listeria_weihenstephanensis ACTCTGTACTTGTGAAGTACGTTAAATCCGATTTAGAGTACCTCAAAACAAAAGAGGACTAAAAC------------------------------------------------------------------CTCTTTTGT
Listeria_newyorkensis       AAAGCTTCTAAATGGTGGCGCGTTACGCCGATTTAGAATACCTCAAAACAAAAGAGGACTAAAACCTAGCAAGCCGGTCGCCGCGCTCAAAGTAAGATTTAGAGTACCTCAAAACAAAAGAGGACTAAAACCTCTTTTGT

Listeria_weihenstephanensis GGATAAGTATTCGAAATAAAGCCATAAAAACTGTGATCCAAAGAACTGGATTATTGGTTTTTATGGCTTTATTCAATTCTTAGTATTGTAGATGAACTGTCAGCGAATGTTGTCTTGCAACGTGCCTTCTTGTATAATGA
Listeria_newyorkensis       GGATAAGTATTCGAAATAAAGCCATAAAAACTGTGATCCAAAGAGCTGGATTATTGGTTTTTATGGCTTTATTCAATTCTTAGTATTGTAGATGAACCATCAGTGAATGTTGTCTTGCAACGTGCCTTCTTGTATAATGA

Listeria_weihenstephanensis ATATATTGATAAATAATAGAAATTTCATACACGCATGAAGAAACCAATTAAAGTTTCAGCAATAATGAAGCATTAGGTACATGACTATAAAACCAAATGGAGCTGAGTAGACAGATGAAAATCACAAAGATGAGAGTAGA
Listeria_newyorkensis       ATATATTGATAAATAATAGAAATTTCATACACGCATGAAGAAACCAATTAAATTTTCAGCATTAATGAAGCATTAGGTACATGACTATAAAACCAAATGGAGCTGAGTAGACAGATGAAAATCACAAAGATGAGAGTAGA

Listeria_weihenstephanensis TGGAAGAACTATCGTAATGGAGAGGACAAGTAAGGAAGGTCAACTGGTTTATGAAGGTATCGATGGAAATAAGACAACAGAAATTATATTTGATAAGAAAAAAGAATCGTTTTATAAGAGTATCCTCAATAAAACTGTGA
Listeria_newyorkensis       TGGAAGAACTATCGTAATGGAGAGGACAAGCAAGGAAGGTCAACTGGGTTATGAAGGTATCGATGGAAATAAGACAACAGAAATTATATTTGATAAGAAAAAAGAGTCATTTTATAAGAGTATCCTCAATAAAACTGTGA

Listeria_weihenstephanensis GAAAACCTGATGAAAAAAGAAAAAAAATAGGCGTAAGCAGGCAATTAATAAAGCGATTAATAAAGAAATAACAGAATTAATGTTGGCGCTGTTACATCAAGAAGTGCCAAGCCAAAAGTTACATAATTTAAAGAGTCTAA
Listeria_newyorkensis       GAAAACCCGATGAAAAA--GAAAAGAATAGGCGTAAGCAGGCAATTAATAAAGCGATTAATAAAGAAATAACAGAATTAATGTTGGCGGTGTTACATCAAGAAGTGCCAAGCCAAAAGTTACATAATTTAAAGAGTCTAA

Listeria_weihenstephanensis ATACGGAATCTTTAACTAAACTATTTAAACCGAAGTTCCAAAACATGATTTCTTATCCGCCTAGCAAAGGTGCCGAACATGTTCAATTTTGCCTTACAGATATAGCGGTACCAGCGATTCGAGATTTAGATGAAATTAAG
Listeria_newyorkensis       ATACGGAATCTTTAACTAAACTATTTAAACCGAAGTTCCAAAACATGATTTCTTATCCGCCTAGCAAAGGTGCCGAACATGTTCAGTTTTGCCTTACAGATATAGCGGTACCAGCGATTCGAGATTTAGATGAAATTAAG

Listeria_weihenstephanensis CCAGATTGGGGCATTTTTTTTGAAAAATTGAAACCCTATACGGATTGGGCAGAATCATACATTCACTATAAGCAGACAACCATACAGAAATCCATTGAGCAAAACAAAATACAGTCCCCTGATTCGCCAAGGAAATTAGT
Listeria_newyorkensis       CCAGATTGGGGCATTTTTTTTGAAAAATTGAAACCCTATACGGATTGGGCAGAATCATACATTCACTATAAGCAGACAACCATACAGAAATCCATTGAGCAAAACAAAATACAGTCCCCTGATTCGCCAAGGAAATTAGT

Listeria_weihenstephanensis ATTGCAAAAATATGTCACAGCCTTTTTGAATGGAGAACCGCTGGGACTCGATCTTGTGGCGAAAAAATATAAACTGGCAGACTTAGCGGAGTCGTTTAAAGTAGTAGATTTGAACGAGGATAAAAGTGCAAACTATAAAA
Listeria_newyorkensis       ATTGCAAAAATATGTCACAGCCTTTTTGAATGGAGAACCGCTGGGACTCGATCTTGTGGCGAAAAAATATAAACTGGCAGACTTAGCGGAGTCGTTTAAATTAGTAGATTTGAACGAGGATAAAAGTGCAAACTATAAAA

Listeria_weihenstephanensis TTAAAGCGTGCTTGCAACAACATCAGCGAAATATTTTGGATGAATTGAAAGAAGATCCAGAGTTAAATCAATATGGTATAGAAGTGAAGAAGTATATACAGCGATATTTCCCAATCAAACGTGCACCGAATAGAAGTAAA
Listeria_newyorkensis       TTAAAGCGTGCTTGCAACAACATCAGCGAAATATTTTGGATGAATTGAAAGAAGATCCGGAGTTAAATCAATATGGTATAGAAGTGAAGAAATATATACAGCGATATTTCCCAATCAAACGTGCACCGAATAGAAGTAAA

Listeria_weihenstephanensis CATGCGCGAGCGGACTTTTTGAAAAAGGAATTAATTGAGTCTACAGTGGAGCAGCAATTTAAAAATGCTGTATATCATTATGTACTGGAACAAGGAAAAATGGAGGCATATGAGCTAACAGATCCTAAAACAAAAGACTT
Listeria_newyorkensis       CATGCACGAGCGGACTTTTTGAAAAAGGAATTAATTGAGTCTACAGTGGAGCAACAATTTAAAAATGCTGTATATCATTATGTACTGGAACAAGGCAAAATGGAGGCATATGAGCTAACAGATCCTAAAACAAAAGACTT

Listeria_weihenstephanensis GCAGGATATTAGATCTGGTGAGGCATTTAGCTTCAAATTTATTAATGCTTGCGCCTTCGCATCCAATAATTTGAAGATGATTTTAAACCCTGAATGTGAAAAGGATATTTTAGGTAAGGGCGATTTTAAAAAGAATTTGC
Listeria_newyorkensis       GCAGGATATTAGATCTGGTGAGGCATTTAGCTTCAAATTTATTAATGCTTGCGCCTTCGCATCGAATAATTTGAAGATGATTTTAAACCCTGAATGTGAAAAGGATATCCTAGGTAAGGGCAATTTTAAAAAGAATTTGC

Listeria_weihenstephanensis CAAACAGTACTACGCAGTCTGATGTTGTGAAAAAAATGATTCCTTTTTTCTCGGATGAGATTCAAAATGTGAATTTTGATGAAGCTATCTGGGCGATTAGGGGCTCTATTCAGCAAATTAGAAATGAGGTTTACCATTGC
Listeria_newyorkensis       CAAACAGTACTACGCGATCTGATGTTGTGAAGAAAATGATTCCCTTTTTCTCGGATGAGCTTCAAAATGTGAATTTTGATGAAGCTATCTGGGCGATTAGGGGCTCTATTCAGCAAATTAGAAATGAGGTTTACCATTGT

Listeria_weihenstephanensis AAAAAGCATTCTTGGAAAAGCATACTTAAAATAAAAGGCTTTGAATTTGAACCTAACAATATGAAATATACGGATTCTGATATGCAAAAATTGATGGATAAAGATATCGCCAAAATTCCAGACTTCATCGAAGAAAAACT
Listeria_newyorkensis       AAAAAGCATTCTTGGAAAAGCATACTTAAAATAAAAGGCTTTGAATTTGAACCTAACAATATGAAATATGCGGATTCTGATATGCAAAAATTGATGGATAAAGATATCGCCAAAATTCCAGAGTTCATCGAAGAAAAACT

Listeria_weihenstephanensis TAAAAGTAGTGGGATAATAAGGTTCTACAGTCATGATAAATTGCAGTCTATCTGGGAAATGAAGCAAGGGTTTTCGTTGTTGACTACTAATGCGCCGTTTGTCCCAAGCTTTAAACGTGTCTACGCAAAAGGGCACGACT
Listeria_newyorkensis       TAAAAGTAGTGGAGTAGTAAGGTTCTACAGGCATGATGAGTTGCAATCCATATGGGAAATGAAACAAGGATTTTCGTTGCTGACTACTAATGCGCCGTTTGTCCCAAGCTTTAAGCGTGTCTACGCAAAAGGGCACGACT

Listeria_weihenstephanensis ACCAAACTTCTAAAAATAGATATTATGATTTAGGTTTGACTACTTTTGATATTTTGGAATATGGAGAAGAAGATTTTCGTGCACGCTATTTCCTGACGAAGCTAGTTTATTATCAACAATTTATGCCATGGTTTACAGCT
Listeria_newyorkensis       ACCAAACTTCTAAAAATAGATACTATAATTTGGATTTGACTACTTTTGATATTTTGGAATATGGAGAAGAAGATTTTCGTGCACGCTATTTCCTGACGAAGCTAGTTTATTATCAGCAATTTATGCCATGGTTTACAGCT

Listeria_weihenstephanensis GATAATAATGCTTTCCGAGATGCTGCCAATTTTGTATTGCGATTAAATAAAAATAGACAGCAGGATGCAAAAGCTTTTATTAACATTAGAGAAGTTGAAGAAGGTGAGATGCCTAGAGACTATATGGGCTATGTCCAAGG
Listeria_newyorkensis       GATAATAATGCTTTCCGAGATGCTGCCAATTTTGTATTGCGATTAAATAAAAATAGACAGCAGGATGCAAAAGCTTTTATTAACATTAGAGAAGTTGAAGAAGGTGAGATGCCTAGAGACTATATGGGTTATGTCCAAGG

Listeria_weihenstephanensis TCAAATAGCGATACATGAGGATTCAACTGAGGATACACCGAATCATTTTGAAAAATTTATTAGCCAGGTTTTTATTAAGGGATTTGATAGTCATATGAGATCTGCTGATTTAAAATTTATTAAAAATCCAAGAAATCAGG
Listeria_newyorkensis       TCAAATAGCGATACATGAGGATTCAATTGAGGATACACCGAATCATTTTGAGAAATTTATTAGTCAGGTTTTTATTAAGGGCTTTGATAGGCATATGAGATCTGCTAATTTAAAATTTATTAAAAATCCAAGAAATCAGG

Listeria_weihenstephanensis GGCTAGAACAAAGTGAAATTGAGGAAATGAGCTTTGATATTAAAGTAGAGCCATCATTTTTGAAAAATAAAGATGACTATATTGCATTTTGGACATTCTGCAAAATGCTGGATGCTAGGCATTTAAGCGAGCTAAGAAAC
Listeria_newyorkensis       GGCTAGAACAAAGTGAGATTGAGGAAATGAGCTTTGATATTAAAGTGGAGCCGTCATTTTTGAAAAATAAAGATGACTATATTGCATTTTGGATATTCTGCAAAATGCTTGATGCTAGGCATTTAAGCGAGCTAAGAAAC

Listeria_weihenstephanensis GAAATGATTAAGTATGACGGTCATTTAACTGGAGAACAAGAAATCATTGGTTTAGCATTGCTTGGAGTGGATTCACGAGAGAATGATTGGAAGCAATTTTTTAGCTCAGAACGGGAATACGAGAAAATTATGAAGGGCTA
Listeria_newyorkensis       GAAATGATTAAGTATGACGGTCATTTAACTGGAGAACAAGAAATCATTGGTTTAGCATTGCTCGGAGTGGATTCACGAGAGAATGATTGGAAGCAGTTTTTTAGCTCAGAACGGGAATACGAGAAAATTATGAAGGGCTA

Listeria_weihenstephanensis TGTTGGAGAGGAATTGTATCAGCGGGAACCGTACCGACAAAGTGATGGCAAAACACCGATTCTTTTTCGTGGTGTAGAGCAAGCGAGGAAGTATGGTACTGAAACAGTGATTCAACGGCTTTTTGATGCTAGTCCTGAGT
Listeria_newyorkensis       TGTTGTAGAGGAATTGTATCAGCGGGAACCGTACCGACAAAGTGATGGCAAAACACCGATTCTTTTTCGTGGTGTAGAGCAAGCGAGGAAGTATGGTACTGAAACAGTGATTCAACGGCTTTTTGATGCTAATCCTGAGT
```

Figure S2. Alignment of *Listeria* loci encoding putative Type VI CRISPR-Cas system.

The aligned syntenic region corresponds to *Listeria weihenstephanensis* FSL R9-0317 contig AODJ01000004.1, coordinates 42281-46274 and *Listeria newyorkensis* strain FSL M6-0635 contig JNFB01000012.1, coordinates 169489-173541. Color coding: C2c2 gene is highlighted by blue, CRISPR repeats - red, degenerated repeat – magenta, spacers - bold.

FIGURE S3 (related to Figure 2)

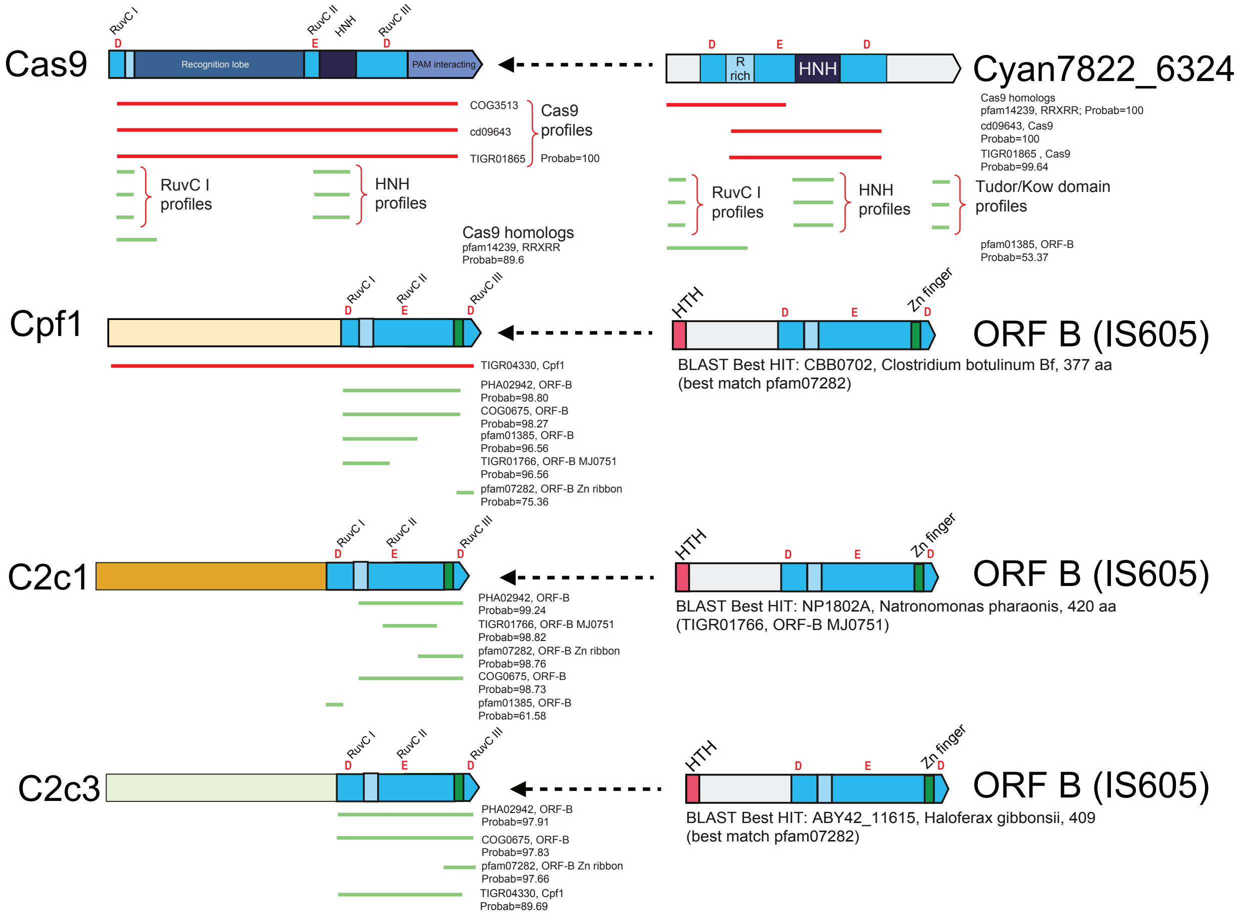

Figure S3 | The closest homologs of the new type V effector proteins among the transposon-encoded proteins: non-overlapping sets of homologs.

FIGURE S4 (related to Figure 2)

```
544884152_Alicyclobacillus_acidoterrestris         ------------------------MAVKSIKVKLRLDDMPE---IRAG------LWKLHKEVNAGVRYYTEWLSLLRQEN---LYRRSPNGDGEQECDKT
652589596_Alicyclobacillus_contaminans             ----------------------------------------------------------------------------------------------------
652932497_Desulfovibrio_inopinatus                 ------------------------MPTRTINLKLVLGKNPENATLRRA------LFSTHRLVNQATKRIEEFLLLCRGEA------YRTVDNEGKEAEIP
667765471_Desulfonatronum_thiodismutans            ---------------------------------MVLGRKDDTAELRRA------LWTTHEHVNLAVAEVERVLLRCRGRS---YWTLDR---RGDPVHVP
497199019_Opitutaceae_bacterium_TAV5               ------------------MSLNRIYQGRVAAVETGTALAKGNVEWMPAAGGDEVLWQHHELFQAAINYYLVALLALADKNNPVLGPLISQMDNPQSPYHV
654153037_Tuberibacillus_calidus                   ------------------------MATKSFILKMKTKNNPQ---LRLS------LWKTHELFNFGVAYYMDLLSLFRQKD---LYMHNDE-DPDHPVVLK
754485389_Bacillus_thermoamylovorans               ------------------------MATRSFILKIEP--NEE---VKKG------LWKTHEVLNHGIAYYMNILKLIRQEA---IYEHHEQ-DPKNPKKVS
495056180_Brevibacillus_sp-_CF112                  ----------------------------------------------------------------------------------------------------
651512544_Bacillus_sp-_NSP2-1                      ------------------------MAIRSIKLKLKTHTGPEAQNLRKG------IWRTHRLLNEGVAYYMKMLLLFRQES---TGERPKEELQEELICHI
Secondary_structure_for_651512544_(Jpred)          *---------------------------EEEEEEEE----HHHHHHHH------HHHHHHHHHHHHHHHHHHHHHHH-----------HHHHHHHHHHHH
654874074_Desulfatirhabdium_butyrativorans         ----------------MPLSNNPPVTQRAYTLRLR-GADPSDLSWREA------LWHTHEAVNKGAKVFGDWLLTLRGGLDHTLADTKVKGGKGKPDRDP
652569729_Alicyclobacillus_herbarius               MLKQAVLGNGPLINWEKNVKRGKGMATKSIKVKLRLGKHPD---IRAG------IWQLHKAANAGVRYYTEWLSLMRQKN---LYTRGP--KGEQQLYRS
652589403_Alicyclobacillus_contaminans             ------------------------MSVKSIKFKLMIG-GPQYTRIRRG------IYKTHEVFNEGVRYYQEWLLLMRQGD---VYRYQDD---KPEIVLS
411770298_Citrobacter_freundii_ATCC_8090           ----------------------------------------------------------------------------------------------------
696372964_Citrobacter_freundii                     ----------------------------------------------------------------------------------------------------
492410745_Brevibacillus_agri                       ------------------------MEKRDERFQL------------------------HQRVKFQIRVLAQIMRMANKQ---------------------
492410748_Brevibacillus_agri                       ------------------------MAIRSIKLKLKTHTGPEAQNLRKG------IWRTHRLLNEGVAYYMKMLLLFRQES---TGERPKEELQEELICHI
495062547_Brevibacillus_sp-_CF112                  ------------------------MAIRSIKLKLKTHTGPEAQNLRKG------IWRTHRLLNEGVAYYMKMLLLFRQES---TGERPKEELQEELICHI
506407588_Methylobacterium_nodulans                -------------------------------------------------------------------------MLTKQD---------------------
219945206_Methylobacterium_nodulans_ORS_2060       ------------------------MPVRSLKLKIVVPRHPSELEKAQA------LWSTHRLVNEAVSFYEQKLLLLRGET-----------YSTSDGSVP
760065057_Methylobacterium_nodulans                ----------------------------------------------------------------------------------------------------
CONSENSUS_0.8                                      *.........................................................H.............L...........................
RuvC-like_motifs                                   //..................................................................................................

544884152_Alicyclobacillus_acidoterrestris         AEECKAELLERLRAR----------------------------------------------------QVENGHRGPAGSDDELLQLARQL----------
652589596_Alicyclobacillus_contaminans             ------------------------------------------------------------------------------MGFNTAELLRKV----------
652932497_Desulfovibrio_inopinatus                 RHAVQEEALAFAKAA-----------------------------------------------------QRHNGCISTYEDQEILDVLRQL----------
667765471_Desulfonatronum_thiodismutans            ESQVAEDALAMAREA----------------------------------------------------QRRNGWP-VVGEDEEILLALRYL----------
497199019_Opitutaceae_bacterium_TAV5               WGSFRRQGRQRTGLS----------------------------------------------------QAVAPYITPGNNAPTLDEVFRSILAGNPTDRAT
654153037_Tuberibacillus_calidus                   KEEIQERLWMKVRET----------------------------------------------------QQKNGFHGEV-SKDEVLETLRAL----------
754485389_Bacillus_thermoamylovorans               KAEIQAELWDFVLKM----------------------------------------------------QKCNSFTHEV-DKDVVFNILREL----------
495056180_Brevibacillus_sp-_CF112                  ----------------------------------------------------------------------------------------------------
651512544_Bacillus_sp-_NSP2-1                      REQQQRNQADKNTQA----------------------------------------------------LPL----------DKALEALRQL----------
Secondary_structure_for_651512544_(Jpred)          HHHHHH---------------------------------------------------------------H----------HHHHHHHHHH----------
654874074_Desulfatirhabdium_butyrativorans         TPEERKARRILLALSWLSVESKLGAPSSYIVASGDEPAKDRNDNVVSALEEILQSRKVAKSEIDDWKRDCSASLSAAIRDDAVWVNRSKV----------
652569729_Alicyclobacillus_herbarius               GEQCRRELLQRLRER----------------------------------------------------QRLNGRTDEPGTDEELLKVARQI----------
652589403_Alicyclobacillus_contaminans             AEHCKRELLRRLRQV----------------------------------------------------QKENVGR-TSHTDEELLQVMRAL----------
411770298_Citrobacter_freundii_ATCC_8090           ----------------------------------------------------------------------------------------------------
696372964_Citrobacter_freundii                     ----------------------------------------------------------------------------------------------------
492410745_Brevibacillus_agri                       ----------------------------------------------------------------------------------------------------
492410748_Brevibacillus_agri                       REQQQRNQADKNTQA----------------------------------------------------LPL----------DKALEALRQL----------
495062547_Brevibacillus_sp-_CF112                  REQQQRNQADKNTQA--------------------------------------------------------------LPLDKALEALRQL----------
506407588_Methylobacterium_nodulans                ----------------------------------------------------------------------------------------------------
219945206_Methylobacterium_nodulans_ORS_2060       QDEVRRQLLEQAREA----------------------------------------------------QARNGG--SGGSDDEIVRLCRSL----------
760065057_Methylobacterium_nodulans                -----------------------------------------------------------------------------------------M----------
CONSENSUS_0.8                                      ....................................................................................................
RuvC-like_motifs                                   ....................................................................................................

544884152_Alicyclobacillus_acidoterrestris         YELLVPQ---AIGAK------GDAQQIARKFLSPLADKDA------------------------------------------------------------
652589596_Alicyclobacillus_contaminans             EEEMRKT---SVGFD-------------------------------------------------------------------------------------
652932497_Desulfovibrio_inopinatus                 YERLVPSVNENNE--------AGDAQAANAWVSPLMSAESEGGLSVYDKVLDPPPVWMKLKEEKAPGWEAASQIWIQSD---------------------
667765471_Desulfonatronum_thiodismutans            YEQIVPS---CLLDDLGKPLKGDAQKIGTNYAGPLFDSD--TCRRDEGKDVACCGPFHEVAGKYLGALPEWATPISKQEFDGKDASHLRFKATGGDDAFF
497199019_Opitutaceae_bacterium_TAV5               LDAALMQLLKACDGA------GAIQQEGRSYWPKFCDPDSTANFAGDPAMLRREQHRLLLPQVLHDPAITHDSPALGSFDTYSIAT--------------
654153037_Tuberibacillus_calidus                   YEELVPS---AVGKS------GEANQISNKYLYPLTDPA--S----------------------------------------------------------
754485389_Bacillus_thermoamylovorans               YEELVPS---SVEKK------GEANQLSNKFLYPLVDPN--S----------------------------------------------------------
495056180_Brevibacillus_sp-_CF112                  ----------------------------------------------------------------------------------------------------
651512544_Bacillus_sp-_NSP2-1                      YELLVPS---SVGQS------GDAQIISRKFLSPLVDPN--S----------------------------------------------------------
Secondary_structure_for_651512544_(Jpred)          HHHHHHH---HH-----------HHHHHHHH---------------------------------------------------------------------
654874074_Desulfatirhabdium_butyrativorans         FDEAVKSVGSSLTREEAWDMLERFFGSRDAYLTPMKDPEDKSSETEQEDKAKDLVQKAGQWLSSRYGTSEGADFCRMSDIYGKIAAWADNASQGGSSTVD
652569729_Alicyclobacillus_herbarius               YEVLVPQ---SIGKS------GDAQQLASNFLSPLVDPN-------------------------------------------------------------
652589403_Alicyclobacillus_contaminans             YELIVPS---AVGKK------GDAASLSRKFLSPLAWKD--S----------------------------------------------------------
411770298_Citrobacter_freundii_ATCC_8090           ----------------------------------------------------------------------------------------------------
696372964_Citrobacter_freundii                     ----------------------------------------------------------------------------------------------------
492410745_Brevibacillus_agri                       ----------------------------------------------------------------------------------------------------
492410748_Brevibacillus_agri                       YELLVPS---SVGQS------GDAQIISRKFLSPLVDPN--S----------------------------------------------------------
495062547_Brevibacillus_sp-_CF112                  YELLVPS---SVGQS------GDAQIISRKFLSPLVDPNS------------------------------------------------------------
506407588_Methylobacterium_nodulans                ----------------------------------------------------------------------------------------------------
219945206_Methylobacterium_nodulans_ORS_2060       YEAIVLA-------------DDANAQLANAFLGPLTDPNSAGFLEAFNKVDRPAPSWLDQVPASDPIDPAVLAEANAWLDTD------------------
760065057_Methylobacterium_nodulans                YEAIVLA-------------DDANAQLANAFLGPLTDPNSAGFLEAFNKVDRPAPSWLDQVPASDPIDPAVLAEANAWLDTD------------------
CONSENSUS_0.8                                      ....................................................................................................
RuvC-like_motifs                                   ....................................................................................................

544884152_Alicyclobacillus_acidoterrestris         ---------------VGGLGIAKAGNKPR---------WVRMREAGEPGWEEEKEKAETRKSADRTA---DVLRALA--------------------DFG
652589596_Alicyclobacillus_contaminans             -------------------------------------------------------------TDNPFA---------------------------------
652932497_Desulfovibrio_inopinatus                 ---------------EGQSLLNKPGSPPR---------WIRKLRSGQP-WQDDFVSDQKKKQDELTKGNAPLIKQLK--------------------EMG
667765471_Desulfonatronum_thiodismutans            RVSIEKANAWYEDPANQDALKNKAYNKDD---------WKKEKDKGISSWAVKYIQKQLQLGQDPRT---EVRRKLWL-------------------ELG
497199019_Opitutaceae_bacterium_TAV5               ---------------PDTRTPQLTGPKARARLEQAITLWRVRLPESAADFDRLASSLKKIPDDDSRLNLQGYVGSSAKGEVQARLFALLLFRHLERSSFT
654153037_Tuberibacillus_calidus                   ---------------QSGKGTANSGRKPR---------WKKLKEAGDPSWKDAYEKWEKERQEDPKL---KILAALQ--------------------SFG
754485389_Bacillus_thermoamylovorans               ---------------QSGKGTASSGRKPR---------WYNLKIAGDPSWEEEKKKWEEDKKKDPLA---KILGKLA--------------------EYG
495056180_Brevibacillus_sp-_CF112                  ----------------------------------------------------------------------------------------------------
651512544_Bacillus_sp-_NSP2-1                      ---------------EGGKGTSKAGAKPT---------WQKKKEANDPTWEQDYEKWKKRREEDPTA---SVITTLE--------------------EYG
Secondary_structure_for_651512544_(Jpred)          -------------------EEE----------------HHHHHH-------HHHHHHHHHH----HH---HHHHHHH--------------------H--
654874074_Desulfatirhabdium_butyrativorans         DLVSELRQHFDTKESKATNGLDWIIGLSS---------YTGHTPNPVHELLRQNTSLNKSHLDDLKKKANTRAESCKS-------------------KIG
652569729_Alicyclobacillus_herbarius               --------------SKGGQGQSNAGRKPA---------WQKMRDEGNPGWVAAKERYEQRKATDPTK---KMIEMLD--------------------GLG
652589403_Alicyclobacillus_contaminans             ---------------KGLTGESKAGNKPR---------WKRLQEQGLP-YEEEYNRWLREKESDPAK---HIPAQLA--------------------SMG
411770298_Citrobacter_freundii_ATCC_8090           ----------------------------------------------------------------------------------------------------
696372964_Citrobacter_freundii                     ----------------------------------------------------------------------------------------------------
492410745_Brevibacillus_agri                       --------------------------------------------------------------------------------------------------YG
492410748_Brevibacillus_agri                       ---------------EGGKGTSKAGAKPT---------WQKKKEANDPTWEQDYEKWKKRREEDPTA---SVITTLE--------------------EYG
495062547_Brevibacillus_sp-_CF112                  ---------------EGGKGTSKAGAKPT---------WQKKKEANDPTWEQDYEKWKKRREEDPTA---SVITTLE--------------------EYG
506407588_Methylobacterium_nodulans                ----------------------------------------------------------------------------------------------------
219945206_Methylobacterium_nodulans_ORS_2060       ---------------AGRAWLVDTGAPPR---------WRSLAAKQDPIWPREFARKLGELRKEAASGTSAIIKALKR-------------------DFG
760065057_Methylobacterium_nodulans                ---------------AGRAWLVDTGAPPR---------WRSLAAKQDPIWPREFARKLGELRKEAASGTSAIIKALKR-------------------DFG
CONSENSUS_0.8                                      ....................................................................................................
RuvC-like_motifs                                   ....................................................................................................
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FIGURE S4 (con't)

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544884152_Alicyclobacillus_acidoterrestris      ---LKPLMRVYTDSE---MSSVEWKPLRKGQAVRTWD------------------RDMFQQAIERMMSWE-------SWNQRVGQEYAKLVEQKNRFEQK
652589596_Alicyclobacillus_contaminans          ----------------------------------------------------------------------------------------------------
652932497_Desulfovibrio_inopinatus              ---LLPLVNPF----------FRHLLDPEGKGVSPWD------------------RLAVRAAVAHFISWE-------SWNHRTRAEYNSLKLRRDEFEAA
667765471_Desulfonatronum_thiodismutans         ---LLPLFIPVFDK---------------TMVGNLWN------------------RLAVRLALAHLLSWE-------SWNHRAVQDQALARAKRDELAAL
497199019_Opitutaceae_bacterium_TAV5            LGLLRSATPPPKNAETPPPAGVPLPAASAADPVRIARGK----------------RSFVFRAFTSLPCWHGGDNIHPTWKSFDIAAFKYALTVINQIEEK
654153037_Tuberibacillus_calidus                ---LIPLFRPFTENDHKAVISVKWMPKSKNQSVRKFD------------------KDMFNQAIERFLSWE-------SWNEKVAEDYEKTVSIYESLQKE
754485389_Bacillus_thermoamylovorans            ---LIPLFIPFTDSNEPIVKEIKWMEKSRNQSVRRLD------------------KDMFIQALERFLSWE-------SWNLKVKEEYEKVEKEHKTLEER
495056180_Brevibacillus_sp-_CF112               -------------------------------------------------------------------------------------------------MPK
651512544_Bacillus_sp-_NSP2-1                   ---IRPIFPLYTNT----VTDIAWLPLQSNQFVRTWD------------------RDMLQQAIERLLSWE-------SWNKRVQEEYAKLKEKMAQLNEQ
Secondary_structure_for_651512544_(Jpred)       -----HHHHHH-----------EE----------HHH------------------HHHHHHHHHHHH-HH-------HHHHHHHHHHHHHHHHHHHHHHH
654874074_Desulfatirhabdium_butyrativorans      SKGQRPYSDAILNDVES-VCGFTYRVDKDGQPVSVADYSKYDVDYKWGTARHYIFAVMLDHAARRISLAH-------KWIKRAEAERHKFEEDAKRIANV
652569729_Alicyclobacillus_herbarius            ---LKPLFSVFTET---YTTGVKWKDLSKRQGVRTWD---------------------------------------------------------------
652589403_Alicyclobacillus_contaminans          ---LKPFLKVFTES----TEGIAWLPLAKDQGVRTWD------------------RDMFQQAIEGLLSWE-------SWNRRV-----------------
411770298_Citrobacter_freundii_ATCC_8090        ----------------------------------------------------------------------------------------------------
696372964_Citrobacter_freundii                  ----------------------------------------------------------------------------------------------------
492410745_Brevibacillus_agri                    ----------------------------------------------------------------------------------------------------
492410748_Brevibacillus_agri                    ---IRPIFPLYTNT----VTDIAWLPLQSNQFVRTWD------------------RDMLQQAIERLLSWE-------SWNKRVQEEYAKLKEKMAQLNEQ
495062547_Brevibacillus_sp-_CF112               ---IRPIFPLYTNT----VTDIAWLPLQSNQFVRTWD------------------RDMLQQAIERLLSWE-------SWNKRV-----------------
506407588_Methylobacterium_nodulans             ----------------------------------------------------------------------------------------------------
219945206_Methylobacterium_nodulans_ORS_2060    ---VLPLFQP----------SLAPRILGSRSSLTPWD------------------RLAFRLAVGHLLSWE-------SWCTRARDEHTARVQRLEQFSSA
760065057_Methylobacterium_nodulans             ---VLPLFQP----------SLAPRILGSRSSLTPWD------------------RLAFRLAVGHLLSWE-------SWCTRARDEHTARVQRLEQFSSA
CONSENSUS_0.8                                   ....................................................................................................
RuvC-like_motifs                                ....................................................................................................

544884152_Alicyclobacillus_acidoterrestris      NF--VGQEHLVHLVNQLQQDMKEASPGLESKEQTA----------------------------------HYVTGRALRGSDKVFEKWGKLAPDAP-----
652589596_Alicyclobacillus_contaminans          ---------------------------------------------------------------------HRITRRAIRGWDRIAEAWRRLPPDAP-----
652932497_Desulfovibrio_inopinatus              S---DEFKDDFTLLRQYEAKRHSTLKSIALADDSNP---------------------------------YRIGVRSLRAWNRVREEWIDKGAT-------
667765471_Desulfonatronum_thiodismutans         FL--GMEDGFAGLREYELRRNESIKQHAFEPVDRP----------------------------------YVVSGRALRSWTRVREEWLRHGDT-------
497199019_Opitutaceae_bacterium_TAV5            TKERQKECAELETDFDYMHGRLAKIPVKYTTGEAEPPPILANDLRIPLLRELLQNIKVDTALTDGEAVSYGLQRRTIRGFRELRRIWRGHAPAGTVFSSE
654153037_Tuberibacillus_calidus                LK--GISTKAFEIMERVEKAYEAHLRE-ITFSNST----------------------------------YRIGNRAIRGWTEIVKKWMKLDPSAP-----
754485389_Bacillus_thermoamylovorans            IK--E-DIQAFKSLEQYEKERQEQLLR-DTLNTNE----------------------------------YRLSKRGLRGWREIIQKWLKMDENEP-----
495056180_Brevibacillus_sp-_CF112               IL--RGHK-WISLLEQYEENRERELRENMTAANDK----------------------------------YRITKRQMKGWNELYELWSTFPASAS-----
651512544_Bacillus_sp-_NSP2-1                   LE--GGQE-WISLLEQYEENRERELRENMTAANDK----------------------------------YRITKRQMKGWNELYELWSTFPASAS-----
Secondary_structure_for_651512544_(Jpred)       ------HH-HHHHHHHHHHHHHHHHH--------H----------------------------------HHHHHEEE---HHHHHHH-------------
654874074_Desulfatirhabdium_butyrativorans      PARA-----------REWLDSFCKERSVTSGAVEP----------------------------------YRIRRRAVDGWKEVVAAWSKSDCKST-----
652569729_Alicyclobacillus_herbarius            ----------------------------------------------------------------------------------------------------
652589403_Alicyclobacillus_contaminans          ----------------------------------------------------------------------------------------------------
411770298_Citrobacter_freundii_ATCC_8090        ----------------------------------------------------------------------------------MYELWSTFPASAS-----
696372964_Citrobacter_freundii                  ----------------------------------------------------------------------------------LYELWSTFPASAS-----
492410745_Brevibacillus_agri                    ------------------------------------------------------------------------------------DRWDE-----------
492410748_Brevibacillus_agri                    LE--GGQE-WISLLEQYEENRERELRENMTAANDK----------------------------------YRITKRQMKGWNELYELWSTFPASAS-----
495062547_Brevibacillus_sp-_CF112               ----------------------------------------------------------------------------------------------------
506407588_Methylobacterium_nodulans             ----------------------------------------------------------------------------------------------------
219945206_Methylobacterium_nodulans_ORS_2060    HLKGDLATKVSTLREYERARKEQIAQLGLPMGERD----------------------------------FLITVRMTRGWDDLREKWRRSGDKG------
760065057_Methylobacterium_nodulans             HLKGDLATKVSTLREYERARKEQIAQLGLPMGERD----------------------------------FLITVRMTRGWDDLREKWRRSGDKG------
CONSENSUS_0.8                                   ..........................................................................R...........W.............
RuvC-like_motifs                                ....................................................................................................

544884152_Alicyclobacillus_acidoterrestris      -FDLYDAEIKNVQRRNTRRFGSHDLF-AKLAEPEYQALW--------RE------DA-SFLTRYAVYNSILRKLNHAK-MFATFTLPDATAHPIWTRFDK
652589596_Alicyclobacillus_contaminans          -ESEYIEAFKDIQRKNPRKIGSEPLF-KNLAAPGVRSEL--------LN------NP-QVLITFAKYNELQRQLAKAK-QFAQKTLPHPVFHPVWVRYDK
652932497_Desulfovibrio_inopinatus              -EEQRVTILSKLQTQLRGKFGDPDLF-NWLAQDRHVHLW----------------SPRDSVTPLVRINAVDKVLRRRK-PYALMTFAHPRFHPRWILYEA
667765471_Desulfonatronum_thiodismutans         -QESRKNICNRLQDRLRGKFGDPDVF-HWLAEDGQEALW--------KE-------R-DCVTSFSLLNDADGLLEKRK-GYALMTFADARLHPRWAMYEA
497199019_Opitutaceae_bacterium_TAV5            LKEKLAGELRQFQTDNSTTIGSVQLFNELIQNPKYWPIWQAPDVETARQWADAGFAD-DPLAALVQEAELQEDIDALK-APVKLTPADPEYSRRQYDFNA
654153037_Tuberibacillus_calidus                -QGNYLDVVKDYQRRHPRESGDFKLF-ELLSRPENQAAW--------RE------YP-EFLPLYVKYRHAEQRMKTAK-KQATFTLCDPIRHPLWVRYEE
754485389_Bacillus_thermoamylovorans            -SEKYLEVFKDYQRKHPREAGDYSVY-EFLSKKENHFIW--------RN------HP-EYPYLYATFCEIDKKKKDAK-QQATFTLADPINHPLWVRFEE
495056180_Brevibacillus_sp-_CF112               -HEQYKEALKRVQQRLRGRFGDAHFF-QYLMEEKNRLIW--------KG------NP-QRIHYFVARNELTKRLEEAK-QSATMTLPNARKHPLWVRFDA
651512544_Bacillus_sp-_NSP2-1                   -HEQYKEALKRVQQRLRGRFGDAHFF-QYLMEEKNRLIW--------KG------NP-QRIHYFVARNELTKRLEEAK-QSATMTLPNARKHPLWVRFDA
Secondary_structure_for_651512544_(Jpred)       ---HHHHHHHHHHHH-------HHHH-HHHHHHH-HHH---------------------EEEEEHHHHHHHHHHHHHH-HH--E---------EEEEEE-
654874074_Desulfatirhabdium_butyrativorans      -EDRIAAARALQDDSEIDKFGDIQLF-EALAEDDALCVW--------HKDGEATNEP-DFQPLIDYSLAIEAEFKKRQFKVPAYRHPDELLHPVFCDFGK
652569729_Alicyclobacillus_herbarius            -RDMFQSL-----------------------SERSGVID--------VG-------S-HTVHHIDLATASDAQIQYEL----------------------
652589403_Alicyclobacillus_contaminans          -REEYDALSARVYAYHAKHFAD---------QPGWAVYW--------PQ------SQ-P-----------------------------------------
411770298_Citrobacter_freundii_ATCC_8090        -HEQYKEALKRVQQRLRGRFGDAHFF-QYLMEEKNRLIW--------KG------NP-QRIHYFVARNELTKRLEEAK-QSATMTLPNARKHPLWVRFDA
696372964_Citrobacter_freundii                  -HEQYKEALKRVQQRLRGRFGDAHFF-QYLMEEKNRLIW--------KG------NP-QRIHYFVARNELTKRLEEAK-QSATMTLPNARKHPLWVRFDA
492410745_Brevibacillus_agri                    -LDSLKQAVEQKKSPL---------------DQTDRTFW--------EG----------------IVCDLTKVLPRNE----------------------
492410748_Brevibacillus_agri                    -HEQYKEALKRVQQRLRGRFGDAHFF-QYLMEEKNRLIW--------KG------NP-QRIHYFVARNELTKRLEEAK-QSATMTLPNARKHPLWVRFDA
495062547_Brevibacillus_sp-_CF112               -QEEYAKLKEKMA--------------QLNEQLEGGQEW----------------------------CTLSR----------------------------
506407588_Methylobacterium_nodulans             -KQQKITYCTNMNEVFEAKLGSADLL----------LNW--------DH----------------LRGRIRDRVDAGDIGSAFLKLALDVAHVLPDGVDD
219945206_Methylobacterium_nodulans_ORS_2060    -QEALHAIIATEQTRKRGRFGDPDLF-RWLARPENHHVW-------ADG------HA-DAVGVLARVNAMERLVERSR-DTALMTLPDPVAHPRSAQWEA
760065057_Methylobacterium_nodulans             -QEALHAIIATEQTRKRGRFGDPDLF-RWLARPENHHVW-------ADG------HA-DAVGVLARVNAMERLVERSR-DTALMTLPDPVAHPRSAQWEA
CONSENSUS_0.8                                   ....................G....F...L........W....................................................H........
RuvC-like_motifs                                ....................................................................................................

544884152_Alicyclobacillus_acidoterrestris      LGG-NLHQYT-FLFNEFGERRHAIRFHKLLKV-------ENGVAREVDDVTVPISMSEQLDNL----------------LPRDPNEPIALYFRDYGAEQ-
652589596_Alicyclobacillus_contaminans          LGG-NLHHYQ-IEPAVHANDTHKVKFSSLL------LPQEDGSYAEVKDVTVSLAPSLQFPTGLVHPKVTTPPRTGLVTVMDEEAGKPVVCYRDRGHDA-
652932497_Desulfovibrio_inopinatus              PGGSNLRQYA-------LDCTENALHITLPLL----VDDAHGTWIEKK-IRVPLAPSGQIQDLT---------------LEKLEKKKNRLYY--RSGFQ-
667765471_Desulfonatronum_thiodismutans         PGGSNLRTYQ-------IRKTENGLWADVVLL----SPRNESAAVEEKTFNVRLAPSGQLSNVSFDQ------------IQKGSKMVGRCRY--QSANQ-
497199019_Opitutaceae_bacterium_TAV5            VSKFGAGSRS---ANRHEPGQTERGHNTFTTEIAARNAADGNRWRATH-VRIHYSAPRLLRDGLRRP------------DTDGNEALEAVPWLQPMMEAL
654153037_Tuberibacillus_calidus                RSGTNLNKYRLIMNE-------KEKVVQFDRLICLN---ADGHYEEQEDVTVPLAPSQQFDDQIKFS------------SEDTGKGKHNFSYYHKGINY-
754485389_Bacillus_thermoamylovorans            RSGSNLNKYRILTEQLHTEKLKKKLTVQLDRLIYPT---ESGGWEEKGKVDIVLLPSRQFYNQIFLD------------IEE--KGKHAFTYKDESIKF-
495056180_Brevibacillus_sp-_CF112               RGG-NLQDY---YLTAEADKPRSRRFVTFSQL----IWPSESGWMEKKDVEVELALSRQFYQQV--K------------LLKNDKGKQKIEFKDKGSGS-
651512544_Bacillus_sp-_NSP2-1                   RGG-NLQDY---YLTAEADKPRSRRFVTFSQL----IWPSESGWMEKKDVEVELALSRQFYQQV--K------------LLKNDKGKQKIEFKDKGSGS-
Secondary_structure_for_651512544_(Jpred)       --------E---EEEEE-------HEEEE---------------EE---EEEEEEHHHHHHHHH--H------------H--------EEEEEE------
654874074_Desulfatirhabdium_butyrativorans      SRWKI---NYDVHKNVQAPFYRGLCLTLWTGSEIK---PVPLCWQSKR-LTRDLALGNNHRNDAASA------------VTRADRLGRAASNVTKSDMV-
652569729_Alicyclobacillus_herbarius            ----------------------------------------------------------------------------------------------------
652589403_Alicyclobacillus_contaminans          ---------------------------------------RQKGWVKMK----------------------------------------------------
411770298_Citrobacter_freundii_ATCC_8090        RGG-NLQDY---YLTAEADKPRSRRFVTFSQL----IWPSESGWMEKKDVEVELALSRQFYQQV--K------------LLKNDKGKQKIEFKDKGSGS-
696372964_Citrobacter_freundii                  RGG-NLQDY---YLTAEADKPRSRRFVTFSQL----IWPSESGWMEKKDVEVELALSRQFYQQV--K------------LLKNDKGKQKIEFKDKGSGS-
492410745_Brevibacillus_agri                    -----------------------------------------ADW--------------------------------------------------------
492410748_Brevibacillus_agri                    RGG-NLQDY---YLTAEADKPRSRRFVTFSQL----IWPSESGWMEKKDVEVELALSRQFYQQV--K------------LLKNDKGKQKIEFKDKGSGS-
495062547_Brevibacillus_sp-_CF112               ----------------------------------------------------------------------------------------------------
506407588_Methylobacterium_nodulans             Q-----------------------------------LARAAFHFQSAKGAKSKHADSVQA----------------------------------------
219945206_Methylobacterium_nodulans_ORS_2060    EGGSNLRNYQ------------------------------------------------------------------------------------------
760065057_Methylobacterium_nodulans             EGGSNLRNYQ------------------------------------------------------------------------------------------
CONSENSUS_0.8                                   ....................................................................................................
RuvC-like_motifs                                ....................................................................................................
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FIGURE S4 (con’t)

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544884152_Alicyclobacillus_acidoterrestris         ----HFTGEFGGA----KIQCRRDQLA--------------HMHR--RRGARDVYLNVSVRVQSQSE--ARGERRPPYAAVFRLVG-----DNHRAFVHF
652589596_Alicyclobacillus_contaminans             ----LVPVAFGGA----KLQFNRAHLS-----------AGYRKGVLSAGGGGSIYFNVTLDVQVPNE---------------------RDVSKTFSFSRD
652932497_Desulfovibrio_inopinatus                 ----QFAGLAGGA----EVLFHRPYME-----------HDERSEESLLERPGAVWFKLTLDVATQAP---------------------PNWLDGKGRVRT
667765471_Desulfonatronum_thiodismutans            ----QFEGLLGGA----EILFDRKRIA-----------NEQHGATDLASKPGHVWFKLTLDVRPQAP---------------------QGWLDGKGRPAL
497199019_Opitutaceae_bacterium_TAV5               APLPTLPQDLTG-----MPVFLMPDVT--------------------LSGERRILLNLPVTLEPAALVEQLGNAGRWQNQFFG--------SREDPFALR
654153037_Tuberibacillus_calidus                   ----ELKGTLGGA----RIQFDREHLL-----------R-RQGVK--AGNVGRIFLNVTLNIEPMQPFSRSGNLQTSVGKALKVYV--DGYPKVVNFKPK
754485389_Bacillus_thermoamylovorans               ----PLKGTLGGA----RVQFDRDHLR-----------RYPHKVE--SGNVGRIYFNMTVNIEPT---------ESPVSKSLKIHR--DDFPKFVNFKPK
495056180_Brevibacillus_sp-_CF112                  ----TFNGHLGGA----KLQLERGDLE-----------KEEKNFE--DGEIGSVYLNVVIDFEPL-QEVKNGRVQAPYGQVLQLIRRPNEFPKVTTYKSE
651512544_Bacillus_sp-_NSP2-1                      ----TFNGHLGGA----KLQLERGDLE-----------KEEKNFE--DGEIGSVYLNVVIDFEPL-QEVKNGRVQAPYGQVLQLIRRPNEFPKVTTYKSE
Secondary_structure_for_651512544_(Jpred)          ----EEEEEE--E----EEEE----HH-----------HHHH----------EEEEEEEEEE-----HH--------HHHHHHHHHH---------HHHH
654874074_Desulfatirhabdium_butyrativorans         ----NITGLFEQADWNGRLQAPRQQLEAIAVVRDNPRLSEQERNLRMCGMIEHIRWLVTFSVKLQPQ-------GPWCAYAEQ--------HGLNTNPQY
652569729_Alicyclobacillus_herbarius               ----------------------------------------------------------------------------------------------------
652589403_Alicyclobacillus_contaminans             ----------------------------------------------------------------------------------------------------
411770298_Citrobacter_freundii_ATCC_8090           ----TFNGHLGGA----KLQLERGDLE-----------KEEKTSR--TGKSAAFTLTL------------------------------------------
696372964_Citrobacter_freundii                     ----TFNGHLGGA----KLQLERGDLE-----------KEEKTSR--TGKSAAFTLTL------------------------------------------
492410745_Brevibacillus_agri                       ----------------------------------------------------------------------------------------------------
492410748_Brevibacillus_agri                       ----TFNGHLGGA----KLQLERGDLE-----------KEEKNFE--DGEIGSVYLNVVIDFEPL-QEVKNGRVQAPYGQVLQLIRRPNEFPKVTTYKSE
495062547_Brevibacillus_sp-_CF112                  ----------------------------------------------------------------------------------------------------
506407588_Methylobacterium_nodulans                ----------------------------------------------------------------------------------------------------
219945206_Methylobacterium_nodulans_ORS_2060       ------LEAVGG-----ELQITLPLLK--------------------AADDGRC----------------------------------------------
760065057_Methylobacterium_nodulans                ------LEAVGG-----ELQITLPLLK--------------------AADDGRC----------------------------------------------
CONSENSUS_0.8                                      ....................................................................................................
RuvC-like_motifs                                   ....................................................................................................

544884152_Alicyclobacillus_acidoterrestris         DKLSDYLAEHPDDGKLGSEGLLSGLRVMSVDLGLRTSASISVFRVARKDELK-------------------------------PNSKGRVPFFFPIKGND
652589596_Alicyclobacillus_contaminans             RDLVSLKAEELKRYMETKPLGMPGVRVMSVDLGVRYGAAISVFEVKPFAEVR-------------------------------KDK-----LHYPITGCE
652932497_Desulfovibrio_inopinatus                 PPEVHHFKTALSNKSKHTRTLQPGLRVLSVDLGMRTFASCSVFELIEGKPETG--------------------------------------RAFPVADER
667765471_Desulfonatronum_thiodismutans            PPEAKHFKTALSNKSKFADQVRPGLRVLSVDLGVRSFAACSVFELVRGGPDQ-------------------------------G-------TYFPAADGR
497199019_Opitutaceae_bacterium_TAV5               WPADGAVKTAKGKTHIPWHQDRDHFTVLGVDLGTRDAGALALLNVTAQKPAK------------------------------------------PVHRII
654153037_Tuberibacillus_calidus                   ELTEHIKESEKNTLTLGVESLPTGLRVMSVDLGQRQAAAISIFEVVSEKPD--------------------------------DNK-----LFYPVKDTD
754485389_Bacillus_thermoamylovorans               ELTEWIKDSKGKKLKSGIESLEIGLRVMSIDLGQRQAAAASIFEVVDQKPDI-------------------------------EGK-----LFFPIKGTE
495056180_Brevibacillus_sp-_CF112                  QLVEWIKASPQHSA--GVESLASGFRVMSIDLGLRAAAATSIFSVEESSDKN-------------------------------AAD-----FSYWIEGTP
651512544_Bacillus_sp-_NSP2-1                      QLVEWIKASPQHSA--GVESLASGFRVMSIDLGLRAAAATSIFSVEESSDKN-------------------------------AAD-----FSYWIEGTP
Secondary_structure_for_651512544_(Jpred)          HHHHHHH-----------HHHHHHHHHEEE---HHHH--EEEEEE----------------------------------------------EEEE-----
654874074_Desulfatirhabdium_butyrativorans         WPHADTNRDRKVHARLILPRLP-GLRVLSVDLGHRYAAACAVWEAVNTETVKEACQNVGRDMPKEHDLYLHIKVKKQGIGKQTEVDKTTIYRRIGADTLP
652569729_Alicyclobacillus_herbarius               ----------------------------------------------------------------------------------------------------
652589403_Alicyclobacillus_contaminans             ----------------------------------------------------------------------------------------------------
411770298_Citrobacter_freundii_ATCC_8090           ----------------------------------------------------------------------------------------------------
696372964_Citrobacter_freundii                     ----------------------------------------------------------------------------------------------------
492410745_Brevibacillus_agri                       ----------------------------------------------------------------------------------------------------
492410748_Brevibacillus_agri                       QLVEWIKASPQHSA--GVESLASGFRVMSIDLGLRAAAATSIFL--------------------------------------------------------
495062547_Brevibacillus_sp-_CF112                  ----------------------------------------------------------------------------------------------------
506407588_Methylobacterium_nodulans                -----------------------GLRVLSIDLGVRSFATCSVFELKDTAPTT-------------------------------G-------VAFPLAEFR
219945206_Methylobacterium_nodulans_ORS_2060       ----------------------------------------------------------------------------------------------------
760065057_Methylobacterium_nodulans                ----------------------------------------------------------------------------------------------------
CONSENSUS_0.8                                      ..........................V..VDLG.R.................................................................
RuvC-like_motifs                                   ..............................D.....................................................................

544884152_Alicyclobacillus_acidoterrestris         N------LVAVHERSQLLKLPGET------------------ESKDLRAIREERQRTLRQLRTQLAYLRLLVRCGS-EDVGRR-----ERSWAKLIEQPV
652589596_Alicyclobacillus_contaminans             G------FVAEHERSVILKLPGE--------------------GVRTAGKQSERKQALAAIRAEMSILRKWLRVSQVTEEDRA-----KAVRGLLEDERG
652932497_Desulfovibrio_inopinatus                 SMDSPNKLWAKHERSFKLTLPGET------------------PSRKEEEERSIARAEIYALKRDIQRLKSLLRLGEEDNDNRR-----DALLEQFFKGWG
667765471_Desulfonatronum_thiodismutans            TVDDPEKLWAKHERSFKITLPGEN------------------PSRKEEIARRAAMEELRSLNGDIRRLKAILRLSVLQEDDPR-----TEHLRLFMEAIV
497199019_Opitutaceae_bacterium_TAV5               GEADGRTWYASLADARMIRLPGEDARLFVRGKLVQEPYGERGRNASLLEWEDARNIILRLGQNPDELLGADPRRHSYPEINDKLLVALRRAQARLARLQN
654153037_Tuberibacillus_calidus                   -------LFAVHRTSFNIKLPGEK------------------RTERRMLEQQKRDQAIRDLSRKLKFLKNVLNMQKLEKTDER-----EKRVNRWIKDRE
754485389_Bacillus_thermoamylovorans               -------LYAVHRASFNIKLPGET------------------LVKSREVLRKAREDNLKLMNQKLNFLRNVLHFQQFEDITER-----EKRVTKWISRQE
495056180_Brevibacillus_sp-_CF112                  -------LVAVHHRSYMLRLPGEQ------------------VEKQVMEKRDERFQLHQRVKFQIRVLAQIMRMAN-KQYGDR-----WDELDSLKQAVE
651512544_Bacillus_sp-_NSP2-1                      -------LVAVHQRSYMLRLPGEQ------------------VEKQVMEKRDERFQLHQRVKFQIRVLAQIMRMAN-KQYGDR-----WDELDSLKQAVE
Secondary_structure_for_651512544_(Jpred)          -------EEEEE--EEEEE-----------------------HHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHH------HHH-----HHHHHHHHHHHH
654874074_Desulfatirhabdium_butyrativorans         DGRPHPAPWARLDRQFLIKLQGE--------------------EKDAREASNEEIWALHQMECKLDRTKPLIDRLIASGWGLL-----KRQMARLDALKE
652569729_Alicyclobacillus_herbarius               ----------------------------------------------------------------------------------------------------
652589403_Alicyclobacillus_contaminans             ----------------------------------------------------------------------------------------------------
411770298_Citrobacter_freundii_ATCC_8090           ----------------------------------------------------------------------------------------------------
696372964_Citrobacter_freundii                     ----------------------------------------------------------------------------------------------------
492410745_Brevibacillus_agri                       ----------------------------------------------------------------------------------------------------
492410748_Brevibacillus_agri                       ----------------------------------------------------------------------------------------------------
495062547_Brevibacillus_sp-_CF112                  ----------------------------------------------------------------------------------------------------
506407588_Methylobacterium_nodulans                -------LWAVHERSFTLELPGEN------------------VGAAGQQWRAQADAELRQLRGGLNRHRQLLRAATVQ----------KGERDAYLTDLR
219945206_Methylobacterium_nodulans_ORS_2060       ----------------------------------------------------------------------------------------------------
760065057_Methylobacterium_nodulans                ----------------------------------------------------------------------------------------------------
CONSENSUS_0.8                                      .........A.........L.GE.............................................................................
RuvC-like_motifs                                   ....................................................................................................

544884152_Alicyclobacillus_acidoterrestris         DAANHMTPDWREAFENELQK-----------------------------------------------LKSLHGICSDKE--------W------------
652589596_Alicyclobacillus_contaminans             GGWTMDPGEDSDHQPLQQFL-----------------------------------------------HEARLAVGELVNLVHLSPAEW------------
652932497_Desulfovibrio_inopinatus                 EEDVVPGQA----------------------------------------------------------FPRSLFQGLGAAPFRSTPELW------------
667765471_Desulfonatronum_thiodismutans            DDPAKSA------------------------------------------------------------LNAELFKGFGDDRFRSTPDLW------------
497199019_Opitutaceae_bacterium_TAV5               RSWRLRDLAESDKALDEIHAERAGE------------------------------------------KPSPLPPLARDDAIKSTDEA-------------
654153037_Tuberibacillus_calidus                   REEENP------VYVQEFEM-----------------------------------------------ISKVLY-SPHSV--------W------------
754485389_Bacillus_thermoamylovorans               NSDVPL------VYQDELIQ-----------------------------------------------IRELMY-KPYKD--------W------------
495056180_Brevibacillus_sp-_CF112                  QKKSPLDQTDRTFWEGIVCD-----------------------------------------------LTKVLP-RNEAD--------W------------
651512544_Bacillus_sp-_NSP2-1                      QKKSPLDQTDRTFWEGIVCD-----------------------------------------------LTKVLP-RNEAD--------W------------
Secondary_structure_for_651512544_(Jpred)          --------------------------------------------------------------------EEEE---------------H------------
654874074_Desulfatirhabdium_butyrativorans         LGWIPAPDSSENLSREDGEAKDYRESLAVDDLMFSAVRTLRLALQRHGNRARIAYYLISEVKIRPGGIQEKLDENGRIDLLQDALALWHELFSSPGWRDE
652569729_Alicyclobacillus_herbarius               ----------------------------------------------------------------------------------------------------
652589403_Alicyclobacillus_contaminans             ----------------------------------------------------------------------------------------------------
411770298_Citrobacter_freundii_ATCC_8090           ---------------SLISN-----------------------------------------------LCKK-----------------------------
696372964_Citrobacter_freundii                     ---------------SLISN-----------------------------------------------LCKK-----------------------------
492410745_Brevibacillus_agri                       ----------------------------------------------------------------------------------------------------
492410748_Brevibacillus_agri                       ----------------------------------------------------------------------------------------------------
495062547_Brevibacillus_sp-_CF112                  ----------------------------------------------------------------------------------------------------
506407588_Methylobacterium_nodulans                EAWSAKE-----LWPFEASL-----------------------------------------------LSELERCSTVADPL------W------------
219945206_Methylobacterium_nodulans_ORS_2060       -------------------------------------------------------------------IDTPL----------------------------
760065057_Methylobacterium_nodulans                -------------------------------------------------------------------IDTPL----------------------------
CONSENSUS_0.8                                      ....................................................................................................
RuvC-like_motifs                                   ....................................................................................................
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FIGURE S4 (con’t)

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544884152_Alicyclobacillus_acidoterrestris    ----------------------------------MDAVYESVRRVWRHMGKQVRDWRKDVRSGERPKIRGYAKDV------------------------V
652589596_Alicyclobacillus_contaminans        ----------------------------------ERAVIERHRRLERITASHIRVFQTMRKVWGKRRNEDAAH--------------------------T
652932497_Desulfovibrio_inopinatus            ----------------------------------RQHCQTYYDKAEACLAKHISDWRKRTRPRPTSREMWYKTRSY-----------------------H
667765471_Desulfonatronum_thiodismutans       ----------------------------------KQHCHFFHDKAEKVVAERFSRWRTETRPKSSSWQDWRERRGYA-----------------------
497199019_Opitutaceae_bacterium_TAV5          ----------------------------------LLSQRDIIRRSFVQIANLILPLRGRRWEWRPHVEVPDCHILA--------QSDPGTDDTKRLVAGQ
654153037_Tuberibacillus_calidus              ----------------------------------VDQLKSIHRKLEEQLGKEISKWRQSISQ-GRQG--------------------------------V
754485389_Bacillus_thermoamylovorans          ----------------------------------VAFLKQLHKRLEVEIGKEVKHWRKSLSD-GRKG--------------------------------L
495056180_Brevibacillus_sp-_CF112             ----------------------------------EQAVVQIHRKAEEYVGKAVQAWRKRFAA-DERKG-------------------------------I
651512544_Bacillus_sp-_NSP2-1                 ----------------------------------EQAVVQIHRKAEEYVGKAVQAWRKRFAA-DERKG-------------------------------I
Secondary_structure_for_651512544_(Jpred)     ----------------------------------HHHHHHHHHHHHHHHHHHHHHHHHHHHH--------------------------------------
654874074_Desulfatirhabdium_butyrativorans    AAKQLWDSRIATLAGYKAPEENGDNVSDVAYRKKQQVYREQLRNVAKTLSGDVITCKELSDAWKERWEDEDQRWKKLLRWFKDWVLPSGTQANNATIRNV
652569729_Alicyclobacillus_herbarius          ----------------------------------------------------------------------------------------------------
652589403_Alicyclobacillus_contaminans        ----------------------------------------------------------------------------------------------------
411770298_Citrobacter_freundii_ATCC_8090      ----------------------------------------------------------------------------------------------------
696372964_Citrobacter_freundii                ----------------------------------------------------------------------------------------------------
492410745_Brevibacillus_agri                  ----------------------------------EQAVVQIHRKAEEYVGKAVQAWRKRFAADERKG--------------------------------I
492410748_Brevibacillus_agri                  ----------------------------------------------------------------------------------------------------
495062547_Brevibacillus_sp-_CF112             ----------------------------------------------------------------------------------------------------
506407588_Methylobacterium_nodulans           ----------------------------------QDTCKRAARLYRTEFGAVVSEWRSRTRSREDRK--------------------------------Y
219945206_Methylobacterium_nodulans_ORS_2060  ----------------------------------------------------------------------------------------------------
760065057_Methylobacterium_nodulans           ----------------------------------------------------------------------------------------------------
CONSENSUS_0.8                                 ....................................................................................................
RuvC-like_motifs                              ....................................................................................................

544884152_Alicyclobacillus_acidoterrestris    GGNSIEQIEYLERQYKFLKSWSFFGKVSGQ-----VIRAEKGSR--FAITLREHIDHAKEDRLKKLADRIIMEALGYVYALDERGKGKW-----------
652589596_Alicyclobacillus_contaminans        GGISLAHIEHLIQQRKLFIRWSTHARTYGE-----VRRLPKHEG--FAKRLQKHTNHVKEDRIKKLADMIVMAARGYRF---LDKRARW----------V
652932497_Desulfovibrio_inopinatus            GGKSIWMLEYLDAVRKLLLSWSLRGRTYGA-----INRQDTARFGSLASRLLHHINSLKEDRIKTGADSIVQAARGYIP---LPHGKGW-----------
667765471_Desulfonatronum_thiodismutans       GGKSYWAVTYLEAVRGLILRWNMRGRTYGE-----VNRQDKKQFGTVASALLHHINQLKEDRIKTGADMIIQAARGFVP---RKNGAGW-----------
497199019_Opitutaceae_bacterium_TAV5          RGISHERIEQIEELRRRCQSLNRALRHKPGERPVLGRPAKGEEIADPCPALLEKINRLRDQRVDQTAHAILAAALGVRLRAPSKDRAER--RHRDIHGEY
654153037_Tuberibacillus_calidus              YGISLKNIEDIEKTRRLLFRWSMRPENPGE-----VKQLQPGER--FAIDQQNHLNHLKDDRIKKLANQIVMTALGYRY---DGKRKKW----------I
754485389_Bacillus_thermoamylovorans          YGISLKNIDEIDRTRKFLLRWSLRPTEPGE-----VRRLEPGQR--FAIDQLNHLNALKEDRLKKMANTIIMHALGYCY---DVRKKKW----------Q
495056180_Brevibacillus_sp-_CF112             AGLSMWNIEELEGLRKLLISWSRRSRNPQE-----VNRFERGHT--SHQRLLTHIQNVKEDRLKQLSHAIVMTALGYVY---DERKQEW----------C
651512544_Bacillus_sp-_NSP2-1                 AGLSMWNIEELEGLRKLLISWSRRTRNPQE-----VNRFERGHT--SHQRLLTHIQNVKEDRLKQLSHAIVMTALGYVY---DERKQEW----------C
Secondary_structure_for_651512544_(Jpred)     --HHHHHHHHHHHHHHHHHHHHHHHHHH--------------------HHHHHHHHHHHHHHHHHHHHHHHHHHHHHHH---H----EE----------E
654874074_Desulfatirhabdium_butyrativorans    GGLSLSRLATITEFRRKVQVGFF-TRLRPD-----GTRHEIGEQ--FGQKTLDALELLREQRVKQLASRIAEAALGIG----SEGGKGWDGGKRPRQRIN
652569729_Alicyclobacillus_herbarius          ----------------------------------------------------------------------------------------------------
652589403_Alicyclobacillus_contaminans        ----------------------------------------------------------------------------------------------------
411770298_Citrobacter_freundii_ATCC_8090      ----------------------------------------------------------------------------------------------------
696372964_Citrobacter_freundii                ----------------------------------------------------------------------------------------------------
492410745_Brevibacillus_agri                  AGLSMWNIEELEGLRKLLISWSRRTRNPQE-----VNRFERGHT--SHQRLLTHIQNVKEDRLKQLSHAIVMTALGYVY---DERKQEW-----------
492410748_Brevibacillus_agri                  ----------------------------------------------------------------------------------------------------
495062547_Brevibacillus_sp-_CF112             ----------------------------------------------------------------------------------------------------
506407588_Methylobacterium_nodulans           AGKSMWSVQHLTDVRRFLQSWSLAGRASGD-----IRRLDRERGGVFAKDLLDHIDALKDDRLKTGADLIVQAARGF-----QRNEFGY----------W
219945206_Methylobacterium_nodulans_ORS_2060  ----------------------------------------------------------------------------------------------------
760065057_Methylobacterium_nodulans           ----------------------------------------------------------------------------------------------------
CONSENSUS_0.8                                 .G.S.........................................................R....A..I...A.G........................
RuvC-like_motifs                              ....................................................................................................

544884152_Alicyclobacillus_acidoterrestris    VAKYPPCQLILLEELSEYQFNNDRPPSENNQLMQWSHRGVFQELINQAQVHDLL-------------------VGTMYAAFSSRFDARTGAPGIRCRRVP
652589596_Alicyclobacillus_contaminans        KTRHAPCDLILFEDLSRYRFTMDRPPTENSQLMNWSHRELLKTVKMQAALFGIG-------------------VGTVPAAFTSRFDAQTGAPGLRCKRVT
652932497_Desulfovibrio_inopinatus            EQRYEPCQLILFEDLARYRFRVDRPRRENSQLMQWNHRAIVAETTMQAELYGQI-------------------VENTAAGFSSRFHAATGAPGVRCRFLL
667765471_Desulfonatronum_thiodismutans       VQVHEPCRLILFEDLARYRFRTDRSRRENSRLMRWSHREIVNEVGMQGELYGLH-------------------VDTTEAGFSSRYLASSGAPGVRCRHLV
497199019_Opitutaceae_bacterium_TAV5          ERFRAPADFVVIENLSRYLSSQDRARSENTRLMQWCHRQIVQKLRQLCETYGIP-------------------VLAVPAAYSSRFSSRDGSAGFRAVHLT
654153037_Tuberibacillus_calidus              A-KHPACQLVLFEDLSRYAFYDERSRLENRNLMRWSRREIPKQVAQIGGLYGLL-------------------VGEVGAQYSSRFHAKSGAPGIRCRVVK
754485389_Bacillus_thermoamylovorans          A-KNPACQIILFEDLSNYNPYEERSRFENSKLMKWSRREIPRQVALQGEIYGLQ-------------------VGEVGAQFSSRFHAKTGSPGIRCSVVT
495056180_Brevibacillus_sp-_CF112             A-EYPACQVILFENLSQYRSNLDRSTKENSTLMKWAHRSIPKYVHMQAEPYGIQ-------------------IGDVRAEYSSRFYAKTGTPGIRCKKVR
651512544_Bacillus_sp-_NSP2-1                 A-EYPACQVILFENLSQYRSNLDRSTKENSTLMKWAHRSIPKYVHMQAEPYGIQ-------------------IGDVRAEYSSRFYAKTGTPGIRCKKVR
Secondary_structure_for_651512544_(Jpred)     --------EEEEHH---H-------HHHHHHHHHHHHHHHHHHHHHHHHH-----------------------EEEE----------------E------
654874074_Desulfatirhabdium_butyrativorans    DSRFAPCHAVVIENLANYRPDETRTRLENRRLMTWSASKVHKYLSEACQLNGLY-------------------LCTVSAWYTSRQDSRTGAPGIRCQDVS
652569729_Alicyclobacillus_herbarius          ----------------------------------------------------------------------------------------------------
652589403_Alicyclobacillus_contaminans        ----------------------------------------------------------------------------------------------------
411770298_Citrobacter_freundii_ATCC_8090      ----------------------------------------------------------------------------------------------------
696372964_Citrobacter_freundii                ----------------------------------------------------------------------------------------------------
492410745_Brevibacillus_agri                  CAEYPACQVILFENLSQYRSNLDRSTKENSTLMKWAHRSIPKYVHMQAEPYGIQ-------------------IGDVRAEYSSRFYAKTGTPGIRCKKVR
492410748_Brevibacillus_agri                  ----------------------------------------------------------------------------------------------------
495062547_Brevibacillus_sp-_CF112             ----------------------------------------------------------------------------------------------------
506407588_Methylobacterium_nodulans           VQKHAPCHVILFEDLSRYRMRTDRPRRENSQLMQWAHRGVPDMVGMQGEIYGIQDRRDPDSARKHARQPLAAFCLDTPAAFSSRYHASTMTPGIRCHPLR
219945206_Methylobacterium_nodulans_ORS_2060  ----------------------------------------------------------------------------------------------------
760065057_Methylobacterium_nodulans           ----------------------------------------------------------------------------------------------------
CONSENSUS_0.8                                 .........I..E.L..Y.....R...EN..LM.W....I......................................A...SR.....G..G.R.....
RuvC-like_motifs                              ............E.......................................................................................

544884152_Alicyclobacillus_acidoterrestris    ARCTQEHNPEPFPWWLNKFV-----------------VEHTLDACPLRADD---------LIPTGEGEIFVSP-FSAEEGDFHQIHADLNAAQNLQQRLW
652589596_Alicyclobacillus_contaminans        KQDKEKTPFWLI----------------------QFAEITGVNVTNVEPGQ---------LIPVDGGEWFVSPKGPRAADGLKCVHADINAAHNLQRRFW
652932497_Desulfovibrio_inopinatus            ERDFDNDLPKPYLLRELSWMLGNTKV-------ESEEEKLRLLSEKIRPGS---------LVPWDGGEQFATL--HPKRQTLCVIHADMNAAQNLQRRFF
667765471_Desulfonatronum_thiodismutans       EEDFHDGLPGMHLVGELDWLLPKDKD-------RTANEARRLLGGMVRPGM---------LVPWDGGELFATL---NAASQLHVIHADINAAQNLQRRFW
497199019_Opitutaceae_bacterium_TAV5          PDHRHRMPWSRILARLKAHEEDGKRLEKTVLDEARAVRGLFDRLDRFNAGHVPGKPWRTLLAPLPGGPVFVPL------GDATPMQADLNAAINIALRGI
654153037_Tuberibacillus_calidus              EHELYITEGGQKVRNQKFLD----SL-------VENNIIEPDDARRLEPGD---------LIRDQGGDKFATL---DERGELVITHADINAAQNLQKRFW
754485389_Bacillus_thermoamylovorans          K---------EKLQDNRFFK----NL-------QREGRLTLDKIAVLKEGD---------LYPDKGGEKFISL---SKDRKLVTTHADINAAQNLQKRFW
495056180_Brevibacillus_sp-_CF112             GQDL------QGRRFENLQK----RL-------VNEQFLTEEQVKQLRPGD---------IVPDDSGELFMTLTDGSGSKEVVFLQADINAAHNLQKRFW
651512544_Bacillus_sp-_NSP2-1                 GQDL------QGRRFENLQK----RL-------VNEQFLTEEQVKQLRPGD---------IVPDDSGELFMTLTDGSGSKEVVFLQADINAAHNLQKRFW
Secondary_structure_for_651512544_(Jpred)     -----------------HHH----HH-------HH---------------------------------EEEE----------EEEHHHHHHHHHHHHHHH
654874074_Desulfatirhabdium_butyrativorans    VREFMQSPFWRKQVKQAEAKHDENKG------DARERFLCELNKTWKAKTPAEWKKAGFVRIPLRGGEIFVSA--DSKSPSAKGIHADLNAAANIGLRAL
652569729_Alicyclobacillus_herbarius          ----------------------------------------------------------------------------------------------------
652589403_Alicyclobacillus_contaminans        ----------------------------------------------------------------------------------------------------
411770298_Citrobacter_freundii_ATCC_8090      ----------------------------------------------------------------------------------------------------
696372964_Citrobacter_freundii                ----------------------------------------------------------------------------------------------------
492410745_Brevibacillus_agri                  GQDL------QGRRFENLQK----RL-------VNEQFLTEEQVKQLRPGD---------IVPDDSGELFMTLTDGSGSKEVVFLQADINAAHNLQKRFW
492410748_Brevibacillus_agri                  ----------------------------------------------------------------------------------------------------
495062547_Brevibacillus_sp-_CF112             ----------------------------------------------------------------------------------------------------
506407588_Methylobacterium_nodulans           KREFEDQGFLELLKREN----------------------EGLDLNGYKPGD---------LVPLPGGEVFVCL----NANGLSRIHADINAAQNLQRRFW
219945206_Methylobacterium_nodulans_ORS_2060  ----------------------------------------------------------------------------------------------------
760065057_Methylobacterium_nodulans           ----------------------------------------------------------------------------------------------------
CONSENSUS_0.8                                 ..............................................................P...G..F................AD.NAA.N...R..
RuvC-like_motifs                              .....................................................<--...............................D............
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FIGURE S4 (con't)

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544884152_Alicyclobacillus_acidoterrestris         SDFDISQIRLRCDWGEVDGELVLIPRLTGKRT--------------------ADSYSNKVFYTNTGVTYYERERGKKRRKVFAQEKLSEEEAELLVEADE
652589596_Alicyclobacillus_contaminans             IP---RLPSVKCRRYVEAEGFAAVPSSTAFMKVHGKG-------------AFVSVDGEFYEYQKGRRVAV----NRADRTSSTLDEDEGDIGEEMLVSSN
652932497_Desulfovibrio_inopinatus                 GRCG-EAFRLVCQPHGDDVLRLASTPGARLLGALQQL---------ENGQGAFELVRDMGSTSQMNRFVMKSLGKKKIKPLQDNNGDDELEDVLSVLPEE
667765471_Desulfonatronum_thiodismutans            GRCG-EAIRIVCNQLSVDGSTRYEMAKAPKARLLGALQQLKNGDAPFHLTSIPNSQKPENSYVMTPTNAGKKYRAGPGEKSSGEE--DELALDIVEQAEE
497199019_Opitutaceae_bacterium_TAV5               AAP--DRHDIHHRLRAENKKRILSLR--------------------------LGTQREKARWPGGAPAVTLSTPNNGASPEDSDALPERVSNLFVDIAGV
654153037_Tuberibacillus_calidus                   TRTH-GLYRIRCESREIKDAVVLVPSDKDQKEKMENL-------FGIGYLQPFKQENDVYKWVKGEKIKG---KKTSSQSDDKELV-SEILQEASVMADE
754485389_Bacillus_thermoamylovorans               TRTH-GFYKVYCKAYQVDGQTVYIPESKDQKQKIIEE-------FGEGY---FILKDGVYEWGNAGKLKI---KKGSSKQSSSELVDSDILKDSFDLASE
495056180_Brevibacillus_sp-_CF112                  QRYN-ELFKVSCRVIVRDEEEYLVPKTKSVQAKLGKG-------LFVKKS--DTAWKDVYVWDSQAKLKG---KTTFTEESESPEQ-LEDFQEIIEEAEE
651512544_Bacillus_sp-_NSP2-1                      QRYN-ELFKVSCRVIVRDEEEYLVPKTKSVQAKLGKG-------LFVKKS--DTAWKDVYVWDSQAKLKG---KTTFTEESESPEQ-LEDFQEIIEEAEE
Secondary_structure_for_651512544_(Jpred)          H--------EE--EEEE---EEEEE----HHHHH------------EEE--------EEEEEE----HH-----HEHHH-----HH-HHHHHHHHHHHH-
654874074_Desulfatirhabdium_butyrativorans         TDP------------DWPGKWWYVPCD-------------------------PVSFESKMDYVKGCAAVKVGQPLRQPAQTNADGAASKIRKGKKNRTAG
652569729_Alicyclobacillus_herbarius               ----------------------------------------------------------------------------------------------------
652589403_Alicyclobacillus_contaminans             ----------------------------------------------------------------------------------------------------
411770298_Citrobacter_freundii_ATCC_8090           ----------------------------------------------------------------------------------------------------
696372964_Citrobacter_freundii                     ----------------------------------------------------------------------------------------------------
492410745_Brevibacillus_agri                       QRYN-ELFKVSCRVIVRDEEEYLVPKTKSVQAKLGKG---------LFVKKSDTAWKDVYVWDSQAKLKG---KTTFTEESESPEQ-LEDFQEIIEEAEE
492410748_Brevibacillus_agri                       ----------------------------------------------------------------------------------------------------
495062547_Brevibacillus_sp-_CF112                  ----------------------------------------------------------------------------------------------------
506407588_Methylobacterium_nodulans                TQHG-DAFRLPCGKSAVQGQIRWAPLSMGKRQAGALG--------GFGYLEPTGHDSGSCQWRKTTEAEWRRLSGAQKDRDEAAAAEDEELQGLEEELLE
219945206_Methylobacterium_nodulans_ORS_2060       ----------------------------------------------------------------------------------------------------
760065057_Methylobacterium_nodulans                ----------------------------------------------------------------------------------------------------
CONSENSUS_0.8                                      ....................................................................................................
RuvC-like_motifs                                   ....................................................................................................

544884152_Alicyclobacillus_acidoterrestris         AREKSVVLMRDPSGIINRGN----WTRQKEFWSMVNQRIEGYLVKQIRSRVPLQDSACENTGDI--------
652589596_Alicyclobacillus_contaminans             GAGEFVRMFYDESGYVGYG----RWMDSKVFWGKVRQIVHRAIQDQVEKRAAARGENGATSSR---------
652932497_Desulfovibrio_inopinatus                 DDTGRITVFRDSSGIFFPCN---VWIPAKQFWPAVRAMIWKVMASHSLG-----------------------
667765471_Desulfonatronum_thiodismutans            LAQGRKTFFRDPSGVFFAPD---RWLPSEIYWSRIRRRIWQVTLERNSSGRQERAEMDEMPY----------
497199019_Opitutaceae_bacterium_TAV5               ANFERVTIEGVSQ----------KFATGRGLWASVKQRAWNRVARLNETVTDNNRNEEEDDIPM--------
654153037_Tuberibacillus_calidus                   LKGNRKTLFRDPSGYVFPKD---RWYTGGRYFGTLEHLLKRKLAER---RLFDGGSSRRGLFNGTDSNTNVE
754485389_Bacillus_thermoamylovorans               LKGEKLMLYRDPSGNVFPSD---KWMAAGVFFGKLERILISKLTNQYSISTIEDDSSKQSM-----------
495056180_Brevibacillus_sp-_CF112                  AKGTYRTLFRDPSGVFFPES---VWYPQKDFWGEVKRKLYGKLRERFLTKAR--------------------
651512544_Bacillus_sp-_NSP2-1                      AKGTYRTLFRDPSGVFFPES---VWYPQKDFWGEVKRKLYGKLRERFLTKAR--------------------
Secondary_structure_for_651512544_(Jpred)          ---EEEEEEE----EEE----------HHHHHHHHHHHHHHHHHHHHHH-----------------------
654874074_Desulfatirhabdium_butyrativorans         TSKEKVYLWRDISAFPLESNEIGEWKETSAYQNDVQYRVIRMLKEHIKSLDNRTGDNVEG------------
652569729_Alicyclobacillus_herbarius               ------------------------------------------------------------------------
652589403_Alicyclobacillus_contaminans             ------------------------------------------------------------------------
411770298_Citrobacter_freundii_ATCC_8090           ------------------------------------------------------------------------
696372964_Citrobacter_freundii                     ------------------------------------------------------------------------
492410745_Brevibacillus_agri                       AKGTYRTLFRDPSGVFFPES---VWYPQKDFWGEVKRKLYGKLRERFLTKAR--------------------
492410748_Brevibacillus_agri                       ------------------------------------------------------------------------
495062547_Brevibacillus_sp-_CF112                  ------------------------------------------------------------------------
506407588_Methylobacterium_nodulans                RSGERVVFFRDPSGVVLPTD---LWFPSAAFWSIVRAKTVGRLRSHLDAQAEASYAVAAGL-----------
219945206_Methylobacterium_nodulans_ORS_2060       ------------------------------------------------------------------------
760065057_Methylobacterium_nodulans                ------------------------------------------------------------------------
CONSENSUS_0.8                                      ........................................................................
RuvC-like_motifs                                   ........................................................................
```

Figure S4. Multiple alignment of C2c1 protein family.

The alignment was built using MUSCLE program and modified manually on the basis of local PSI-BLAST pairwise alignments. Each sequence is labelled with GenBank Identifier (GI) number and systematic name of an organism. Secondary structure was predicted by Jpred and shown underneath the sequence which was used as a query (designations: H- alpha helix, E – beta strand). CONSENSUS was calculated for each alignment column by scaling the sum-of-pairs score within the column between those of a homogeneous column (the same residue in all aligned sequences) and a random column with homogeneity cutoff 0.8. Active site motifs of RuvC-like domain are shown below alignment.

FIGURE S5 (related to Figure 2)

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100000002  CEPX01008730.1  --------------MRSNYHGGRNARQWRKQISGLA-RRTKETVFTYKFPLETDAAEI--DFDKAVQTYGIAEGVGHGSLIGLVCAFHLSGFRLFSKAGEAMAFRNRSRYPTDAFAEKLSAIMGI
100020996 AUXO013399408.1  -----MKKFELKQNFRNNYSG-KTLRNFRQTLAQIANKKSSDSILTIKFKLDCSKTGKLPKYENLISLYDTIEDIKKGTLSYYLFTLIVSGFKFFGSASQAKAFSTKDIFKDNDFYNQFKIQSHL
100022927  CEQE01148443.1  --------------MRSNYHGGRNARQWRKQISGLA-RRTKETVFTYKFPLETDAAEI--DFDKAVQTYGIAEGVGHGSLIGLVCAFHLSGFRLFSKAGEAMAFRNRSRYPTDAFAEKLSAIMGI
100000004  CEVA01036528.1  ----------------------MNARDWRKHVGVLA-QQHKETTRTYTFPLDTTGSAI--DFDAALQAYNAVEGVGYGSLLGLACAVHLSGFRLFSTGKEAATFRNRARYPNAAFQAALRKELGT
100021577  CEPS01188136.1  MVAGLKKIKRDGVTMKSNYHGGVKARAWRKRIGGLA-RRQKETVFTYKFPLETEEAGI--DFDKAVQTYGIAEGISQGSLIGLVCAFHLSGFRLFSKADETKAFCNQGRYPNQAFAEKLRNELSV
Jpred Secondary structure  ----HHHH----EEE--------HHHHHHHH----H-H----EEEEEE--------------HHHHHHHEE--------HHHHHHHHHH------------HHHH-------HHHHHHHHHHHHH
CONSENSUS_0.8              .........................R..RK.I..LA.....ET..T..F.L..........FD..I..Y...E.V..G.L........LSGFR.F....EA..F.....Y....F..........

100000002  CEPX01008730.1  QLPTLSPEGLDLIFQSPPRSRDGIAPVWSENEVRNRLYTNWTGRGPANKPDEHLL-EIAGEIAKQVFPKFGGWDDLASDPDKALAAADKYFQSQ-GDFPSIASLPAAIMLSPANSTVDFEGD--Y
100020996 AUXO013399408.1  DLPDFVPSKIYQRLKKNVRSTNGKDNAFKASVIVAEYRKEIGKLKNKDESSEHQCEELFKKIGTALETRFSSWQDLINNCSTGCEIIDEILNDSFGTLPSIKKM--VLASTTQSSDGEQDGI--A
100022927  CEQE01148443.1  QLPTLSPEGLDLIFQSPPRSRDGIAPVWSENEVRNRLYTNWTGRGPANKPDEHLL-EIAGEIAKQVFPKFGGWDDLASDPDKALAAADKYFQSQ-GDFPSIASLPAAIMLSPANSTVDFEGD--Y
100000004  CEVA01036528.1  TITTLTPETLDRLFSSRPKRRNGVPLPWNQDSIRDRLYTNWVKPRPGDTPDAVLF-QIATGIAQEITEDVSSWTDLAKNSDRGLKAAHRYFARV-GGFPAFDNLTPPATVQPTDTTIDYDPNAPF
100021577  CEPS01188136.1  TLPKLSPQSLDVLFQSSPKSKNGVAPEWSKNAIRNRLYTNWTGKGAGTNPDEHLL-EIAEDIAAEIDSDLDGWKDLEEHPEKGLSAADRYFQAQ-GDFPSLTGLPPSVPLTPQNSTVAFEGD--P
Jpred Secondary structure  E--------HHHHH---------------HHHHHHHHHH------------HHHH-HHHHHHHHHH--------------------HHHHHHH----------------------EEEE------
CONSENSUS_0.8              .L....P..L............G.........I.......................EI...I...I......W.DL...................G..PS...L..........S..........

100000002  CEPX01008730.1  IAIDPAAETL----LHQAVSRCAARLGRERPDLDQNKGPFVSSLQDALVSSQNNGLSWLFGVGFQHWKEKSPKELIDEYKVPADQHGAVTQVKSFVDAIPLNPLFDTTH----YGEFRASVAGKV
100020996 AUXO013399408.1  IAYDPDSTFIKSDELLNPYFAVATILKSMPPEIQQDKKS--AYVKANLTTPTHNALSWIFGKGLTLFQTESTEKLCAMFNV--SDKRVIEQVQDAAKAVKLPAELDLNHCTLKFQDFRSSLGGHL
100022927  CEQE01148443.1  IAIDPAAETL----LHQAVSRCAARLGRERPDLDQNKGPFVSSLQDALVSSQNNGLSWLFGVGFQHWKEKSPKELIDEYKVPADQHGAVTQVKSFVDAIPLNPLFDTTH----YGEFRASVAGKV
100000004  CEVA01036528.1  HLVSHADQTL----IHQSISLCAHRIRQEDPALDPNKSGFIKQLQNNFLSQTFYGLSWLFGAGYVHFRECTANDLAIQYGIPNNCRDGIHQIKSFADAILPNTFFEKKH----YRKDSRSVGKKA
100021577  CEPS01188136.1  VCLNPSDNTL----LHQAVARCAGRILQEQPNLSPDKNRFINQLQDELVSSQNNGLSWLFGVGFKYWKEMSVDQLADDYKVKSTDLDALKQVKSFIDAIPLNPLFDTPH----YGEFRASVAGKM
Jpred Secondary structure  EEE------H----HHHHHHHHHHHHHHH--------HHHHHHHHHHHH-------EEEEE---HHHH---HHHHHHH--------HHHHHHHHHHHH---------------------HHHHHH
CONSENSUS_0.8              .........L....L.......A..L....P.L...K......L...L.......LSWLFG.G.......S...L...Y.V.......I.QVK....AI......D..H....Y.....SV....

100000002  CEPX01008730.1  RSWVANYWKRLLDLKSLLATTE-FTLPESISDPKAVSLFSGLLVDPQG-----LKKVADSL--PARLVSAEEAIDRLMGVGIP--TAADIAQVERVADEIGAFIGQVQQFNNQVKQKLENLQDAD
100020996 AUXO013399408.1  DSWTTNYLKRLDELNDLL-----LNLPKNLSLPDIFMIDGKDFIEYSGCNRDEIQQMIDFVVNEQNRIKLQESLNALLGKGNNQICSDDISTVKDFSEIVNSLHSFVQQIDNSLEQSSNEANSIF
100022927  CEQE01148443.1  RSWVANYWKRLLDLKSLLATTE-FTLPESISDPKAVSLFSGLLVDPQG-----LKKVADSL--PARLVSAEEAIDRLMGVGIP--TAADIAQVERVADEIGAFIGQVQQFNNQVKQKLENLQDAD
100000004  CEVA01036528.1  KSWISNYWQRLLQLQTWVDDHTWVTLPQELTEAQFKPLFRGLLVDAVE-----LMAIAERL--PQRLADCRDSLDCLMGKGPQAATKNDVEIVEKVREEIESFVGQIEQLGNQLRHQLENENN--
100021577  CEPS01188136.1  RSWVKNYWKRLLDLKSQLGTAN-INLPEGLDEQRAENLFSGLLIDSKG-----LRQVTDKL--PSRLKKAEDTIDRLMGDGNP--TSDDIEQVETVAAEISAFIGQVEQFNNQLEQRLENPLEGD
Jpred Secondary structure  HHHHHHHHHHHHHHHHH--------------HHHHHHHH-HEEE----------HHHHHHH--HHHHHHHHHHHHHH------------HHHHHHHHHHHHHHHHHHHHHHHHHHHHH-------
CONSENSUS_0.8              .SW..NY.KRL..L...L.......LP..L.......L.....VD........L....D.L............L..LMG.G.......DI..V......I......V.Q..N.L.Q.........

100000002  CEPX01008730.1  DE---EFLKGLKIEL-PSGDKEPPAINRISGGAPDAAAEISELEEKLQRLLDARSEHFQTISEWAEENAVTLDPIAAMVELER-LRLAERGATGDPEEYALRLLLQRIGRLANRVSPVSAGSIRE
100020996 AUXO013399408.1  SELKKIEKNEKWDIWKNNLKKIPKLNKLSGGVPDAWKEIREIEQKFHEISENQKKHFTEVMEWIDAGNGTIDIFESRFKYDELLKKSKKNNLQSADELAFRSVLNKLGRFARQGNDLVCEKIKN
100022927  CEQE01148443.1  DE---EFLKGLKIEL-PSGDKEPPAINRISGGAPDAAAEISELEEKLQRLLDARSEHFQTISEWAEENAVTLDPIAAMVELER-LRLAERGATGDPEEYALRLLLQRIGRLANRVSPVSAGSIRE
100000004  CEVA01036528.1  DQVHRDNLHQLKNRL-PLDLRRPQALNKISGGVPDVAKSIRGLETQLDQVLKERRSHFGRLTKWAKECGITLDPLQPLIESEK-QRVAERGSAHDAKELAIRLLLQRIGRLGHRLSPTNATAIQE
100021577  CEPS01188136.1  DE---TFLKQLKIDL-PAEFKKPPAINRISGGSPDPTAEIAELEEKLDRLMSARKEHYETIAEWASANKVTLDPMEAMTTLEA-QRLTERGAEGDQEEFALRLLLQRIGRLANRLSPQGATAIRD
Jpred Secondary structure  HH---HHHHHHH-------------------------HHHHHHHHHHHHHHH--HHHHHHHHHHH----------HHHHHH-HHHHHH-------HHHHHHHHHHHHHHHHH-------HHHHHH
CONSENSUS_0.8              .E.........K..L.....K....LN.ISGG.PD...EI..LE.K..........HF..I.EW......TLD........E...R...R.......E.A.R.LL.RIGR............I..

100000002  CEPX01008730.1  LLKP--VFMEEREFNLFFHNRLGSLYRSPYSTSRHQPFSIDVG-KAKAIDWIAGLDQISSDIEKALSGAGEALGDQLRDWINLAGFAISQRLRGLP--DTVPNALAQVRCPD---DVRIPPLLAM
100020996 AUXO013399408.1  WFKEQNIFDSSKDFNRYFINQKGFIFKHPSSKKDNSPYNLSANLLEKRYEVTNTVGALLEQCESDPAIVNDPFS--MRSLVEFRALWFSINISGISKEQHIPTKIAQPKLDDSTYQESVSPTLKY
100022927  CEQE01148443.1  LLKP--VFMEEREFNLFFHNRLGSLYRSPYSTSRHQPFSIDVG-KAKAIDWIAGLDQISSDIEKALSGAGEALGDQLRDWINLAGFAISQRLRGLP--DTVPNALAQVRCPD---DVRIPPLLAM
100000004  CEVA01036528.1  LLRP--VFAVKREFNLFFHNHMGALYRSPYSTSRHQPFQINVD-VAHGTDWIGTIETLIQNLFTQIQ--DDAL---LRDLVQLEGFVFSHKLRALP--GVIPSELARPNNLQ---QMGLPALLLV
100021577  CEPS01188136.1  LLRP--VFTEKREFNLFFHNRMGSLYRSPYSTSRHQPFTIDVA-VAKNTDWMDALDGIAETIMKGLSQAGDELSLRLRDWINISGFSLSQRLRGLP--DTVPGELALVRSAD---DVRIPPMLAL
Jpred Secondary structure  HHHH--HHH---HHHHHHHHH----------------EEEEEE-E------HHHHHHHHHHHHHHHHH---HHHHHHHHHH------HHHHH------------EEEEE------------HHHH
CONSENSUS_0.8              ......VF...REFN.FF.N..G.LYR.P.S.....PF.I.........D.......L............D.....LR..V.......S..L.GL.....IP..LA.....D......I...L..

100000002  CEPX01008730.1  LLEEDDIARDVCLKAFNLYVSAINGCLFGALREGFIVRTRFQRIGTDQIHYVPKDKAWEYPDRLNTAKGPINAAVSSD---WIEK--DGAVIKPVETVRNL-SSTGFAGAG-VSEYLVQAPHDWY
100020996 AUXO013399408.1  RLEKEQITSSELNSIFTVYKSLLSGLSIRLSRNSFYLRTKFSWIGNNSLIYCPKETTWKIPAAYFKSDLWNEYKDKQILIVNEEY--DVDVVKTFESVYKIVKSKDNNEKNRILPLLKQLPHDWM
100022927  CEQE01148443.1  LLEEDDIARDVCLKAFNLYVSAINGCLFGALREGFIVRTRFQRIGTDQIHYVPKDKAWEYPDRLNTAKGPINAAVSSD---WIEK--DGAVIKPVETVRNL-SSTGFAGAG-VSEYLVQAPHDWY
100000004  CEVA01036528.1  LLQADQVHRETVLRVFNLYGSAINGYLFQALRPGFIVRAGFQRLETKKLRYVPKAQSWQYPDRLHHAKSAIKNSLSAG---WIKKNHQGAIL-PQKTLTALVKQKSLKDTG-VPEYLVQAPHDWY
100021577  CEPS01188136.1  QLEEDEVSREVCLKAFNLYVSAINGCLFRALREGFIVRTKFQRLERDVLSYVPKTKLWNYPQRLDTARGPIHSALAAA---WINK--EGSVIDPVETVTAL-SDTGFSDDG-IPEYLVQAPHDWY
Jpred Secondary structure  H--------HHHHHHHHHHHHHH--HHHHHHH---EEE-HHHHHHHHHHHH---------------------HHHHHHH---HH-------EE-HHHHHHH--------------HHH-------
CONSENSUS_0.8              .LE.D.I........F.LY.S.I.G......R..F.VR..F..I....L.Y.PK...W..P.............................VI...ETV..L...........V...L.Q.PHDW.

100000002  CEPX01008730.1  TPLDLRDV-AHLVTGLPVEK---NITKLKRL--TNRTAFRMVGASSFKTHLDSVLLSDKIKLGDFTIIIDQHYRQSVTY-GGKVKISYEPERLQVEAAVPVVDTRDRTVPEPDTLFDHIVAIDLG
100020996 AUXO013399408.1  FKLPFGASNAEKCKVLKLEK---NNKKFKPLSVSKDSLARLSGPSTYFNQIDEIMMNDESELSEMTLLADEPVRQQMS--NGKIEII--PDDYVMSLAIPIT-RSLKKGNTESFPFKNIVSIDQG
100022927  CEQE01148443.1  TPLDLRDV-AHLVTGLPVEK---NITKLKRL--TNRTAFRMVGASSFKTHLDSVLLSDKIKLGDFTIIIDQHYRQSVTY-GGKVKISYEPERLQVEAAVPVVDTRDRTVPEPDTLFDHIVAIDLG
100000004  CEVA01036528.1  VPIDLRGP-AIPIEGLTVGTEGPELTQLGPM--KDDCAFRAIGPSSFKSKIDAGLLPQDVKYGDMTLIFDQHYQQSISFANGTFSIQYQPTSLQVKAAIPVVDKRPRDTRNNSHLYDRIVAIDLG
100021577  CEPS01188136.1  TPIDLRDI-SKPVSGLPVKK---NITGLKRQ--KKQTAFRMVGPSSFKSHLDSTLLSEEVKLGDFTLIFDQYYKQRVSY-NGRVKITFEPDRLHVEAAVPVIDKRVRPSTEEDALFDHLLAIDLG
Jpred Secondary structure  ----------------------------HHH--HH---EEEE----------HHHH--------EEEEHHHHHHHHH------EEEEEE----E-EE----E----------HHHHHHHHHH---
CONSENSUS_0.8              ..L......A.....L.V.....................R..G.S.F...ID..LL....K..D.TLI.DQ...Q..S...G...I...P....V..AIPV.....R........F..IV.ID.G
RuvC-like_motifs           ..........................................................................................................................D..

100000002  CEPX01008730.1  ERSVGFAVFDIKSCLRTGEVKPIHDNNGNPVVGTVAVPSIRRLMKAVRSHRRRRQPNQKVNQTYSTALQNYRENVIGDVCNRIDTLMERYNAFPVLEFQIKNFQAGAKQLEIVYGS---------
100020996 AUXO013399408.1  EAGFAYAVFKLSDC-GNERAEPIAT-------GLIPIPSIRRLIHSVKKYRGKKQRIQNFNQKFDSTMFTLRENVTGDICGLIVALMKKYNAFPILEKQVGNLESGSKQLMLVYKAVNSKFLAAK
100022927  CEQE01148443.1  ERSVGFAVFDIKSCLRTGEVKPIHDNNGNPVVGTVAVPSIRRLMKAVRSHRRRRQPNQKVNQTYSTALQNYRENVIGDVCNRIDTLMERYNAFPVLEFQIKNFQAGAKQLEIVYGSVLHRYTFSG
100000004  CEVA01036528.1  ERKIGYAIFDLKQVLKSEQLEPMRE-DGKPLIGSISIRSIRGLMKAVQTHRNRRQPNYRIDQTYSKALMHYRESVIGDVCNAIDTLCARYGGFPVLESSVRNFEVGSAQLKTVYGSVSRRYTWSA
100021577  CEPS01188136.1  EKRVGYAVYDIKACLRTGDIKPLEDGDGKPIVGSVAVPSIRRLMKAVRSHRQQRQPNQKVNQTYSTALMNYRENVIGDVCNRIDTLMEKYNAFPVLESSVMNFEAGSRQLEMVYGSVLHRYTYSK
Jpred Secondary structure  ----EEEEEEEHHHH--------------EEEEEE----HHHHHHHHHHHHH------HHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHH-------------------EEEHH-HHHHHHH---
CONSENSUS_0.8              E....YAVF.L..........P..........G.I.I.SIR.L...V..HR..RQ.....NQ.Y...L...RENV.GDVC..I..L...Y..FPVLE..V.N.E.GS.QL..VY..V........
RuvC-like_motifs           ................................................................................................E............................

100000002  CEPX01008730.1  -----------------------------------------------------------------------------------------------------------------------------
100020996 AUXO013399408.1  VDMQNDQRRSWWYQGN-----SWNTPILRISNPNQSNNKNIVKNINGKKYEELKIYPGYSVSAYMTSCICHVCGRNALELLKNDDSTGKVKKYQINQDGEVTIGGEVIKLY--------------
100022927  CEQE01148443.1  VDAHKAKRREYWYNGE-----LWEHPYLMAKKWNEETNS------MSGAPKPVSLFPGVTVNAARTSQICHQCQRNPMSHLRG--LTGTI---EISSDGLLELDDGTIRLFETSDYDEDKFKQSR
100000004  CEVA01036528.1  VDAHKNQRQQYWLGGTKDKIPIWTHPYLMTREWDEKNSK------WSNRSKPLKMHPGVEVHPAGTSQICHQCKRNPIGALWN--VADTV---VLDDQGQLDLDDGTIRLNSGY-IDTTEIKRAR
100021577  CEPS01188136.1  IDAHTAKRKEYWYTGE-----YWDHPYLMAHKWNERTRS------YSGSLSALTLYPGVMVHPAGTSQRCHQCKRNPMVEIKQ--LTGQV---EINADGSLELDDGTICLYEGYDYSPEEYKKAK
Jpred Secondary structure  ----------EEE---------------EH--------------------EEEEE----EE----------------HHHEEE-----EE---EE------------EEEEE-------HHHHHH
CONSENSUS_0.8              VD.....R...W..G.......W..P.L............................PG..V....TS..CH.C.RN....L........V........G........I.L...............

100000002  CEPX01008730.1  -------------------------------------------------------------------------------------------
100020996 AUXO013399408.1  RKPDRLTPVKNLA--KKGNRERTYASINERAP-#--MSKDTTQSRYFCVFKNCPCHNKEQHADVNAAINIGRRFLKDCILDDNKEKD----
100022927  CEQE01148443.1  REKRRLDANVLLSGRHRAEYIYTVAKRNLRRPPKNVMTKDTTQSRYTCLYKNCS---WTGHADENAAINIGRRYLAERIDMPASKTKAAV-
100000004  CEVA01036528.1  RKKIRLPENKPLTGSHKTSHVRAVARRNLRQPPKSTRAKDTTQSRYTCLYVDCG---HECHADENAAINIGRKYLQERIHIEASRQALSTR
100021577  CEPS01188136.1  REKRRLDPNVPLSGRHQAKHVSAVAKRNLRRPTVSMMSGDTTQARYVCLYTDCD---FTGHADENAAINIGWKYLTERIALSESKDKAGV-
Jpred Secondary structure  HH-----------------EE-HHHHH------EEEE-------EEEEEEE--------------------HHHHHHHHHH----------
CONSENSUS_0.8              R...RL.....L............A..N.R.P.......DTTQ.RY.C....C.......HAD.NAAINIG...L...I............
RuvC-like_motifs           ..............................................................D............................
```

Figure S5. Multiple alignment of C2c3 protein family.

The alignment was built using MUSCLE program. Each sequence is labelled with local assigned number and the Genbank ID for metagenomics contig coding for respective C2c3 protein. Secondary structure was predicted by Jpred and shown underneath the alignment (designations: H- alpha helix, E – beta strand). CONSENSUS was calculated for each alignment column by scaling the sum-of-pairs score within the column between those of a homogeneous column (the same residue in all aligned sequences) and a random column with homogeneity cutoff 0.8. Active site motifs of RuvC-like domain are shown below alignment for the C-terminal domain.

FIGURE S6 (related to Figure 2)

```
564875111 Rhodobacter capsulatus R121       --------------------------MQIGKVQGRTISEFGD--PAGGLKRKISTDGKNRKELPAHLSSD-PKALIGQWISG-------ID--------K
769144435 Lachnospiraceae bacterium MA2020   --------------------------MQISKVNHKH--------VAVGQKDRERITGFIYNDPVGDEKSL-EDVVAKRANDTKVLFNVFNT--------K
551041827 Lachnospiraceae bacterium NK4A179  --------------------------MKISKVREENRGAKLTVNAKTAVVSENRSQEGILYNDPSRYGKS-RKNDEDRDRYI--ESRLKSS--------G
671463495 Clostridium  aminophilum          --------------------------MKFSKVDHTRS-------AVGIQKATDSVHGMLYTDPKKQEVNDLDKRFDQLNVKAKRLYNVFNQ--------S
Secondary structure for 671463495 (Jpred)   -----------------------------EE-------------EEEEEE----EEEEEE----------HHHHHHHH---HHHHHHHH-----------
652829192 Lachnospiraceae bacterium NK4A144  --------------------------MKISKVDHTRMAV-----AKGNQHRRDEISGILYKDPTKTGSIDFDERFKKLNCSAKILYHVFNGIAEGSNKYK
736546968 Carnobacterium gallinarum         --------------------------MRITKVKIKLDNK-----LYQVTMQKEEKYGTLKLNEESRKSTA-EILRLKKASFNKSFHSKTIN---------
736550717 Carnobacterium gallinarum         --------------------------MRMTKVKIN---------GSPVSMNRSKLNGHLVWNGTTNTVNI-LTKKEQS------FAASFLN--------K
503209049 Paludibacter propionicigenes      --------------------------MRVSKVKVKDGGK-----DKMVLVHRKTTGAQLVYSGQPVSNET-SNILPEKKRQS--FDLSTLN--------K
502750493 Listeria seeligeri                MWISIKTLIHHLGVLFFCDYMYNRREKKIIEVKTMRITKVEVD-RKKVLISRDKNGGKLVYENEMQDNTE-QIMHHKKSS----FYKSVVN--------K
738100542 Listeria weihenstephanensis       -----------------------------------------------------------MLALLHQEVPS-QKLHNLK------SLNTESL--------T
738133341 Listeria newyorkensis             --------------------------MKITKMRVD---------GRTIVMERTSKEGQLGYEGIDGNKTT-EIIFDKKKES---FYKSILN--------K
544240864 Leptotrichia wadei F0279          ------------------------MYMKITKIDGVSHYKK----QDKGILKKKWKDLDERKQREKIEARY-NKQIESKIYKE--FFRLKNK--------K
738101039 Leptotrichia wadei                --------------------------MKITKIDGVSHYKK----QDKGILKKKWKDLDERKQREKIEARY-NKQIESKIYKE--FFRLKNK--------K
545623740 Leptotrichia wadei                --------------------------MKVTKIDGLSHK-------------KFEDEGKLVKFRNNKNINE-IKERLKK------LKELKLD--------N
545623306 Leptotrichia wadei                --------------------------MKVTKVDGISHK-------------KYIEEGKLVKSTSEENRTS-ERLSE--------LLSIRLD--------I
506250229 Leptotrichia buccalis             --------------------------MKVTKVGGISHK-------------KYTSEGRLVKSESEENRTD-ERLSA--------LLNMRLD--------M
Secondary structure for 506250229 (Jpred)   ----------------------------EE---------------------------EEEEE-HHHHHHH-HHHHH--------HHHHHHH--------H
545661797 Leptotrichia sp  oral taxon 225    ----------------------------------------------------------------------------------------------------
545620493 Leptotrichia sp  oral taxon 879    -------------------MGNLFGHKRWYEVRDKKDFK-----IKRKVKVKRNYDGNKYILNINENNNK-EKIDNNKFIGE--FVNYKKN--------N
517262777 Leptotrichia shahii               -------------------MGNLFGHKRWYEVRDKKDFK-----IKRKVKVKRNYDGNKYILNINENNNK-EKIDNNKFIRK--YINYKKN--------D
CONSENSUS                                   ..............................KV....................................................................
HEPN (predicted RNAse) motifs               //..................................................................................................

564875111 Rhodobacter capsulatus R121       IYRKPDSRKSDGKAIHSPTPSKMQFDARDDL--------------------------------------------------------GEAFWKLVSEAGL
769144435 Lachnospiraceae bacterium MA2020   DLYDSQESDKSEKDKEIISKGAKFVAKSFNS--------------------------------------------AITILKKQNKIYSTLTSQQVIKELK
551041827 Lachnospiraceae bacterium NK4A179  KLYRIFNEDKNKRETDELQWFLSEIVKKINRRNGLVLSDMLSVDDRAFEKAFEKYAELSYTNRRNKVSGSPAFETCGVDAATAERLKGIISETNFINRIK
671463495 Clostridium  aminophilum          KAEEDDDEKRFGKVVKKLNRELKDLLFHREV------------------------------------------SRYNSIGNAKYNYYGIKSNPEEIVSNL
Secondary structure for 671463495 (Jpred)   ------HHHHHHHHHHHHHHHHHHHHHHHHH------------------------------------------HHHH--------EEE----HHHHHHHH
652829192 Lachnospiraceae bacterium NK4A144  NIVDKVNNNLDRVLFTGKSYDRKSIIDIDTV---------------------------------------------------LRNVEKINAFDRISTEER
736546968 Carnobacterium gallinarum         -SQKENKNATIKKNGDYISQIFEKLVGVDTN-------------------------------------------------KNIRKPKMSLTDLKDLPKKD
736550717 Carnobacterium gallinarum         TLVKADQVKGYKVLAENIFIIFEQLEKSNSE--------------------------------------------------------KPSVYLNNIRRLK
503209049 Paludibacter propionicigenes      TIIKFDTAKKQKLNVDQYKIVEKIFKYPKQE------------------------------------------------------------LPKQIKAEE
502750493 Listeria seeligeri                TICRPEQKQMKKLVHGLLQENSQEKIKVSDV-----------------------------------------------------------------TKLN
738100542 Listeria weihenstephanensis       KLFKPK----------------------------------------------------------------------------------------------
738133341 Listeria newyorkensis             TVRKPDEKEKNRRKQAINKAINKEITELMLA------------------------------------------------VLHQEVPSQKLHNLKSLNTES
544240864 Leptotrichia wadei F0279          RIEKEEDQNIKS------LYFFIKELYLNEK-------------------------------------------------NEEWELKNINLE---ILDDK
738101039 Leptotrichia wadei                RIEKEEDQNIKS------LYFFIKELYLNEK-------------------------------------------------NEEWELKNINLE---ILDDK
545623740 Leptotrichia wadei                YIKNPENVKNKDKDAEKETKIRRTNLKKYFS--------------------------------------------------------EIILRKEDEKYIL
545623306 Leptotrichia wadei                YIKNPDNASEEE------NRIRRENLKKFFS-------------------------------------------------NKVLHLKDSVLYLKNRKEKN
506250229 Leptotrichia buccalis             YIKNPSSTETKE------NQKRIGKLKKFFS-------------------------------------------------NKMVYLKDNTLSLKNGKKEN
Secondary structure for 506250229 (Jpred)   HH------HHHH------HHHHHHHHHHHHH-------------------------------------------------HHHHHHHHHHHHH---HHHH
545661797 Leptotrichia sp  oral taxon 225    ----------------------------------------------------------------------------------------------------
545620493 Leptotrichia sp  oral taxon 879    NVLKEFKRKFHAGNILFKLKGKEEIIRIENN------------DDFLETEEVVLYIE-----------VYGKSEKLKALEITKKKIIDEAIRQGITKDDK
517262777 Leptotrichia shahii               NILKEFTRKFHAGNILFKLKGKEGIIRIENN------------DDFLETEEVVLYIE-----------AYGKSEKLKALGITKKKIIDEAIRQGITKDDK
CONSENSUS                                   ....................................................................................................
HEPN (predicted RNAse) motifs               ....................................................................................................

564875111 Rhodobacter capsulatus R121       A-------QDSDYDQFKRRLHPYGDKFQPADSGAKLKFEADP---------------------------------PEPQAFHGRWYGAMSKRGNDAKELA
769144435 Lachnospiraceae bacterium MA2020   DKFGGARIYDDDIEEALTETLKKSFRKENVRNSIKVLIENAA------------GIRSSLSKDEEELIQEYFVKQLVEEYTKTKLQKNVVKSIKNQNMVI
551041827 Lachnospiraceae bacterium NK4A179  N-NIDNKVSEDIIDRIIAKYLKKSLCRERVKRGLKKLLMNAF------------D---LPYSDPDIDVQRDFIDYVLEDFYHVRAKSQVSRSIKNMNMPV
671463495 Clostridium  aminophilum          GMVESLKGERDPQKVISKLLLYYLRKGLKPGTDGLRMILEAS-----------------------CGLRKLSGDEKELKVFLQTLDEDFEKKTFKKNLIR
Secondary structure for 671463495 (Jpred)   HHHHHH------HHHHHHHHHHHHHH--HHHHHHHHHHHHHH--------------------------------HHHHHHHHHHHHHHHHHHHHHHHHHH
652829192 Lachnospiraceae bacterium NK4A144  EQIIDDLLEIQLRKGLRKGKAGLREVLLIGAGVIVRTDKKQE--------------------------IADFLEILDEDFNKTNQAKNIKLSIENQGLVV
736546968 Carnobacterium gallinarum         LALFIKRKFKNDDIVEIKNLDLISLFYNALQKVPGEHFTDES------------------------------WADFCQEMMPYREYKNKFIE--RKIILLA
736550717 Carnobacterium gallinarum         E--AGLKRFFKSKYHEEIKYTSEKNQSVPTKLNLIPLFFNAV-----------------DRIQEDKFDEKNWSYFCKEMSPYLDYKKSYLN--RKKEILA
503209049 Paludibacter propionicigenes      ILPFLNHKFQEPVKYWKNGKEESFNLTLLIVEAVQAQDKRKL-------------------------------------QPYYDWKTWYIQ--TKSDLLK
502750493 Listeria seeligeri                ISNFLNHRFKKSLYYFPENSPDKSEEYRIEINLSQLLEDSLK---------------------KQQGTFICWESFSKDMELYINWAENYIS--SKTKLIK
738100542 Listeria weihenstephanensis       --------FQNMISYPPSKGAEHVQFCLTDIAVPAIRDLDEI--------------------------KPDWGIFFEKLKPYTDWAESYIH--YKQTTIQ
738133341 Listeria newyorkensis             LTKLFKPKFQNMISYPPSKGAEHVQFCLTDIAVPAIRDLDEI--------------------------KPDWGIFFEKLKPYTDWAESYIH--YKQTTIQ
544240864 Leptotrichia wadei F0279          ERVIKGYKFKEDVYFFKEGYKEYYLRILFNNLIEKVQNENRE-------------------------KVRKNKEFLDLKEIFKKYKN------RKIDLLL
738101039 Leptotrichia wadei                ERVIKGYKFKEDVYFFKEGYKEYYLRILFNNLIEKVQNENRE-------------------------KVRKNKEFLDLKEIFKKYKN------RKIDLLL
545623740 Leptotrichia wadei                KKTKKFKDINQEIDYYDVKSKKNQQEIFDVLKEILELKIKET--------------------------EKEEIITFDSEKLKKVFGEDFVKKEAKIKAIE
545623306 Leptotrichia wadei                A--------VQDKNYSEEDISEYDLKNKNSFSVLKKILLNED----------------------------------VNSEELEIFRKDVEAKLNKINSLK
506250229 Leptotrichia buccalis             I----------DREYSETDILESDVRDKKNFAVLKKIYLNEN----------------------------------VNSEELEVFRNDIKKKLNKINSLK
Secondary structure for 506250229 (Jpred)   --------------------HHHH-----HHHHHHHHHH----------------------------------------HHHHHHHHHHHHHHHHHHHHH
545661797 Leptotrichia sp  oral taxon 225    ----------------------------------------------------------------------------------------------------
545620493 Leptotrichia sp  oral taxon 879    K--IEIKRQENEEEIEIDIRDEYTNKTLNDCSIILRIIENDELETKKSIYEIFKNINMSLYKIIEKIIENETEKVFENRYYEEHLREKLLKD-NKIDVIL
517262777 Leptotrichia shahii               K--IEIKRQENEEEIEIDIRDEYTNKTLNDCSIILRIIENDELETKKSIYEIFKNINMSLYKIIEKIIENETEKVFENRYYEEHLREKLLKD-DKIDVIL
CONSENSUS                                   ....................................................................................................
HEPN (predicted RNAse) motifs               ....................................................................................................

564875111 Rhodobacter capsulatus R121       AALYEHLHVDEKRIDG-------------QPKRNPKTDKFAPGLVV-------ARALGIESSVLPRGMARLARNWGEEEIQTYFVVDVAASVKEVAKAAV
769144435 Lachnospiraceae bacterium MA2020   QPDSDSQVLSLSESRREKQSSAVSSDTLVNCKEKDVLKAFLTDYAV---------------------LDEDERNSLLWKLRNLVNLYFYG-SESIRDYSY
551041827 Lachnospiraceae bacterium NK4A179  QPEGDGKF-AITVSKGGTESGNK------RSAEKEAFKKFLSDYAS---------------------LDERVRDDMLRRMRRLVVLYFYGSDDSKLS---
671463495 Clostridium  aminophilum          SIENQNMAVQPSNEGDPIIGITQGRFNSQKNEEKSAIERMMSMYAD---------------------LNEDHREDVLRKLRRLNVLYFNVDTEKTEEPT-
Secondary structure for 671463495 (Jpred)   HHH-------------EEEEEE---------HHHHHHHHHHHHH-------------------------HHHHHHHHHHHHHHEEEEEE-----------
652829192 Lachnospiraceae bacterium NK4A144  SPVSRGEERIFDVSGAQKGKSSK------KAQEKEALSAFLLDYAD---------------------LDKNVRFEYLRKIRRLINLYFYVKNDDVMSLTE
736546968 Carnobacterium gallinarum         NSIEQNKGFSINPET--------------FSKRKRVLHQWAIEVQE-----------RGDFSILDEKLSKLAEIYNFKKMCKRVQDELNDLEKSMKKG--
736550717 Carnobacterium gallinarum         NSIQQNRGFSMPTAEEPNL----------LSKRKQLFQQWAMKFQESPLIQQNNFAVEQFNKEFANKINELAAVYNVDELCTAITEKL------------
503209049 Paludibacter propionicigenes      KSIENNRI-DLTEN---------------LSKRKKALLAWETEFTA----------------SGSIDLTHYHKVYMTDVLCKMLQDV-------------
502750493 Listeria seeligeri                KSIRNNRIQST------------------ESRSGQLMDRYMKDILN---------------KNKPFDIQSVSEKYQLEKLTSALKATFK-----------
738100542 Listeria weihenstephanensis       KSIEQNKI-QSP-----------------DSPRKLVLQKYVTAFLN----------------GEPLGLDLVAKKYKLADLAESFKVV-------------
738133341 Listeria newyorkensis             KSIEQNKI-QSP-----------------DSPRKLVLQKYVTAFLN----------------GEPLGLDLVAKKYKLADLAESFKLV-------------
544240864 Leptotrichia wadei F0279          KSINNNKI-NLEYKKENVNEEIYGINP--TNDREMTFYELLKEIIE-------------KKDEQKSILEEKLDNFDITNFLENIEKIFNEETE-----IN
738101039 Leptotrichia wadei                KSINNNKI-NLEYKKENVNEEIYGINP--TNDREMTFYELLKEIIE-------------KKDEQKSILEEKLDNFDITNFLENIEKIFNEETE-----IN
545623740 Leptotrichia wadei                KSLKINKA-NYKKDSIKIGDDKYS-NVKGENKRSRIYEYYKKSENL-----------KKFEENIREAFEKLYTEENIKELYSKIEEILKKTHLKSIVREF
545623306 Leptotrichia wadei                YSFEENKA-NYQKINENNVEKVGG-----KSKRNIIYDYYRESAKR-----------NDYINNVQEAFDKLYKKEDIEKLFFLIENSKKHEKYKIREYYH
506250229 Leptotrichia buccalis             YSFEKNKA-NYQKINENNIEKVEG-----KSKRNIIYDYYRESAKR-----------DAYVSNVKEAFDKLYKEEDIAKLVLEIENLTKLEKYKIREFYH
Secondary structure for 506250229 (Jpred)   HHHHH-----HHHHH--HHH-------------HHHHHHHHHHHHH-----------HHHHHHHHHHHHH--HHHHHHHHHHHHHHHHHH---HHHHHHH
545661797 Leptotrichia sp  oral taxon 225    ----------------------------------------------------------------------------------------------------
545620493 Leptotrichia sp  oral taxon 879    TNFMEIRE-KIKSNLEIMGFVKFYLNVSGDKKKSENKKMFVEKI-------LN-TNVDLTVEDIVDFIVKELKFWNITKRIEKVKKFNNEFLENRRNRTY
517262777 Leptotrichia shahii               TNFMEIRE-KIKSNLEILGFVKFYLNVGGDKKKSKNKKMLVEKI-------LN-INVDLTVEDIADFVIKELEFWNITKRIEKVKKVNNEFLEKRRNRTY
CONSENSUS                                   ....................................................................................................
HEPN (predicted RNAse) motifs               ....................................................................................................
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FIGURE S6 (con't)

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564875111 Rhodobacter capsulatus R121         SAAQAFDPP------------------------------------RQVSGRSLSPKV--GFALAEHLERV-----------------TGSKRCSFDPAAG
769144435 Lachnospiraceae bacterium MA2020    TKEKSVWKEHDEQK------ANKTLFIDEICHITK----------IGKNGKEQKVLD--YEENRSRCRKQ---------------NINYYRSALNYAKNN
551041827 Lachnospiraceae bacterium NK4A179   -----DVNEKFDVW------EDHAARRVDNREFIKLPLENKLA--NGKTDKDAERIR--KNTVKELYRNQ---------------NIGCYRQAVKAVEED
671463495 Clostridium  aminophilum            LPGEVDTNPVFEVW------HDHEKGKENDRQFATFAKILTEDRETRKKEKLAVKEA--LNDLKSAIRDH---------------NIMAYRCSIKVTEQD
Secondary structure for 671463495 (Jpred)     -------------H------HHHH-------HHHHHHHHHHHHHH----HHHHHHHH--HHHHHHHHH------------------HHHHHHEEEEEE--
652829192 Lachnospiraceae bacterium NK4A144   IPAEVNLEKDFDIW------RDHEQRKEENGDFVGCPDILLADRDVKKSNSKQVKIA--ERQLRESIREK---------------NIKRYRFSIKTIEKD
736546968 Carnobacterium gallinarum           ---------------------------------------------KNPEKEKEAYKKQKNFKIKTIWKDY---------------PYKTHIGLI------
736550717 Carnobacterium gallinarum           ---------------------------------------------MNFDKDKSNKTR--NFEIKKLWKQH---------------PHNKDKALI------
503209049 Paludibacter propionicigenes        ---------------------------------------------KPLTDDKGKINT--NAYHRGLKKAL-----------------QNHQPAIFGTREV
502750493 Listeria seeligeri                  ---------------------------------------------EAKKNDKEI-----NYKLKSTLQNH-------------------ERQII------
738100542 Listeria weihenstephanensis         -------------------------------------------------DLNEDKSA--NYKIKACLQQH-------------------QRNIL------
738133341 Listeria newyorkensis               -------------------------------------------------DLNEDKSA--NYKIKACLQQH-------------------QRNIL------
544240864 Leptotrichia wadei F0279            IIKGKVLNELREYI------KEKEE--------------------NNSDNKLKQIY---NLELKKYIENN-----------------FSYKK--------
738101039 Leptotrichia wadei                  IIKGKVLNELREYI------KEKEE--------------------NNSDNKLKQIY---NLELKKYIENN-----------------FSYKK--------
545623740 Leptotrichia wadei                  YQNEIIGESEFSKKNGDGISILYNQIKDSI---------------KKEENFIEFIENTGNLELKELTKSQ---------------IFYKYFL--------
545623306 Leptotrichia wadei                  KIIGRKNDKENFAK------IIYEEI-------------------QNVNNIKELIEK--IPDMSELKKSQ---------------VFYKYYL--------
506250229 Leptotrichia buccalis               EIIGRKNDKENFAK------IIYEEI-------------------QNVNNMKELIEK--VPDMSELKKSQ---------------VFYKYYL--------
Secondary structure for 506250229 (Jpred)     HHH--------HHH------HHHHHH-------------------H--HHHHHHHH-----------HH-----------------HHHHHH--------
545661797 Leptotrichia sp  oral taxon 225     --------------------------------------------------MKELIEK--VPNVSELKKSQ---------------VFYKYYL--------
545620493 Leptotrichia sp  oral taxon 879     IKSYVLLDKHEKFK------IERENKKDKIVKFFVENIKN-----NSIKEKIEKILA--EFKINELIKKLEKELKKGNCDTEIFGIFKKHYKVNFDSKKF
517262777 Leptotrichia shahii                 IKSYVLLDKHEKFK------IERENKKDKIVKFFVENIKN-----NSIKEKIEKILA--EFKIDELIKKLEKELKKGNCDTEIFGIFKKHYKVNFDSKKF
CONSENSUS                                     ....................................................................................................
HEPN (predicted RNAse) motifs                 ....................................................................................................

564875111 Rhodobacter capsulatus R121         PSVLAL---------------HDEVKKT----------YKRLCARGKNAARAFPADKTELLAL-MRHTHENRVRNQMVRM-------GRVSEYRGQQAGD
769144435 Lachnospiraceae bacterium MA2020    TSGIFE--NEDSNHFWIHLI-ENEVERLYNGIENGEEFKFETGYISEKVWKAV-INHLSIKYIALGKAVYNYAMKELSSP-------GDIEPG--KIDDS
551041827 Lachnospiraceae bacterium NK4A179   NNGRYF-DDKMLNMFFIHRI-EYGVEKIYANLKQVTEFKARTGYLSEKIWKDL-INYISIKYIAMGKAVYNYAMDELNASDKKEIELGKISEE--YLSG-
671463495 Clostridium  aminophilum            KDGLFF-EDQRINRFWIHHI-ESAVERILASINPEKLYKLRIGYLGEKVWKDL-LNYLSIKYIAVGKAVFHFAMEDLGKT-GQDIELGKLSNS--VSGG-
Secondary structure for 671463495 (Jpred)     ---------HHHHHHHHHHH-HHHHHHHHH-----HHHHHHH----HHHHHHH-HHHHHHHHHHHHHHHHHHHHHHH------EEEE--HHHH--H----
652829192 Lachnospiraceae bacterium NK4A144   -DGTYFFANKQISVFWIHRI-ENAVERILGSINDKKLYRLRLGYLGEKVWKDI-LNFLSIKYIAVGKAVFNFAMDDLQEK-DRDIEPGKISEN--AVNGL
736546968 Carnobacterium gallinarum           -EKIKE--NEELNQF------NIEIGKY---FEHYFPIKKERCTEDEPYY----LNSETIATT-VNYQLKNALISYLMQI-------GKYKQF--GLENQ
736550717 Carnobacterium gallinarum           -KLFNQEGNEALNQF------NIELGKY---FEHYFPKTGKKESAES----YY-LNPQTIIKT-VGYQLRNAFVQYLLQV-------GKLHQY----NKG
503209049 Paludibacter propionicigenes        PNEANR-ADNQLSIY------HLEVVKY---LEHYFPIKTSKRRNTADDIAHY-LKAQTLKTT-IEKQLVNAIRANIIQQ-------GKTNHH--ELKAD
502750493 Listeria seeligeri                  -EELKE--NSELNQF------NIEIRKH---LETYFPIKKTNRKVGDIRN----LEIGEIQKI-VNHRLKNKIVQRILQE-------GKLASY---EIES
738100542 Listeria weihenstephanensis         -DELKE--DPELNQY------GIEVKKY---IQRYFPIKRAPNR-SKHARADF-LKKELIEST-VEQQFKNAVYHYVLEQ-------GKMEAY--ELTD-
738133341 Listeria newyorkensis               -DELKE--DPELNQY------GIEVKKY---IQRYFPIKRAPNR-SKHARADF-LKKELIEST-VEQQFKNAVYHYVLEQ-------GKMEAY--ELTDP
544240864 Leptotrichia wadei F0279            -QKSKS--KNGKNDYL------------------YLNFLKKIMFIEEVDEKKE-INKEKFKNK-INSNFKNLFVQHILDY-------GKLLYY--KENDE
738101039 Leptotrichia wadei                  -QKSKS--KNGKNDYL------------------YLNFLKKIMFIEEVDEKKE-INKEKFKNK-INSNFKNLFVQHILDY-------GKLLYY--KENDE
545623740 Leptotrichia wadei                  -ENEEL--NDENIKFAFCYFVEIEVNNL---LKENVYKIKRFNESNKKRIENI-FEYGKLKKL-IVYKLENKLNNYVRNC-------GKYNYH--MENGD
545623306 Leptotrichia wadei                  -DKEEL--NDKNIKYAFCHFVEIEMSQL---LKNY--VYKRLSNISNDKIKRI-FEYQNLKKL-IENKLLNKLDTYVRNC-------GKYNYY--LQVGE
506250229 Leptotrichia buccalis               -DKEEL--NDKNIKYAFCHFVEIEMSQL---LKNY--VYKRLSNISNDKIKRI-FEYQNLKKL-IENKLLNKLDTYVRNC-------GKYNYY--LQDGE
Secondary structure for 506250229 (Jpred)     -HHHH--------EEEEEHHHHHHHHHH---HHHH--H--------HHHHHHH-HHH--HHHH-HHHHHHHHHHHHHHH----------EEEH--HH---
545661797 Leptotrichia sp  oral taxon 225     -NKEKL--NDENIKYVFCHFVEIEMSKL---LKNY--VYKKPSNISNDKVKRI-FEYQSLKKL-IENKLLNKLDTYIRNC-------GKYSFY--LQDGE
545620493 Leptotrichia sp  oral taxon 879     SNKSDE--EKELYKIIYRYL-KGRIEKI---LVNE--QKVRLKKMEKIEIEKI-LNESILSEK-ILKRVKQYTLEHIMYL-------GKLRHN--DIVKM
517262777 Leptotrichia shahii                 SKKSDE--EKELYKIIYRYL-KGRIEKI---LVNE--QKVRLKKMEKIEIEKI-LNESILSEK-ILKRVKQYTLEHIMYL-------GKLRHN--DIDMT
CONSENSUS                                     ................................................................I.....N................GK...........
HEPN (predicted RNAse) motifs                 ....................................................................................................

564875111 Rhodobacter capsulatus R121         LAQ-SHYWTSAGQTEIKESEIFVRLWVGAFALAGRSM-KAWIDP----------------MGKIVNTEKNDRDLTAAVNIRQVISNKEMVAEAMARR---
769144435 Lachnospiraceae bacterium MA2020    YIN---GITSFDYEIIKAEESLQRDISMNVVFATNYLACATVDT----------------DKDFLLFS-----KEDIRS---CTKKDGNLCKNIMQF---
551041827 Lachnospiraceae bacterium NK4A179   -IS------SFDYELIKAEEMLQRETAVYVAFAARHLSSQTVE-------------LDSENSDFLLLKPKGTMDKNDKNKLASNNILNFLKDKETLR---
671463495 Clostridium  aminophilum            -LT------SFDYEQIRADETLQRQLSVEVAFAANNLFRAVVGQ---TGKKIEQSKSEENEEDFLLWK-----AEKIAESIKKEGEGNTLKSILQFF---
Secondary structure for 671463495 (Jpred)     ------------HHHHHHHHHHHHHHHHHHHHHHHHHHHHHH---------------------EEEE-------HHHHHHHH----HHHHHHHHHHH---
652829192 Lachnospiraceae bacterium NK4A144   T--------SFDYEQIKADEMLQREVAVNVAFAANNLARVTVDI-----------PQNGEKEDILLWN-----KSDIKK--YKKNSKKGILKSILQF---
736546968 Carnobacterium gallinarum           VLD------SKKLQEIGIYEGFQTKFMDACVFATSSL-KNIIEP--------------MRSGDILGKR---EFKEAIATSSFVN------YHHFFPY-FP
736550717 Carnobacterium gallinarum           VLD------SQTLQEIGMYEGFQTKFMDACVFASSSL-RNIIQA--------------TTNEDILTREKFKKELEKNVELKHDLFFKTEIVEERDEN---
503209049 Paludibacter propionicigenes        TT-------SNDLIRIKTNEAFVLNLTGTCAFAANNI-RNMVDN--------------EQTNDILGKG---DFIKSLLK--------DNTNSQLYSF---
502750493 Listeria seeligeri                  TVN------SNSLQKIKIEEAFALKFINACLFASNNL-RNMVYP--------------VCKKDILMIGEFKNSFKEIKH------------KKFIRQ---
738100542 Listeria weihenstephanensis         -PK------TKDLQDIRSGEAFSFKFINACAFASNNL-KMILNP--------------ECEKDILGKG---DFKKNLPN----STTQSDVVKKMIPF---
738133341 Listeria newyorkensis               K--------TKDLQDIRSGEAFSFKFINACAFASNNL-KMILNP--------------ECEKDILGKG---NFKKNLPN----STTRSDVVKKMIPF---
544240864 Leptotrichia wadei F0279            YIKNTGQLETKDLEYIKTKETLIRKMAVLVSFAANSY-YNLFGR---------------VSGDILGTEVVKSSKTNVIK------VGSHIFKEKMLN---
738101039 Leptotrichia wadei                  YIKNTGQLETKDLEYIKTKETLIRKMAVLVSFAANSY-YNLFGR---------------VSGDILGTEVVKSSKTNV------IKVGSHIFKEKMLN---
545623740 Leptotrichia wadei                  IAT------SDINMRNRQTEAFLRSIIGVSSFGYFSL-RNILGV--------NDDDFYETEEDLTKKE-----RRNLEKAKEDITIKNTFDEVVVKS---
545623306 Leptotrichia wadei                  IAT------SDFIARNRQNEAFLRNIIGVSSVAYFSL-RNILET--------------ENENDITGRMRGKTVKNNKGEEKYVSGEVDKIYNENKQN---
506250229 Leptotrichia buccalis               IAT------SDFIARNRQNEAFLRNIIGVSSVAYFSL-RNILET--------------ENENDITGRMRGKTVKNNKGEEKYVSGEVDKIYNENKKN---
Secondary structure for 506250229 (Jpred)     ---------HHHHHHH---HHHHHHHHHHHHHHHHHH-HHH--------------------------------------EEEEEE----E------E---
545661797 Leptotrichia sp  oral taxon 225     IAT------SDFIVGNRQNEAFLRNIIGVSSAAYFSL-RNILET--------------ENENDITGKMRGKTVKNKKGEEKYISGEIDKLYDNNKQN---
545620493 Leptotrichia sp  oral taxon 879     TVN------TDDFSRLHAKEELDLELITFFASTNMEL-NKIFNGKEKVTD---FFGFNLNGQKITLKEKVPSFKLNILKKLNFINNENNIDEKLSHF---
517262777 Leptotrichia shahii                 TVN------TDDFSRLHAKEELDLELITFFASTNMEL-NKIFSRENINNDENIDFFGGDREKNYVLDKKILNSKIKIIRDLDFIDNKNNITNNFIRK---
CONSENSUS                                     .........S.........E............A...L.........................D.....................................
HEPN (predicted RNAse) motifs                 ....................................................................................................

564875111 Rhodobacter capsulatus R121         -------------GIYFGETPELDRLGAEGNEGFVFALLRYLRGCRNQTFHLGARAGFLKE---------------------------------------
769144435 Lachnospiraceae bacterium MA2020    ------WGGYSTWKN-FCE--EYLKDDKD-ALELLYSLKSMLYSMRNSSFHFSTENVDNG----------------------------------------
551041827 Lachnospiraceae bacterium NK4A179   DTILQYFGGHSLWTDFPFD--KYLAGGKD-DVDFLTDLKDVIYSMRNDSFHYATENHNNG----------------------------------------
671463495 Clostridium  aminophilum            -GGASSWDLN-HFCAAYGN--ESSALGYE--TKFADDLRKAIYSLRNETFHFTTLNKGSF----------------------------------------
Secondary structure for 671463495 (Jpred)     ---------H-HHHHH---------------HHHHHHHHHHHHHH----EEEEE----------------------------------------------
652829192 Lachnospiraceae bacterium NK4A144   ------FGGASTWNMKMFEI-AYHDQPGDYEENYLYDIIQIIYSLRNKSFHFKTYDHGDK----------------------------------------
736546968 Carnobacterium gallinarum           FELKGMKDRESELIP-FGE--QTEAKQMQ---NIWA-LRGSVQQIRNEIFHSFDKNQKFN-----------------------L----------------
736550717 Carnobacterium gallinarum           ----------------PAK--KIAMTPNE--LDLWA-IRGAVQRVRNQIFHQ-QINKRHEP---------------------------------------
503209049 Paludibacter propionicigenes        ---------------FFGE--GLSTNKAEKETQLWG-IRGAVQQIRNNVNHY--KKDALK----------------------------------------
502750493 Listeria seeligeri                  ------------WSQFFSQ--EITVDDIE--LASWG-LRGAIAPIRNEIIHL--KKHSWKKF-------------------FNN----------------
738100542 Listeria weihenstephanensis         ----------------FSD--EIQNVNFD--EAIWA-IRGSIQQIRNEVYHC--KKHSWK----------------------------------------
738133341 Listeria newyorkensis               ----------------FSD--ELQNVNFD--EAIWA-IRGSIQQIRNEVYHC--KKHSWK----------------------------------------
544240864 Leptotrichia wadei F0279            ----------------YFF--DFEIFDANKIVEILESISYSIYNVRNGVGHF-NKLILGK----------------------------------------
738101039 Leptotrichia wadei                  ----------------YFF--DFEIFDANKIVEILESISYSIYNVRNGVGHF-NKLILGK----------------------------------------
545623740 Leptotrichia wadei                  FQKKGIYNIKENLKMFYGD--SFDNADKDELKQFFVNMLNAITSIRHRVVHY-NMNTNSE----------------------------------------
545623306 Leptotrichia wadei                  -------EVKENLKMFYSY--DFNMDNKNEIEDFFANIDEAISSIRHGIVHF-NLELEGK----------------------------------------
506250229 Leptotrichia buccalis               -------EVKENLKMFYSY--DFNMDNKNEIEDFFANIDEAISSIRHGIVHF-NLELEGK----------------------------------------
Secondary structure for 506250229 (Jpred)     -------EEE----EEE----------HHHHHHHHHHHHHHHHHHH--HHEE------------------------------------------------
545661797 Leptotrichia sp  oral taxon 225     -------EVKKNLKMFYSY--DFNMNSKKEIEDFFSNIDEAISSIRHGIVHF-NLELEGK----------------------------------------
545620493 Leptotrichia sp  oral taxon 879     -----------------------------------YSFQKEGYLLRNKILHNS--------YGNIQETKNLKGEYENVEKLIKELKVSDEEI-SKSLSLD
517262777 Leptotrichia shahii                 -------------------------------------FTKIGTNERNRILHA---------ISKERDLQGTQDDYNKVINIIQNLKISDEEV-SKALNLD
CONSENSUS                                     .............................................RN...H.................................................
HEPN (predicted RNAse) motifs                 .............................................R....H.................................................
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FIGURE S6 (con’t)

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564875111 Rhodobacter capsulatus R121              IRKELEKTRWGKAKEAEHVVLTDKTVAAIRAIIDNDAK--ALGARLLADLSGAFVAHYAS-----KEHF-------STLY------SEIVKAVKDAPEVS
769144435 Lachnospiraceae bacterium MA2020         ----------------------SWDTELIGKLFEEDCN--RAARIEKEKFYNNNLHMFYS-----SSLL---EKVLERLY------SSHHER---ASQV-
551041827 Lachnospiraceae bacterium NK4A179        ----------------------KWNKELISAMFEHETE--RMTVVMKDKFYSNNLPMFYK-----NDDL---KKLLIDLY------KDNVER---ASQV-
671463495 Clostridium  aminophilum                 ----------------------DWNAKLIGDMFSHEAA--TGIAVERTRFYSNNLPMFYR-----ESDL---KRIMDHLY------NTYHPR---ASQV-
Secondary structure for 671463495 (Jpred)          ----------------------HHHHHHHHHHHHHHHH--HHHHHHHHHHHH------HH-----HHHH---HHHHHHHH------H-------------
652829192 Lachnospiraceae bacterium NK4A144        ----------------------NWNRELIGKMIEHDAE--RVISVEREKFHSNNLPMFYK-----DADL---KKILDLLY------SDYAGR---ASQV-
736546968 Carnobacterium gallinarum                PQLDKSNFEFDASENSTGKSQ-SYIETDYKFLFEAEKN--QLEQFFIERIKSSGALEYYP-----LKSLEKLFAKKEMKF------SLGSQV---VAFA-
736550717 Carnobacterium gallinarum                NQLKVGSFENGDLGNV------SYQKTIYQKLFDAEIK--DIEIYFAEKIKSSGALEQYS-----MKDLEKLFSNKELTL------SLGGQV---VAFA-
503209049 Paludibacter propionicigenes             TVFNISNFENPTITDPKQQT--NYADTIYKARFINELE--KIPEAFAQQLKTGGAVSYYT-----IENL--KSLLTTFQF------SLCRST---IPFA-
502750493 Listeria seeligeri                       PTFKVKKSKIINGKTKDVTSEFLYKETLFKDYFYSELD--SVPELIINKMESSKILDYYS-----SDQLNQVFTIPNFEL------SLLTSA---VPFA-
738100542 Listeria weihenstephanensis              SILKIKGFEFEPNNM-------KYTDSDMQKLMDKDIA--KIPDFIEEKLKSSGIIRFYS-----HDKL-QSIWEMKQGF------SLLTTN---APFV-
738133341 Listeria newyorkensis                    SILKIKGFEFEPNNM-------KYADSDMQKLMDKDIA--KIPEFIEEKLKSSGVVRFYR-----HDEL-QSIWEMKQGF------SLLTTN---APFV-
544240864 Leptotrichia wadei F0279                 --YKKKDINTNKRIEED-----LNNNEEIKGYFIKKRG--EIERKVKEKFLSNNLQYYYS-----KEKI--ENYFEVYEF------EILKRK---IPFA-
738101039 Leptotrichia wadei                       --YKKKDINTNKRIEED-----LNNNEEIKGYFIKKRG--EIERKVKEKFLSNNLQYYYS-----KEKI--ENYFEVYEF------EILKRK---IPFA-
545623740 Leptotrichia wadei                       NIFNFSG---------------IEVSKLLKSIFEKETDKRELKLKIFRQLNSAGVFDYWE-----NRKI--DKYLENIEF------KFVNKN---IPFV-
545623306 Leptotrichia wadei                       DIFAFKN---------------IAPSEISKKMFQNEINEKKLKLKIFKQLNSANVFNYYE-----KDVI--IKYLKNTKF------NFVNKN---IPFV-
506250229 Leptotrichia buccalis                    DIFAFKN---------------IAPSEISKKMFQNEINEKKLKLKIFRQLNSANVFRYLE-----KYKI--LNYLKRTRF------EFVNKN---IPFV-
Secondary structure for 506250229 (Jpred)          --------------------------HHHHHHHHH---HHHHHHHHHHHHH----HHHHH-----HHHH--HHHHHHHHH------HHH-----------
545661797 Leptotrichia sp  oral taxon 225          DIFTFKN---------------IVPSQISKKMFHDEINEKKLKLKIFKQLNSANVFRYLE-----KYKI--LNYLNRTRF------EFVNKN---IPFV-
545620493 Leptotrichia sp  oral taxon 879          VIFEGKVDIINKINS-------LKIGEYKDKKYLPSFS--KIVLEITRKFREINKDKLFD-IESEKIILNAVKYVNKILY------EKITSNEE-NEFLK
517262777 Leptotrichia shahii                      VVFKDKKNIITKINDIK-----ISEENNNDIKYLPSFS--KVLPEILNLYRNNPKNEPFDTIETEKIVLNALIYVNKELYKKLILEDDLEENESKNIFL-
CONSENSUS                                          ....................................................................L...............................
HEPN (predicted RNAse) motifs                      ....................................................................................................

564875111 Rhodobacter capsulatus R121              SGLPRLKLLLKRADGVRGYVHGLRDTRKHAFATKLPPPPAPRELDDPATKARYIALLRLYDGPFRA-----------------YASGITGTALAGPAARA
769144435 Lachnospiraceae bacterium MA2020         ---PSFNRVFVRKNFPSSLSEQR----------ITPKFTDSK-DEQIWQSAVYYLCKEIYYNDFLQ-----------------SK--EAYKLFREGVKNL
551041827 Lachnospiraceae bacterium NK4A179        ---PSFNKVFVRKN-FPALVRDKDNLGIELD--LKADADKGE-NELKFYNALYYMFKEIYYNAFLNDKNVRERFITKATKVADNYDRNKERNLKDRIKSA
671463495 Clostridium  aminophilum                 ---PSFNSVFVRKNFRLFLSNTLN---------TNTSFDTE--VYQKWESGVYYLFKEIYYNSFLP-----------------SG--DAHHLFFEGLRRI
Secondary structure for 671463495 (Jpred)          -------EEEE--------------------------------HHHHHHHHHHHHHHHHHHH---------------------------HHHHHHHHHHH
652829192 Lachnospiraceae bacterium NK4A144        ---PAFNTVLVRKNFPEFLRKDMG---------YKVHFNNPE-VENQWHSAVYYLYKEIYYNLFLR-----------------DK--EVKNLFYTSLKNI
736546968 Carnobacterium gallinarum                ---PSYKKLVKKGH---SYQTATEGTAN-YL--GLSYYNRYE-LKEESFQAQYYLLKLIYQYVFLP-----------------NFSQGNSPAFRETVKAI
736550717 Carnobacterium gallinarum                ---PSYKKLYKQGY---FYQNEKT------I--ELEQFTDYD-FSNDVFKANYYLIKLIYHYVFLP-----------------QFSQANNKLFKDTVHYV
503209049 Paludibacter propionicigenes             ---PGFKKVFNGGI---NYQNAKQDES--FYELMLEQYLRKENFAEESYNARYFMLKLIYNNLFLP-----------------GFT-TDRKAFADSVGFV
502750493 Listeria seeligeri                       ---PSFKRVYLKGF---DYQNQDEAQPDYNL--KLNIYNEKA-FNSEAFQAQYSLFKMVYYQVFLP-----------------QFT-TNNDLFKSSVDFI
738100542 Listeria weihenstephanensis              ---PSFKRVYAKGH---DYQTSKNR----YYDLGLTTFDILE-YGEEDFRARYFLTKLVYYQQFMP-----------------WFT-ADNNAFRDAANFV
738133341 Listeria newyorkensis                    ---PSFKRVYAKGH---DYQTSKNR----YYNLDLTTFDILE-YGEEDFRARYFLTKLVYYQQFMP-----------------WFT-ADNNAFRDAANFV
544240864 Leptotrichia wadei F0279                 ---PNFKRIIKKGE---DLFNNKNNKKYEYF--KNFDKNSAE-EKKEFLKTRNFLLKELYYNNFYK-----------------EFL-SKKEEFEKIVLEV
738101039 Leptotrichia wadei                       ---PNFKRIIKKGE---DLFNNKNNKKYEYF--KNFDKNSAE-EKKEFLKTRNFLLKELYYNNFYK-----------------EFL-SKKEEFEKIVLEV
545623740 Leptotrichia wadei                       ---PSFTKLYNRID---NLKGNNAL--------NLGYINIPK--RKEARDSQIYLLKNIYYGEFVE-----------------KFV-NNNDNFEKIFREI
545623306 Leptotrichia wadei                       ---PSFTKLYNKIE---DLRNTLKF----FW--SVP-------KDKEEKDAQIYLLKNIYYGEFLN-----------------KFV-KNSKVFFKITNEV
506250229 Leptotrichia buccalis                    ---PSFTKLYSRID---DLKNSLGI----YW--KTPKTNDDN-KTKEIIDAQIYLLKNIYYGEFLN-----------------YFM-SNNGNFFEISKEI
Secondary structure for 506250229 (Jpred)          -----HHHHHHHHH---HHHHH-------EE------------------HHHHHHHHHHHHHHHHH-----------------HH-----HHHHHHHHHH
545661797 Leptotrichia sp  oral taxon 225          ---PSFTKLYSRID---DLKNSLCI----YW--KIPKANDNN-KTKEITDAQIYLLKNIYYSEFLN-----------------YFM-SNNGNFFEIIKEI
545620493 Leptotrichia sp  oral taxon 879          TLPDKLVKKSNNKK---ENKNLLSIEE--YY--KNAQVSSSK-GDKKAIKKYQNKVTNAYLEYLEN-----------------TF--TEIIDFSKFNLNY
517262777 Leptotrichia shahii                      ---QELKKTLGNID---EIDENI--IEN-YY--KNAQISASK-GNNKAIKKYQKKVIECYIGYLRK-----------------NY--EELFDFSDFKMNI
CONSENSUS                                          ...P.......................................................Y...F............................F.......
HEPN (predicted RNAse) motifs                      ....................................................................................................

564875111 Rhodobacter capsulatus R121              ----KEAATALAQSVNVTKAYSDVMEGRSSRLRPPNDGETLREYLSALTGETATEFRVQIGYESDSENARKQAEF--IENYRRDMLAF---MFEDYI--R
769144435 Lachnospiraceae bacterium MA2020         ----DKNDINNQKAAD-SFKQ------AVVYYGKAIGNATLSQVCQAIMTEYNRQNNDGLKKKSAYAEKQNSNKYKHYPLFLKQVLQS---AFWEYLDEN
551041827 Lachnospiraceae bacterium NK4A179        ---GSDEKKKLREQLQ-NYIAENDFGQRIKNIVQVNPDYTLAQICQLIMTEYNQQNNGCMQKKSAARKDINKDSYQHYKMLLLVNLRK---AFLEFI--K
671463495 Clostridium  aminophilum                 ---RKEADNLPIVGKE-AKKR--NAVQDFGRRCDELKNLSLSAICQMIMTEYNEQNNGNRKVKSTREDKRKPDIFQHYKMLLLRTLQE---AFAIYI--R
Secondary structure for 671463495 (Jpred)          ---HHHHHHH-----H-HHHH--HHHHHHHHHHHHHHHHHHHHHHHHHHHHHHH-----HHHHHHHHHH-----HHHHHHHHHHHHHH---HHHHHH--H
652829192 Lachnospiraceae bacterium NK4A144        --------RSEVSDKK-QKLA----SDDFASRCEEIEDRSLPEICQIIMTEYNAQNFGNRKVKSQRVIEKNKDIFRHYKMLLIKTLAG---AFSLYL--K
736546968 Carnobacterium gallinarum                ----LRINKDEARKKM-KKNKKFLRKYAFEQVREMEFKETPDQYMSYLQSEMREEKVRKAEKNDKGFEKNITMNF---EKLLMQIFVK---GFDVFLTTF
736550717 Carnobacterium gallinarum                IQQNKELNTTEKDKKN-NKKI---RKYAFEQVK-LMKNESPEKYMQYLQREMQEERT----IKEAKKTNEEKPNY-NFEKLLIQIFIK---GFDTFL--R
503209049 Paludibacter propionicigenes             ----QMQNKKQAEKVN-PRKK---EAYAFEAVRPMTAADSIADYMAYVQSELMQEQN----KKEEKVAEETRINF---EKFVLQVFIK---GFDSFL--R
502750493 Listeria seeligeri                       ----LTLNKERKGYAK-----------AFQDIRKMNKDEKPSEYMSYIQSQLML-------YQKKQEEKEKINHF---EKFINQVFIK---GFNSFI--E
738100542 Listeria weihenstephanensis              ----LRLNKNRQQDAK-----------AFINIREVEEGEMPRDYMGYVQGQIAI---------HEDSTEDTPNHF---EKFISQVFIK---GFDSHM--R
738133341 Listeria newyorkensis                    ----LRLNKNRQQDAK-----------AFINIREVEEGEMPRDYMGYVQGQIAI---------HEDSIEDTPNHF---EKFISQVFIK---GFDRHM--R
544240864 Leptotrichia wadei F0279                 ----KEEKKSRGNINN-KKSG-----VSFQSIDDYDTKINISDYIASIHKKEME-------RVEKYNEEKQKDTAKYIRDFVEEIFLT---GFINYL--E
738101039 Leptotrichia wadei                       ----KEEKKSRGNINN-KKSG-----VSFQSIDDYDTKINISDYIASIHKKEME-------RVEKYNEEKQKDTAKYIRDFVEEIFLT---GFINYL--E
545623740 Leptotrichia wadei                       ----IEINKKDGTNTK-TKF------YKLEKFETLKANA-PIEYLEKLQSLHQI-------NYNREKVEEDKDIY---VDFVQKIFLK---GFINYL--Q
545623306 Leptotrichia wadei                       ----IKINKQ--RNQK-TGH------YKYQKFENIEKTV-PVEYLAIIQSREMI----------NNQDKEEKNTY---IDFIQQIFLK---GFIDYL--N
506250229 Leptotrichia buccalis                    ----IELNKNDKRNLK-TGF------YKLQKFEDIQEKI-PKEYLANIQSLYMI--------NAGNQDEEEKDTY---IDFIQKIFLK---GFMTYL--A
Secondary structure for 506250229 (Jpred)          ----HHHHHHHH---------------EEEHHHHHH----HHHHHHHHHHHHHH--------HHH-------HHH---HHHHHHHHHH---HHHHHH--H
545661797 Leptotrichia sp  oral taxon 225          ----IELNKNDKRNLK-TGF------YKLQKFENLQEKT-PKEYLANIQSFYMI--------DAGNKDEEEKDAY---IDFIQKIFLK---GFMTYL--A
545620493 Leptotrichia sp  oral taxon 879          ----DEIKTKIEERKD-NKSK--------IIIDSISTNINITNDIEYIISIFAL-------LNSNTYINKIRNRF-----FATSVWLEKQNGTKEYDYEN
517262777 Leptotrichia shahii                      ----QEIKKQIKDIND-NKT------YERITVKTSDKTIVINDDFEYIISIFAL-------LNSNAVINKIRNRF-----FATSVWLN----TSEYQ---
CONSENSUS                                          ...............................................I............................................F..Y....
HEPN (predicted RNAse) motifs                      ....................................................................................................

564875111 Rhodobacter capsulatus R121              AK------GFDWILKIEP------------GATAMTRAPVLPEPIDTRG-----------------------QYEHWQAAL----YLVMHFVPASDVSNL
769144435 Lachnospiraceae bacterium MA2020         KE------IYGFISAQIH------------KSNVEIKAEDFIANYSSQQ--YKKLVDKVK-------------KTPELQKW----YTLGRLINPRQANQF
551041827 Lachnospiraceae bacterium NK4A179        E-------NYAFVLKP--------------YKHDLCDKADFVPDFAKYVKPYAGLISRVA-------------GSSELQKW----YIVSRFLSPAQANHM
671463495 Clostridium  aminophilum                 RE------EFKFIFDLPK------------TLYVMKPVEEFLPNWKSGM--FDSLVERVK-------------QSPDLQRW----YVLCKFLNGRLLNQL
Secondary structure for 671463495 (Jpred)          HH------HHHHHH--------------------------HHHHHHHHH--HHHHHHH-------------------HHHH----HHHHHH--HHHHHHH
652829192 Lachnospiraceae bacterium NK4A144        QE------RFAFIGKATP------------IPYETTDVKNFLPEWKSGM--YASFVEEIK-------------NNLDLQEW----YIVGRFLNGRMLNQL
736546968 Carnobacterium gallinarum                AG------KELLLSSEEKV-----------IKETEISLSKKINEREKTLKASIQVEHQLV-------------ATNSAISY----WLFCKLLDSRHLNEL
736550717 Carnobacterium gallinarum                --------NFDLNLNPAEE-----------LVGTVKEKAEGLRKRKERIAKILNVDEQIK-------------TGDEEIAF----WIFAKLLDARHLSEL
503209049 Paludibacter propionicigenes             AK------EFDFVQMPQPQLT---------ATASNQQKADKLNQLEASITADCKLTPQYA-----------KADDATHIAF----YVFCKLLDAAHLSNL
502750493 Listeria seeligeri                       KN------RLTYICHP--------------TKNTVPENDNIEIPFHTDM-------------------------DDSNIAF----WLMCKLLDAKQLSEL
738100542 Listeria weihenstephanensis              SA------DLKFIKNPRNQG----------LEQSEIEEMSFDIKVEPSF----------------------LKNKDDYIAF----WTFCKMLDARHLSEL
738133341 Listeria newyorkensis                    SA------NLKFIKNPRNQG----------LEQSEIEEMSFDIKVEPSF----------------------LKNKDDYIAF----WIFCKMLDARHLSEL
544240864 Leptotrichia wadei F0279                 KDK-----RLHFLKEEFSI-----------LCNNNNNVVDFNINI-----NEEKIKEFLK------------ENDSKTLNL----YLFFNMIDSKRISEF
738101039 Leptotrichia wadei                       KDK-----RLHFLKEEFSI-----------LCNNNNNVVDFNINI-----NEEKIKEFLK------------ENDSKTLNL----YLFFNMIDSKRISEF
545623740 Leptotrichia wadei                       GSDLLKSLNLLNLKKDEA------------IANKKSFYDEKLKLWQNNGSNLSKMPEEIYDYIKKIKINK-INYSDRMSIF----YLLLKLIDHKELTNL
545623306 Leptotrichia wadei                       KN------NLKYIESNNNNDNNDIFSKIKIKKDNKEKYDKILKNYEKHN-RNKEIPHEINEFVREIKLGKILKYTENLNMF----YLILKLLNHKELTNL
506250229 Leptotrichia buccalis                    NNGRL---SLIYIGSDEETNTS--------LAEKKQEFDKFLKKYEQNN--NIKIPYEINEFLREIKLGNILKYTERLNMF----YLILKLLNHKELTNL
Secondary structure for 506250229 (Jpred)          ----H---HHHH------------------HHHHHHHHHHHHH---------------HHHHHHHHH----------HHHH----HHHHHH--HHHHHHH
545661797 Leptotrichia sp  oral taxon 225          NNGRL---SLMYIGNDEQINTS--------LAEKKQEFDKFLKKYEQNN--NIKIPYEINEFLREIKLGNILKYTERLNMF----YLILKLLNHKELTNL
545620493 Leptotrichia sp  oral taxon 879          IISILDEVLLINLLRENNITDILDLKNAIIDAKIVENDETYIKNYIFES-NEEKLKKRLF-------CEELVDKEDIRKIFEDENFKFKSFIKKNEIGNF
517262777 Leptotrichia shahii                      --------NIIDILDEIMQLN---------TLRNECITENWNLNLEEFIQKMKEIEKDFDD----------FKIQTKKEIF----NNYYEDIKNNILTEF
CONSENSUS                                          ...........................................................................................L........
HEPN (predicted RNAse) motifs                      ....................................................................................................
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FIGURE S6 (con't)

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564875111 Rhodobacter capsulatus R121          L---HQLRKWEALQGKYELV----QDGDATDQADARREALDLVKRFRDVLVLFLKTGEARFEGR-----AAPFDLKPFRALFANPATFDRLFMATP----
769144435 Lachnospiraceae bacterium MA2020     L---GSIRNYVQFVKDIQRR-----AKENGNPIRNYYEVLESDSIIK--ILEMCTKLNGTTSND-------------IHDYFRDEDEYAEYISQFV----
551041827 Lachnospiraceae bacterium NK4A179    L---GFLHSYKQYVWDIYRRASETGTEINHSIAEDKIAGVDITDVDA--VIDLSVKLCGTISSE-------------ISDYFKDDEVYAEYISSYL----
671463495 Clostridium  aminophilum            S---GVIRSYIQFAGDIQRRAKANHNRLYM---DNTQRVEYYSNVLE--VVDFCIKGTSRFSNV-------------FSDYFRDEDAYADYLDNYL--QF
Secondary structure for 671463495 (Jpred)      H---HHHHHHHHHHHHHHHHH-HHHHHHHH---HHHHHHHHH----H--HEEEEE-----------------------HHHHHHHHHHHHHHH-------
652829192 Lachnospiraceae bacterium NK4A144    A---GSLRSYIQYAEDIERR---AAENRNKLFSKPDEKIEACKKAVR--VLDLCIKISTRISAE-------------FTDYFDSEDDYADYLEKYLKYQD
736546968 Carnobacterium gallinarum            R---NEMIKFKQSRIKFNHT----------------QHAELIQNLLP--IVELTILSNDYDEKN--------------DSQNVDVSAYFEDKSLYE----
736550717 Carnobacterium gallinarum            R---NEMIKFKQSSVKKGLI-----------------KNGDLIEQMQP-ILELCILSNDSESM--------------EKESFDKIEVFLE----------
503209049 Paludibacter propionicigenes         R---NELIKFRESVNEFKFH-----------------------HLLE--IIEICLLSADVVPTD-------------YRDLYSSEADCLARLRPFI----
502750493 Listeria seeligeri                   R---NEMIKFSCSLQSTEEI-------------------STFTKARE--VIGLALLNGEKGCND-------------WKELFDDKEAWKKNMSLYV----
738100542 Listeria weihenstephanensis          R---NEMIKYDGHLTGEQE------------------------------IIGLALLGVDSREND-------------WKQFFSSEREYEKIMKGYV----
738133341 Listeria newyorkensis                R---NEMIKYDGHLTGEQE------------------------------IIGLALLGVDSREND-------------WKQFFSSEREYEKIMKGYV----
544240864 Leptotrichia wadei F0279             R---NELVKYKQFTKKRLDE---------------EKEFLGIKIELYETLIEFVILTREKLDTKKSEEIDAWLVDKLYVKDSNEYKEYEEILKLFV----
738101039 Leptotrichia wadei                   R---NELVKYKQFTKKRLDE---------------EKEFLGIKIELYETLIEFVILTREKLDTKKSEEIDAWLVDKLYVKDSNEYKEYEEILKLFV----
545623740 Leptotrichia wadei                   R---GNLEKYVSMNKNKIYS-----------------------EELN--IVNLVSLDNNKVRAN-------------FNLKPEDIGKFLKTETSIR----
545623306 Leptotrichia wadei                   K---GSLEKYQSANKEETFS-----------------------DELE--LINLLNLDNNRVTED-------------FELEANEIGKFLDFNENKI----
506250229 Leptotrichia buccalis                K---GSLEKYQSANKEEAFS-----------------------DQLE--LINLLNLDNNRVTED-------------FELEADEIGKFLDFNGNKV----
Secondary structure for 506250229 (Jpred)      ------EEEEE--HHHHHHH-----------------------HHHH--HHHEEE---------------------------HHH---------------
545661797 Leptotrichia sp  oral taxon 225      K---GSLEKYQSANKEEAFS-----------------------DQLE--LINLLNLDNNRVTED-------------FELEADEIGKFLDFNGNKV----
545620493 Leptotrichia sp  oral taxon 879      KINFGILSNLECNSEVEAKK-----------------IIGKNSKKLESFIQNIIDEYKSNIRTL-------------FSSEF--LEKYKEEIDNLV----
517262777 Leptotrichia shahii                  K---DDINGCDVLEKKLEKIVIFDDETKFEIDKKSNILQDEQRKLSNINKKDLKKKVDQYIKDKDQEIKSKILCRIIFNSDF--LKKYKKEIDNLI----
CONSENSUS                                      ......L.............................................................................................
HEPN (predicted RNAse) motifs                  ....................................................................................................

564875111 Rhodobacter capsulatus R121          ----------TTARPAEDDPE----------GD-GASEPELRVARTLRGLRQI------ARYNHMAVLSDLFAKHKVRDEEVARLAEIEDET-------Q
769144435 Lachnospiraceae bacterium MA2020     ---NFGDVHSGAALNAFCNSES-EGKKNGIYYD-GIN-----PIV-NRNWVLC------KLYGSPDLISKIIS-----R---VNENMIHDFH--------
551041827 Lachnospiraceae bacterium NK4A179    -DFEYDGGNYKDSLNRFCNSDAVNDQKVALYYD-GEH-----PKL-NRNIILS------KLYGERRFLEKITD-----R---VSRSDIVEYY-------K
671463495 Clostridium  aminophilum            KDEKIAEVSSFAALKTFCNEE---EVKAGIYMD-GEN-----PVM-QRNIVMA------KLFGPDEVLKNVVP-----K---VTREEIEEYY-------Q
Secondary structure for 671463495 (Jpred)      ----------HHHHH----------------------------HH-HHHHHHH------H---HHHHHHHHH------------HHHHHHHH-------H
652829192 Lachnospiraceae bacterium NK4A144    DAIKELSGSSYAALDHFCNKD---DLKFDIYVNAGQK-----PIL-QRNIVMA------KLFGPDNILSEVME-----K---VTESAIREYY-------D
736546968 Carnobacterium gallinarum            -----------------TAPY--------VQTD-DRT-----RVS-FRPILKL------EKYHTKSLIEALLKDNPQFR---VAATDIQEWM-------H
736550717 Carnobacterium gallinarum            -----------KVELAKNEPY--------MQED-KLT-----PVK-FRFMKQL------EKYQTRNFIENLVIENPEFK---VSEKIVLNWH-------E
503209049 Paludibacter propionicigenes         --------EQGADITNWSDLF--------VQSD-KHS-----PVI-HANIELS------VKYGTTKLLEQIINKDTQFK---TTEANFTAWN-------T
502750493 Listeria seeligeri                   -----------SEELLQSLPY--------TQED-GQT-----PVI-NRSIDLV------KKYGTETILEKLFSSSDDYK---VSAKDIAKLH-------E
738100542 Listeria weihenstephanensis          -----------GEELYQREPY--------RQSD-GKT-----PIL-FRGVEQA------RKYGTETVIQRLFDASPEFK---VSKCNITEWE-------R
738133341 Listeria newyorkensis                -----------VEELYQREPY--------RQSD-GKT-----PIL-FRGVEQA------RKYGTETVIQRLFDANPEFK---VSKCNLAEWE-------R
544240864 Leptotrichia wadei F0279             ---------DEKILSSKEAPY--------YATD-NKT-----PIL-LSNFEKT------RKYGTQSFLSEIQSNYKYSK---VEKENIEDYNKKEEIEQK
738101039 Leptotrichia wadei                   ---------DEKILSSKEAPY--------YATD-NKT-----PIL-LSNFEKT------RKYGTQSFLSEIQSNYKYSK---VEKENIEDYNKKEEIEQK
545623740 Leptotrichia wadei                   -----------NINQLNNFSE--------IFAD-GEN-----VIK-HRSFYNI------KKYGILDLLEKIVD-KADLK---ITKEEIKKYE-------N
545623306 Leptotrichia wadei                   --------KDRKELKKFDTNK--------IYFD-GEN-----IIK-HRAFYNI------KKYGMLNLLEKIAD-KAKYK---ISLKELKEYS-------N
506250229 Leptotrichia buccalis                --------KDNKELKKFDTNK--------IYFD-GEN-----IIK-HRAFYNI------KKYGMLNLLEKIAD-KAGYK---ISIEELKKYS-------N
Secondary structure for 506250229 (Jpred)      ----------HHHHH-----E--------EE-----------EEE----HHHH------HHHHHHHHHHHHHH-----------HHHHHHHH-------H
545661797 Leptotrichia sp  oral taxon 225      --------KDNKELKKFDTNK--------IYFD-GEN-----IIK-HRAFYNI------KKYGMLNLLEKISD-EAKYK---ISIEELKNYS-------N
545620493 Leptotrichia sp  oral taxon 879      --------EDTESENKNKFEK--------IYYP-KEHKNELYIYK-KNLFLNIGNPNFDKIYGLISKDIKNVDTKILFD------DDIKK---------N
517262777 Leptotrichia shahii                  --------EDMESENENKFQE--------IYYP-KERKNELYIYK-KNLFLNIGNPNFDKIYGLISNDIKMADAKFLFN---IDGKNIRK---------N
CONSENSUS                                      ................................D............................YG........................I............
HEPN (predicted RNAse) motifs                  ....................................................................................................

564875111 Rhodobacter capsulatus R121          EKSQIVAA--QELRTDLHDKV--MK---------------CHPKTISPEERQS---YAAAIKTIEEHRFLVGRVYLGDHLRLHRLMMDVIGRLIDYAGAY
769144435 Lachnospiraceae bacterium MA2020     ------------KQEDLIREY-------------------------QIKGICS---NKKEQQDLRTFQVLKNRVELRDIVEYSEIINELYGQLIKWCYLR
551041827 Lachnospiraceae bacterium NK4A179    LKKETSQ--------------------------------------YQTKGIFD---SEDEQKNIKKFQEMKNIVEFRDLMDYSEIADELQGQLINWIYLR
671463495 Clostridium  aminophilum            LEKQIAP--------------------------------------YRQNGYCK---SEEDQKKLLRFQRIKNRVEFQTITEFSEIINELLGQLISWSFLR
Secondary structure for 671463495 (Jpred)      HHHHHHH--------------------------------------------------HHHHHHHHHHHHHHH-HHHHHHHHHHHHHHHHHHHHHHHHHHH
652829192 Lachnospiraceae bacterium NK4A144    YLKKVSG--------------------------------------YRVRGKCS---TEKEQEDLLKFQRLKNAVEFRDVTEYAEVINELLGQLISWSYLR
736546968 Carnobacterium gallinarum            KREEIGEL--VEKRKNLHTEW--AE----------------GQQTLGAEKREE---YRDYCKKIDRFNWKANKVTLTYLSQLHYLITDLLGRMVGFSALF
736550717 Carnobacterium gallinarum            EKEKIADL--VDKRTKLHEEW--ASKAREIEEYNEKIKKNKSKKLDKPAEFAKFAEYKIICEAIENFNRLDHKVRLTYLKNLHYLMIDLMGRMVGFSVLF
503209049 Paludibacter propionicigenes         AQKSIEQL--IKQREDHHEQWVKAKNADDKEKQERKREKSNFAQKFIEKHGDD---YLDICDYINTYNWLDNKMHFVHLNRLHGLTIELLGRMAGFVALF
502750493 Listeria seeligeri                   Y--DVTEK--IAQQESLHKQW--IE----------------KPGLARDSAWTK--KYQNVINDISNYQWAKTKVELTQVRHLHQLTIDLLSRLAGYMSIA
738100542 Listeria weihenstephanensis          QKETIEET--IERRKELHNEW--EK----------------NPKKPQNNAFFK--EYKECCDAIDAYNWHKNKTTLVYVNELHHLLIEILGRYVGYVAIA
738133341 Listeria newyorkensis                QKETIEET--IKRRKELHNEW--AK----------------NPKKPQNNAFFK--EYKECCDAIDAYNWHKNKTTLAYVNELHHLLIEILGRYVGYVAIA
544240864 Leptotrichia wadei F0279             KKSNIEKL--QDLKVELHKKW--------------------EQNKITEKEIEK---YNNTTRKINEYNYLKNKEELQNVYLLHEMLSDLLARNVAFFNKW
738101039 Leptotrichia wadei                   KKSNIEKL--QDLKVELHKKW--------------------EQNKITEKEIEK---YNNTTRKINEYNYLKNKEELQNVYLLHEMLSDLLARNVAFFNKW
545623740 Leptotrichia wadei                   LQNELKRNDFYKIQERIHRNY--NQKP--------------FLIKNNEKDFND---YKKAIENIQNYTQLKNKIEFNDLNLLQSLLFRILHRLAGYTSLW
545623306 Leptotrichia wadei                   KKNEIEKN--YTMQQNLHRKY--ARPK--------------KDEKFNDEDYKE---YEKAIGNIQKYTHLKNKVEFNELNLLQGLLLKILHRLVGYTSIW
506250229 Leptotrichia buccalis                KKNEIEKN--HKMQENLHRKY--ARPR--------------KDEKFTDEDYES---YKQAIENIEEYTHLKNKVEFNELNLLQGLLLRILHRLVGYTSIW
Secondary structure for 506250229 (Jpred)      HHHHHHHH--HHHHHHHHHHH--H-----------------------HHHHHH---HHHHHHHHHHH-H----HHHHHHHHHHHHHHHHHHHHHHHHHHH
545661797 Leptotrichia sp  oral taxon 225      KKNEIEKN--HTNQENLHRKY--ARPR--------------KDEKFNDEDYKK---YEKAIRNIQQYTHLKNKVEFNELNLLQSLLLRILHRLVGYTSIW
545620493 Leptotrichia sp  oral taxon 879      KISEIDAI--LKNLNDKLNGY--SNDYKAKYVNKLKENDDFFAKNIQNENYSSFGEFEKDYNKVSEYKKIRDLVEFNYLNKIESYLIDINWKLAIQMARF
517262777 Leptotrichia shahii                  KISEIDAI--LKNLNDKLNGY--SKEYKEKYIKKLKENDDFFAKNIQNKNYKS---FEKDYNRVSEYKKIRDLVEFNYLNKIESYLIDINWKLAIQMARF
CONSENSUS                                      ....I..........................................................I..Y.....................L...........
HEPN (predicted RNAse) motifs                  ....................................................................................................

564875111 Rhodobacter capsulatus R121          ERDTGTFLIN-----ASKQLGAGADW--------------------------------------------------------------------------
769144435 Lachnospiraceae bacterium MA2020     ERDLMYFQLGFHYLCLNNASSKEADYI---KINVDDRNISGAILYQIAAMYINGLPVYYKKDDMYVALKSGKKASDELNSNE----QTSKKINYFLKYGN
551041827 Lachnospiraceae bacterium NK4A179    ERDLMNFQLGYHYACLNNDSNKQATYVTLDYQGKKNRKINGAILYQICAMYINGLPLYYVDKDSSEWTVSDGKE------------STGAKIGEFYRYAK
671463495 Clostridium  aminophilum            ERDLLYFQLGFHYLCLHNDTEKPAEYK--EISREDGTVIRNAILHQVAAMYVGGLPVYTLAD--KKLAAFEKGEADCKLSISKDTAGAGKKIKDFFRYSK
Secondary structure for 671463495 (Jpred)      HHHHHHHHHHHHHHHH-------EEEE--EEEE----EE-HHHHHHHHHHH------HHHHH--HHHHE--------EEEE--------------H----
652829192 Lachnospiraceae bacterium NK4A144    ERDLLYFQLGFHYMCLKNKSFKPAEYV--DIRRNNGTIIHNAILYQIVSMYINGLDFYSCDKEGKTLKPIETGK------------GVGSKIGQFIKYSQ
736546968 Carnobacterium gallinarum            ERDLVYFSRS--FSELGGETYHISDYKNLSGVLRLNAEVKPIKIKNIK--------------------------------------VIDNEENPYKGNEP
736550717 Carnobacterium gallinarum            ERDFVYMGRS--YSALKKQSIYLNDY----DTFANIRDWEVNENKHLF--------------------------------------GTSSSDLTFQETAE
503209049 Paludibacter propionicigenes         DRDFQFFDEQ-----QIADEFKLHGFVNLHSIDKKLNEVPTKKIKEIY--------------------------------------DIRNKIIQINGNKI
502750493 Listeria seeligeri                   DRDFQFSSNY--ILERENSEYRVTSWI-LLSENKNKNKYNDYELYNLK--------------------------------------NASIKVSSK--NDP
738100542 Listeria weihenstephanensis          DRDFQCMANQ--YFKHSGITERVEYW-----------------------------------------------------------------------GDN
738133341 Listeria newyorkensis                DRDFQCMANQ--YFKHSGITERVEYW-----------------------------------------------------------------------GDN
544240864 Leptotrichia wadei F0279             ERDFKFIVIAIKQFLRENDKEKVNEFLNPPDNSKGKKVYFSVSKYK----------------------------------------NTVENIDGI--HKN
738101039 Leptotrichia wadei                   ERDFKFIVIAIKQFLRENDKEKVNEFLNPPDNSKGKKVYFSVSKYK----------------------------------------NTVENIDGI--HKN
545623740 Leptotrichia wadei                   ERDLQFKLKG--EYPENKYIDEIFNF----DNSKNKIYNEKNERGG----------------------------------------SVVSKYGYFLVEKD
545623306 Leptotrichia wadei                   ERDLRFRLKG--EFPENHYIEEIFNF----DNSKNVKYKSG---------------------------------------------QIVEKYINF--YKE
506250229 Leptotrichia buccalis                ERDLRFRLKG--EFPENQYIEEIFNF----ENKKNVKYKGG---------------------------------------------QIVEKYIKF--YKE
Secondary structure for 506250229 (Jpred)      H--HHHHHH------HHHHHHHHH-----------------------------------------------------------------HHHHHH--HHH
545661797 Leptotrichia sp  oral taxon 225      ERDLRFRLKG--EFPENQYIEEIFNF----NNSKNVKYKNG---------------------------------------------QIVEKYISF--YKE
545620493 Leptotrichia sp  oral taxon 879      ERDMHYIVNG----LRELGIIKLSGY----NTGISRAYPKRNGSDGFY--------------------------------------TTTAYYKFF--DEE
517262777 Leptotrichia shahii                  ERDMHYIVNG----LRELGIIKLSGY----NTGISRAYPKRNGSDGFY--------------------------------------TTTAYYKFF--DEE
CONSENSUS                                      ERD.................................................................................................
HEPN (predicted RNAse) motifs                  ....................................................................................................
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FIGURE S6 (con’t)

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564875111 Rhodobacter capsulatus R121              ----------------AVTIAGAANTDARTQ-------TRKDLAHFNVLDRA--DGTPDLTALVNRARE-MMAYDRKRKNAVPRSILDMLARLGLTLKWQ
769144435 Lachnospiraceae bacterium MA2020         N-------ILGDK-KDQLYLAGLELFENVAEHENIII-FRNEIDHFHYFYDR----DRSMLDLYSEVFDRFFTYDMKLRKNVVNMLYNILLDHNIVSSFV
551041827 Lachnospiraceae bacterium NK4A179        S-------FENTS---DCYASGLEIFENISEHDNITE-LRNYIEHFRYYSSF----DRSFLGIYSEVFDRFFTYDLKYRKNVPTILYNILLQHFVNVRFE
671463495 Clostridium  aminophilum                 YVLIKDRMLTDQNQKYTIYLAGLELFENTDEHDNITD-VRKYVDHFKYYATS-DENAMSILDLYSEIHDRFFTYDMKYQKNVANMLENILLRHFVLIRPE
Secondary structure for 671463495 (Jpred)          HEHHHH-HHHHHHHHHHHHHHH-HH---------HHH-HHHHHHH---------HHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHH-EEEEEE
652829192 Lachnospiraceae bacterium NK4A144        Y------LYNDPSYKLEIYNAGLEVFENIDEHDNITD-LRKYVDHFKYYAYG---NKMSLLDLYSEFFDRFFTYDMKYQKNVVNVLENILLRHFVIFYPK
736546968 Carnobacterium gallinarum                E-------VKPFLDRLHAYLENVIGIKAVH-----GK-IRNQTAHLSVLQLE-----LSMIESMNNLRD-LMAYDRKLKNAVTKSMIKILDKHGMILKLK
736550717 Carnobacterium gallinarum                --------FKNLKKPMENQLKALLGVTNHS-----FE-IRNNIAHLHVLRNDGKGEGVSLLSCMNDLRK-LMSYDRKLKNAVTKAIIKILDKHGMILKLT
503209049 Paludibacter propionicigenes             NESVRANLIQFISSKRNYYNNAFLHVSNDEIKEKQMYDIRNHIAHFNYLTKD--AADFSLIDLINELRE-LLHYDRKLKNAVSKAFIDLFDKHGMILKLK
502750493 Listeria seeligeri                       Q-------LKVDLKQLRLTLEYLELFDNRL-----KE-KRNNISHFNYLNGQ---LGNSILELFDDARD-VLSYDRKLKNAVSKSLKEILSSHGMEVTFK
738100542 Listeria weihenstephanensis              R-------LKSIK-KLDTFLKKEGLFVSEK------N-ARNHIAHLNYLSLK---SECTLLYLSERLRE-IFKYDRKLKNAVSKSLIDILDRHGMSVVFA
738133341 Listeria newyorkensis                    R-------LKSIK-KLDTFLKKEGLFVSEK------N-ARNHIAHLNYLSLK---SECTLLYLSERLRE-IFKYDRKLKNAVSKSLIDILDRHGMSVVFA
544240864 Leptotrichia wadei F0279                 --------FMNLIFLNNKFMNRKIDKMNCAIW---VY-FRNYIAHFLHLHTK--NEKISLISQMNLLIK-LFSYDKKVQNHILKSTKTLLEKYNIQINFE
738101039 Leptotrichia wadei                       --------FMNLIFLNNKFMNRKIDKMNCAIW---VY-FRNYIAHFLHLHTK--NEKISLISQMNLLIK-LFSYDKKVQNHILKSTKTLLEKYNIQINFE
545623740 Leptotrichia wadei                       G-------EIQRKNARDKKKNKIIKKEGLE--------IRNYIAHFNYIPDA----TKSILEILEELRN-LLKYDRKLKNAVMKSIKDIFKEYGLIIEFK
545623306 Leptotrichia wadei                       L-------YKDNVEKRSIYSDKKVKKLKQEKKD--LY-IRNYIAHFNYIPHA----EISLLEVLENLRK-LLSYDRKLKNAIMKSIVDILKEYGFVATFK
506250229 Leptotrichia buccalis                    L-------HQNDEVKINKYSSANIKVLKQEKKD--LY-IRNYIAHFNYIPHA----EISLLEVLENLRK-LLSYDRKLKNAVMKSVVDILKEYGFVATFK
Secondary structure for 506250229 (Jpred)          H-------HHH-HHHH-----HHHHHHHH------EE-EEE-HHHH------------HHHHHHHHHHH-HHHH-HHHHH-HHHHHHHHHHH--EEEEEE
545661797 Leptotrichia sp  oral taxon 225          L-------YKDDTEKISIYSDKKVKELKKEKKD--LY-IRNYIAHFNYIPNA----EISLLEVLENLRK-LLSYDRKLKNAIMKSIVDILKEYGFVVTFK
545620493 Leptotrichia sp  oral taxon 879          S-------YKKFE--KICYGFGIDLSENSEINKPENESIRNYISHFYIVRNP--FADYSIAEQIDRVSN-LLSYSTRYNNSTYASVFEVFKK-DVNLDYD
517262777 Leptotrichia shahii                      S-------YKKFE--KICYGFGIDLSENSEINKPENESIRNYISHFYIVRNP--FADYSIAEQIDRVSN-LLSYSTRYNNSTYASVFEVFKK-DVNLDYD
CONSENSUS                                          .......................................RN.I.HF............S..............YD.K....V......IL..........
HEPN (predicted RNAse) motifs                      .......................................R....H.......................................................

564875111 Rhodobacter capsulatus R121              ----------------MKDHL----LQDATIT--QAAIKHLDKV-------RLTVGGPAAVTEARFSQ------DYLQMVAAVFNGSVQNPKPRRRDDGD
769144435 Lachnospiraceae bacterium MA2020         FETGEKKVGRGDSEVIKPSAK----IRLRANNGVSSDVFTYKVG-------SKDELKIAT--LPAKNE------EFLLNVARLIYYPDMEAVSENMVREG
551041827 Lachnospiraceae bacterium NK4A179        FVSGKKMIGIDKKDRKIAKEKECARITIREKNGVYSEQFTYKL--------KNGTVY-----VDARDK------RYLQSIIRLLFYPEKVNMDEMIEVKE
671463495 Clostridium  aminophilum                 FFTGSKKVGEGKKITCKARAQ----IEIAENGMRSEDFTYKL---------SDGKKNISTCMIAARDQ------KYLNTVARLLYYPHEAKKSIV-----
Secondary structure for 671463495 (Jpred)          EE----E--------HHEEEE----EEE---------EEEEE----------------EEEEEEHHHH------HHHHHHHHHH----HH----------
652829192 Lachnospiraceae bacterium NK4A144        FGSGKKDVGIRDCK--KERAQ----IEISEQSLTSEDFMFKLD--------DKAGEEAKK--FPARDE------RYLQTIAKLLYYPNEIEDMNR-----
736546968 Carnobacterium gallinarum                ID--------------ENHKN----FEIESLI--PKEIIHL----------KDKAIK-----TNQVSE------EYCQLVLALLTTNPGNQLN-------
736550717 Carnobacterium gallinarum                NN--------------DHTKP----FEIESLK--PKKIIHLEK--------SNHSFP-----MDQVSQ------EYCDLVKKMLVFTN------------
503209049 Paludibacter propionicigenes             L---------------NADHK----LKVESLE--PKKIYHLGS--------SAKDKPEYQYCTNQVMM------AYCNMCRSLLEMKK------------
502750493 Listeria seeligeri                       PLY-------------QTNHH----LKIDKLQ--PKKIHHLG---------EKSTVS-----SNQVSN------EYCQLVRTLLTMK-------------
738100542 Listeria weihenstephanensis              NLK-------------ENKHR----LVIKSLE--PKKLRHLGE--------KKIDNGYIE--TNQVSE------EYCGIVKRLLEI--------------
738133341 Listeria newyorkensis                    NLK-------------ENKHR----LVIKSLE--PKKLRHLGG--------KKIDGGYIE--TNQVSE------EYCGIVKRLLEM--------------
544240864 Leptotrichia wadei F0279                 ----------------ISNDK----NEVFKYK--IKNRLY-----------SKKGKM-----LGKNNKFEILENEFLENVKAMLEYSE------------
738101039 Leptotrichia wadei                       ----------------ISNDK----NEVFKYK--IKNRLY-----------SKKGKM-----LGKNNKFEILENEFLENVKAMLEYSE------------
545623740 Leptotrichia wadei                       ISHV------------NNSEK----IEVLNVD--SEKIKHL----------KNNGLV-----TTRNSE------DLCELIKMMLEYKKS-----------
545623306 Leptotrichia wadei                       I---------------GADKK----IEIQTLE--SEKIVHLKNL-------KKKKLM-----TDRNSE------ELCELVKVMFEYKALE----------
506250229 Leptotrichia buccalis                    I---------------GADKK----IGIQTLE--SEKIVHLKNL-------KKKKLM-----TDRNSE------ELCKLVKIMFEYKMEEKKSEN-----
Secondary structure for 506250229 (Jpred)          E-------------------E----EEEE-------HHH------------------------HHHHH------HHHHHHHHHHHHHHHH----------
545661797 Leptotrichia sp  oral taxon 225          I---------------EKDKK----IRIESLK--SEEVVHLKKLKLKDNDKKKEPIK-----TYRNSK------ELCELVKVMFEYKMKEKKSEN-----
545620493 Leptotrichia sp  oral taxon 879          ----------------ELKKK----FRLIGNNDILERLMKPK---------KVSVLE-----LESYNS------DYIKNLIIELLTKIENTNDTL-----
517262777 Leptotrichia shahii                      ----------------ELKKK----FKLIGNNDILERLMKPK---------KVSVLE-----LESYNS------DYIKNLIIELLTKIENTNDTL-----
CONSENSUS                                          ...............................................................................V...L................
HEPN (predicted RNAse) motifs                      ....................................................................................................

564875111 Rhodobacter capsulatus R121              AWHKPPKPATAQSQPDQKPPNKAPSAGSRLPPPQVGEVYEGVVVKVIDTGSLGFLAVEGVAGNIGLHISRLRRIREDAIIVGRRYRFRVEIYVPPKSNTS
769144435 Lachnospiraceae bacterium MA2020         VVKV------------------------------------------------------EKSNDKKGKISRGSNTRSSNQSKYNNKSKNRMNYSMGS----
551041827 Lachnospiraceae bacterium NK4A179        KKKP------------------------------------------------------SDNNTGKGYSKRDRQQDRKEYDKYKEKKKKEGNFLSGMGGNI
671463495 Clostridium  aminophilum                 --------------------------------------------------------DTREKKNNKKTNRGDGTFNKQKGTARKEKDNGPREFNDTGFSNT
Secondary structure for 671463495 (Jpred)          ----------------------------------------------------------------------------------------------------
652829192 Lachnospiraceae bacterium NK4A144        -----------------------------------------------------------------FMKKGETINKKVQFNRKKKITRKQKNNSSNEVLSS
736546968 Carnobacterium gallinarum                ----------------------------------------------------------------------------------------------------
736550717 Carnobacterium gallinarum                ----------------------------------------------------------------------------------------------------
503209049 Paludibacter propionicigenes             ----------------------------------------------------------------------------------------------------
502750493 Listeria seeligeri                       ----------------------------------------------------------------------------------------------------
738100542 Listeria weihenstephanensis              ----------------------------------------------------------------------------------------------------
738133341 Listeria newyorkensis                    ----------------------------------------------------------------------------------------------------
544240864 Leptotrichia wadei F0279                 ----------------------------------------------------------------------------------------------------
738101039 Leptotrichia wadei                       ----------------------------------------------------------------------------------------------------
545623740 Leptotrichia wadei                       ----------------------------------------------------------------------------------------------------
545623306 Leptotrichia wadei                       ----------------------------------------------------------------------------------------------------
506250229 Leptotrichia buccalis                    ----------------------------------------------------------------------------------------------------
Secondary structure for 506250229 (Jpred)          ----------------------------------------------------------------------------------------------------
545661797 Leptotrichia sp  oral taxon 225          ----------------------------------------------------------------------------------------------------
545620493 Leptotrichia sp  oral taxon 879          ----------------------------------------------------------------------------------------------------
517262777 Leptotrichia shahii                      ----------------------------------------------------------------------------------------------------
CONSENSUS                                          ....................................................................................................
HEPN (predicted RNAse) motifs                      ....................................................................................................

564875111 Rhodobacter capsulatus R121              KLNAADLVRID
769144435 Lachnospiraceae bacterium MA2020         IFEKMDLKFD-
551041827 Lachnospiraceae bacterium NK4A179        NWDEINAQLKN
671463495 Clostridium  aminophilum                 PFAGFDPFRNS
Secondary structure for 671463495 (Jpred)          -----------
652829192 Lachnospiraceae bacterium NK4A144        TMGYLFKNIKL
736546968 Carnobacterium gallinarum                -----------
736550717 Carnobacterium gallinarum                -----------
503209049 Paludibacter propionicigenes             -----------
502750493 Listeria seeligeri                       -----------
738100542 Listeria weihenstephanensis              -----------
738133341 Listeria newyorkensis                    -----------
544240864 Leptotrichia wadei F0279                 -----------
738101039 Leptotrichia wadei                       -----------
545623740 Leptotrichia wadei                       -----------
545623306 Leptotrichia wadei                       -----------
506250229 Leptotrichia buccalis                    -----------
Secondary structure for 506250229 (Jpred)          -----------
545661797 Leptotrichia sp  oral taxon 225          -----------
545620493 Leptotrichia sp  oral taxon 879          -----------
517262777 Leptotrichia shahii                      -----------
CONSENSUS                                          ...........
HEPN (predicted RNAse) motifs                      ...........
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Supplementary Figure S6. Multiple alignment of C2c2 protein family

The alignment was built using MUSCLE program and modified manually on the basis of local PSI- BLAST pairwise alignments. Each sequence is labelled with GenBank Identifier (GI) number and systematic name of an organism. Secondary structure was predicted by Jpred and shown underneath the sequence which was used as a query (designations: H- alpha helix, E – beta strand). CONSENSUS was calculated for each alignment column by scaling the sum-of-pairs score within the column between those of a homogeneous column (the same residue in all aligned sequences) and a random column with homogeneity cutoff 0.8. Active site motifs of HEPN domain are shown below alignment.

FIGURE S7 (Related to Figures 3 and 4)

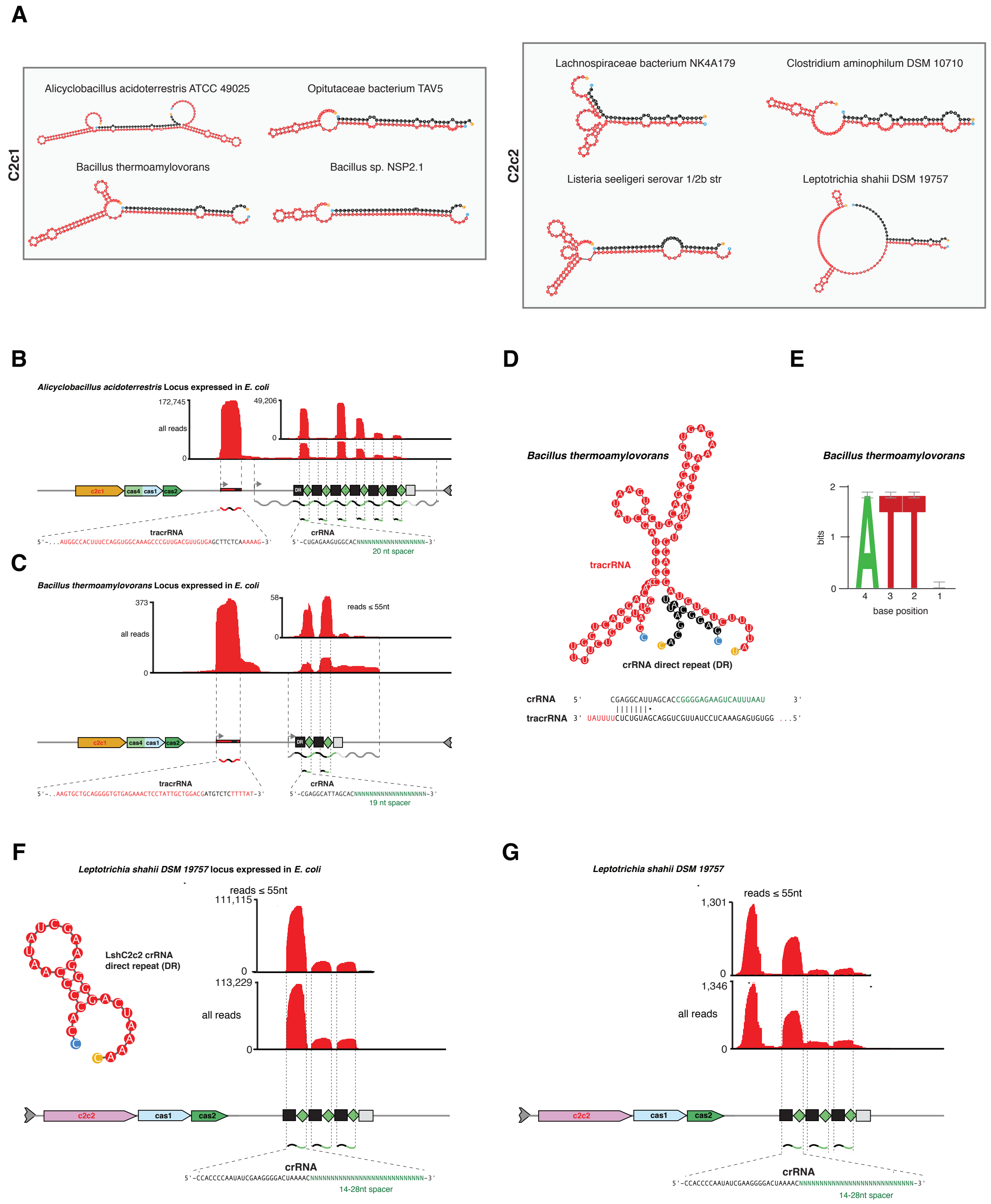

Figure S7. Additional functional validation off type V-B (C2c1 loci) and type VI (C2c2 loci) CRISPR-Cas systems.

(A) Predicted structures of tracrRNAs base-paired with the repeats. TracrRNA for Alicyclobacillus acidoterrestric was identified using RNAseq. For the remaining loci, putative tracrRNAs were identified based on presence of an anti-direct repeat (DR) sequence. Anti-DRs were identified using Geneious (www.geneious.com) by searching for sequences within each respective CRISPR locus that are highly homologus to DR. The 5' and 3' ends of each putative tracrRNA was determined though computational prediction of bacterial transcription start and termination sites using BPROM (www.softberry.com) and ARNOLD (rna.igmors.u-psud.fr/toolbox/arnold/) respectively. Co-folding predictions were generated using Geneious. 5' ends are colored blue and 3' ends are colored orange.

(B) Heterologous expression of the Alicyclobacillus acideoterrestris C2c1 locus in pACYC- 184 transformed into E. coli shows identical results to the expression observed in the endogenous strain (Fig. 4A). Processed crRNAs have a 5' 14-nt DR and 20-nt spacer and a putative 79-nt tracrRNA is expressed robustly.

(C) The Bacillus thermoamylovorans locus was heterologously expressed in E. coli. The putative tracrRNA is significantly expressed and is processed to 91 nt. Processed crRNAs are also present with a 5' 14 nt DR and 19nt spacer.

(D) In silico co-folding of the crRNA direct repeat and putative tracrRNA shows stable secondary structure and complementarity between the two RNAs. 5' bases are colored blue and 3' bases are colored orange.

(E) Depletion from the 5' left PAM library reveals a 5' ATTN PAM. Depletion is measured as the negative log2 fold ratio and PAMs above a threshold of 3.5 are used to calculate the entropy score at each position.

(F) RNA-sequencing of the Leptotrichia shahii DSM 19757 locus expressed in E. coli shows processing of the CRISPR array in the 3' to 5' direction (direction of the locus). crRNAs are processed to have a 5' DR that is 28nt in length and spacers with lengths 14-28nt. *Inset:* In silico folding of the L. shahii crRNA DR predicts stable secondary structure.

(G) RNA-sequencing of the endogenous Leptotrichia shahii DSM 19757 C2c2 locus shows similar results to (A).

Table S1 (related to Figure 1)

The discovered Class 2 CRISPR-Cas loci. Please see accompanying Excel spreadsheet.

SUPPLEMENTAL EXPERIMENTAL PROCEDURES

Computational sequence analysis

The multiple alignments of the C2c1, C2c2, C2c3 and Cas1 proteins in the Fasta format and the complete phylogenetic tree for Cas1 proteins in the Newick format are available at ftp://ftp.ncbi.nih.gov/pub/wolf/_suppl/Class2/.

Growth of Bacterial Strains

For RNA-sequencing, *Alicyclobacillus acidoterrestris*(ATCC) was cultured using ATCC Medium 1655 in suspension at 50°C and 300 rpm. *E. coli* containing heterologous constructs were cultured in Luria broth supplemented with appropriate antibiotics in suspension at 37°C and 300rpm. Both strains were grown in aerobic conditions and harvested in stationary growth phase.

For the PAM screen, *E. coli* were grown on LB-agar plates supplemented with ampicillin and the appropriate antibiotics (chloramphenicol or kanamycin) for maintenance of the C2c1 locus plasmid at 37°C.

Generation of heterologous plasmids

To generate the AacC2c1 locus for heterologous expression, genomic DNA was purified from *Alicyclobacillus acidoterrestris* using the Qiagen DNeasy Blood and Tissue kit and the C2c1 locus was PCR amplified for cloning into pACYC-184. The BthC2c1 and LseC2c2 locus was synthesized by Genscript into a pET-28 vector. Cells harboring plasmids were made competent using the Z-competent kit (Zymo).

RNA extraction and Northern blotting

The procedure was performed essentially as described previously (Pougach and Severinov, 2012). *E. coli* BL21 AI cells were transformed with plasmids pACYCduet-1 containing, under inducible T7 promoters, *A. ac.* or *L. sh.* cas operons and plasmids pCDF-1b containing the respective minimal CRISPR cassettes with single spacers. Total RNA was extracted from 5 mL of *E. coli* cells induced with 1 mM arabinose/0.2 mM IPTG and grown until OD_{600} 0.8 – 1.0. The cells were lysed by 5-minute treatment using Max Bacterial Enhancement Reagent followed by RNA purification with the TRIzol reagent (Thermo Fisher Scientific). 15 mg of total RNA were separated on a denaturing 8 M urea - 12% polyacrylamide gel and electrophoretically transferred to Hybond-XL membrane (GE Healthcare) using a Mini Trans-Blot Electrophoretic Transfer Cell (Bio-Rad). The membrane was dried and then UV cross-linked. ExpHyb hybridization solution (Clontech) was used for hybridization according to manufacturer's instructions for 1 hour at 40 °C with ^{32}P-end labeled oligonucleotide probes.

Preparation of C2c1 Protein Lysate

C2c1 proteins codon optimized for human expression and designed with an N-terminal nuclear localization tag. The protein sequences were synthesized and cloned into the pcDNA3.1 expression plasmid by Genscript. Using Lipofectamine 2000 reagent (Life Technologies), 2,000ng of the expression plasmids were transfected into HEK293FT cells (6-well plates at 90% confluence). After 48 hours, cells were washed with DPBS (Left Technologies), lysed using lysis buffer [20mM Hepes pH 7.5, 100mM KCl, 5mM $MgCl_2$, 1 mM DTT, 5% glycerol, 0.1% Triton X-100, 1X cOmplete Protease Inhibitor Cocktail Tablets (Roche)]. After sonicating for 10 minutes in a Biorupter sonicators (Diagenod) (50% duty cycle on high), the lysate was centrifuged and the supernatant was frozen at -80°C for later use in cleavage assays.

Primers used in this work

Primer Description	**Sequence (5' to 3')**
PAM library generation	
Oligo for 5' AacC2c1 PAM library (forward)	`ggccagtgaattcgagctcggtacccgggNNNNNNNtgtttggtaaaggtaaaaagacgaatgatgcatccagcttggcgtaatcatggtcatagctgtt`
Oligo for 3' AacC2c1 PAM library (forward)	`ggccagtgaattcgagctcggtacccgggtgtttggtaaaggtaaaaagacgaatgatgcatccNNNNNNNagcttggcgtaatcatggtcatagctgtt`
Oligo for 5' BsC2c1 PAM library (forward)	`ggccagtgaattcgagctcggtacccgggNNNNNNNcggggagaagtcatttaataaggccactgttaaaagcttggcgtaatcatggtcatagctgtt`
Oligo for 3' BsC2c1 PAM library (forward)	`ggccagtgaattcgagctcggtacccggggagaagtcatttaataaggccactgttaaaaNNNNNNNNagcttggcgtaatcatggtcatagctgttt`
Oligo for reverse strand synthesis of PAM library (reverse)	`AAACAGCTATGACCATGATTACGCCAA`
Northern Blot Probes	

Aac_tracrRNA_probe1	tctttttgagaagctcaacggg
Aac_crRNA_probe2	cctttaccaaacagtgccacttctcagatcgctc
Aac_crRNA_probe3	tcagtgatccgacggatgcatcattcgtctttttacc
Lsh_crRNA_probe1	ggtagaacagcaatctagttttagtccccttcgat
Lsh_crRNA_probe2	attggggtggtctatatcaatatggattacttggt
Lsh_crRNA_probe3	atcgaaggggactaaaactagattgctgttctacc
Lsh_crRNA_probe4	accaagtaatccatattgatatagaccaccccaat
Cloning	
Aac_cas_Nco_d	acgtccatggccgtcaaatccatcaaagtg
Aac_cas_Kpn_r	cgtaggtacctcaaaataccaatcccttcaaatccaatgg
Aac_cas_Nde_d	cagctggctcatatgcaccgacg
Aac_cas_Nde_r	cgtcggtgcatatgagccagctg
AacC2c1 PAM Validation Target TTT Forward	ctagTTtgtttggtaaaggtaaaaagacgaatgatgcatcc
AacC2c1 PAM Validation Target TTA Forward	ctagTtatgtttggtaaaggtaaaaagacgaatgatgcatcc
AacC2c1 PAM Validation Target TTC Forward	ctagTTctgtttggtaaaggtaaaaagacgaatgatgcatcc
AacC2c1 PAM Validation Target TTG Forward	ctagTTgtgtttggtaaaggtaaaaagacgaatgatgcatcc
AacC2c1 PAM Validation Target GGA Forward	ctagGgatgtttggtaaaggtaaaaagacgaatgatgcatcc
AacC2c1 PAM Validation Target TTT Reverse	agctggatgcatcattcgtctttttacctttaccaaacaaaa
AacC2c1 PAM Validation Target TTA Reverse	agctggatgcatcattcgtctttttacctttaccaaacataa
AacC2c1 PAM Validation Target TTC Reverse	agctggatgcatcattcgtctttttacctttaccaaacagaa
AacC2c1 PAM Validation Target TTG Reverse	agctggatgcatcattcgtctttttacctttaccaaacacaa
AacC2c1 PAM Validation Target GGA Reverse	agctggatgcatcattcgtctttttacctttaccaaacatcc

crRNA/tracrRNA IVT	
AacC2c1 crRNA targeting EMX1 target 1	gaaatTAATACGACTCACTATAGGGCGAGCGATCTGAGAAGTGGCACCAGAACCGGAGGACAAAGTA
AacC2c1 crRNA targeting AacC2c1 spacer 1	gaaatTAATACGACTCACTATAGGGCGAGCGATCTGAGAAGTGGCACTGTTTGGTAAAGGTAAAAAG
AacC2c1 tracrRNA 151nt	GTCTAGAGGACAGAATTTTTCAACGGGTGTGCCAATGGCCACTTTCCAGGTGGCAAAGCCCGTTGAGCTTCTCAAAAAGAACGCTCGCTCAGTGTTCTGACCTTTCGAGCGCCTGTTCAGGGCGAAAACCCTGGGAGGCGCTCGAATCATA
AacC2c1 tracrRNA 96nt	GTCTAGAGGACAGAATTTTTCAACGGGTGTGCCAATGGCCACTTTCCAGGTGGCAAAGCCCGTTGAGCTTCTCAAAAAGAACGCTCGCTCAGTGTT
AacC2c1 tracrRNA 90nt	GTCTAGAGGACAGAATTTTTCAACGGGTGTGCCAATGGCCACTTTCCAGGTGGCAAAGCCCGTTGAGCTTCTCAAAAAGAACGCTCGCTC
AacC2c1 tracrRNA 78nt	GTCTAGAGGACAGAATTTTTCAACGGGTGTGCCAATGGCCACTTTCCAGGTGGCAAAGCCCGTTGAGCTTCTCAAAAA
AacC2c1 tracrRNA 67nt	GTCTAGAGGACAGAATTTTTCAACGGGTGTGCCAATGGCCACTTTCCAGGTGGCAAAGCCCGTTGAG
AacC2c1 sgRNA targeting EMX1 target 1	gaaatTAATACGACTCACTATAGGGGTCTAGAGGACAGAATTTTTCAACGGGTGTGCCAATGGCCACTTTCCAGGTGGCAAAGCCCGTTGAGCTTCTCAAATCTGAGAAGTGGCACCAGAACCGGAGGACAAAGTA
AacC2c1 sgRNA targeting AacC2c1 spacer 1	gaaatTAATACGACTCACTATAGGGGTCTAGAGGACAGAATTTTTCAACGGGTGTGCCAATGGCCACTTTCCAGGTGGCAAAGCCCGTTGAGCTTCTCAAATCTGAGAAGTGGCACTGTTTGGTAAAGGTAAAAAG

Plasmid and codon-optimized C2c1/C2c2 protein-coding sequences used in this work

Constructs used for RNA-sequencing, Bacterial Interference, and Lysate Cleavage	
C2c1 locus constructs	*Permanent Sequence Links*
AacC2c1 locus cloned in pACYC184	https://benchling.com/s/YfJMfbu2/edit
BtC2c1 locus in pET28a	https://benchling.com/s/7SJzEUPG/edit
C2c2 locus constructs	
LshC2c2 locus cloned in pACYC184	https://benchling.com/s/gco8u7H8/edit
LseC2c2 locus cloned in pET28a	https://benchling.com/s/3NojkRem/edit

C2c1 human codon optimized constructs	
AacC2c1 Human Codon Optimized Protein	https://benchling.com/s/WivDaYfG/edit
Constructs used for Northern Blotting	
AacC2c1 and Cas genes in pACYCduet	https://benchling.com/s/wgbYgHeZ/edit
AacC2c1 CRISPR array in pCDF	https://benchling.com/s/kjfElooT/edit
LshC2c2 and Cas genes in pACYCduet	https://benchling.com/s/mFzf1E7u/edit
LshC2c2 CRISPR array in pCDF	https://benchling.com/s/v26xY1KC/edit

SUPPLEMENTAL REFERENCES

Pougach, K., and Severinov, K. (2012). Use of semi-quantitative Northern blot analysis to determine relative quantities of bacterial CRISPR transcripts. Methods Mol Biol *905*, 73-86.